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Gender makes the difference in exertional heat illness: A Systematic Review

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1 Gender makes the difference in exertional heat illness: A Systematic Review

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33
34 Word count: 3992

35 36 **Abstract**

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2
3 37 **Objectives:** The aim of this review is to describe the epidemiology of all heat related illnesses
4
5 38 in women compared to men in the armed forces and to identify risk factors and gender
6
7 39 differences in heat illness and heat tolerance.
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11 40 **Design:** A systematic review of multiple databases (MEDLINE, Emtree, CINAHL,
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13 41 PsycINFO, Informit, and Scopus) was conducted from inception of the databases to the 1st of
14
15 42 April 2019.
16
17

18 43 **Eligibility criteria:** Studies investigating heat illness and heat tolerance in women in the armed
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20 44 forces.
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23 45 **Results:** Twenty-seven (27) studies were included in the review. Measures used to describe
24
25 46 heat illness were proportions and incidence rates. The average proportion of heat stroke events
26
27 47 in women was lower than in men (12% vs 88%). In addition, men had significantly higher heat
28
29 48 stroke incidence compared to women (median = 0.27, interquartile range = 0.11 vs median =
30
31 49 0.15, interquartile range = 0.03; U= 10.50, P < 0.001). However, the incidence of other heat
32
33 50 injuries was similar between men and women (median = 1.41, interquartile range = 0.37 vs
34
35 51 median = 1.62, interquartile range = 0.97; U = 47.50, P = 0.058). Investigated factors associated
36
37 52 with heat illness and tolerance included gender, age, level of education, ethnicity, body mass
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39 53 index (BMI), maximal aerobic capacity (VO_{2max}), positive sickle cell trait, being in service for
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41 54 less than 1 year, and unit of service. Women were more likely to be heat intolerant compared
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43 55 to men using the standard heat tolerance test.
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49 56 **Conclusion:** The findings of this review suggest that women have a greater risk of heat illness
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51 57 and show higher rates of heat intolerance than men on the standard heat tolerance test. There
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53 58 is a need to re-evaluate the heat tolerance test protocol for women with further investigation of
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55 59 the factors that make women more susceptible to heat illness than men.
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59 60 **Article summary**

61 **Strengths and limitations of this study**

- 62 • This is the first known systematic review investigating the impact of gender on
63 exertional heat illness and heat tolerance in the armed forces.
- 64 • We conducted a comprehensive search and identified potential risk factors that are
65 associated with exertional heat illness.
- 66 • Most of the included studies utilized retrospective data with an increased likelihood of
67 misclassification bias which may have underestimated or overestimated the association
68 between heat-related illness and risk factors.
- 69 • We could not perform a metaanalysis due to the heterogeneity in the study designs.

70 **Trial registration** None

71 **Key words**

72 Heat stress; Heat stroke; Heat exhaustion; Heat tolerance; Women; Armed Forces

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80 **Introduction**

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3 81 Heat illness is a spectrum of disorders that arise when there is a disruption in the regulation of
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5 82 body temperature.[1] These illnesses may arise from a combination of prolonged exposure to
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7 83 heat/humidity and increased metabolic activity.[2] When body temperature rises, conduction,
8
9 84 convection, radiation and evaporation mechanisms help to cool the body and maintain
10
11 85 normothermia.[1] However, heat loss is susceptible to prevailing environmental conditions and
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13 86 type of clothing worn. Without adequate cooling a number of syndromes may occur ranging
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15 87 from heat cramps, heat syncope and heat exhaustion through to heat stroke, a potentially life-
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17 88 threatening disorder.[1]
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22 89 Heat stroke is a medical emergency.[3] It is characterized by elevated core temperature of 40°C
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24 90 and above, central nervous system disturbances and multi-organ damage that may result in
25
26 91 death.[3] Heat stroke has been classified as either classic or exertional.[4] Classical heat stroke
27
28 92 is insidious in onset and occurs in vulnerable populations such as young children, the elderly
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30 93 and patients with chronic diseases.[5] On the other hand, exertional heat stroke occurs more
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32 94 rapidly and affects apparently healthy, active people such as athletes, factory workers,
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34 95 construction workers, agricultural workers, firefighters and military recruits.[6, 7] The workers
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36 96 in these industries often require high levels of physical exertion to perform jobs and tasks. A
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38 97 combination of rigorous activities and extreme exposure to heat places the workers at increased
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40 98 risk of heat stress and heat stroke.[8]
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46 99 However, the ability to cope with heat stress varies between individuals.[3] Individuals who
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48 100 are unable to cope with heat stress may have elevated body temperature under extreme
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50 101 conditions in the heat, which may cause heat exhaustion or heat stroke.[3] The inability to
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52 102 withstand heat stress during exertion in hot environments is defined as heat intolerance.[3]
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54 103 Evidence in the published literature suggests that heat stroke may be preceded or accompanied
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56 104 by a state of heat intolerance.[3] The Israeli Defence Force developed the heat tolerance test
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58 105 in 1979 as an index of the ability of soldiers to cope with exertional heat.[9] Individuals who

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3 106 have suffered heat stroke are sent for a heat tolerance test after a minimum recovery period of
4
5 107 6 to 8 weeks as part of the return to duty process.[9] Criteria used to define heat intolerance
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7 108 include an elevation in rectal temperature above 38.5°C and heart rate above 150 bpm or when
8
9 109 rectal temperature or heart rate fail to stabilize during the test. The current heat tolerance test
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11 110 criteria are based on previous studies by Shapiro et al.[10] and Epstein et al.,[11] which utilised
12
13 111 only male military participants.[10, 11]
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17 112 Globally, increasing numbers of women are joining the armed forces following the inclusive
18
19 113 approach to recruiting and creation of more roles for women.[12] Women are required to
20
21 114 operate in austere environments with heat illnesses becoming more frequent.[12] This has
22
23 115 raised the question about gender differences in thermoregulation during heat stress.[12] During
24
25 116 prolonged heat exposure, the body's thermal inertia is determined by complex interactions
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27 117 between the body's morphological characteristics (body composition, body mass and surface
28
29 118 area) and heat load. Evidence suggests that women differ from men in thermal responses to
30
31 119 heat.[13] These difference may be because women have a lower rate of whole body evaporative
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33 120 heat loss, higher body fat mass, body mass ratio,[14] number of sweat glands and lower aerobic
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35 121 fitness.[15] In addition, hormonal variations due to menstrual cyclic patterns and the use of
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37 122 contraceptive pills may all be associated with the differences in response to heat stress.[16]
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43 123 Although these gender differences exist, they have not been considered when conducting the
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45 124 heat tolerance test (HTT) for women who have had a heat stroke.[15] Furthermore, heat illness
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47 125 can impact defence operational effectiveness and may result in acute loss of manpower and
48
49 126 possible medical discharge from service.[17] A previous review on the risk of heat illness in
50
51 127 women compared with men focused on the general population.[18] The findings of the review
52
53 128 suggested that men are at increased risk of heat illness compared to women.[18] However,
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55 129 there is a dearth of research investigating heat illness in women compared to men in the armed
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60 130 forces.

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3 131 Therefore, the aims of this systematic review are:
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6 132 To describe the epidemiology of heat stroke and other heat related illnesses in women
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8 133 compared to men in the armed forces.
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10 134 To identify predisposing risk factors and gender differences in heat illness and heat
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12 135 tolerance
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18 19 137 **Methods**

20 21 22 138 **Search Strategy**

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25 139 This review utilised the Preferred Reporting Items for Systematic Review and Meta-analysis
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27 140 protocols (PRISMA-P) 2015 statement[19] and explored all literature published in English
28
29 141 from inception of the different databases to the 1st of April 2019. Databases searched included
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31 142 MEDLINE, CINAHL, PsycINFO, Emcare, Informit and Scopus. A preliminary search was
32
33 143 conducted in Medline, Emcare and CINAHL to identify relevant key words contained in the
34
35 144 titles, abstracts and subject descriptors. These search terms were used to conduct the search in
36
37 145 other databases without subject headings. The search strategy used in Medline is presented in
38
39 146 supplemental table 1. No review protocol exists.
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44 147 **Eligibility criteria**

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47 148 Studies included in the review were assessed according to the following inclusion criteria: Peer-
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49 149 reviewed literature comparing heat illness in women to men in the Armed Forces. Exclusions
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51 150 included literature discussing heat illness in other occupations, or studies where data on heat
52
53 151 illness in women could not be separated from men or studies reporting heat illness in men or
54
55 152 literature reviews, conference abstracts and grey literature. In addition, additional primary data
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3 153 sources were identified from the reference lists of the included studies using a hand-search
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5 154 technique.

8 155 **Selection of studies and data extraction**

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11 156 FA and BMA identified all included studies and data extraction was performed using a standard
12
13 157 abstraction form. Data extracted from the studies included: study location and design,
14
15 158 population, proportion and incidence of heat illnesses, factors associated with heat illness and
16
17 159 heat tolerance, and heat tolerance in men and women. All authors cross-checked the extracted
18
19 160 data for consistency.

23 161 **Quality assessment**

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26 162 The methodological quality assessment was assessed by FA in consultation with MC using the
27
28 163 modified quality assessment tool for studies with diverse designs (QATSDD) critical appraisal
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30 164 tool.[20] Any disagreement about any article was reviewed by BMA and AMA and discussed
31
32 165 until consensus was reached. The QATSDD tool is a 16-item tool which assesses the quality
33
34 166 of diverse studies (both quantitative and qualitative).[20] The tool was modified to exclude two
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36 167 items relating to qualitative studies as well as two items relating to quantitative studies that
37
38 168 were not applicable to the studies included in the review. The items excluded comprised
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40 169 statistical assessment of reliability and validity of measurement tool(s) (Quantitative only), fit
41
42 170 between stated research question and format and content of data collection tool e.g. interview
43
44 171 schedule (Qualitative), assessment of reliability of analytical process (Qualitative only) and
45
46 172 evidence of user involvement in design. Each criterion in the modified QATSDD tool was
47
48 173 awarded a score of 0 to 3 with 0 = not at all, 1 = very slightly, 2 = moderately and 3 = complete.
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50 174 The scores of each criterion were summed to assess the methodological quality of included
51
52 175 studies with a maximum score of 36. The criteria included were (1) theoretical framework; (2)
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54 176 statement of aims/objectives; (3) description of research setting; (4) evidence of sample size;

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3 177 (5) representative sample of target group of a reasonable size, (6) description of procedure for
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5 178 data collection; (7) rationale for choice of data collection tool(s); (8) detailed recruitment data;
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8 179 (9) fit between research question and method of data collection (Quantitative only); (10) fit
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10 180 between research question and method of analysis (Quantitative only); (11) good justification
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12 181 for analytical method selected; and (12) strengths and limitations. For ease of interpretation,
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14 182 the scores were converted to percentages and classified as low (<50%), medium (50-80%) or
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16 183 high (>80%) quality of evidence.
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20 184 **Data analysis and synthesis**

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23 185 Data analysis was conducted using SPSS version 25. Heat illness was reported as either all
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25 186 heat related illnesses or heat stroke versus other heat illnesses. Measures used to describe heat
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27 187 illness were proportions and rates. The mean proportion of heat stroke and other heat illness
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29 188 were reported for studies published between 1995 and 1997. A Mann-Whitney U test was used
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31 189 to assess the median differences in the incidence of heat stroke and other heat illnesses between
32
33 190 men and women from 2006 to 2018. Level of significance was set at 0.05. The incidence rates
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35 191 and proportions of all heat related illness (where heat stroke was not differentiated from other
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37 192 heat illnesses) were reported using frequency tables. Due to the heterogeneity of the included
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39 193 studies, a meta-analysis was not conducted.
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46 195 **Results**

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48 196 An initial search identified 3801 papers. After removing duplicates, screening titles and
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50 197 abstracts, 47 papers remained for full text review with twenty-seven (27) included in the
51
52 198 systematic review (Figure 1). Twenty-five (25) of the reviewed articles originated from the
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54 199 United States of America, while the other two studies were conducted in the United Kingdom
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56 200 and Israel respectively (Supplemental Table 2). All included studies were conducted among
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3 201 armed forces personnel, however, one study focused on armed force personnel with sickle cell
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5 202 trait (SCT),[21] while another study included university staff and armed forces personnel in
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7 203 the study.[22] Twenty-four (24) articles examined heat illnesses and injuries in women and
8
9 204 men. Eight (8) of these studies described all heat related illnesses in men and women,[21, 23-
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11 205 29] while 16 studies included information on heat stroke and other heat injuries (including
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13 206 “heat exhaustion” and “unspecified effects of heat”) in relation to both genders.[30-45] Six (6)
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15 207 studies identified risk factors associated with heat stroke,[21, 25, 28, 29, 46, 47] and 2 studies
16
17 208 compared heat tolerance in men and women.[15, 47]

209 **Epidemiology of heat stroke and other heat related illnesses in women compared to men**

210 Table 1 shows the proportions and incidences of all heat-related illness in men and women in
211 the armed forces. Six (6) studies reported higher incidences and proportions of heat illness in
212 men compared to women[21, 23, 25, 26, 28, 29] while two studies reported higher incidences
213 of heat illness in women.[24, 27] Between 1995 and 1997, the mean proportion of all reported
214 heat stroke events in women was approximately 12% compared to 88% of heat stroke events
215 in men. Similarly, men reported a higher mean proportion of heat exhaustion (96%) compared
216 to women (4%).[31-33] Between 2006 and 2018, overall median incidence for heat illness was
217 higher than heat stroke for both men and women (Figure 2). However, men had significantly
218 higher heat stroke incidence compared to women with a mean rank of 19.19 for men and 7.81
219 for women (median = 0.27, IQR = 0.11 vs median = 0.15 respectively, IQR = 0.03; U = 10.50,
220 $P < 0.001$). Although, the incidence of other heat injuries was similar between men and women;
221 there was a trend for women to report a slightly higher median incidence of other heat injuries
222 compared to men (median = 1.41 IQR = 0.37 vs median = 1.62, IQR = 0.97; mean rank = 10.65
223 vs 16.35, U = 47.50, P = 0.058).

224 **Table 1: Proportion and incidence of heat related illnesses in women and men in the** 225 **Defence Force**

Reference, year	Country	Study design	Study duration	Population	All heat injuries	
					Women	Men
Dickson, 1994[23]	UK	Descriptive epidemiology	1981-1991 (10yrs)	Royal Air force, Royal Navy and Army (1448 cases)	11.43*	41.87*
Army Medical Surveillance Activity, 1998[24]	USA	Descriptive epidemiology	1997 – 1998 (1 year)	US Army (1433 cases) 1997	12.8†	8.6†
Army Medical Surveillance Activity, 2000[27]	USA	Descriptive epidemiology	1997 – 1999 (2 years)	US Army and Marine Corps (3386 cases)	15.8†	12.0†
Army Medical Surveillance Activity, 2002[25]	USA	Descriptive epidemiology	1990 – 1997 (7 years)	US Army (2290 cases)	14.0%§	86.0%§
Army Medical Surveillance Activity, 2003[26]	USA	Case control	1998 – 2001 (3 years)	US Army (5021 cases and 10,042 controls)	20.7%§	79.3%§
Army Medical Surveillance Activity, 2003[26]	USA	Descriptive epidemiology	2002 (1 year)	US Army (1816 cases)	3.5†	5.1†
Carter et al, 2005[28]	USA	Cross-sectional	1980 – 2002 (22 years)	US Army (5246 cases)	13.7%§	86.3%§
Bedno et al, 2014[29]	USA	Analytical cross-sectional	2005 - 2006	US Armed Forces (80 exertional heat illness cases) 9455 men 1913 women	0.680%	0.71%
Singer et al, 2018[21]	USA	Retrospective cohort	1992 - 2012	SCT and non-SCT US Armed Forces SCT: 214 exertional heat illness cases Non-SCT: 577 exertional heat illness cases	13.89† 13.14†	14.79† 7.79†

226 § Proportions and incidences reported are of the total cases reported in the articles

227 * Incidence rate reported per 100,000 person-years; † Incidence rate per 100,000 person- months;

228 † Incidence rate reported per 1000 person-years

229 UK = United Kingdom; USA = United States of America

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234 Risk factors for heat illness and heat intolerance

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3 235 As shown in Table 2, six (6) studies identified the risk factors associated with heat-related
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5 236 illness and heat tolerance.[21, 25, 28, 29, 46, 47] However, one study identified the risk for
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7 237 heat illness in association with SCT status.[21] The odds of females experiencing heat illness
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9 238 ranged from 1.04 to 1.36 and were 3.68 times more likely to be heat intolerant (using the
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11 239 standard heat tolerance test protocol) compared to males.[21, 25, 28, 29, 47] Other identified
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13 240 risk factors for heat illness (Table 2) included younger and older age,[21, 25] lower level of
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15 241 education,[25] ethnicity,[25, 28] higher body mass index (BMI),[46] lower VO_{2max},[47] being
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17 242 SCT positive,[21] being in service for less than 1 year,[25] and serving in combat units as an
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19 243 infantry or gun crew soldier.[25, 28]
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256 **Table 2: Risk factors associated with heat illness and tolerance**

Reference, year	Country	Study design and duration	Study population	Risk factors	OR or IDR (95% CI)
Army Medical Surveillance Activity, 2002[25]	USA	Case-control 1998 – 2001 (3 years)	US Army 5021 cases and 10,042 controls	Female	1.5 (1.4 - 1.7)
				Age < 20 years	2.1 (1.4 - 3.1)
				Other ethnicity*	1.2 (1.0 - 1.4)
				Combat	1.5 (1.4 - 1.6)
				Lower level of education	2.0 (1.2 – 3.1)
Carter et al, 2005[28]	USA	Cross-sectional 1980 – 2002 (22 years)	US Army 5246 cases of heat illness; 4521 males and 725 females	Less than 1 year of service	2.3 (2.0 – 2.6)
				Female	1.21 (1.09 – 1.40)
				Infantry soldiers and gun crew men	2.69 (1.71 – 2.89)
				African and Hispanic ethnicity	0.76 (0.71 – 0.82)
Wallace et al, 2006[46]	USA	Case-control 1988 – 1996 (8 years)	US Marine Corps Male (627 cases and 1679 controls) Female (49 cases and 123 controls)	Northern state of origin	1.69 (1.42 – 1.90)
				BMI ≥ 26 kg/m ² (males)	2.10 (1.59 – 2.78)
				Run time ≥ 12.9 minutes (males)	5.61 (3.73 – 8.45)
Bedno et al, 2014[29]	USA	Analytical cross-sectional 2005 - 2006	US Armed Forces 9455 men (67 exertional heat illness cases) 1913 women (13 exertional heat illness cases)	Run time ≥ 6.9 minutes (females)	5.30 (1.59 – 17.64)
				Female	1.04 (0.57 – 1.89)
Kazman et al, 2015[47]	USA	Analytical cross-sectional (Duration not stated)	Military and university community members 55 males and 20 females	Female	3.68 (1.21 – 11.24)
				VO _{2max}	0.9 (0.76 – 0.96)
Singer et al, 2018[21] †	USA	Retrospective cohort study	SCT and non-SCT US Armed Forces SCT: 214 exertional heat illness cases Non-SCT: 577 exertional heat illness cases	Female	1.36 (1.17 – 1.50)
				SCT positive	1.24 (1.06 – 1.45)
				Age at enlistment: 30+ years	1.57 (1.07 – 2.33)
				Marines vs Army	1.51 (1.15 – 2.13)
				Occupation: Combat vs repair/engineer	1.57 (1.15 – 2.13)

257 *non- White, non-Black, non-Hispanic; OR = Odds ratio; IDR = Incidence density ratio; BMI= Body Mass Index; CI=Confidence Interval; USA = United States of America; † The risk factors
258 associated with EHI and SCT status

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3 **259 Heat tolerance in women and men**
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6 260 Two studies compared heat tolerance in males and females using the most commonly used test,
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8 261 the HTT developed by the Israeli Armed Forces.[15, 47] The findings reported in Table 3
9
10 262 revealed that a greater proportion of women were classified as heat intolerant compared to men
11
12 263 (45% vs 18% and 66% vs 25.79%).[15, 47] In addition, women had higher baseline
13
14 264 temperature (37.18°C vs 37.07°C and 37.1°C vs 36.9°C respectively)[15, 47] and heart rate
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16 265 (82.11 bpm vs 73.94 bpm and 76 bpm vs 68 bpm). In addition, the endpoint heart rates for
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18 266 women were higher compared to their male counterparts (141.5 bpm vs 126.5 bpm and 137
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20 267 bpm vs 122 bpm respectively).[15, 47] The end point temperature varied between the two
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22 268 studies; one study reported a higher endpoint temperature for females[15] and the other study
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24 269 reported similar endpoint temperature between males and females.[47]
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270 **Table 3: Heat tolerance in women and men**

Reference, year	Country	Study design and duration	Study population	Parameters	Women	Men
Druyan et al, 2012[15]	Israel	Retrospective cross-sectional 2008 – 2010 (2 years)	170 males and 9 females	Heat intolerance rate	66.6%	25.79%
				Baseline T _{rec} (° C)	37.18 ± 0.09	37.07 ± 0.02
				Endpoint T _{rec} (° C)	38.14 ± 0.14	37.93 ± 0.03
				Baseline HR (bpm)	82.11 ± 4.88	73.94 ± 1.17
				Endpoint HR (bpm)	141.50 ± 7.84	126.50 ± 1.79
Kazman et al, 2015[47]	USA	Analytical cross-sectional (duration not stated)	Military and university community members; 55 males and 20 females	Heat intolerance rate	45%	18%
				Baseline T _{rec} (° C)	37.1 ± 0.4	36.9 ± 0.4
				Endpoint T _{rec} (° C)	38.1 ± 0.4	38.1 ± 0.4
				Baseline HR (bpm)	76 ± 15.0	68 ± 12.1
				Endpoint HR (bpm)	137 ± 20.1	122 ± 20.2

271 HR = Heart rate; Bpm = beats per minute; T_{rec} = Rectal temperature; USA = United States of America

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3 272 **Assessment of methodological quality**
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6 273 The QATSDD scores ranged from 0 to 97.2% (Supplemental Table 3). Only six studies scored
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8 274 above 50% and included details about recruitment, data analysis, strengths and limitations of
9
10 275 the research. The other studies had lower scores because they lacked detailed justification for
11
12 276 the analytical methods, data collection, analysis, strengths and limitations. However, results of
13
14 277 the methodological assessment should be interpreted with caution. Although the tool assesses
15
16 278 methodological quality, it is more likely to be dependent on how the paper was written. In this
17
18 279 review, 80% of the studies included were military reports on heat-related illnesses in the Armed
19
20 280 Forces. These reports were published in a peer-reviewed journal and were retrospective
21
22 281 analyses of data collected by Defence Medical Surveillance Systems. These studies may not
23
24 282 have reported details about data collection, strengths and limitations, but they presented valid
25
26 283 information on heat- related illness.
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284 Discussion

285 The findings of this review suggest a higher rate of heat stroke in men compared to women in
286 the armed forces. On the other hand, the incidence of other exertional heat injuries (heat
287 exhaustion and unspecified heat illnesses) were similar for both men and women. However,
288 women were more likely to be heat intolerant compared to men. Other risk factors found to be
289 associated with exertional heat illness include age, lower level of education, ethnicity, higher
290 BMI, lower VO_{2max} , positive SCT, shorter duration of service, and service unit. The association
291 between these factors and exertional heat illness is weak given the small number of articles that
292 investigated the relationship.

293 The reported higher incidence of heat stroke in men compared to women could possibly
294 indicate that men may have comparatively tolerated working in the heat beyond the endurance
295 limits than women.[17] Conversely, the women may not have ignored the early warning signs
296 of heat illness and may have sought earlier treatment compared to men. This reinforces the
297 presumption that women are more inclined to make use of health services and report ill health
298 than men.[48] In addition, the consultation rates of men were 30% lower than women,
299 confirming the assumption that men are less likely to consult and may present at a later stage
300 with more severe forms of diseases.[48] Although, previously published literature have
301 reported a higher rate of all types of heat illnesses in men in the general population (including
302 some armed forces personnel) compared to women; heat stroke was not considered separately
303 from other forms of heat illnesses.[18]

304 However, despite the lower rate of heat stroke, women had a greater risk of heat illness and
305 were more likely to be heat intolerant than men.[21, 25, 28, 29, 47] The higher risk of exertional
306 heat illness in women may likely be due to differences in physiological and physical
307 characteristics between men and women.[49] Physiological characteristics such as hormones,

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3 308 use of contraceptive pills and lower evaporative heat loss may make women more susceptible
4
5 309 to heat illness. [14, 16] Physical characteristics such as lower aerobic fitness and greater body
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7 310 fat are predictors of exertional heat illness.[49] Generally, men have less body fat and greater
8
9 311 lean body mass compared to women. Furthermore, women have lower aerobic fitness levels
10
11 312 and lower overall work capacity which may contribute to the increased risk of exertional heat
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13 313 illness.[49]

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17 314 Other risk factors for heat illness and intolerance identified in the studies include higher
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19 315 BMI,[46] lower VO_{2max} ,[47] age,[21, 25] lower level of education,[25] non-White, non-Black,
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21 316 non-Hispanic ethnic groups,[25] less than one year of service,[25] service unit.[25, 28] and
22
23 317 positive SCT.[21] Individuals with higher BMI (indicating higher body fat) have been reported
24
25 318 to be at increased risk of exertional heat illness and are less heat tolerant.[50] Evidence shows
26
27 319 that high body fat increases metabolic heat production and decreases heat loss leading to heat
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29 320 illness.[51] However, individuals with a low BMI may or may not be fit. Individuals with low
30
31 321 aerobic fitness levels are likely to exert themselves beyond their physical limit and are at
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33 322 increased risk of heat illness.[51] During exercise, relative physiological strain is increased,
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35 323 peripheral blood flow decreases which in turn hinders thermoregulation and increasing the risk
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37 324 of heat illness.[51]

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43 325 The association between age, duration of service, occupational roles, level of education and
44
45 326 heat illness may be explained by the level of aerobic fitness. Age as a risk factor varied in this
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47 327 review, with younger age and older age (at enlistment) considered as factors that increase the
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49 328 risk of heat illness.[21, 25] Evidence suggests that aerobic fitness decreases with older age,
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51 329 especially if older adults are sedentary.[52] However, aerobic fitness improves with regular
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53 330 physical exercise and the age related differences between younger and older adults are
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55 331 reversed.[53] The younger Armed Forces personnel in the review had been in service for less
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57 332 than a year and may not be as physically fit as the older and long serving personnel.[25] The
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3 333 physical fitness requirements for recruits vary from the fitness standards for longer serving
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5 334 personnel. For example, in Australia, Army recruits are required to pass the pre-enlistment
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7 335 fitness assessment (PFA) which comprises of push-ups, sit-ups and the beep test during the
8
9 336 initial stages of their training.[54] In contrast, the older serving personnel undergo regular
10
11 337 fitness training which consists of push-ups, sit-ups, 2.4 km run, 5km walk and weight
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13 338 lifting.[55] The intense and regular training the older personnel have undergone may be
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15 339 responsible for their higher level of fitness and lower risks of heat illness.[56] Furthermore,
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17 340 occupational roles such as serving as in Marine Corps and physically demanding jobs such as
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19 341 infantry, combat and gun crew had an increased risk of heat illness compared to personnel in
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21 342 administrative or support jobs. This may be associated with the rigorous and strenuous training
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23 343 requirements for these jobs.[29]

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29 344 Similarly, the association between lower level of education and heat illness may be due to
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31 345 aerobic fitness. Research has identified educational attainment as a major predictor of health
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33 346 outcomes.[57] Education provides the opportunity for individuals to learn more about their
34
35 347 health and to make healthy lifestyle choices. Individuals with a higher level of education are
36
37 348 more likely to engage in healthy behaviours such as healthy diet and regular exercise.[57]
38
39 349 Regular exercise is necessary to maintain and improve aerobic fitness.[58] High aerobic fitness
40
41 350 may reduce the risk of exertional heat illness; however, some fit individuals may be at increased
42
43 351 risk of heat illness because of their ethnic status. The effect of ethnicity on heat illness varied
44
45 352 in this review. One study reported that minor ethnic groups (non-White, non-Black, non-
46
47 353 Hispanic) were more susceptible to heat illness[25], while another study reported that
48
49 354 Caucasians had an increased risk of heat illness compared to other ethnic groups.[28] Genetic
50
51 355 adaptation may play a role in the differences between ethnic groups.[59] Evidence shows that
52
53 356 a disruption in the cell protective mechanism of heat shock proteins may increase the risk of
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55 357 heat illness.[59]

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3 358 Another role genetics plays in predisposition to heat illness was evident in the review with SCT
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5 359 positive armed force members at increased risk of exertional heat illness compared to SCT
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8 360 negative members.[21] SCT is an inherited blood disorder where an individual has a wild type
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10 361 haemoglobin A and haemoglobin S. Individuals with the SCT are considered heterozygous for
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12 362 the sickle cell mutation in the subunit beta gene of the haemoglobin.[60] Evidence has linked
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14 363 positive SCT with exercise related adverse health outcomes such as exertional heat illness
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16 364 (including exertional rhabdomyolysis, heat stroke and hyperthermia) in military personnel.[60]
17
18 365 However, the biological pathway by which SCT is associated with heat illness is still
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20 366 unknown.[21] More in depth research is needed to elucidate the role of genetics in exertional
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23 367 heat illness.

