BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-031825
Article Type:	Research
Date Submitted by the Author:	20-May-2019
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Keywords:	OCCUPATIONAL & INDUSTRIAL MEDICINE, ACCIDENT & EMERGENCY MEDICINE, Heat Stroke, Armed Forces, Women

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

Type of article: Review

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Word count: 3992

Abstract

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

Design: A systematic review of multiple databases (MEDLINE, Emcare, CINAHL, PsycINFO, Informit, and Scopus) was conducted from inception of the databases to the 1st of April 2019.

Eligibility criteria: Studies investigating heat illness and heat tolerance in women in the armed forces.

Results: Twenty-seven (27) studies were included in the review. Measures used to describe heat illness were proportions and incidence rates. The average proportion of heat stroke events in women was lower than in men (12% vs 88%). In addition, men had significantly higher heat stroke incidence compared to women (median = 0.27, interquartile range = 0.11 vs median = 0.15, interquartile range = 0.03; $U= 10.50$, $P < 0.001$). However, the incidence of other heat injuries was similar between men and women (median = 1.41, interquartile range = 0.37 vs median = 1.62, interquartile range = 0.97; $U = 47.50$, $P = 0.058$). Investigated factors associated with heat illness and tolerance included gender, age, level of education, ethnicity, body mass index (BMI), maximal aerobic capacity (VO_{2max}), positive sickle cell trait, being in service for less than 1 year, and unit of service. Women were more likely to be heat intolerant compared to men using the standard heat tolerance test.

Conclusion: The findings of this review suggest that women have a greater risk of heat illness and show higher rates of heat intolerance than men on the standard heat tolerance test. There is a need to re-evaluate the heat tolerance test protocol for women with further investigation of the factors that make women more susceptible to heat illness than men.

Article summary

Strengths and limitations of this study

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

Trial registration None

Key words

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

Introduction

Heat illness is a spectrum of disorders that arise when there is a disruption in the regulation of body temperature.[1] These illnesses may arise from a combination of prolonged exposure to heat/humidity and increased metabolic activity.[2] When body temperature rises, conduction, convection, radiation and evaporation mechanisms help to cool the body and maintain normothermia.[1] However, heat loss is susceptible to prevailing environmental conditions and type of clothing worn. Without adequate cooling a number of syndromes may occur ranging from heat cramps, heat syncope and heat exhaustion through to heat stroke, a potentially life-threatening disorder.[1]

Heat stroke is a medical emergency.[3] It is characterized by elevated core temperature of 40°C and above, central nervous system disturbances and multi-organ damage that may result in death.[3] Heat stroke has been classified as either classic or exertional.[4] Classical heat stroke is insidious in onset and occurs in vulnerable populations such as young children, the elderly and patients with chronic diseases.[5] On the other hand, exertional heat stroke occurs more rapidly and affects apparently healthy, active people such as athletes, factory workers, construction workers, agricultural workers, firefighters and military recruits.[6, 7] The workers in these industries often require high levels of physical exertion to perform jobs and tasks. A combination of rigorous activities and extreme exposure to heat places the workers at increased risk of heat stress and heat stroke.[8]

However, the ability to cope with heat stress varies between individuals.[3] Individuals who are unable to cope with heat stress may have elevated body temperature under extreme conditions in the heat, which may cause heat exhaustion or heat stroke.[3] The inability to withstand heat stress during exertion in hot environments is defined as heat intolerance.[3] Evidence in the published literature suggests that heat stroke may be preceded or accompanied by a state of heat intolerance.[3] The Israeli Defence Force developed the heat tolerance test in 1979 as an index of the ability of soldiers to cope with exertional heat.[9] Individuals who have suffered heat stroke are sent for a heat tolerance test after a minimum recovery period of 6 to 8 weeks as part of the return to duty process.[9] Criteria used to define heat intolerance include an elevation in rectal temperature above 38.5°C and heart rate above 150 bpm or when rectal temperature or heart rate fail to stabilize during the test. The current heat tolerance test criteria are based on previous studies by Shapiro et al.[10] and Epstein et al.,[11] which utilised only male military participants.[10, 11]

Globally, increasing numbers of women are joining the armed forces following the inclusive approach to recruiting and creation of more roles for women.[12] Women are required to operate in austere environments with heat illnesses becoming more frequent.[12] This has raised the question about gender differences in thermoregulation during heat stress.[12] During prolonged heat exposure, the body's thermal inertia is determined by complex interactions between the body's morphological characteristics (body composition, body mass and surface area) and heat load. Evidence suggests that women differ from men in thermal responses to heat.[13] These difference may be because women have a lower rate of whole body evaporative heat loss, higher body fat mass, body mass ratio,[14] number of sweat glands and lower aerobic fitness.[15] In addition, hormonal variations due to menstrual cyclic patterns and the use of contraceptive pills may all be associated with the differences in response to heat stress.[16]

Although these gender differences exist, they have not been considered when conducting the heat tolerance test (HTT) for women who have had a heat stroke.[15] Furthermore, heat illness can impact defence operational effectiveness and may result in acute loss of manpower and possible medical discharge from service.[17] A previous review on the risk of heat illness in women compared with men focused on the general population.[18] The findings of the review suggested that men are at increased risk of heat illness compared to women.[18] However, there is a dearth of research investigating heat illness in women compared to men in the armed forces.

Therefore, the aims of this systematic review are:

- To describe the epidemiology of heat stroke and other heat related illnesses in women compared to men in the armed forces.
- To identify predisposing risk factors and gender differences in heat illness and heat tolerance

Methods

Search Strategy

This review utilised the Preferred Reporting Items for Systematic Review and Meta-analysis protocols (PRISMA-P) 2015 statement[19] and explored all literature published in English from inception of the different databases to the 1st of April 2019. Databases searched included MEDLINE, CINAHL, PsycINFO, Emcare, Informit and Scopus. A preliminary search was conducted in Medline, Emcare and CINAHL to identify relevant key words contained in the titles, abstracts and subject descriptors. These search terms were used to conduct the search in other databases without subject headings. The search strategy used in Medline is presented in supplemental table 1. No review protocol exists.

Eligibility criteria

Studies included in the review were assessed according to the following inclusion criteria: Peer-reviewed literature comparing heat illness in women to men in the Armed Forces. Exclusions included literature discussing heat illness in other occupations, or studies where data on heat illness in women could not be separated from men or studies reporting heat illness in men or literature reviews, conference abstracts and grey literature. In addition, additional primary data sources were identified from the reference lists of the included studies using a hand-search technique.

Selection of studies and data extraction

FA and BMA identified all included studies and data extraction was performed using a standard abstraction form. Data extracted from the studies included: study location and design, population, proportion and incidence of heat illnesses, factors associated with heat illness and heat tolerance, and heat tolerance in men and women. All authors cross-checked the extracted data for consistency.

Quality assessment

The methodological quality assessment was assessed by FA in consultation with MC using the modified quality assessment tool for studies with diverse designs (QATSDD) critical appraisal tool.[20] Any disagreement about any article was reviewed by BMA and AMA and discussed until consensus was reached. The QATSDD tool is a 16-item tool which assesses the quality of diverse studies (both quantitative and qualitative).[20] The tool was modified to exclude two items relating to qualitative studies as well as two items relating to quantitative studies that were not applicable to the studies included in the review. The items excluded comprised statistical assessment of reliability and validity of measurement tool(s) (Quantitative only), fit between stated research question and format and content of data collection tool e.g. interview schedule (Qualitative), assessment of reliability of analytical process (Qualitative only) and evidence of user involvement in design. Each criterion in the modified QATSDD tool was awarded a score of 0 to 3 with 0 = not at all, 1 = very slightly, 2 = moderately and 3 = complete. The scores of each criterion were summed to assess the methodological quality of included studies with a maximum score of 36. The criteria included were (1) theoretical framework; (2) statement of aims/objectives; (3) description of research setting; (4) evidence of sample size;

(5) representative sample of target group of a reasonable size, (6) description of 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; and (12) strengths and limitations. For ease of interpretation, the scores were converted to percentages and classified as low (<50%), medium (50-80%) or high (>80%) quality of evidence.

Data analysis and synthesis

Data analysis was conducted using SPSS version 25. Heat illness was reported as either all heat related illnesses or heat stroke versus other heat illnesses. Measures used to describe heat illness were proportions and rates. The mean proportion of heat stroke and other heat illness were reported for studies published between 1995 and 1997. A Mann-Whitney U test was used to assess the median differences in the incidence of heat stroke and other heat illnesses between men and women from 2006 to 2018. Level of significance was set at 0.05. The incidence rates and proportions of all heat related illness (where heat stroke was not differentiated from other heat illnesses) were reported using frequency tables. Due to the heterogeneity of the included studies, a meta-analysis was not conducted.

Results

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

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

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

Table 1: Proportion and incidence of heat related illnesses in women and men in the 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	12.8ǂ	8.6ǂ
				1998	15.8ǂ	12.0ǂ
Army Medical Surveillance Activity, 2000[27]	USA	Descriptive epidemiology	1997 – 1999 (2 years)	US Army and Marine Corps (3386 cases)		
				Army (1896 cases)	2.0†	1.5†
				Marine Corps (1104 cases)	4.4†	2.0†
Army Medical Surveillance Activity, 2002[25]	USA	Descriptive epidemiology	1990 – 1997 (7 years)	US Army (2290 cases)	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[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	13.89†	14.79†
				Non-SCT: 577 exertional heat illness cases	13.14†	7.79†

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

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

† Incidence rate reported per 1000 person-years

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

Risk factors for heat illness and heat intolerance

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

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	US Army	Female	1.5 (1.4 - 1.7)
		1998 – 2001 (3 years)	5021 cases and 10,042 controls	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)
				Less than 1 year of service	2.3 (2.0 – 2.6)
Carter et al, 2005[28]	USA	Cross-sectional 1980 – 2002 (22 years)	US Army	Female	1.21 (1.09 – 1.40)
				Infantry soldiers and gun crew men	2.69 (1.71 – 2.89)
			5246 cases of heat illness; 4521 males and 725 females	African and Hispanic ethnicity	0.76 (0.71 – 0.82)
				Northern state of origin	1.69 (1.42 – 1.90)
Wallace et al, 2006[46]	USA	Case-control 1988 – 1996 (8 years)	US Marine Corps	BMI ≥ 26 kg/m² (males)	2.10 (1.59 – 2.78
			Male (627 cases and 1679 controls)	Run time ≥ 12.9 minutes (males)	5.61 (3.73 – 8.45)
			Female (49 cases and 123 controls)	Run time ≥ 6.9 minutes (females)	5.30 (1.59 – 17.64)
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	Female	1.04 (0.57 – 1.89)
Kazman et al, 2015[47]	USA	Analytical cross-sectional (Duration not stated)	Military and university community members	Female	3.68 (1.21 – 11.24)
			55 males and 20 females	VO_{2max}	0.9 (0.76 – 0.96)
Singer et al, 2018[21] ǂ	USA	Retrospective cohort study	SCT and non-SCT US Armed Forces	Female	1.36 (1.17 – 1.50)
			SCT: 214 exertional heat illness cases	SCT positive	1.24 (1.06 – 1.45)
			Non-SCT: 577 exertional heat illness cases	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)

*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; ǂ The risk factors associated with EHI and SCT status

Heat tolerance in women and men

Two studies compared heat tolerance in males and females using the most commonly used test, the HTT developed by the Israeli Armed Forces.[15, 47] The findings reported in Table 3 revealed that a greater proportion of women were classified as heat intolerant compared to men (45% vs 18% and 66% vs 25.79%).[15, 47] In addition, women had higher baseline temperature (37.18°C vs 37.07°C and 37.1°C vs 36.9°C respectively)[15, 47] and heart rate (82.11 bpm vs 73.94 bpm and 76 bpm vs 68 bpm). In addition, the endpoint heart rates for women were higher compared to their male counterparts (141.5 bpm vs 126.5 bpm and 137 bpm vs 122 bpm respectively).[15, 47] The end point temperature varied between the two studies; one study reported a higher endpoint temperature for females[15] and the other study reported similar endpoint temperature between males and females.[47]

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	170 males and 9 females			
		2008 – 2010 (2 years)		Heat intolerance rate	66.6%	25.79%
				Baseline T_{rec} (º C)	37.18 ± 0.09	37.07 ± 0.02
				Endpoint T_{rec} (º 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} (º C)	37.1 ± 0.4	36.9 ± 0.4
				Endpoint T_{rec} (º 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

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

Assessment of methodological quality

The QATSDD scores ranged from 0 to 97.2% (Supplemental Table 3). Only six studies scored above 50% and included details about recruitment, data analysis, strengths and limitations of the research. The other studies had lower scores because they lacked detailed justification for the analytical methods, data collection, analysis, strengths and limitations. However, results of the methodological assessment should be interpreted with caution. Although the tool assesses methodological quality, it is more likely to be dependent on how the paper was written. In this review, 80% of the studies included were military reports on heat-related illnesses in the Armed Forces. These reports were published in a peer-reviewed journal and were retrospective analyses of data collected by Defence Medical Surveillance Systems. These studies may not have reported details about data collection, strengths and limitations, but they presented valid information on heat- related illness.

Discussion

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

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

However, despite the lower rate of heat stroke, women had a greater risk of heat illness and were more likely to be heat intolerant than men.[21, 25, 28, 29, 47] The higher risk of exertional heat illness in women may likely be due to differences in physiological and physical characteristics between men and women.[49] Physiological characteristics such as hormones, use of contraceptive pills and lower evaporative heat loss may make women more susceptible to heat illness. [14, 16] Physical characteristics such as lower aerobic fitness and greater body fat are predictors of exertional heat illness.[49] Generally, men have less body fat and greater lean body mass compared to women. Furthermore, women have lower aerobic fitness levels and lower overall work capacity which may contribute to the increased risk of exertional heat illness.[49]

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

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

Similarly, the association between lower level of education and heat illness may be due to aerobic fitness. Research has identified educational attainment as a major predictor of health outcomes.[57] Education provides the opportunity for individuals to learn more about their health and to make healthy lifestyle choices. Individuals with a higher level of education are more likely to engage in healthy behaviours such as healthy diet and regular exercise.[57] Regular exercise is necessary to maintain and improve aerobic fitness.[58] High aerobic fitness may reduce the risk of exertional heat illness; however, some fit individuals may be at increased risk of heat illness because of their ethnic status. The effect of ethnicity on heat illness varied in this review. One study reported that minor ethnic groups (non-White, non-Black, non-Hispanic) were more susceptible to heat illness[25], while another study reported that Caucasians had an increased risk of heat illness compared to other ethnic groups.[28] Genetic adaptation may play a role in the differences between ethnic groups.[59] Evidence shows that a disruption in the cell protective mechanism of heat shock proteins may increase the risk of heat illness.[59]

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

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

Strengths and limitations

To the authors' current knowledge, this is the first known systematic review investigating the impact of gender on exertional heat illness and heat tolerance in the armed forces. In addition, we identified potential risk factors that are associated with exertional heat illness. However, the heterogeneity in the study designs contributed to the variable methodological quality of the included studies. Most of the articles in this review were military reports and may not be considered of high methodological quality when assessed using a formal critical appraisal tool. In addition, most of the included studies utilized retrospective data as the data source with an increased likelihood of incompleteness and inaccuracy. There is a likelihood that misclassification bias could have been introduced into the studies. Three studies that explored the risk factors associated with heat-related illness used retrospective data. [25, 28, 46] The retrospective data may have been misclassified or incomplete at the time of entry and may have introduced misclassification bias into the studies. This type of bias may underestimate or overestimate the association between heat-related illness and risk factors. Although the risk factors associated with heat illness were discussed; the review provided limited evidence of these factors, given the few numbers of studies that investigated the association. Furthermore, we included only studies published in English language; studies published in other languages were excluded.

