

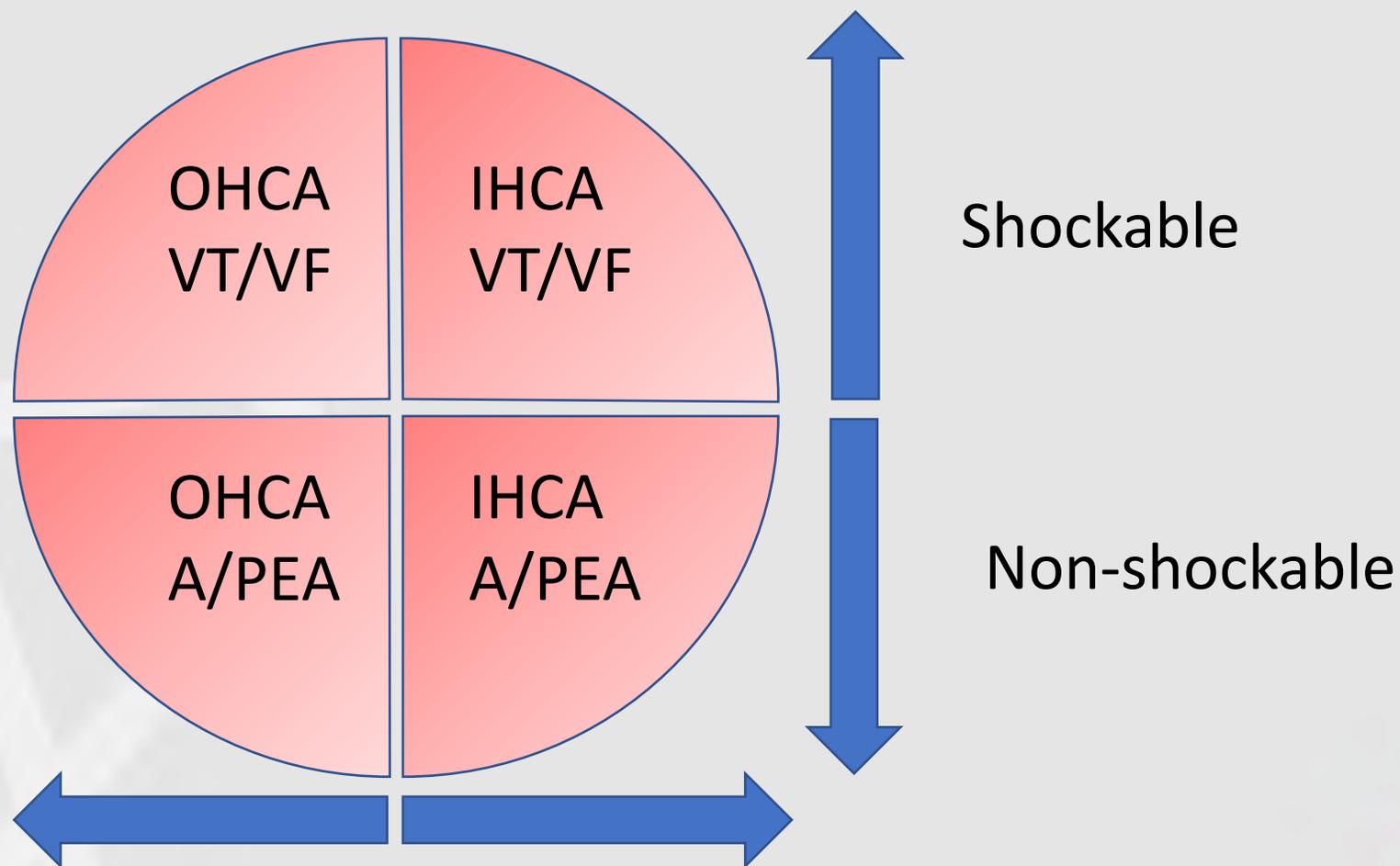


# Temperatur och hjärtstopp

NIKLAS NIELSEN, LUNDS UNIVERSITET, HELSINGBORGS LASARETT

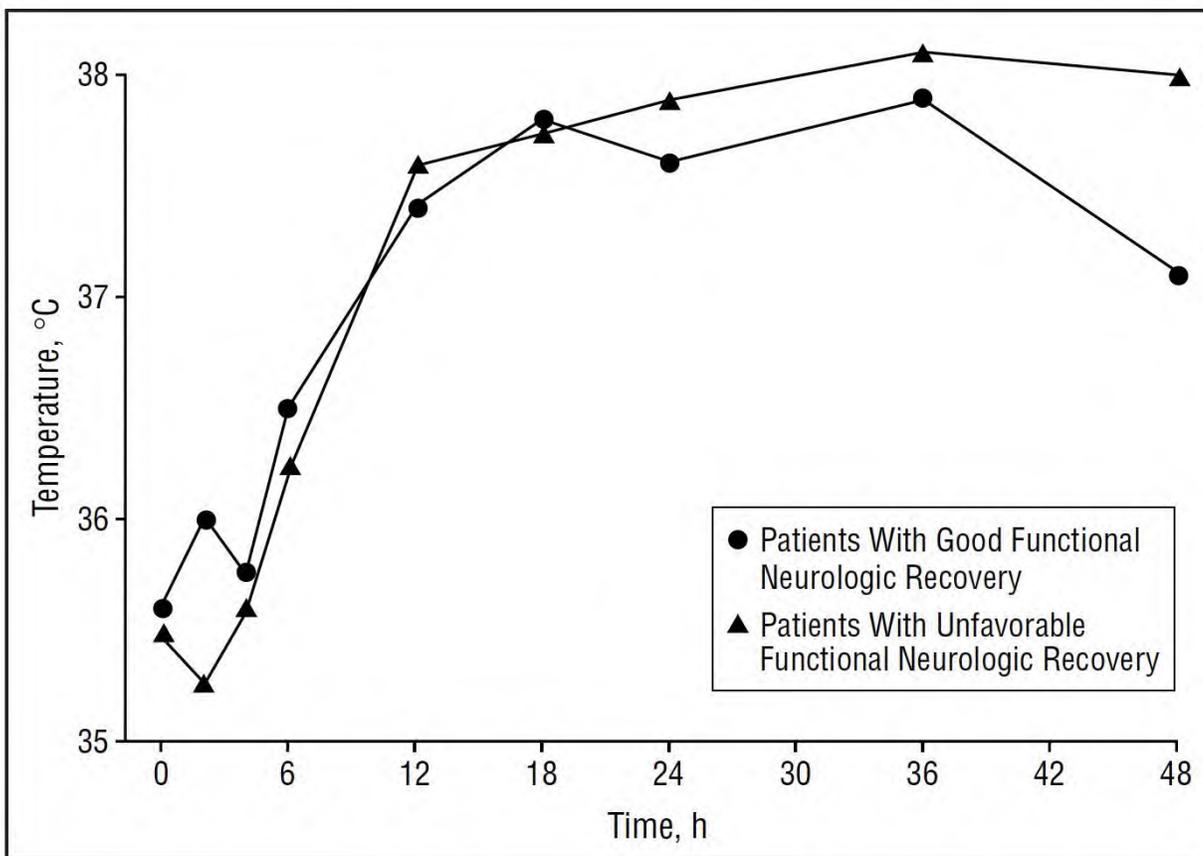


# Hjärtstopp som behandlas på IVA

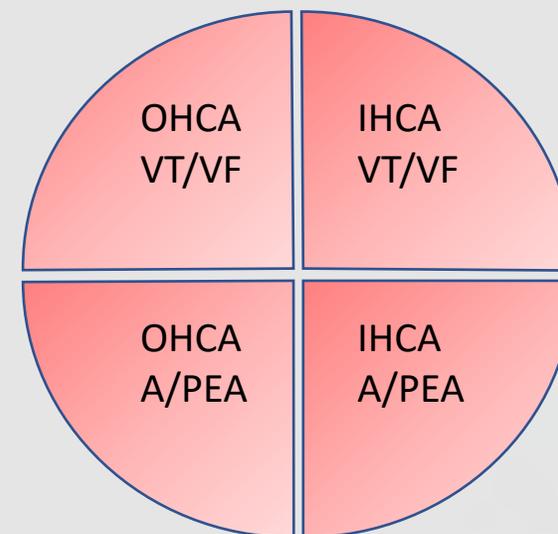


Out-of-hospital cardiac arrest    In-hospital cardiac arrest

