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The Heat Illness Avatar: An Open, Interactive Resource for Characterisation of Heat-Related Illness

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Abstract

Heat-related illnesses (HRI) are a growing public health concern in our warming world. Timely treatment is critical but early recognition and management of secondary complications remains challenging due to the heterogeneous nature of its clinical presentation. We present the Heat Illness Avatar (HIA), an open interactive digital resource developed from 610 clinically diagnosed exertional HRI cases reported across 248 studies. The HIA integrates data from diverse exertional contexts, climates, and geographic locations, encompassing patients with varied demographics, disease severity, and clinical outcomes. As an open-access resource and clinical decision-support tool, it enables generation of reference HRI phenotypes, quantification of frequency and mortality risk across 588 clinical features, and stratification by user-defined variables including age, environment, activity, and exercise intensity. These capabilities establish the HIA as an integrated platform to support future research and to facilitate early recognition and informed management of HRI, with the potential to improve patient outcomes.

Introduction

Climate change is the most pressing global public health challenge of the 21st century [1,2], driving elevations in global temperature and increasing the frequency, duration and intensity of heatwaves [3,4]. Between 1980 to 2022, global heatwave frequency increased by 0.92 events per decade, while annual heatwave days increased by 4.23 days per decade [5]. Such trends are associated with numerous adverse health impacts [6], including elevated morbidity and mortality [7,8], increased heat-related illness (HRI) incidences [9], greater cardiovascular, respiratory and renal disease risk [10,11], and increased mental health issues [12]. Military personnel, first-responders, outdoor workers and athletes, bear a disproportionate share of this burden due to the combination of high metabolic heat production, thick personal protective attire and prolonged environmental heat exposure in their daily activities. This risk is exacerbated by heightened motivation in these populations, which may suppress thermoregulatory behaviour and elevate physiological strain [13]. As global temperatures continue to rise, exertional HRI incidences are expected to increase commensurately, imposing substantial operational and economic costs that threaten the safety and performance of physically active populations worldwide [14,15].

Exertional HRI symptoms range in severity from mild heat cramps and syncope, through heat exhaustion, leading up to the life-threatening extreme of exertional heat stroke (EHS) [16,17]. Unlike classic heat stroke, which results from passive exposure to extreme environmental temperatures, EHS arises from excessive metabolic heat production and impaired dissipation during intense physical exertion and can occur in temperate climates [18]. Without rapid recognition and aggressive cooling, EHS leads to severe clinical consequences, including multi-organ system dysfunction and even death [19]. Nevertheless, its mortality and morbidity burden are highly modifiable and linked to the timeliness of intervention [20,21]. Therefore, early and accurate clinical recognition remains critical for improving patient survival and minimising long-term sequelae.

Despite its severity and need for immediate intervention, EHS is frequently misdiagnosed in real-world settings where contextual information is incomplete or difficult to ascertain [21]. Additionally, limited understanding of EHS pathophysiology may hinder recognition and management of secondary complications, which can substantially influence clinical outcomes [22]. Currently, clinical understanding of EHS centres on several hallmark features, including hyperthermia, neurological dysfunction, cardiovascular instability, renal impairment and coagulopathy [19,23]. However, this framework does not capture the heterogeneity of EHS presentation and progression in the real-world, which varies considerably across individuals. Furthermore, these features often overlap with and present alongside competing diagnoses such as rhabdomyolysis, hyponatraemia, sepsis and other central nervous system pathologies [23]. These complexities underscore the need for systematic characterisation of diverse EHS clinical manifestations to improve diagnostic accuracy, support clinical decision-making and monitoring, and guide evidence-based treatment.

We conducted a systematic review of published exertional HRI cases following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, to aggregate and characterise clinical features associated with exertional HRI from published case literature. Given the heterogeneity and breadth of clinical features across cases, an interactive digital dashboard known as the Heat Illness Avatar (HIA) was developed to synthesise and visualise the extracted dataset. The HIA dynamically generates a reference HRI phenotype based on user-defined characteristics including age, environment, activity type and exercise intensity, and provides a clinical feature map illustrating co-presences, associations, and mortality risks. Together, these capabilities establish the HIA as a structured research and clinical decision support tool to advance understanding of EHS pathophysiology, improve early recognition and triage of exertional heat illness (EHI), and guide treatment of complex cases that persist after immediate cooling. Future refinement of the HIA through incorporation of newly published exertional HRI studies and classic heat stroke cases will ensure continued relevance while expanding its utility across exertional and classic heat stroke.

Results

Establishing a robust HRI dataset to facilitate HIA development

We systematically reviewed relevant scientific databases from inception up to 01 March 2025 to construct the HIA. This revealed 6728 unique articles, of which 248 studies were eligible for inclusion. From these studies, 610 HRI cases involving individuals aged 18 to 65 years were identified and extracted to our database. All HRI cases occurred between 1933 to 2025, spanning across 43 countries. Majority of cases originated from the United States (33%), followed by South Africa (15%), Israel (10%) and United Kingdom (7%) (Fig. 1a). While disparities in the number of HRI reports by country may suggest fewer incidences, they more plausibly reflect systematic underreporting in the literature and the

need to strengthen global HRI documentation efforts. These disparities may also be influenced by language restrictions applied in the review inclusion criteria.