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27 368 The risk of heat illness is dependent on thermal tolerance.[3] The HTT is conducted for
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29 369 members of the armed forces after a heat stroke event as part of the return to duty process.[9]
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31 370 The test criteria defines heat intolerance as peak rectal temperature > 38.5°C, peak heart rate
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33 371 > 150 bpm, or the inability of these values to reach a plateau.[10, 11] However, using the
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35 372 current protocol, there were more women in the armed forces classified as heat intolerant than
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37 373 men.[15, 47] In addition, women had higher baseline temperature and heart rate compared to
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39 374 men. The higher baseline core temperature increases the likelihood of being intolerant and at-
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41 375 risk of heat illness.[47] Two studies acknowledge that sex differences in thermoregulation may
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43 376 account for the higher intolerance rates in women.[15, 47] Given that the test protocol was
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45 377 developed using male subjects, there is a need to re-evaluate the criteria for women to reduce
46
47 378 false positive results.[15, 47]

379 **Strengths and limitations**

380 To the authors' current knowledge, this is the first known systematic review investigating the
381 impact of gender on exertional heat illness and heat tolerance in the armed forces. In addition,

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3 382 we identified potential risk factors that are associated with exertional heat illness. However,
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5 383 the heterogeneity in the study designs contributed to the variable methodological quality of the
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7 384 included studies. Most of the articles in this review were military reports and may not be
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9 385 considered of high methodological quality when assessed using a formal critical appraisal tool.
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11
12 386 In addition, most of the included studies utilized retrospective data as the data source with an
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14 387 increased likelihood of incompleteness and inaccuracy. There is a likelihood that
15
16 388 misclassification bias could have been introduced into the studies. Three studies that explored
17
18 389 the risk factors associated with heat-related illness used retrospective data. [25, 28, 46] The
19
20 390 retrospective data may have been misclassified or incomplete at the time of entry and may have
21
22 391 introduced misclassification bias into the studies. This type of bias may underestimate or
23
24 392 overestimate the association between heat-related illness and risk factors. Although the risk
25
26 393 factors associated with heat illness were discussed; the review provided limited evidence of
27
28 394 these factors, given the few numbers of studies that investigated the association. Furthermore,
29
30 395 we included only studies published in English language; studies published in other languages
31
32 396 were excluded.

397 **Implication for policy and future research**

398 This systematic review demonstrates that there is limited research on exertional heat illness in
399 women in the Armed Forces. Although men had a higher reported incidence of heat stroke; this
400 may be a reflection that women are more likely to report poorer health earlier than men.[48]
401 Further research is needed to establish if this reflects physiological or behavioural differences.
402 Given that women have an increased risk of heat illness; they should be encouraged to
403 participate in cardiovascular training programs to improve physical fitness. Nonetheless, more
404 research is needed to understand the roles of underlying factors such as menstrual cycle phase,
405 use of contraceptive pills and cardiovascular function in heat illness.[15, 47] Furthermore, the
406 limited evidence revealed that more women were classified as heat intolerant using the current

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3 407 heat tolerance test protocol. The current criteria may be unfair to women given that it was
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5 408 developed using male participants. Therefore, it is important that the protocol is re-evaluated
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7 409 for women or a new protocol is developed that puts the gender specific factors into
8
9 410 consideration.[15] The re-evaluation of the protocol for women would reduce false positive
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11 411 results and the likelihood of ending the careers of these otherwise healthy women.[15]
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15 412 **Conclusion**

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18 413 In conclusion, this review shows that men experienced a higher incidence of heat stroke but
19
20 414 women in the armed forces may have a greater risk of heat illness and are more likely to be
21
22 415 heat intolerant than their male counterparts using the standard heat tolerance test. Further
23
24 416 research is needed to evaluate the heat tolerance test protocol for women and to further
25
26 417 investigate the influence of gender differences on heat intolerance and heat illness.
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30 418 **Authors' contribution**

31
32 419 All authors contributed substantially to the study concept, design, data extraction, quality
33
34 420 assessment and writing of the manuscript.
35

36 421 **Conceptualization:** Faith O. Alele, Bunmi S. Malau-Aduli, Aduli E. Malau-Aduli, Melissa
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38 422 Crowe

39 423 **Methodology:** Faith O. Alele, Bunmi S. Malau-Aduli, Aduli E. Malau-Aduli, Melissa Crowe

40 424 **Writing** - Original draft: Faith O. Alele

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42 425 **Writing – review & editing:** Faith O. Alele, Bunmi S. Malau-Aduli, Aduli E. Malau-Aduli,
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44 426 Melissa Crowe

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46 427 All authors read and approved the manuscript for submission.
47

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49
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52
53 431 **Patient consent for publication:** Not required

54
55 432 **Data sharing statement:** There are no additional or unpublished data available.
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11 577 **Figure legends**

12
13 578 Figure 1: PRISMA flow chart of the study selection protocol

14
15 579 Figure 2: Comparison of the incidence rate of heat stroke and other heat illnesses between
16 580 women and men. This figure shows the median incidence rate for heat stroke and other heat
17 581 injuries between 2006 and 2018. Men had significantly higher heat stroke incidence compared
18 582 to women with a mean rank of 19.19 for men and 7.81 for women (median = 0.27, IQR = 0.11
19 583 vs median = 0.15, IQR = 0.03; U= 10.50, P < 0.001). However, there was no significant
20 584 difference between men and women, in the incidence of other heat injuries (median = 1.41 IQR
21 585 = 0.37 vs median = 1.62, IQR = 0.97; mean rank = 10.65 vs 16.35, U = 47.50, P = 0.058.
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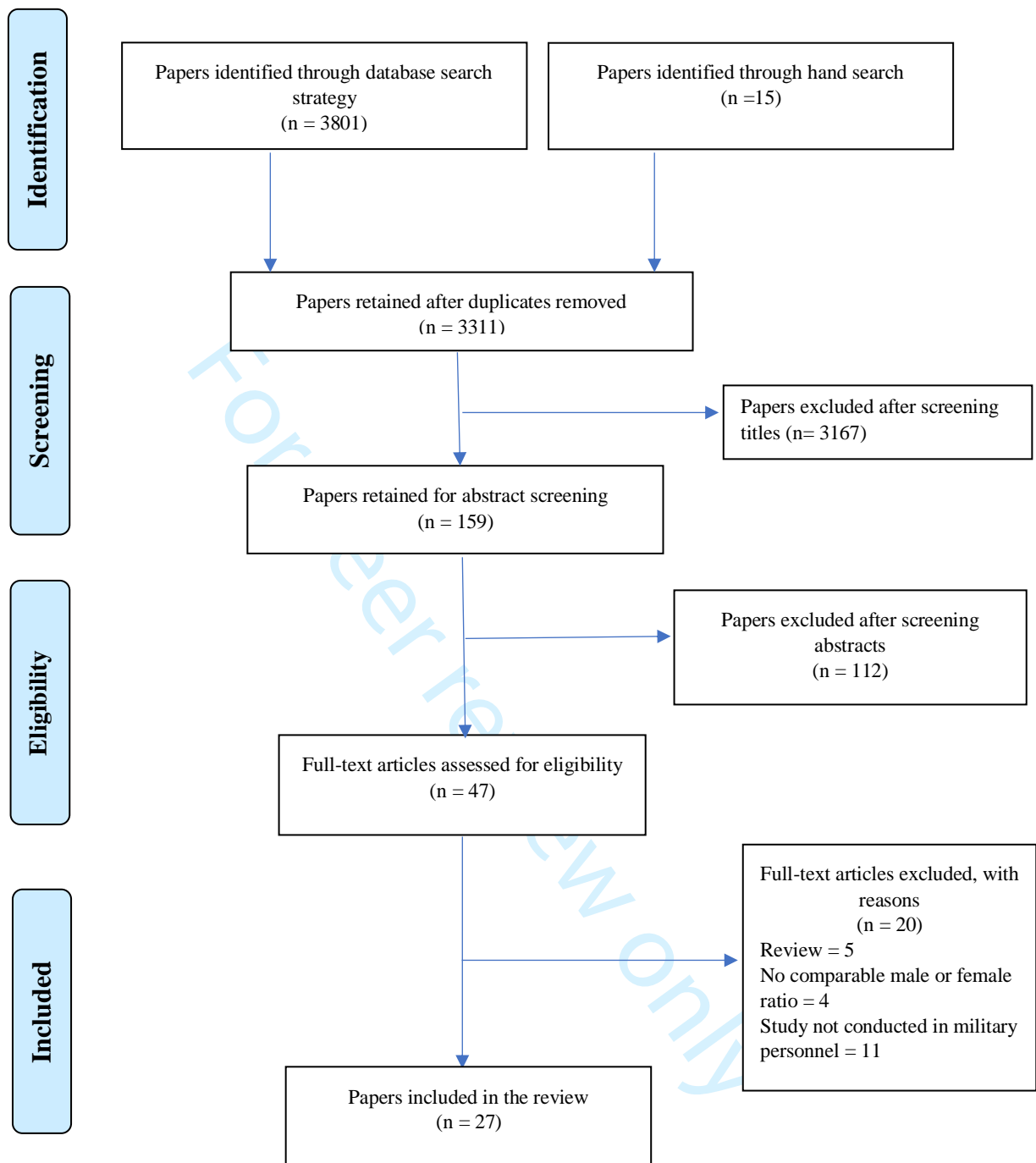
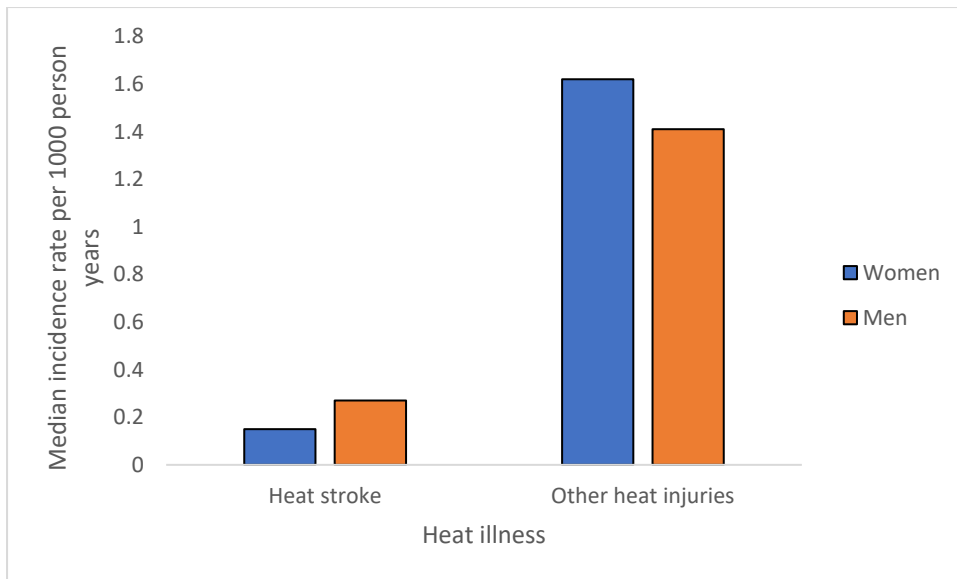


Figure 1: PRISMA flow chart of the study selection protocol



*** P < 0.001

Figure 2

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Supplemental Table 1

Medline search strategy	
1.	Women (MeSH)
2.	Gender expression
3.	Gender identity (MeSH)
4.	Gender
5.	Wom\$
6.	Sex
7.	Heat strok*
8.	Heatstrok*
9.	Heat collapse
10.	Heat exhaustion
11.	Heat prostration
12.	Heat cramp
13.	Heat cramps
14.	Heat stress disorder
15.	Heat stress disorders (MeSH)
16.	Thermal stress
17.	Heat illness
18.	Heat illnesses
19.	Heat injury
20.	Heat injuries
21.	Heat related diseases
22.	Heat disorder
23.	Heat disorders
24.	Heat related disorder
25.	Heat related disorders
26.	Heat related illness
27.	Heat related illnesses
28.	Heat related injuries
29.	Heat related injury
30.	Environmental heat illness
31.	Heat stress
32.	Heat adaptation
33.	Heat tolerance
34.	Heat tolerances
35.	Heat resistance
36.	Thermal resistance
37.	Thermoresistance
38.	Thermotolerance (MeSH)
39.	Heat endurance
40.	1 OR 2 OR 3 OR 4 OR 5 OR 6
41.	7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39
42.	40 AND 41

Supplemental Table 2
Summary of all included studies

Reference, year	Country	Study design and duration	Population	Study findings [§]
Dickson. G, 1994	UK	Descriptive epidemiology 1981-1991	Royal Airforce, Royal Navy and Army; 1448 all heat injuries cases [†]	<u>Women</u> All heat injuries: 11.43 [#] <u>Men</u> All heat injuries: 41.87 [#]
Army Medical Surveillance Activity, 1995	USA	Descriptive epidemiology; 1994	US Army; 23 heat stroke cases 12 heat exhaustion cases	<u>Women</u> Heat stroke: 13% Heat exhaustion: 0% <u>Men</u> Heat stroke: 87% Heat exhaustion: 100%
Army Medical Surveillance Activity, 1996	USA	Descriptive epidemiology; 1995	US Army; 81 heat stroke cases 39 heat exhaustion cases	<u>Women</u> Heat stroke: 17.3% Heat exhaustion: 7.7% <u>Men</u> Heat stroke: 82.7% Heat exhaustion: 92.3%
Army Medical Surveillance Activity, 1997	USA	Descriptive epidemiology; 1996	US Army; 45 heat stroke cases 24 heat exhaustion cases	<u>Women</u> Heat stroke: 4.4% Heat exhaustion: 4.2% <u>Men</u> Heat stroke: 95.6% Heat exhaustion: 95.8%
Army Medical Surveillance Activity, 1998	USA	Descriptive epidemiology; 1997 - 1998	US Army; 1433 all heat injuries cases (1997-1998) [†] 1997 1998	<u>Women</u> All heat injuries: 12.8 [‡] <u>Men</u> All heat injuries: 8.6 [‡] <u>Women</u> All heat injuries: 15.8 [‡] <u>Men</u> All heat injuries: 12.0 [‡]

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Army Medical Surveillance Activity, 2000	USA	Descriptive epidemiology; 1997 - 1999	US Army and Marine Corps; 3386 all heat injuries cases [†] Army (1896 cases) Marine Corps (1104 cases)	Women All heat injuries: 2.0 [†] Men All heat injuries: 1.5 [†] Women All heat injuries: 4.4 [†] Men All heat injuries: 2.0 [†]
Army Medical Surveillance Activity, 2002	USA	Descriptive epidemiology 1990 - 1997	US Army; 2290 all heat injuries cases [†]	Women All heat injuries: 14.0% Men All heat injuries: 86.0%
		Case – control 1998 - 2001	US Army; 5021 cases and 10,042 controls (all heat injuries) [†]	Women All heat injuries: 20.7% Men All heat injuries: 79.3% Risk factors Female: OR; 1.5 (1.4 - 1.7) Age < 20 years: OR; 2.1 (1.4 - 3.1) Other ethnicity*: OR; 1.2 (1.0 -1.4) Combat: OR; 1.5 (1.4 - 1.6) Lower level of education: OR; 2.0 (1.2 – 3.1) Less than 1 year of service: OR; 2.3 (2.0 – 2.6)
Army Medical Surveillance Activity, 2003	USA	Descriptive epidemiology; 2002	US Army; 1816 all heat injuries cases [†]	Women All heat injuries: 3.5 [†] Men All heat injuries: 5.1 [†]
Carter et al, 2005	USA	Cross-sectional 1980 - 2002	US Army; 5246 all heat injuries cases [†] 4521 males and 725 females	Women All heat injuries: 13.7% Men All heat injuries: 86.3% Risk factors

				Female: IDR: 1.21 (1.09 – 1.40) Infantry soldiers and gun crew men: IDR; 2.69 (1.71 – 2.89) African and Hispanic ethnicity: IDR; 0.76 (0.71 – 0.82) Northern state of origin: IDR; 1.69 (1.42 – 1.90)
7	Army Medical Surveillance Activity, 2006	USA	Descriptive epidemiology; 2005	US Armed Forces; 204 heat stroke cases 958 heat exhaustion cases
8				Women Heat stroke: 0.26† Heat exhaustion: 2.89†
9				Men Heat stroke: 0.48† Heat exhaustion: 1.98†
13	Wallace et al, 2005	USA	Case-control 1988 - 1996	US Army; 5246 cases of heat illness; 4521 males and 725 females
14				Risk factors Females Run time ≥ 6.9 minutes: OR; 5.30 (1.59 – 17.64)
15				Males Run time ≥ 12.9 minutes: OR; 5.61 (3.73 – 8.45)
16				BMI ≥ 26 kg/m ² : OR; 2.10 (1.59 – 2.78)
23	Army Medical Surveillance Activity, 2007	USA	Descriptive epidemiology; 2006	US Armed Forces; 259 heat stroke cases 1854 heat exhaustion cases
24				Women Heat stroke: 0.14† Heat exhaustion: 1.49†
25				Men Heat stroke: 0.22† Heat exhaustion: 1.34†
29	Army Medical Surveillance Activity, 2008	USA	Descriptive epidemiology; 2007	US Armed Forces; 329 heat stroke cases 1853 heat exhaustion cases
30				Women Heat stroke: 0.14† Heat exhaustion: 1.62†
31				Men Heat stroke: 0.26† Heat exhaustion: 1.34†
35	Army Medical Surveillance Activity, 2009	USA	Descriptive epidemiology; 2008	US Armed Forces; 299 heat stroke cases 1467 heat exhaustion cases
36				Women Heat stroke: 0.16† Heat exhaustion: 1.35†
37				Men Heat stroke: 0.22† Heat exhaustion: 0.98†

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Army Medical Surveillance Activity, 2010	USA	Descriptive epidemiology; 2009	US Armed Forces; 323 heat stroke cases 2038 other heat injuries cases*	Women Heat stroke: 0.15† Other heat injuries: 1.78† Men Heat stroke: 0.22† Other heat injuries: 1.35†
Army Medical Surveillance Activity, 2011	USA	Descriptive epidemiology; 2010	US Armed Forces; 311 heat stroke cases 2576 other heat injuries cases*	Women Heat stroke: 0.12† Other heat injuries: 2.32† Men Heat stroke: 0.23† Other heat injuries: 1.67†
Army Medical Surveillance Activity, 2012	USA	Descriptive epidemiology; 2011	US Armed Forces; 362 heat stroke cases 2652 other heat injuries cases*	Women Heat stroke: 0.10† Other heat injuries: 2.63† Men Heat stroke: 0.27† Other heat injuries: 1.68†
Druyan et al, 2012	Israael	Retrospective cross-sectional 2008 – 2010	Israeli Defence Forces; 170 males and 9 females	Heat tolerance parameters Women Heat intolerance rate: 66.6% Baseline Trec (° C): 37.18 ± 0.09 Endpoint Trec (° C): 38.14 ± 0.14 Baseline HR (bpm): 82.11 ± 4.88 Endpoint HR (bpm): 141.50 ± 7.84 Men Heat intolerance rate: 25.79% Baseline Trec (° C): 37.07 ± 0.02 Endpoint Trec (° C): 37.93 ± 0.03 Baseline HR (bpm): 73.94 ± 1.17 Endpoint HR (bpm): 126.50 ± 1.79
Army Medical Surveillance Activity, 2013	USA	Descriptive epidemiology; 2012	US Armed Forces; 365 heat stroke cases 2257 other heat injuries cases*	Women Heat stroke: 0.15† Other heat injuries: 2.35† Men Heat stroke: 0.27† Other heat injuries: 1.44†

1 2 3 4 5 6 7 8	Army Medical Surveillance Activity, 2014	USA	Descriptive epidemiology; 2013	US Armed Forces; 324 heat stroke cases 1701 other heat injuries cases*	<u>Women</u> Heat stroke: 0.15† Other heat injuries: 1.30† <u>Men</u> Heat stroke: 0.24† Other heat injuries: 1.19†
9 10 11 12	Bedno et al, 2014	USA	Analytical cross-sectional	US Armed Forces; 80 exertional heat illness cases	<u>Women</u> Heat illness: 0.680% <u>Men</u> Heat illness: 0.71%
13 14 15 16 17 18	Army Medical Surveillance Activity, 2015	USA	Descriptive epidemiology; 2014	US Armed Forces; 314 heat stroke cases 1410 other heat injuries cases*	<u>Women</u> Heat stroke: 0.14† Other heat injuries: 1.31† <u>Men</u> Heat stroke: 0.27† Other heat injuries: 1.21†
19 20 21 22 23 24 25 26 27 28 29 30 31 32 33	Kazman et al, 2015	USA	Analytical cross-sectional	Military and university community members; 55 males and 20 females	<u>Heat tolerance parameters</u> <u>Women</u> Heat intolerance rate: 45% Baseline Trec (° C): 37.1 ± 0.4 Endpoint Trec (° C): 38.1 ± 0.4 Baseline HR (bpm): 76 ± 15.0 Endpoint HR (bpm): 137 ± 20.1 <u>Men</u> Heat intolerance rate: 18% Baseline Trec (° C): 36.9 ± 0.4 Endpoint Trec (° C): 38.1 ± 0.4 Baseline HR (bpm): 68 ± 12.1 Endpoint HR (bpm): 122 ± 20.2 <u>Risk factors</u> Female: OR; 3.68 (1.21 – 11.24) VO _{2max} : OR; 0.9 (0.76 – 0.96)
34 35 36 37 38 39 40 41 42 43 44 45 46	Army Medical Surveillance Activity, 2016	USA	Descriptive epidemiology; 2015	US Armed Forces; 417 heat stroke cases 1625 other heat injuries cases*	<u>Women</u> Heat stroke: 0.16† Other heat injuries: 1.54† <u>Men</u> Heat stroke: 0.35† Other heat injuries: 1.48†

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Army Medical Surveillance Activity, 2017	USA	Descriptive epidemiology; 2016	US Armed Forces; 401 heat stroke cases 2135 other heat injuries cases*	Women Heat stroke: 0.19† Other heat injuries: 1.90† Men Heat stroke: 0.33† Other heat injuries: 1.61†
Army Medical Surveillance Activity, 2018	USA	Descriptive epidemiology; 2017	US Armed Forces; 464 heat stroke cases 1699 heat exhaustion cases	Women Heat stroke: 0.25† Other heat injuries: 1.38† Men Heat stroke: 0.41† Other heat injuries: 1.41†
Singer et al, 2018	USA	Retrospective cohort 1992 - 2012	SCT and non-SCT US Armed Forces SCT: 214 exertional heat illness cases Non-SCT: 577 exertional heat illness cases	Women Exertional heat illness: 13.89† Men Exertional heat illness: 14.79† Women Exertional heat illness: 13.14† Men Exertional heat illness: 7.79†

§ Proportions and incidences reported are of the total cases reported in the articles
Incidence rate reported per 100,000 person-years.
‡ Incidence rate per 100,000 person- months.
† Incidence rate reported per 1000 person-years.
* Other heat injuries include “heat exhaustion” and “unspecified effects of heat”.
‡ heat injuries include heat stroke and other heat injuries.
SCT = Sickle cell trait
US = United States of America; 2006 to date, heat injuries was reported in the US Armed Forces (Army, Navy, Air Force and Marine Corps).
UK = United Kingdom; USA = United States of America

Supplemental Table 3: Quality assessment of included studies using the quality assessment tool for studies with diverse designs (QATSDD)

QATSDD Criteria	1	2	3	4	5	6	7	8	9	10	11	12	Total score	% of total score
Dickinson' 94[23]	0	1	2	0	1	3	0	0	3	2	0	2	14/36	38.9
AMSA'95[31]	0	0	0	0	0	0	0	0	0	0	0	0	0/36	0
AMSA' 96[32]	0	0	0	0	0	0	0	0	0	0	0	0	0/36	0
AMSA'97[33]	0	0	0	0	0	0	0	0	0	0	0	0	0/36	0
AMSA'98[24]	2	1	1	0	0	0	0	0	2	2	0	0	8/36	22.2
AMSA'00[27]	2	1	2	0	0	1	0	0	2	3	0	0	11/36	30.6
AMSA'02[25]	3	0	2	0	1	1	0	0	2	0	2	0	11/36	30.6
AMSA'03[26]	2	1	1	0	1	1	0	0	2	2	0	0	10/36	27.8
Carter et al' 05[28]	3	3	3	2	2	3	1	2	3	3	2	0	27/36	75
AMSA'06[30]	2	1	1	0	1	1	0	0	2	2	0	0	10/36	27.8
Wallace et al' 06[46]	3	3	3	2	2	3	1	2	3	3	2	2	29/36	80.6
AMSA'07[34]	1	1	1	0	0	1	0	0	2	2	0	0	8/36	22.2
AMSA' 08[35]	1	1	1	0	0	1	0	0	2	2	0	0	8/36	22.2
AMSA' 09[36]	1	1	1	0	0	1	0	0	2	2	0	0	8/36	22.2
AMSA' 10[37]	1	1	2	0	0	1	0	0	2	2	0	2	11/36	30.6
AMSA' 11[38]	2	1	2	0	0	1	0	0	2	2	0	2	12/36	33.3
Druyan et al'12[15]	3	3	3	1	0	2	0	3	3	2	2	1	23/36	63.9
AMSA' 12[39]	2	1	2	0	0	1	0	0	2	2	0	2	12/36	33.3
AMSA' 13[40]	2	2	2	0	0	2	0	0	2	2	0	2	14/36	38.9
AMSA' 14[41]	2	2	2	0	0	2	0	0	2	3	0	2	15/36	41.7
AMSA' 15[42]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4
Bedno et al, 2015[29]	3	3	3	2	2	3	3	3	3	3	3	3	34/36	94.4
Kazman et al' 15[47]	3	3	3	2	2	3	2	3	3	3	3	3	33/36	91.7
AMSA' 16[43]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4
AMSA' 17[44]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4
AMSA' 18[45]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4
Singer et al,18[21]	3	3	3	3	3	3	2	3	3	3	3	3	35/36	97.2

QATSDD Criteria

- (1) Theoretical framework; (6) Procedure for data collection (11) Good justification for analytical method selected
(2) Aims/objectives; (7) Rationale for choice of data collection tool(s) (12) Strengths and limitations.
(3) Description of research setting (8) Detailed recruitment data
(4) Sample size; (9) Fit between research question and method of data collection (Quantitative only)
(5) Representative sample of target group (10) Fit between research question and method of analysis (Quantitative only)
QATSDD rating scale: 0=not at all; 1=very slightly; 2=moderately; 3=complete; AMSA = Army Medical Surveillance Activity



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6, supplementary file 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Figure 1
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8



PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8
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Page 1 of 2

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8, Supplementary file 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	15, 16
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10, 12, 14, Supplementary file 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9, 10, 11, 12, 13, 14
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	16
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	17, 18, 19
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	20, 21
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	21, 22
FUNDING			



PRISMA 2009 Checklist

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Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	22
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From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

Page 2 of 2

For peer review only

BMJ Open

Gender makes the difference in exertional heat illness in the armed forces: A systematic review and meta-analysis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-031825.R1
Article Type:	Original research
Date Submitted by the Author:	30-Aug-2019
Complete List of Authors:	Alele, Faith; James Cook University, College of Healthcare Sciences Malau-Aduli, Bunmi; James Cook University, College of Medicine and Dentistry Malau-Aduli, Aduli; James Cook University, College of Public Health, Medical and Veterinary Sciences Crowe, Melissa; James Cook University, Division of Tropical Health and Medicine
Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Sports and exercise medicine
Keywords:	OCCUPATIONAL & INDUSTRIAL MEDICINE, ACCIDENT & EMERGENCY MEDICINE, Heat Stroke, Armed Forces, Women

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3 1 **Gender makes the difference in exertional heat illness in the armed forces:**
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6 2 **A systematic review and meta-analysis**
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9 3 **Type of article:** Review
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58 35 Word count: 4723
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60 36

37 Abstract

38 **Objectives:** The aim of this review is to describe the epidemiology of all heat related illnesses
39 in women compared to men in the armed forces and to identify risk factors and gender
40 differences in heat illness and heat tolerance.

41 **Design:** Systematic review and meta-analysis.

42 **Data sources and eligibility criteria:** A search of multiple databases (MEDLINE, Emcare,
43 CINAHL, PsycINFO, Informit, and Scopus) was conducted from inception of the databases to
44 1 April 2019 for studies investigating and comparing heat illness and heat tolerance in women
45 and men in the armed forces.

46 **Results:** Twenty-seven (27) studies were included in the systematic review and 13 of these
47 studies were included in the meta-analysis. Meta-analysis of the 13 studies identified a 43%
48 decreased risk of heat stroke in women compared to men (risk ratio = 0.56, 95% CI 0.47 to
49 0.66). The overall risk of other heat illnesses (heat exhaustion and unspecified effects of heat
50 and light) was 26% higher in women compared to men (risk ratio = 1.26, 95% CI 1.15 to 1.38).
51 The factors significantly associated with heat illness were gender, age, level of education,
52 ethnicity, body mass index (BMI), positive sickle cell trait, being in service for less than 1 year,
53 and unit of service. Although there was a higher proportion of women who were heat intolerant
54 compared to men; this finding needs to be interpreted with caution due to the limited evidence.

55 **Conclusion:** In relation to armed forces personnel, the findings of this review suggest that men
56 experienced a higher risk of heat stroke than women. However, women have a greater risk of
57 other heat illnesses. Despite the limited evidence, further research is required to investigate the
58 influence of gender differences on heat intolerance and heat illness.