# Före 2002 – ingen temperaturbehandling



Temperature curves within 48 hours after successful cardiopulmonary resuscitation. Data are expressed as the median.



# 2002

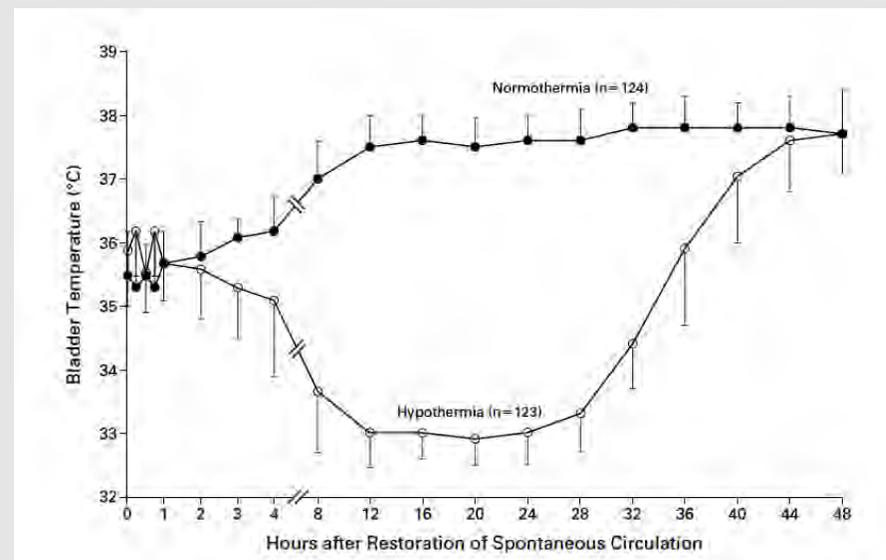
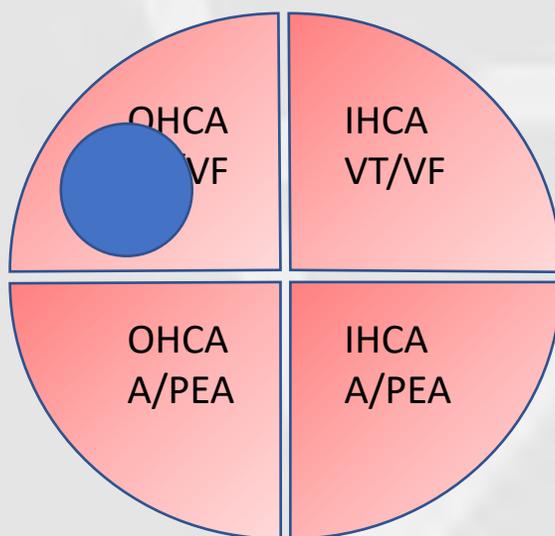
ORIGINAL ARTICLE