Environmental reporting was inconsistent across studies, with dry bulb temperature (T_{db}) documented in 57% of cases and other environmental indices reported in fewer than one-third of studies. Our dataset captured a broad spectrum of environmental conditions, with T_{db}, relative humidity (RH) and wet-bulb globe temperatures (WBGT) ranging from 3.0 to 45.6°C (Fig. 1b), 13 to 100% (Fig. 1c) and 2.0 to 36.1°C respectively (Fig. 1d). Most HRI incidences occurred at T_{db} and WBGT between 25 and 35°C (T_{db} = 61%, 221 of 361 cases, Fig. 1b; WBGT = 74%, 100 of 135 cases, Fig. 1d), with few cases reported above 35°C. This may be attributed to protective behavioural adaptations (e.g. seeking shade and minimising physical activity) and heat mitigation strategies implemented during high heat conditions [24,25]. HRIs were also observed in temperate climates, reinforcing that risk persists beyond exercise in hot environments. HRI incidence peaked at RH of 50 to 70% (44%, 87 of 197 cases, Fig. 1c) and remained high at > 70% RH (34%, 67 of 197 cases). This reflects impaired evaporative heat loss during exercise in humid conditions, limiting metabolic heat dissipation and elevating HRI risk [26].

Occupational activities accounted for 72% of 610 HRI cases (Fig. 1e), with military training the dominant contributor (54% of 437 cases). These cases typically involved marching, running, or unspecified physical training with varying loads. This was followed by outdoor physical work (37%), mainly mining and construction work. The predominance of military cases reflects both the training rigour and better-established reporting infrastructure within the armed forces relative to civilian contexts. Athletic-related cases accounted for 15% of 610 HRI cases, mainly from marathon running (66%). Recreational activities contributed 7%, refugee movement/forced migration 1%, while 5% were not specified (Fig. 1e). Notably, among cases with WBGT ≥ 31°C, occupational activities made up 44 of 48 cases, with four unspecified. All athletic-related and recreational activity-related HRI cases occurred at WBGT < 31°C.

Casualty demographics were well documented for age (100%) and sex (89%). Most exertional HRI cases occurred in individuals aged 18 to 30 years (68%, 416 cases, Fig. 1f), with mean age at 28 ± 9 years. Most casualties were male (83%, 506 cases), while 6% were females (36 cases) (Fig. 1g). Sex was not reported in the remaining 68 cases (11%). This sex imbalance may be attributed to the large proportion of military- and construction-based incidences, which are traditionally male-dominated industries. Reporting of anthropometric parameters, including height, body mass, and/or BMI, were limited to 12% of cases. Among the 76 cases with available data, 88% were classified as overweight (BMI 23-27.4 kg/m^2; 43 cases) or obese (BMI ≥ 27.5 kg/m^2 [27]; 24 cases, Fig. 1h). Given that elevated BMI is an established EHI risk factor [28,29], consistent BMI documentation in case reports is needed to strengthen obesity prevalence estimates among HRI cases and enhance risk characterisation.

Among 449 cases with documented health statuses, 90% involved otherwise healthy individuals (Fig. 1i). Acute illnesses were reported in a minority, including coryza, influenza, malaise, sore throat, among others. Prior HRI incidence was documented in 26 cases, with four occurring 3 days to 6 weeks before the subsequent incident. Chronic comorbidities were reported in 48 of the 610 cases, including

hypertension, malignant hyperthermia genetic susceptibility, and psychiatric disorders (i.e. schizophrenia, depression, attention deficit hyperactivity disorder and chronic alcohol abuse). Sixty-three cases reported medication use at the time of HRI, including antipsychotics, CNS stimulants, non-steroidal anti-inflammatory drugs (NSAIDs), selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs) and Ephedra based supplements, many of which impair thermoregulation and increase heat illnesses risk [30]. Other predisposing EHI factors, including inadequate heat acclimatisation, poor physical fitness, sleep deprivation and excessive motivation were also noted [28,31,32].

Patient diagnoses were derived from the published cases. Eighty-three percent of the cases were diagnosed as EHS and 16% as EHI (Fig. 1k). The remaining 1% (eight cases) had no explicit diagnosis beyond HRI. This aligns with evidence that milder HRI cases are underrepresented in the literature [33]. The overall survival rate was 68% (Fig. 1j). Most EHS cases survived (69%) highlighting that HRI-related mortality is largely preventable with timely recognition and appropriate patient management, even in cases with severe clinical manifestations [34].

Mapping acute clinical features to understand the immediate organ- and system-level impact of HRI

Characterization of known and novel acute clinical features could guide biomarker research towards prevention of HRI. Of the 610 cases, 588 reported acute clinical features, defined as features presented within 24 hours from HRI onset. These were predominantly observed in the nervous system, with 1831 reported manifestations across 98 unique clinical features, and the cardiovascular system (1124 manifestations across 80 clinical features). Acute features were also commonly reported in the urinary (622 manifestations across 45 clinical features), digestive (445 manifestations across 49 clinical features), respiratory (366 manifestations across 44 clinical features), integumentary (276 manifestations across 14 clinical features), and muscular systems (264 manifestations across 16 clinical features). None were identified in the skeletal or reproductive systems. Multiple organ system injury was documented in 76% of the 588 cases. Frequency counts were determined from these 588 cases, whereas mortality risk ratios were calculated from 508 cases with reported patient outcomes. An overview of notable acute HRI clinical features is illustrated in Fig. 2.

Nervous system – Neurological manifestations were the most prominent feature of HRI, with altered consciousness (32%, RR = 0.49, 95% CI [0.31, 0.76]), loss of consciousness (29%, RR = 1.69, 95% CI [1.21, 2.38]), and collapse of unknown origin (27%, RR = 1.54, 95% CI [1.09, 2.17]) the most frequently reported. Comas and seizures were reported in 18% (RR = 1.86, 95% CI [1.32, 2.64]) and 15% (RR = 1.69, 95% CI [1.17, 2.44]) of cases, respectively, underscoring the impact of HRI on brain function. Gait instability was noted in 3% (RR = 0.91, 95% CI [0.32, 2.57]) of cases. Casualties also displayed evidence of irritability (9%, RR = 0.56, 95% CI [0.26, 1.21]), delirium (5%, RR = 1.24, 95% CI [0.64, 2.41]), irregular speech (2%, RR = 1.34, 95% CI [0.50, 3.58]), and restlessness (2%, RR = 0.98, 95% CI [0.28, 3.41]), suggesting that behavioural and emotional alterations could be an indicator of HRI onset. Acute ocular features include

sluggish pupil reflexes reported in 14 cases (2%, RR = 2.16, 95% CI [1.15, 4.06]), abnormal pupil dilation in 11 cases (2%, RR = 1.81, 95% CI [0.81, 4.03]) and abnormal eye deviation in 7 cases (1%, RR = 1.40, 95% CI [0.43, 4.59]).

