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SPECIAL ARTICLE

## Targeted temperature management in patients with intracerebral haemorrhage, subarachnoid haemorrhage, or acute ischaemic stroke: consensus recommendations

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### Abstract

**Background:** A modified Delphi approach was used to identify a consensus on practical recommendations for the use of non-pharmacological targeted temperature management in patients with intracerebral haemorrhage, subarachnoid haemorrhage, or acute ischaemic stroke with non-infectious fever (assumed neurogenic fever).

**Methods:** Nine experts in the management of neurogenic fever participated in the process, involving the completion of online questionnaires, face-to-face discussions, and summary reviews, to consolidate a consensus on targeted temperature management.

**Results:** The panel's recommendations are based on a balance of existing evidence and practical considerations. With this in mind, they highlight the importance of managing neurogenic fever using a single protocol for targeted temperature management. Targeted temperature management should be initiated if the patient temperature increases above 37.5°C, once an appropriate workup for infection has been undertaken. This helps prevent prophylactic targeted temperature management use and ensures infection is addressed appropriately. When neurogenic fever is detected, targeted temperature management should be initiated rapidly if antipyretic agents fail to control the temperature within 1 h, and should then be maintained for as long as there is potential for secondary brain damage. The recommended target temperature for targeted temperature management is 36.5–37.5°C. The use of advanced targeted temperature management methods that enable continuous, or near continuous, temperature measurement and precise temperature control is recommended.

**Conclusions:** Given the limited heterogeneous evidence currently available on targeted temperature management use in patients with neurogenic fever and intracerebral haemorrhage, subarachnoid haemorrhage, or acute ischaemic stroke, a

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#### 2 | Andrews et al.

Delphi approach was appropriate to gather an expert consensus. To aid in the development of future investigations, the panel provides recommendations for data gathering.

Keywords: stroke; subarachnoid hemorrhage; intracerebral hemorrhage; Delphi technique

Targeted temperature management (TTM) is the process of controlling the core body temperature at a specific level. It can be used to achieve hypothermia  $(TTM_{hypo})$  or maintain normal body temperature (TTM<sub>norm</sub>). TTM has been used in several clinical situations, such as out-of-hospital cardiac arrest, traumatic brain injury (TBI), and cerebral vascular accidents, in an attempt to reduce neurological damage and enhance functional outcomes.<sup>1</sup> The evidence base for TTM use in patients with intracerebral haemorrhage (ICH), subarachnoid haemorrhage (SAH), or acute ischaemic stroke (AIS) is limited and difficult to interpret given the range of TTM methods used, the different target temperatures used, the heterogeneity of the patient groups, and the presence or absence of neurogenic or infectious fever. A similar amount of heterogeneity exists in the limited number of clinical guidelines published in France and the USA.

Fever is common in critically ill patients with neurological conditions.<sup>2,3</sup> In those with AIS or TBI, fever can contribute to secondary brain injury, and is associated with poorer functional outcomes and higher morbidity and mortality.<sup>4–6</sup> Fever has an infectious cause in about half of all cases.<sup>2,3,7,8</sup> It has also been shown to have a strong independent association with poor outcomes.<sup>7,9,10</sup> Most evidence on fever prevention in patients in critical care is observational in nature, so the specific role fever plays in causing secondary brain injury is unclear. The Impact of Fever Prevention in Brain Injured Patients study (NCT02996266) is a US study that may provide some answers to this question, as it is designed to assess the impact of fever prevention on fever burden and short- and long-term neurological outcomes in brain-injured patients.<sup>11</sup>

The goal of this modified Delphi consensus—'establishing consensus in health outcomes (ECHO) for TTM in patients with neurogenic fever'—was to identify common expert practice recommendations for the use of non-pharmacological TTM in patients with ICH, SAH, or AIS who develop fever. The panel of experts were drawn from UK centres and reflect UK-specific practice, although their recommendations may be extrapolated to other high-income countries with similar healthcare systems.

#### Methods

A modified Delphi consensus approach was used, which involved a combination of online questionnaires, a face-toface meeting, and post-meeting reviews. The process consisted of two rounds of a Delphi questionnaire (questions are in supplementary data) plus a final validation stage, as shown in Table 1. Rounds 1 and 2 were conducted at a face-to-face meeting held at the De Vere Grand Connaught Rooms in London on July 5, 2017. P.J.D.A. acted as Chair, with an independent Delphi facilitator moderating the meeting. After the initial meeting, the outcomes report (Round 3) and manuscript validations were conducted asynchronously, with documents shared by e-mail and feedback collected from each participant independently by the facilitator. The agreed cut-off of for the consensus was 70% of experts in agreement; this was in keeping with recent consensus initiatives in this field.<sup>12</sup>

#### Participants

A total of nine experts in the management of neurogenic fever participated in the consensus process. The participants were selected on the basis of their clinical role, and their experience of managing patients with ICH, SAH, and AIS; managing fever in these patients; and using TTM. The nine participants were drawn from leading intensive and neurocritical care groups in the UK. Five participants attended Rounds 1 and 2. Of these five participants, one felt that they had insufficient breadth of relevant expertise to respond to the questions, and therefore, withdrew from voting to avoid bias. This participant did, however, engage in the discussions and provided insight into infection-related issues. Nine participants were involved in the final manuscript validation.

#### Rounds 1 and 2 questions

Statements and questions for each round were prepared by the facilitator in consultation with P.J.D.A. and delivered by SurveyMonkey<sup>®</sup> to each attendee's e-mail address for them to complete anonymously online and without collaboration

Step	Format	Description	n
Round 1	Face-to-face meeting; SurveyMonkey questionnaire	Questionnaire completed anonymously; 25 statements/questions	4
Round 2	Face-to-face meeting; SurveyMonkey questionnaire	Revised questionnaire completed anonymously; 14 revised/new consensus statements	4
Round 3	Independent, asynchronous review via e-mail	Consensus summary document for review and comment	9
Manuscript validation	Independent, asynchronous review via e-mail	Final manuscript review and validation	9

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