Implication for policy and future research

This systematic review demonstrates that there is limited research on exertional heat illness in women in the Armed Forces. Although men had a higher reported incidence of heat stroke; this may be a reflection that women are more likely to report poorer health earlier than men.[48] Further research is needed to establish if this reflects physiological or behavioural differences. Given that women have an increased risk of heat illness; they should be encouraged to participate in cardiovascular training programs to improve physical fitness. Nonetheless, more research is needed to understand the roles of underlying factors such as menstrual cycle phase, use of contraceptive pills and cardiovascular function in heat illness.[15, 47] Furthermore, the limited evidence revealed that more women were classified as heat intolerant using the current heat tolerance test protocol. The current criteria may be unfair to women given that it was developed using male participants. Therefore, it is important that the protocol is re-evaluated for women or a new protocol is developed that puts the gender specific factors into consideration.[15] The re-evaluation of the protocol for women would reduce false positive results and the likelihood of ending the careers of these otherwise healthy women.[15]

Conclusion

In conclusion, this review shows that men experienced a higher incidence of heat stroke but women in the armed forces may have a greater risk of heat illness and are more likely to be heat intolerant than their male counterparts using the standard heat tolerance test. Further research is needed to evaluate the heat tolerance test protocol for women and to further investigate the influence of gender differences on heat intolerance and heat illness.

Authors' contribution

All authors contributed substantially to the study concept, design, data extraction, quality assessment and writing of the manuscript.

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All authors read and approved the manuscript for submission.

Funding: The first author (FA) is supported by the Australian Government International Research Training Program Scholarship

Competing Interests: The authors declare that they have no competing interests.

Patient consent for publication: Not required

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

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Figure legends

Figure 1: PRISMA flow chart of the study selection protocol

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

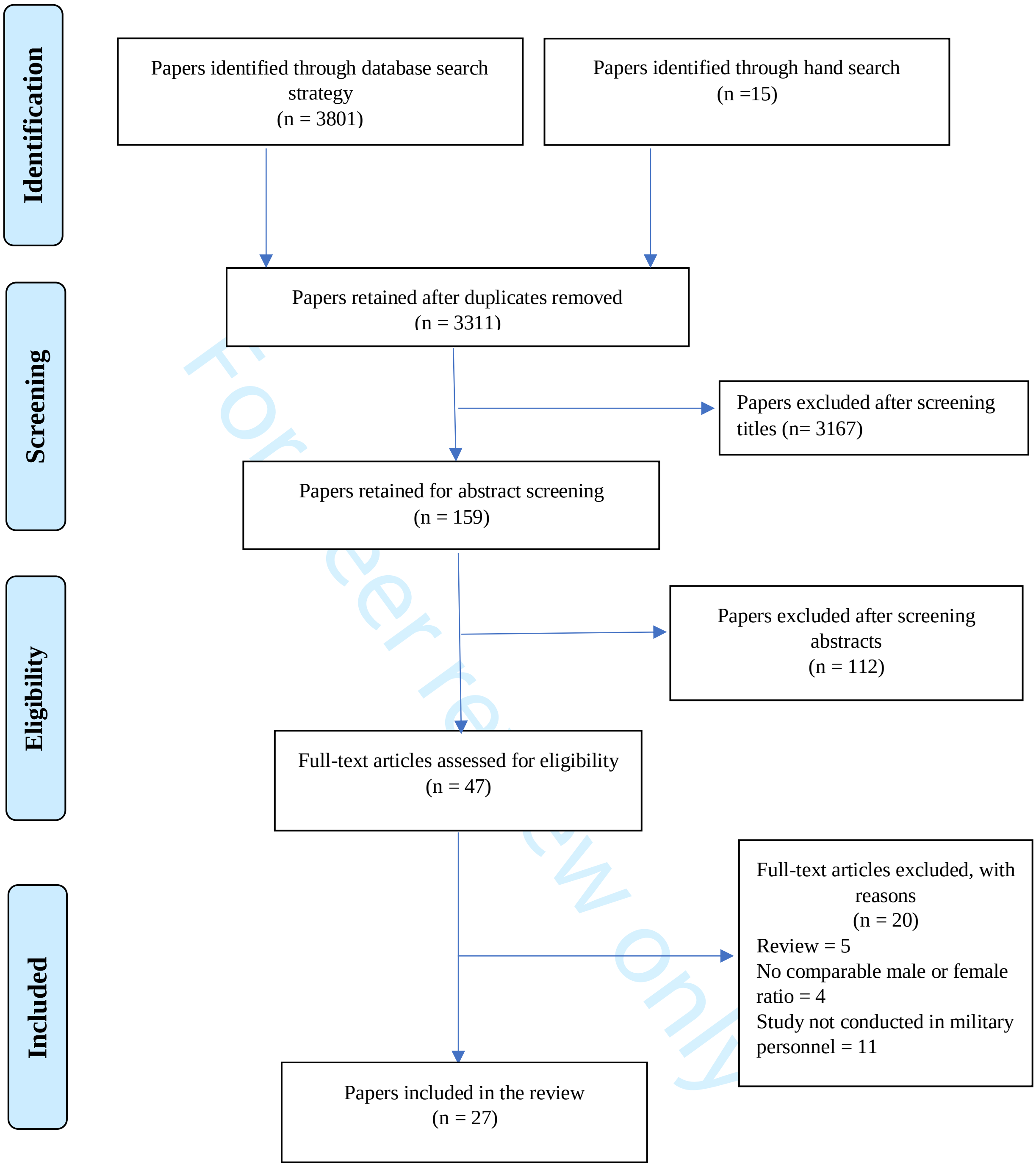
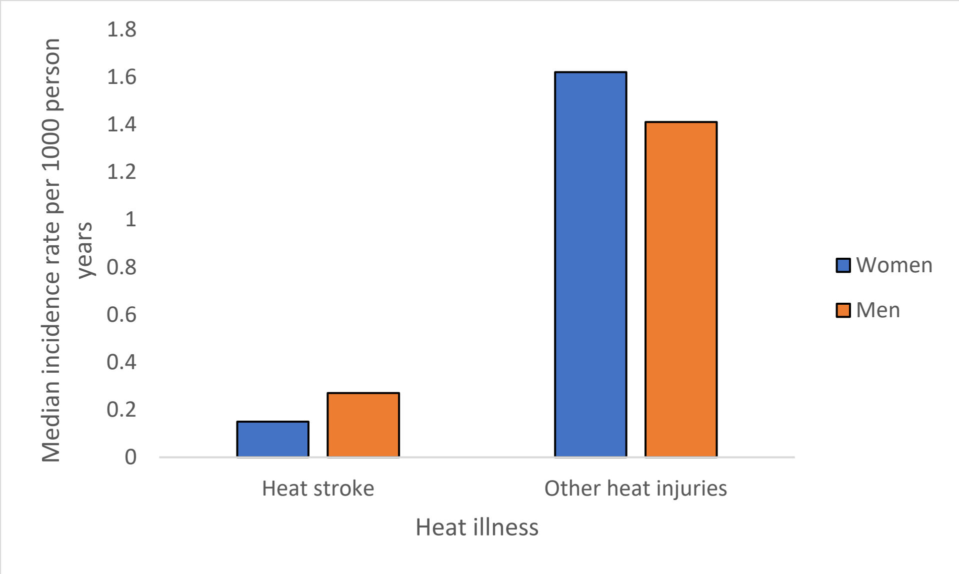


Figure 1: PRISMA flow chart of the study selection protocol



*** P < 0.001

Figure 2

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	**Women** All heat injuries: 12.8[ǂ] **Men** All heat injuries: 8.6[ǂ]
			1998	**Women** All heat injuries: 15.8[ǂ] **Men** All heat injuries: 12.0[ǂ]

Army Medical Surveillance Activity, 2000	USA	Descriptive epidemiology; 1997 - 1999	US Army and Marine Corps; 3386 all heat injuries cases⁋	
			Army (1896 cases)	**<u>Women</u>** All heat injuries: 2.0† **<u>Men</u>** All heat injuries: 1.5†
			Marine Corps (1104 cases)	**<u>Women</u>** All heat injuries: 4.4† **<u>Men</u>** All heat injuries: 2.0†
Army Medical Surveillance Activity, 2002	USA	Descriptive epidemiology 1990 - 1997	US Army; 2290 all heat injuries cases⁋	**<u>Women</u>** All heat injuries: 14.0% **<u>Men</u>** All heat injuries: 86.0%
		Case – control 1998 - 2001	US Army; 5021 cases and 10,042 controls (all heat injuries)⁋	**<u>Women</u>** All heat injuries: 20.7% **<u>Men</u>** All heat injuries: 79.3% **<u>Risk factors</u>** 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⁋	**<u>Women</u>** 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	**<u>Women</u>** All heat injuries: 13.7% **<u>Men</u>** All heat injuries: 86.3% **<u>Risk factors</u>**

				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)
Army Medical Surveillance Activity, 2006	USA	Descriptive epidemiology; 2005	US Armed Forces; 204 heat stroke cases 958 heat exhaustion cases	**Women** Heat stroke: 0.26† Heat exhaustion: 2.89† **Men** Heat stroke: 0.48† Heat exhaustion: 1.98†
Wallace et al, 2005	USA	Case-control 1988 - 1996	US Army; 5246 cases of heat illness; 4521 males and 725 females	**Risk factors** ***Females*** Run time ≥ 6.9 minutes: OR; 5.30 (1.59 – 17.64) ***Males*** Run time ≥ 12.9 minutes: OR; 5.61 (3.73 – 8.45) BMI ≥ 26 kg/m^2: OR; 2.10 (1.59 – 2.78)
Army Medical Surveillance Activity, 2007	USA	Descriptive epidemiology; 2006	US Armed Forces; 259 heat stroke cases 1854 heat exhaustion cases	**Women** Heat stroke: 0.14† Heat exhaustion: 1.49† **Men** Heat stroke: 0.22† Heat exhaustion: 1.34†
Army Medical Surveillance Activity, 2008	USA	Descriptive epidemiology; 2007	US Armed Forces; 329 heat stroke cases 1853 heat exhaustion cases	**Women** Heat stroke: 0.14† Heat exhaustion: 1.62† **Men** Heat stroke: 0.26† Heat exhaustion: 1.34†
Army Medical Surveillance Activity, 2009	USA	Descriptive epidemiology; 2008	US Armed Forces; 299 heat stroke cases 1467 heat exhaustion cases	**Women** Heat stroke: 0.16† Heat exhaustion: 1.35† **Men** Heat stroke: 0.22† Heat exhaustion: 0.98†

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	Israeal	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†

Army Medical Surveillance Activity, 2014	USA	Descriptive epidemiology; 2013	US Armed Forces; 324 heat stroke cases 1701 other heat injuries cases*	**Women** Heat stroke: 0.15† Other heat injuries: 1.30† **Men** Heat stroke: 0.24† Other heat injuries: 1.19†
Bedno et al, 2014	USA	Analytical cross-sectional	US Armed Forces; 80 exertional heat illness cases	**Women** Heat illness: 0.680% **Men** Heat illness: 0.71%
Army Medical Surveillance Activity, 2015	USA	Descriptive epidemiology; 2014	US Armed Forces; 314 heat stroke cases 1410 other heat injuries cases*	**Women** Heat stroke: 0.14† Other heat injuries: 1.31† **Men** Heat stroke: 0.27† Other heat injuries: 1.21†
Kazman et al, 2015	USA	Analytical cross-sectional	Military and university community members; 55 males and 20 females	**Heat tolerance parameters** ***Women*** 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 ***Men*** 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 **Risk factors** Female: OR; 3.68 (1.21 – 11.24) VO_{2max}: OR; 0.9 (0.76 – 0.96)
Army Medical Surveillance Activity, 2016	USA	Descriptive epidemiology; 2015	US Armed Forces; 417 heat stroke cases 1625 other heat injuries cases*	**Women** Heat stroke: 0.16† Other heat injuries: 1.54† **Men** Heat stroke: 0.35† Other heat injuries: 1.48†

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	**Women** Exertional heat illness: 13.89† **Men** Exertional heat illness: 14.79†
			Non-SCT: 577 exertional heat illness cases	**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.
ǂ 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;
(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

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

Section/topic	#	Checklist item	Reported on page #
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

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

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

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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BMJ Open

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

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

Type of article: Review

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Word count: 4723

Abstract

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

Design: Systematic review and meta-analysis.

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

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

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

Article summary

Strengths and limitations of this study

- This is the first known systematic review and meta-analysis investigating the impact of gender on exertional heat illness and heat tolerance in the armed forces.
- We conducted a comprehensive search and identified potential risk factors that are associated with exertional heat illness.
- Most of the included studies utilized retrospective data with an increased likelihood of misclassification bias which may have underestimated or overestimated the association between heat-related illness and risk factors.

