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SPECIAL ARTICLE

Targeted temperature management in patients with intracerebral haemorrhage, subarachnoid haemorrhage, or acute ischaemic stroke: updated consensus guideline recommendations by the Neuroprotective Therapy Consensus Review (NTCR) group

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*This is a consensus document produced by expert members of the Neuroprotective Therapy Consensus Review group and has been seen and approved by the Council of Neuro Anaesthesia and Critical Care Society (NACCS).

Abstract

Background: There is a lack of consistent, evidence-based guidelines for the management of patients with fever after brain injury. The aim was to update previously published consensus recommendations on targeted temperature management after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke in patients who require admission to critical care.

Methods: A modified Delphi consensus, the Neuroprotective Therapy Consensus Review (NTCR), included 19 international neuro-intensive care experts with a subspecialty interest in the acute management of intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke. An online, anonymised survey was completed ahead of the meeting before the group came together to consolidate consensus and finalise recommendations on targeted temperature management. A threshold of $\geq$80% for consensus was set for all statements.

Results: Recommendations were formulated based on existing evidence, literature review, and consensus. After intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke in patients who require critical care admission, core temperature should ideally be monitored continuously and maintained between 36.0°C and 37.5°C using automated feedback-controlled devices, where possible. Targeted temperature management should be commenced within 1 h of first fever identification with appropriate diagnosis and treatment of infection, maintained for as long as the brain remains at risk of secondary injury, and rewarming should be controlled. Shivering should be monitored and managed to limit risk of secondary injury. Following a single protocol for targeted temperature

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management across intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke is desirable.

Conclusions: Based on a modified Delphi expert consensus process, these guidelines aim to improve the quality of targeted temperature management for patients after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke in critical care, highlighting the need for further research to improve clinical guidelines in this setting.

Keywords: guidelines; intensive care; intracerebral haemorrhage; neurocritical care; normothermia; stroke; subarachnoid haemorhhage; targeted temperature management

Editor's key points

- Consensus recommendations were developed on targeted temperature management after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke in patients who require admission to critical care.
- A modified Delphi consensus process involving 19 international neurocritical care experts formulated recommendations based on existing evidence, literature review, and consensus.
- Core temperature should be monitored continuously and targeted temperature management commenced within 1 h of first fever with temperature maintained between 36.0°C and 37.5°C using automated feedback-controlled devices, where possible, with shivering managed to limit risk of secondary injury.
- These guidelines aim to improve the quality of targeted temperature management for patients after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke in critical care, and highlight the need for further research to improve clinical guidelines in this setting.

Stroke, a heterogenous syndrome caused by a disruption of cerebral blood flow, can be followed by sustained loss of neurological function and tissue damage.[1,2] It is a leading cause of disability with a significant economic burden, and one of the top causes of years of life lost, along with ischaemic heart disease, lower respiratory infections, and diabetes mellitus.[3,4] Stroke is categorised as haemorrhagic or ischaemic stroke, with haemorrhagic stroke being sub-categorised as subarachnoid haemorrhage and intracerebral haemorrhage.[5]

Targeted temperature management (TTM) is a complex intervention that aims to minimise further brain injury and improve neurological outcomes after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke.[6] It involves controlling core body temperature at a specific level to achieve the desired temperature[7] to prevent fever, maintain normothermia, or induce hypothermia.[6–8]

Fever is frequently observed in the neuro-intensive care unit (NICU). Neurogenic fever is a non-infectious fever that is common after severe brain insult from intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke,[9] and has been linked to both higher clinical severity and worse outcome,[10,11] including increased risk of death, longer ICU and hospital length of stay, lower functional status, and dependence in activities of daily living.[12,13] There are, however, conflicting opinions in the current literature with regards to whether treating fever leads to improved outcome for patients.[3,10] Sample sizes in published studies are often small, with few randomised controlled trials (RCTs), and different definitions of fever or therapeutic approaches to addressing fever.[3,10,13]