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3 60 **Article summary**
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6 61 **Strengths and limitations of this study**
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- 9 62 • This is the first known systematic review and meta-analysis investigating the impact of
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11 gender on exertional heat illness and heat tolerance in the armed forces.
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14 64 • We conducted a comprehensive search and identified potential risk factors that are
15
16 associated with exertional heat illness.
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19 66 • Most of the included studies utilized retrospective data with an increased likelihood of
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21 misclassification bias which may have underestimated or overestimated the association
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23 between heat-related illness and risk factors.
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26 69 **Trial registration** None
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29 70 **Key words**
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32 71 Heat stress; Heat stroke; Heat exhaustion; Heat tolerance; Women; Armed forces
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80 Introduction

81 Heat illnesses are disorders that arise after prolonged exposure to heat/humidity and/or
82 increased physical activity.[1] When body temperature rises, conduction, convection, radiation
83 and evaporation mechanisms help to cool the body and maintain normothermia.[1] However,
84 heat loss is susceptible to prevailing environmental conditions and type of clothing worn.
85 Without adequate cooling heat illnesses may occur including exercise-associated muscle
86 cramps (EAMC), heat syncope, heat exhaustion and heat stroke, a potentially life-threatening
87 disorder.[1]

88 Heat stroke is a medical emergency.[2] The condition is characterized by elevated core
89 temperature of 40°C and above, central nervous system disturbances and multi-organ damage
90 that may result in death.[2] Heat stroke has been classified as either classic or exertional.[3]
91 Classical heat stroke is insidious in onset and occurs in vulnerable populations such as young
92 children, the elderly and patients with chronic diseases.[4] On the other hand, exertional heat
93 stroke occurs more rapidly and affects apparently healthy, active people such as athletes,
94 factory workers, construction workers, agricultural workers, firefighters and military
95 recruits.[5] The workers in these industries often require high levels of physical exertion to
96 perform jobs and tasks. A combination of rigorous activities and extreme exposure to heat
97 places the workers at increased risk of heat stress and heat stroke.[6]

98 However, the ability to cope with heat stress varies between individuals.[2] Individuals who
99 are unable to cope with heat stress may be affected by heat exhaustion or heat stroke as a result
100 of a combination of factors including an elevation in body temperature, cardiovascular
101 insufficiency, hypotension and fatigue [7]. The inability to withstand heat stress during
102 exertion in hot environments is defined as heat intolerance.[2] Evidence in the published
103 literature suggests that heat intolerance may be as a direct result of heat stroke or due to

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3 104 predisposing inherent factors (genetics).[2] The Israeli Defence Force developed the heat
4
5 105 tolerance test in 1979 as an index of the ability of soldiers to cope with exertional heat.[8]
6
7
8 106 Individuals who have suffered heat stroke are sent for a heat tolerance test after a minimum
9
10 107 recovery period of 6 to 8 weeks as part of the return to duty process.[8] Criteria used to define
11
12 108 heat intolerance include an elevation in rectal temperature above 38.5°C and heart rate above
13
14
15 109 150 bpm or when rectal temperature or heart rate fail to stabilize during the test. The current
16
17 110 heat tolerance test criteria are based on previous studies by Shapiro et al.[9] which utilised only
18
19 111 male military participants.[8, 9] According to these studies, the heat tolerance test is a useful
20
21 112 tool to determine return to duty and to prevent subsequent exertional heat stroke. [8,9] Given
22
23
24 113 that heat stroke may be fatal; it is essential to identify individuals who are at high risk of
25
26 114 exertional heat illness. [8]

27
28
29 115 Globally, increasing numbers of women are joining the armed forces as inclusive approaches
30
31 116 to recruiting are adopted and more roles for women are created.[10] Women are required to
32
33 117 operate in austere environments with heat illnesses becoming more frequent.[10] This has
34
35
36 118 raised the question about gender differences in thermoregulation during heat stress.[10] During
37
38 119 prolonged heat exposure, the body's thermal inertia is determined by complex interactions
39
40 120 between morphological characteristics (body composition, body mass and surface area) and
41
42
43 121 heat load. Evidence suggests that women differ from men in thermal responses to heat.[11]
44
45 122 These difference may be because women have a lower rate of whole body evaporative heat
46
47 123 loss, higher body fat mass, body mass ratio,[12] number of sweat glands and lower aerobic
48
49
50 124 fitness.[13] In addition, hormonal variations due to menstrual cyclic patterns and the use of
51
52 125 contraceptive pills may all be associated with the differences in response to heat stress.[14]
53
54
55 126 Although these gender differences exist, they have not been considered when conducting the
56
57 127 heat tolerance test (HTT) for women who have had a heat stroke.[13] Furthermore, heat illness
58
59 128 can impact defence operational effectiveness and may result in acute loss of manpower and

1
2
3 129 possible medical discharge from service.[15] A previous review of the risk of heat illness in
4
5 130 women compared with men focused on the general population.[16] The findings of the review
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7
8 131 suggested that men are at increased risk of heat illness compared to women.[16] However, no
9
10 132 systematic review has investigated gender differences among armed forces personnel in
11
12 133 relation to heat illness. Given that heat intolerance may predispose to or accompany heat stroke,
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14
15 134 it is important to understand the role gender plays in heat intolerance.

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18 135 Therefore, the objective of this systematic review and meta-analysis was to provide a
19
20 136 comprehensive summary of the epidemiology of heat illness and heat intolerance in women
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22 137 and men in the armed forces.

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25 138 Specific aims were

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28 139 To determine the relative risk of heat illness in women compared to men in the armed
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30 140 forces and

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33 141 To identify predisposing risk factors associated with heat illness and heat tolerance in
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35 142 the armed forces

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41 144 **Methods**

45 145 **Search Strategy**

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47
48 146 This review utilised the Preferred Reporting Items for Systematic Review and Meta-analysis
49
50 147 (PRISMA) guidelines [17] and the MOOSE (Meta-analysis Of Observational Studies in
51
52 148 Epidemiology) checklist [18] to explore all literature published in English from inception of
53
54 149 the different databases to 1 April 2019. Databases searched included MEDLINE, CINAHL,
55
56 150 PsycINFO, Emcare, Informit and Scopus. A preliminary search was conducted in Medline,
57
58 151 Emcare and CINAHL to identify relevant key words contained in the titles, abstracts and
59
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2
3 152 subject descriptors. These search terms were used to conduct the search in other databases
4
5 153 without subject headings. The search strategy used in Medline is presented in supplemental
6
7
8 154 Table 1. No review protocol exists.
9

10 11 155 **Eligibility criteria**

12
13 156 Studies included in the review were assessed according to the following inclusion criteria: Peer-
14
15
16 157 reviewed literature comparing heat illness in women to men in the armed forces or reporting
17
18 158 heat tolerance in women and men of the armed forces. Exclusions included literature discussing
19
20 159 heat illness in other occupations, or studies where data on heat illness in women could not be
21
22
23 160 separated from men or studies reporting heat illness in men or literature reviews, conference
24
25 161 abstracts and grey literature. In addition, additional primary data sources were also identified
26
27 162 from the reference lists of the included studies using a hand-search technique (Figure 1).
28
29

30 31 163 **Selection of studies and data extraction**

32
33 164 FA and BMA identified all included studies and data extraction was performed using a standard
34
35 165 abstraction form. Data extracted from the studies included: study location and design,
36
37 166 population, proportion and incidence of heat illnesses, factors associated with heat illness and
38
39 167 heat tolerance, and heat tolerance in men and women. All authors cross-checked the extracted
40
41 168 data for consistency.
42
43
44

45 46 169 **Quality assessment**

47
48 170 The methodological quality assessment was assessed by FA in consultation with MC using the
49
50 171 modified quality assessment tool for studies with diverse designs (QATSDD) critical appraisal
51
52 172 tool.[19] Disagreement about any article was reviewed by BMA and AMA and discussed until
53
54 173 consensus was reached. The QATSDD tool is a 16-item tool which assesses the quality of
55
56 174 diverse studies (both quantitative and qualitative).[19] The tool was modified to exclude two
57
58 175 items relating to qualitative studies as well as two items relating to quantitative studies that
59
60

1
2
3 176 were not applicable to the studies included in the review. The items excluded were statistical
4
5 177 assessment of reliability and validity of measurement tool(s) (Quantitative only), fit between
6
7
8 178 stated research question and format and content of data collection tool e.g. interview schedule
9
10 179 (Qualitative), assessment of reliability of analytical process (Qualitative only) and evidence of
11
12 180 user involvement in design. Each criterion in the modified QATSDD tool was awarded a score
13
14
15 181 of 0 to 3 with 0 = not at all, 1 = very slightly, 2 = moderately and 3 = complete. The scores of
16
17 182 each criterion were summed to assess the methodological quality of included studies with a
18
19 183 maximum score of 36. The criteria included were (1) theoretical framework; (2) statement of
20
21 184 aims/objectives; (3) description of research setting; (4) evidence of sample size; (5)
22
23 185 representative sample of target group of a reasonable size, (6) description of procedure for data
24
25 186 collection; (7) rationale for choice of data collection tool(s); (8) detailed recruitment data; (9)
26
27 187 fit between research question and method of data collection (Quantitative only); (10) fit
28
29 188 between research question and method of analysis (Quantitative only); (11) good justification
30
31 189 for analytical method selected; and (12) strengths and limitations. For ease of interpretation,
32
33 190 the scores were converted to percentages and classified as low (<50%), medium (50-80%) or
34
35 191 high (>80%) quality of evidence.
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40 192 **Patient and public involvement**

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42
43 193 There was no public or patient involvement in this study.
44
45

46 194 **Data analysis and synthesis**

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49 195 In this review, the International Classification of Diseases ICD 9 or ICD 10 diagnosis codes
50
51 196 [20, 21] for the effects of heat and light were used to classify heat illnesses. All included studies
52
53 197 in the review utilized either the ICD 9 or ICD 10 codes to classify heat illnesses depending on
54
55 198 the year of publication. Heat illnesses were categorised as all heat illnesses, heat stroke and
56
57 199 other heat illnesses (including heat exhaustion and unspecified effects of heat and light). For
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2
3 200 this analysis, all heat illness was defined as cases where diagnosis of heat stroke (992.0, T67.0),
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5 201 heat exhaustion (992.3–5, T67.3 -5), heat syncope (992.1, T67.1), heat cramps (992.2, T67.2),
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7
8 202 heat fatigue, transient (992.6, T67.6), heat oedema (992.7, T67.7), other specified heat effects
9
10 203 (992.8, T67.8) and unspecified effects of heat and light (992.9, T67.9) were reported. Heat
11
12 204 stroke was identified and defined using the ICD diagnosis codes 992.0 (ICD 9) and T67.0 (ICD
13
14 205 10). While other heat illnesses were defined as heat exhaustion (992.3-5, T67 3-5) and
15
16 206 unspecified effects of heat and light (992.9 and T67.9). Incidence rates and proportions were
17
18 207 extracted from the data reported in each study and used for the analysis in this review. Studies
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20 208 reporting all heat illnesses and the risk factors associated with heat illnesses and heat tolerance
21
22 209 were not pooled due to variation in the study designs, populations, and measures reported.

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24
25
26 210 A meta-analysis was conducted to provide an overview of the risk of heat stroke and other heat
27
28 211 illnesses (heat exhaustion and unspecified effects of heat) in women compared to men in the
29
30 212 armed forces. A pooled analysis of the risk of heat stroke was conducted separately from other
31
32 213 heat illnesses. For other heat illnesses, a subgroup analysis was performed according to
33
34 214 classifications used in the included studies (1 – heat exhaustion and unspecified effects of heat
35
36 215 and light and 2 – heat exhaustion). The risk ratio for each study and the pooled risk ratios (RR)
37
38 216 with 95% CI were calculated using Review Manager 5.3.[22] The risk ratios were presented as
39
40 217 the ratio of the incident rates of heat illness in women to men. A random effects model was
41
42 218 used taking into account the heterogeneity of the included studies. I^2 was used to measure the
43
44 219 heterogeneity (between study variations) of the included studies. Where the percentage of
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46 220 variation between the included studies was greater than 50%, a sensitivity analysis was
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48 221 performed.

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225 **Results**

226 **Systematic review**

227 An initial search identified 3801 papers. After removing duplicates, screening titles and
228 abstracts, 47 papers remained for full text review with twenty-seven (27) included in the
229 systematic review (Figure 1). Twenty-five (25) of the reviewed articles originated from the
230 United States of America, while the other two studies were conducted in the United Kingdom
231 and Israel respectively (Supplemental Table 2). All included studies were conducted among
232 armed forces personnel, however, one study focused on armed force personnel with sickle cell
233 trait (SCT),[23] while another study included university staff and armed forces personnel in
234 the study.[24] Twenty- four (24) articles examined heat illnesses and injuries in women and
235 men. Eight (8) of these studies described all heat related illnesses in men and women,[23, 25-
236 31] while 16 studies included information on heat stroke and other heat injuries (including
237 “heat exhaustion” and “unspecified effects of heat”) in relation to both genders.[32-47] Six (6)
238 studies identified risk factors associated with heat stroke,[23, 27, 30, 31, 48, 49] and two studies
239 compared heat tolerance in men and women.[16, 49]

240 **Heat illnesses in women compared to men**

241 Table 1 shows the proportions and incidences of all heat-related illness in men and women in
242 the armed forces. Six (6) studies reported higher incidences and proportions of heat illness in
243 men compared to women[23, 25, 27, 28, 30, 31] while two studies reported higher incidences
244 of heat illness in women.[26, 29] Between 1995 and 1997, the mean proportion of all reported
245 heat stroke events in women was approximately 12% compared to 88% of heat stroke events
246 in men. Similarly, men reported a higher mean proportion of heat exhaustion (96%) compared
247 to women (4%).[33-35] Between 2006 and 2018, the average incidence rate of heat stroke in
248 women and men was 0.16/1000 person years and 0.29/ 1000 person years. The average
249 incidence of other heat illnesses (including heat exhaustion and unspecified effects of heat and

1
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3 250 light) was 1.84/1000 person years and 1.44/ 1000 person years for women and men
4
5 251 respectively.
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252 **Table 1: Proportion and incidence of heat related illnesses in women and men in the Armed Force**

Reference, year	Country	Study design	Study duration	Population	ICD codes	All heat injuries	
						Women	Men
Dickson. 1994[25]	UK	Descriptive epidemiology	1981-1991 (10yrs)	Royal Air force, Royal Navy and Army (1448 cases)	ICD-9-CM: 992.0 – 992.9	11.43*	41.87*
Army Medical Surveillance Activity, 1998[26]	USA	Descriptive epidemiology	1997 – 1998 (1 year)	US Army (1433 cases) 1997	ICD-9-CM: 992.0 – 992.9	12.8†	8.6†
			1998			15.8†	12.0†
Army Medical Surveillance Activity, 2000[29]	USA	Descriptive epidemiology	1997 – 1999 (2 years)	US Army and Marine Corps (3386 cases)	ICD-9-CM: 992.0 – 992.9		
				Army (1896 cases) Marine Corps (1104 cases)			2.0† 1.5† 4.4† 2.0†
Army Medical Surveillance Activity, 2002[27]	USA	Descriptive epidemiology	1990 – 1997 (7 years)	US Army (2290 cases)	ICD-9-CM: 992.0 – 992.9	14.0%§	86.0%§
		Case control	1998 – 2001 (3 years)	US Army (5021 cases and 10,042 controls)		20.7%§	79.3%§
Army Medical Surveillance Activity, 2003[28]	USA	Descriptive epidemiology	2002 (1 year)	US Army (1816 cases)	ICD-9-CM: 992.0 – 992.9	3.5†	5.1†
Carter et al, 2005[30]	USA	Cross-sectional	1980 – 2002 (22 years)	US Army (5246 cases)	ICD-9-CM: 992.0 – 992.9	13.7%§	86.3%§
Bedno et al, 2014[31]	USA	Analytical cross-sectional	2005 - 2006	US Armed forces (80 exertional heat illness cases) 9455 men 1913 women	ICD-9-CM: 992.0 – 992.9	0.680%	0.71%
Singer et al, 2018[23]	USA	Retrospective cohort	1992 - 2012	SCT and non-SCT US Armed forces	ICD-9-CM: 992.0 – 992.9		
				SCT: 214 exertional heat illness cases Non-SCT: 577 exertional heat illness cases			13.89† 14.79† 13.14† 7.79†

253 § Proportions and incidences reported are of the total cases reported in the articles

254 * Incidence rate reported per 100,000 person-years; † Incidence rate per 100,000 person- months; ‡ Incidence rate reported per 1000 person-years

255 UK = United Kingdom; USA = United States of America

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3 256 **Risk factors for heat illness and heat intolerance**
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6 257 As shown in Table 2, five (5) studies identified the risk factors associated with heat illness,[23,
7
8 258 27, 30, 31, 48] while one (1) study identified the predictors of heat intolerance.[49] Of the five
9
10 259 (5) studies reporting the risk factors associated with heat illness, one study identified the risk
11
12 260 for heat illness in association with SCT status.[23] The odds of females experiencing heat
13
14 261 illness ranged from 1.04 to 1.5 compared to males.[23, 27, 30, 31] Other identified risk factors
15
16 262 for heat illness (Table 2) included younger and older age,[23, 27] lower level of education,[27]
17
18 263 ethnicity,[27, 30] higher body mass index (BMI),[48] being SCT positive,[23] being in service
19
20 264 for less than 1 year,[27] and serving in combat units as an infantry or gun crew soldier.[27, 30]
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24 265 The factor that predicted heat intolerance was lower VO_{2max} .[49]
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278 **Table 2: Risk factors associated with heat illness and tolerance**

Reference, year	Country	Study design and duration	Study population	Risk factors	OR or IDR (95% CI)
Army Medical Surveillance Activity, 2002[27]	USA	Case-control 1998 – 2001 (3 years)	US Army 5021 cases and 10,042 controls	Female	1.5 (1.4 - 1.7)
				Age < 20 years	2.1 (1.4 - 3.1)
				Other ethnicity*	1.2 (1.0 - 1.4)
				Combat	1.5 (1.4 - 1.6)
				Lower level of education	2.0 (1.2 – 3.1)
Carter et al, 2005[30]	USA	Cross-sectional 1980 – 2002 (22 years)	US Army 5246 cases of heat illness; 4521 males and 725 females	Less than 1 year of service	2.3 (2.0 – 2.6)
				Female	1.21 (1.09 – 1.40)
				Infantry soldiers and gun crew men	2.69 (1.71 – 2.89)
				African and Hispanic ethnicity	0.76 (0.71 – 0.82)
Wallace et al, 2006[48]	USA	Case-control 1988 – 1996 (8 years)	US Marine Corps Male (627 cases and 1679 controls) Female (49 cases and 123 controls)	Northern state of origin	1.69 (1.42 – 1.90)
				BMI ≥ 26 kg/m ² (males)	2.10 (1.59 – 2.78)
				Run time ≥ 12.9 minutes (males)	5.61 (3.73 – 8.45)
Bedno et al, 2014[31]	USA	Analytical cross-sectional 2005 - 2006	US Armed forces 9455 men (67 exertional heat illness cases) 1913 women (13 exertional heat illness cases)	Run time ≥ 6.9 minutes (females)	5.30 (1.59 – 17.64)
				Female	1.04 (0.57 – 1.89)
Kazman et al, 2015[49]	USA	Analytical cross-sectional (Duration not stated)	Military and university community members 55 males and 20 females	VO _{2max}	0.9 (0.76 – 0.96)
Singer et al, 2018[23] †	USA	Retrospective cohort study	SCT and non-SCT US Armed forces SCT: 214 exertional heat illness cases Non-SCT: 577 exertional heat illness cases	Female	1.36 (1.17 – 1.50)
				SCT positive	1.24 (1.06 – 1.45)
				Age at enlistment: 30+ years	1.57 (1.07 – 2.33)
				Marines vs Army	1.51 (1.15 – 2.13)
				Occupation: Combat vs repair/engineer	1.57 (1.15 – 2.13)

279 *non- White, non-Black, non-Hispanic; OR = Odds ratio; IDR = Incidence density ratio; BMI= Body Mass Index; CI=Confidence Interval; USA = United States of America; † The risk factors
280 associated with EHI and SCT status

281 **Heat tolerance in women and men**

282 Two studies compared heat tolerance classification in males and females using the most
283 common test, the HTT developed by the Israeli Defence Force. [13, 49] Druyan et al.
284 investigated gender differences in Israeli Defence Force personnel who had sustained heat
285 injury. The study reported that 67% of the women were found to be heat intolerant compared
286 to 26% of their male counterparts.[13] In the study by Kazman et al. the study population
287 comprised of participants from the university and military communities. The findings of the
288 study reported that a greater proportion of women were classified as heat intolerant compared
289 to men (45% vs 18% respectively). [49] Although the mean physiological parameters for
290 women and men in both studies were below the test threshold (rectal temperature >38.5C and
291 HR >150 bpm); women had higher mean baseline temperature and mean heart rate (Table 3)
292 in both studies [13, 49]. In addition, the mean endpoint heart rates for women were higher
293 compared to their male counterparts.[13, 49] However, the mean end point temperature varied
294 between the two studies; one study reported a higher endpoint temperature for females
295 compared to males [13] and the other study reported similar endpoint temperatures for males
296 and females.[49]

297

298 **Table 3: Heat tolerance in women and men**

Reference, year	Country	Study design and duration	Study population	Parameters	Women	Men
Druyan et al, 2012[13]	Israel	Retrospective cross-sectional 2008 – 2010 (2 years)	170 males and 9 females	Heat intolerance rate	66.67%	25.79%
				<u>Physiological measurements (mean ± SD)</u>		
				Baseline T _{rec} (° C)	37.18 ± 0.09	37.07 ± 0.02
				Endpoint T _{rec} (° C)	38.14 ± 0.14	37.93 ± 0.03
				Baseline HR (bpm)	82.11 ± 4.88	73.94 ± 1.17
				Endpoint HR (bpm)	141.50 ± 7.84	126.44 ± 1.79
				Kazman et al, 2015[49]	USA	Analytical cross-sectional (duration not stated)
<u>Physiological measurements (mean ± SD)</u>						
Baseline T _{rec} (° C)	37.1 ± 0.4	36.9 ± 0.4				
Endpoint T _{rec} (° C)	38.1 ± 0.4	38.1 ± 0.4				
Baseline HR (bpm)	76 ± 15.0	68 ± 12.1				
Endpoint HR (bpm)	137 ± 20.1	122 ± 20.2				

299 HR = Heart rate; Bpm = beats per minute; T_{rec} = Rectal temperature; USA = United States of America

300 **Meta-analysis findings**

301 Of the 27 studies, 13 were included in the meta-analysis. The incidence rate data were extracted
302 from the included studies and pooled together to perform the meta-analysis (Supplemental
303 Table 3 and Supplemental Table 4).

304 **Risk of heat stroke in women and men in the armed forces**

305 In the pooled analysis, the risk ratio of heat stroke in women compared to men in the armed
306 forces was 0.56 (95% CI 0.47 to 0.66). There was no heterogeneity ($I^2 = 0\%$) in the studies
307 reporting heat stroke (Figure 2).

308 **Risk of other heat illnesses in women and men in the armed forces**

309 The overall pooled risk ratio of other heat illness was 1.26 (95% CI 1.15 to 1.38) in women
310 compared to men in the armed forces (Figure 3). The women to men risk ratio of studies
311 reporting heat exhaustion and unspecified effects of heat and light was 1.28 (95% CI 1.14, to
312 1.45). In studies reporting only heat exhaustion, the risk of heat exhaustion in women compared
313 to men was 1.22 (95% CI 1.06 to 1.42). The percentage of variance between the included studies
314 due to heterogeneity (I^2) was 53%; a sensitivity analysis was conducted where three of the
315 included studies with the largest rates: AMSA 2006, AMSA 2012, and AMSA 2013 [36, 42,
316 43] were excluded. The heterogeneity test was lower ($I^2 = 7\%$) after excluding the studies from
317 the pooled analysis (Supplemental Figure 1), however the effect did not change (pooled RR =
318 1.18, 95% CI 1.09 to 1.27).

319 **Assessment of methodological quality**

320 The QATSDD scores ranged from 0 to 97.2% (Supplemental Table 5). Only six studies scored
321 above 50% and included details about recruitment, data analysis, strengths and limitations of
322 the research. The other studies had lower scores because they lacked detailed justification for

1
2
3 323 the analytical methods, data collection, analysis, strengths and limitations. However, results of
4
5 324 the methodological assessment should be interpreted with caution. Although the tool assesses
6
7
8 325 methodological quality, it is more likely to be dependent on how the paper was written. In this
9
10 326 review, 80% of the studies included were military reports on heat-related illnesses in the Armed
11
12 327 forces. These reports were published in a peer-reviewed journal and were retrospective
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14 328 analyses of data collected by Defence Medical Surveillance Systems. These studies may not
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17 329 have reported details about data collection, strengths and limitations, but they presented valid
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19 330 information on heat-related illness.
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332 **Discussion**

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28 333 This systematic review and meta-analysis provide an overview on the available evidence on
29
30 334 epidemiology of heat illnesses and heat tolerance in women compared to men in the armed
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33 335 forces.
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336 **Summary of findings**

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39 337 The findings of this systematic review suggest a higher rate of all heat illnesses (defined as cases
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41 338 where a combined diagnosis of all heat illnesses was reported) in men compared to women as
42
43 339 evidenced by the outcomes reported in six (6) of eight (8) studies. The meta-analysis of 13
44
45 340 studies demonstrated that women had 44% less risk of heat stroke compared men in the armed
46
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48 341 forces. On the other hand, the overall pooled analysis revealed that women had 26% increase
49
50 342 in risk of other heat illnesses (heat exhaustion and unspecified heat illnesses) Risk factors found
51
52 343 to be associated with exertional heat illness include age, lower level of education, ethnicity,
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54 344 higher BMI, positive SCT, shorter duration of service, and service unit. The reported predictor
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56 345 of heat intolerance was lower VO_{2max} . However, the association between these factors and
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59 346 exertional heat illness and heat intolerance is weak given the small number of articles that

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3 347 investigated the relationship. Furthermore, despite the higher proportion of heat intolerance
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5 348 reported among women; this finding should be interpreted with caution given the small sample
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8 349 size for females in both studies and the differences in occupations of the women in the two
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10 350 studies. One study included women in the armed forces with a previous history of heat stroke,
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12 351 [13] while the other study recruited women from the general population as well as military
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15 352 members with no previous history of heat stroke. [49]

17 353 **Heat illnesses in women compared to men**

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20 354 The lower risk of heat stroke in women compared to men could possibly indicate that men can
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23 355 tolerate working in the heat beyond the endurance limits than women.[15] Conversely, the
24
25 356 women may not have ignored the early warning signs of heat illness and may have sought
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27 357 earlier treatment compared to men. This reinforces the presumption that women are more
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29
30 358 inclined to make use of health services and report ill health than men.[50] In addition, the
31
32 359 consultation rates of men were 30% lower than women, confirming the assumption that men
33
34 360 are less likely to consult and may present at a later stage with more severe forms of
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37 361 diseases.[50] Although, previously published literature have reported a higher rate of all types
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39 362 of heat illnesses in men in the general population (including some armed forces personnel)
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41 363 compared to women; heat stroke was not considered separately from other forms of heat
42
43 364 illnesses.[16]

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46 365 However, despite the lower risk of heat stroke, women had a greater risk of other heat illnesses
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48 366 (heat exhaustion and unspecified effects of heat and light) than men.[32, 36 – 47] The higher
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50 367 risk of other heat illnesses in women may likely be due to differences in physiological and
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53 368 physical characteristics between men and women.[51] Physiological characteristics such as
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56 369 hormones, use of contraceptive pills and lower evaporative heat loss may make women more
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58 370 susceptible to heat illness. [12, 14] Physical characteristics such as lower aerobic fitness and
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3 371 greater body fat are predictors of exertional heat illness.[51] Generally, men have less body fat
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5 372 and greater lean body mass compared to women. Furthermore, women have lower aerobic
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8 373 fitness levels and lower overall work capacity which may contribute to the increased risk of
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10 374 exertional heat illness.[51]
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13 375 **Risk factors for heat illness and heat intolerance**

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16 376 The risk factors for heat illness identified in the studies include higher BMI,[48] lower age,[23,
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18 377 27] lower level of education,[27] non-White, non-Black, non-Hispanic ethnic groups,[27] less
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20 378 than one year of service,[27] service unit.[27, 29] and positive SCT.[23] On the other hand,
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23 379 lower VO_{2max} , was identified as a predictor of heat intolerance.[49] Evidence suggest that
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25 380 individuals with higher BMI (indicating higher body fat) have been reported to be at increased
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27 381 risk of exertional heat illness and are less heat tolerant.[52] However, individuals with a low
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29 382 BMI may or may not be fit. Individuals with low aerobic fitness levels are likely to exert
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31 383 themselves beyond their physical limit and are at increased risk of heat illness.[53] During
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33 384 exercise, relative physiological strain is increased, peripheral blood flow decreases which in
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35 385 turn hinders thermoregulation and increasing the risk of heat illness.[53]
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40 386 The association between age, duration of service, occupational roles, level of education and
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42 387 heat illness may be explained by the level of aerobic fitness. Age as a risk factor varied in this
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44 388 review, with younger age and older age (at enlistment) considered as factors that increase the
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46 389 risk of heat illness.[23, 27] Evidence suggests that aerobic fitness decreases with older age,
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48 390 especially if older adults are sedentary.[54] However, aerobic fitness improves with regular
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50 391 physical exercise and the age related differences between younger and older adults are
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52 392 reversed.[55] The association between shorter duration in service and the increased risk of heat
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54 393 illness was inconclusive given that only one study investigated and reported its findings.
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56 394 However, the findings are in contrast to a previous study that reported that individuals with
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3 395 more years of service in the army had poorer physiological characteristics (lower aerobic
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5 396 capacity, lower maximum heart rate and higher percentage body fat).[56] These poorer
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8 397 physiological characteristics may place armed forces personnel at risk of heat illness.[52, 53]
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10 398 Furthermore, occupational roles such as serving as in Marine Corps and physically demanding
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12 399 jobs such as infantry, combat and gun crew had an increased risk of heat illness compared to
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14 400 personnel in administrative or support jobs. This may be associated with the rigorous and
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16 401 strenuous training requirements for these jobs.[31]

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20 402 Similarly, the association between lower level of education and heat illness may be due to
21
22 403 aerobic fitness. Research has identified educational attainment as a major predictor of health
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24 404 outcomes.[57] Education provides the opportunity for individuals to learn more about their
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26 405 health and to make healthy lifestyle choices. Individuals with a higher level of education are
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28 406 more likely to engage in healthy behaviours such as healthy diet and regular exercise.[57]
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30 407 Regular exercise is necessary to maintain and improve aerobic fitness.[58] High aerobic fitness
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32 408 may reduce the risk of exertional heat illness; however, some fit individuals may be at increased
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34 409 risk of heat illness because of their ethnic status. The effect of ethnicity on heat illness varied
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36 410 in this review. One study reported that minor ethnic groups (non-White, non-Black, non-
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38 411 Hispanic) were more susceptible to heat illness[27], while another study reported that
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40 412 Caucasians had an increased risk of heat illness compared to other ethnic groups.[30] The
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42 413 association between ethnicity and heat illness is not fully understood and other factors like
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44 414 acclimatisation and genetic adaptation may play a role in the differences between ethnic
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46 415 groups.[59]

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52 416 In addition, the role of genetics in heat illness was evident in the review with SCT positive
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54 417 armed force members at increased risk of exertional heat illness compared to SCT negative
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56 418 members.[23] SCT is an inherited blood disorder where an individual has a wild type
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58 419 haemoglobin A and haemoglobin S. Individuals with the SCT are considered heterozygous for

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3 420 the sickle cell mutation in the subunit beta gene of the haemoglobin.[60] Evidence has linked
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5 421 positive SCT with exercise related adverse health outcomes such as exertional heat illness
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7 422 (including exertional rhabdomyolysis, heat stroke and hyperthermia) in military personnel.[60]
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10 423 However, the biological pathway by which SCT is associated with heat illness is still
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12 424 unknown.[23] More in depth research is needed to elucidate the role of genetics in exertional
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15 425 heat illness.

