Society of Critical Care Medicine Guidelines for the Treatment of Heat Stroke

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RATIONALE: Predicted increases in heat-related weather phenomena will result in increasing heat exposures and heat injuries, like heat stroke. Prompt recognition, early intervention, and evidence-based management are necessary to optimize outcomes.

OBJECTIVES: The objective of these guidelines was to develop evidence-based recommendations for the treatment of patients with heat stroke.

DESIGN: The Society of Critical Care Medicine convened a multidisciplinary panel of 18 international clinicians, comprising expertise in critical care, emergency medicine, neurocritical care, surgery, trauma/burn surgery, sports medicine, athletic training, military medicine, nursing, pharmacy, respiratory therapy, and one patient representative. The panel also included a guidelines methodologist specialized in developing evidence-based recommendations in alignment with the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology. Conflict-of-interest policies were strictly followed during all phases of guidelines development including panel selection and voting.

METHODS: The panel members identified Patient, Intervention, Comparison, and Outcomes questions in two main areas: cooling modalities and medications that affect temperature. A systematic review for each question was conducted to identify the best available evidence, statistically analyze the evidence, and assess the certainty of the evidence using the GRADE methodology. The GRADE evidence-to-decision framework was used to formulate the recommendations. Good practice statements were included to provide additional clinical guidance.

RESULTS: The panel generated two strong recommendations, five good practice statements and one "only-in-the-context of research" statement. Active cooling measures are recommended over passive cooling methods, with cold- or ice-water immersion achieving the fastest cooling rate. This method should be prioritized where available. In heat stroke patients, there is no evidence to support pharmacological interventions that affect temperature control and they should be avoided.

CONCLUSIONS: The guidelines task force provided recommendations for the management of patients with heat stroke. These recommendations should be considered along with the patient's clinical status and available resources.

KEYWORDS: cold-water immersion; cooling methods; emergency medicine; heat stroke; heat-related illness; intensive care unit

Heat-related illness is a leading cause of weather-related fatalities and its prevalence is expected to increase (1). Heat stroke, the most severe form of heat-related illness, is defined as a core temperature greater than 40°C presenting with CNS abnormalities. Heat stroke can be accompanied by burn injury, caused by direct contact with pavement or other surfaces, which can reach temperatures in excess of 71°C (2). Heat stroke is subclassified as either classic (i.e., nonexertional) or exertional and can affect anyone. Certain populations though are at higher risk including infants, elderly,

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athletes, domestically displaced, and outdoor workers such as firefighters, construction workers, landscapers, and military personnel (3).

The increasing prevalence of heat stroke has emphasized the need for timely critical care and emergency services (4). Rapid cooling is an essential intervention to restore normal physiologic activity and minimize morbidity and mortality (5). Cold-water immersion is frequently cited as the preferred modality, but cold-water immersion may not be feasible in some settings or when mass casualty events occur, raising questions on the best alternative strategy (6). Once cooling has been achieved, the management of heat stroke is often centered around maintenance of organ support with minimal direct evidence to guide clinical decision-making.

Building on prior work conducted by the Society of Critical Care Medicine (SCCM) (6), a multidisciplinary panel was commissioned to develop evidence-based guidelines for the treatment of heat stroke highlighting recommendations for critical care management that occurs across a continuum of settings.

METHODOLOGY

Intended Audience

The intended audience for these guidelines is all individuals who provide care for patients with heat stroke in both the pre-hospital and acute care settings. This includes physicians, advanced practice providers, pharmacists, nurses, respiratory therapists, medical and nursing directors, athletic trainers, coaches, and other allied health and/or administrative professionals.

Composition of the Guidelines Development Group

The SCCM commissioned an international panel of experts in critical care, emergency medicine, neurocritical care, surgery, trauma/burn surgery, sports medicine, athletic training, military medicine, nursing, pharmacy and respiratory therapy, and plus one patient representative. Practice locations included pre-hospital, emergency, and inpatient settings. A methodologist from the Guidelines in Intensive Care Development and Evaluation group of McMaster University assisted with the development of the guidelines.