Therapeutic hypothermia is suggested to provide robust neuroprotection because of its multifaceted physiological mechanism of action. Although laboratory and preclinical studies have contributed useful knowledge to the practice of TTM within the complex clinical scenario of stroke, there are obstacles that hinder its routine application in clinical practice.[14] Despite the need for efficient and effective fever management, there is a lack of consistent, evidence-based guidelines for management of patients with fever after brain insult.[13,15] The goal of this modified Delphi consensus, the Neuroprotective Therapy Consensus Review (NTCR), was to build on existing data[7] and to discuss and identify practice recommendations for the application of TTM in patients after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke managed within a critical care environment.

Methods

A modified Delphi consensus method was used, involving a combination of an online survey (Round 1), a face-to-face meeting (Round 2), and post-meeting reviews of the consensus results (Round 3). The questions asked at Round 1 are in Supplementary data, and the results from validation at the face-to-face meeting are in Table 1. Round 1 was conducted via the SurveyMonkey® online platform, and Round 2 was held at the Park Plaza London Waterloo Hotel on October 11, 2022. AL acted as Chair, with an independent facilitator moderating the meeting. There were 10 panel members present in person, and nine panel members who joined virtually via Microsoft Teams. After the initial meeting, the recommendations and final manuscript (Round 3) were developed, with documents shared by e-mail and feedback collected independently from each participant by the facilitator. The agreed cut-off for the consensus was to have ≥80% of panel members in agreement, with methodology adopted from the manuscript published by Andrews and colleagues (2018).[7] The process for the Delphi panel and subsequent manuscript development is shown in Figure 1.

Participants

A total of 19 experts in the management of intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke in the critical care setting participated

Table 1 Summary of panel recommendations.

Topic	Level of consensus (%)	Stage reached
How to use targeted temperature management (TTM)		
Temperature should be measured in patients with intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke managed in a critical care setting continuously, or at least hourly	100	Round 2
In the absence of direct measurements, core temperature is the most useful surrogate measure of brain temperature	89.5	Round 1
An automated device for TTM is indicated for high-quality temperature control for the treatment of neurogenic fever in adult patients with intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke	100	Round 2
TTM should be used reactively and using an automated device to maintain normothermia after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke	100	Round 2
The target temperature for patients with intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke should be between 36.0°C and 37.5°C	100	Round 2
The maximum temperature variation that these patients should ideally experience during TTM is less than plus or minus 0.5°C per hour, and <1°C per 24-h period	100	Round 2
Temperature control should be used for as long as the brain is at risk in patients after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke who are admitted in a critical care setting	89.5	Round 1
An automated TTM device that enables precise temperature control is desirable for maintaining temperature in patients after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke	94.7	Round 1
The maximum temperature variation that a patient should experience during normothermia is less than or equal to plus or minus 0.5°C per hour and ≤1°C per 24-h period	100	Round 2
Targeted temperature management for neurogenic fever		
Neurogenic fever in patients with intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke can adversely affect patient outcome	94.7	Round 1
It is important to prevent, treat, or both neurogenic fever in patients with intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke in the acute setting	94.7	Round 1
It is important for neurogenic fever in intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke to be treated with a single local TTM protocol	84.2	Round 1
Once fever is detected in patients with intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke, controlled temperature management should be initiated with an automated device as soon as possible, ideally within 1 h	100	Round 2
When used reactively once fever is detected, TTM should be initiated with an automated device in these patients at 37.5°C	100	Round 2
Shivering		
It is important to manage shivering in these patient groups during temperature control	100	Round 1
Which first-line therapeutic option should be included in a protocol to manage shivering?	No consensus	No consensus
Controlled but passive rewarming should be used to rewarm shivering patients, as opposed to spontaneous, uncontrolled rewarming	94.7	Round 1
Controlled rewarming should take place at a speed of ≤1°C per day	88	Round 2
Normothermia should be applied in a slow and controlled fashion for as long as the brain is at risk once the patient is rewarmed	100	Round 2
Outcome assessment		
What is a valid metric for measuring the quality of TTM delivery in patients after acute stroke severe enough to be admitted to critical care?	No consensus	No consensus

in the consensus process. The participants were selected based on their clinical role, and both their experience of managing stroke severe enough to warrant admission to critical care, managing fever in these patients, and using TTM. All of the participants were selected from leading intensive and neurocritical care groups: 17 from within the Neuro Anaesthesia and Critical Care Society (NACCS) UK network, and two from Italy.