## Treatment of Comatose Survivors of Out-of-Hospital Cardiac Arrest with Induced Hypothermia

Stephen A. Bernard, M.B., B.S., Timothy W. Gray, M.B., B.S., Michael D. Bunn, M.B., B.S., Bruce M. Jones, M.B., B.S., William Stiles, M.B., B.S., Geoff Gutteridge, M.B., B.S., and Karen Smith, B.Sc.  
N Engl J Med 2002; 346:557-563 | February 21, 2002

## Mild Therapeutic Hypothermia to Improve the Neurologic Outcome after Cardiac Arrest

The Hypothermia after Cardiac Arrest Study Group  
N Engl J Med 2002; 346:554-562 | February 21, 2002



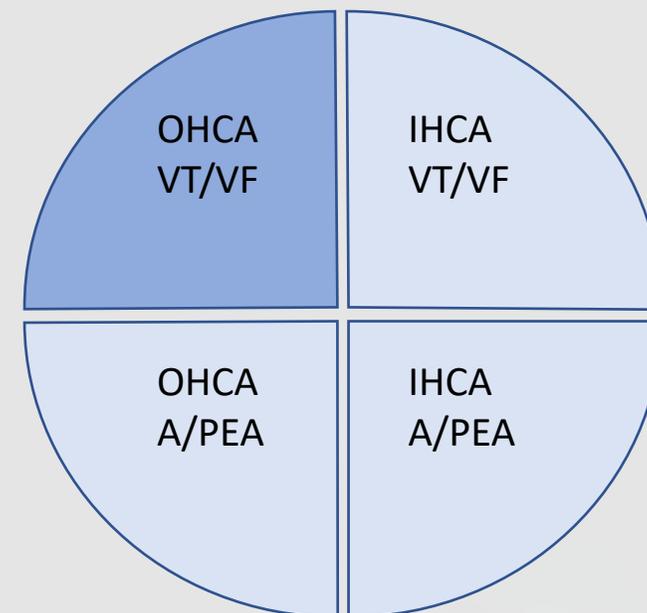
# 2003 – ILCOR rekommendation

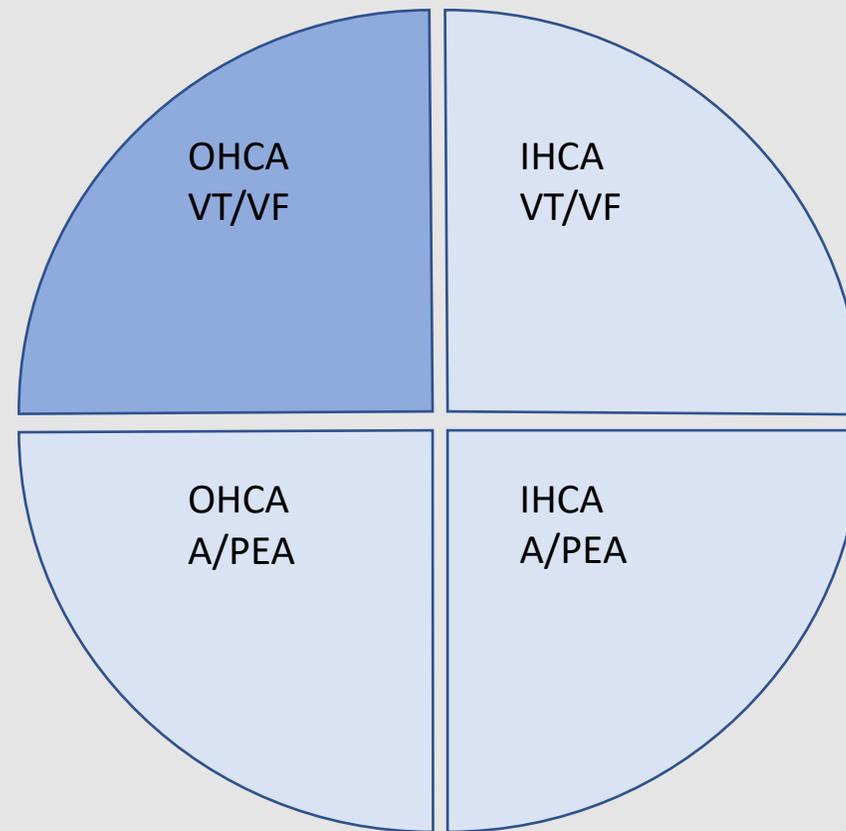
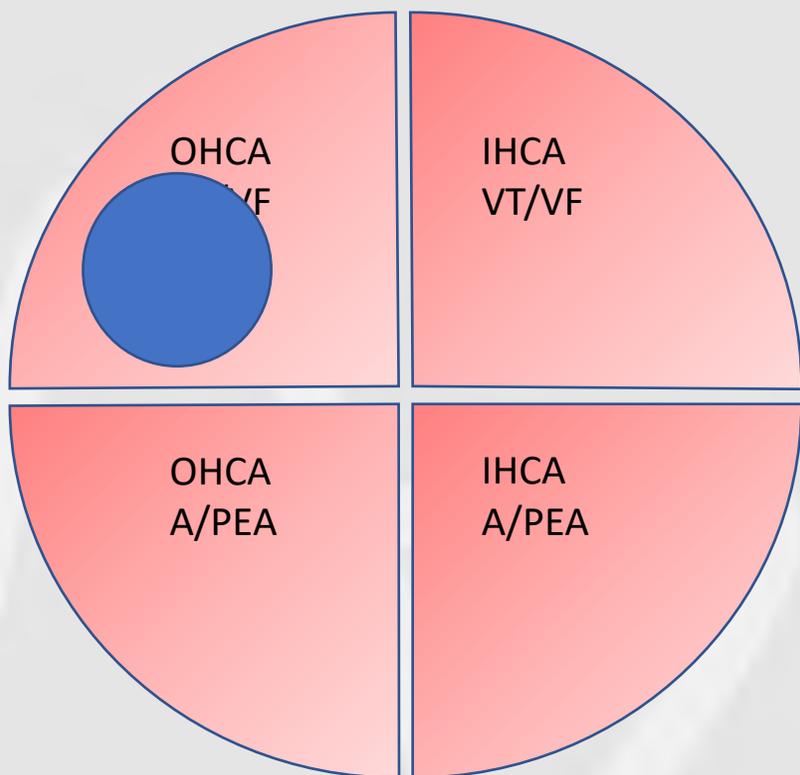
## ILCOR Advisory Statement