16 17 18 426 **Heat tolerance in women and men**

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20 427 The risk of heat illness is dependent on thermal tolerance.[2] The HTT is conducted for
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22 428 members of the armed forces after a heat stroke event as part of the return to duty process.[8]
23
24 429 The test criteria defines heat intolerance as peak rectal temperature $> 38.5^{\circ}\text{C}$, peak heart rate
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26 430 > 150 bpm, or the inability of these values to reach a plateau.[8, 9] Although in the two studies,
27
28 431 a higher proportion of women were classified as heat intolerant; this evidence should be
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30 432 interpreted with caution given that the female populations included in each study varied with
31
32 433 respect to heat illness and occupations.[13, 49] However, both studies acknowledge that gender
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34 434 differences in thermoregulation may account for the higher intolerance rates in women.[13, 49]
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36 435 Furthermore, both studies reported using the Israeli Defence Force heat tolerance test protocol
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38 436 and given that the test protocol was developed using male participants, there may be a need to
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40 437 re-evaluate the criteria for women to reduce false positive results.[13, 49]

41 42 43 44 438 **Strengths and limitations**

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49 439 To the authors' current knowledge, this is the first known systematic review and meta-analysis
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51 440 investigating the impact of gender on exertional heat illness and heat tolerance in the armed
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53 441 forces. In addition, we identified potential risk factors that are associated with exertional heat
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55 442 illness. However, the heterogeneity in the study designs contributed to the variable
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57 443 methodological quality of the included studies. Most of the articles in this review were military
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3 444 reports and may not be considered of high methodological quality when assessed using a formal
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5 445 critical appraisal tool. In addition, most of the included studies utilized retrospective data as
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7 446 the data source with an increased likelihood of incompleteness and inaccuracy.
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9 447 Misclassification bias is likely to have been introduced into the studies. Three studies that
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11 448 explored the risk factors associated with heat-related illness used retrospective data. [27, 30,
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13 449 48] These retrospective data may have been misclassified or incomplete at the time of entry
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15 450 and may have introduced misclassification bias into the studies. This type of bias may
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17 451 underestimate or overestimate the association between heat-related illness and risk factors.
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19 452 Although the risk factors associated with heat illness were discussed; the review provided
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21 453 limited evidence of these factors, given the few numbers of studies that investigated the
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23 454 association. Furthermore, we included only studies published in English language; studies
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25 455 published in other languages were excluded.
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31 456 **Implication for policy and future research**

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34 457 This systematic review and meta-analysis demonstrate that there is limited research on
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36 458 exertional heat illness in women in the armed forces. Although men had a higher risk of heat
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38 459 stroke; women had a higher risk of other heat illnesses. This may be a reflection that women
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40 460 are more likely to report poorer health earlier than men.[50] Further research is needed to
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42 461 establish if this reflects physiological or behavioural differences. In addition , more research is
43
44 462 needed to understand the roles of underlying factors such as menstrual cycle phase, use of
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46 463 contraceptive pills and cardiovascular function in heat illness.[13, 49] Furthermore, the limited
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48 464 and inconclusive evidence suggests that more women were classified as heat intolerant
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50 465 compared to men using the Israeli Defence Force heat tolerance test protocol. The current
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52 466 criteria may be unfair to women given that it was developed using male participants. More
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54 467 research is needed to determine the gender differences in heat tolerance as well as to consider
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3 468 re-evaluating the heat tolerance test protocol or the development of a new protocol that
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5 469 considers gender specific factors.[13]
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8 470 **Conclusion**

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11 471 In conclusion, this review shows that men had a higher risk of heat stroke but women in the
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13 472 armed forces had a greater risk of other heat illness. Despite the limited evidence, further
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15 473 research is required to investigate the influence of gender differences on heat tolerance and
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17 474 heat illness. Further research is needed to evaluate the heat tolerance test protocol for women.
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23 24 476 **Authors' contribution**

25
26 477 All authors contributed substantially to the study concept, design, data extraction, quality assessment
27
28 478 and writing of the manuscript.

29 479 **Conceptualization and design:** FOA, BSMA, AEMA and MC

30 480 **Methodology:** FOA, BSMA, AEMA and MC

31 481 **Writing - Original draft:** FOA

32 482 **Writing – critical review & editing:** FOA, BSMA, AEMA and MC

33 483 All authors read and approved the manuscript for submission.

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35
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37 486 **Competing Interests:** The authors declare that they have no competing interests.

38 487 **Patient consent for publication:** Not required

39 488 **Data sharing statement:** There are no additional or unpublished data available.

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632 **Figure legends**

633 Figure 1: PRISMA flow chart of the study selection protocol

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3 634 Figure 2: Forest plot of studies investigating the risk of heat stroke in women compared to men
4 635 in the armed forces. Incidence data were extracted from tables provided in the original articles.
5
6 636 M-H = Mantel-Haenszel; CI = confidence interval.

7
8 637 Figure 3: Forest plot of studies investigating the risk of heat exhaustion and unspecified effect
9 638 of heat and light (1.1.1) and heat exhaustion (1.1.2) in women compared to men in the armed
10 639 forces. Incidence data were extracted from tables provided in the original articles. M-H =
11 640 Mantel-Haenszel; CI = confidence interval.

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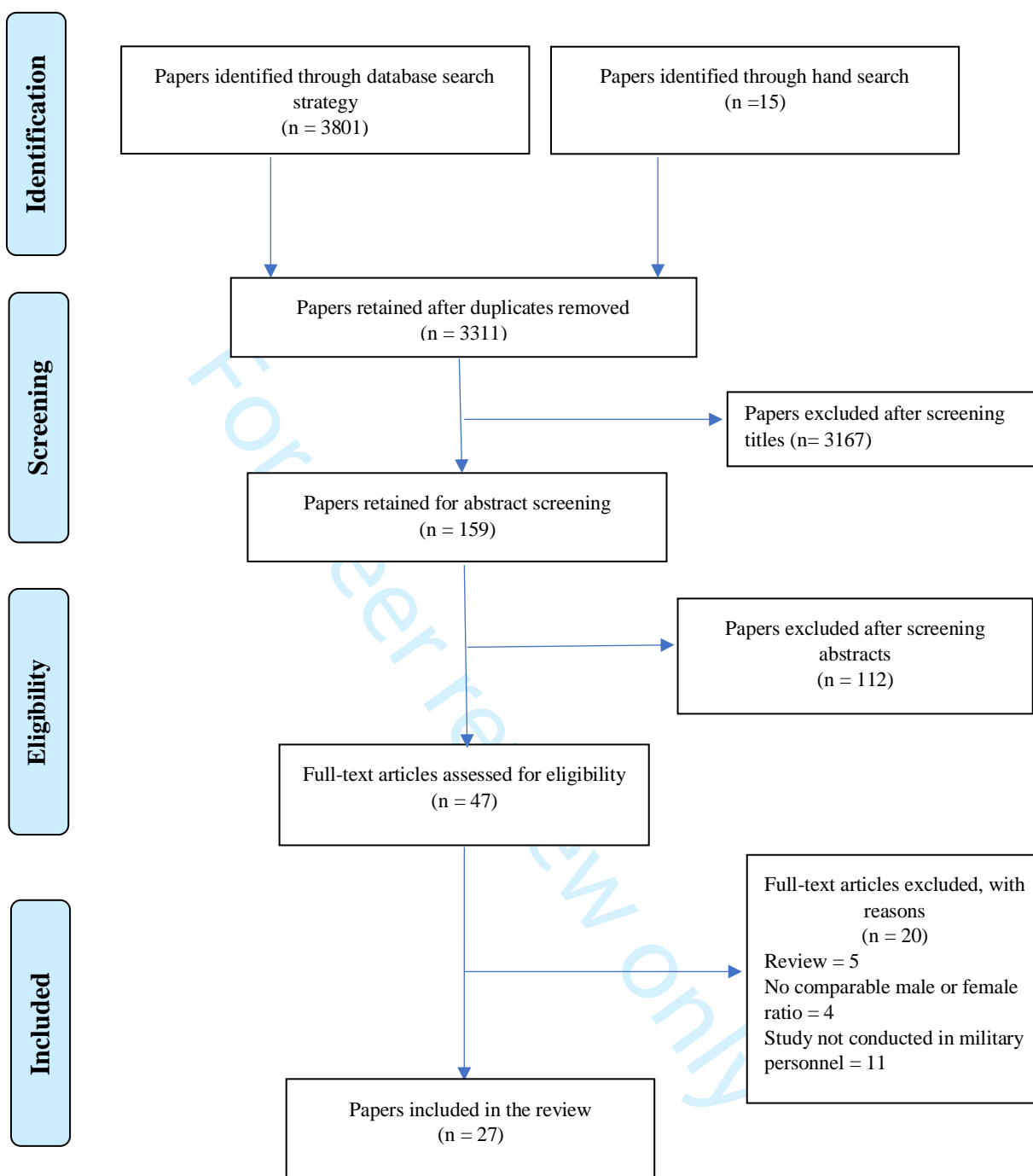


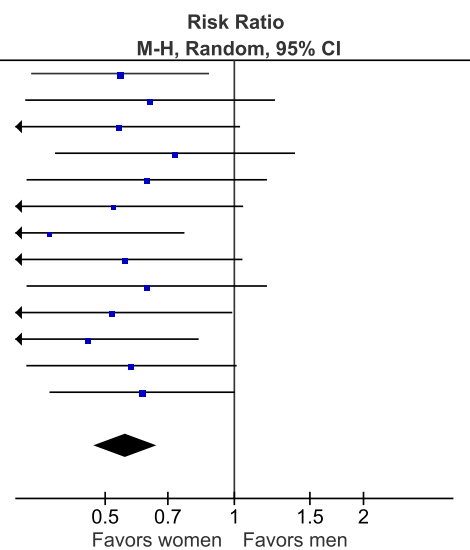
Figure 1: PRISMA flow chart of the study selection protocol

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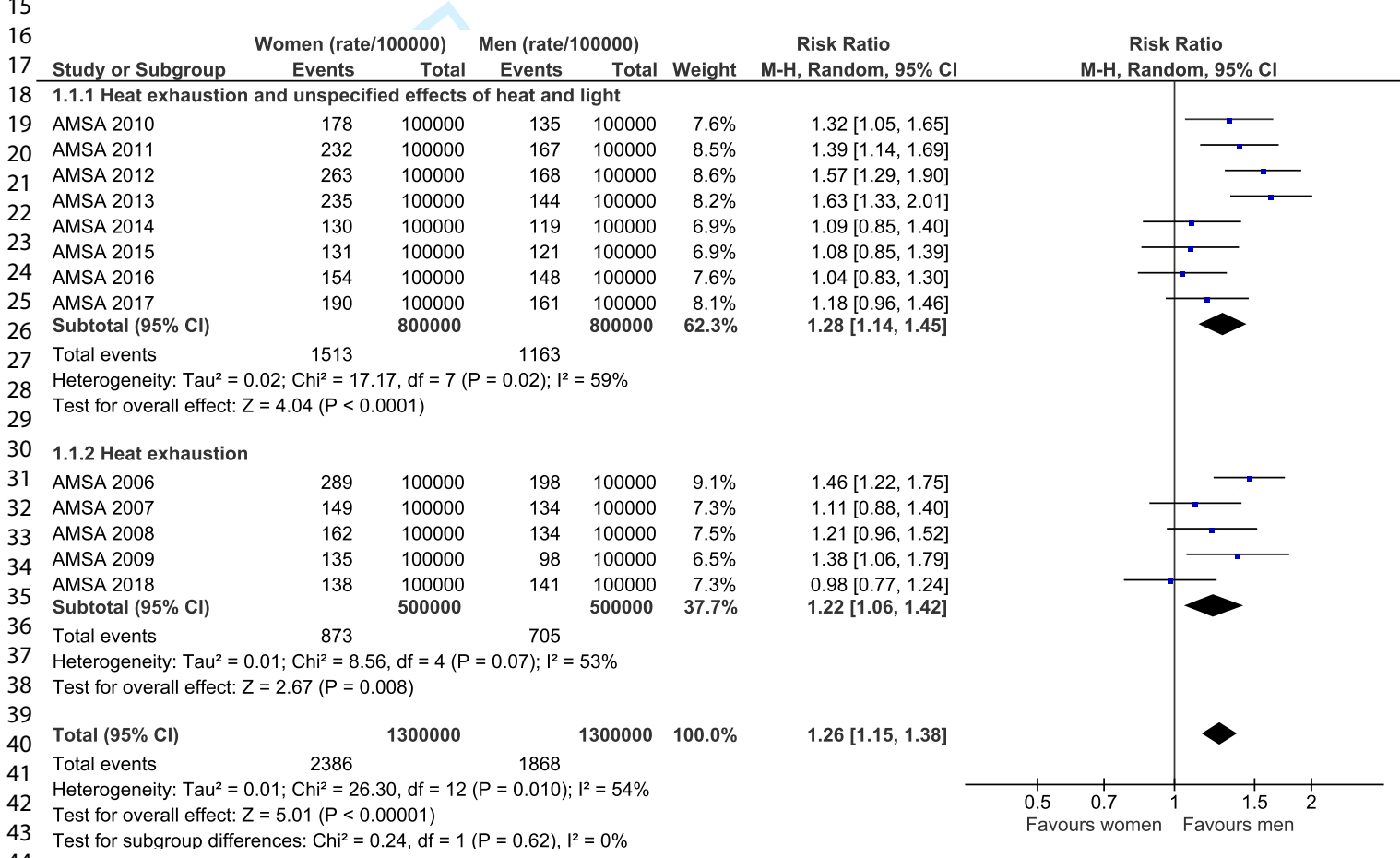
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Study or Subgroup	Women (rate/100000)		Men (rate/100000)		Weight	Risk Ratio		Risk Ratio	
	Events	Total	Events	Total		M-H, Random, 95% CI	Year	M-H, Random, 95% CI	
AMSA 2006	26	100000	48	100000	12.5%	0.54 [0.34, 0.87]	2006		
AMSA 2007	14	100000	22	100000	6.3%	0.64 [0.33, 1.24]	2007		
AMSA 2008	14	100000	26	100000	6.7%	0.54 [0.28, 1.03]	2008	←	
AMSA 2009	16	100000	22	100000	6.9%	0.73 [0.38, 1.38]	2009		
AMSA 2010	15	100000	24	100000	6.8%	0.63 [0.33, 1.19]	2010		
AMSA 2011	12	100000	23	100000	5.8%	0.52 [0.26, 1.05]	2011	←	
AMSA 2012	10	100000	27	100000	5.4%	0.37 [0.18, 0.77]	2012	←	
AMSA 2013	15	100000	27	100000	7.2%	0.56 [0.30, 1.04]	2013	←	
AMSA 2014	15	100000	24	100000	6.8%	0.63 [0.33, 1.19]	2014		
AMSA 2015	14	100000	27	100000	6.8%	0.52 [0.27, 0.99]	2015	←	
AMSA 2016	16	100000	35	100000	8.1%	0.46 [0.25, 0.83]	2016	←	
AMSA 2017	19	100000	33	100000	8.9%	0.58 [0.33, 1.01]	2017		
AMSA 2018	25	100000	41	100000	11.5%	0.61 [0.37, 1.00]	2018		
Total (95% CI)		1300000		1300000	100.0%	0.56 [0.47, 0.66]			
Total events	211		379						

Heterogeneity: Tau² = 0.00; Chi² = 2.95, df = 12 (P = 1.00); I² = 0%
 Test for overall effect: Z = 6.76 (P < 0.00001)



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Supplemental Table 1

Medline search strategy	
1.	Women (MeSH)
2.	Gender expression
3.	Gender identity (MeSH)
4.	Gender
5.	Wom\$
6.	Sex
7.	Heat strok*
8.	Heatstrok*
9.	Heat collapse
10.	Heat exhaustion
11.	Heat prostration
12.	Heat cramp
13.	Heat cramps
14.	Heat stress disorder
15.	Heat stress disorders (MeSH)
16.	Thermal stress
17.	Heat illness
18.	Heat illnesses
19.	Heat injury
20.	Heat injuries
21.	Heat related diseases
22.	Heat disorder
23.	Heat disorders
24.	Heat related disorder
25.	Heat related disorders
26.	Heat related illness
27.	Heat related illnesses
28.	Heat related injuries
29.	Heat related injury
30.	Environmental heat illness
31.	Heat stress
32.	Heat adaptation
33.	Heat tolerance
34.	Heat tolerances
35.	Heat resistance
36.	Thermal resistance
37.	Thermoresistance
38.	Thermotolerance (MeSH)
39.	Heat endurance
40.	1 OR 2 OR 3 OR 4 OR 5 OR 6
41.	7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39
42.	40 AND 41

Supplemental Table 2
Summary of all included studies

Reference, year	Country	Study design and duration	Population	Study findings [§]
Dickson. G, 1994	UK	Descriptive epidemiology 1981-1991	Royal Airforce, Royal Navy and Army; 1448 all heat injuries cases [†]	Women All heat injuries: 11.43 [#] Men All heat injuries: 41.87 [#]
Army Medical Surveillance Activity, 1995	USA	Descriptive epidemiology; 1994	US Army; 23 heat stroke cases 12 heat exhaustion cases	Women Heat stroke: 13% Heat exhaustion: 0% Men Heat stroke: 87% Heat exhaustion: 100%
Army Medical Surveillance Activity, 1996	USA	Descriptive epidemiology; 1995	US Army; 81 heat stroke cases 39 heat exhaustion cases	Women Heat stroke: 17.3% Heat exhaustion: 7.7% Men Heat stroke: 82.7% Heat exhaustion: 92.3%
Army Medical Surveillance Activity, 1997	USA	Descriptive epidemiology; 1996	US Army; 45 heat stroke cases 24 heat exhaustion cases	Women Heat stroke: 4.4% Heat exhaustion: 4.2% Men Heat stroke: 95.6% Heat exhaustion: 95.8%
Army Medical Surveillance Activity, 1998	USA	Descriptive epidemiology; 1997 - 1998	US Army; 1433 all heat injuries cases (1997-1998) [†] 1997 1998	Women All heat injuries: 12.8 [‡] Men All heat injuries: 8.6 [‡] Women All heat injuries: 15.8 [‡] Men All heat injuries: 12.0 [‡]

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Army Medical Surveillance Activity, 2000	USA	Descriptive epidemiology; 1997 - 1999	US Army and Marine Corps; 3386 all heat injuries cases [†] Army (1896 cases) Marine Corps (1104 cases)	Women All heat injuries: 2.0 [†] Men All heat injuries: 1.5 [†] Women All heat injuries: 4.4 [†] Men All heat injuries: 2.0 [†]
Army Medical Surveillance Activity, 2002	USA	Descriptive epidemiology 1990 - 1997	US Army; 2290 all heat injuries cases [†]	Women All heat injuries: 14.0% Men All heat injuries: 86.0%
		Case – control 1998 - 2001	US Army; 5021 cases and 10,042 controls (all heat injuries) [†]	Women All heat injuries: 20.7% Men All heat injuries: 79.3% Risk factors Female: OR; 1.5 (1.4 - 1.7) Age < 20 years: OR; 2.1 (1.4 - 3.1) Other ethnicity*: OR; 1.2 (1.0 -1.4) Combat: OR; 1.5 (1.4 - 1.6) Lower level of education: OR; 2.0 (1.2 – 3.1) Less than 1 year of service: OR; 2.3 (2.0 – 2.6)
Army Medical Surveillance Activity, 2003	USA	Descriptive epidemiology; 2002	US Army; 1816 all heat injuries cases [†]	Women All heat injuries: 3.5 [†] Men All heat injuries: 5.1 [†]
Carter et al, 2005	USA	Cross-sectional 1980 - 2002	US Army; 5246 all heat injuries cases [†] 4521 males and 725 females	Women All heat injuries: 13.7% Men All heat injuries: 86.3% Risk factors

				Female: IDR: 1.21 (1.09 – 1.40) Infantry soldiers and gun crew men: IDR; 2.69 (1.71 – 2.89) African and Hispanic ethnicity: IDR; 0.76 (0.71 – 0.82) Northern state of origin: IDR; 1.69 (1.42 – 1.90)
7	Army Medical Surveillance Activity, 2006	USA	Descriptive epidemiology; 2005	US Armed Forces; 204 heat stroke cases 958 heat exhaustion cases
8				Women Heat stroke: 0.26† Heat exhaustion: 2.89†
9				Men Heat stroke: 0.48† Heat exhaustion: 1.98†
13	Wallace et al, 2005	USA	Case-control 1988 - 1996	US Army; 5246 cases of heat illness; 4521 males and 725 females
14				Risk factors Females Run time ≥ 6.9 minutes: OR; 5.30 (1.59 – 17.64)
15				Males Run time ≥ 12.9 minutes: OR; 5.61 (3.73 – 8.45)
16				BMI ≥ 26 kg/m ² : OR; 2.10 (1.59 – 2.78)
23	Army Medical Surveillance Activity, 2007	USA	Descriptive epidemiology; 2006	US Armed Forces; 259 heat stroke cases 1854 heat exhaustion cases
24				Women Heat stroke: 0.14† Heat exhaustion: 1.49†
25				Men Heat stroke: 0.22† Heat exhaustion: 1.34†
29	Army Medical Surveillance Activity, 2008	USA	Descriptive epidemiology; 2007	US Armed Forces; 329 heat stroke cases 1853 heat exhaustion cases
30				Women Heat stroke: 0.14† Heat exhaustion: 1.62†
31				Men Heat stroke: 0.26† Heat exhaustion: 1.34†
35	Army Medical Surveillance Activity, 2009	USA	Descriptive epidemiology; 2008	US Armed Forces; 299 heat stroke cases 1467 heat exhaustion cases
36				Women Heat stroke: 0.16† Heat exhaustion: 1.35†
37				Men Heat stroke: 0.22† Heat exhaustion: 0.98†

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Army Medical Surveillance Activity, 2010	USA	Descriptive epidemiology; 2009	US Armed Forces; 323 heat stroke cases 2038 other heat injuries cases*	Women Heat stroke: 0.15† Other heat injuries: 1.78† Men Heat stroke: 0.22† Other heat injuries: 1.35†
Army Medical Surveillance Activity, 2011	USA	Descriptive epidemiology; 2010	US Armed Forces; 311 heat stroke cases 2576 other heat injuries cases*	Women Heat stroke: 0.12† Other heat injuries: 2.32† Men Heat stroke: 0.23† Other heat injuries: 1.67†
Army Medical Surveillance Activity, 2012	USA	Descriptive epidemiology; 2011	US Armed Forces; 362 heat stroke cases 2652 other heat injuries cases*	Women Heat stroke: 0.10† Other heat injuries: 2.63† Men Heat stroke: 0.27† Other heat injuries: 1.68†
Druyan et al, 2012	Israael	Retrospective cross-sectional 2008 – 2010	Israeli Defence Forces; 170 males and 9 females	Heat tolerance parameters Women Heat intolerance rate: 66.6% Baseline Trec (° C): 37.18 ± 0.09 Endpoint Trec (° C): 38.14 ± 0.14 Baseline HR (bpm): 82.11 ± 4.88 Endpoint HR (bpm): 141.50 ± 7.84 Men Heat intolerance rate: 25.79% Baseline Trec (° C): 37.07 ± 0.02 Endpoint Trec (° C): 37.93 ± 0.03 Baseline HR (bpm): 73.94 ± 1.17 Endpoint HR (bpm): 126.50 ± 1.79
Army Medical Surveillance Activity, 2013	USA	Descriptive epidemiology; 2012	US Armed Forces; 365 heat stroke cases 2257 other heat injuries cases*	Women Heat stroke: 0.15† Other heat injuries: 2.35† Men Heat stroke: 0.27† Other heat injuries: 1.44†

1 2 3 4 5 6 7 8	Army Medical Surveillance Activity, 2014	USA	Descriptive epidemiology; 2013	US Armed Forces; 324 heat stroke cases 1701 other heat injuries cases*	<u>Women</u> Heat stroke: 0.15† Other heat injuries: 1.30† <u>Men</u> Heat stroke: 0.24† Other heat injuries: 1.19†
9 10 11 12	Bedno et al, 2014	USA	Analytical cross-sectional	US Armed Forces; 80 exertional heat illness cases	<u>Women</u> Heat illness: 0.680% <u>Men</u> Heat illness: 0.71%
13 14 15 16 17 18	Army Medical Surveillance Activity, 2015	USA	Descriptive epidemiology; 2014	US Armed Forces; 314 heat stroke cases 1410 other heat injuries cases*	<u>Women</u> Heat stroke: 0.14† Other heat injuries: 1.31† <u>Men</u> Heat stroke: 0.27† Other heat injuries: 1.21†
19 20 21 22 23 24 25 26 27 28 29 30 31 32 33	Kazman et al, 2015	USA	Analytical cross-sectional	Military and university community members; 55 males and 20 females	<u>Heat tolerance parameters</u> <u>Women</u> Heat intolerance rate: 45% Baseline Trec (° C): 37.1 ± 0.4 Endpoint Trec (° C): 38.1 ± 0.4 Baseline HR (bpm): 76 ± 15.0 Endpoint HR (bpm): 137 ± 20.1 <u>Men</u> Heat intolerance rate: 18% Baseline Trec (° C): 36.9 ± 0.4 Endpoint Trec (° C): 38.1 ± 0.4 Baseline HR (bpm): 68 ± 12.1 Endpoint HR (bpm): 122 ± 20.2 <u>Risk factors</u> Female: OR; 3.68 (1.21 – 11.24) VO _{2max} : OR; 0.9 (0.76 – 0.96)
34 35 36 37 38 39 40 41 42 43 44 45 46	Army Medical Surveillance Activity, 2016	USA	Descriptive epidemiology; 2015	US Armed Forces; 417 heat stroke cases 1625 other heat injuries cases*	<u>Women</u> Heat stroke: 0.16† Other heat injuries: 1.54† <u>Men</u> Heat stroke: 0.35† Other heat injuries: 1.48†

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Army Medical Surveillance Activity, 2017	USA	Descriptive epidemiology; 2016	US Armed Forces; 401 heat stroke cases 2135 other heat injuries cases*	Women Heat stroke: 0.19† Other heat injuries: 1.90† Men Heat stroke: 0.33† Other heat injuries: 1.61†
Army Medical Surveillance Activity, 2018	USA	Descriptive epidemiology; 2017	US Armed Forces; 464 heat stroke cases 1699 heat exhaustion cases	Women Heat stroke: 0.25† Other heat injuries: 1.38† Men Heat stroke: 0.41† Other heat injuries: 1.41†
Singer et al, 2018	USA	Retrospective cohort 1992 - 2012	SCT and non-SCT US Armed Forces SCT: 214 exertional heat illness cases Non-SCT: 577 exertional heat illness cases	Women Exertional heat illness: 13.89† Men Exertional heat illness: 14.79† Women Exertional heat illness: 13.14† Men Exertional heat illness: 7.79†

§ Proportions and incidences reported are of the total cases reported in the articles
Incidence rate reported per 100,000 person-years.
‡ Incidence rate per 100,000 person- months.
† Incidence rate reported per 1000 person-years.
* Other heat injuries include “heat exhaustion” and “unspecified effects of heat”.
‡ heat injuries include heat stroke and other heat injuries.
SCT = Sickle cell trait
US = United States of America; 2006 to date, heat injuries was reported in the US Armed Forces (Army, Navy, Air Force and Marine Corps).
UK = United Kingdom; USA = United States of America

Supplemental Table 3: Incidence rates of Heat stroke in women compared to men in the Armed Forces