Rounds 1 and 2

Statements and questions for each round were prepared by the independent facilitator in consultation with AL and delivered by SurveyMonkey® to each attendee by e-mail for them to complete anonymously online. Statements and questions were informed by a literature search, which identified publications relevant to the specific topics under discussion. The literature search focused on publications released since 2017.

Round 1 comprised 23 statements and questions related to the clinical use of TTM for neurogenic fever in patients with intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke. These had been created in consultation with the meeting chair. All Round 1 questions were in a multiple-choice format. All questions were mandatory and included a comment box where participants could provide additional comments or insights.

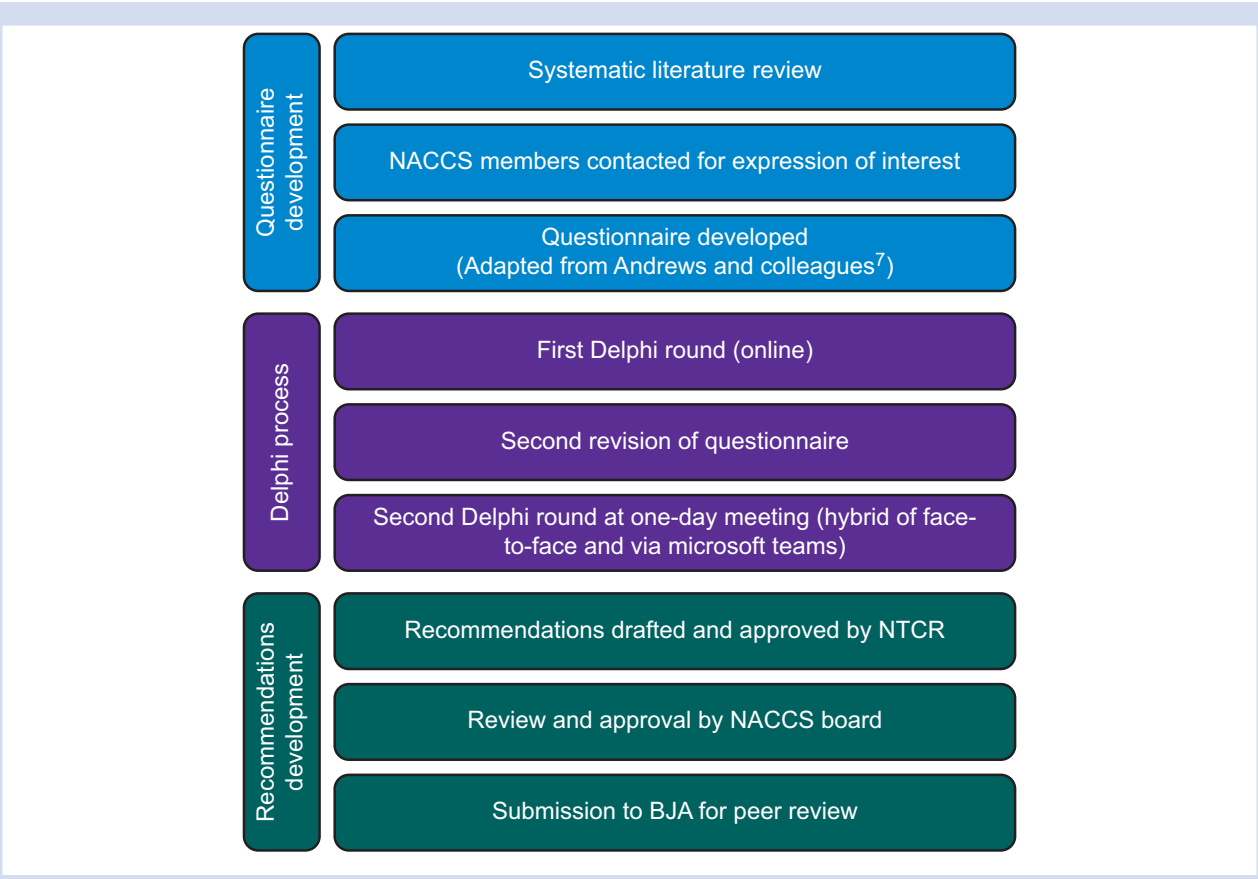

Fig 1. Summary of Delphi process. BJA, *British Journal of Anaesthesia;* NACCS, Neuro Anaesthesia and Critical Care Society; NTCR, Neuroprotective Therapy Consensus Review.

Pooled responses to the Round 1 questions were displayed on screen to the whole group during the face-to-face meeting, and the results and comments were discussed during Round 2. All responses were reviewed and discussed regardless of the level of consensus. Where consensus (≥80% agreement) was achieved, the discussion focused on improvements in the phrasing or scope of the initial question to arrive at a final statement that clearly captured the consensus views of all experts. Where consensus was not reached, detailed facilitated discussion was undertaken to identify the reasons behind the lack of agreement.

Round 3 and final validation

The responses from the meeting were captured in a summary document that showed how the consensus evolved ahead of, and during the meeting. For Round 3, this summary was distributed to all participants via e-mail, with meeting attendees asked to review and confirm the accuracy of the content in relation to the meeting discussions and provide any comments. Areas requiring additional discussion were identified, and the process for addressing these was guided by AL. A manuscript was prepared, structuring the recommendations, offering additional narrative, and providing context in relation to current clinical practice. The manuscript was distributed to all authors for parallel data analysis and interpretation, review of the article, and final validation and approval.