### Therapeutic Hypothermia After Cardiac Arrest

An Advisory Statement by the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation

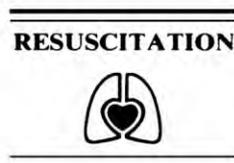
- Unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest should be cooled to 32°C to 34°C for 12 to 24 hours when the initial rhythm was ventricular fibrillation (VF).
- Such cooling may also be beneficial for other rhythms or in-hospital cardiac arrest.





# Guidelines 2005

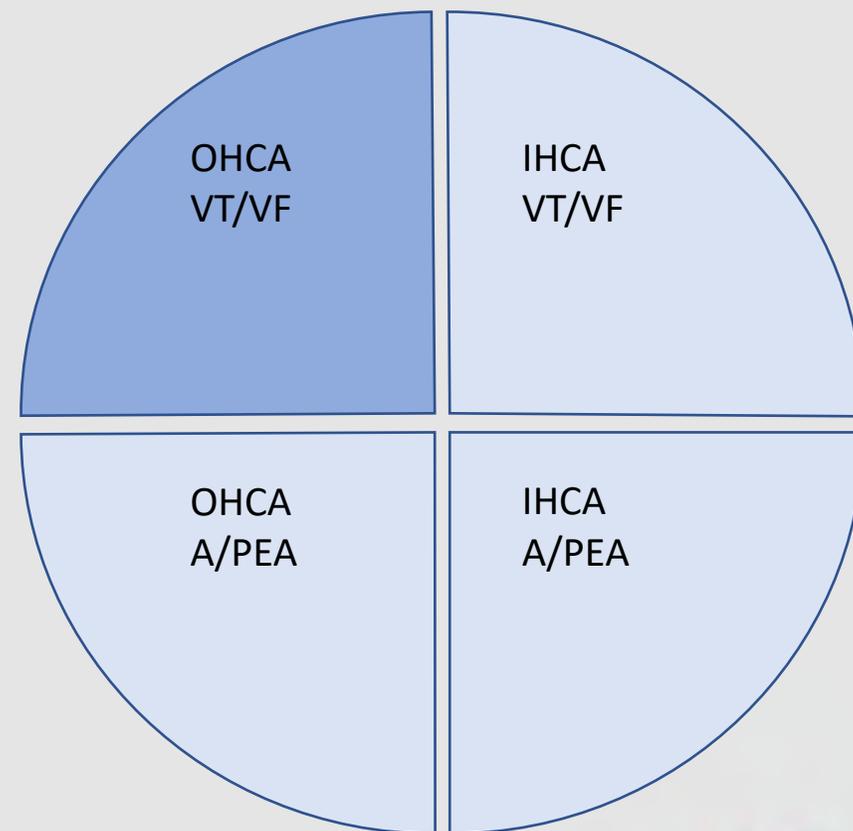
Resuscitation (2005) 67S1, S39–S86



[www.elsevier.com/locate/resuscitation](http://www.elsevier.com/locate/resuscitation)

## European Resuscitation Council Guidelines for Resuscitation 2005 Section 4. Adult advanced life support

Jerry P. Nolan, Charles D. Deakin, Jasmeet Soar,  
Bernd W. Böttiger, Gary Smith



# Guidelines 2010



## European Resuscitation Council Guidelines for Resuscitation 2010 Section 4. Adult advanced life support

Charles D. Deakin<sup>a,1</sup>, Jerry P. Nolan<sup>b,\*,1</sup>, Jasmeet Soar<sup>c</sup>, Kjetil Sunde<sup>d</sup>, Rudolph W. Koster<sup>e</sup>, Gary B. Smith<sup>f</sup>, Gavin D. Perkins<sup>f</sup>