Cardiovascular system – Cardiovascular clinical features were the second most common among HRI cases. These were reported at rest, and after the HRI incident occurred. Tachycardia was the most common, observed in 39% of cases (RR = 1.31, 95% CI [0.93, 1.84]). This was followed by hypotension and diastolic hypotension, observed in 20% (RR = 1.20, 95% CI [0.82, 1.76]) and 18% of cases (RR = 0.94, 95% CI [0.60, 1.45]) respectively, indicative of hemodynamic instability. Leucocytosis (11%, RR = 1.45, 95% CI [0.94, 2.24]), thrombocytopenia (7%, RR = 1.57, 95% CI [0.95, 2.60]), hypertension (11%, RR = 0.67, 95% CI [0.36, 1.26]) and disseminated intravascular coagulation (9%, RR = 2.42, 95% CI [1.67, 3.53]) were also reported in a significant proportion of patients. Severe cardiovascular complications, including myocardial injury (3%, RR = 2.58, 95% CI [1.57, 4.23]) and myocardial infarction (3%, RR = 0.98, 95% CI [0.40, 2.39]), were evident in our review and prior heat stroke research [35], highlighting the profound impact of HRI on the cardiovascular system. *Is it*

Urinary system – The most common clinical feature from the urinary system was acute renal injury, which was observed in 29% of HRI cases (RR = 0.94, 95% CI [0.65, 1.36]). Metabolic acidosis (13%, RR = 1.33, 95% CI [0.87, 2.05]) was the primary acid-base disorder reported among patients whereas lactic acidosis (4%, RR = 0.60, 95% CI [0.20, 1.75]) was less common. Abnormalities in sodium and potassium levels were the most common among measured plasma electrolytes. These imbalances culminated in 36 cases of hyponatremia (6%, RR = 1.24, 95% CI [0.69, 2.25]), 26 cases of hyperkalaemia (4%, RR = 1.61, 95% CI [0.88, 2.93]), and 19 cases of hypokalaemia (3%, RR = 1.03, 95% CI [0.42, 2.50]). Low urine output (oliguria) was recorded in 3% (RR = 1.03, 95% CI [0.42, 2.50]) of HRI casualties with a further 3% (RR = 2.01, 95% CI [1.06, 3.83]) exhibiting absence of urine production (anuria). Other notable urinary disorders included proteinuria (7%, RR = 1.54, 95% CI [0.95, 2.52]) and haemoglobinuria (2%, RR = 1.05, 95% CI [0.38, 2.90]), reflecting abnormal protein and haemoglobin presence in the urine respectively.

Digestive system – Acute liver dysfunction was the most common acute clinical feature of the digestive system, reported in 16% (RR = 1.37, 95% CI [0.93, 2.04]) of cases. Gastrointestinal features such as vomiting (10%, RR = 1.09, 95% CI [0.65, 1.82]), diarrhoea (6%, RR = 2.28, 95% CI [1.49, 3.49]), and nausea (6%, RR = 0.27, 95% CI [0.07, 1.06]) were also commonly reported. Abdominal tenderness and gastrointestinal haemorrhaging were reported in 7 patients (1%, RR = 0.69, 95% CI [0.11, 4.30]) and 6 patients (1%, RR = 2.49, 95% CI [1.10, 5.64]), respectively.

Respiratory system – Tachypnoea was reported in 16% of cases (RR = 0.98, 95% CI [0.63, 1.53]). In relation, both hypercapnia (RR = 0.68, 95% CI [0.32, 1.45]) and respiratory acidosis (RR = 1.38, 95% CI [0.81, 2.36]) were reported in 7% of cases. Severe respiratory manifestations were also reported with 16 cases of pulmonary oedema (3%, RR = 3.64, 95% CI [2.49, 5.31]), 11 cases of pulmonary haemorrhage (2%, RR = 4.81, 95% CI [3.70, 6.24]) and 7 cases of acute respiratory distress syndrome (1%, RR = 2.13, 95% CI [0.89, 5.09]).

Lymphatic system - An inflammatory response was documented in 20 patients (3%, RR = 0.98, 95% CI [0.40, 2.39]). Splenic congestion was also observed in 3 cases (1%, RR = 5.00, 95% CI [4.20, 5.95]).

Integumentary system - Eighteen percent of HRI cases presented with sweaty skin (RR = 0.88, 95% CI [0.56, 1.38]) while 10% presented with dry skin (RR = 1.81, 95% CI [1.21, 2.72]). A subset exhibited hot (9%, RR = 1.42, 95% CI [0.88, 2.31]) and pale (3%, RR = 0.76, 95% CI [0.27, 2.19]) skin. Other cutaneous manifestations included cyanosis (2%, RR = 2.55, 95% CI [1.46, 4.43]) and flushed red skin (2%, RR = 0.44, 95% CI [0.07, 2.87]).