Results

The results of the final consensus agreements are presented in Table 1. To provide additional context around each recommendation, and the debate that took place ahead of reaching consensus, further explanation is given in the discussion section. Because of the expertise and specialities of the panel and the wide varieties of patients seen in non-critical care settings, the group agreed that their recommendations would focus solely on patients who had suffered a brain insult as a result of intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke serious enough to warrant admission to a critical care environment.

Discussion

To date, a relatively small amount of homogenous data has been published around the use of TTM with an automated feedback-controlled device for managing neurogenic fever in intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke, leading to the development of this consensus discussion. The Delphi method is an iterative process allowing the anonymous inclusion of a number of individuals across diverse locations and areas of expertise and avoiding dominance by any one individual. It uses a systematic progression of repeated rounds of voting and is an effective process for determining expert group

consensus where there is little or no definitive evidence and where opinion is important.[16,17]

The modified Delphi approach used in this case combined the early flow of structured information and submission of anonymous responses with the face-to-face discussion of responses and further voting to gain consensus and expert insight into usual practice regarding non-pharmacological TTM with an automated feedback-controlled device.

How to use targeted temperature management.

(i) An automated feedback-controlled device for targeted temperature management is indicated for high-quality temperature control for the treatment of neurogenic fever in adult patients with intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke in a critical care setting.
(ii) Temperature should be measured in ventilated patients with intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke managed in an ICU or high dependency unit (HDU) setting continuously, or at least hourly.