Trial registration None

Key words

Heat stress; Heat stroke; Heat exhaustion; Heat tolerance; Women; Armed forces

Introduction

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

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

However, the ability to cope with heat stress varies between individuals.[2] Individuals who are unable to cope with heat stress may be affected by heat exhaustion or heat stroke as a result of a combination of factors including an elevation in body temperature, cardiovascular insufficiency , hypotension and fatigue [7]. The inability to withstand heat stress during exertion in hot environments is defined as heat intolerance.[2] Evidence in the published literature suggests that heat intolerance may be as a direct result of heat stroke or due to predisposing inherent factors (genetics).[2] The Israeli Defence Force developed the heat tolerance test in 1979 as an index of the ability of soldiers to cope with exertional heat.[8] Individuals who have suffered heat stroke are sent for a heat tolerance test after a minimum recovery period of 6 to 8 weeks as part of the return to duty process.[8] Criteria used to define heat intolerance include an elevation in rectal temperature above 38.5°C and heart rate above 150 bpm or when rectal temperature or heart rate fail to stabilize during the test. The current heat tolerance test criteria are based on previous studies by Shapiro et al.[9] which utilised only male military participants.[8, 9] According to these studies, the heat tolerance test is a useful tool to determine return to duty and to prevent subsequent exertional heat stroke. [8,9] Given that heat stroke may be fatal; it is essential to identify individuals who are at high risk of exertional heat illness. [8]

Globally, increasing numbers of women are joining the armed forces as inclusive approaches to recruiting are adopted and more roles for women are created.[10] Women are required to operate in austere environments with heat illnesses becoming more frequent.[10] This has raised the question about gender differences in thermoregulation during heat stress.[10] During prolonged heat exposure, the body's thermal inertia is determined by complex interactions between morphological characteristics (body composition, body mass and surface area) and heat load. Evidence suggests that women differ from men in thermal responses to heat.[11] These difference may be because women have a lower rate of whole body evaporative heat loss, higher body fat mass, body mass ratio,[12] number of sweat glands and lower aerobic fitness.[13] In addition, hormonal variations due to menstrual cyclic patterns and the use of contraceptive pills may all be associated with the differences in response to heat stress.[14]

Although these gender differences exist, they have not been considered when conducting the heat tolerance test (HTT) for women who have had a heat stroke.[13] Furthermore, heat illness can impact defence operational effectiveness and may result in acute loss of manpower and possible medical discharge from service.[15] A previous review of the risk of heat illness in women compared with men focused on the general population.[16] The findings of the review suggested that men are at increased risk of heat illness compared to women.[16] However, no systematic review has investigated gender differences among armed forces personnel in relation to heat illness. Given that heat intolerance may predispose to or accompany heat stroke, it is important to understand the role gender plays in heat intolerance.

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

Specific aims were

- To determine the relative risk of heat illness in women compared to men in the armed forces and
- To identify predisposing risk factors associated with heat illness and heat tolerance in the armed forces

Methods

Search Strategy

This review utilised the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines [17] and the MOOSE (Meta-analysis Of Observational Studies in Epidemiology) checklist [18] to explore all literature published in English from inception of the different databases to 1 April 2019. Databases searched included MEDLINE, CINAHL, PsycINFO, Emcare, Informit and Scopus. A preliminary search was conducted in Medline, Emcare and CINAHL to identify relevant key words contained in the titles, abstracts and subject descriptors. These search terms were used to conduct the search in other databases without subject headings. The search strategy used in Medline is presented in supplemental Table 1. No review protocol exists.

Eligibility criteria

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

Selection of studies and data extraction

FA and BMA identified all included studies and data extraction was performed using a standard abstraction form. Data extracted from the studies included: study location and design, population, proportion and incidence of heat illnesses, factors associated with heat illness and heat tolerance, and heat tolerance in men and women. All authors cross-checked the extracted data for consistency.

Quality assessment

The methodological quality assessment was assessed by FA in consultation with MC using the modified quality assessment tool for studies with diverse designs (QATSDD) critical appraisal tool.[19] Disagreement about any article was reviewed by BMA and AMA and discussed until consensus was reached. The QATSDD tool is a 16-item tool which assesses the quality of diverse studies (both quantitative and qualitative).[19] The tool was modified to exclude two items relating to qualitative studies as well as two items relating to quantitative studies that were not applicable to the studies included in the review. The items excluded were statistical assessment of reliability and validity of measurement tool(s) (Quantitative only), fit between stated research question and format and content of data collection tool e.g. interview schedule (Qualitative), assessment of reliability of analytical process (Qualitative only) and evidence of user involvement in design. Each criterion in the modified QATSDD tool was awarded a score of 0 to 3 with 0 = not at all, 1 = very slightly, 2 = moderately and 3 = complete. The scores of each criterion were summed to assess the methodological quality of included studies with a maximum score of 36. The criteria included were (1) theoretical framework; (2) statement of aims/objectives; (3) description of research setting; (4) evidence of sample size; (5) representative sample of target group of a reasonable size, (6) description of 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; and (12) strengths and limitations. For ease of interpretation, the scores were converted to percentages and classified as low (<50%), medium (50-80%) or high (>80%) quality of evidence.

Patient and public involvement

There was no public or patient involvement in this study.

Data analysis and synthesis

In this review, the International Classification of Diseases ICD 9 or ICD 10 diagnosis codes [20, 21] for the effects of heat and light were used to classify heat illnesses. All included studies in the review utilized either the ICD 9 or ICD 10 codes to classify heat illnesses depending on the year of publication. Heat illnesses were categorised as all heat illnesses, heat stroke and other heat illnesses (including heat exhaustion and unspecified effects of heat and light). For this analysis, all heat illness was defined as cases where diagnosis of heat stroke (992.0, T67.0), heat exhaustion (992.3–5, T67.3 -5), heat syncope (992.1, T67.1), heat cramps (992.2, T67.2), heat fatigue, transient (992.6, T67.6), heat oedema (992.7, T67.7), other specified heat effects (992.8, T67.8) and unspecified effects of heat and light (992.9, T67.9) were reported. Heat stroke was identified and defined using the ICD diagnosis codes 992.0 (1CD 9) and T67.0 (ICD 10). While other heat illnesses were defined as heat exhaustion (992.3-5, T67 3-5) and unspecified effects of heat and light (992.9 and T67.9). Incidence rates and proportions were extracted from the data reported in each study and used for the analysis in this review. Studies reporting all heat illnesses and the risk factors associated with heat illnesses and heat tolerance were not pooled due to variation in the study designs, populations, and measures reported.

A meta-analysis was conducted to provide an overview of the risk of heat stroke and other heat illnesses (heat exhaustion and unspecified effects of heat) in women compared to men in the armed forces. A pooled analysis of the risk of heat stroke was conducted separately from other heat illnesses. For other heat illnesses, a subgroup analysis was performed according to classifications used in the included studies (1 – heat exhaustion and unspecified effects of heat and light and 2 – heat exhaustion). The risk ratio for each study and the pooled risk ratios (RR) with 95% CI were calculated using Review Manager 5.3.[22] The risk ratios were presented as the ratio of the incident rates of heat illness in women to men. A random effects model was used taking into account the heterogeneity of the included studies. I^2 was used to measure the heterogeneity (between study variations) of the included studies. Where the percentage of variation between the included studies was greater than 50%, a sensitivity analysis was performed.

Results

Systematic review

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

Heat illnesses in women compared to men

Table 1 shows the proportions and incidences of all heat-related illness in men and women in the armed forces. Six (6) studies reported higher incidences and proportions of heat illness in men compared to women[23, 25, 27, 28, 30, 31] while two studies reported higher incidences of heat illness in women.[26, 29] Between 1995 and 1997, the mean proportion of all reported heat stroke events in women was approximately 12% compared to 88% of heat stroke events in men. Similarly, men reported a higher mean proportion of heat exhaustion (96%) compared to women (4%).[33-35] Between 2006 and 2018, the average incidence rate of heat stroke in women and men was 0.16/1000 person years and 0.29/ 1000 person years. The average incidence of other heat illnesses (including heat exhaustion and unspecified effects of heat and light) was 1.84/1000 person years and 1.44/ 1000 person years for women and men respectively.

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	12.8ǂ	8.6ǂ
				1998		15.8ǂ	12.0ǂ
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)		2.0†	1.5†
				Marine Corps (1104 cases)		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		13.89†	14.79†
				Non-SCT: 577 exertional heat illness cases		13.14†	7.79†

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

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

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

Risk factors for heat illness and heat intolerance

As shown in Table 2, five (5) studies identified the risk factors associated with heat illness,[23, 27, 30, 31, 48] while one (1) study identified the predictors of heat intolerance.[49] Of the five (5) studies reporting the risk factors associated with heat illness, one study identified the risk for heat illness in association with SCT status.[23] The odds of females experiencing heat illness ranged from 1.04 to 1.5 compared to males.[23, 27, 30, 31] Other identified risk factors for heat illness (Table 2) included younger and older age,[23, 27] lower level of education,[27] ethnicity,[27, 30] higher body mass index (BMI),[48] being SCT positive,[23] being in service for less than 1 year,[27] and serving in combat units as an infantry or gun crew soldier.[27, 30] The factor that predicted heat intolerance was lower VO_{2max}.[49]

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 Age < 20 years Other ethnicity* Combat Lower level of education Less than 1 year of service	1.5 (1.4 - 1.7) 2.1 (1.4 - 3.1) 1.2 (1.0 -1.4) 1.5 (1.4 - 1.6) 2.0 (1.2 – 3.1) 2.3 (2.0 – 2.6)
Carter et al, 2005[30]	USA	Cross-sectional 1980 – 2002 (22 years)	US Army 5246 cases of heat illness; 4521 males and 725 females	Female Infantry soldiers and gun crew men African and Hispanic ethnicity Northern state of origin	1.21 (1.09 – 1.40) 2.69 (1.71 – 2.89) 0.76 (0.71 – 0.82) 1.69 (1.42 – 1.90)
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)	BMI ≥ 26 kg/m² (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)
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	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] ǂ	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 SCT positive Age at enlistment: 30+ years Marines vs Army Occupation: Combat vs repair/engineer	1.36 (1.17 – 1.50) 1.24 (1.06 – 1.45) 1.57 (1.07 – 2.33) 1.51 (1.15 – 2.13) 1.57 (1.15 – 2.13)

*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; ǂ The risk factors associated with EHI and SCT status

Heat tolerance in women and men

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

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	170 males and 9 females			
		2008 – 2010 (2 years)		Heat intolerance rate	66.67%	25.79%
				Physiological measurements (mean ± SD)		
				Baseline T_{rec} (º C)	37.18 ± 0.09	37.07 ± 0.02
				Endpoint T_{rec} (º 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)	Military and university community members; 55 males and 20 females	Heat intolerance rate	45%	18%
				Physiological measurements (mean ± SD)		
				Baseline T_{rec} (º C)	37.1 ± 0.4	36.9 ± 0.4
				Endpoint T_{rec} (º 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

Meta-analysis findings

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

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

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

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

The overall pooled risk ratio of other heat illness was 1.26 (95% CI 1.15 to 1.38) in women compared to men in the armed forces (Figure 3). The women to men risk ratio of studies reporting heat exhaustion and unspecified effects of heat and light was 1.28 (95% CI 1.14, to 1.45). In studies reporting only heat exhaustion, the risk of heat exhaustion in women compared to men was 1.22 (95% CI 1.06 to1.42). The percentage of variance between the included studies due to heterogeneity (I^2) was 53%; a sensitivity analysis was conducted where three of the included studies with the largest rates: AMSA 2006, AMSA 2012, and AMSA 2013 [36, 42, 43] were excluded. The heterogeneity test was lower (I^2 = 7%) after excluding the studies from the pooled analysis (Supplemental Figure 1), however the effect did not change (pooled RR = 1.18, 95% CI 1.09 to 1.27).

Assessment of methodological quality

The QATSDD scores ranged from 0 to 97.2% (Supplemental Table 5). Only six studies scored above 50% and included details about recruitment, data analysis, strengths and limitations of the research. The other studies had lower scores because they lacked detailed justification for the analytical methods, data collection, analysis, strengths and limitations. However, results of the methodological assessment should be interpreted with caution. Although the tool assesses methodological quality, it is more likely to be dependent on how the paper was written. In this review, 80% of the studies included were military reports on heat-related illnesses in the Armed forces. These reports were published in a peer-reviewed journal and were retrospective analyses of data collected by Defence Medical Surveillance Systems. These studies may not have reported details about data collection, strengths and limitations, but they presented valid information on heat- related illness.

Discussion

This systematic review and meta-analysis provide an overview on the available evidence on epidemiology of heat illnesses and heat tolerance in women compared to men in the armed forces.

Summary of findings

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

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

Heat illnesses in women compared to men

The lower risk of heat stroke in women compared to men could possibly indicate that men can tolerate working in the heat beyond the endurance limits than women.[15] Conversely, the women may not have ignored the early warning signs of heat illness and may have sought earlier treatment compared to men. This reinforces the presumption that women are more inclined to make use of health services and report ill health than men.[50] In addition, the consultation rates of men were 30% lower than women, confirming the assumption that men are less likely to consult and may present at a later stage with more severe forms of diseases.[50] Although, previously published literature have reported a higher rate of all types of heat illnesses in men in the general population (including some armed forces personnel) compared to women; heat stroke was not considered separately from other forms of heat illnesses.[16]

However, despite the lower risk of heat stroke, women had a greater risk of other heat illnesses (heat exhaustion and unspecified effects of heat and light) than men.[32, 36 – 47] The higher risk of other heat illnesses in women may likely be due to differences in physiological and physical characteristics between men and women.[51] Physiological characteristics such as hormones, use of contraceptive pills and lower evaporative heat loss may make women more susceptible to heat illness. [12, 14] Physical characteristics such as lower aerobic fitness and greater body fat are predictors of exertional heat illness.[51] Generally, men have less body fat and greater lean body mass compared to women. Furthermore, women have lower aerobic fitness levels and lower overall work capacity which may contribute to the increased risk of exertional heat illness.[51]

Risk factors for heat illness and heat intolerance

The risk factors for heat illness identified in the studies include higher BMI,[48] lower age,[23, 27] lower level of education,[27] non-White, non-Black, non-Hispanic ethnic groups,[27] less than one year of service,[27] service unit.[27, 29] and positive SCT.[23] On the other hand, lower VO_{2max}, was identified as a predictor of heat intolerance.[49] Evidence suggest that individuals with higher BMI (indicating higher body fat) have been reported to be at increased risk of exertional heat illness and are less heat tolerant.[52] However, individuals with a low BMI may or may not be fit. Individuals with low aerobic fitness levels are likely to exert themselves beyond their physical limit and are at increased risk of heat illness.[53] During exercise, relative physiological strain is increased, peripheral blood flow decreases which in turn hinders thermoregulation and increasing the risk of heat illness.[53]

The association between age, duration of service, occupational roles, level of education and heat illness may be explained by the level of aerobic fitness. Age as a risk factor varied in this review, with younger age and older age (at enlistment) considered as factors that increase the risk of heat illness.[23, 27] Evidence suggests that aerobic fitness decreases with older age, especially if older adults are sedentary.[54] However, aerobic fitness improves with regular physical exercise and the age related differences between younger and older adults are reversed.[55] The association between shorter duration in service and the increased risk of heat illness was inconclusive given that only one study investigated and reported its findings. However, the findings are in contrast to a previous study that reported that individuals with more years of service in the army had poorer physiological characteristics (lower aerobic capacity, lower maximum heart rate and higher percentage body fat).[56] These poorer physiological characteristics may place armed forces personnel at risk of heat illness.[52, 53] Furthermore, occupational roles such as serving as in Marine Corps and physically demanding jobs such as infantry, combat and gun crew had an increased risk of heat illness compared to personnel in administrative or support jobs. This may be associated with the rigorous and strenuous training requirements for these jobs.[31]

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

In addition, the role of genetics in heat illness was evident in the review with SCT positive armed force members at increased risk of exertional heat illness compared to SCT negative members.[23] SCT is an inherited blood disorder where an individual has a wild type haemoglobin A and haemoglobin S. Individuals with the SCT are considered heterozygous for the sickle cell mutation in the subunit beta gene of the haemoglobin.[60] Evidence has linked positive SCT with exercise related adverse health outcomes such as exertional heat illness (including exertional rhabdomyolysis, heat stroke and hyperthermia) in military personnel.[60] However, the biological pathway by which SCT is associated with heat illness is still unknown.[23] More in depth research is needed to elucidate the role of genetics in exertional heat illness.