Muscular system – Rhabdomyolysis was the most common clinical feature of the muscular system, reported in 11% of cases (RR = 0.66, 95% CI [0.35, 1.24]). Other physical manifestations included cramps (5%, RR = 0.17, 95% CI [0.02, 1.15]), myalgia (2%, RR = 1.23, 95% CI [0.36, 4.12]), and muscle tenderness (1%, RR = 1.23, 95% CI [0.36, 4.12]).

Endocrine system – Hyperglycaemia (6%, RR = 1.01, 95% CI [0.51, 1.99]) and hypoglycaemia (1%, RR = 0.61, 95% CI [0.10, 3.83]) were the two primary endocrine system complications reported, suggesting abnormal insulin regulation as an acute clinical feature of HRI.

Non-specific organ system – Certain clinical features could not be assigned to a specific organ system. Malaise (3%, RR = 0.28, 95% CI [0.04, 1.89]), shock (unspecified) (1%, RR = 2.47, 95% CI [0.91, 6.68]), and coagulative necrosis (1%, RR = 5.04, 95% CI [4.23, 6.01]) were observed in several cases.

As HRI clinical features seldom present in isolation[36], pairwise co-occurrence frequencies of clinical features and their corresponding pairwise risk ratios were calculated. To minimise sparse-data bias and ensure robust estimation, only feature pairs occurring concurrently in at least 26 cases (5% of 508 cases) were interpreted. The highest mortality risk was observed when dry skin co-occurred with loss of consciousness (6%, RR = 2.57, 95% CI [1.69, 3.91]). This was followed by disseminated intravascular coagulation (DIC) with acute renal injury/dysfunction (6%, RR = 2.51, 95% CI [1.66, 3.79]), and collapse of unknown origin co-occurring with seizures (7%, RR = 2.46, 95% CI [1.64, 3.69]). DIC co-occurring with unconscious state (7%, RR = 2.53, 95% CI [1.69, 3.79]) was also associated with elevated mortality risk. Higher-order co-occurrence combinations involving up to five simultaneous clinical features are available for interactive exploration in the HIA Digital Dashboard.

Discussion

The heat illness avatar (HIA) is a first-of-its-kind interactive visualization tool that captures the full array of documented exertional HRI clinical features in the published literature (Fig. 3). We systematically reviewed relevant scientific databases from inception to 01 March 2025 to construct the HIA. This yielded 610 exertional HRI cases across 243 studies, from which 578 clinical features were identified and extracted. The HIA draws on a diverse dataset of HRI cases occurring across various exertional contexts, climates, and geographical locations. This yielded a dataset encompassing patients with broad demographics, varying illness severities, and survival outcomes, strengthening its relevance in clinical

and research domains. Designed as an open-access living database and clinical decision support tool, the HIA dynamically generates reference HRI phenotypes, highlighting common clinical features present and their associated mortality risk based on user defined characteristics, including age, environment, activity, and exercise intensity. Given the heterogeneity of clinical HRI features between cases, the HIA includes a map layer illustrating the co-presences and associations between features of interest and their respective mortality risk ratio. Accordingly, we have developed an interactive platform that may enable timely detection and treatment of co-occurring clinical features within the HRI phenotype to improve patient outcomes.

The HIA is a robust, centralized database of 610 documented exertional HRI cases in the English language. Efforts to characterize HRI etiology have been limited by discordant use of terminology and case definitions across published reports [33]. By consolidating and aligning these clinical cases within the HIA, we provide a harmonized resource to improve recognition and management of HRI and its diverse clinical manifestations. Considering the multitude of exertional HRI cases in the HIA, a dynamic filtering capability was developed to support feature-specific queries and enable efficient case retrieval (Fig. 3a). To extend its applicability beyond exertional HRI, future iterations of the HIA will incorporate classic heat stroke cases to capture key differences between exertional and classic heat stroke etiology and pathophysiology [18]. Moreover, the database is open to published contributions from the wider research and clinical community to extend the comprehensiveness and recency of our dataset. Such engagement may promote systematic reporting of HRI, addressing the underrepresentation of untreated or undocumented cases that impedes epidemiological research [33]. Importantly, development of clear guidelines for reporting future HRI cases is necessary to enhance the rigour and consistency within the database. This serves to retain data quality and interpretability of the HIA by minimizing reporter subjectivity when defining HRI cases and their clinical manifestations.

The primary intent for the HIA is to facilitate pattern recognition and clinical assistance in diagnosing multiorgan failure. This was achieved through systematic visualization of documented HRI clinical features, mapping their associations across organ systems, organs, and patient presentations. The HIA clusters clinical features into various organ systems (e.g., cardiovascular system, digestive system) to provide an evidence-based overview of the multi-organ system impact of HRI. Clinical features are further classified at the organ level, offering greater granularity and elucidating the organs within each system that are most impacted (Fig. 3a). By aggregating reported clinical HRI features in the literature, the HIA also enables identification of less common clinical features that could aid in diagnosing unique clinical phenotypes and serve as novel markers for early HRI detection. Taken together, these capabilities enable users to explore the systemic manifestations of HRI, while offering deeper insight into its aetiology and pathophysiology.

The HIA also features a dynamic network graph (Fig. 3b) to elucidate the strength of associations between a clinical feature of interest and other HRI-related features, based on their co-occurrence frequency. These associations can greatly enhance recognition and management of exertional HRIs by enabling identification of common clinical feature clusters. On a broader scale, this tool also highlights

the associations between organ systems, such as the frequent co-involvement of the cardiovascular and central nervous systems. This offers deeper insight into the multi-system manifestations of HRI and supports more informed clinical decision-making. Identified associations between organ systems may also guide future investigations into the complex, multi-system pathophysiology of exertional HRIs.