Reference, year	Country	Study design	Study duration	Population	ICD codes	Heat stroke	
						Women	Men
Army Medical Surveillance Activity, 2006	USA	Descriptive epidemiology;	2005 (1 year)	US Armed Forces; 204 heat stroke cases	ICD-9-CM: 992.0	0.26	0.48
Army Medical Surveillance Activity, 2007	USA	Descriptive epidemiology;	2006 (1 year)	US Armed Forces; 259 heat stroke cases	ICD-9-CM: 992.0	0.14	0.22
Army Medical Surveillance Activity, 2008	USA	Descriptive epidemiology;	2007 (1 year)	US Armed Forces; 329 heat stroke cases	ICD-9-CM: 992.0	0.14	0.26
Army Medical Surveillance Activity, 2009	USA	Descriptive epidemiology;	2008 (1 year)	US Armed Forces; 299 heat stroke cases	ICD-9-CM: 992.0	0.16	0.22
Army Medical Surveillance Activity, 2010	USA	Descriptive epidemiology;	2009 (1 year)	US Armed Forces; 323 heat stroke cases	ICD-9-CM: 992.0	0.15	0.24
Army Medical Surveillance Activity, 2011	USA	Descriptive epidemiology;	2010 (1 year)	US Armed Forces; 311 heat stroke cases	ICD-9-CM: 992.0	0.12	0.23
Army Medical Surveillance Activity, 2012	USA	Descriptive epidemiology;	2011 (1 year)	US Armed Forces; 362 heat stroke cases	ICD-9-CM: 992.0	0.10	0.27
Army Medical Surveillance Activity, 2013	USA	Descriptive epidemiology;	2012 (1 year)	US Armed Forces; 365 heat stroke cases	ICD-9-CM: 992.0	0.15	0.27
Army Medical Surveillance Activity, 2014	USA	Descriptive epidemiology; 2013	2013 (1 year)	US Armed Forces; 324 heat stroke cases	ICD-9-CM: 992.0	0.15	0.24
Army Medical Surveillance Activity, 2015	USA	Descriptive epidemiology;	2014 (1 year)	US Armed Forces; 314 heat stroke cases	ICD-9-CM: 992.0	0.14	0.27
Army Medical Surveillance Activity, 2016	USA	Descriptive epidemiology;	2015 (1 year)	US Armed Forces; 417 heat stroke cases	ICD-9-CM: 992.0 ICD 10: T67.0	0.16	0.35

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Army Medical Surveillance Activity, 2017	USA	Descriptive epidemiology;	2016 (1 year)	US Armed Forces; 401 heat stroke cases	ICD-9-CM: 992.0 ICD 10: T67.0	0.19	0.33
Army Medical Surveillance Activity, 2018	USA	Descriptive epidemiology;	2017 (1 year)	US Armed Forces; 464 heat stroke cases 1699 heat exhaustion cases	ICD-9-CM: 992.0 ICD 10: T67.0	0.25	0.41

For peer review only

Supplemental Table 4: Incidence rates of other heat injuries (heat exhaustion and unspecified effects of heat and light) in women compared to men in the Armed Forces

Reference, year	Country	Study design	Study duration	Population	ICD codes	Other heat injuries	
						Women	Men
Army Medical Surveillance Activity, 2006	USA	Descriptive epidemiology;	2005 (1 year)	US Armed Forces; 958 heat exhaustion cases	ICD-9-CM: 992.3 – 992.5	2.89	1.98
Army Medical Surveillance Activity, 2007	USA	Descriptive epidemiology;	2006 (1 year)	US Armed Forces; 1854 heat exhaustion cases	ICD-9-CM: 992.3 – 992.5	1.49	1.34
Army Medical Surveillance Activity, 2008	USA	Descriptive epidemiology;	2007 (1 year)	US Armed Forces; 1853 heat exhaustion cases	ICD-9-CM: 992.3 – 992.5	1.62	1.34
Army Medical Surveillance Activity, 2009	USA	Descriptive epidemiology;	2008 (1 year)	US Armed Forces; 1467 heat exhaustion cases	ICD-9-CM: 992.3 – 992.5	1.35	0.98
Army Medical Surveillance Activity, 2010	USA	Descriptive epidemiology;	2009 (1 year)	US Armed Forces; 2038 other heat injuries cases*	ICD-9-CM: 992.3 – 992.5; 992.9	1.78	1.35
Army Medical Surveillance Activity, 2011	USA	Descriptive epidemiology;	2010 (1 year)	US Armed Forces; 2576 other heat injuries cases*	ICD-9-CM: 992.3 – 992.5; 992.9	2.32	1.67
Army Medical Surveillance Activity, 2012	USA	Descriptive epidemiology;	2011 (1 year)	US Armed Forces; 2652 other heat injuries cases*	ICD-9-CM: 992.3 – 5; 992.9	2.63	1.68
Army Medical Surveillance Activity, 2013	USA	Descriptive epidemiology;	2012 (1 year)	US Armed Forces; 2257 other heat injuries cases*	ICD-9-CM: 992.3 – 992.5; 992.9	2.35	1.44
Army Medical Surveillance Activity, 2014	USA	Descriptive epidemiology;	2013 (1 year)	US Armed Forces; 1701 other heat injuries cases*	ICD-9-CM: 992.3 – 992.5; 992.9	1.30	1.19
Army Medical Surveillance Activity, 2015	USA	Descriptive epidemiology;	2014 (1 year)	US Armed Forces; 1410 other heat injuries cases*	ICD-9-CM: 992.3 – 992.5; 992.9	1.31	1.21

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For peer review only

Army Medical Surveillance Activity, 2016	USA	Descriptive epidemiology;	2015 (1 year)	US Armed Forces; 1625 other heat injuries cases*	ICD-9-CM: 992.3 – 992.5; 992.9 ICD 10: T67.3 – T67.5; T67.9	1.54	1.48
Army Medical Surveillance Activity, 2017	USA	Descriptive epidemiology;	2016 (1 year)	US Armed Forces; 2135 other heat injuries cases*	ICD-9-CM: 992.3 – 992.5; 992.9 ICD 10: T67.3 – T67.5; T67.9	1.90	1.61
Army Medical Surveillance Activity, 2018	USA	Descriptive epidemiology;	2017 (1 year)	US Armed Forces; 1699 heat exhaustion cases	ICD-9-CM: 992.3 – 992.5 ICD 10: T67.3 – T67.5	1.38	1.41

Supplemental Table 3: Quality assessment of included studies using the quality assessment tool for studies with diverse designs (QATSDD)

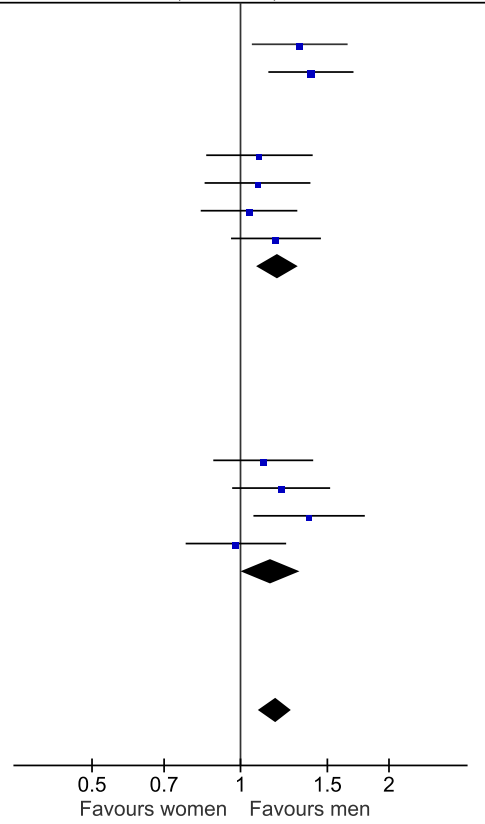
QATSDD Criteria	1	2	3	4	5	6	7	8	9	10	11	12	Total score	% of total score
Dickinson' 94[23]	0	1	2	0	1	3	0	0	3	2	0	2	14/36	38.9
AMSA'95[31]	0	0	0	0	0	0	0	0	0	0	0	0	0/36	0
AMSA' 96[32]	0	0	0	0	0	0	0	0	0	0	0	0	0/36	0
AMSA'97[33]	0	0	0	0	0	0	0	0	0	0	0	0	0/36	0
AMSA'98[24]	2	1	1	0	0	0	0	0	2	2	0	0	8/36	22.2
AMSA'00[27]	2	1	2	0	0	1	0	0	2	3	0	0	11/36	30.6
AMSA'02[25]	3	0	2	0	1	1	0	0	2	0	2	0	11/36	30.6
AMSA'03[26]	2	1	1	0	1	1	0	0	2	2	0	0	10/36	27.8
Carter et al' 05[28]	3	3	3	2	2	3	1	2	3	3	2	0	27/36	75
AMSA'06[30]	2	1	1	0	1	1	0	0	2	2	0	0	10/36	27.8
Wallace et al' 06[46]	3	3	3	2	2	3	1	2	3	3	2	2	29/36	80.6
AMSA'07[34]	1	1	1	0	0	1	0	0	2	2	0	0	8/36	22.2
AMSA' 08[35]	1	1	1	0	0	1	0	0	2	2	0	0	8/36	22.2
AMSA' 09[36]	1	1	1	0	0	1	0	0	2	2	0	0	8/36	22.2
AMSA' 10[37]	1	1	2	0	0	1	0	0	2	2	0	2	11/36	30.6
AMSA' 11[38]	2	1	2	0	0	1	0	0	2	2	0	2	12/36	33.3
Druyan et al'12[15]	3	3	3	1	0	2	0	3	3	2	2	1	23/36	63.9
AMSA' 12[39]	2	1	2	0	0	1	0	0	2	2	0	2	12/36	33.3
AMSA' 13[40]	2	2	2	0	0	2	0	0	2	2	0	2	14/36	38.9
AMSA' 14[41]	2	2	2	0	0	2	0	0	2	3	0	2	15/36	41.7
AMSA' 15[42]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4
Bedno et al, 2015[29]	3	3	3	2	2	3	3	3	3	3	3	3	34/36	94.4
Kazman et al' 15[47]	3	3	3	2	2	3	2	3	3	3	3	3	33/36	91.7
AMSA' 16[43]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4
AMSA' 17[44]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4
AMSA' 18[45]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4
Singer et al,18[21]	3	3	3	3	3	3	2	3	3	3	3	3	35/36	97.2

QATSDD Criteria

- (1) Theoretical framework; (6) Procedure for data collection (11) Good justification for analytical method selected
(2) Aims/objectives; (7) Rationale for choice of data collection tool(s) (12) Strengths and limitations.
(3) Description of research setting (8) Detailed recruitment data
(4) Sample size; (9) Fit between research question and method of data collection (Quantitative only)
(5) Representative sample of target group (10) Fit between research question and method of analysis (Quantitative only)
QATSDD rating scale: 0=not at all; 1=very slightly; 2=moderately; 3=complete; AMSA = Army Medical Surveillance Activity

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Study or Subgroup	Women (rate/100000)		Men (rate/100000)		Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
	Events	Total	Events	Total			
1.1.1 Heat exhaustion and unspecified effects of heat and light							
AMSA 2010	178	100000	135	100000	10.5%	1.32 [1.05, 1.65]	
AMSA 2011	232	100000	167	100000	13.0%	1.39 [1.14, 1.69]	
AMSA 2012	263	100000	168	100000	0.0%	1.57 [1.29, 1.90]	
AMSA 2013	235	100000	144	100000	0.0%	1.63 [1.33, 2.01]	
AMSA 2014	130	100000	119	100000	8.6%	1.09 [0.85, 1.40]	
AMSA 2015	131	100000	121	100000	8.7%	1.08 [0.85, 1.39]	
AMSA 2016	154	100000	148	100000	10.3%	1.04 [0.83, 1.30]	
AMSA 2017	190	100000	161	100000	11.8%	1.18 [0.96, 1.46]	
Subtotal (95% CI)		600000		600000	62.8%	1.19 [1.08, 1.31]	
Total events	1015		851				
Heterogeneity: Tau ² = 0.00; Chi ² = 5.52, df = 5 (P = 0.36); I ² = 9%							
Test for overall effect: Z = 3.56 (P = 0.0004)							
1.1.2 Heat exhaustion							
AMSA 2006	289	100000	198	100000	0.0%	1.46 [1.22, 1.75]	
AMSA 2007	149	100000	134	100000	9.7%	1.11 [0.88, 1.40]	
AMSA 2008	162	100000	134	100000	10.0%	1.21 [0.96, 1.52]	
AMSA 2009	135	100000	98	100000	7.9%	1.38 [1.06, 1.79]	
AMSA 2018	138	100000	141	100000	9.6%	0.98 [0.77, 1.24]	
Subtotal (95% CI)		400000		400000	37.2%	1.15 [1.01, 1.32]	
Total events	584		507				
Heterogeneity: Tau ² = 0.00; Chi ² = 3.93, df = 3 (P = 0.27); I ² = 24%							
Test for overall effect: Z = 2.05 (P = 0.04)							
Total (95% CI)		1000000		1000000	100.0%	1.18 [1.09, 1.27]	
Total events	1599		1358				
Heterogeneity: Tau ² = 0.00; Chi ² = 9.66, df = 9 (P = 0.38); I ² = 7%							
Test for overall effect: Z = 4.24 (P < 0.0001)							
Test for subgroup differences: Chi ² = 0.14, df = 1 (P = 0.71), I ² = 0%							





PRISMA 2009 Checklist

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Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6, supplementary file 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Figure 1
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8



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Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8
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Page 1 of 2

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8, Supplementary file 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	15, 16
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10, 12, 14, Supplementary file 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9, 10, 11, 12, 13, 14
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	16
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	17, 18, 19
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	20, 21
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	21, 22
FUNDING			



PRISMA 2009 Checklist

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Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	22
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From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

Page 2 of 2

For peer review only

MOOSE Checklist for Meta-analyses of Observational Studies

Item No	Recommendation	Reported on Page No
Reporting of background should include		
1	Problem definition	4
2	Hypothesis statement	6
3	Description of study outcome(s)	7
4	Type of exposure or intervention used	7 - 9
5	Type of study designs used	7 - 8
6	Study population	7
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	Title page
8	Search strategy, including time period included in the synthesis and key words	6, supplemental Table 1
9	Effort to include all available studies, including contact with authors	7, Figure 1
10	Databases and registries searched	6
11	Search software used, name and version, including special features used (eg, explosion)	6, supplemental Table 1
12	Use of hand searching (eg, reference lists of obtained articles)	7
13	List of citations located and those excluded, including justification	8, Table 2, Figure 1
14	Method of addressing articles published in languages other than English	6-
15	Method of handling abstracts and unpublished studies	7
16	Description of any contact with authors	Figure 1
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	7-8
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	7-9
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	8-9
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	7-8
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	7-8
22	Assessment of heterogeneity	9
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	9
24	Provision of appropriate tables and graphics	Tables 1-3, Figs 2-3
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	Figs 2-3
26	Table giving descriptive information for each study included	Supplemental Table 2
27	Results of sensitivity testing (eg, subgroup analysis)	Supplemental Figure 1

28	Indication of statistical uncertainty of findings	15-17
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Item No	Recommendation	Reported on Page No
Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	23
30	Justification for exclusion (eg, exclusion of non-English language citations)	6
31	Assessment of quality of included studies	7-8; 17-18
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	19-24
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	24
34	Guidelines for future research	24
35	Disclosure of funding source	25

From: Stroup DF, Berlin JA, Morton SC, et al, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. *JAMA*. 2000;283(15):2008-2012. doi: 10.1001/jama.283.15.2008.

BMJ Open

A Systematic Review of the Gender Differences in the Epidemiology and Risk Factors of Exertional Heat Illness and Heat tolerance in the Armed Forces

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-031825.R2
Article Type:	Original research
Date Submitted by the Author:	11-Dec-2019
Complete List of Authors:	Alele, Faith; James Cook University, College of Healthcare Sciences Malau-Aduli, Bunmi; James Cook University, College of Medicine and Dentistry Malau-Aduli, Aduli; James Cook University, College of Public Health, Medical and Veterinary Sciences Crowe, Melissa; James Cook University, Division of Tropical Health and Medicine
Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Sports and exercise medicine
Keywords:	OCCUPATIONAL & INDUSTRIAL MEDICINE, ACCIDENT & EMERGENCY MEDICINE, Heat Stroke, Armed Forces, Women

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3 1 **A Systematic Review of the Gender Differences in the Epidemiology and Risk Factors of**
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5 2 **Exertional Heat Illness and Heat tolerance in the Armed Forces**
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8 3 **Type of article:** Review
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56 34 Word count: 3993
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3 **Abstract**
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6 **Objectives:** The aim of this review was to describe the epidemiology of all heat related
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8 illnesses in women compared to men in the armed forces and to identify gender specific risk
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10 factors and differences in heat tolerance.
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14 **Design:** A systematic review of multiple databases (MEDLINE, Emtree, CINAHL,
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16 PsycINFO, Informit, and Scopus) was conducted from inception of the databases to 1 April
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18 2019 using the preferred reporting items for systematic review and meta-analysis (PRISMA)
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20 guidelines.
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24 **Eligibility criteria:** All relevant studies investigating and comparing heat illness and heat
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26 tolerance in women and men in the armed forces were included in the review.
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29 **Results:**
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32 Twenty-four (24) studies were included in the systematic review. The incidence of heat stroke
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34 in women ranged from 0.10 to 0.26 per 1000 person years, while the incidence of heat stroke
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36 ranged from 0.22 to 0.48 per 1000 person years in males. The incidence of other heat illnesses
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38 in women compared to men ranged from 1.30 to 2.89 per 1000 person years vs 0.98 to 1.98 per
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40 1000 person years. The limited evidence suggests that women had a greater risk of exertional
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42 heat illness compared to men. Other gender specific risk factors were slower run times and
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44 body mass index. Although there was a higher proportion of women who were heat intolerant
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46 compared to men; this finding needs to be interpreted with caution due to the limited evidence.
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51 **Conclusion:** In relation to armed forces personnel, the findings of this review suggest that men
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53 experienced a higher incidence of heat stroke than women. Although the evidence is limited, a
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55 higher proportion of women were heat intolerant and had a greater risk of exertional heat
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3 58 illnesses. Despite the limited evidence, further research is required to investigate the influence
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5 59 of gender differences on heat intolerance and heat illness.
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8 **Article summary**

9 **Strengths and limitations of this study**

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15 62 • This is the first known systematic review investigating the impact of gender on
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17 63 exertional heat illness and heat tolerance in the armed forces.
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19 64 • We conducted a comprehensive search and identified potential risk factors that are
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21 65 associated with exertional heat illness.
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24 66 • Most of the included studies utilized retrospective data with an increased likelihood of
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26 67 misclassification bias which may have underestimated or overestimated the association
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28 68 between heat-related illness and risk factors.
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32 69 **Trial registration** None
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34 **Key words**

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37 71 Heat stress; Heat stroke; Heat exhaustion; Heat tolerance; Women; Armed Forces
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79 Introduction

80 Heat illnesses are disorders that arise after prolonged exposure to heat/humidity and/or
81 increased physical activity.[1] When body temperature rises, conduction, convection, radiation
82 and evaporation mechanisms help to cool the body and maintain normothermia.[1] However,
83 heat loss is susceptible to prevailing environmental conditions and type of clothing worn.
84 Without adequate cooling heat illnesses may occur including exercise-associated muscle
85 cramps (EAMC), heat syncope, heat exhaustion and heat stroke, a potentially life-threatening
86 disorder.[1]

87 Heat stroke is a medical emergency.[2] It is characterized by elevated core temperature of 40°C
88 and above, central nervous system disturbances and multi-organ damage that may result in
89 death.[2] Heat stroke has been classified as either classic or exertional.[3] Classic heat stroke
90 is insidious in onset and occurs in vulnerable populations such as young children, the elderly
91 and patients with chronic diseases.[4] On the other hand, exertional heat stroke occurs more
92 rapidly and affects apparently healthy, active people such as athletes, factory workers,
93 construction workers, agricultural workers, firefighters and armed forces personnel.[5] The
94 workers in these industries often require high levels of physical exertion to perform jobs and
95 tasks. A combination of rigorous activities and extreme exposure to heat places the workers at
96 increased risk of heat stroke.[6]

97 Among armed forces personnel, exertional heat illness continues to pose as a significant cause
98 of morbidity and mortality [7]. Operations and training may involve exposure to high ambient
99 temperature and high workload which may result in heat illness.[7] Historically, men have
100 occupied military roles and responsibilities with fewer proportion of women in the armed
101 forces.[8] However, more women are joining the armed forces globally following the inclusive
102 approach to recruiting and creation of more roles for women.[9] Women are required to operate

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3 103 in austere environments with heat illnesses becoming more frequent.[9] This has raised the
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5 104 question about gender differences in thermoregulation during heat stress.[9] Evidence suggests
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8 105 that women differ from men in thermal responses to heat.[10] This difference may be because
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10 106 women have a lower rate of whole body evaporative heat loss, higher body fat mass, body mass
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12 107 ratio,[11] number of sweat glands and lower aerobic fitness.[12] In addition, hormonal
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14 108 variations due to menstrual cyclic patterns and the use of contraceptive pills may be associated
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17 109 with the differences in response to heat stress.[13]

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20 110 When exertional heat illness occurs, it may be challenging to determine if an individual may
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22 111 return to duty. An inaccurate determination of complete recovery among armed forces
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24 112 personnel may negatively impact military readiness.[14] While, there are no evidence-based
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27 113 recommendations for return to duty, the American College of Sports Medicine (ACSM)
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29 114 guidelines states that exertional heat stroke patients may return to duty after re-establishing
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31 115 heat tolerance.[15] Individuals vary in their ability to cope with heat stress and the inability to
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33 116 withstand heat stress during exertion in hot environments is defined as heat intolerance.[2]
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36 117 Evidence suggests that heat intolerance may be as a direct result of heat stroke or due to
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38 118 predisposing inherent factors (genetics).[2] However, the objective criteria or measure for
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40
41 119 defining heat tolerance or intolerance remains a subject of controversy.[14] The current return
42
43 120 to duty guidelines for military personnel varies across countries.[16] For example, in the United
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45 121 States, military return to duty process is based on clinical assessments with gradual
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47 122 acclimatization and re-introduction of duties.[17] By contrast, return to duty in the Israeli
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50 123 Defence Force requires a heat tolerance test to determine if an individual is heat tolerant.[18]
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52 124 Therefore, it is important to develop evidence based return to duty protocols across the globe.
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54
55 125 The Israeli Defence Force originally developed the heat tolerance test in 1979 as an index of
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57 126 the ability of soldiers to cope with exertional heat.[18] Individuals who have suffered heat
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60 127 stroke are sent for a heat tolerance test after a minimum recovery period of 6 to 8 weeks as part

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3 128 of the return to duty process.[18] Criteria used to define heat intolerance include an elevation
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5 129 in rectal temperature above 38.5°C and heart rate above 150 bpm or when rectal temperature
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7 130 or heart rate fail to stabilize during the test. The heat tolerance test criteria are based on previous
8
9 131 studies by Shapiro et al.[19] which utilised only male military participants.[18, 19] While the
10
11 132 test may be considered as a useful tool to determine return to duty and to prevent subsequent
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13 133 exertional heat stroke, [18,19] there is no consensus on the validity of the tool as a diagnostic
14
15 134 test for heat tolerance.[14] Furthermore, the heat tolerance test does not account for predicting
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17 135 factors such as gender.[14] Given the limitation, questions have been raised about the validity
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19 136 of the protocol in determining return to duty for females in the armed forces. It has been
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21 137 suggested that more research is required to determine whether or not a new protocol should be
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23 138 developed for women.[12]

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29 139 As restrictions on gender based-exclusions from military specializations are lifted,[20] it is
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31 140 imperative to understand and evaluate exertional heat illness in women compared to men and
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33 141 identify the gender specific risk factors. Furthermore, it is important to understand how women
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35 142 respond to the heat tolerance test compared to men. According to a recent review on the risk
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37 143 of heat illness in women compared with men in the general population, men are at increased
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39 144 risk of heat illness compared to women.[21] However, no previous review has investigated the
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41 145 epidemiology and risk factors of heat illness as well as gender responses to the heat tolerance
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43 146 test in men and women in the armed forces. Given that, heat illness can impact defence
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45 147 operational effectiveness and may result in acute loss of manpower and possible medical
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47 148 discharge from service,[22] it is essential that the review should be conducted to inform
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49 149 policies.

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55 150 Therefore, the objective of this systematic review was to provide a comprehensive summary of
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57 151 the epidemiology of heat illness and heat intolerance in women and men in the armed forces.
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3 152 Specific aims were
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6 153 To determine the incidence and prevalence of heat illness in women compared to men
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8 154 in the armed forces:
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11 155 To identify gender differences in heat tolerance in the armed forces and
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14 156 To identify gender specific predisposing risk factors associated with heat illness in the
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16 157 armed forces
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22 159 **Methods**

23 160 **Search Strategy**

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26 161 This review utilised the Preferred Reporting Items for Systematic Review and Meta-analysis
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28 162 (PRISMA) guidelines [23] to explore all literature published in English from inception of the
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30 163 different databases to 1 April 2019. Databases searched were MEDLINE, CINAHL,
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32 164 PsycINFO, Emcare, Informit and Scopus. A preliminary search was conducted in Medline,
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34 165 Emcare and CINAHL to identify relevant key words contained in the titles, abstracts and
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36 166 subject descriptors. These search terms were used to conduct the search in other databases
37
38 167 without subject headings. The search strategy used in Medline is presented in supplemental
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40 168 Table 1. No review protocol exists.
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48 169 **Eligibility criteria**

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51 170 Studies included in the review were assessed according to the following inclusion criteria: Peer-
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53 171 reviewed literature comparing heat illness in women to men in the armed forces or reporting
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55 172 heat tolerance in women and men of the armed forces. Exclusions included literature discussing
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57 173 heat illness in other occupations, or studies where data on heat illness in women could not be
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3 174 separated from men or studies reporting heat illness in men or literature reviews, conference
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5 175 abstracts and grey literature. In addition, additional primary data sources were identified from
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8 176 the reference lists of the included studies using a hand-search technique (Figure 1).
9

10 11 177 **Selection of studies and data extraction**

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14 178 FA and BMA identified all included studies and data extraction was performed using a standard
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16 179 abstraction form. Data extracted from the studies included: study location and design,
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18 180 population, proportion and incidence of heat illnesses, factors associated with heat illness and
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20 181 heat tolerance, and heat tolerance in men and women. All authors cross-checked the extracted
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23 182 data for consistency.
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26 183 **Quality assessment**

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29 184 The methodological quality assessment was assessed by FA in consultation with MC using the
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31 185 modified quality assessment tool for studies with diverse designs (QATSDD) critical appraisal
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33 186 tool.[24] Any disagreement about any article was reviewed by BMA and AMA and discussed
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35 187 until consensus was reached. The QATSDD tool is a 16-item tool which assesses the quality
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37 188 of diverse studies (both quantitative and qualitative).[24] The tool was modified to exclude two
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39 189 items relating to qualitative studies as well as two items relating to quantitative studies that
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41 190 were not applicable to the studies included in the review. The items excluded comprised
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43 191 statistical assessment of reliability and validity of measurement tool(s) (Quantitative only), fit
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45 192 between stated research question and format and content of data collection tool e.g. interview
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47 193 schedule (Qualitative), assessment of reliability of analytical process (Qualitative only) and
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49 194 evidence of user involvement in design. Each criterion in the modified QATSDD tool was
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51 195 awarded a score of 0 to 3 with 0 = not at all, 1 = very slightly, 2 = moderately and 3 = complete.
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53 196 The scores of each criterion were summed to assess the methodological quality of included
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55 197 studies with a maximum score of 36. The criteria included were (1) theoretical framework; (2)
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3 198 statement of aims/objectives; (3) description of research setting; (4) evidence of sample size;
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5 199 (5) representative sample of target group of a reasonable size, (6) description of procedure for
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7 200 data collection; (7) rationale for choice of data collection tool(s); (8) detailed recruitment data;
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10 201 (9) fit between research question and method of data collection (Quantitative only); (10) fit
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12 202 between research question and method of analysis (Quantitative only); (11) good justification
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14 203 for analytical method selected; and (12) strengths and limitations. For ease of interpretation,
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16 204 the scores were converted to percentages and classified as low (<50%), medium (50-80%) or
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18 205 high (>80%) quality of evidence.
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22 206 **Patient and public involvement**

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25 207 There was no public or patient involvement in this study.
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28 208 **Data analysis and synthesis**

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31 209 In this review, the International Classification of Diseases ICD 9 or ICD 10 diagnosis codes
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33 210 [25, 26] for the effects of heat and light were used to classify heat illnesses. All included studies
34
35 211 utilized either the ICD 9 or ICD 10 codes to classify heat illnesses depending on the year of
36
37 212 publication. Heat illnesses were categorised as heat stroke and other heat illnesses. Heat stroke
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39 213 was defined using the ICD diagnosis codes 992.0 (ICD 9) and T67.0 (ICD 10). While other
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41 214 heat illnesses were defined as heat exhaustion (992.3-5, T67 3-5) and unspecified effects of
42
43 215 heat and light (992.9 and T67.9). In addition, some studies presented findings for all heat illness
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45 216 without categorizing them into heat stroke and other heat illnesses. These findings were
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47 217 presented separately. Incidence rates and proportions were extracted from the data reported in
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49 218 each study and used for the analysis in this review.
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222 **Results**

223 An initial search identified 3816 papers. After removing duplicates, screening titles and
224 abstracts, 47 papers remained for full text review with twenty-four (24) included in the
225 systematic review (Figure 1). Twenty-two (22) of the reviewed articles originated from the
226 United States of America (USA), while the other two studies were conducted in the United
227 Kingdom (UK) and Israel respectively (Supplemental Table 2). All included studies were
228 conducted among armed forces personnel, however, two studies included university staff and
229 armed forces personnel in the studies.[27, 28] Twenty- one (21) articles examined heat illnesses
230 and injuries in women and men. Seven (7) of these studies described all heat related illnesses
231 in men and women,[29-35] while 13 studies included information on heat stroke and other heat
232 injuries in relation to both genders.[36-48] Four (4) studies identified gender specific risk
233 factors associated with heat stroke,[31, 34, 35, 49] and three (3) studies compared heat
234 tolerance in men and women.[12, 27, 28]

235 **Incidence of heat stroke in women compared to men in the armed forces**

236 Thirteen studies conducted among US army personnel compared the incidence of heat stroke
237 between men and women.[36 – 48] The incidence of heat stroke among females ranged from
238 0.10 to 0.26 per 1000 person years. Among males, the incidence of heat stroke ranged from
239 0.22 to 0.48 per 1000 person years (Figure 2). Between 2015 and 2018, the incidence of heat
240 stroke increased steadily for both men and women.

241 **Incidence of other heat illnesses in women compared to men in the armed forces**

242 The incidence of other heat illnesses was reported by 13 studies conducted by the US Army.
243 The incidence of other heat illnesses in women ranged from 1.30 to 2.89 per 1000 person years.
244 In men, the incidence rate of other heat illness ranged from 0.98 to 1.98 per 1000 person years
245 (Figure 3).