Heat tolerance in women and men

The risk of heat illness is dependent on thermal tolerance.[2] The HTT is conducted for members of the armed forces after a heat stroke event as part of the return to duty process.[8] The test criteria defines heat intolerance as peak rectal temperature > 38.5°C, peak heart rate > 150 bpm, or the inability of these values to reach a plateau.[8, 9] Although in the two studies, a higher proportion of women were classified as heat intolerant; this evidence should be interpreted with caution given that the female populations included in each study varied with respect to heat illness and occupations.[13, 49] However, both studies acknowledge that gender differences in thermoregulation may account for the higher intolerance rates in women.[13, 49] Furthermore, both studies reported using the Israeli Defence Force heat tolerance test protocol and given that the test protocol was developed using male participants, there may be a need to re-evaluate the criteria for women to reduce false positive results.[13, 49]

Strengths and limitations

To the authors' current knowledge, this is the first known systematic review and meta-analysis investigating the impact of gender on exertional heat illness and heat tolerance in the armed forces. In addition, we identified potential risk factors that are associated with exertional heat illness. However, the heterogeneity in the study designs contributed to the variable methodological quality of the included studies. Most of the articles in this review were military reports and may not be considered of high methodological quality when assessed using a formal critical appraisal tool. In addition, most of the included studies utilized retrospective data as the data source with an increased likelihood of incompleteness and inaccuracy. Misclassification bias is likely to have been introduced into the studies. Three studies that explored the risk factors associated with heat-related illness used retrospective data. [27, 30, 48] These retrospective data may have been misclassified or incomplete at the time of entry and may have introduced misclassification bias into the studies. This type of bias may underestimate or overestimate the association between heat-related illness and risk factors. Although the risk factors associated with heat illness were discussed; the review provided limited evidence of these factors, given the few numbers of studies that investigated the association. Furthermore, we included only studies published in English language; studies published in other languages were excluded.

Implication for policy and future research

This systematic review and meta-analysis demonstrate that there is limited research on exertional heat illness in women in the armed forces. Although men had a higher risk of heat stroke; women had a higher risk of other heat illnesses. This may be a reflection that women are more likely to report poorer health earlier than men.[50] Further research is needed to establish if this reflects physiological or behavioural differences. In addition , more research is needed to understand the roles of underlying factors such as menstrual cycle phase, use of contraceptive pills and cardiovascular function in heat illness.[13, 49] Furthermore, the limited and inconclusive evidence suggests that more women were classified as heat intolerant compared to men using the Israeli Defence Force heat tolerance test protocol. The current criteria may be unfair to women given that it was developed using male participants. More research is needed to determine the gender differences in heat tolerance as well as to consider re-evaluating the heat tolerance test protocol or the development of a new protocol that considers gender specific factors.[13]

Conclusion

In conclusion, this review shows that men had a higher risk of heat stroke but women in the armed forces had a greater risk of other heat illness. Despite the limited evidence, further research is required to investigate the influence of gender differences on heat tolerance and heat illness. Further research is needed to evaluate the heat tolerance test protocol for women.

Authors' contribution

All authors contributed substantially to the study concept, design, data extraction, quality assessment and writing of the manuscript.

Conceptualization and design: FOA, BSMA, AEMA and MC

Methodology: FOA, BSMA, AEMA and MC

Writing - Original draft: FOA

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

All authors read and approved the manuscript for submission.

Funding: The first author (FA) is supported by the Australian Government International Research Training Program Scholarship

Competing Interests: The authors declare that they have no competing interests.

Patient consent for publication: Not required

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

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Figure legends

Figure 1: PRISMA flow chart of the study selection protocol

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

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

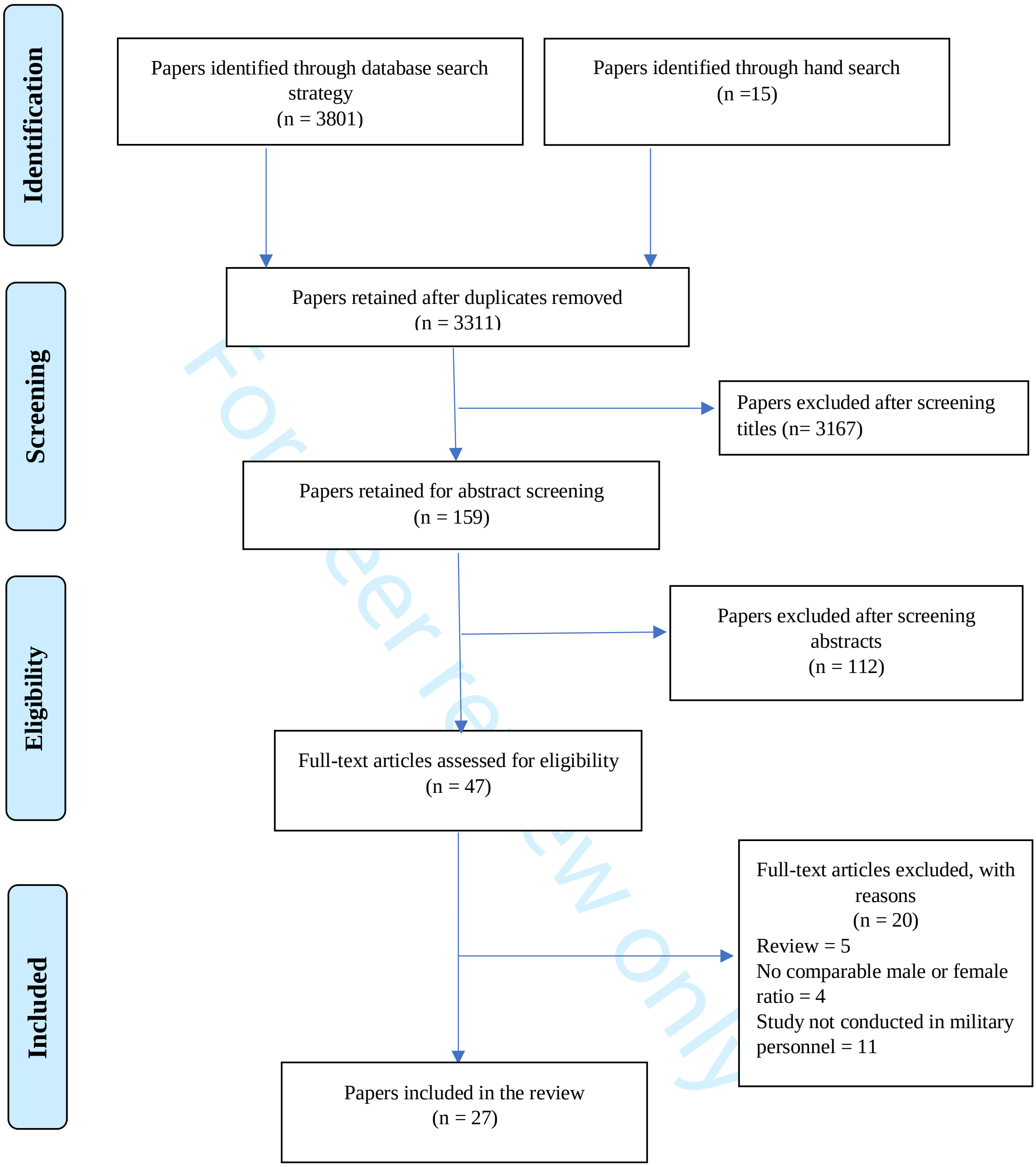
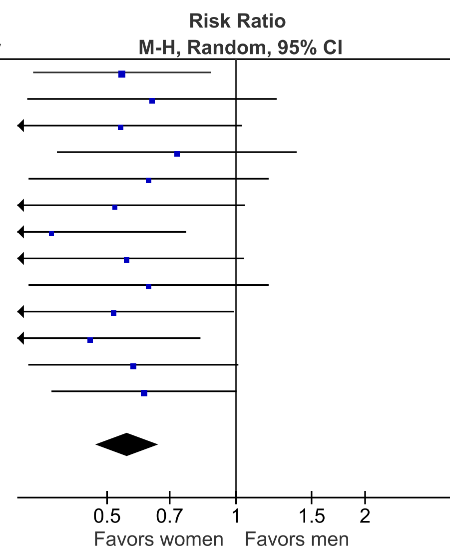


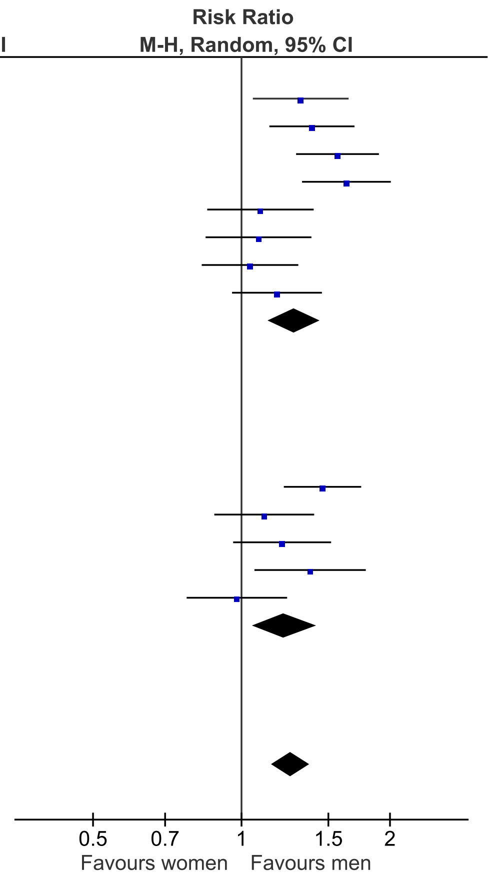
Figure 1: PRISMA flow chart of the study selection protocol

	Women (rate/100000)		Men (rate/100000)			Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year
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)



Study or Subgroup	Women (rate/100000) Events	Women (rate/100000) Total	Men (rate/100000) Events	Men (rate/100000) Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Heat exhaustion and unspecified effects of heat and light						
AMSA 2010	178	100000	135	100000	7.6%	1.32 [1.05, 1.65]
AMSA 2011	232	100000	167	100000	8.5%	1.39 [1.14, 1.69]
AMSA 2012	263	100000	168	100000	8.6%	1.57 [1.29, 1.90]
AMSA 2013	235	100000	144	100000	8.2%	1.63 [1.33, 2.01]
AMSA 2014	130	100000	119	100000	6.9%	1.09 [0.85, 1.40]
AMSA 2015	131	100000	121	100000	6.9%	1.08 [0.85, 1.39]
AMSA 2016	154	100000	148	100000	7.6%	1.04 [0.83, 1.30]
AMSA 2017	190	100000	161	100000	8.1%	1.18 [0.96, 1.46]
Subtotal (95% CI)		**800000**		**800000**	**62.3%**	**1.28 [1.14, 1.45]**
Total events	1513		1163			
Heterogeneity: Tau² = 0.02; Chi² = 17.17, df = 7 (P = 0.02); I² = 59%						
Test for overall effect: Z = 4.04 (P < 0.0001)						
1.1.2 Heat exhaustion						
AMSA 2006	289	100000	198	100000	9.1%	1.46 [1.22, 1.75]
AMSA 2007	149	100000	134	100000	7.3%	1.11 [0.88, 1.40]
AMSA 2008	162	100000	134	100000	7.5%	1.21 [0.96, 1.52]
AMSA 2009	135	100000	98	100000	6.5%	1.38 [1.06, 1.79]
AMSA 2018	138	100000	141	100000	7.3%	0.98 [0.77, 1.24]
Subtotal (95% CI)		**500000**		**500000**	**37.7%**	**1.22 [1.06, 1.42]**
Total events	873		705			
Heterogeneity: Tau² = 0.01; Chi² = 8.56, df = 4 (P = 0.07); I² = 53%						
Test for overall effect: Z = 2.67 (P = 0.008)						
Total (95% CI)		**1300000**		**1300000**	**100.0%**	**1.26 [1.15, 1.38]**
Total events	2386		1868			
Heterogeneity: Tau² = 0.01; Chi² = 26.30, df = 12 (P = 0.010); I² = 54%						
Test for overall effect: Z = 5.01 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.24, df = 1 (P = 0.62), I² = 0%						



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	**Women** All heat injuries: 12.8[ǂ] **Men** All heat injuries: 8.6[ǂ]
			1998	**Women** All heat injuries: 15.8[ǂ] **Men** All heat injuries: 12.0[ǂ]

Army Medical Surveillance Activity, 2000	USA	Descriptive epidemiology; 1997 - 1999	US Army and Marine Corps; 3386 all heat injuries cases⁋	
			Army (1896 cases)	**Women** All heat injuries: 2.0† **Men** All heat injuries: 1.5†
			Marine Corps (1104 cases)	**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)
Army Medical Surveillance Activity, 2006	USA	Descriptive epidemiology; 2005	US Armed Forces; 204 heat stroke cases 958 heat exhaustion cases	**Women** Heat stroke: 0.26† Heat exhaustion: 2.89† **Men** Heat stroke: 0.48† Heat exhaustion: 1.98†
Wallace et al, 2005	USA	Case-control 1988 - 1996	US Army; 5246 cases of heat illness; 4521 males and 725 females	**Risk factors** ***Females*** Run time ≥ 6.9 minutes: OR; 5.30 (1.59 – 17.64) ***Males*** Run time ≥ 12.9 minutes: OR; 5.61 (3.73 – 8.45) BMI ≥ 26 kg/m^2: OR; 2.10 (1.59 – 2.78)
Army Medical Surveillance Activity, 2007	USA	Descriptive epidemiology; 2006	US Armed Forces; 259 heat stroke cases 1854 heat exhaustion cases	**Women** Heat stroke: 0.14† Heat exhaustion: 1.49† **Men** Heat stroke: 0.22† Heat exhaustion: 1.34†
Army Medical Surveillance Activity, 2008	USA	Descriptive epidemiology; 2007	US Armed Forces; 329 heat stroke cases 1853 heat exhaustion cases	**Women** Heat stroke: 0.14† Heat exhaustion: 1.62† **Men** Heat stroke: 0.26† Heat exhaustion: 1.34†
Army Medical Surveillance Activity, 2009	USA	Descriptive epidemiology; 2008	US Armed Forces; 299 heat stroke cases 1467 heat exhaustion cases	**Women** Heat stroke: 0.16† Heat exhaustion: 1.35† **Men** Heat stroke: 0.22† Heat exhaustion: 0.98†