Beyond clinical feature prevalence, the HIA incorporates risk ratios to quantify the prognostic significance of individual and up to five co-occurring clinical features for HRI mortality (Fig. 3c). Notably, clinical feature frequency did not consistently align with mortality risk, underscoring the importance of considering both metrics in parallel. While several features were frequently reported among patients with exertional HRI (e.g. acute renal dysfunction, tachycardia, and altered conscious state), a subset of less frequent manifestations was associated with markedly higher risk of death (e.g. splenic congestion, renal haemorrhage, and coagulative necrosis). By integrating clinical feature prevalence with risk ratios, the HIA enables a more objective assessment of clinical severity across heterogeneous HRI presentations. This highlights the direct clinical utility of our resource to enable efficient evidence-based decision-making for patient management, particularly in mass gatherings, sporting events, and military training settings where medical resources may be limited. Collectively, these features support early identification of patients at the greatest risk of adverse outcomes, supporting triage and additional medical testing where needed to enable timely escalation of care.

All cases in the HIA can also be filtered by case characteristics (age, sex, BMI, prior health status, patient outcome, day of reported value) to enable stratified analysis. This capability is valuable in generating a more nuanced understanding of HRI within populations of interest, such as older adults, or individuals with high BMI, where differential risks may have important implications for HRI recognition and treatment. Stratification based on patient outcome (Recovered or Passed Away) is also purposeful to determine whether presence of certain clinical features (e.g., loss of consciousness) are more commonly associated with mortality, thereby offering valuable insights into potential prognostic indicators of HRI severity. Similarly, filtering by day of reported clinical features allows differentiation between acute manifestations and longer-term deleterious effects of HRI. Therefore, the HIA provides novel insights into specific case characteristics and the time course of HRI feature manifestation, improving the understanding of its clinical progression.

Limitations

Certain HRI clinical features manifest across multiple organs and/or organ systems (e.g., jaundice, unstable gait), but were assigned to their most relevant organ and organ system only. The HIA may thus underestimate the true extent of multi-organ involvement when HRI clinical features affecting multiple organs or systems are present. Similarly, variability exists in clinical reporting, terminology, and clinical practices. This gives rise to the possibility that certain features were present but not recorded, described differently, or not assessed at all, which leads to underestimation of their true prevalence. As the HIA was also limited to published cases, we may not have captured the full spectrum of HRI features, particularly in milder cases that are often not reported or treated in medical facilities. Additionally, case

reports and series rarely document absent clinical features, limiting our ability to distinguish between true absence and non-reporting. In the HIA dataset, features were classified as “present”, “absent”, or “not reported” to facilitate accurate analyses of co-occurrence and mortality risk. While exhaustive reporting of all absent clinical features is unfeasible, documenting the absence of key HRI features remains crucial for a comprehensive understanding of HRI pathophysiology. It should also be acknowledged that the current HIA dataset is restricted by its inclusion and exclusion criteria and may have limited applicability to individuals under 18 or above 65 years of age, classic heat stroke patients, and cases involving recreational drug use.

Online Methods

HIA dataset development

We conducted a systematic review of the aetiology, clinical features, biomarkers, treatment and outcomes of EHI in adults to form the HIA dataset. This review adhered to the updated 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and meta-analyses [37]. The 2020 PRISMA flow diagram is presented in Extended Data Fig. 1. The protocol for this review was registered a priori with the International Prospective Register of Systematic Review (PROSPERO; CRD42024560456).

Literature search strategy

A systematic literature search of Medline (PubMed), Embase, Web of Science Core Collection, Scopus and CINAHL for relevant English publications was conducted initially in July 2024 and then updated in March 2025 to identify all studies published from database inception to 01 March 2025. The reference lists of included studies were manually searched for additional eligible studies. A search string was developed using the population, intervention, comparison, outcome (PICO) framework [38] with keywords and search terms combined with Boolean operators and (*) to denote a wild card search (or specifically a truncation search) whereby the asterisk represents other letters or variations after a given root word. The key words and search terms were adapted from Yezli and colleagues [35] and refined through consultation with a university research librarian. An initial search strategy was developed for Medline (Pubmed), comprising of the following keywords: (“Heat Stress Disorders” [Mesh term]) OR (“exertional heat” OR “heat syncope” OR “heat exhaustion” OR “heat stroke” OR “heat illness*” OR “heat injur*”) AND (“case report” OR “case series” OR “case reports” OR “case*” OR “incident report*” OR “case study” OR “case studies”). The search strategy was then adapted for the other databases.

Study Selection

After duplicates were removed, two reviewers (AR & SCCT) independently applied the inclusion criteria to titles and abstracts and subsequently to full-text articles using the Covidence systematic review

software (Veritas Health Innovation, Melbourne, Australia). Discrepancies were resolved by consensus and a third reviewer (NR) arbitrated when consensus was not reached.

Only full-text original case reports and case series written in English that met the inclusion criteria were included in this review. The inclusion criteria were: i) case reports and/or case series with a clinical diagnosis of EHS, EHI or exercise-related HRI; and ii) studies involving a human adult population aged 18 to 65 years. Studies were excluded based on the following criteria: i) cases of classic heat illness and/or heat stroke; ii) non-English language articles; iii) studies that did not report individual patient data and corresponding authors could not be contacted for clarification; iv) editorials, conference abstracts, and review articles; and v) studies that reported recreational drug use. Reference lists from review articles were cross-checked for relevant articles missed in the search.