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3 **246 Incidence and prevalence of all heat illnesses in women compared to men**
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6 247 Table 1 shows the proportions and incidences of all heat-related illness in men and women in
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8 248 the armed forces. Five (5) studies reported higher incidences and proportions of all heat illness
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10 249 in men compared to women[29, 31, 32, 34, 35] while two studies reported higher incidences
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13 250 of all heat illness in women.[30, 33]
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251 **Table 1: Incidence and Proportion of all heat related illnesses in women and men in the Armed Force**

Reference, year	Country	Study design	Study duration	Population	ICD codes	All heat injuries	
						Women	Men
Dickson. 1994[29]	UK	Descriptive epidemiology	1981-1991 (10yrs)	Royal Air force, Royal Navy and Army (1448 cases)	ICD-9-CM: 992.0 – 992.9	11.43*	41.87*
Army Medical Surveillance Activity, 1998[30]	USA	Descriptive epidemiology	1997 – 1998 (1 year)	US Army (1433 cases) 1997	ICD-9-CM: 992.0 – 992.9	12.8†	8.6†
						1998	15.8†
Army Medical Surveillance Activity, 2000[33]	USA	Descriptive epidemiology	1997 – 1999 (2 years)	US Army and Marine Corps (3386 cases) Army (1896 cases) Marine Corps (1104 cases)	ICD-9-CM: 992.0 – 992.9	2.0†	1.5†
						4.4†	2.0†
Army Medical Surveillance Activity, 2002[31]	USA	Descriptive epidemiology	1990 – 1997 (7 years)	US Army (2290 cases)	ICD-9-CM: 992.0 – 992.9	14.0%§	86.0%§
		Case control	1998 – 2001 (3 years)	US Army (5021 cases and 10,042 controls)		20.7%§	79.3%§
Army Medical Surveillance Activity, 2003[32]	USA	Descriptive epidemiology	2002 (1 year)	US Army (1816 cases)	ICD-9-CM: 992.0 – 992.9	3.5†	5.1†
Carter et al, 2005[34]	USA	Cross-sectional	1980 – 2002 (22 years)	US Army (5246 cases)	ICD-9-CM: 992.0 – 992.9	13.7%§	86.3%§
Bedno et al, 2014[35]	USA	Analytical cross-sectional	2005 - 2006	US Armed Forces (80 exertional heat illness cases) 9455 men 1913 women	ICD-9-CM: 992.0 – 992.9	0.680%	0.71%

252 § Proportions and incidences reported are of the total cases reported in the articles
 253 * Incidence rate reported per 100,000 person-years; † Incidence rate per 100,000 person- months; ‡ Incidence rate reported per 1000 person-years
 254 UK = United Kingdom; USA = United States of America

255 Gender specific risk factors for heat illness

256 Three (3) studies identified the gender specific risk factors that were associated with heat illness
 257 (Table 2). [31, 34, 49] Two of the studies compared the risk of heat illness between males and
 258 females while one study identified risk factors within each gender. In the two studies that
 259 compared the risk of heat illness by gender, females had a greater risk of experiencing heat
 260 illness (OR 1.5, 95% CI 1.4 to 1.7 and IDR 1.21, 95% CI 1.09 to 1.40) compared to males.[31,
 261 34] Within gender, males with body mass index (BMI) of $\geq 26 \text{ kgm}^{-2}$ had a greater risk of
 262 experiencing heat illness compared to males with BMI $< 22 \text{ kgm}^{-2}$ (OR 2.10, 95% CI 1.59 to
 263 2.78).[49] In addition, males with run times of ≥ 12.9 minutes had almost six times the risk of
 264 exertional heat illness compared to males with run times of < 10.3 minutes (OR 5.61, 95% CI
 265 1.92 to 6.85). While females with run times of ≥ 6.9 minutes had five times the risk of
 266 exertional heat illness compared to females with run times of < 5.8 minutes (OR 5.30, 95% CI
 267 1.59 to 17.64).[49]

268 **Table 2: Gender specific risk factors associated with heat illness**

Reference, year	Country	Study design and duration	Study population	Risk factors	OR or IDR (95% CI)
Army Medical Surveillance Activity, 2002[31]	USA	Case-control 1998 – 2001 (3 years)	US Army 5021 cases and 10,042 controls	Female	1.5 (1.4 - 1.7)
Carter et al, 2005[34]	USA	Cross-sectional 1980 – 2002 (22 years)	US Army 5246 cases of heat illness; 4521 males and 725 females	Female	1.21 (1.09 – 1.40)
Wallace et al, 2006[49]	USA	Case-control 1988 – 1996 (8 years)	US Marine Corps Male (627 cases and 1679 controls) Female (49 cases and 123 controls)	BMI $\geq 26 \text{ kg/m}^2$ (males) Run time ≥ 12.9 minutes (males) Run time ≥ 6.9 minutes (females)	2.10 (1.59 – 2.78) 5.61 (3.73 – 8.45) 5.30 (1.59 – 17.64)

269 Odds ratio; IDR = Incidence density ratio; BMI= Body Mass Index; CI=Confidence Interval; USA = United States of America

270 **Heat tolerance in women and men**

271 Three studies compared heat tolerance classification in males and females using the HTT
 272 developed by the Israeli Defence Force (Table 3). [12, 27, 28] Druyan et al. investigated gender
 273 differences in Israeli Defence Force personnel who had sustained heat injury. The study
 274 reported that 67% of the women were found to be heat intolerant compared to 26% of their
 275 male counterparts.[12] In the studies conducted by Lisman et al. and Kazman et al. the study
 276 population comprised of participants from the university and military communities who had
 277 either no heat illness or a previous history of heat illness. Both studies reported that a greater
 278 proportion of women were classified as heat intolerant compared to men (42% vs 27% and
 279 45% vs 18% respectively). [27, 28]

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281 **Table 3: Heat tolerance in women and men**

Reference, year	Country	Study design and duration	Study population	Heat in tolerance rate Women	Heat in tolerance rate Men
Druyan et al, 2012[12]	Israel	Retrospective cross-sectional 2008 – 2010 (2 years)	170 males and 9 females	66.67%	25.79%
Lisman et al, 2014 [27]	USA	Analytical cross-sectional	Military and university community members; 34 males and 12 females	42%	27%
Kazman et al, 2015[28]	USA	Analytical cross-sectional (duration not stated)	Military and university community members; 55 males and 20 females	45%	18%

282 USA = United States of America

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3 287 **Assessment of methodological quality**
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6 288 The QATSDD scores ranged from 22.2% to 94.4% (Supplemental Table 3). Only six studies
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8 289 scored above 50% and included details about recruitment, data analysis, strengths and
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10 290 limitations of the research. The other studies had lower scores because they lacked detailed
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12 291 justification for the analytical methods, data collection, analysis, strengths and limitations.
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14 292 However, results of the methodological assessment should be interpreted with caution.
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16 293 Although the tool assesses methodological quality, it is more likely to be dependent on how
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18 294 the paper was written. In this review, 70% of the studies included were military reports on heat-
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20 295 related illnesses in the Armed Forces. These reports were published in a peer-reviewed journal
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22 296 and were retrospective analyses of data collected by Defence Medical Surveillance Systems.
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24 297 These studies may not have reported details about data collection, strengths and limitations,
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26 298 but they presented valid information on heat-related illness.
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308 **Discussion**

309 The findings of this systematic review suggest that men have a slightly higher incidence of heat
310 stroke compared to women. By contrast women report a slightly higher incidence of other heat
311 illness compared to men. In addition, among studies that reported all heat illnesses (where heat
312 stroke and other heat illnesses have been combined) there was a higher rate of all heat illnesses
313 in men compared to women as evidenced by the outcomes reported in five (5) of seven (7)
314 studies. However, women had a greater risk of experiencing exertional heat illness and were
315 more likely to be heat intolerant compared to men. Other gender specific risk factors were
316 longer run times for both men and women while higher BMI was associated with exertional
317 heat illness for men only. However, the association between these factors and exertional heat
318 illness is weak given the small number of articles that investigated the relationship.
319 Furthermore, despite the higher proportion of heat intolerance reported among women; this
320 finding should be interpreted with caution given the small sample size for females in the
321 included studies and the differences in occupations of the women in the three studies. One
322 study included women in the armed forces with a previous history of heat stroke, [12] while
323 the other two studies recruited women from the general population as well as military members
324 with either no history or a previous history of heat stroke. [27, 28]

325 **Incidence and prevalence of exertional heat illnesses in women compared to men**

326 In this review, women had a lower incidence of heat stroke, but a slightly higher incidence of
327 other heat illness compared to men. The reported lower incidence of heat stroke/higher
328 incidence of other heat illness in women compared to men could possibly be due to the fact
329 that women in the military in the United States were excluded from combat positions until 2013
330 when the ban was lifted.[20] Evidence in the literature suggests that service members who were
331 engaged in roles such as infantry or gun crew had an increased risk of heat illness, possibly

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3 332 reflecting a greater risk of heat illness for those in combat roles.[34] Furthermore, during
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5 333 military training exercises men may have comparatively tolerated working in the heat beyond
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7 334 the endurance limits.[22] This finding was re-echoed in a previous systematic review that men
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9 335 in the general population had a higher rate of all types of heat illnesses compared to women.[21]
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11 336 Although, the incidence of heat stroke was lower in women compared to men in this review,
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13 337 the incidence of heat stroke among women has increased over the past four years. This implies
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15 338 that as more women engage in specialised military roles their risk of exertional heat illness
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17 339 increases.
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22 340 **Gender specific risk factors for heat illness**

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25 341 Despite the lower incidence of heat stroke, women had a greater risk of exertional heat illnesses
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27 342 compared to men.[30, 33] In addition one study attempted to investigate intra gender risk
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29 343 factors for exertional heat illness.[49] Slower run time duration was associated with exertional
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31 344 heat illness among males and females respectively, while higher BMI was identified as a risk
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33 345 factor among males only.[49] The higher risk of exertional heat illnesses in women may likely
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35 346 be due to differences in physiological and physical characteristics between men and
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37 347 women.[50] Physiological characteristics such as hormones, use of contraceptive pills and
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39 348 lower evaporative heat loss may make women more susceptible to heat illness. [11, 13]
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41 349 However, conflicting evidence suggests that in highly trained women, exercise performance
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43 350 and heat loss is not affected by the menstrual cycle phase but is impaired in humid
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45 351 conditions.[51] In addition, physical characteristics such as lower aerobic fitness is a predictor
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47 352 of exertional heat illness.[50] Generally, women have lower aerobic fitness levels and lower
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49 353 overall work capacity which may contribute to the increased risk of exertional heat illness.[50]
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51 354 Individuals with low aerobic fitness levels are likely to exert themselves beyond their physical
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53 355 limit and are at increased risk of heat illness.[52] Other intra gender risk factors that were
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55 356 identified were longer run time duration and higher BMI.[49] Evidence suggests that slower
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3 357 run time duration which may be a reflection of lower aerobic fitness and higher BMI increases
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5 358 the risk of heat illness.[49, 53] However, the evidence is limited given that this was reported
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8 359 by only one study.[49]
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10 360 **Heat tolerance in women and men**

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14 361 The risk of heat illness is dependent on thermal tolerance.[2] In order to determine the recovery
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16 362 and return to duty for HTT is conducted for members of the armed forces after a heat stroke
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18 363 event.[18] The test criteria defines heat intolerance as peak rectal temperature > 38.5°C, peak
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20 364 heart rate > 150 bpm, or the inability of these values to reach a plateau.[18, 19] Although in
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23 365 the three studies, a higher proportion of women were classified as heat intolerant; this evidence
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25 366 should be interpreted with caution given that the female populations included in each study
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27 367 varied with respect to heat illness and occupations.[12, 27, 28] However, the studies
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29 368 acknowledged that gender differences in cardiorespiratory fitness, body fat percentage and
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31 369 surface area to mass ratio may account for the higher intolerance rates in women.[12, 27, 28] In
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34 370 addition,, the three studies reported using the Israeli Defence Force heat tolerance test protocol
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37 371 and given that the test protocol was developed using male participants, there may be a need to
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39 372 re-evaluate the criteria for women to reduce false positive results.[12, 27, 28] Furthermore,
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41 373 incomplete recovery and inaccurate determination of return to duty may negatively affect
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43 374 military operations and may end the careers of armed forces personnel.[14] Therefore, it is
44
45 375 important to ensure that the heat tolerance test is valid and fair for females, if it is to be used to
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48 376 determine return to duty for females in the armed forces.
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50 51 377 **Strengths and limitations**

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54 378 To the authors' current knowledge, this is the first known systematic review investigating
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56 379 gender differences in exertional heat illness and heat tolerance in the armed forces. In addition,
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59 380 we identified potential gender specific risk factors that are associated with exertional heat
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3 381 illness. However, the heterogeneity in the study designs contributed to the variable
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5 382 methodological quality of the included studies. Most of the articles in this review were military
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7 383 reports and may not be considered of high methodological quality when assessed using a formal
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9 384 critical appraisal tool. In addition, most of the included studies utilized retrospective data as
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11 385 the data source with an increased likelihood of incompleteness and inaccuracy. There is a
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13 386 likelihood that misclassification bias could have been introduced into the studies. Three studies
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15 387 that explored the risk factors associated with heat-related illness used retrospective data. [31,
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17 388 34, 49] The retrospective data may have been misclassified or incomplete at the time of entry
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19 389 and may have introduced misclassification bias into the studies. This type of bias may
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21 390 underestimate or overestimate the association between heat-related illness and risk factors.
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23 391 Although the gender specific risk factors associated with heat illness were discussed; the review
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25 392 provided limited evidence of these factors, given the few numbers of studies that investigated
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27 393 the association. Furthermore, we included only studies published in English language; studies
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29 394 published in other languages were excluded.
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36 395 **Implication for policy and future research**

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39 396 This systematic review demonstrates that there is limited research on exertional heat illness in
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41 397 women in the armed forces. Although men had a higher incidence of heat stroke; women had
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43 398 a higher incidence of other heat illnesses. Further research is needed to establish if this reflects
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45 399 physiological or behavioural differences. In addition, the limited and inconclusive evidence
46
47 400 suggests that more women were classified as heat intolerant compared to men using the Israeli
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49 401 Defence Force heat tolerance test protocol. The current criteria may be unfair to women given
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51 402 that it was developed using male participants. More research is needed to determine the gender
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53 403 differences in heat tolerance as well as to consider re-evaluating the heat tolerance test protocol
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55 404 or the development of a new protocol that considers gender specific factors.[12] Given that the
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3 405 heat tolerance test was conducted in a laboratory setting, more research is needed to replicate
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5 406 the findings in field based setting.
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8 407 **Conclusion**

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11 408 In conclusion, this review shows that men had a higher incidence of heat stroke but women in
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13 409 the armed forces had a greater risk of exertional heat illness. Despite the limited evidence,
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15 410 further research is required to investigate the influence of gender differences on heat tolerance
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17 411 and heat illness. Further research is needed to evaluate the heat tolerance test protocol for
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19 412 women.
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25 26 27 414 **Authors' contribution**

28
29 415 All authors contributed substantially to the study concept, design, data extraction, quality
30
31 416 assessment and writing of the manuscript.

32 417 **Conceptualization:** Faith O. Alele, Bunmi S. Malau-Aduli, Aduli E. Malau-Aduli, Melissa
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34 418 Crowe

35 419 **Methodology:** Faith O. Alele, Bunmi S. Malau-Aduli, Aduli E. Malau-Aduli, Melissa Crowe

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37 420 **Writing** - Original draft: Faith O. Alele

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39 421 **Writing – review & editing:** Faith O. Alele, Bunmi S. Malau-Aduli, Aduli E. Malau-Aduli,
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41 422 Melissa Crowe

42 423 All authors read and approved the manuscript for submission.

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48
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41 562

563 Figure legends

564 Figure 1: PRISMA flow chart of the study selection protocol

565 Figure 2: The incidence rate of exertional heat stroke between men and women in the armed
566 forces from 2006 to 2018

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567 Figure 3: Incidence rate of other heat illnesses (including heat exhaustion and unspecified
568 effects of heat and light) between men and women in the armed forces from 2006 to 2018

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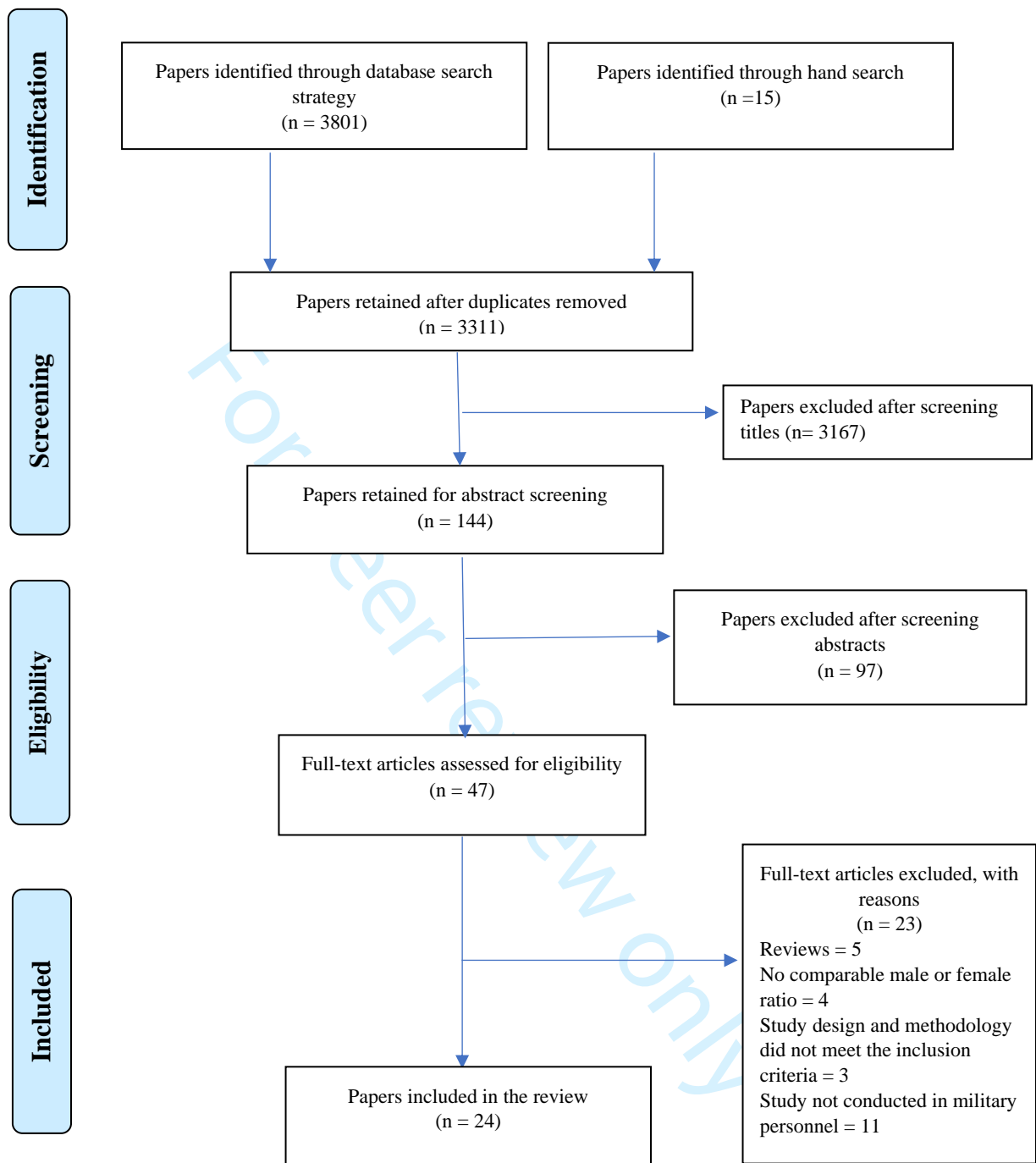


Figure 1: PRISMA flow chart of the study selection protocol

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Figure 2

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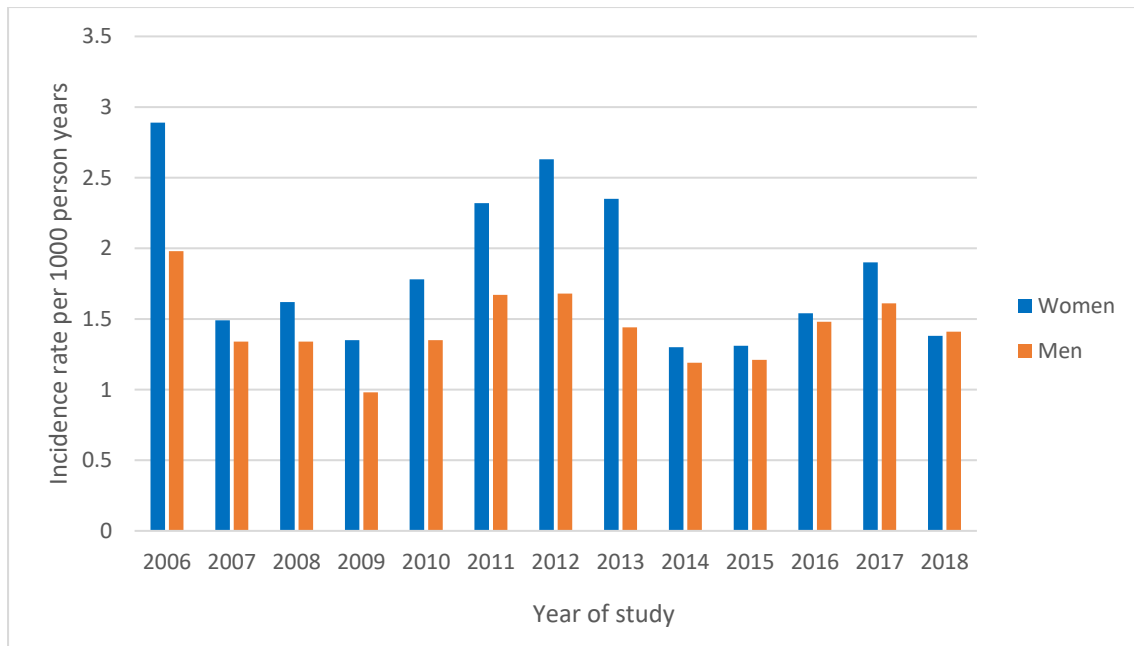


Figure 3

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Supplemental Table 1

Medline search strategy	
1.	Women (MeSH)
2.	Gender expression
3.	Gender identity (MeSH)
4.	Gender
5.	Wom\$
6.	Sex
7.	Heat strok*
8.	Heatstrok*
9.	Heat collapse
10.	Heat exhaustion
11.	Heat prostration
12.	Heat cramp
13.	Heat cramps
14.	Heat stress disorder
15.	Heat stress disorders (MeSH)
16.	Thermal stress
17.	Heat illness
18.	Heat illnesses
19.	Heat injury
20.	Heat injuries
21.	Heat related diseases
22.	Heat disorder
23.	Heat disorders
24.	Heat related disorder
25.	Heat related disorders
26.	Heat related illness
27.	Heat related illnesses
28.	Heat related injuries
29.	Heat related injury
30.	Environmental heat illness
31.	Heat stress
32.	Heat adaptation
33.	Heat tolerance
34.	Heat tolerances
35.	Heat resistance
36.	Thermal resistance
37.	Thermoresistance
38.	Thermotolerance (MeSH)
39.	Heat endurance
40.	1 OR 2 OR 3 OR 4 OR 5 OR 6
41.	7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39
42.	40 AND 41

Supplemental Table 2
Summary of all included studies

Reference, year	Country	Study design and duration	Population	Study findings [§]
Dickson. G, 1994[29]	UK	Descriptive epidemiology 1981-1991	Royal Airforce, Royal Navy and Army; 1448 all heat injuries cases [¶]	Women All heat injuries: 11.43 [#] Men All heat injuries: 41.87 [#]
Army Medical Surveillance Activity, 1998[30]	USA	Descriptive epidemiology; 1997 - 1998	US Army; 1433 all heat injuries cases (1997-1998) [¶] 1997 1998	Women All heat injuries: 12.8 [‡] Men All heat injuries: 8.6 [‡] Women All heat injuries: 15.8 [‡] Men All heat injuries: 12.0 [‡]
Army Medical Surveillance Activity, 2000[33]	USA	Descriptive epidemiology; 1997 - 1999	US Army and Marine Corps; 3386 all heat injuries cases [¶] Army (1896 cases) Marine Corps (1104 cases)	Women All heat injuries: 2.0 [†] Men All heat injuries: 1.5 [†] Women All heat injuries: 4.4 [†] Men All heat injuries: 2.0 [†]
Army Medical Surveillance Activity, 2002[31]	USA	Descriptive epidemiology 1990 - 1997 Case – control 1998 - 2001	US Army; 2290 all heat injuries cases [¶] US Army; 5021 cases and 10,042 controls (all heat injuries) [¶]	Women All heat injuries: 14.0% Men All heat injuries: 86.0% Women All heat injuries: 20.7% Men All heat injuries: 79.3%

				<u>Risk factors</u> Female: OR; 1.5 (1.4 - 1.7)
5	Army Medical Surveillance Activity, 2003[32]	USA	Descriptive epidemiology; 2002	US Army; 1816 all heat injuries cases [†]
6				<u>Women</u> All heat injuries: 3.5 [†]
7				<u>Men</u> All heat injuries: 5.1 [†]
10	Carter et al, 2005[34]	USA	Cross-sectional 1980 - 2002	US Army; 5246 all heat injuries cases [†] 4521 males and 725 females
11				<u>Women</u> All heat injuries: 13.7%
12				<u>Men</u> All heat injuries: 86.3%
13				<u>Risk factors</u> Female: IDR: 1.21 (1.09 – 1.40)
16	Army Medical Surveillance Activity, 2006[36]	USA	Descriptive epidemiology; 2005	US Armed Forces; 204 heat stroke cases 958 heat exhaustion cases
17				<u>Women</u> Heat stroke: 0.26 [†] Heat exhaustion: 2.89 [†]
18				<u>Men</u> Heat stroke: 0.48 [†] Heat exhaustion: 1.98 [†]
22	Wallace et al, 2005[49]	USA	Case-control 1988 - 1996	US Army; 5246 cases of heat illness; 4521 males and 725 females
23				<u>Risk factors</u> <i>Females</i> Run time ≥ 6.9 minutes: OR; 5.30 (1.59 – 17.64)
24				<i>Males</i> Run time ≥ 12.9 minutes: OR; 5.61 (3.73 – 8.45)
25				BMI ≥ 26 kg/m ² : OR; 2.10 (1.59 – 2.78)
30	Army Medical Surveillance Activity, 2007[37]	USA	Descriptive epidemiology; 2006	US Armed Forces; 259 heat stroke cases 1854 heat exhaustion cases
31				<u>Women</u> Heat stroke: 0.14 [†] Heat exhaustion: 1.49 [†]
32				<u>Men</u> Heat stroke: 0.22 [†] Heat exhaustion: 1.34 [†]
36	Army Medical Surveillance Activity, 2008[38]	USA	Descriptive epidemiology; 2007	US Armed Forces; 329 heat stroke cases 1853 heat exhaustion cases
37				<u>Women</u> Heat stroke: 0.14 [†] Heat exhaustion: 1.62 [†]
38				<u>Men</u>

				Heat stroke: 0.26† Heat exhaustion: 1.34†
5	Army Medical Surveillance Activity, 2009[39]	USA	Descriptive epidemiology; 2008	US Armed Forces; 299 heat stroke cases 1467 heat exhaustion cases
6				<u>Women</u> Heat stroke: 0.16† Heat exhaustion: 1.35†
7				<u>Men</u> Heat stroke: 0.22† Heat exhaustion: 1.78†
11	Army Medical Surveillance Activity, 2010[40]	USA	Descriptive epidemiology; 2009	US Armed Forces; 323 heat stroke cases 2038 other heat injuries cases*
12				<u>Women</u> Heat stroke: 0.15† Other heat injuries: 1.78†
13				<u>Men</u> Heat stroke: 0.24† Other heat injuries: 1.35†
17	Army Medical Surveillance Activity, 2011[41]	USA	Descriptive epidemiology; 2010	US Armed Forces; 311 heat stroke cases 2576 other heat injuries cases*
18				<u>Women</u> Heat stroke: 0.12† Other heat injuries: 2.32†
19				<u>Men</u> Heat stroke: 0.23† Other heat injuries: 1.67†
23	Army Medical Surveillance Activity, 2012[42]	USA	Descriptive epidemiology; 2011	US Armed Forces; 362 heat stroke cases 2652 other heat injuries cases*
24				<u>Women</u> Heat stroke: 0.10† Other heat injuries: 2.63†
25				<u>Men</u> Heat stroke: 0.27† Other heat injuries: 1.68†
28	Druyan et al, 2012[12]	Israel	Retrospective cross-sectional 2008 – 2010	Israeli Defence Forces; 170 males and 9 females
29				<u>Heat tolerance parameters</u> <u>Women</u> Heat intolerance rate: 66.6%
32				<u>Men</u> Heat intolerance rate: 25.79%
34	Army Medical Surveillance Activity, 2013[43]	USA	Descriptive epidemiology; 2012	US Armed Forces; 365 heat stroke cases 2257 other heat injuries cases*
35				<u>Women</u> Heat stroke: 0.15† Other heat injuries: 2.35†
36				<u>Men</u> Heat stroke: 0.27† Other heat injuries: 1.44†

1 2 3 4 5 6 7 8	Army Medical Surveillance Activity, 2014[44]	USA	Descriptive epidemiology; 2013	US Armed Forces; 324 heat stroke cases 1701 other heat injuries cases*	<u>Women</u> Heat stroke: 0.15† Other heat injuries: 1.30† <u>Men</u> Heat stroke: 0.24† Other heat injuries: 1.19†
9 10 11 12	Bedno et al, 2014[35]	USA	Analytical cross-sectional	US Armed Forces; 80 exertional heat illness cases	<u>Women</u> Heat illness: 0.680% <u>Men</u> Heat illness: 0.71%
13 14 15 16 17	Lisman et al, 2014[27]	USA	Analytical cross-sectional	Military and university community members; 34 males and 12 females	<u>Heat tolerance parameters</u> <i>Women</i> Heat intolerance rate: 42% <i>Men</i> Heat intolerance rate: 27%
18 19 20 21 22	Army Medical Surveillance Activity, 2015[45]	USA	Descriptive epidemiology; 2014	US Armed Forces; 314 heat stroke cases 1410 other heat injuries cases*	<u>Women</u> Heat stroke: 0.14† Other heat injuries: 1.31† <u>Men</u> Heat stroke: 0.27† Other heat injuries: 1.21†
23 24 25 26 27 28 29	Kazman et al, 2015[28]	USA	Analytical cross-sectional	Military and university community members; 55 males and 20 females	<u>Heat tolerance parameters</u> <i>Women</i> Heat intolerance rate: 45% <i>Men</i> Heat intolerance rate: 18%
30 31 32 33 34 35	Army Medical Surveillance Activity, 2016[46]	USA	Descriptive epidemiology; 2015	US Armed Forces; 417 heat stroke cases 1625 other heat injuries cases*	<u>Women</u> Heat stroke: 0.16† Other heat injuries: 1.54† <u>Men</u> Heat stroke: 0.35† Other heat injuries: 1.48†
36 37 38 39 40	Army Medical Surveillance Activity, 2017[47]	USA	Descriptive epidemiology; 2016	US Armed Forces; 401 heat stroke cases 2135 other heat injuries cases*	<u>Women</u> Heat stroke: 0.19† Other heat injuries: 1.90† <u>Men</u> Heat stroke: 0.33†

1				Other heat injuries: 1.61†
2				
3				
4	Army Medical	USA	Descriptive epidemiology;	Women
5	Surveillance Activity,		US Armed Forces;	Heat stroke: 0.25†
6	2018[48]		464 heat stroke cases	Other heat injuries: 1.38†
7			1699 heat exhaustion cases	Men
8				Heat stroke: 0.41†
9				Other heat injuries: 1.41†

10 § Proportions and incidences reported are of the total cases reported in the articles

11 # Incidence rate reported per 100,000 person-years.

