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Targeted temperature management after out-of-hospital cardiac arrest, no de-implementation required based on network meta analysis

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With great interest, we read the systematic review and network meta-analysis performed by Fernando et al. [1]. The effect of targeted temperature management in out-of-hospital cardiac arrest (OHCA) is a greatly debated subject, recently implemented in international guidelines [2]. The authors conclude that the effect of the targeted temperature management is not beneficial, and might even cause harm by increasing the incidence of arrhythmias. These findings warrant de-implementation of this intervention and changing of many national guidelines. Therefore, critical evaluation of the used methodology is required. Although the authors clearly report and performed their study in accordance with relevant guidelines, we believe the chosen methodology is not perfectly suited to evaluate this question.

First, we believe that the exposure is handled inappropriately. The authors present targeted temperature management as an intervention which focuses on targeting temperatures at 31–32 °C ('deep hypothermia'), 33–34 °C ('moderate hypothermia'), 35–36 °C ('mild hypothermia'), and 37–37.8 °C ('normothermia'). However, it is unnatural and statistically inefficient to categorize temperature into distinct categories. The researchers now assume that patients held at 32.9 °C have different metabolism due to their temperature than patients held at 33 °C. Moreover, they assume that patients between 31 °C and 32.9 °C have completely similar metabolism compared to normothermia. Since metabolic rate scales with temperature, these

assumptions are not likely to hold. "The losses involved in dichotomizing (= categorization) are not negligible and the gains are illusory" [3]. Furthermore, evaluating the effect of hypothermia on outcome often is evaluated in clinical trials by efforts to keep patient-body temperatures within certain ranges. Therefore, not the effect of temperature on outcome is evaluated (which is of most clinical interest), but the effect of the efforts of caregivers to keep temperatures within that range. This introduces measurement error, and the authors do not address or discuss this limitation.

Second, also the primary outcome is handled sub-optimal within this study. The authors categorize MRS and CPC score to "good" and "bad" functional outcome. Although this categorization numerically allows the authors to pool studies which use different outcome measures, it introduces an important limitation: by not exploiting the full range of functional outcome, the analysis loses substantial power [4]. The authors conclude that there is no significant effect, thereby disregarding this substantial loss of power.

We appreciate the efforts of the researchers to summarize and pool estimates from multiple randomized trials to provide a more definitive answer to this debate. However, we feel that the network meta-analysis performed in its current form does not provide a definitive answer. To better evaluate the relationship between temperature and functional outcome, an individual patient data meta-analysis would be more appropriate [5]. Such a design would have more statistical power, would not be limited by unnatural assumptions about categorized exposures, and would be able to address the measurement error

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biasing the results of these studies. Based on current evidence, we are not in favor of de-implementation of targeted temperature management for OHCA as currently recommended in international guidelines [2].

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Declarations

Conflicts of interest

The authors declare to have no conflicts of interest.

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Received: 16 August 2021 Accepted: 27 August 2021

Published online: 18 September 2021

References

1. Fernando SM, Di SP, Sadeghirad B, Lascarrou JB (2021) Targeted temperature management following out-of-hospital cardiac arrest: a systematic review and network meta-analysis of temperature targets. *Intensive Care Med*. <https://doi.org/10.1007/s00134-021-06505-z>
2. Nolan JP, Sandroni C, Böttiger BW et al (2021) European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2021: post-resuscitation care. *Intensive Care Med* 47:369–421. <https://doi.org/10.1007/s00134-021-06368-4>
3. Senn SJ (2005) Dichotomania: an obsessive compulsive disorder that is badly affecting the quality of analysis of pharmaceutical trials. *Proc Int Stat Institute*, 55th Sess, pp. 1–13
4. Roozenbeek B, Lingsma HF, Perel P et al (2011) The added value of ordinal analysis in clinical trials: an example in traumatic brain injury. *Crit Care*. <https://doi.org/10.1186/cc10240>
5. Riley RD, Lambert PC, Abo-Zaid G (2010) Meta-analysis of individual participant data: rationale, conduct, and reporting. *BMJ* 340:521–525. <https://doi.org/10.1136/bmj.c221>