<sup>a</sup> Cardiothoracic Anaesthesia, Southampton General Hospital, Southampton, UK

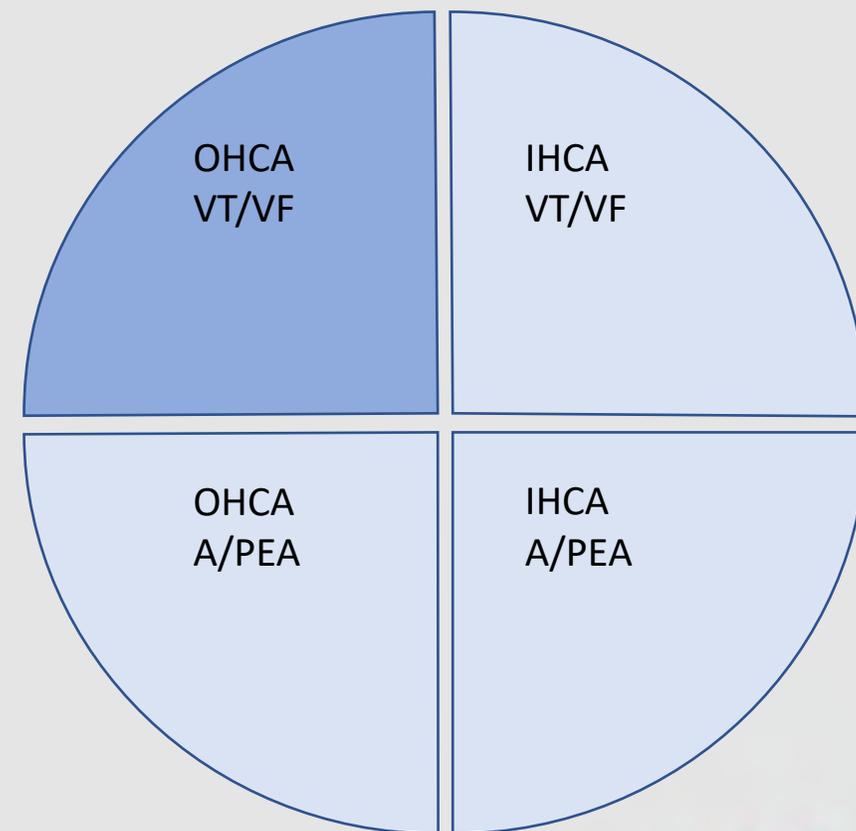
<sup>b</sup> Anaesthesia and Intensive Care Medicine, Royal United Hospital, Bath, UK

<sup>c</sup> Anaesthesia and Intensive Care Medicine, Southmead Hospital, Bristol, UK

<sup>d</sup> Surgical Intensive Care Unit, Oslo University Hospital Ulleval, Oslo, Norway

<sup>e</sup> Department of Cardiology, Academic Medical Center, Amsterdam, The Netherlands

<sup>f</sup> Critical Care and Resuscitation, University of Warwick, Warwick Medical School, Warwick, UK



# Hur bra var egentligen studierna??

Contents lists available at ScienceDirect

**International Journal of Cardiology**

journal homepage: [www.elsevier.com/locate/ijcard](http://www.elsevier.com/locate/ijcard)

**Hypothermia after cardiac arrest should be further evaluated—A systematic review of randomised trials with meta-analysis and trial sequential analysis**

Niklas Nielsen <sup>a,\*</sup>, Hans Friberg <sup>b</sup>, Christian Gluud <sup>c</sup>, Johan Herlitz <sup>d</sup>, Jørn Wetterslev <sup>c</sup>

<sup>a</sup> Department of Clinical Sciences, Section of Anesthesia and Intensive Care, Lund University, S-221 85 Lund, Sweden and Department of Anesthesia and Intensive Care, Helsingborg Hospital, S-251 87 Helsingborg, Sweden

<sup>b</sup> Department of Clinical Sciences, Section of Anesthesia and Intensive Care, Lund University, S-221 85 Lund, Sweden and Department of Emergency Medicine, Lund University Hospital, S-221 85 Lund, Sweden

<sup>c</sup> Copenhagen Trial Unit, Center for Clinical Intervention Research, Rigshospitalet, Copenhagen University Hospital, DK-2100 Copenhagen, Denmark

<sup>d</sup> Department of Cardiology, Sahlgrenska University Hospital, S-413 19 Gothenburg, Sweden

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**ARTICLE INFO**

*Article history:*  
Received 29 March 2010  
Accepted 4 June 2010  
Available online xxx

