

# Targeted Temperature Management






## Finding the Right Temperature for Patients: The Right Choice, Right Now

The TTM2 study, published in June 2021, examined the use of targeted temperature management (TTM) in 1,900 out-of-hospital cardiac arrest adult patients.<sup>1</sup> The trial results have led to discussions about assessing target temperature and tailoring TTM therapy based on injury severity. Below are two examples of **Fit Factors** for clinicians to consider when utilizing TTM strategies.

### Fit Factor 1: Injury Severity

As seen below, three studies were consistent in their findings regarding the level of brain injury and the selection of target temperatures during TTM.

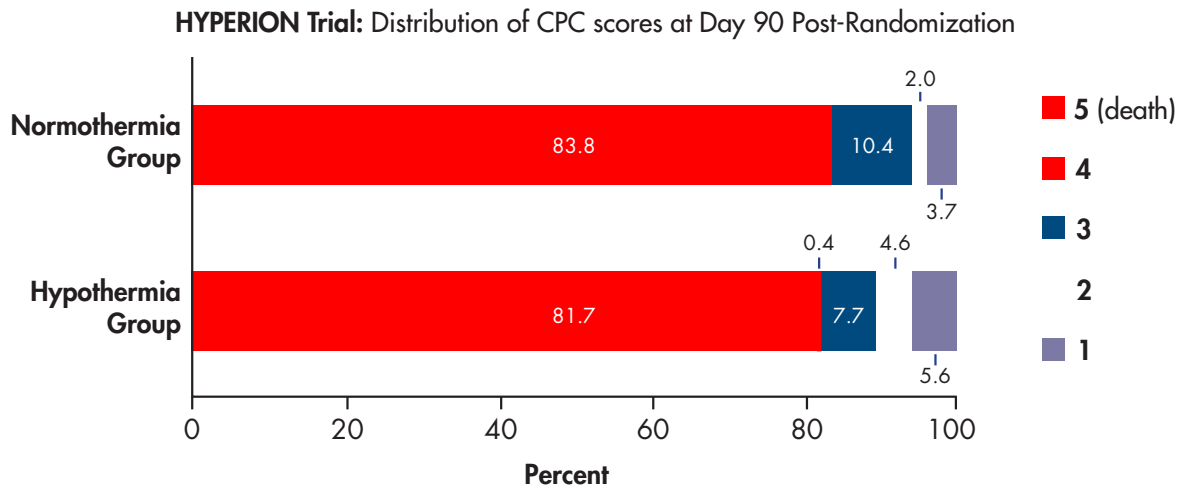
- These trials, which show consistency regardless of geography, suggest that a more severe brain injury needs more aggressive TTM strategies (i.e., 33° C), and their findings support the need to stratify the severity of the patient's brain injury in order to determine the most appropriate target temperature.
- A post-hoc meta-analysis of the combined TTM and TTM2 patient cohorts showed that patients without bystander resuscitation (i.e., with more severe ischemic injury) had better rates of survival and functional outcomes at 6 months with hypothermia administered, compared to those who received bystander resuscitation.<sup>2</sup>

Study Characteristics	Callaway CW, et al. <sup>3</sup>	Nishikimi M, et al. <sup>4</sup>	Nutma S, et al. <sup>5</sup>
 <b>Geography</b>	North America (U.S.)	Asia (Japan)	Europe (Netherlands)
 <b>Number of Subjects (N)</b>	1,319	1,111	479
 <b>Target Temperatures</b>	33° C or 36° C	33–34° C or 35–36° C	33° C or 36° C
 <b>Primary Outcome</b>	Survival to discharge	Neurological outcomes (CPC score) at 30 days	Neurological outcomes (CPC score) at 6 months
 <b>Results</b>	TTM at 33° C associated with better survival in patients with more severe injury; TTM at 36° C associated with better survival for patients with mild to moderate injury.	In patients with moderate initial injury, TTM at 33–34° C was associated with better neurological response vs. TTM at 35–36° C.	Patients with moderate encephalopathy showed significantly better neurological outcomes with TTM at 33° C vs. 36° C.