Conflict of Interest Policy

Members of the panel were required to disclose conflicts of interest (COI) per the SCCMs COI policy. COI was assessed at each phase of the guidelines process and at every panel meeting. Panel members with a COI were excluded from voting on a specific recommendation if a COI was present. There were no COIs that prohibited participation in discussion or voting. There was no input from industry to produce these guidelines.

Formulating Recommendations

The panel prioritized Patient, Intervention, Comparison, and Outcomes (PICO) questions based on those that had important implications for clinical practice and evidence was available. The specific population of interest were patients with heat stroke as opposed to other less severe forms of heat-related illness (e.g., heat exhaustion, heat syncope, etc). The PICO selection process is presented in **Table S1** (http://links.lww.com/CCM/H657). The panel also rated the relative importance of each outcome to determine which outcomes were critical for decision-making. A summary of searched outcomes for all PICO questions is presented in **Table S2** (http://links.lww.com/CCM/H657). The final PICO questions selected ($n = 7$) are listed in **Table 1**.

After PICO questions were finalized, an extensive review of the scientific literature was performed from inception (of each database) through May 2024 to retrieve articles that addressed the PICO questions. The search was conducted by a medical librarian using MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), ClinicalTrials.gov, and World Health Organization International Clinical Trials Registry Platform (search queries are provided in the **Supplemental Materials**, http://links.lww.com/CCM/H657). The search strategy included all ages and did not restrict to subpopulations. Search results were then uploaded to Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, VIC, Australia) (7) for screening, full-text review, and data extraction, following the procedure for systematic review.

Clinical data were systematically reviewed for each PICO question. This was done by performing de novo systematic reviews or updating recently published high-quality reviews from peer-reviewed journals if they were available. Meta-analyses were performed using a random effects model with RevMan, Version

TABLE 1.
Patient, Intervention, Comparison, and Outcomes Questions

Patient, Intervention, Comparison, and Outcomes
P–Patients with heat stroke I–Active cooling methods C–Passive cooling methods O–Survival with good neurologic function long-term (i.e., after 6 mo), survival with good neurologic function at discharge, hospital survival, rate of temperature reduction, time to target temperature, achievement of target temperature within 30 min, organ dysfunction, adverse effects/complications, or hospital length of stay
P–Patients with heat stroke I–Cold-water immersion (or other active method if not cold-water immersion) C–Method other than cold-water immersion O–Survival with good neurologic function long-term (i.e., after 6 mo), survival with good neurologic function at discharge, hospital survival, rate of temperature reduction, time to target temperature, achievement of target temperature within 30 min, organ dysfunction, adverse effects/complications, or hospital length of stay
P–Patients with classic heat stroke I–Cold-water immersion (or other active method if not cold-water immersion) C–Method other than cold-water immersion O–Survival with good neurologic function long-term (i.e., after 6 mo), survival with good neurologic function at discharge, hospital survival, rate of temperature reduction, time to target temperature, achievement of target temperature within 30 min, organ dysfunction, adverse effects/complications, or hospital length of stay
P–Patients with exertional heat stroke I–Cold-water immersion (or other active method if not cold-water immersion) C–Method other than cold-water immersion O–Survival with good neurologic function long-term (i.e., after 6 mo), survival with good neurologic function at discharge, hospital survival, rate of temperature reduction, time to target temperature, achievement of target temperature within 30 min, organ dysfunction, adverse effects/complications, or hospital length of stay
P–Patients with heat stroke I–Reaching the target temperature within 30 min C–Not reaching the target temperature within 30 min O–Survival with good neurologic function long-term (i.e., after 6 mo), survival with good neurologic function at discharge, survival, organ dysfunction, adverse effects/complications, or hospital length of stay
P–Patients with heat stroke I–Achieving a faster cooling rate ($\geq$ 0.155°C/min) C–Not achieving a faster cooling rate ($<$ 0.155°C/min) O–Survival with good neurologic function long-term (i.e., after 6 mo), survival with good neurologic function at discharge, survival, organ dysfunction, adverse effects/complications, or hospital length of stay
P–Patients with heat stroke I–Medications that either directly or indirectly affect temperature control C–No medications O–Survival with good neurologic function long-term (i.e., after 6 mo), survival with good neurologic function at discharge, hospital survival, rate of temperature reduction, time to target temperature, achievement of target temperature within 30 min, organ dysfunction, adverse effects/complications, or hospital length of stay