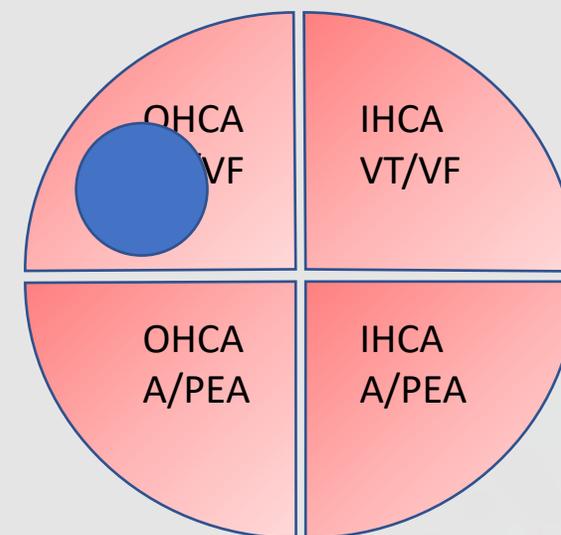
*Keywords:*  
Induced hypothermia  
Heart arrest  
Mortality  
Neurological outcome  
Intensive care  
Critical care

**ABSTRACT**

*Background:* Guidelines recommend mild induced hypothermia (MIH) to reduce mortality and neurological impairment after out-of-hospital cardiac arrest. Our objective was to systematically evaluate the evidence for MIH taking into consideration the risks of systematic and random error and to GRADE the evidence.

*Methods:* Systematic review with meta-analysis and trial sequential analysis of randomised trials evaluating MIH after cardiac arrest in adults. We searched CENTRAL, MEDLINE, and EMBASE databases until May 2009. Retrieved trials were evaluated with Cochrane methodology. Meta-analytic estimates were calculated with random- and fixed-effects models and random errors were evaluated with trial sequential analysis (TSA).

*Results:* Five randomised trials (478 patients) were included. All trials had substantial risk of bias. The relative risk (RR) for death was 0.84 (95% confidence interval (CI) 0.70 to 1.01) and for poor neurological outcome 0.78 (95% CI 0.64 to 0.95). For the two trials with least risk of bias the RR for death was 0.92 (95% CI 0.56 to 1.51) and for poor neurological outcome 0.92 (95% confidence interval 0.56 to 1.50). TSA indicated lack of firm evidence for a beneficial effect. The substantial risk of bias and concerns with directness rated down the quality of the evidence to low.