## Fit Factor 2: Initial Shockable vs. Nonshockable Rhythms

The presence of initial shockable vs. nonshockable rhythms should also be considered. Initial nonshockable rhythms are associated with longer no-flow times, which can increase susceptibility to more severe ischemic injury.<sup>6</sup>

- HYPERION trial, which looked at the use of TTM at 33° C compared to normothermia (37° C) in initial nonshockable rhythms, showed that patients treated at 33°C survived with a more favorable CPC score of 1 or 2 compared to those who received normothermia (10.2% vs. 5.7% respectively,  $p=0.04$ )<sup>7</sup> (Figure 1).
- Data from a nationwide registry in Japan suggested that the use of intravascular cooling was associated with better 30-day neurological outcomes in patients with initial nonshockable rhythms.<sup>8</sup>



**Figure 1.** Distribution of cerebral performance category (CPC) scores on day 90 after randomization. Cerebral performance category scores range from 1 to 5, with higher scores indicating greater disability. Patients who were lost to follow-up (one in the hyperthermia group and two in the normothermia group) were assigned a score of 5, indicating death. For this trial, a favorable neurologic outcome was defined as a CPC score of 1 (good cerebral performance or minor disability) or 2 (moderate disability). Percentages may not total to 100 because of rounding.<sup>7</sup>

## Conclusion

The importance of providing tailored TTM therapy has been well documented in recent studies and is applicable to any brain injury. Both **Fit Factors** are key considerations in deciding target temperature and the course of patient treatment. Clinicians should feel supported to make the best decisions and find the right TTM fit for their patients.

## Additional Resources



**Webinar (English): Beyond One Size Fits All:  
The Era of High-Quality Temperature Management**



<sup>1</sup>Dankiewicz, et al. Hypothermia versus normothermia after out-of-hospital cardiac arrest. *NEJM*. 2021; 384:2283–2294

<sup>2</sup>Holgersson J, et al. Hypothermic versus normothermic temperature control after cardiac arrest. *NEJM Evid*. 2022 Jun 15; [e-pub] <https://doi.org/10.1056/EVIDoa2200137>.

<sup>3</sup>Callaway CW, et al. Association of initial illness severity and outcomes after cardiac arrest with targeted temperature management at 36° C or 33° C. *JAMA Netw Open*. 2020;3:7:e208215. doi:10.1001/jamanetworkopen.2020.8215

<sup>4</sup>Nishikimi M, et al. Outcome related to level of targeted temperature management in postcardiac arrest syndrome of low, moderate, and high severities: a nationwide multicenter prospective registry. *Crit Care Med*. 2021 Aug 1;49(8):e741–e750. doi: 10.1097/CCM.0000000000005025.

<sup>5</sup>Nutma S, et al. Effects of targeted temperature management at 33° C vs. 36° C on comatose patients after cardiac arrest stratified by the severity of encephalopathy. *Resuscitation*. 2022;173:147–153. doi: <https://doi.org/10.1016/j.resuscitation.2022.01.026>

<sup>6</sup>Granfeldt A, et al. Clinical predictors of shockable versus non-shockable rhythms in patients with out-of-hospital cardiac arrest. *Resuscitation*. 2016;108:40–7.

<sup>7</sup>Lascarrou JB, et al. Targeted temperature management for cardiac arrest with nonshockable rhythm. *NEJM*. 2019;381:2327–37.

<sup>8</sup>Watanabe, et al. Impact of cooling method on the outcome of shockable or non-shockable out of hospital cardiac arrest patients receiving target temperature management: a nationwide multicentre cohort study. *Annals of Intensive Care*. 2021;11:163. <https://doi.org/10.1186/s13613-021-00953-y>.