5.4 (Review Manager [RevMan]. Version 5.4. The Cochrane Collaboration, 2020) (8). Data that could not be quantitatively pooled or outcomes with insufficient studies to analyze were addressed narratively.

The clinical practice recommendations were then developed according to the Grading of Recommendations, Assessment, Development, and Evaluation process (9). The Evidence to Decision framework was completed by the panel using GRADEpro software (GRADEpro GDT: GRADEpro Guideline Development Tool [Software]. McMaster University and Evidence Prime, 2024) (10) for each PICO to develop a draft recommendation considering the balance of desirable and undesirable effects, certainty of the evidence, resource considerations, feasibility, acceptability, and equity considerations (Supplemental Materials, http://links.lww.com/CCM/H657, for evidence to decision worksheets). Recommendations had to receive at least 80% of the vote of the panel to be approved.

The recommendations in these guidelines are based on the balance of desirable and undesirable effects that should meet the needs of most patients in most situations. Remarks are provided, as necessary, to guide clinicians in the implementation of these recommendations. Each recommendation statement was assigned a strength ("strong" or "weak"). A "strong" recommendation is one that clinicians should follow for almost all patients (i.e., something that might qualify as a quality measure). A "weak" or "conditional" recommendation reflects a lower degree of certainty in the appropriateness of the patient care strategy for all patients. It implies that not all individuals will benefit from the recommended intervention and necessitates a careful assessment of the individual circumstances, values, and preferences. Several factors can determine the strength and direction of a recommendation including the balance between desirable and undesirable effects, confidence in the magnitude of estimates of effect on important outcomes, and confidence in values and preferences and their variability and resource use. In some situations, it may be appropriate to have a strong recommendation despite low or very low confidence in effect estimates (e.g., a circumstance where low quality evidence suggests benefit in a life-threatening situation) (9). Guidelines panels may also make good practice statements and only-in-the-context of research statements. Good practice statements are made when there is high certainty that the desirable effects of an intervention clearly outweigh the undesirable effects, but the body of supporting evidence is indirect or limited. Only-in-the-context of research statements are those where there is insufficient evidence to make a recommendation, but further research has the potential to reduce uncertainty and is of good value.

These clinical practice guidelines reflect the state of knowledge at the time of publication. Judgment regarding any specific care must be made by the treating clinician and the patient, taking into consideration the individual circumstances of the patient, available treatment options, and resources.

RECOMMENDATIONS

Cooling Modalities

Recommendation 1. We recommend active cooling methods over passive cooling in patients with heat stroke (strong recommendation, very low certainty of evidence).

Remarks. Cold-water immersion or ice-water immersion will result in the fastest rate of temperature reduction and shortest time to target temperature (< 39°C).

A meta-analysis of randomized controlled trials (11–43) was performed that compared cooling rates of various active cooling methods to passive cooling in participants with experimental exertional hyperthermia. A faster cooling rate was recognized with active vs. passive cooling by a mean of 0.04°C/min (95% CI, 0.03–0.05°C/min) (**Fig. S1**, http://links.lww.com/CCM/H657). The overall certainty of evidence for the recommendation is very low, primarily due to indirectness (experimental exertional hyperthermia vs. actual heat stroke subjects), imprecision, and inconsistency (**Table S3**, http://links.lww.com/CCM/H657). The evidence to decision framework used to derive the recommendation is presented in **Table S4** (http://links.lww.com/CCM/H657).