The group debated the strength of indication of a TTM device for precise temperature control for the treatment of neurogenic fever, and concluded, after extensive discussion, that in these vulnerable patients, the reactive use of an automated feedback-controlled device is indicated for TTM for fever control and to re-establish normothermia. As a second wave of the discussion, the group agreed that it may, in fact, be essential. Automated feedback-controlled devices for TTM are powerful tools, encouraging the delivery of quality care and aiming to improve neurological outcome. The TTM process can be divided into three phases: induction, maintenance, and rewarming.8 Although non-automated methods of temperature control such as the infusion of ice-cold fluids are cheaper and easier to apply, the level of control offered is poor and their use should be limited to the induction phase, in combination with automated devices.[18]

The group agreed that, fundamentally, temperature is an important vital parameter after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke. Active temperature control should continue for as long as the brain is at risk of secondary injury. The group confirmed that the determination of risk of secondary injury was to be based on local expertise but should include neuroimaging and neuromonitoring where available, including bedside indices of autoregulation such as the pressure reactivity index, brain metabolism such as microdialysis, and brain oximetry.[19] Discussions initially focused on grouping patients into ventilated and non-ventilated cohorts, which led to agreement on a question re-phrase to avoid focusing on a widely heterogenous patient population. Consensus was reached on continuous monitoring of temperature in patients who are mechanically ventilated whenever feasible, and where continuous monitoring is not possible, at least hourly monitoring was recommended. Supporting literature describing the use of TTM after cardiac arrest emphasises the recommendation of continuous monitoring where possible, highlighting the likelihood of intermittent recording missing large fluctuations in temperature, and resulting in the potential for harm.[18] In patients who have had a stroke but are not mechanically ventilated, consensus was reached on the pragmatic measuring of temperature at least every 4 h, acknowledging the importance of allowing the patient to rest. However, such patients found to be clinically unstable or deteriorating should have temperature measured more frequently.

Temperature measurement

(i) In the absence of direct measurements, core temperature is the most useful surrogate measure of brain temperature.

The panel debated the various surrogates for the measure of brain temperature in the absence of direct measurements, focusing on core, tympanic, and axillary temperature, with core temperature being accepted as the most useful surrogate measure. Within the core temperature option, discussions centred around oesophageal, bladder, rectal, and intravascular measurements. After acknowledgement of their limitations,[20] bladder and oesophageal were singled out as the favoured core temperature measurements. Rectal temperature monitoring was widely regarded as impractical for reasons such as the lag time, a high rate of dislocation, and potential embarrassment for the patient.8,20 Peripheral sites were unanimously deemed to be insufficiently accurate to guide temperature treatment in this context.8 In non-ventilated subjects, and in particular where oesophageal or bladder temperature measurements are not available, tympanic temperature measurement is preferred.

Temperature maintenance

(i) The target temperature for patients with intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke should be between 36.0°C and 37.5°C.

The main aims of TTM in a critical care setting, while the brain is at risk, should be maintenance of temperature between 36.0°C and 37.5°C and prevention of an increase in temperature above 37.5°C. The panel noted that temperature should ideally be centred at 36.5°C on the understanding that the maintained temperature will be susceptible to the accuracy of the device and the variability of individual techniques, and that brain temperature can be up to 2°C higher than core temperature. The group agreed that the maximum temperature variation that these patients should experience during TTM for normothermia is ideally less than plus or minus 0.5°C per hour, and <1°C per 24-h period. Practically, this translates as a recommendation to initiate TTM when core temperature exceeds 37.5°C, and to select a target temperature between 36.5°C and 37.0°C.

The group noted that there is a level of pragmatism to be adopted in avoiding fever, discussing that while more time spent in fever can negatively impact neurological outcome, fluctuations in temperature can also affect outcome. Fluctuations and increases in body temperature have been associated with poor outcome after stroke, worse modified Rankin Scale scores, and increased morbidity and mortality.[21,22] Consensus was reached on the importance of maintaining temperature at a consistent level to ensure optimal recovery in patients with intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke.

Targeted temperature management for neurogenic fever

(i) Neurogenic fever in patients with intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke can adversely affect patient outcome.
(ii) When used reactively once fever is detected, targeted temperature management should be initiated with an automated feedback-controlled device in these patients at 37.5°C, and ideally within 1 h from fever onset.