12 ‡ Incidence rate per 100,000 person- months.

13 † Incidence rate reported per 1000 person-years.

14 * Other heat injuries include “heat exhaustion” and “unspecified effects of heat”.

15 ¶ heat injuries include heat stroke and other heat injuries.

16 US = United States of America; 2006 to date, heat injuries was reported in the US Armed Forces (Army, Navy, Air Force and Marine Corps).

17 UK = United Kingdom; USA = United States of America

Supplemental Table 3: Quality assessment of included studies using the quality assessment tool for studies with diverse designs (QATSDD)

QATSDD Criteria	1	2	3	4	5	6	7	8	9	10	11	12	Total score	% of total score
Dickinson' 94[29]	0	1	2	0	1	3	0	0	3	2	0	2	14/36	38.9
AMSA'98[30]	2	1	1	0	0	0	0	0	2	2	0	0	8/36	22.2
AMSA'00[33]	2	1	2	0	0	1	0	0	2	3	0	0	11/36	30.6
AMSA'02[31]	3	0	2	0	1	1	0	0	2	0	2	0	11/36	30.6
AMSA'03[32]	2	1	1	0	1	1	0	0	2	2	0	0	10/36	27.8
Carter et al' 05[34]	3	3	3	2	2	3	1	2	3	3	2	0	27/36	75
AMSA'06[36]	2	1	1	0	1	1	0	0	2	2	0	0	10/36	27.8
Wallace et al' 06[49]	3	3	3	2	2	3	1	2	3	3	2	2	29/36	80.6
AMSA'07[37]	1	1	1	0	0	1	0	0	2	2	0	0	8/36	22.2
AMSA' 08[38]	1	1	1	0	0	1	0	0	2	2	0	0	8/36	22.2
AMSA' 09[39]	1	1	1	0	0	1	0	0	2	2	0	0	8/36	22.2
AMSA' 10[40]	1	1	2	0	0	1	0	0	2	2	0	2	11/36	30.6
AMSA' 11[41]	2	1	2	0	0	1	0	0	2	2	0	2	12/36	33.3
Druyan et al'12[12]	3	3	3	1	0	2	0	3	3	2	2	1	23/36	63.9
AMSA' 12[42]	2	1	2	0	0	1	0	0	2	2	0	2	12/36	33.3
AMSA' 13[43]	2	2	2	0	0	2	0	0	2	2	0	2	14/36	38.9
AMSA' 14[44]	2	2	2	0	0	2	0	0	2	3	0	2	15/36	41.7
Lisman et al,'14 [27]	3	3	3	2	2	3	2	3	3	3	3	3	33/36	91.7
AMSA' 15[45]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4
Bedno et al, 2015[35]	3	3	3	2	2	3	3	3	3	3	3	3	34/36	94.4
Kazman et al' 15[28]	3	3	3	2	2	3	2	3	3	3	3	3	33/36	91.7
AMSA' 16[46]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4
AMSA' 17[47]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4
AMSA' 18[48]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4

QATSDD Criteria

- (1) Theoretical framework;
 - (2) Aims/objectives;
 - (3) Description of research setting
 - (4) Sample size;
 - (5) Representative sample of target group
 - (6) Procedure for data collection
 - (7) Rationale for choice of data collection tool(s)
 - (8) Detailed recruitment data
 - (9) Fit between research question and method of data collection (Quantitative only)
 - (10) Fit between research question and method of analysis (Quantitative only)
 - (11) Good justification for analytical method selected
 - (12) Strengths and limitations.
- QATSDD rating scale: 0=not at all; 1=very slightly; 2=moderately; 3=complete; AMSA = Army Medical Surveillance Activity*



PRISMA 2009 Checklist

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Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4,5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7, 8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7, supplementary file 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Figure 1
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8, 9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	9



PRISMA 2009 Checklist

Page 1 of 2

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10, Supplementary file 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	15
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10, 11, 12, 13, 14, Figure 1 and Figure 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	15
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18, 19
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16, 17, 18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	22



PRISMA 2009 Checklist

For more information, visit: www.prisma-statement.org. Page 2 of 2

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BMJ Open

A Systematic Review of the Gender Differences in the Epidemiology and Risk Factors of Exertional Heat Illness and Heat tolerance in the Armed Forces

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-031825.R3
Article Type:	Original research
Date Submitted by the Author:	06-Feb-2020
Complete List of Authors:	Alele, Faith; James Cook University, College of Healthcare Sciences Malau-Aduli, Bunmi; James Cook University, College of Medicine and Dentistry Malau-Aduli, Aduli; James Cook University, College of Public Health, Medical and Veterinary Sciences Crowe, Melissa; James Cook University, Division of Tropical Health and Medicine
Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Sports and exercise medicine
Keywords:	OCCUPATIONAL & INDUSTRIAL MEDICINE, ACCIDENT & EMERGENCY MEDICINE, Heat Stroke, Armed Forces, Women

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3 1 **A Systematic Review of the Gender Differences in the Epidemiology and Risk Factors of**
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5 2 **Exertional Heat Illness and Heat tolerance in the Armed Forces**
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7

8 3 **Type of article:** Review
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56 34 Word count: 3993
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3 36 **Abstract**
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6 37 **Objectives:** This review aimed to describe the epidemiology of all heat related illnesses in
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9 38 women compared to men in the armed forces and to identify gender-specific risk factors and
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11 39 differences in heat tolerance.
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14 40 **Design:** A systematic review of multiple databases (MEDLINE, Emtree, CINAHL,
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16 41 PsycINFO, Informit, and Scopus) was conducted from the inception of the databases to 1 April
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18 42 2019 using the preferred reporting items for systematic review and meta-analysis (PRISMA)
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20 43 guidelines.
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24 44 **Eligibility criteria:** All relevant studies investigating and comparing heat illness and heat
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26 45 tolerance in women and men in the armed forces were included in the review.
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29 46 **Results:**
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32 47 Twenty-four (24) studies were included in the systematic review. The incidence of heat stroke
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34 48 in women ranged from 0.10 to 0.26 per 1000 person-years, while the incidence of heat stroke
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36 49 ranged from 0.22 to 0.48 per 1000 person-years in men. The incidence of other heat illnesses
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38 50 in women compared to men ranged from 1.30 to 2.89 per 1000 person-years vs 0.98 to 1.98
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40 51 per 1000 person-years. The limited evidence suggests that women had a greater risk of
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42 52 exertional heat illness compared to men. Other gender-specific risk factors were slower run
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44 53 times and body mass index. Although there was a higher proportion of women who were heat
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46 54 intolerant compared to men; this finding needs to be interpreted with caution due to the limited
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48 55 evidence.
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53 56 **Conclusion:** The findings of this review suggest that men experienced a slightly higher
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55 57 incidence of heat stroke than women in the armed forces. In addition, the limited available
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57 58 evidence suggests that a higher proportion of women were heat intolerant and being a female
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3 59 was associated with a greater risk of exertional heat illnesses. Given the limited evidence
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5 60 available, further research is required to investigate the influence of gender differences on heat
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7 61 intolerance and heat illness.
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10 62 **Article summary**

13 63 **Strengths and limitations of this study**

- 17 64 • This is the first known systematic review investigating the impact of gender on
18 65 exertional heat illness and heat tolerance in the armed forces.
- 21 66 • We conducted a comprehensive search and identified potential risk factors that are
22 67 associated with exertional heat illness.
- 25 68 • Most of the included studies utilized retrospective data with an increased likelihood of
26 69 misclassification bias which may have underestimated or overestimated the association
27 70 between heat-related illness and risk factors.

31 71 **Trial registration:** None

34 72 **Key words**

37 73 Heat stress; Heat stroke; Heat exhaustion; Heat tolerance; Women; Armed Forces
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80 Introduction

81 Heat illnesses are disorders that arise after prolonged exposure to heat/humidity and/or
82 increased physical activity.[1] When body temperature rises, conduction, convection, radiation
83 and evaporation mechanisms help to cool the body and maintain normothermia.[1] However,
84 heat loss is susceptible to prevailing environmental conditions and type of clothing worn.
85 Without adequate cooling heat illnesses may occur including exercise-associated muscle
86 cramps (EAMC), heat syncope, heat exhaustion and heat stroke, a potentially life-threatening
87 disorder.[1]

88 Heat stroke is a medical emergency.[2] It is characterized by elevated core temperature of 40°C
89 and above, central nervous system disturbances and multi-organ damage that may result in
90 death.[2] Heat stroke has been classified as either classic or exertional.[3] Classic heat stroke
91 is insidious in onset and occurs in vulnerable populations such as young children, the elderly
92 and patients with chronic diseases.[4] On the other hand, exertional heat stroke occurs more
93 rapidly and affects healthy, active people such as athletes, factory workers, construction
94 workers, agricultural workers, firefighters and armed forces personnel.[5] The workers in these
95 industries often require high levels of physical exertion to perform jobs and tasks. A
96 combination of rigorous activities and extreme exposure to heat place the workers at increased
97 risk of heat stroke.[6]

98 Among armed forces personnel, exertional heat illness continues to pose as a significant cause
99 of morbidity and mortality. [7] Operations and training may involve exposure to high ambient
100 temperature and heavy workload which may result in heat illness.[7] Historically, men have
101 occupied military roles and responsibilities with fewer proportion of women in the armed
102 forces.[8] However, more women are joining the armed forces globally following the inclusive
103 approach to recruiting and creation of more roles for women.[9] Women are required to operate

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3 104 in austere environments with heat illnesses becoming more frequent.[9] This has raised the
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5 105 question about gender differences in thermoregulation during heat stress.[9] Evidence suggests
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7 106 that women differ from men in thermal responses to heat.[10] This difference may be because
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9 107 women have a lower rate of whole-body evaporative heat loss, higher body fat mass, body
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11 108 mass ratio,[11] number of sweat glands and lower aerobic fitness.[12] Also, hormonal
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13 109 variations due to menstrual cyclic patterns and the use of contraceptive pills may be associated
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15 110 with the differences in response to heat stress.[13]

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20 111 When exertional heat illness occurs, it may be challenging to determine if an individual may
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22 112 return to duty. An inaccurate determination of complete recovery among armed forces
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24 113 personnel may negatively impact military readiness.[14] While, there are no evidence-based
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26 114 recommendations for return to duty, the American College of Sports Medicine (ACSM)
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28 115 guidelines states that exertional heat stroke patients may return to duty after re-establishing
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30 116 heat tolerance.[15] Individuals vary in their ability to cope with heat stress and the inability to
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32 117 withstand heat stress during exertion in hot environments is defined as heat intolerance.[2]
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34 118 Evidence suggests that heat intolerance may be as a direct result of heat stroke or due to
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36 119 predisposing inherent factors (genetics).[2] However, the objective criteria or measure for
37
38 120 defining heat tolerance or intolerance remains a subject of controversy.[14] The current return
39
40 121 to duty guidelines for military personnel varies across countries.[16] For example, in the United
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42 122 States, the military return to duty process is based on clinical assessments with gradual
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44 123 acclimatization and re-introduction of duties.[17] By contrast, return to duty in the Israeli
45
46 124 Defence Force requires a heat tolerance test to determine if an individual is heat tolerant.[18]
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48 125 Therefore, it is important to develop evidence-based return to duty protocols across the globe.
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50 126 The Israeli Defence Force originally developed the heat tolerance test in 1979 as an index of
51
52 127 the ability of soldiers to cope with exertional heat.[18] Individuals who have suffered heat
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54 128 stroke are sent for a heat tolerance test after a minimum recovery period of 6 to 8 weeks as part

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3 129 of the return to duty process.[18] Criteria used to define heat intolerance include an elevation
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5 130 in rectal temperature above 38.5°C and heart rate above 150 bpm or when rectal temperature
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8 131 or heart rate fails to stabilize during the test. The heat tolerance test criteria are based on
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10 132 previous studies by Shapiro et al.[19] which utilised only male military participants.[18, 19]
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12 133 While the test may be considered as a useful tool to determine return to duty and to prevent
13
14 134 subsequent exertional heat stroke, [18,19] there is no consensus on the validity of the tool as a
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16 135 diagnostic test for heat tolerance.[14] Furthermore, the heat tolerance test does not account for
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18 136 predicting factors such as gender.[14] Given the limitation, questions have been raised about
19
20 137 the validity of the protocol in determining return to duty for females in the armed forces. It has
21
22 138 been suggested that more research is required to determine whether or not a new protocol
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24 139 should be developed for women.[12]

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29 140 As restrictions on gender based-exclusions from military specializations are lifted,[20] it is
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31 141 imperative to understand and evaluate exertional heat illness in women compared to men and
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33 142 identify the gender-specific risk factors. Furthermore, it is important to understand how women
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35 143 respond to the heat tolerance test compared to men. According to a recent review on the risk
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37 144 of heat illness in women compared with men in the general population, men are at increased
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39 145 risk of heat illness compared to women.[21] However, no previous review has investigated the
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41 146 epidemiology and risk factors of heat illness as well as gender responses to the heat tolerance
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43 147 test in men and women in the armed forces. Given that, heat illness can impact defence
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45 148 operational effectiveness and may result in acute loss of manpower and possible medical
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47 149 discharge from service,[22] the review should be conducted to inform policies.

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52 150 Therefore, the objective of this systematic review was to provide a comprehensive summary of
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54 151 the epidemiology of heat illness and heat intolerance in women and men in the armed forces.
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58 152 Specific aims were
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3 153 To determine the incidence and prevalence of heat illness in women compared to men
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5 154 in the armed forces:
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8 155 To identify gender differences in heat tolerance in the armed forces and
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11 156 To identify gender-specific predisposing risk factors associated with heat illness in the
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13 157 armed forces
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19 159 **Methods**

20 160 **Search Strategy**

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23 161 This review utilised the Preferred Reporting Items for Systematic Review and Meta-analysis
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25 162 (PRISMA) guidelines [23] to explore all literature published in English from the inception of
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27 163 the different databases to 1 April 2019. Databases searched were MEDLINE, CINAHL,
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29 164 PsycINFO, Emcare, Informit and Scopus. A preliminary search was conducted in Medline,
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31 165 Emcare and CINAHL to identify relevant keywords contained in the titles, abstracts and subject
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33 166 descriptors. These search terms were used to conduct the search in other databases without
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35 167 subject headings. The search strategy used in Medline is presented in supplemental Table 1.
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37 168 No review protocol exists.
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45 169 **Eligibility criteria**

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48 170 Studies included in the review were assessed according to the following inclusion criteria: Peer-
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50 171 reviewed literature comparing heat illness in women to men in the armed forces or reporting
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52 172 heat tolerance in women and men of the armed forces. Exclusions included literature discussing
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54 173 heat illness in other occupations, or studies where data on heat illness in women could not be
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56 174 separated from men or studies reporting heat illness in men or literature reviews, conference
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3 175 abstracts and grey literature. In addition, additional primary data sources were identified from
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5 176 the reference lists of the included studies using a hand-search technique (Figure 1).
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8 177 **Selection of studies and data extraction**

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11 178 FA and BMA identified all included studies and data extraction was performed using a standard
12
13 179 abstraction form. Data extracted from the studies included: study location and design,
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15 180 population, proportion and incidence of heat illnesses, factors associated with heat illness and
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17 181 heat tolerance, and heat tolerance in men and women. All authors cross-checked the extracted
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19 182 data for consistency.
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23 183 **Quality assessment**

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26 184 The methodological quality assessment was assessed by FA in consultation with MC using the
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28 185 modified quality assessment tool for studies with diverse designs (QATSDD) critical appraisal
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30 186 tool.[24] Any disagreement about any article was reviewed by BMA and AMA and discussed
31
32 187 until consensus was reached. The QATSDD tool is a 16-item tool which assesses the quality
33
34 188 of diverse studies (both quantitative and qualitative).[24] The tool was modified to exclude two
35
36 189 items relating to qualitative studies as well as two items relating to quantitative studies that did
37
38 190 not to the studies included in the review. The items excluded comprised statistical assessment
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40 191 of the reliability and validity of measurement tool(s) (Quantitative only), fit between stated
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42 192 research question and format and content of data collection tool e.g. interview schedule
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44 193 (Qualitative), assessment of reliability of analytical process (Qualitative only) and evidence of
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46 194 user involvement in design. Each criterion in the modified QATSDD tool was awarded a score
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48 195 of 0 to 3 with 0 = not at all, 1 = very slightly, 2 = moderately and 3 = complete. The scores of
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50 196 each criterion were summed to assess the methodological quality of included studies with a
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52 197 maximum score of 36. The criteria included were (1) theoretical framework; (2) statement of
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54 198 aims/objectives; (3) description of research setting; (4) evidence of sample size; (5)
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3 199 representative sample of target group of a reasonable size, (6) description of procedure for data
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5 200 collection; (7) rationale for choice of data collection tool(s); (8) detailed recruitment data; (9)
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7 201 fit between research question and method of data collection (Quantitative only); (10) fit
8
9 202 between research question and method of analysis (Quantitative only); (11) good justification
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11 203 for analytical method selected; and (12) strengths and limitations. For ease of interpretation,
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13 204 the scores were converted to percentages and classified as low (<50%), medium (50-80%) or
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15 205 high (>80%) quality of evidence.
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20 206 **Patient and public involvement**

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23 207 Patients and the public were not involved in the design or planning of the study.
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26 208 **Data analysis and synthesis**

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29 209 In this review, the International Classification of Diseases ICD 9 or ICD 10 diagnosis codes
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31 210 [25, 26] for the effects of heat and light were used to classify heat illnesses. All included studies
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33 211 utilized either the ICD 9 or ICD 10 codes to classify heat illnesses depending on the year of
34
35 212 publication. Heat illnesses were categorised as heat stroke and other heat illnesses. Heat stroke
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37 213 was defined using the ICD diagnosis codes 992.0 (ICD 9) and T67.0 (ICD 10). While other
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39 214 heat illnesses were defined as heat exhaustion (992.3-5, T67 3-5) and unspecified effects of
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41 215 heat and light (992.9 and T67.9). In addition, some studies presented findings for all heat illness
42
43 216 without categorizing them into heat stroke and other heat illnesses. These findings were
44
45 217 presented separately. Incidence rates and proportions were extracted from the data reported in
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47 218 each study and used for the analysis in this review. Due to the heterogeneity of the included
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49 219 studies, a meta-analysis was not conducted.
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223 **Results**

224 An initial search identified 3816 papers. After removing duplicates, screening titles and
225 abstracts, 47 papers remained for full-text review with twenty-four (24) included in the
226 systematic review (Figure 1). Twenty-two (22) of the reviewed articles originated from the
227 United States of America (USA), while the other two studies were conducted in the United
228 Kingdom (UK) and Israel respectively (Supplemental Table 2). All included studies were
229 conducted among armed forces personnel, however, two studies included university staff and
230 armed forces personnel in the studies.[27, 28] Twenty- one (21) articles examined heat illnesses
231 and injuries in women and men. Seven (7) of these studies described all heat -related illnesses
232 in men and women,[29-35] while 13 studies included information on heat stroke and other heat
233 injuries in relation to both genders.[36-48] Four (4) studies identified gender-specific risk
234 factors associated with heat stroke,[31, 34, 35, 49] and three (3) studies compared heat
235 tolerance in men and women.[12, 27, 28]

236 **Incidence of heat stroke in women compared to men in the armed forces**

237 Thirteen studies conducted among US army personnel compared the incidence of heat stroke
238 between men and women.[36 – 48] The incidence of heat stroke among females ranged from
239 0.10 to 0.26 per 1000 person-years. Among males, the incidence of heat stroke ranged from
240 0.22 to 0.48 per 1000 person years (Figure 2). Between 2015 and 2018, the incidence of heat
241 stroke increased steadily for both men and women.

242 **Incidence of other heat illnesses in women compared to men in the armed forces**

243 The incidence of other heat illnesses was reported by 13 studies conducted by the US Army.
244 [36 – 48] The incidence of other heat illnesses in women ranged from 1.30 to 2.89 per 1000
245 person-years. In men, the incidence rate of other heat illness ranged from 0.98 to 1.98 per 1000
246 person years (Figure 3).

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3 **247 Incidence and prevalence of all heat illnesses in women compared to men**
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6 248 Table 1 shows the proportions and incidences of all heat-related illness in men and women in
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8 249 the armed forces. Five (5) studies reported higher incidences and proportions of all heat illness
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10 250 in men compared to women[29, 31, 32, 34, 35] while two studies reported higher incidences
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13 251 of all heat illness in women.[30, 33]
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For peer review only

252 **Table 1: Incidence and Proportion of all heat related illnesses in women and men in the Armed Force**

Reference, year	Country	Study design	Study duration	Population	ICD codes	All heat injuries	
						Women	Men
Dickson. 1994[29]	UK	Descriptive epidemiology	1981-1991 (10yrs)	Royal Air force, Royal Navy and Army (1448 cases)	ICD-9-CM: 992.0 – 992.9	11.43*	41.87*
Army Medical Surveillance Activity, 1998[30]	USA	Descriptive epidemiology	1997 – 1998 (1 year)	US Army (1433 cases) 1997	ICD-9-CM: 992.0 – 992.9	12.8†	8.6†
				1998		15.8†	12.0†
Army Medical Surveillance Activity, 2000[33]	USA	Descriptive epidemiology	1997 – 1999 (2 years)	US Army and Marine Corps (3386 cases)	ICD-9-CM: 992.0 – 992.9		
				Army (1896 cases) Marine Corps (1104 cases)		2.0†	1.5†
Army Medical Surveillance Activity, 2002[31]	USA	Descriptive epidemiology	1990 – 1997 (7 years)	US Army (2290 cases)	ICD-9-CM: 992.0 – 992.9	14.0%§	86.0%§
		Case-control	1998 – 2001 (3 years)	US Army (5021 cases and 10,042 controls)		20.7%§	79.3%§
Army Medical Surveillance Activity, 2003[32]	USA	Descriptive epidemiology	2002 (1 year)	US Army (1816 cases)	ICD-9-CM: 992.0 – 992.9	3.5†	5.1†
Carter et al, 2005[34]	USA	Cross-sectional	1980 – 2002 (22 years)	US Army (5246 cases)	ICD-9-CM: 992.0 – 992.9	13.7%§	86.3%§
Bedno et al, 2014[35]	USA	Analytical cross-sectional	2005 - 2006	US Armed Forces (80 exertional heat illness cases) 9455 men 1913 women	ICD-9-CM: 992.0 – 992.9	0.680%	0.71%

253 § Proportions and incidences reported are of the total cases reported in the articles
 254 * Incidence rate reported per 100,000 person-years; † Incidence rate per 100,000 person- months; ‡ Incidence rate reported per 1000 person-years
 255 UK = United Kingdom; USA = United States of America

256 Gender-specific risk factors for heat illness

257 Three (3) studies identified the gender-specific risk factors that were associated with heat
 258 illness (Table 2). [31, 34, 49] Two of the studies compared the risk of heat illness between
 259 males and females while one study identified risk factors within each gender. In the two studies
 260 that compared the risk of heat illness by gender, females had a greater risk of experiencing heat
 261 illness (OR 1.5, 95% CI 1.4 to 1.7 and IDR 1.21, 95% CI 1.09 to 1.40) compared to males.[31,
 262 34] Within gender, males with body mass index (BMI) of $\geq 26 \text{ kgm}^{-2}$ had a greater risk of
 263 experiencing heat illness compared to males with BMI $< 22 \text{ kgm}^{-2}$ (OR 2.10, 95% CI 1.59 to
 264 2.78).[49] In addition, males with run times of ≥ 12.9 minutes had almost six times the risk of
 265 exertional heat illness compared to males with run times of < 10.3 minutes (OR 5.61, 95% CI
 266 1.92 to 6.85). While females with run times of ≥ 6.9 minutes had five times the risk of
 267 exertional heat illness compared to females with run times of < 5.8 minutes (OR 5.30, 95% CI
 268 1.59 to 17.64).[49]

269 **Table 2: Gender-specific risk factors associated with heat illness**

Reference, year	Country	Study design and duration	Study population	Risk factors	OR or IDR (95% CI)
Army Medical Surveillance Activity, 2002[31]	USA	Case-control 1998 – 2001 (3 years)	US Army 5021 cases and 10,042 controls	Female	1.5 (1.4 - 1.7)
Carter et al, 2005[34]	USA	Cross-sectional 1980 – 2002 (22 years)	US Army 5246 cases of heat illness; 4521 males and 725 females	Female	1.21 (1.09 – 1.40)
Wallace et al, 2006[49]	USA	Case-control 1988 – 1996 (8 years)	US Marine Corps Male (627 cases and 1679 controls) Female (49 cases and 123 controls)	BMI $\geq 26 \text{ kg/m}^2$ (males) Run time ≥ 12.9 minutes (males) Run time ≥ 6.9 minutes (females)	2.10 (1.59 – 2.78) 5.61 (3.73 – 8.45) 5.30 (1.59 – 17.64)

270 Odds ratio; IDR = Incidence density ratio; BMI= Body Mass Index; CI=Confidence Interval; USA = United States of America

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3 **271 Heat tolerance in women and men**
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6 272 Three studies compared heat tolerance classification in males and females using the HTT
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8 273 developed by the Israeli Defence Force (Table 3). [12, 27, 28] Druyan et al. investigated gender
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10 274 differences in Israeli Defence Force personnel who had sustained heat injury. The study
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12 275 reported that 67% of the women were found to be heat intolerant compared to 26% of their
13
14 276 male counterparts.[12] In the studies conducted by Lisman et al. and Kazman et al. the study
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16 277 population comprised of participants from the university and military communities who had
17
18 278 either no heat illness or a previous history of heat illness. Both studies reported that a greater
19
20 279 proportion of women were classified as heat intolerant compared to men (42% vs 27% and
21
22 280 45% vs 18% respectively). [27, 28]
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30 **282 Table 3: Heat tolerance in women and men**
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Reference, year	Country	Study design and duration	Study population	Heat in tolerance rate Women	Heat in tolerance rate Men
Druyan et al, 2012[12]	Israel	Retrospective cross-sectional 2008 – 2010 (2 years)	170 males and 9 females	66.67%	25.79%
Lisman et al, 2014 [27]	USA	Analytical cross-sectional (duration not stated)	Military and university community members; 34 males and 12 females	42%	27%
Kazman et al, 2015[28]	USA	Analytical cross-sectional (duration not stated)	Military and university community members; 55 males and 20 females	45%	18%

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288 **Assessment of methodological quality**

289 The QATSDD scores ranged from 22.2% to 94.4% (Supplemental Table 3). Only six studies
290 scored above 50% and included details about recruitment, data analysis, strengths and
291 limitations of the research. The other studies had lower scores because they lacked detailed
292 justification for the analytical methods, data collection, analysis, strengths and limitations.
293 However, results of the methodological assessment should be interpreted with caution.
294 Although the tool assesses methodological quality, it is more likely to be dependent on how
295 the paper was written. In this review, 70% of the studies included were military reports on heat-
296 related illnesses in the Armed Forces. These reports were published in a peer-reviewed journal
297 and were retrospective analyses of data collected by Defence Medical Surveillance Systems.
298 These studies may not have reported details about data collection, strengths and limitations,
299 but they presented valid information on heat-related illness.

300

301 **Discussion**

302 The findings of this systematic review suggest that men have a slightly higher incidence of heat
303 stroke compared to women. By contrast, women report a slightly higher incidence of other heat
304 illness compared to men. In addition, among studies that reported all heat illnesses (where heat
305 stroke and other heat illnesses have been combined), there was a higher rate of all heat illnesses
306 in men compared to women as evidenced by the outcomes reported in five (5) of seven (7)
307 studies. However, women had a greater risk of experiencing exertional heat illness and were
308 more likely to be heat intolerant compared to men. Other gender-specific risk factors were
309 longer run times for both men and women while higher BMI was associated with exertional
310 heat illness for men only. However, the association between these factors and exertional heat
311 illness is weak given the small number of articles that investigated the relationship.