Army Medical Surveillance Activity, 2010	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: 0.22† 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*	**<u>Women</u>** Heat stroke: 0.12† Other heat injuries: 2.32† **<u>Men</u>** 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*	**<u>Women</u>** Heat stroke: 0.10† Other heat injuries: 2.63† **<u>Men</u>** Heat stroke: 0.27† Other heat injuries: 1.68†
Druyan et al, 2012	Israeal	Retrospective cross-sectional 2008 – 2010	Israeli Defence Forces; 170 males and 9 females	**<u>Heat tolerance parameters</u>** ***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*	**<u>Women</u>** Heat stroke: 0.15† Other heat injuries: 2.35† **<u>Men</u>** Heat stroke: 0.27† Other heat injuries: 1.44†

Army Medical Surveillance Activity, 2014	USA	Descriptive epidemiology; 2013	US Armed Forces; 324 heat stroke cases 1701 other heat injuries cases*	**Women** Heat stroke: 0.15† Other heat injuries: 1.30† **Men** Heat stroke: 0.24† Other heat injuries: 1.19†
Bedno et al, 2014	USA	Analytical cross-sectional	US Armed Forces; 80 exertional heat illness cases	**Women** Heat illness: 0.680% **Men** Heat illness: 0.71%
Army Medical Surveillance Activity, 2015	USA	Descriptive epidemiology; 2014	US Armed Forces; 314 heat stroke cases 1410 other heat injuries cases*	**Women** Heat stroke: 0.14† Other heat injuries: 1.31† **Men** Heat stroke: 0.27† Other heat injuries: 1.21†
Kazman et al, 2015	USA	Analytical cross-sectional	Military and university community members; 55 males and 20 females	**Heat tolerance parameters** ***Women*** Heat intolerance rate: 45% Baseline Trec (º C): 37.1 ± 0.4 Endpoint Trec (º C): 38.1 ± 0.4 Baseline HR (bpm): 76 ± 15.0 Endpoint HR (bpm): 137 ± 20.1 ***Men*** Heat intolerance rate: 18% Baseline Trec (º C): 36.9 ± 0.4 Endpoint Trec (º C): 38.1 ± 0.4 Baseline HR (bpm): 68 ± 12.1 Endpoint HR (bpm): 122 ± 20.2 **Risk factors** Female: OR; 3.68 (1.21 – 11.24) VO_{2max}: OR; 0.9 (0.76 – 0.96)
Army Medical Surveillance Activity, 2016	USA	Descriptive epidemiology; 2015	US Armed Forces; 417 heat stroke cases 1625 other heat injuries cases*	**Women** Heat stroke: 0.16† Other heat injuries: 1.54† **Men** Heat stroke: 0.35† Other heat injuries: 1.48†

Army Medical Surveillance Activity, 2017	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† 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	**<u>Women</u>** Heat stroke: 0.25† Other heat injuries: 1.38† **<u>Men</u>** 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	**<u>Women</u>** Exertional heat illness: 13.89† **<u>Men</u>** Exertional heat illness: 14.79†
			Non-SCT: 577 exertional heat illness cases	**<u>Women</u>** Exertional heat illness: 13.14† **<u>Men</u>** 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.
ǂ 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 (I 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

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

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 (I 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	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

Army Medical Surveillance Activity, 2016	USA	Descriptive epidemiology;	2015 (1year)	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)

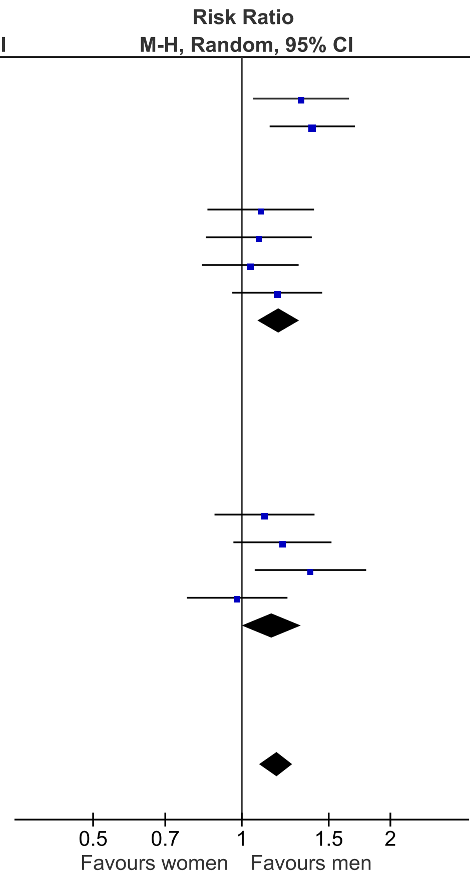
QATSDD Criteria	1	2	3	4	5	6	7	8	9	10	11	12	Total score	% of total score
Dickinson' 94[23]	0	1	2	0	1	3	0	0	3	2	0	2	14/36	38.9
AMSA'95[31]	0	0	0	0	0	0	0	0	0	0	0	0	0/36	0
AMSA' 96[32]	0	0	0	0	0	0	0	0	0	0	0	0	0/36	0
AMSA'97[33]	0	0	0	0	0	0	0	0	0	0	0	0	0/36	0
AMSA'98[24]	2	1	1	0	0	0	0	0	2	2	0	0	8/36	22.2
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;
(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

	Women (rate/100000)		Men (rate/100000)			Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
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: Tau² = 0.00; Chi² = 5.52, df = 5 (P = 0.36); I² = 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: Tau² = 0.00; Chi² = 3.93, df = 3 (P = 0.27); I² = 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: Tau² = 0.00; Chi² = 9.66, df = 9 (P = 0.38); I² = 7%						
Test for overall effect: Z = 4.24 (P < 0.0001)						
Test for subgroup differences: Chi² = 0.14, df = 1 (P = 0.71), I² = 0%						



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

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

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

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**.

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
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Item No	Recommendation	Reported on Page No
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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:	*BMJ Open*
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

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

Type of article: Review

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Word count: 3993

Abstract

Objectives: The aim of this review was to describe the epidemiology of all heat related illnesses in women compared to men in the armed forces and to identify gender specific risk factors and differences in heat tolerance.

Design: A systematic review of multiple databases (MEDLINE, Emcare, CINAHL, PsycINFO, Informit, and Scopus) was conducted from inception of the databases to 1 April 2019 using the preferred reporting items for systematic review and meta-analysis (PRISMA) guidelines.

Eligibility criteria: All relevant studies investigating and comparing heat illness and heat tolerance in women and men in the armed forces were included in the review.

Results:

Twenty-four (24) studies were included in the systematic review. The incidence of heat stroke in women ranged from 0.10 to 0.26 per 1000 person years, while the incidence of heat stroke ranged from 0.22 to 0.48 per 1000 person years in males. The incidence of other heat illnesses in women compared to men ranged from 1.30 to 2.89 per 1000 person years vs 0.98 to 1.98 per 1000 person years. The limited evidence suggests that women had a greater risk of exertional heat illness compared to men. Other gender specific risk factors were slower run times and body mass index. Although there was a higher proportion of women who were heat intolerant compared to men; this finding needs to be interpreted with caution due to the limited evidence.

Conclusion: In relation to armed forces personnel, the findings of this review suggest that men experienced a higher incidence of heat stroke than women. Although the evidence is limited, a higher proportion of women were heat intolerant and had a greater risk of exertional heat

illnesses. Despite the limited evidence, further research is required to investigate the influence of gender differences on heat intolerance and heat illness.

Article summary

Strengths and limitations of this study

- This is the first known systematic review investigating the impact of gender on exertional heat illness and heat tolerance in the armed forces.
- We conducted a comprehensive search and identified potential risk factors that are associated with exertional heat illness.
- Most of the included studies utilized retrospective data with an increased likelihood of misclassification bias which may have underestimated or overestimated the association between heat-related illness and risk factors.

Trial registration None

Key words

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

Introduction

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

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

Among armed forces personnel, exertional heat illness continues to pose as a significant cause of morbidity and mortality [7]. Operations and training may involve exposure to high ambient temperature and high workload which may result in heat illness.[7] Historically, men have occupied military roles and responsibilities with fewer proportion of women in the armed forces.[8] However, more women are joining the armed forces globally following the inclusive approach to recruiting and creation of more roles for women.[9] Women are required to operate in austere environments with heat illnesses becoming more frequent.[9] This has raised the question about gender differences in thermoregulation during heat stress.[9] Evidence suggests that women differ from men in thermal responses to heat.[10] This difference may be because women have a lower rate of whole body evaporative heat loss, higher body fat mass, body mass ratio,[11] number of sweat glands and lower aerobic fitness.[12] In addition, hormonal variations due to menstrual cyclic patterns and the use of contraceptive pills may be associated with the differences in response to heat stress.[13]

When exertional heat illness occurs, it may be challenging to determine if an individual may return to duty. An inaccurate determination of complete recovery among armed forces personnel may negatively impact military readiness.[14] While, there are no evidence-based recommendations for return to duty, the American College of Sports Medicine (ACSM) guidelines states that exertional heat stroke patients may return to duty after re-establishing heat tolerance.[15] Individuals vary in their ability to cope with heat stress and the inability to withstand heat stress during exertion in hot environments is defined as heat intolerance.[2] Evidence suggests that heat intolerance may be as a direct result of heat stroke or due to predisposing inherent factors (genetics).[2] However, the objective criteria or measure for defining heat tolerance or intolerance remains a subject of controversy.[14] The current return to duty guidelines for military personnel varies across countries.[16] For example, in the United States, military return to duty process is based on clinical assessments with gradual acclimatization and re-introduction of duties.[17] By contrast, return to duty in the Israeli Defence Force requires a heat tolerance test to determine if an individual is heat tolerant.[18] Therefore, it is important to develop evidence based return to duty protocols across the globe.

The Israeli Defence Force originally developed the heat tolerance test in 1979 as an index of the ability of soldiers to cope with exertional heat.[18] Individuals who have suffered heat stroke are sent for a heat tolerance test after a minimum recovery period of 6 to 8 weeks as part of the return to duty process.[18] Criteria used to define heat intolerance include an elevation in rectal temperature above 38.5°C and heart rate above 150 bpm or when rectal temperature or heart rate fail to stabilize during the test. The heat tolerance test criteria are based on previous studies by Shapiro et al.[19] which utilised only male military participants.[18, 19] While the test may be considered as a useful tool to determine return to duty and to prevent subsequent exertional heat stroke, [18,19] there is no consensus on the validity of the tool as a diagnostic test for heat tolerance.[14] Furthermore, the heat tolerance test does not account for predicting factors such as gender.[14] Given the limitation, questions have been raised about the validity of the protocol in determining return to duty for females in the armed forces. It has been suggested that more research is required to determine whether or not a new protocol should be developed for women.[12]

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

Therefore, the objective of this systematic review was to provide a comprehensive summary of the epidemiology of heat illness and heat intolerance in women and men in the armed forces.

Specific aims were

- To determine the incidence and prevalence of heat illness in women compared to men in the armed forces:
- To identify gender differences in heat tolerance in the armed forces and
- To identify gender specific predisposing risk factors associated with heat illness in the armed forces

Methods

Search Strategy

This review utilised the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines [23] to explore all literature published in English from inception of the different databases to 1 April 2019. Databases searched were MEDLINE, CINAHL, PsycINFO, Emcare, Informit and Scopus. A preliminary search was conducted in Medline, Emcare and CINAHL to identify relevant key words contained in the titles, abstracts and subject descriptors. These search terms were used to conduct the search in other databases without subject headings. The search strategy used in Medline is presented in supplemental Table 1. No review protocol exists.

Eligibility criteria

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

Selection of studies and data extraction

FA and BMA identified all included studies and data extraction was performed using a standard abstraction form. Data extracted from the studies included: study location and design, population, proportion and incidence of heat illnesses, factors associated with heat illness and heat tolerance, and heat tolerance in men and women. All authors cross-checked the extracted data for consistency.

Quality assessment

The methodological quality assessment was assessed by FA in consultation with MC using the modified quality assessment tool for studies with diverse designs (QATSDD) critical appraisal tool.[24] Any disagreement about any article was reviewed by BMA and AMA and discussed until consensus was reached. The QATSDD tool is a 16-item tool which assesses the quality of diverse studies (both quantitative and qualitative).[24] The tool was modified to exclude two items relating to qualitative studies as well as two items relating to quantitative studies that were not applicable to the studies included in the review. The items excluded comprised statistical assessment of reliability and validity of measurement tool(s) (Quantitative only), fit between stated research question and format and content of data collection tool e.g. interview schedule (Qualitative), assessment of reliability of analytical process (Qualitative only) and evidence of user involvement in design. Each criterion in the modified QATSDD tool was awarded a score of 0 to 3 with 0 = not at all, 1 = very slightly, 2 = moderately and 3 = complete. The scores of each criterion were summed to assess the methodological quality of included studies with a maximum score of 36. The criteria included were (1) theoretical framework; (2)

statement of aims/objectives; (3) description of research setting; (4) evidence of sample size; (5) representative sample of target group of a reasonable size, (6) description of 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; and (12) strengths and limitations. For ease of interpretation, the scores were converted to percentages and classified as low (<50%), medium (50-80%) or high (>80%) quality of evidence.

Patient and public involvement

There was no public or patient involvement in this study.

Data analysis and synthesis

In this review, the International Classification of Diseases ICD 9 or ICD 10 diagnosis codes [25, 26] for the effects of heat and light were used to classify heat illnesses. All included studies utilized either the ICD 9 or ICD 10 codes to classify heat illnesses depending on the year of publication. Heat illnesses were categorised as heat stroke and other heat illnesses. Heat stroke was defined using the ICD diagnosis codes 992.0 (1CD 9) and T67.0 (ICD 10). While other heat illnesses were defined as heat exhaustion (992.3-5, T67 3-5) and unspecified effects of heat and light (992.9 and T67.9). In addition, some studies presented findings for all heat illness without categorizing them into heat stroke and other heat illnesses. These findings were presented separately. Incidence rates and proportions were extracted from the data reported in each study and used for the analysis in this review.