Fever is commonly found in patients admitted to neurocritical care. It has been found to increase the risk of complications and is often associated with unfavourable clinical outcome,[6,13,23,24] whether the neurological injury was ischaemic, haemorrhagic, or traumatic in origin and whether the outcome being measured was clinical, functional, or economic.[13] Although panel discussions focused on neurogenic fever, the group emphasised that it is important to correctly diagnose central fever *vs* fever of infectious origin because of the ramifications of failing to identify a treatable condition, the negative consequences of antibiotic overuse, and the detrimental effect of hyperthermia on brain-injured patients.[9,25] Equally, TTM can mask development of worsening pyrexia secondary to infection. It was widely agreed by the group that the development of neurogenic fever in patients after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke negatively affects patient outcome, so within critical care settings, it is of utmost importance to prevent or promptly treat fever when detected.

When using core temperature as a proxy of brain temperature, the group agreed that TTM should be initiated at 37.5°C, and whereas the definition of what constitutes pyrexia is debatable, it was flagged that waiting for a higher temperature would result in a potential overshoot and could subsequently be more difficult to correct and control. It was agreed that TTM should be initiated as soon as possible, with the group highlighting that this conveys the urgency but accepts the variability in feasibility across different centres and team settings, such as staff numbers and access to training and equipment.

(i) It is important for neurogenic fever in intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke to be treated with a single local targeted temperature management protocol.

The panel felt that the term 'protocol' implies a large amount of detail, often being used as a 'catch-all' term that may lack clarity. The group discussed in depth whether it would be more beneficial to have a different protocol for intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke. After extensive discussion and acknowledgement of the regional differences in access to resources and for ease of adoption across the multidisciplinary team (MDT), it was agreed that a single protocol for the implementation of TTM for intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke would be the most effective method for managing neurogenic fever.

Targeted temperature management for shivering

(i) It is important to manage shivering in patients after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke during temperature control in a critical care setting.

Shivering is common during TTM, and control of shivering can be challenging if clinicians are not familiar with the available options and recommended approaches. Shivering can cause a decrease in brain tissue oxygen leading to cerebral metabolic stress, potentially eliminating the benefits of the TTM.[26–28]

The group agreed, in line with current literature, that shivering must be managed.[26–28] It was agreed that for effective temperature control, counter warming, paracetamol, sedatives, magnesium, opioids, and neuromuscular blocking agents should be included in a protocol to manage shivering. Such measures could be utilised in a stepwise approach, from non-sedating interventions to sedatives and neuromuscular blocking agents if first-line interventions have no positive effect. The panel highlighted that whilst non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used to manage fever and shivering in clinical practice, there exists a range of contraindications to NSAIDs after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke, and that their use should be based on individual assessment of risks and benefits.

(ii) Controlled rewarming should take place at a speed of $\leq$1°C per day.
(iii) Normothermia should be maintained for as long as the brain is at risk once the patient is rewarmed.

The group highlighted that controlled rewarming is an essential component of high-quality TTM to avoid shivering. Following a second-round vote, the panel agreed that $\leq$1°C per day was the optimum speed to rewarm patients, noting that rebound hyperthermia is common and should be avoided if the brain remains at risk. Reinstating TTM can be considered in the case of rebound hyperthermia. The group advised that the speed of rewarming to normothermia should be slow and controlled, within time-controlled parameters. If body temperature and shivering are not adequately monitored, induction is delayed, body temperature remains variable using non-automated methods, and spontaneous and fast rewarming occur, the patient will be exposed to 'low-quality TTM' and the likelihood of a beneficial effect will be compromised.[18]

Outcome assessment

The group extensively debated the best utility metrics for measuring the quality of TTM in patients after acute stroke. In addition to compliance with local protocols, the group agreed that in a critical care environment the amount of time spent within the target temperature range of 36.0–37.5°C and outcome scores, such as the modified Rankin scale, would be valid measures of the quality of TTM delivery. The quality of TTM is multifactorial, with significant variability induced by human factors, such as staff numbers and access to training and equipment. Adopting a holistic approach to TTM and physiological optimisation is of utmost importance and aims to deliver high-quality care with the aim of ensuring patients achieve the best possible quality of life after brain insult from intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, or acute ischaemic stroke.