**Hypothermia versus strict normothermia after out-of-hospital cardiac arrest.**

**a randomised, parallel groups, assessor blinded clinical trial**

Acronyme: **HNCA-trial**

Version: **1.1**

Date: **2009-04-29**



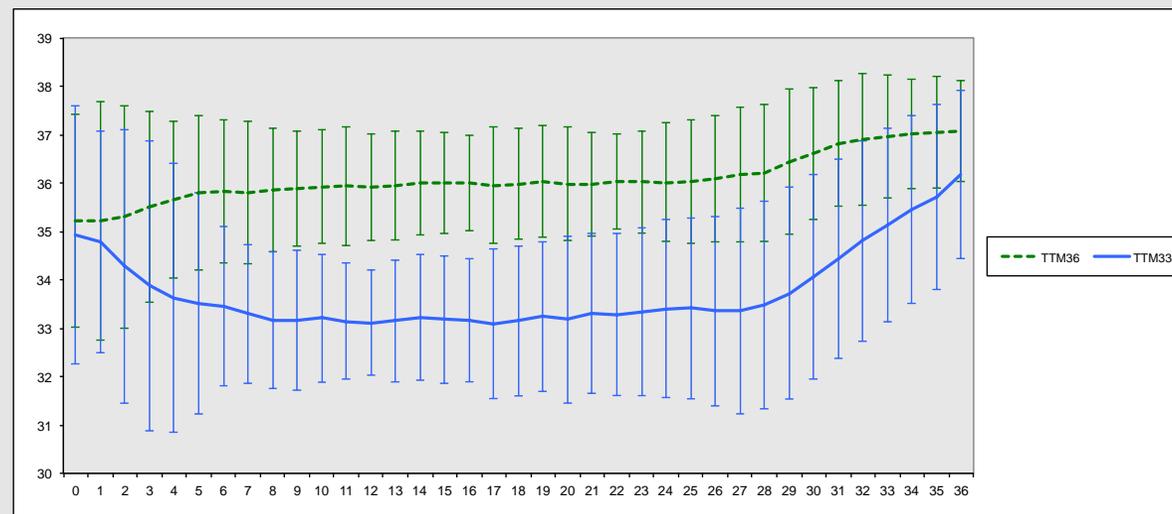
**LUND**  
UNIVERSITY

# TTM-studien

THE NEW ENGLAND JOURNAL OF MEDICINE

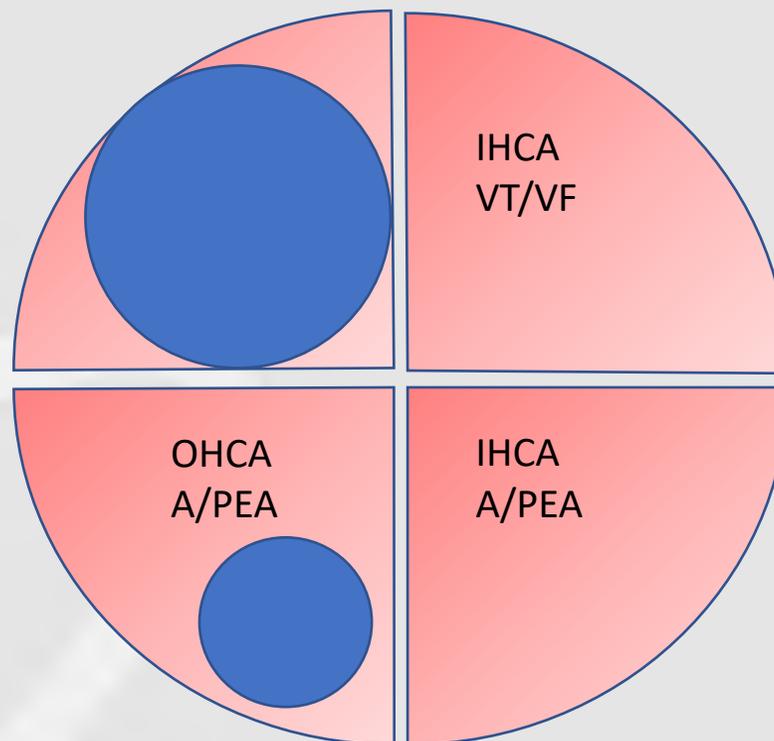
ORIGINAL ARTICLE

Targeted Temperature Management  
at 33°C versus 36°C after Cardiac Arrest

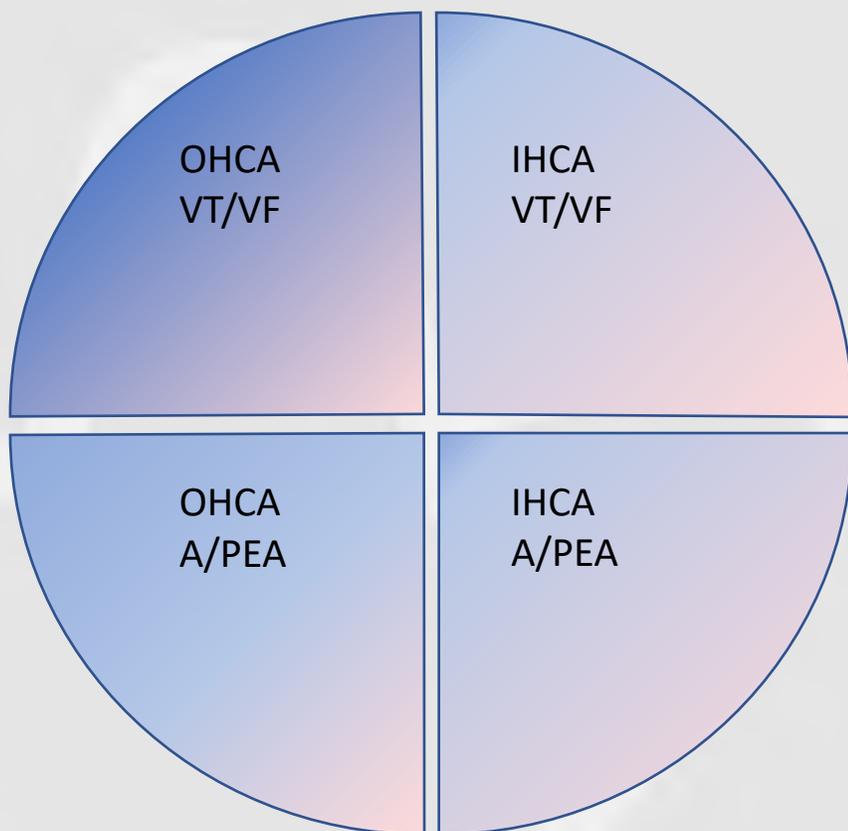


Nedkylning till 33°C förbättrar inte  
överlevnad eller neurologisk funktion  
i jämförelse med att hålla 36°C

# TTM-studien



# Guidelines 2015



## Temperature control

- Maintain a constant, target temperature between 32 °C and 36 °C for those patients in whom temperature control is used (strong recommendation, moderate-quality evidence).
- Whether certain subpopulations of cardiac arrest patients may benefit from lower (32–34 °C) or higher (36 °C) temperatures remains unknown, and further research may help elucidate this.
- TTM is recommended for adults after OHCA with an initial shockable rhythm who remain unresponsive after ROSC (strong recommendation, low-quality evidence).
- TTM is suggested for adults after OHCA with an initial non-shockable rhythm who remain unresponsive after ROSC (weak recommendation, very low-quality evidence).
- TTM is suggested for adults after IHCA with any initial rhythm who remain unresponsive after ROSC (weak recommendation, very low-quality evidence).
- If targeted temperature management is used, it is suggested that the duration is at least 24 h (weak recommendation, very low-quality evidence).



## Changes in Temperature Management of Cardiac Arrest Patients Following Publication of the Target Temperature Management Trial\*

Ryan Salter; Michael Bailey; Rinaldo Bellomo; Glenn Eastwood; Andrew Goodwin; Niklas Nielsen; David I Alistair Nichol; Manoj Saxena; Yahya Shehabi; Paul Young



Original Investigation | Cardiology

## Temporal Trends in the Use of Therapeutic Hypothermia for Out-of-Hospital Cardiac Arrest

Steven M. Bradley, MD, MPH; Wenhui Liu, MS; Bryan McNally, MD, MPH; Kimberly Vellano, MPH; Timothy D. Henry, MD; Michael R. Mooney, MD; M. Nicholas Burke, MD; Emmanouil S. Brilakis, MD, PhD; Gary K. Grunwald, PhD; Mehul Adhaduk, MD; Michael Donnino, MD; Saket Girotra, MD, SM; for the Cardiac Arrest Registry to Enhance Survival (CARES) Surveillance Group