There were insufficient data directly comparing active vs. passive cooling methods on clinical outcomes such as survival, length of stay, organ dysfunction, and complications. Based on limited evidence from a systematic review (3), mortality ranged from 0% to 26.5% in patients with exertional heat stroke who were treated with various cooling methods. For patients with classic heat stroke, mortality ranged from 0% to 71.4% with intensive cooling treatment (3). The review identified two pediatric case series that reported mortality rates of 25% ($n = 7$) and 60% ($n = 50$) despite treatment (3).

Active cooling can be performed via numerous mechanisms. The panel discussed the differences in cooling rates among available therapies and recognized that many methods of active cooling may not be feasible in some settings (e.g., mass casualty events) or readily available (e.g., austere environments, resource-limited regions). Furthermore, patients may not be cooperative with some methods of active cooling like ice- or cold-water immersion. Nevertheless, mortality rates in patients requiring ICU care for heat stroke approach 60% and approximately 30% of heat stroke survivors experience some form of long-term cognitive or motor dysfunction (6). The CNS is particularly vulnerable to excessive heat and cell death increases in an exponential manner as temperature exposure time increases (44). Conversely, recovery of CNS function can occur during aggressive cooling, which is a favorable prognostic sign. It is important to account for the time between symptom onset and the provision of care when selecting a cooling method. The method with the fastest cooling rate is ice-water and cold-water immersion (water temperature ≤ 12°C). In situations where this cannot be done, clinicians should choose a method or combination of methods that will achieve a rapid rate of temperature reduction (**Fig. 1**) and reach the target temperature within 30 minutes of onset of heat stroke symptoms, considering the patient's initial core body temperature, if available (**Fig. 2**). Appropriate event planning and preparation are key to minimize delays in care or avoid having to substitute a secondary option for a preferred method.

There are no direct trials evaluating cost-effectiveness. However, the panel decided this intervention would likely be cost-effective considering the low cost to perform active cooling and the indirect benefits of avoiding a prolonged ICU stay. In one large case series of patients with exertional heat stroke following a running/road race, only 10% required transfer to an emergency department following aggressive onsite cooling with cold-water immersion (45). Cost-effectiveness however may vary particularly in resource-limited areas where ice and clean water may not be available.

There are many, well-known dangers associated with severe hyperthermia and heat stroke (5, 6). Although the overall certainty of evidence for active cooling was very low, restoring body temperature to "normal" physiologic levels (e.g., < 39°C) can reverse life threatening, pathophysiologic processes. The panel ultimately determined the desirable effects strongly outweighed the undesirable effects and issued a strong recommendation in favor of active cooling methods.

Good Practice Statement 1. Clinicians should prioritize cooling methods that achieve the most rapid rate of cooling, which is ice-water immersion (1–5°C) or cold-water immersion (9–12°C).

The results of the subgroup meta-analyses confirmed ice-water immersion (1–5°C) and cold-water immersion (9–12°C) as the most effective cooling approach with a difference in mean cooling rate of 0.14°C/min (95% CI, 0.08–0.21°C/min) and 0.11°C/min (95% CI,