It was agreed that the question of what functional outcome measure was most useful was beyond the scope of the panel. It was agreed, however, that it is important to measure efficacy of TTM, with relevant metrics including compliance to local protocols, time within target temperature range, time to achieve normothermia, and avoidance of fever. Tracking these measures over time and ensuring correction through implementation of measures to improve performance, such as staff training, was also highlighted as a key aspect of quality care.

Limitations

This consensus review was carried out to evaluate current evidence in the literature on the use of TTM in the management of fever after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke in a critical care setting, and to develop a set of practical recommendations addressing the current gaps in published

evidence. Conflicting reports of its safety and feasibility and differing recommendations around its use in clinical settings have led to a range of guidelines and recommendations being developed, with no clear conclusion. Although early clinical trials such as COOL AID and ICTuS offered support for its safety and feasibility, more evidence is needed to help prove its utility in clinical practice.[3] Several surveys have reported that a lack of treatment protocols, knowledge deficiencies, limited access to dedicated equipment, cost, and increased workloads are major barriers to TTM implementation.[6,29]

A key limitation of this report is that the recommendations from the group are based on experience in two relatively high-resource countries, the UK and Italy, so have potentially limited applicability to lower-resource settings and populations noted to be disproportionately at risk of stroke. This highlights the need for future recommendations and reports that address these, and other, underrepresented groups.[10]

This report was written by an expert panel comprised of specialists in neurocritical care, and the recommendations are therefore limited to patients managed in a critical care or high dependency care environment. Although the recommendations are relevant to patients managed in other settings such as acute stroke units or thrombectomy patients managed in postanaesthesia care units, local practice, staff training, and the availability of equipment will differ in such settings. In addition, the heterogenous nature of stroke patients within critical care must be highlighted. The recommendations offered must be contextualised to individual patient and system needs, with treatment and management implemented according to the severity of brain injury and clinical course.[6] Future research and additional studies should allow for recommendations of greater certainty and more definitive standards of TTM care across different hospital care settings.

As the ECHO group noted,[7] the Delphi process has some drawbacks. The group discussion after the anonymous online survey completion can be impacted by social bias, with live voting and displays shown on screen potentially affecting attendees' ability to vote and comment freely. The opinions of the nine panel members who joined virtually might have been unequally weighted in comparison to those joining in person, highlighting the potential need to carry out future panel meetings with all members joining in the same format.

Two important questions '*Which first-line therapeutic option should be included in a protocol to manage shivering?*' and '*What is a valid metric for measuring the quality of TTM delivery in patients following acute stroke severe enough to be admitted to critical care?*' resulted in no consensus. Whereas it was agreed that a variety of measures could be utilised to control shivering in a stepwise approach from non-sedating interventions to sedatives and neuromuscular block, the panel felt that the choice of first-line interventions are context-sensitive. Whilst NSAIDs represent a valid first-line option in many circumstances, there exists a range of contraindications to their use in this clinical context and their use as first-line options should be based on individual assessment of risks and benefits. Although the panel agreed that outcome scores such as the modified Rankin scale would be valid measures of the quality of TTM delivery, they concluded that the question of what functional outcome score was most useful was beyond the scope of the panel, and that the importance of other metrics such as compliance to local protocols, time within target temperature range, time to achieve normothermia, and avoidance of fever should be highlighted.

Conclusions

Targeted temperature management is a complex therapy that could have a role in reducing secondary injury and improving long-term neurological outcome for patients.[6] However, the use of targeted temperature management in specific settings, and the appropriate methods for its implementation, remain relatively understudied, and high-quality and consistent evidence is lacking. Following agreement from the Delphi panel that there is a clear need for clinical guidance, this review aims to serve as a springboard for further evidence and consensus to be developed for the management of fever with targeted temperature management after intracerebral haemorrhage, aneurysmal subarachnoid haemorrhage, and acute ischaemic stroke in the critical care setting, and for how the clinical practice of targeted temperature management can be improved.

Declarations of interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2023.04.030.

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