Results

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

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

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

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

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

Incidence and prevalence of all heat illnesses in women compared to men

Table 1 shows the proportions and incidences of all heat-related illness in men and women in the armed forces. Five (5) studies reported higher incidences and proportions of all heat illness in men compared to women[29, 31, 32, 34, 35] while two studies reported higher incidences of all heat illness in women.[30, 33]

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	12.8ǂ	8.6ǂ
				1998		15.8ǂ	12.0ǂ
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)		2.0†	1.5†
				Marine Corps (1104 cases)		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%

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

Gender specific risk factors for heat illness

Three (3) studies identified the gender specific risk factors that were associated with heat illness (Table 2). [31, 34, 49] Two of the studies compared the risk of heat illness between males and females while one study identified risk factors within each gender. In the two studies that compared the risk of heat illness by gender, females had a greater risk of experiencing heat 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, 34] Within gender, males with body mass index (BMI) of ≥ 26 kgm^{-2} had a greater risk of experiencing heat illness compared to males with BMI < 22 kgm^{-2} (OR 2.10, 95% CI 1.59 to 2.78).[49] In addition, males with run times of ≥ 12.9 minutes had almost six times the risk of exertional heat illness compared to males with run times of < 10.3 minutes (OR 5.61, 95% CI 1.92 to 6.85). While females with run times of ≥ 6.9 minutes had five times the risk of exertional heat illness compared to females with run times of < 5.8 minutes (OR 5.30, 95% CI 1.59 to 17.64).[49]

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	BMI ≥ 26 kg/m^2 (males)	2.10 (1.59 – 2.78
			Male (627 cases and 1679 controls)	Run time ≥ 12.9 minutes (males)	5.61 (3.73 – 8.45)
			Female (49 cases and 123 controls)	Run time ≥ 6.9 minutes (females)	5.30 (1.59 – 17.64)

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

Heat tolerance in women and men

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

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%

USA = United States of America

Assessment of methodological quality

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

Discussion

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

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

In this review, women had a lower incidence of heat stroke, but a slightly higher incidence of other heat illness compared to men. The reported lower incidence of heat stroke/higher incidence of other heat illness in women compared to men could possibly be due to the fact that women in the military in the United States were excluded from combat positions until 2013 when the ban was lifted.[20] Evidence in the literature suggests that service members who were engaged in roles such as infantry or gun crew had an increased risk of heat illness, possibly reflecting a greater risk of heat illness for those in combat roles.[34] Furthermore, during military training exercises men may have comparatively tolerated working in the heat beyond the endurance limits.[22] This finding was re-echoed in a previous systematic review that men in the general population had a higher rate of all types of heat illnesses compared to women.[21] Although, the incidence of heat stroke was lower in women compared to men in this review, the incidence of heat stroke among women has increased over the past four years. This implies that as more women engage in specialised military roles their risk of exertional heat illness increases.

Gender specific risk factors for heat illness

Despite the lower incidence of heat stroke, women had a greater risk of exertional heat illnesses compared to men.[30, 33] In addition one study attempted to investigate intra gender risk factors for exertional heat illness.[49] Slower run time duration was associated with exertional heat illness among males and females respectively, while higher BMI was identified as a risk factor among males only.[49] The higher risk of exertional heat illnesses in women may likely be due to differences in physiological and physical characteristics between men and women.[50] Physiological characteristics such as hormones, use of contraceptive pills and lower evaporative heat loss may make women more susceptible to heat illness. [11, 13] However, conflicting evidence suggests that in highly trained women, exercise performance and heat loss is not affected by the menstrual cycle phase but is impaired in humid conditions.[51] In addition, physical characteristics such as lower aerobic fitness is a predictor of exertional heat illness.[50] Generally, women have lower aerobic fitness levels and lower overall work capacity which may contribute to the increased risk of exertional heat illness.[50] Individuals with low aerobic fitness levels are likely to exert themselves beyond their physical limit and are at increased risk of heat illness.[52] Other intra gender risk factors that were identified were longer run time duration and higher BMI.[49] Evidence suggests that slower

357 run time duration which may be a reflection of lower aerobic fitness and higher BMI increases
358 the risk of heat illness.[49, 53] However, the evidence is limited given that this was reported
359 by only one study.[49]

360 **Heat tolerance in women and men**

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

377 **Strengths and limitations**

378 To the authors' current knowledge, this is the first known systematic review investigating
379 gender differences in exertional heat illness and heat tolerance in the armed forces. In addition,
380 we identified potential gender specific risk factors that are associated with exertional heat

illness. However, the heterogeneity in the study designs contributed to the variable methodological quality of the included studies. Most of the articles in this review were military reports and may not be considered of high methodological quality when assessed using a formal critical appraisal tool. In addition, most of the included studies utilized retrospective data as the data source with an increased likelihood of incompleteness and inaccuracy. There is a likelihood that misclassification bias could have been introduced into the studies. Three studies that explored the risk factors associated with heat-related illness used retrospective data. [31, 34, 49] The retrospective data may have been misclassified or incomplete at the time of entry and may have introduced misclassification bias into the studies. This type of bias may underestimate or overestimate the association between heat-related illness and risk factors. Although the gender specific risk factors associated with heat illness were discussed; the review provided limited evidence of these factors, given the few numbers of studies that investigated the association. Furthermore, we included only studies published in English language; studies published in other languages were excluded.

Implication for policy and future research

This systematic review demonstrates that there is limited research on exertional heat illness in women in the armed forces. Although men had a higher incidence of heat stroke; women had a higher incidence of other heat illnesses. Further research is needed to establish if this reflects physiological or behavioural differences. In addition, the limited and inconclusive evidence suggests that more women were classified as heat intolerant compared to men using the Israeli Defence Force heat tolerance test protocol. The current criteria may be unfair to women given that it was developed using male participants. More research is needed to determine the gender differences in heat tolerance as well as to consider re-evaluating the heat tolerance test protocol or the development of a new protocol that considers gender specific factors.[12] Given that the heat tolerance test was conducted in a laboratory setting, more research is needed to replicate the findings in field based setting.

Conclusion

In conclusion, this review shows that men had a higher incidence of heat stroke but women in the armed forces had a greater risk of exertional heat illness. Despite the limited evidence, further research is required to investigate the influence of gender differences on heat tolerance and heat illness. Further research is needed to evaluate the heat tolerance test protocol for women.

Authors' contribution

All authors contributed substantially to the study concept, design, data extraction, quality assessment and writing of the manuscript.

Conceptualization: Faith O. Alele, Bunmi S. Malau-Aduli, Aduli E. Malau-Aduli, Melissa Crowe

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All authors read and approved the manuscript for submission.

Funding: The first author (FA) is supported by the Australian Government International Research Training Program Scholarship

Competing Interests: The authors declare that they have no competing interests.

Patient consent for publication: Not required

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

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Figure legends

Figure 1: PRISMA flow chart of the study selection protocol

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

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

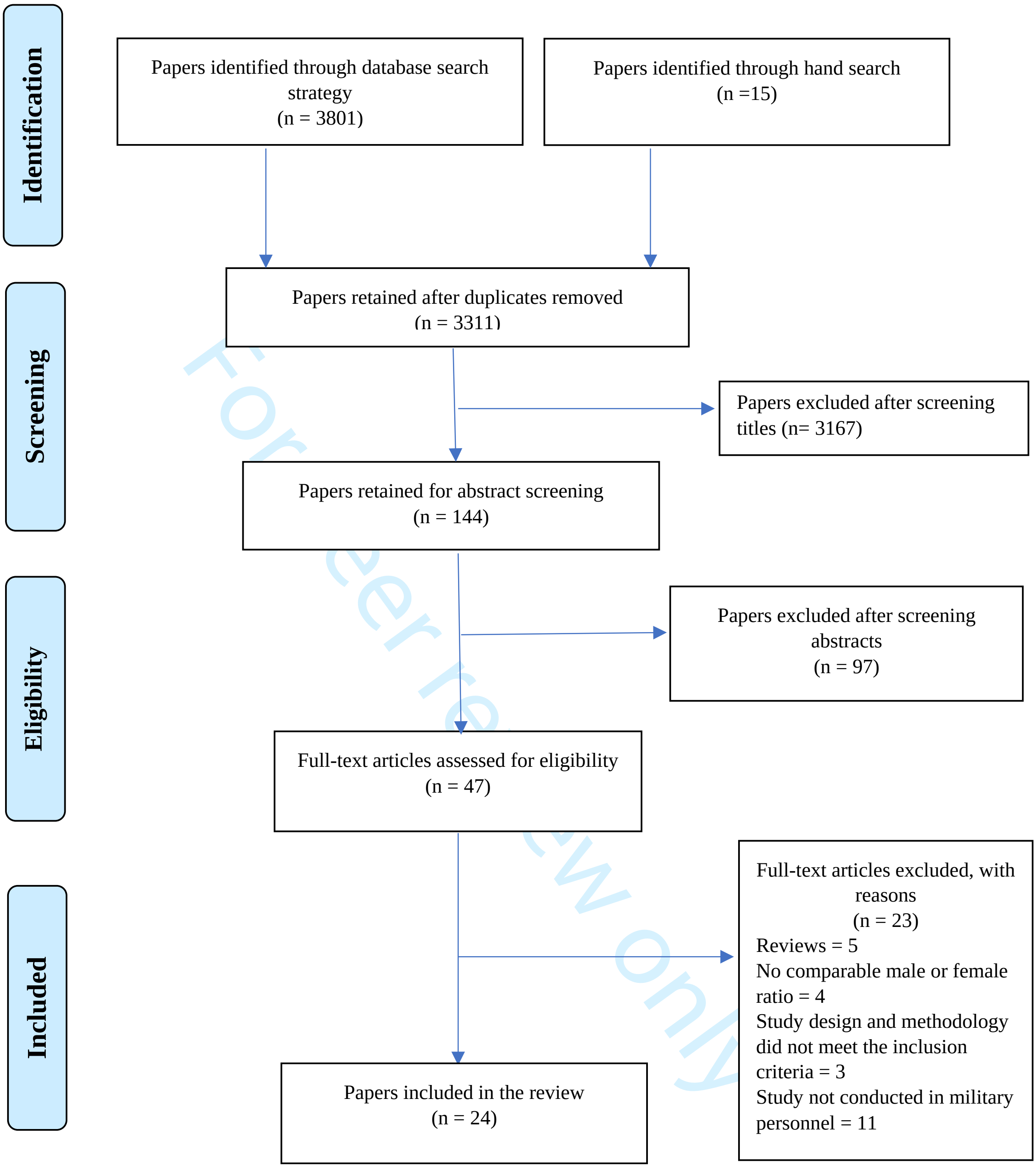

Figure 1: PRISMA flow chart of the study selection protocol

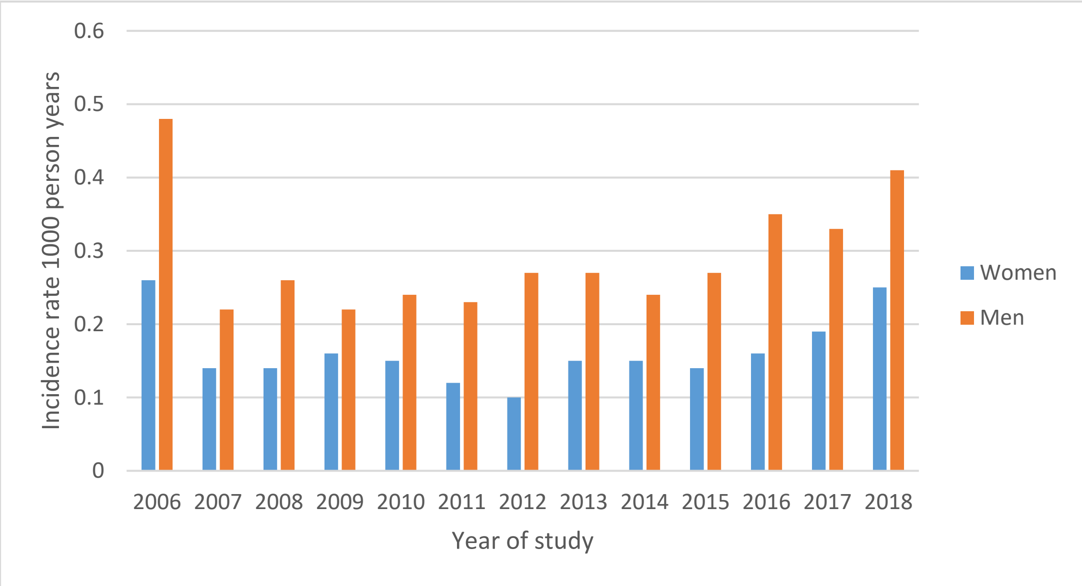
0.6
0.5
0.4
0.3
0.2
0.1
0
Incidence rate 1000 person years
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
Year of study
Women
Men

Figure 2

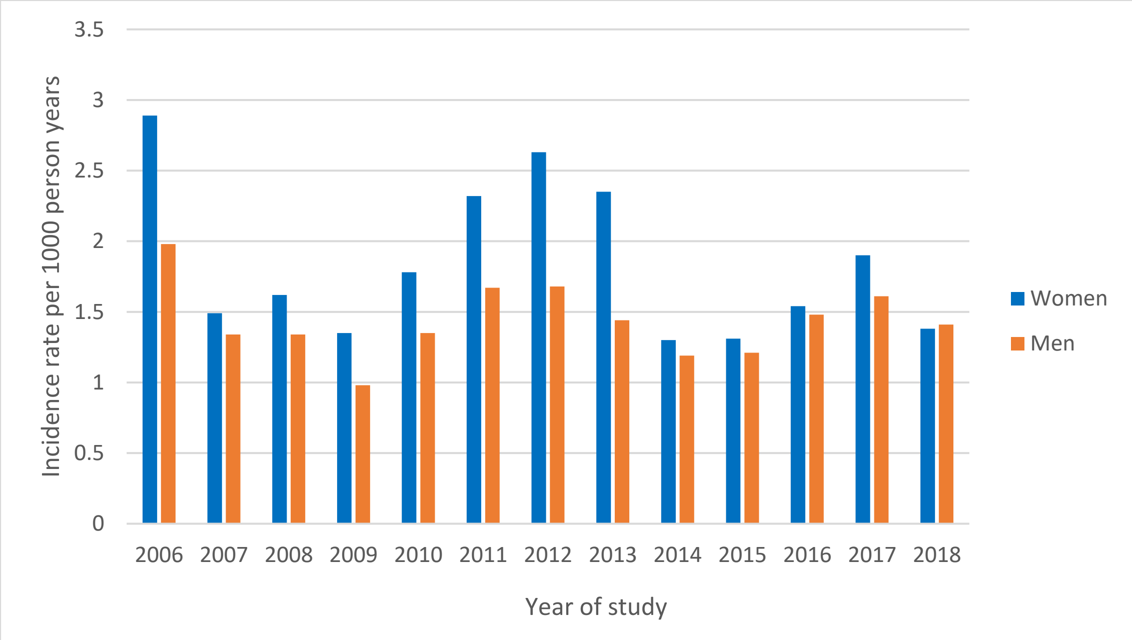
3.5
3
2.5
2
1.5
1
0.5
0
Incidence rate per 1000 person years
2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018
Year of study
Women
Men