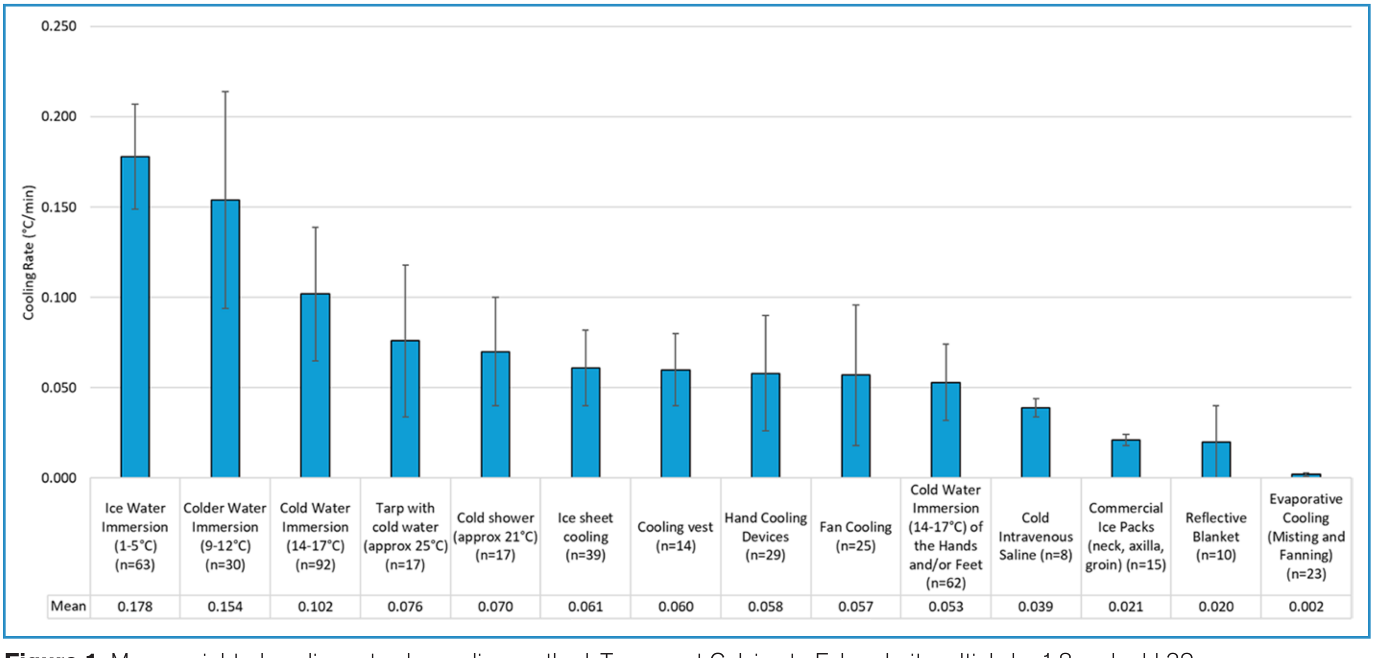

Figure 1. Mean weighted cooling rates by cooling method. To convert Celsius to Fahrenheit multiply by 1.8 and add 32.

	Initial Core Temperature (°C)						
	40.0	40.6	41.1	41.7	42.2	42.8	43.3
Cooling Method	Final Core Temperature (°C)						
Ice Water Immersion (1-5°C)	34.7	35.3	35.8	36.4	36.9	37.5	38.0
Colder Water Immersion (9-12°C)	35.4	36.0	36.5	37.1	37.6	38.2	38.7
Cold Water Immersion (14-17°C)	36.9	37.5	38.0	38.6	39.1	39.7	40.2
Tarp with Cold Water (approx. 25°C)	37.7	38.3	38.8	39.4	39.9	40.5	41.0
Cold Shower (approx. 21°C)	37.9	38.5	39.0	39.6	40.1	40.7	41.2
Ice Sheet Cooling	38.2	38.8	39.3	39.9	40.4	41.0	41.5
Cooling Vest	38.2	38.8	39.3	39.9	40.4	41.0	41.5
Hand Cooling Devices	38.3	38.9	39.4	40.0	40.5	41.1	41.6
Fan Cooling	38.3	38.9	39.4	40.0	40.5	41.1	41.6
Cold Water Immersion (14-17°C) of the Hands and/or Feet	38.4	39.0	39.5	40.1	40.6	41.2	41.7
Cold Intravenous Saline	38.8	39.4	39.9	40.5	41.0	41.6	42.1
Commercial Ice Packs (neck, axilla, groin)	39.4	40.0	40.5	41.1	41.6	42.2	42.7
Reflective Blanket	39.4	40.0	40.5	41.1	41.6	42.2	42.7
Evaporative Cooling (Misting and Fanning)	39.9	40.5	41.0	41.6	42.1	42.7	43.2

Figure 2. Ability to reach target final core temperatures (°C) after 30 min based on each cooling modality and starting temperature. *Green* reflects a final core temperature less than 39°C (preferred), *yellow* reflects a final core temperature between 39°C and 40°C (borderline), and *red* reflects a final core temperature greater than 40°C (inadequate). To convert Celsius to Fahrenheit multiply by 1.8 and add 32.