Data extraction and risk of bias

Three authors (AR, SCCT, and RYTL) independently extracted relevant data from each included study into a bespoke Excel database. Extracted data included: i) study descriptions and details; ii) patient demographics including age, sex, body mass index, prior medical history, medication use and geographical location; iii) case descriptions including modality of exercise prior to the heat-related illness (HRI) and environmental conditions; and iv) case outcomes including primary and secondary diagnoses, patient outcomes, and clinical features of HRI and the day they were reported. For each study, the initial values for each reported biomarker were extracted from the earliest available timepoint (e.g., emergency medical services arrival and/or hospital admission), where possible. Peak values of biomarkers were also extracted, if reported. The WebPlotDigitizer software was used to extract biomarker data from studies that presented figures with no available numerical data [39]. Where HRI cases provided details such as the date, location, or event name but did not specify environmental conditions, an online search of historical records (e.g., marathon event) was conducted to obtain the missing environmental data. All extracted data were then checked and verified by seven authors.

After data extraction, three authors (AR, SCCT and RYTL) evaluated the methodological quality of all included studies using either the Joanna Briggs Institute critical appraisal checklist for Case Reports [40] or Case Series [41], according to the study design. Each article was assigned to and independently evaluated by two of the three authors.

Data coding and processing

Extracted clinical features data were first grouped by the affected body system (primary coding) and then by the associated organ of origin or manifestation within the respective body system (secondary coding). Any overlapping features were first combined and then matched to associated clinical biomarkers (e.g., hyper-and hypotension were matched to systolic/diastolic blood pressure), where possible. A clinical reference dictionary, comprising of the normal clinical ranges and associated diagnoses for each biomarker, was then created and used to back-code the extracted biomarker data when necessary. The clinical reference dictionary was established according to relevant Singaporean

guidelines (e.g., National University Health System (Mayo Clinic Laboratories), SingHealth Singapore General Hospital and HealthHub Singapore). Biomarker data values were then converted to the respective units established in the clinical reference dictionary, as required.

To enhance our understanding of the immediate effects of HRI, acute clinical features were specifically extracted for analysis. Where possible, mortality risk ratio for individual and co-occurring clinical features were calculated and reported. Acute clinical features were defined as clinical features manifesting within 24 hours following the onset of HRI event. These features were grouped based on the human organ system in which they manifested. Features that could not be assigned to a specific organ system were classified as “Non-specific organ system”. To identify which organs were most affected within each organ system, clinical HRI features were further sub-grouped according to the primary organ involved. Co-occurrence, correlations, and clinical feature risk ratios were calculated based on the study data. Where programmatic processing was involved in this section, Python and Jupyter Notebooks were used. All figures were created with Python and BioRender.com.

HIA Dashboard Development

Due to the breadth and depth of the extracted dataset, an interactive digital avatar dashboard was developed to better visualise and provide insights for the published cases of exertional HRI. The digital avatar was created using JavaScript and HTML, viewable at https://nus-hrpc.github.io/heatillnessavatar/. We designed the HIA to support incorporation of new published HRI case studies from the wider research and clinical community. Details regarding submission requirements and data structure are provided at README.md. Following independent expert review, approved submissions will be integrated into the existing HIA dataset.

A hierarchical tree-map was developed to organize the dataset into nested levels, from physiological systems down to individual clinical features, visualizing frequency/proportion, and surfaces corresponding risk ratios via tooltips. This interactive diagram also functions as a navigation panel and filter. Other visualizations, in the form of a network graph depicting the co-occurrence of clinical features or associated physiological systems was also created to visualize the complex nature of related multi-organ/system dysfunctions associated with HRI. Various global filters, such as sex, age, outcome were also made available via a side panel.

Declarations

Competing interests

The authors have no competing financial or non-financial interests to disclose.

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Author contributions

AR and NR conceived the study. AR and SCCT conducted the searches and screened all publications. AR, SCCT, RYTL, YFZ, BWBL, XYC, NY, EYHK extracted the data and analysed the HIA database with inputs from SY and JKWL. NR, YFZ and JHY developed the HIA dashboard. AR, SCCT, RYTL and YFZ wrote the manuscript. NR supervised the work. All authors read, corrected and approved the final paper.

Data availability

Data extracted from the systematic search are made publicly available via the HIA dashboard (link: https://nus-hrpc.github.io/heatillnessavatar/).