Figure 3

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	**Women** All heat injuries: 12.8ǂ **Men** All heat injuries: 8.6ǂ
			1998	**Women** All heat injuries: 15.8ǂ **Men** All heat injuries: 12.0ǂ
Army Medical Surveillance Activity, 2000[33]	USA	Descriptive epidemiology; 1997 - 1999	US Army and Marine Corps; 3386 all heat injuries cases⁋ Army (1896 cases)	**Women** All heat injuries: 2.0† **Men** All heat injuries: 1.5†
			Marine Corps (1104 cases)	**Women** All heat injuries: 4.4† **Men** All heat injuries: 2.0†
Army Medical Surveillance Activity, 2002[31]	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%

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

				Heat stroke: 0.26† Heat exhaustion: 1.34†
Army Medical Surveillance Activity, 2009[39]	USA	Descriptive epidemiology; 2008	US Armed Forces; 299 heat stroke cases 1467 heat exhaustion cases	**Women** Heat stroke: 0.16† Heat exhaustion: 1.35† **Men** Heat stroke: 0.22† Heat exhaustion: 1.78†
Army Medical Surveillance Activity, 2010[40]	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: 0.24† Other heat injuries: 1.35†
Army Medical Surveillance Activity, 2011[41]	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[42]	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[12]	Israel	Retrospective cross-sectional 2008 – 2010	Israeli Defence Forces; 170 males and 9 females	**Heat tolerance parameters** ***Women*** Heat intolerance rate: 66.6% ***Men*** Heat intolerance rate: 25.79%
Army Medical Surveillance Activity, 2013[43]	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†

Army Medical Surveillance Activity, 2014[44]	USA	Descriptive epidemiology; 2013	US Armed Forces; 324 heat stroke cases 1701 other heat injuries cases*	**Women** Heat stroke: 0.15† Other heat injuries: 1.30† **Men** 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	**Women** Heat illness: 0.680% **Men** Heat illness: 0.71%
Lisman et al, 2014[27]	USA	Analytical cross-sectional	Military and university community members; 34 males and 12 females	**Heat tolerance parameters** ***Women*** Heat intolerance rate: 42% ***Men*** Heat intolerance rate: 27%
Army Medical Surveillance Activity, 2015[45]	USA	Descriptive epidemiology; 2014	US Armed Forces; 314 heat stroke cases 1410 other heat injuries cases*	**Women** Heat stroke: 0.14† Other heat injuries: 1.31† **Men** 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	**Heat tolerance parameters** ***Women*** Heat intolerance rate: 45% ***Men*** Heat intolerance rate: 18%
Army Medical Surveillance Activity, 2016[46]	USA	Descriptive epidemiology; 2015	US Armed Forces; 417 heat stroke cases 1625 other heat injuries cases*	**Women** Heat stroke: 0.16† Other heat injuries: 1.54† **Men** Heat stroke: 0.35† Other heat injuries: 1.48†
Army Medical Surveillance Activity, 2017[47]	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[48]	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†

§ *Proportions and incidences reported are of the total cases reported in the articles*
# Incidence rate reported per 100,000 person-years.
ǂ 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.
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[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

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

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

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

PRISMA 2009 Checklist

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:	*BMJ Open*
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

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

Type of article: Review

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Word count: 3993

Abstract

Objectives: This review aimed to describe the epidemiology of all heat related illnesses in women compared to men in the armed forces and to identify gender-specific risk factors and differences in heat tolerance.

Design: A systematic review of multiple databases (MEDLINE, Emcare, CINAHL, PsycINFO, Informit, and Scopus) was conducted from the inception of the databases to 1 April 2019 using the preferred reporting items for systematic review and meta-analysis (PRISMA) guidelines.

Eligibility criteria: All relevant studies investigating and comparing heat illness and heat tolerance in women and men in the armed forces were included in the review.

Results:

Twenty-four (24) studies were included in the systematic review. The incidence of heat stroke in women ranged from 0.10 to 0.26 per 1000 person-years, while the incidence of heat stroke ranged from 0.22 to 0.48 per 1000 person-years in men. The incidence of other heat illnesses in women compared to men ranged from 1.30 to 2.89 per 1000 person-years vs 0.98 to 1.98 per 1000 person-years. The limited evidence suggests that women had a greater risk of exertional heat illness compared to men. Other gender-specific risk factors were slower run times and body mass index. Although there was a higher proportion of women who were heat intolerant compared to men; this finding needs to be interpreted with caution due to the limited evidence.

Conclusion: The findings of this review suggest that men experienced a slightly higher incidence of heat stroke than women in the armed forces. In addition, the limited available evidence suggests that a higher proportion of women were heat intolerant and being a female

was associated with a greater risk of exertional heat illnesses. Given the limited evidence available, further research is required to investigate the influence of gender differences on heat intolerance and heat illness.

Article summary

Strengths and limitations of this study

- This is the first known systematic review investigating the impact of gender on exertional heat illness and heat tolerance in the armed forces.
- We conducted a comprehensive search and identified potential risk factors that are associated with exertional heat illness.
- Most of the included studies utilized retrospective data with an increased likelihood of misclassification bias which may have underestimated or overestimated the association between heat-related illness and risk factors.

Trial registration: None

Key words

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

Introduction

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

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

Among armed forces personnel, exertional heat illness continues to pose as a significant cause of morbidity and mortality. [7] Operations and training may involve exposure to high ambient temperature and heavy workload which may result in heat illness.[7] Historically, men have occupied military roles and responsibilities with fewer proportion of women in the armed forces.[8] However, more women are joining the armed forces globally following the inclusive approach to recruiting and creation of more roles for women.[9] Women are required to operate in austere environments with heat illnesses becoming more frequent.[9] This has raised the question about gender differences in thermoregulation during heat stress.[9] Evidence suggests that women differ from men in thermal responses to heat.[10] This difference may be because women have a lower rate of whole-body evaporative heat loss, higher body fat mass, body mass ratio,[11] number of sweat glands and lower aerobic fitness.[12] Also, hormonal variations due to menstrual cyclic patterns and the use of contraceptive pills may be associated with the differences in response to heat stress.[13]

When exertional heat illness occurs, it may be challenging to determine if an individual may return to duty. An inaccurate determination of complete recovery among armed forces personnel may negatively impact military readiness.[14] While, there are no evidence-based recommendations for return to duty, the American College of Sports Medicine (ACSM) guidelines states that exertional heat stroke patients may return to duty after re-establishing heat tolerance.[15] Individuals vary in their ability to cope with heat stress and the inability to withstand heat stress during exertion in hot environments is defined as heat intolerance.[2] Evidence suggests that heat intolerance may be as a direct result of heat stroke or due to predisposing inherent factors (genetics).[2] However, the objective criteria or measure for defining heat tolerance or intolerance remains a subject of controversy.[14] The current return to duty guidelines for military personnel varies across countries.[16] For example, in the United States, the military return to duty process is based on clinical assessments with gradual acclimatization and re-introduction of duties.[17] By contrast, return to duty in the Israeli Defence Force requires a heat tolerance test to determine if an individual is heat tolerant.[18] Therefore, it is important to develop evidence-based return to duty protocols across the globe.

The Israeli Defence Force originally developed the heat tolerance test in 1979 as an index of the ability of soldiers to cope with exertional heat.[18] Individuals who have suffered heat stroke are sent for a heat tolerance test after a minimum recovery period of 6 to 8 weeks as part of the return to duty process.[18] Criteria used to define heat intolerance include an elevation in rectal temperature above 38.5°C and heart rate above 150 bpm or when rectal temperature or heart rate fails to stabilize during the test. The heat tolerance test criteria are based on previous studies by Shapiro et al.[19] which utilised only male military participants.[18, 19] While the test may be considered as a useful tool to determine return to duty and to prevent subsequent exertional heat stroke, [18,19] there is no consensus on the validity of the tool as a diagnostic test for heat tolerance.[14] Furthermore, the heat tolerance test does not account for predicting factors such as gender.[14] Given the limitation, questions have been raised about the validity of the protocol in determining return to duty for females in the armed forces. It has been suggested that more research is required to determine whether or not a new protocol should be developed for women.[12]

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

Therefore, the objective of this systematic review was to provide a comprehensive summary of the epidemiology of heat illness and heat intolerance in women and men in the armed forces.

Specific aims were

To determine the incidence and prevalence of heat illness in women compared to men in the armed forces:

To identify gender differences in heat tolerance in the armed forces and

To identify gender-specific predisposing risk factors associated with heat illness in the armed forces

Methods

Search Strategy

This review utilised the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines [23] to explore all literature published in English from the inception of the different databases to 1 April 2019. Databases searched were MEDLINE, CINAHL, PsycINFO, Emcare, Informit and Scopus. A preliminary search was conducted in Medline, Emcare and CINAHL to identify relevant keywords contained in the titles, abstracts and subject descriptors. These search terms were used to conduct the search in other databases without subject headings. The search strategy used in Medline is presented in supplemental Table 1. No review protocol exists.

Eligibility criteria

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

Selection of studies and data extraction

FA and BMA identified all included studies and data extraction was performed using a standard abstraction form. Data extracted from the studies included: study location and design, population, proportion and incidence of heat illnesses, factors associated with heat illness and heat tolerance, and heat tolerance in men and women. All authors cross-checked the extracted data for consistency.

Quality assessment

The methodological quality assessment was assessed by FA in consultation with MC using the modified quality assessment tool for studies with diverse designs (QATSDD) critical appraisal tool.[24] Any disagreement about any article was reviewed by BMA and AMA and discussed until consensus was reached. The QATSDD tool is a 16-item tool which assesses the quality of diverse studies (both quantitative and qualitative).[24] The tool was modified to exclude two items relating to qualitative studies as well as two items relating to quantitative studies that did not to the studies included in the review. The items excluded comprised statistical assessment of the reliability and validity of measurement tool(s) (Quantitative only), fit between stated research question and format and content of data collection tool e.g. interview schedule (Qualitative), assessment of reliability of analytical process (Qualitative only) and evidence of user involvement in design. Each criterion in the modified QATSDD tool was awarded a score of 0 to 3 with 0 = not at all, 1 = very slightly, 2 = moderately and 3 = complete. The scores of each criterion were summed to assess the methodological quality of included studies with a maximum score of 36. The criteria included were (1) theoretical framework; (2) statement of aims/objectives; (3) description of research setting; (4) evidence of sample size; (5)

representative sample of target group of a reasonable size, (6) description of 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; and (12) strengths and limitations. For ease of interpretation, the scores were converted to percentages and classified as low (<50%), medium (50-80%) or high (>80%) quality of evidence.

Patient and public involvement

Patients and the public were not involved in the design or planning of the study.

Data analysis and synthesis

In this review, the International Classification of Diseases ICD 9 or ICD 10 diagnosis codes [25, 26] for the effects of heat and light were used to classify heat illnesses. All included studies utilized either the ICD 9 or ICD 10 codes to classify heat illnesses depending on the year of publication. Heat illnesses were categorised as heat stroke and other heat illnesses. Heat stroke was defined using the ICD diagnosis codes 992.0 (1CD 9) and T67.0 (ICD 10). While other heat illnesses were defined as heat exhaustion (992.3-5, T67 3-5) and unspecified effects of heat and light (992.9 and T67.9). In addition, some studies presented findings for all heat illness without categorizing them into heat stroke and other heat illnesses. These findings were presented separately. Incidence rates and proportions were extracted from the data reported in each study and used for the analysis in this review. Due to the heterogeneity of the included studies, a meta-analysis was not conducted.

Results

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

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

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

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

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

Incidence and prevalence of all heat illnesses in women compared to men

Table 1 shows the proportions and incidences of all heat-related illness in men and women in the armed forces. Five (5) studies reported higher incidences and proportions of all heat illness in men compared to women[29, 31, 32, 34, 35] while two studies reported higher incidences of all heat illness in women.[30, 33]

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	12.8ǂ	8.6ǂ
				1998		15.8ǂ	12.0ǂ
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)		2.0†	1.5†
				Marine Corps (1104 cases)		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%

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

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

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

Gender-specific risk factors for heat illness

Three (3) studies identified the gender-specific risk factors that were associated with heat illness (Table 2). [31, 34, 49] Two of the studies compared the risk of heat illness between males and females while one study identified risk factors within each gender. In the two studies that compared the risk of heat illness by gender, females had a greater risk of experiencing heat 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, 34] Within gender, males with body mass index (BMI) of ≥ 26 kgm^{-2} had a greater risk of experiencing heat illness compared to males with BMI < 22 kgm^{-2} (OR 2.10, 95% CI 1.59 to 2.78).[49] In addition, males with run times of ≥ 12.9 minutes had almost six times the risk of exertional heat illness compared to males with run times of < 10.3 minutes (OR 5.61, 95% CI 1.92 to 6.85). While females with run times of ≥ 6.9 minutes had five times the risk of exertional heat illness compared to females with run times of < 5.8 minutes (OR 5.30, 95% CI 1.59 to 17.64).[49]

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	US Marine Corps	BMI ≥ 26 kg/m^2 (males)	2.10 (1.59 – 2.78
		1988 – 1996 (8 years)	Male (627 cases and 1679 controls)	Run time ≥ 12.9 minutes (males)	5.61 (3.73 – 8.45)
			Female (49 cases and 123 controls)	Run time ≥ 6.9 minutes (females)	5.30 (1.59 – 17.64)

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

Heat tolerance in women and men

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

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 (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%

USA = United States of America

Assessment of methodological quality

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

Discussion

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

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

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

In this review, women had a lower incidence of heat stroke, but a slightly higher incidence of other heat illness compared to men. The reported lower incidence of heat stroke/higher incidence of other heat illness in women compared to men could be because women in the military in the United States were excluded from combat positions until 2013 when the ban was lifted.[20] Evidence in the literature suggests that service members who were engaged in roles such as infantry or gun crew had an increased risk of heat illness, possibly reflecting a greater risk of heat illness for those in combat roles.[34] Furthermore, during military training exercises, men may have comparatively tolerated working in the heat beyond the endurance limits.[22] This finding was re-echoed in a previous systematic review that men in the general population had a higher rate of all types of heat illnesses compared to women.[21] Although the incidence of heat stroke was lower in women compared to men in this review, the incidence of heat stroke among women has increased over the past four years. This implies that as more women engage in specialised military roles their risk of exertional heat illness increases.