0.07–0.14°C/min), respectively, compared with passive cooling (Fig. S1, http://links.lww.com/CCM/H657). A ranking of the relative effectiveness of various active cooling methods is presented in Figure 1. These rates may be influenced by the use of experimental designs that do not use the same initial temperatures that are often observed in clinical practice (for ethical and safety reasons) and thereby result in different temperature differentials.

There are numerous case reports describing the benefit of cold-water immersion and this method has been widely endorsed (46–50). Cold-water immersion, although may be associated with adverse effects (e.g., ice directly applied to skin can lead to frostbite), introduce hazards for hospital staff (e.g., falls), interfere with ongoing resuscitation and procedures and complicate patient monitoring (e.g., cardiac monitor leads falling off). Techniques for performing cold-water immersion have been described (50). Nevertheless, the panel determined that the desirable effects of this modality far outweighed the undesirable effects. Cold-water immersion may not be an option in some settings. Secondary alternatives are highlighted in Figure 1. However, cold-water immersion can be successfully implemented in circumstances where mass casualty events might be expected (e.g., sporting events, road-races, etc). Careful planning and foresight are needed so required resources are readily available.

Good Practice Statement 2. Clinicians may use similar cooling strategies for either classic or exertional heat stroke.

Experimental models comparing cooling methods are primarily conducted in climate-controlled exercise laboratories using healthy volunteers. Initial temperatures do not reach the extreme values often encountered in practice and patient comorbidities are often absent. Comparative trials in patients with classic heat stroke are lacking due to the ethical challenges with this experimental design. Given the harmful physiologic sequelae associated with extremes in body temperature, regardless of the root cause (excessive heat gain vs. inability to dissipate heat), the panel decided similar treatment approaches should be sought.

Good Practice Statement 3. Clinicians should choose cooling methods that reach the target temperature within 30 minutes from recognition of heat stroke symptoms.

Direct clinical evidence assessing outcomes in heat stroke patients based on the time to reach target temperature is lacking. This is largely due to the ethical challenges with performing a randomized controlled trial in this setting. One retrospective study, which reported cooling rates using a variety of modalities in 143 patients, reported mortality rates of 6.9% when a temperature of 39°C was reached in 30 minutes vs.10.6% when it was not (p = not significant) (51). A second retrospective study of 39 patients noted a 55% relative reduction in mortality when a temperature less than or equal to 38.9°C was reached within 1 hour ($p = 0.18$) (52). Two large case series reported zero fatalities when target temperatures were reached within 30 minutes (45, 53). Despite the limited direct evidence, the degree and duration of hyperthermia are known to adversely affect normal physiologic processes. The panel decided a time to target temperature within 30 minutes is an appropriate goal.

Good Practice Statement 4. Clinicians should prioritize cooling modalities that achieve a cooling rate greater than or equal to 0.155°C/min.

Data directly comparing cooling rates on clinical outcomes are limited. One review combined case series data and found higher mortality (16% vs. 0%) with insufficient cooling (< 0.15°C/min) and a higher rate of medical complications (risk ratio [RR], 4.57; 95% CI, 3.42–6.28) (46). A lack of comparative trials is attributed to prohibitive ethical concerns with conducting a randomized controlled trial in which aggressive cooling is delayed. Nevertheless, the panel decided the desirable effects of aggressive cooling outweigh the undesirable effects. Additionally, when considering the goal of achieving a target temperature within 30 minutes, cooling methods with a temperature reduction rate greater than or equal to 0.155°C/min will accomplish that goal across a wide range of initial core temperatures. We recognize that cooling strategies that achieve this rate of temperature reduction may not be feasible or available in some settings. Clinicians are advised to select the method or combination of methods that will achieve the fastest rate of temperature reduction.

Medications That Affect Temperature Control

Recommendation 2. We recommend against the use of dantrolene in patients with heat stroke (strong recommendation, very low certainty of evidence).