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Figures

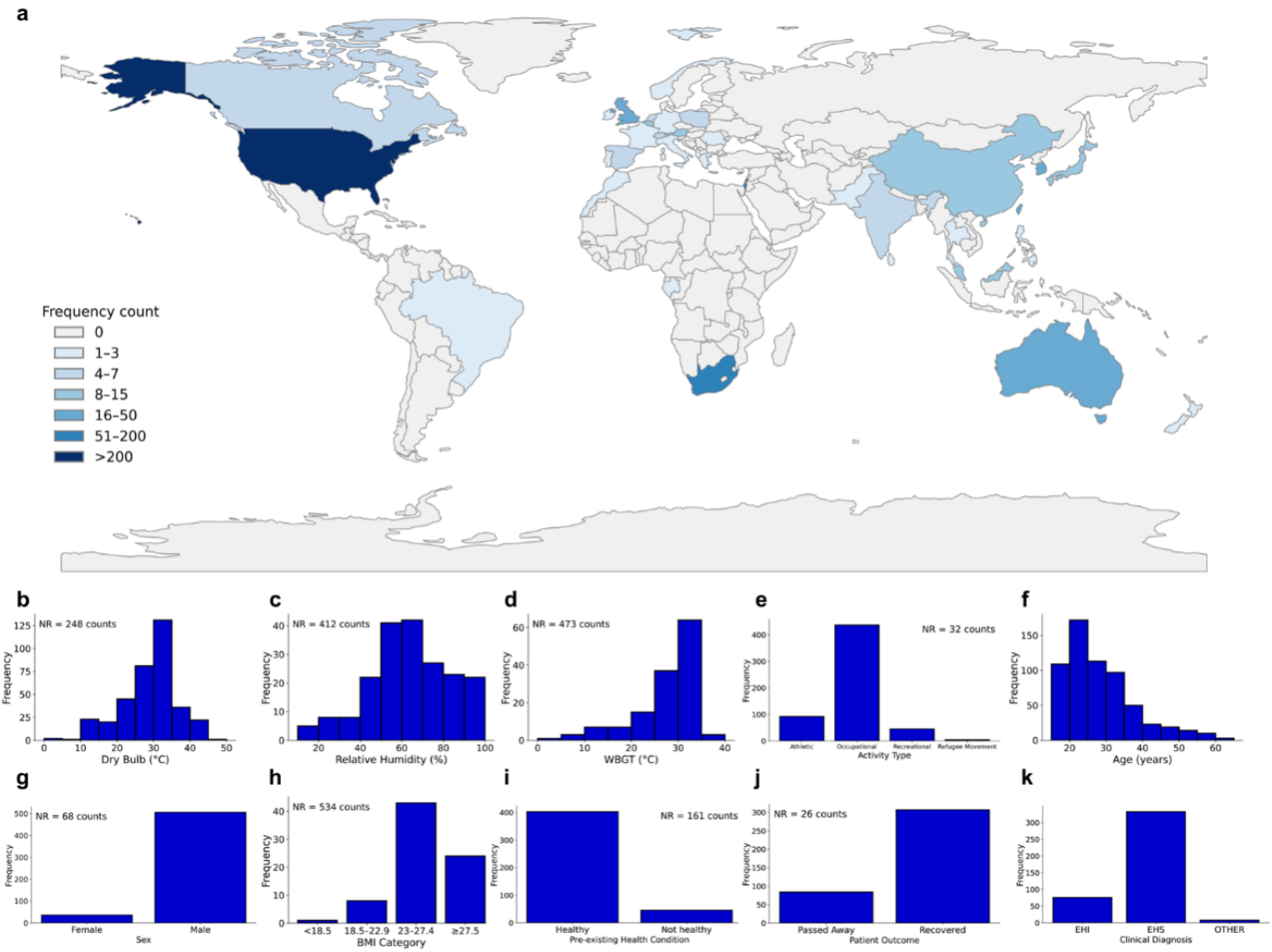


Figure 1

Overview of the global distribution, environmental conditions, exertional activity types and clinical demographic of Heat Illness Avatar (HIA) cases. a, Geographical distribution of reported heat related illness (HRI) cases. **b-d,** Environmental conditions at HRI onset including dry bulb temperature, relative humidity and wet-bulb globe temperature (WBGT) (row above, left to right). **e,** Type of exertional activity resulting in HRI. **f-k,** Clinical demographic of HRI cases including age (row above), biological sex, body mass index (BMI) category, pre-existing health status, patient outcome, and clinical diagnosis (row below, left to right). EHI, Exertional Heat Illness; EHS, Exertional Heat Stroke; NR, Not Reported.