Gender-specific risk factors for heat illness

Despite the lower incidence of heat stroke, women had a greater risk of exertional heat illnesses compared to men.[30, 33] In addition one study attempted to investigate intra gender risk factors for exertional heat illness.[49] The slower run time duration was associated with exertional heat illness among males and females respectively, while higher BMI was identified as a risk factor among males only.[49] The higher risk of exertional heat illnesses in women may likely be due to differences in physiological and physical characteristics between men and women.[50] Physiological characteristics such as hormones, use of contraceptive pills and lower evaporative heat loss may make women more susceptible to heat illness.[11, 13] However, conflicting evidence suggests that in highly trained women, exercise performance and heat loss is not affected by the menstrual cycle phase but is impaired in humid conditions.[51] In addition, physical characteristics such as lower aerobic fitness is a predictor of exertional heat illness.[50] Generally, women have lower aerobic fitness levels and lower overall work capacity which may contribute to the increased risk of exertional heat illness.[50] Individuals with low aerobic fitness levels are likely to exert themselves beyond their physical limit and are at increased risk of heat illness.[52] Other intra gender risk factors that were identified were longer run time duration and higher BMI.[49] Evidence suggests that slower run time duration which may be a reflection of lower aerobic fitness and higher BMI increases the risk of heat illness.[49, 53] However, the evidence is limited given that this was reported by only one study.[49]

Heat tolerance in women and men

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

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

369 **Strengths and limitations**

370 To the authors' current knowledge, this is the first known systematic review investigating gender differences in exertional heat illness and heat tolerance in the armed forces. In addition, we identified potential gender-specific risk factors that are associated with exertional heat illness. However, the heterogeneity in the study designs contributed to the variable methodological quality of the included studies. Most of the articles in this review were military reports and may not be considered of high methodological quality when assessed using a formal critical appraisal tool. Also, most of the included studies utilized retrospective data as the data source with an increased likelihood of incompleteness and inaccuracy. There is a likelihood that misclassification bias could have been introduced into the studies. Three studies that explored the risk factors associated with heat-related illness used retrospective data. [31, 34, 49] The retrospective data may have been misclassified or incomplete at the time of entry and may have introduced misclassification bias into the studies. This type of bias may underestimate or overestimate the association between heat-related illness and risk factors. Although the gender-specific risk factors associated with heat illness were discussed; the review provided limited evidence of these factors, given the few numbers of studies that

investigated the association. Furthermore, we included only studies published in English language; studies published in other languages were excluded.

Implication for policy and future research

This systematic review demonstrates that there is limited research on exertional heat illness in women in the armed forces. Although men had a higher incidence of heat stroke; women had a higher incidence of other heat illnesses. Further research is needed to establish if this reflects physiological or behavioural differences. In addition, the limited and inconclusive evidence suggests that more women were classified as heat intolerant compared to men using the Israeli Defence Force heat tolerance test protocol. The current criteria may be unfair to women given that it was developed using male participants. More research is needed to determine the gender differences in heat tolerance as well as to consider re-evaluating the heat tolerance test protocol or the development of a new protocol that considers gender-specific factors.[12] Given that the heat tolerance test was conducted in a laboratory setting, more research is needed to replicate the findings in field based setting.

Conclusion

In conclusion, this review suggests that men had a slightly higher incidence of heat stroke but women in the armed forces may have a greater risk of exertional heat illness. However, the current evidence is limited, and further research is required to investigate the influence of gender differences on heat tolerance and heat illness. In addition, further research is needed to evaluate the heat tolerance test protocol for women.

Authors' contribution

All authors contributed substantially to the study concept, design, data extraction, quality assessment and writing of the manuscript.

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Funding: The first author (FA) is supported by the Australian Government International Research Training Program Scholarship

Competing Interests: The authors declare that they have no competing interests.

Patient consent for publication: Not required

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

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Figure legends

Figure 1: PRISMA flow chart of the study selection protocol

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

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

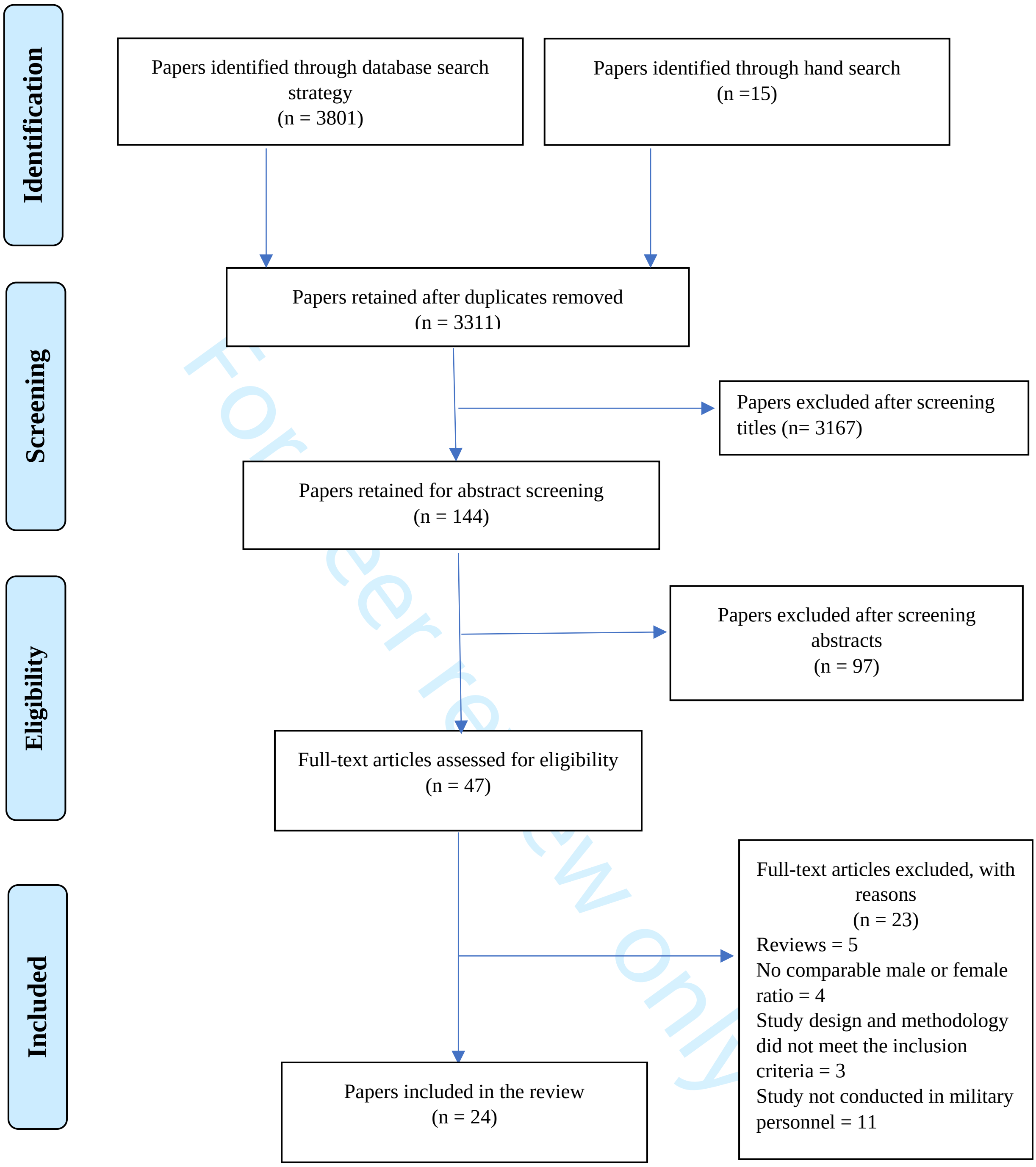

Figure 1: PRISMA flow chart of the study selection protocol

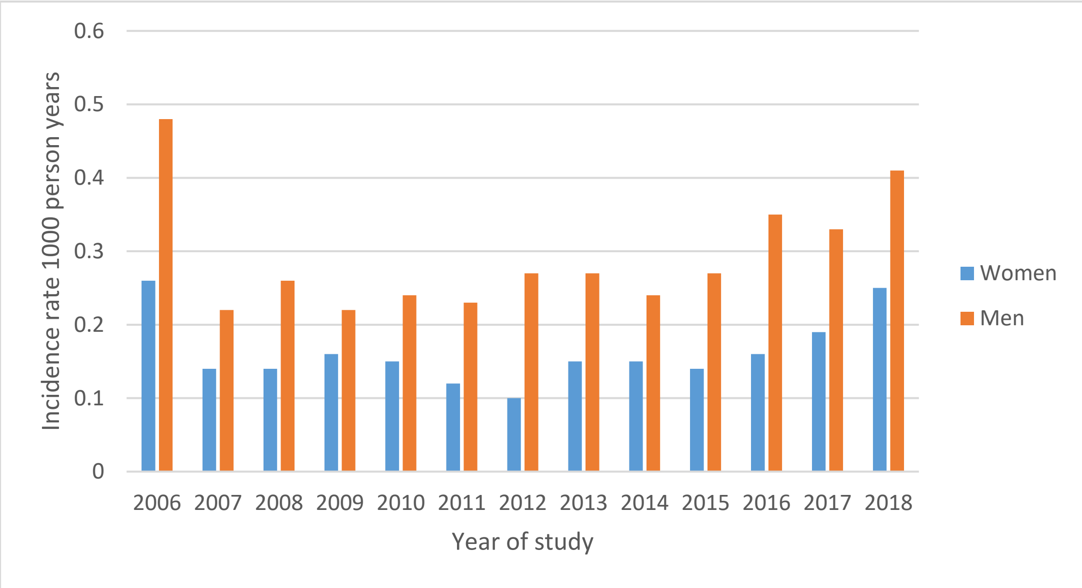
0.6
0.5
0.4
0.3
0.2
0.1
0
Incidence rate 1000 person years
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
Year of study
Women
Men

Figure 2

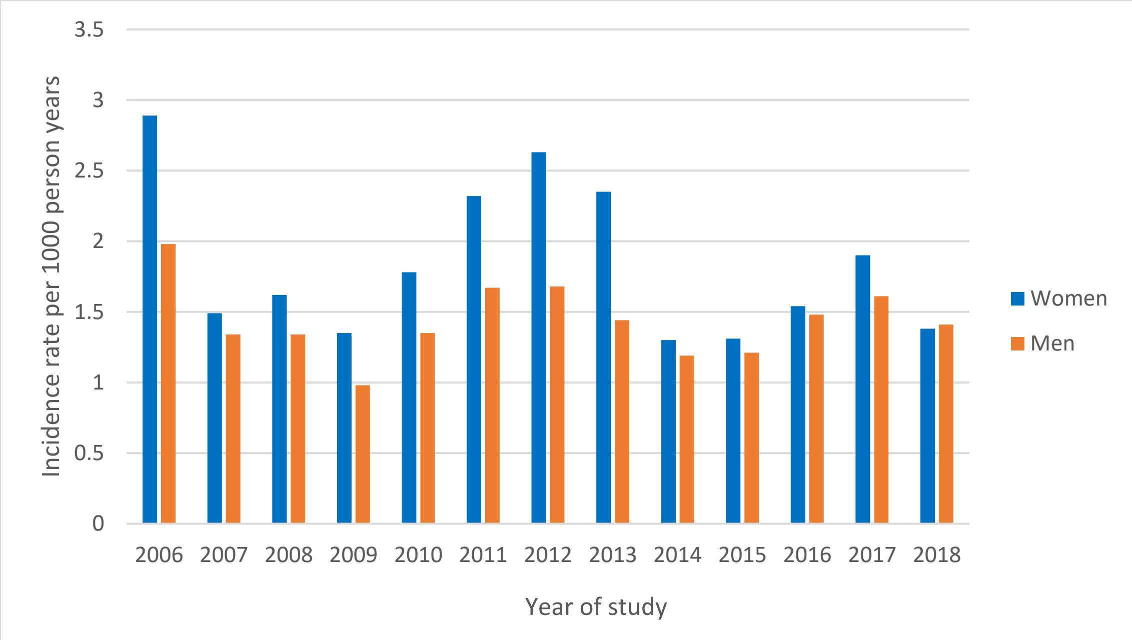
3.5
3
2.5
2
1.5
1
0.5
0
Incidence rate per 1000 person years
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
Year of study
Women
Men

Figure 3

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	**Women** All heat injuries: 12.8ǂ **Men** All heat injuries: 8.6ǂ
			1998	**Women** All heat injuries: 15.8ǂ **Men** All heat injuries: 12.0ǂ
Army Medical Surveillance Activity, 2000[33]	USA	Descriptive epidemiology; 1997 - 1999	US Army and Marine Corps; 3386 all heat injuries cases⁋ Army (1896 cases)	**Women** All heat injuries: 2.0† **Men** All heat injuries: 1.5†
			Marine Corps (1104 cases)	**Women** All heat injuries: 4.4† **Men** All heat injuries: 2.0†
Army Medical Surveillance Activity, 2002[31]	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%

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

				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	**Women** Heat stroke: 0.16† Heat exhaustion: 1.35† **Men** Heat stroke: 0.22† Heat exhaustion: 1.78†
Armed Forces Health Surveillance Branch, 2010[40]	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: 0.24† Other heat injuries: 1.35†
Armed Forces Health Surveillance Branch, 2011[41]	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†
Armed Forces Health Surveillance Branch, 2012[42]	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[12]	Israel	Retrospective cross-sectional 2008 – 2010	Israeli Defence Forces; 170 males and 9 females	**Heat tolerance parameters** ***Women*** Heat intolerance rate: 66.6% ***Men*** Heat intolerance rate: 25.79%
Armed Forces Health Surveillance Branch, 2013[43]	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†

Armed Forces Health Surveillance Branch, 2014[44]	USA	Descriptive epidemiology; 2013	US Armed Forces; 324 heat stroke cases 1701 other heat injuries cases*	**Women** Heat stroke: 0.15† Other heat injuries: 1.30† **Men** 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	**Women** Heat illness: 0.680% **Men** Heat illness: 0.71%
Lisman et al, 2014[27]	USA	Analytical cross-sectional	Military and university community members; 34 males and 12 females	**Heat tolerance parameters** ***Women*** Heat intolerance rate: 42% ***Men*** 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*	**Women** Heat stroke: 0.14† Other heat injuries: 1.31† **Men** 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	**Heat tolerance parameters** ***Women*** Heat intolerance rate: 45% ***Men*** 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*	**Women** Heat stroke: 0.16† Other heat injuries: 1.54† **Men** 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*	**Women** Heat stroke: 0.19† Other heat injuries: 1.90† **Men** Heat stroke: 0.33†

				Other heat injuries: 1.61†
Armed Forces Health Surveillance Branch, 2018[48]	USA	Descriptive epidemiology; 2017	US Armed Forces; 464 heat stroke cases 1699 heat exhaustion cases	**<u>Women</u>** Heat stroke: 0.25† Other heat injuries: 1.38† **<u>Men</u>** Heat stroke: 0.41† Other heat injuries: 1.41†

§ *Proportions and incidences reported are of the total cases reported in the articles*
# Incidence rate reported per 100,000 person-years.
ǂ 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;
(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

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.	9

PRISMA 2009 Checklist

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