Dantrolene is a treatment option for patients with malignant hyperthermia and its use in heat stroke has garnered some attention due to overlap in pathophysiologic mechanisms. Three randomized controlled trials have compared dantrolene with placebo in heat stroke patients (54–56). Of those, one is only available in abstract form. Meta-analyses have demonstrated no reduction in the risk of mortality (three trials; RR, 1.01; 95% CI, 0.11–9.31; and **Fig. S2**, http://links.lww.com/CCM/H657), a mean difference in cooling time (two trials) of −10.5 minutes (95% CI, −28.5 to 7.6 min; and **Fig. S3**, http://links.lww.com/CCM/H657), a difference in hospital length of stay (one trial) of 1.85 days (95% CI, 0.99–2.70 d; and **Fig. S4**, http://links.lww.com/CCM/H657), no difference in the risk of adverse events (two trials; RR, 0.99; 95% CI, 0.46–2.15; and **Fig. S5**, http://links.lww.com/CCM/H657), and a difference in incidence of recovery of consciousness as defined by a Glasgow Coma Score of greater than or equal to 13 points at less than or equal to 90 minutes (one trial; RR, 2.5; 95% CI, 0.56–11.16; and **Fig. S6**, http://links.lww.com/CCM/H657). The overall certainty of evidence was very low due to risk of bias, imprecision, and inconsistency (**Table S5**, http://links.lww.com/CCM/H657).

When considering the recommendation, the panel discussed the quality of available evidence and the fact that one trial is only available in abstract form. CIs were wide, and in all cases, differences were not statistically significant. Some outcomes were only analyzed via one study. The panel deliberated a strong vs. a weak recommendation but decided a strong recommendation was more appropriate because a weak recommendation would imply dantrolene may be acceptable in some situations. After evaluating the certainty of data,

TABLE 2.
Research Agenda

Category	Research question
Cooling strategy	What is the most optimal rate of cooling?
	What is the most desirable time to reach target temperature?
	What is the best combination of cooling methods if cold-water immersion is not feasible?
	What is the role of novel cooling devices such as intranasal cooling devices, endovascular cooling devices, blankets engineered from heat-conductive biomaterials, etc?
Medications	What is the role of antimicrobial prophylaxis?
	What is the role of seizure prophylaxis?
	Can other medications be used to prevent organ failure (e.g., N-acetylcysteine)?
	What is the role of immunomodulators to treat the inflammatory response?
Other	What is the role of biomarkers to identify organ failure and prognosticate outcomes?
	Can artificial intelligence be used to systems that create rapid, predictable cooling and minimize adverse effects?
	Can precision medicine be used to identify patients at higher risk for heat stroke?

cost and required resources though, the panel was unable to cite what that acceptable situation might be. The complete evidence to decision framework used to derive the recommendation is presented in **Table S6** (http://links.lww.com/CCM/H657).

Good Practice Statement 5. The routine use of acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDS), and salicylates for temperature reduction should be avoided.

Antipyretics such as acetaminophen, NSAIDS, or salicylates, have no evidence supporting a desirable effect in the setting of heat stroke (57). Further, the panel recognized the risk for known adverse effects (e.g., hepatotoxicity, acute kidney injury, bleeding), which may be particularly evident in patients with heat stroke due to their high risk for organ dysfunction. Given the potential imbalance of undesirable-to-desirable effects, antipyretic medications should be avoided.

Only-in-the-Context of Research Statement 1. Prophylactic antibiotics or prophylactic antiseizure medications should only be used in the context of research.

The rationale behind antibiotic prophylaxis is related to translocation of intestinal bacterial that is common with extreme temperatures coupled with the increased permeability of the blood-brain barrier. The rationale for antiseizure medications is based on seizures being a common CNS manifestation of heat stroke. There are no studies in humans evaluating the benefit of prophylactic antibiotics or prophylactic antiseizure medications (58). Further research is needed to determine the role of these therapies.

RESEARCH AGENDA

Future research is needed on several topic areas covered by these guidelines. A summary of research priorities is presented in **Table 2**.

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