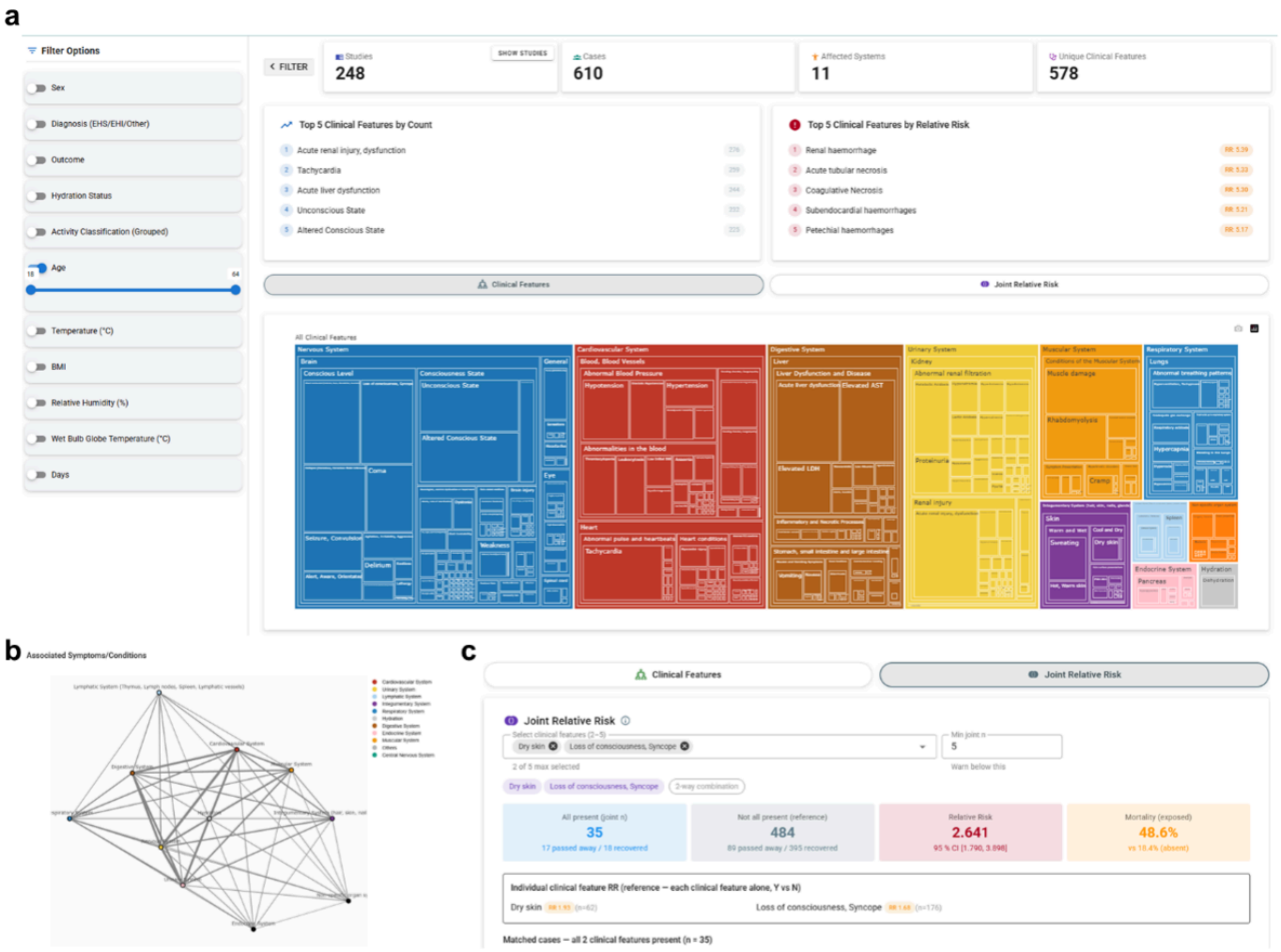


Figure 2

Digital interface for Heat Illness Avatar (HIA). a, Interactive visualization tool with dynamic filtering capability (left). The HIA highlights the top five heat-related illness (HRI) clinical features based on frequency count and relative risk ratio. The HIA also enables organ- and system-level mapping of HRI clinical features and calculation of joint relative risk for features of interest. **b,** The HIA's dynamic network graph illustrating associations between clinical features of interest and other HRI features, quantified by co-occurrence frequency. **c,** The HIA's dynamic joint relative risk ratio allowing quantification of mortality risk for individual and up to five co-occurring clinical features.

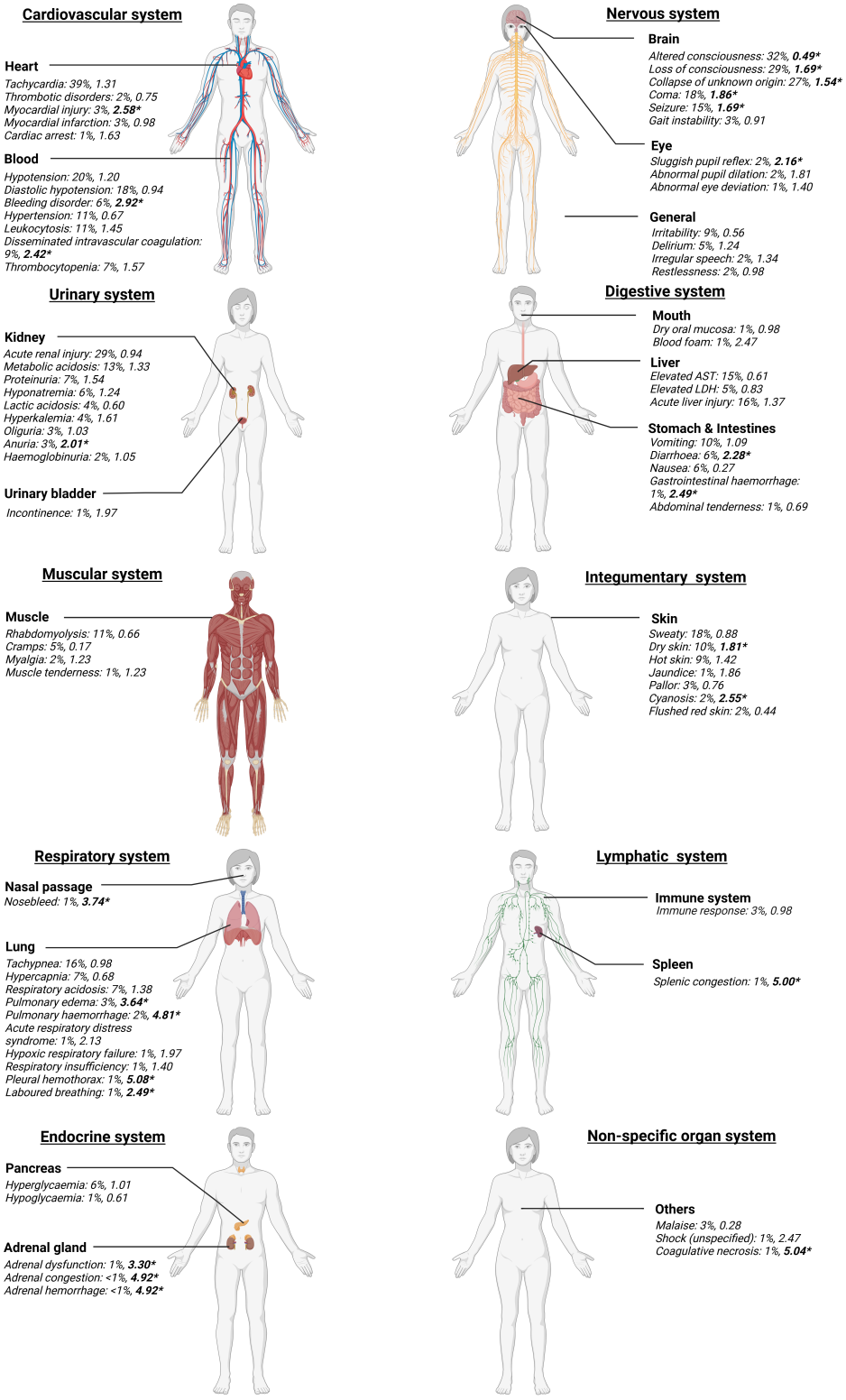


Figure 3

Organ- and system-level mapping of acute clinical features of heat-related illness (HRI) using the Heat Illness Avatar (HIA). Frequency distributions (presented as percentages) and associated risk ratios for key clinical features of HRI across affected organs and systems. *P < 0.05.

Supplementary Files

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- Extendeddatafigure1.PRISMA.tif