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3 312 Furthermore, despite the higher proportion of heat intolerance reported among women; this
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5 313 finding should be interpreted with caution given the small sample size for females in the
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8 314 included studies and the differences in occupations of the women in the three studies. One
9
10 315 study included women in the armed forces with a previous history of heat stroke, [12] while
11
12 316 the other two studies recruited women from the general population as well as military members
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14
15 317 with either no history or a previous history of heat stroke. [27, 28]

18 318 **Incidence and prevalence of exertional heat illnesses in women compared to men**

20 319 In this review, women had a lower incidence of heat stroke, but a slightly higher incidence of
21
22 320 other heat illness compared to men. The reported lower incidence of heat stroke/higher
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24 321 incidence of other heat illness in women compared to men could be because women in the
25
26 322 military in the United States were excluded from combat positions until 2013 when the ban
27
28 323 was lifted.[20] Evidence in the literature suggests that service members who were engaged in
29
30 324 roles such as infantry or gun crew had an increased risk of heat illness, possibly reflecting a
31
32 325 greater risk of heat illness for those in combat roles.[34] Furthermore, during military training
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34 326 exercises, men may have comparatively tolerated working in the heat beyond the endurance
35
36 327 limits.[22] This finding was re-echoed in a previous systematic review that men in the general
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38 328 population had a higher rate of all types of heat illnesses compared to women.[21] Although
39
40 329 the incidence of heat stroke was lower in women compared to men in this review, the incidence
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42 330 of heat stroke among women has increased over the past four years. This implies that as more
43
44 331 women engage in specialised military roles their risk of exertional heat illness increases.

51 332 **Gender-specific risk factors for heat illness**

54 333 Despite the lower incidence of heat stroke, women had a greater risk of exertional heat illnesses
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56 334 compared to men.[30, 33] In addition one study attempted to investigate intra gender risk
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58 335 factors for exertional heat illness.[49] The slower run time duration was associated with
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3 336 exertional heat illness among males and females respectively, while higher BMI was identified
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5 337 as a risk factor among males only.[49] The higher risk of exertional heat illnesses in women
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7 338 may likely be due to differences in physiological and physical characteristics between men and
8
9 339 women.[50] Physiological characteristics such as hormones, use of contraceptive pills and
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11 340 lower evaporative heat loss may make women more susceptible to heat illness.[11, 13]
12
13 341 However, conflicting evidence suggests that in highly trained women, exercise performance
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15 342 and heat loss is not affected by the menstrual cycle phase but is impaired in humid
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17 343 conditions.[51] In addition, physical characteristics such as lower aerobic fitness is a predictor
18
19 344 of exertional heat illness.[50] Generally, women have lower aerobic fitness levels and lower
20
21 345 overall work capacity which may contribute to the increased risk of exertional heat illness.[50]
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23 346 Individuals with low aerobic fitness levels are likely to exert themselves beyond their physical
24
25 347 limit and are at increased risk of heat illness.[52] Other intra gender risk factors that were
26
27 348 identified were longer run time duration and higher BMI.[49] Evidence suggests that slower
28
29 349 run time duration which may be a reflection of lower aerobic fitness and higher BMI increases
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31 350 the risk of heat illness.[49, 53] However, the evidence is limited given that this was reported
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33 351 by only one study.[49]

352 **Heat tolerance in women and men**

353 The risk of heat illness is dependent on thermal tolerance.[2] To determine the recovery and
354 return to duty for HTT is conducted for members of the armed forces after a heat stroke
355 event.[18] The test criteria define heat intolerance as peak rectal temperature > 38.5°C, peak
356 heart rate > 150 bpm, or the inability of these values to reach a plateau.[18, 19] Although, in
357 the three studies, a higher proportion of women were classified as heat intolerant; this evidence
358 should be interpreted with caution given that the female populations included in each study
359 varied with respect to heat illness and occupations.[12, 27, 28] However, the studies
360 acknowledged that gender differences in cardiorespiratory fitness, body fat percentage and

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3 361 surface area to mass ratio may account for the higher intolerance rates in women.[12, 27, 28]
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5 362 In addition, the three studies reported using the Israeli Defence Force heat tolerance test
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8 363 protocol and given that the test protocol was developed using male participants, there may be
9
10 364 a need to re-evaluate the criteria for women to reduce false-positive results.[12, 27, 28]
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12 365 Furthermore, incomplete recovery and inaccurate determination of return to duty may
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14 366 negatively affect military operations and may end the careers of armed forces personnel.[14]
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17 367 Therefore, it is important to ensure that the heat tolerance test is valid and fair for females if it
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19 368 is to be used to determine return to duty for females in the armed forces.
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22 369 **Strengths and limitations**

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25 370 To the authors' current knowledge, this is the first known systematic review investigating
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27 371 gender differences in exertional heat illness and heat tolerance in the armed forces. In addition,
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29 372 we identified potential gender-specific risk factors that are associated with exertional heat
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31 373 illness. However, the heterogeneity in the study designs contributed to the variable
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33 374 methodological quality of the included studies. Most of the articles in this review were military
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35 375 reports and may not be considered of high methodological quality when assessed using a formal
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37 376 critical appraisal tool. Also, most of the included studies utilized retrospective data as the data
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39 377 source with an increased likelihood of incompleteness and inaccuracy. There is a likelihood
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41 378 that misclassification bias could have been introduced into the studies. Three studies that
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43 379 explored the risk factors associated with heat-related illness used retrospective data. [31, 34,
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45 380 49] The retrospective data may have been misclassified or incomplete at the time of entry and
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47 381 may have introduced misclassification bias into the studies. This type of bias may
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49 382 underestimate or overestimate the association between heat-related illness and risk factors.
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51 383 Although the gender-specific risk factors associated with heat illness were discussed; the
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53 384 review provided limited evidence of these factors, given the few numbers of studies that
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3 385 investigated the association. Furthermore, we included only studies published in English
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5 386 language; studies published in other languages were excluded.
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8 387 **Implication for policy and future research**

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11 388 This systematic review demonstrates that there is limited research on exertional heat illness in
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13 389 women in the armed forces. Although men had a higher incidence of heat stroke; women had
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15 390 a higher incidence of other heat illnesses. Further research is needed to establish if this reflects
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17 391 physiological or behavioural differences. In addition, the limited and inconclusive evidence
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19 392 suggests that more women were classified as heat intolerant compared to men using the Israeli
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21 393 Defence Force heat tolerance test protocol. The current criteria may be unfair to women given
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23 394 that it was developed using male participants. More research is needed to determine the gender
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25 395 differences in heat tolerance as well as to consider re-evaluating the heat tolerance test protocol
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27 396 or the development of a new protocol that considers gender-specific factors.[12] Given that the
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29 397 heat tolerance test was conducted in a laboratory setting, more research is needed to replicate
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31 398 the findings in field based setting.
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36 37 399 **Conclusion**

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40 400 In conclusion, this review suggests that men had a slightly higher incidence of heat stroke but
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42 401 women in the armed forces may have a greater risk of exertional heat illness. However, the
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44 402 current evidence is limited, and further research is required to investigate the influence of
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46 403 gender differences on heat tolerance and heat illness. In addition, further research is needed to
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48 404 evaluate the heat tolerance test protocol for women.
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52 405 **Authors' contribution**

53
54 406 All authors contributed substantially to the study concept, design, data extraction, quality
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56 407 assessment and writing of the manuscript.
57

58 408 **Conceptualization:** Faith O. Alele, Bunmi S. Malau-Aduli, Aduli E. Malau-Aduli, Melissa
59 409 Crowe
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3 410 **Methodology:** Faith O. Alele, Bunmi S. Malau-Aduli, Aduli E. Malau-Aduli, Melissa Crowe

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5 411 **Writing** - Original draft: Faith O. Alele

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7 412 **Writing – review & editing:** Faith O. Alele, Bunmi S. Malau-Aduli, Aduli E. Malau-Aduli,
8 413 Melissa Crowe

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10 414 All authors read and approved the manuscript for submission.

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17 418 **Patient consent for publication:** Not required

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25 422 **References**

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552 **Figure legends**

553 Figure 1: PRISMA flow chart of the study selection protocol

554 Figure 2: The incidence rate of exertional heat stroke between men and women in the armed
555 forces from 2006 to 2018

556 Figure 3: Incidence rate of other heat illnesses (including heat exhaustion and unspecified
557 effects of heat and light) between men and women in the armed forces from 2006 to 2018

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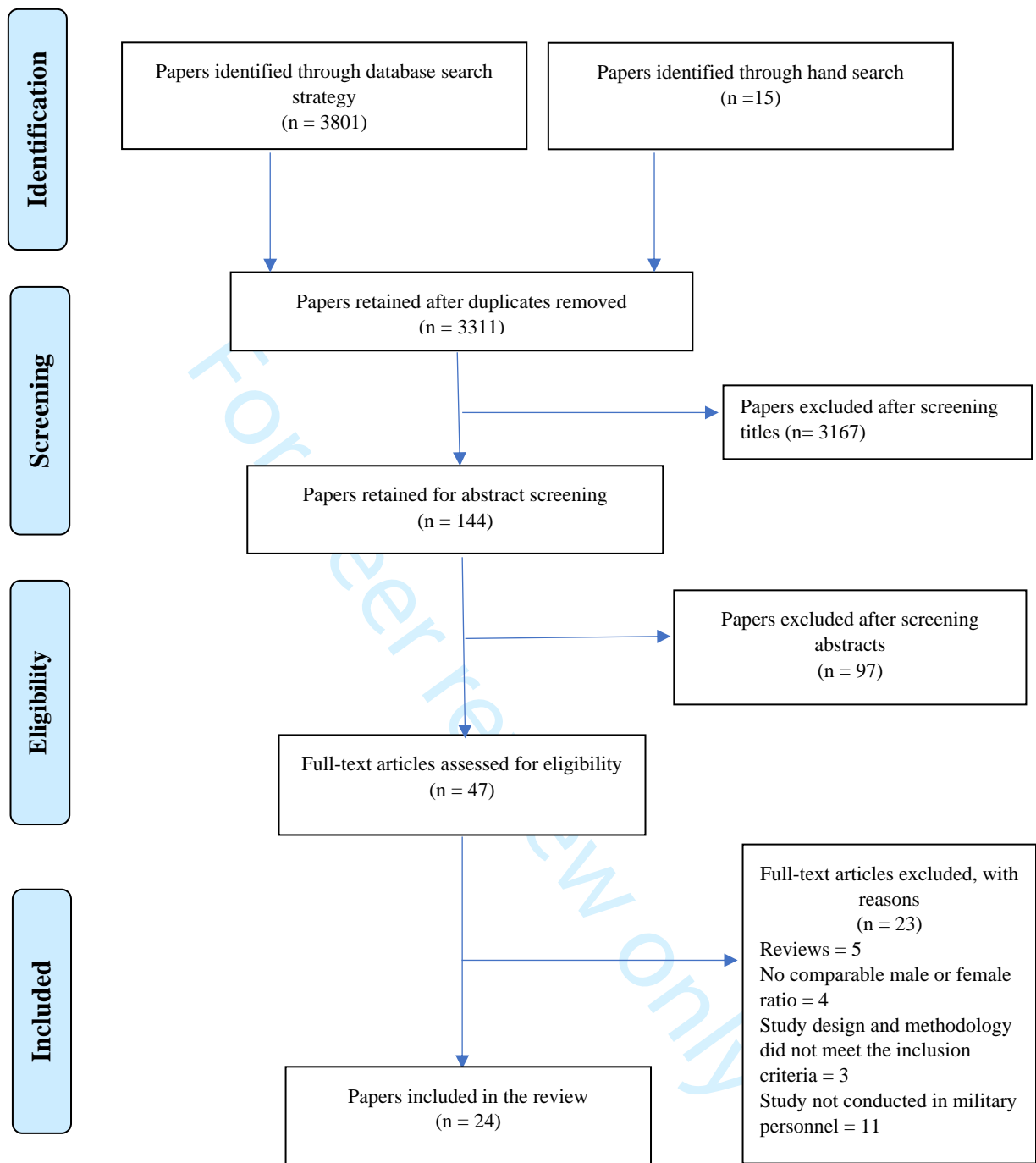


Figure 1: PRISMA flow chart of the study selection protocol

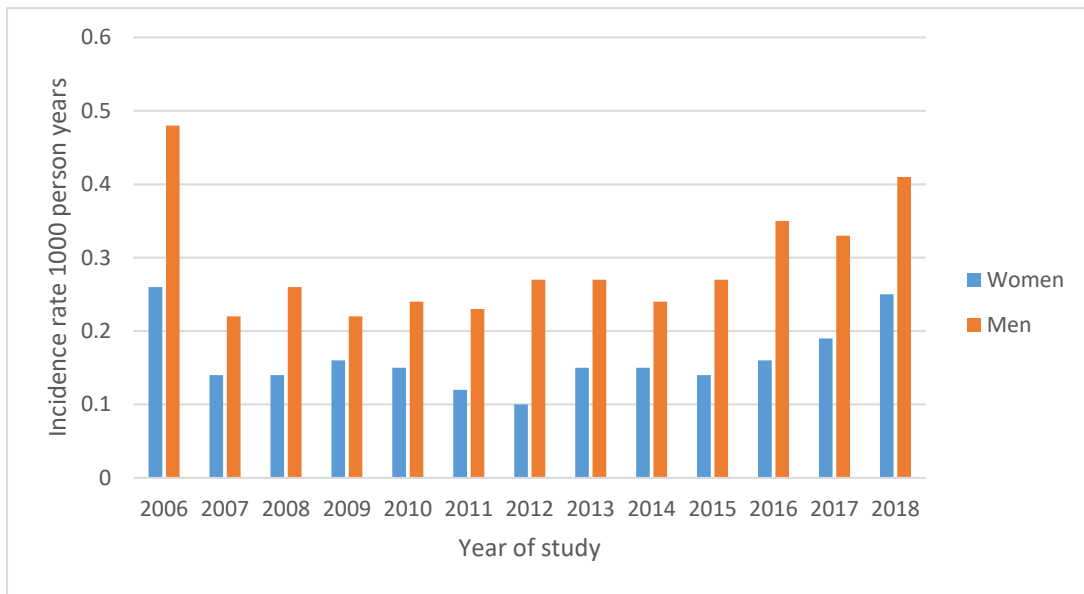


Figure 2

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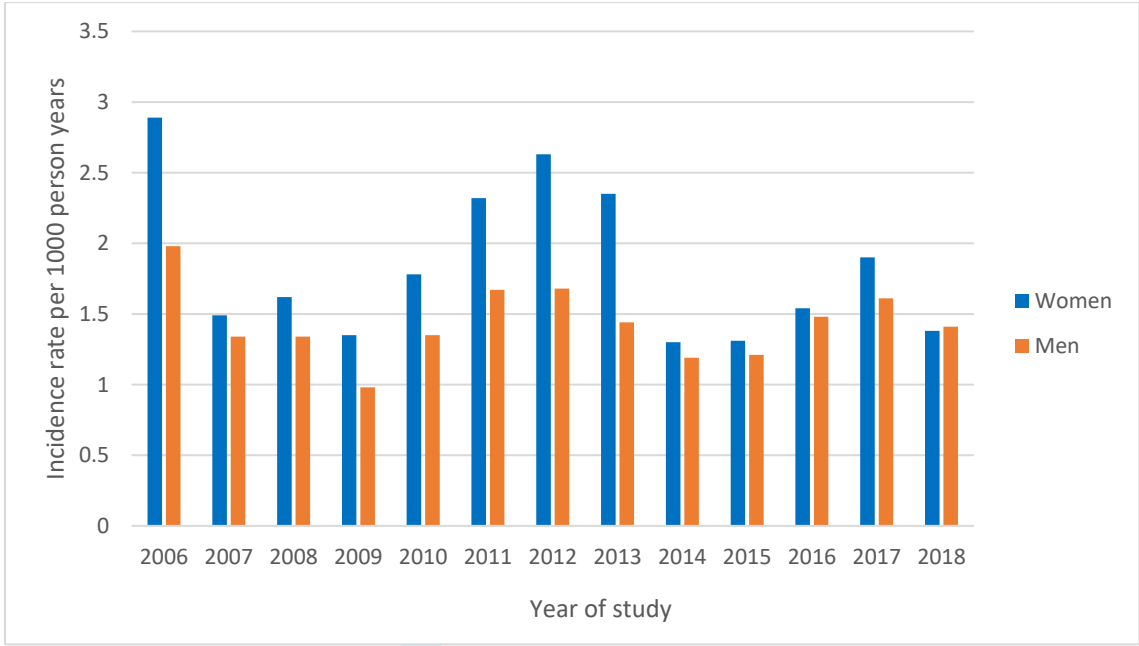


Figure 3

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Supplemental Table 1

Medline search strategy	
1.	Women (MeSH)
2.	Gender expression
3.	Gender identity (MeSH)
4.	Gender
5.	Wom\$
6.	Sex
7.	Heat strok*
8.	Heatstrok*
9.	Heat collapse
10.	Heat exhaustion
11.	Heat prostration
12.	Heat cramp
13.	Heat cramps
14.	Heat stress disorder
15.	Heat stress disorders (MeSH)
16.	Thermal stress
17.	Heat illness
18.	Heat illnesses
19.	Heat injury
20.	Heat injuries
21.	Heat related diseases
22.	Heat disorder
23.	Heat disorders
24.	Heat related disorder
25.	Heat related disorders
26.	Heat related illness
27.	Heat related illnesses
28.	Heat related injuries
29.	Heat related injury
30.	Environmental heat illness
31.	Heat stress
32.	Heat adaptation
33.	Heat tolerance
34.	Heat tolerances
35.	Heat resistance
36.	Thermal resistance
37.	Thermoresistance
38.	Thermotolerance (MeSH)
39.	Heat endurance
40.	1 OR 2 OR 3 OR 4 OR 5 OR 6
41.	7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39
42.	40 AND 41

Supplemental Table 2
Summary of all included studies

Reference, year	Country	Study design and duration	Population	Study findings [§]
Dickson. G, 1994[29]	UK	Descriptive epidemiology 1981-1991	Royal Airforce, Royal Navy and Army; 1448 all heat injuries cases [¶]	Women All heat injuries: 11.43 [#] Men All heat injuries: 41.87 [#]
Army Medical Surveillance Activity, 1998[30]	USA	Descriptive epidemiology; 1997 - 1998	US Army; 1433 all heat injuries cases (1997-1998) [¶] 1997 1998	Women All heat injuries: 12.8 [‡] Men All heat injuries: 8.6 [‡] Women All heat injuries: 15.8 [‡] Men All heat injuries: 12.0 [‡]
Army Medical Surveillance Activity, 2000[33]	USA	Descriptive epidemiology; 1997 - 1999	US Army and Marine Corps; 3386 all heat injuries cases [¶] Army (1896 cases) Marine Corps (1104 cases)	Women All heat injuries: 2.0 [†] Men All heat injuries: 1.5 [†] Women All heat injuries: 4.4 [†] Men All heat injuries: 2.0 [†]
Army Medical Surveillance Activity, 2002[31]	USA	Descriptive epidemiology 1990 - 1997 Case – control 1998 - 2001	US Army; 2290 all heat injuries cases [¶] US Army; 5021 cases and 10,042 controls (all heat injuries) [¶]	Women All heat injuries: 14.0% Men All heat injuries: 86.0% Women All heat injuries: 20.7% Men All heat injuries: 79.3%

				Risk factors Female: OR; 1.5 (1.4 - 1.7)
5	Army Medical Surveillance Activity, 2003[32]	USA	Descriptive epidemiology; 2002	US Army; 1816 all heat injuries cases [†]
6				Women All heat injuries: 3.5 [†]
7				Men All heat injuries: 5.1 [†]
10	Carter et al, 2005[34]	USA	Cross-sectional 1980 - 2002	US Army; 5246 all heat injuries cases [†] 4521 males and 725 females
11				Women All heat injuries: 13.7%
12				Men All heat injuries: 86.3%
13				Risk factors Female: IDR: 1.21 (1.09 – 1.40)
16	Army Medical Surveillance Activity, 2006[36]	USA	Descriptive epidemiology; 2005	US Armed Forces; 204 heat stroke cases 958 heat exhaustion cases
17				Women Heat stroke: 0.26 [†] Heat exhaustion: 2.89 [†]
18				Men Heat stroke: 0.48 [†] Heat exhaustion: 1.98 [†]
22	Wallace et al, 2005[49]	USA	Case-control 1988 - 1996	US Army; 5246 cases of heat illness; 4521 males and 725 females
23				Risk factors Females Run time ≥ 6.9 minutes: OR; 5.30 (1.59 – 17.64)
24				Males Run time ≥ 12.9 minutes: OR; 5.61 (3.73 – 8.45)
25				BMI ≥ 26 kg/m ² : OR; 2.10 (1.59 – 2.78)
30	Armed Forces Health Surveillance Branch, 2007[37]	USA	Descriptive epidemiology; 2006	US Armed Forces; 259 heat stroke cases 1854 heat exhaustion cases
31				Women Heat stroke: 0.14 [†] Heat exhaustion: 1.49 [†]
32				Men Heat stroke: 0.22 [†] Heat exhaustion: 1.34 [†]
36	Armed Forces Health Surveillance Branch, 2008[38]	USA	Descriptive epidemiology; 2007	US Armed Forces; 329 heat stroke cases 1853 heat exhaustion cases
37				Women Heat stroke: 0.14 [†] Heat exhaustion: 1.62 [†]
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Heat stroke: 0.26†
Heat exhaustion: 1.34†

Armed Forces Health Surveillance Branch, 2009[39]	USA	Descriptive epidemiology; 2008	US Armed Forces; 299 heat stroke cases 1467 heat exhaustion cases	<u>Women</u> Heat stroke: 0.16† Heat exhaustion: 1.35† <u>Men</u> Heat stroke: 0.22† Heat exhaustion: 1.78†
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Armed Forces Health Surveillance Branch, 2010[40]	USA	Descriptive epidemiology; 2009	US Armed Forces; 323 heat stroke cases 2038 other heat injuries cases*	<u>Women</u> Heat stroke: 0.15† Other heat injuries: 1.78† <u>Men</u> Heat stroke: 0.24† Other heat injuries: 1.35†
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Armed Forces Health Surveillance Branch, 2011[41]	USA	Descriptive epidemiology; 2010	US Armed Forces; 311 heat stroke cases 2576 other heat injuries cases*	<u>Women</u> Heat stroke: 0.12† Other heat injuries: 2.32† <u>Men</u> Heat stroke: 0.23† Other heat injuries: 1.67†
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Armed Forces Health Surveillance Branch, 2012[42]	USA	Descriptive epidemiology; 2011	US Armed Forces; 362 heat stroke cases 2652 other heat injuries cases*	<u>Women</u> Heat stroke: 0.10† Other heat injuries: 2.63† <u>Men</u> Heat stroke: 0.27† Other heat injuries: 1.68†
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Druyan et al, 2012[12]	Israel	Retrospective cross-sectional 2008 – 2010	Israeli Defence Forces; 170 males and 9 females	<u>Heat tolerance parameters</u> <u>Women</u> Heat intolerance rate: 66.6% <u>Men</u> Heat intolerance rate: 25.79%
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Armed Forces Health Surveillance Branch, 2013[43]	USA	Descriptive epidemiology; 2012	US Armed Forces; 365 heat stroke cases 2257 other heat injuries cases*	<u>Women</u> Heat stroke: 0.15† Other heat injuries: 2.35† <u>Men</u> Heat stroke: 0.27† Other heat injuries: 1.44†
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Armed Forces Health Surveillance Branch, 2014[44]	USA	Descriptive epidemiology; 2013	US Armed Forces; 324 heat stroke cases 1701 other heat injuries cases*	<u>Women</u> Heat stroke: 0.15† Other heat injuries: 1.30† <u>Men</u> Heat stroke: 0.24† Other heat injuries: 1.19†
Bedno et al, 2014[35]	USA	Analytical cross-sectional	US Armed Forces; 80 exertional heat illness cases	<u>Women</u> Heat illness: 0.680% <u>Men</u> Heat illness: 0.71%
Lisman et al, 2014[27]	USA	Analytical cross-sectional	Military and university community members; 34 males and 12 females	<u>Heat tolerance parameters</u> <u>Women</u> Heat intolerance rate: 42% <u>Men</u> Heat intolerance rate: 27%
Armed Forces Health Surveillance Branch, 2015[45]	USA	Descriptive epidemiology; 2014	US Armed Forces; 314 heat stroke cases 1410 other heat injuries cases*	<u>Women</u> Heat stroke: 0.14† Other heat injuries: 1.31† <u>Men</u> Heat stroke: 0.27† Other heat injuries: 1.21†
Kazman et al, 2015[28]	USA	Analytical cross-sectional	Military and university community members; 55 males and 20 females	<u>Heat tolerance parameters</u> <u>Women</u> Heat intolerance rate: 45% <u>Men</u> Heat intolerance rate: 18%
Armed Forces Health Surveillance Branch, 2016[46]	USA	Descriptive epidemiology; 2015	US Armed Forces; 417 heat stroke cases 1625 other heat injuries cases*	<u>Women</u> Heat stroke: 0.16† Other heat injuries: 1.54† <u>Men</u> Heat stroke: 0.35† Other heat injuries: 1.48†
Armed Forces Health Surveillance Branch, 2017[47]	USA	Descriptive epidemiology; 2016	US Armed Forces; 401 heat stroke cases 2135 other heat injuries cases*	<u>Women</u> Heat stroke: 0.19† Other heat injuries: 1.90† <u>Men</u> Heat stroke: 0.33†

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Other heat injuries: 1.61†

Women

Heat stroke: 0.25†

Other heat injuries: 1.38†

Men

Heat stroke: 0.41†

Other heat injuries: 1.41†

Armed Forces Health Surveillance Branch, 2018[48]	USA	Descriptive epidemiology; 2017	US Armed Forces; 464 heat stroke cases 1699 heat exhaustion cases
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§ Proportions and incidences reported are of the total cases reported in the articles
Incidence rate reported per 100,000 person-years.
‡ Incidence rate per 100,000 person- months.
† Incidence rate reported per 1000 person-years.
* Other heat injuries include “heat exhaustion” and “unspecified effects of heat”.
¶ heat injuries include heat stroke and other heat injuries.
UK = United Kingdom; USA = United States of America

Supplemental Table 3: Quality assessment of included studies using the quality assessment tool for studies with diverse designs (QATSDD)

QATSDD Criteria	1	2	3	4	5	6	7	8	9	10	11	12	Total score	% of total score
Dickinson' 94[29]	0	1	2	0	1	3	0	0	3	2	0	2	14/36	38.9
AMSA'98[30]	2	1	1	0	0	0	0	0	2	2	0	0	8/36	22.2
AMSA'00[33]	2	1	2	0	0	1	0	0	2	3	0	0	11/36	30.6
AMSA'02[31]	3	0	2	0	1	1	0	0	2	0	2	0	11/36	30.6
AMSA'03[32]	2	1	1	0	1	1	0	0	2	2	0	0	10/36	27.8
Carter et al' 05[34]	3	3	3	2	2	3	1	2	3	3	2	0	27/36	75
AMSA'06[36]	2	1	1	0	1	1	0	0	2	2	0	0	10/36	27.8
Wallace et al' 06[49]	3	3	3	2	2	3	1	2	3	3	2	2	29/36	80.6
AFHSB'07[37]	1	1	1	0	0	1	0	0	2	2	0	0	8/36	22.2
AFHSB' 08[38]	1	1	1	0	0	1	0	0	2	2	0	0	8/36	22.2
AFHSB' 09[39]	1	1	1	0	0	1	0	0	2	2	0	0	8/36	22.2
AFHSB' 10[40]	1	1	2	0	0	1	0	0	2	2	0	2	11/36	30.6
AFHSB' 11[41]	2	1	2	0	0	1	0	0	2	2	0	2	12/36	33.3
Druyan et al'12[12]	3	3	3	1	0	2	0	3	3	2	2	1	23/36	63.9
AFHSB' 12[42]	2	1	2	0	0	1	0	0	2	2	0	2	12/36	33.3
AFHSB' 13[43]	2	2	2	0	0	2	0	0	2	2	0	2	14/36	38.9
AMSA' 14[44]	2	2	2	0	0	2	0	0	2	3	0	2	15/36	41.7
Lisman et al,'14 [27]	3	3	3	2	2	3	2	3	3	3	3	3	33/36	91.7
AFHSB' 15[45]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4
Bedno et al, 2015[35]	3	3	3	2	2	3	3	3	3	3	3	3	34/36	94.4
Kazman et al' 15[28]	3	3	3	2	2	3	2	3	3	3	3	3	33/36	91.7
AFHSB' 16[46]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4
AFHSB' 17[47]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4
AFHSB' 18[48]	3	2	2	0	0	2	0	0	2	3	0	2	16/36	44.4

QATSDD Criteria

- (1) Theoretical framework; (6) Procedure for data collection (11) Good justification for analytical method selected
 (2) Aims/objectives; (7) Rationale for choice of data collection tool(s) (12) Strengths and limitations.
 (3) Description of research setting (8) Detailed recruitment data
 (4) Sample size; (9) Fit between research question and method of data collection (Quantitative only)
 (5) Representative sample of target group (10) Fit between research question and method of analysis (Quantitative only)
 QATSDD rating scale: 0=not at all; 1=very slightly; 2=moderately; 3=complete; AMSA = Army Medical Surveillance Activity



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4,5,6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7, supplemental table 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Figure 1
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8, 9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis. http://bmjopen.bmj.com/site/about/guidelines.xhtml	9



PRISMA 2009 Checklist

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Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10, Supplemental table 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	15
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10, 11, 12, 13, 14, Figure 1 and Figure 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	15
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18, 19
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15, 16, 17, 18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	20

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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