RESEARCH

Open Access

## Changes in cardiac arrest patients' temperature management after the 2013 "TTM" trial: results from an international survey

Nicolas Deye<sup>1\*</sup>, François Vincent<sup>2</sup>, Philippe Michel<sup>3</sup>, Stephan Ehrmann<sup>4</sup>, Daniel da Silva<sup>5</sup>, Michael Piagnerelli<sup>6</sup>, Antoine Kimmoun<sup>7</sup>, Olfa Hamzaoui<sup>8</sup>, Jean-Claude Lacherade<sup>9</sup>, Bernard de Jonghe<sup>10</sup>, Florence Brouard<sup>3</sup>, Corinne Audoin<sup>11</sup>, Xavier Monnet<sup>12</sup>, Pierre-François Laterre<sup>13</sup> and For the SRLF Trial Group

## Targeted Temperature Management at 33 Versus 36 Degrees: A Retrospective Cohort Study

Nicholas J. Johnson, MD<sup>1,2</sup>; Kyle R. Danielson, MPH, AHNP<sup>3</sup>; Catherine R. Counts, PhD, MHA<sup>1</sup>; Katelyn Ruark, BS<sup>4,5</sup>; Sue Scruggs, RN<sup>1</sup>; Catherine L. Hough, MD, MS<sup>1</sup>; Charles Maynard, PhD<sup>1</sup>; Michael R. Sayre, MD<sup>1,6</sup>; David J. Carlhom, MD<sup>1</sup>

**Objectives:** To determine the association between targeted temperature management goal temperature of 33°C versus 36°C and neurologic outcome after out-of-hospital cardiac arrest.  
**Design:** This was a retrospective, before-and-after, cohort study.  
**Setting:** Urban, academic, level 1 trauma center from 2010 to 2017.  
**Patients:** Adults with nontraumatic out-of-hospital cardiac arrest who received targeted temperature management.

targeted temperature management 33°C were older (57 vs 52 yr;  $p < 0.05$ ) and had more arrests of cardiac etiology (45% vs 35%;  $p < 0.05$ ), but otherwise had similar baseline characteristics, including initial cardiac rhythm. A total of 40% of patients treated during targeted temperature management 33°C survived with favorable neurologic outcome, compared with 30% in the targeted temperature management 36°C group ( $p < 0.05$ ). After adjustment for demographic and cardiac arrest characteristics, targeted temperature management



Contents lists available at ScienceDirect

Resuscitation

journal homepage: [www.elsevier.com/locate/resuscitation](http://www.elsevier.com/locate/resuscitation)



Clinical paper

A survey on general and temperature management of post cardiac arrest patients in large teaching and university hospitals in 14 European countries—The SPAME trial results

Christian Storm<sup>a,\*,1</sup>, J. Nee<sup>a,1</sup>, Kjetil Sunde<sup>b</sup>, Michael Holzer<sup>c</sup>, Pia Hubner<sup>c</sup>, steban Lopez-de-Sa<sup>f</sup>, Alain Cariou<sup>g</sup>, Marko Noc<sup>l</sup>, Dirk W. Donker<sup>k</sup>, Janusz Andres<sup>l</sup>, <sup>h,o</sup>, James Penketh<sup>o</sup>, Alexander Krannich<sup>a</sup>,



## SCIENTIFIC REPORTS

OPEN

## Changes in cardiac arrest patients' temperature management after the publication of 2015 AHA guidelines for resuscitation in China

ed: 16 August 2017  
ed: 6 November 2017  
ed online: 22 November 2017

Lanfang Du<sup>1</sup>, Baolan Ge<sup>1</sup>, Qingbian Ma<sup>1</sup>, Jianzhong Yang<sup>2</sup>, Fengying Chen<sup>3</sup>, Yuhong Mi<sup>4</sup>, Zhang<sup>5</sup>, Rongjia Yang<sup>3</sup>, Jian Guan<sup>10</sup>, Yan Xiong<sup>14</sup>, Guoxing Wang<sup>15</sup>, ing<sup>18</sup>, Jihong Zhu<sup>19</sup>, Jie Li<sup>20</sup>, Chao Lan<sup>21</sup>



Resuscitation

journal homepage: [www.elsevier.com/locate/resuscitation](http://www.elsevier.com/locate/resuscitation)



Clinical paper

Functional outcomes associated with varying levels of targeted temperature management after out-of-hospital cardiac arrest — An INTCAR2 registry analysis

Jesper Johnsson<sup>a,b,\*</sup>, Josefine Wahlström<sup>b</sup>, Josef Dankiewicz<sup>c</sup>, Martin Annborn<sup>a,b</sup>, Sachin Agarwal<sup>d</sup>, Allison Dupont<sup>e</sup>, Sune Forsberg<sup>f</sup>, Hans Friberg<sup>g</sup>, Robert Hand<sup>h</sup>, Karen G. Hirsch<sup>i</sup>, Teresa May<sup>j</sup>, John A. McPherson<sup>k</sup>, Michael R Mooney<sup>l</sup>, Nainesh Patel<sup>m</sup>, Richard R. Riker<sup>l</sup>, Pascal Stammer<sup>n</sup>, Eldar Søreide<sup>o,p</sup>, David R. Soder<sup>l</sup>, Niklas Nielsen<sup>a,b</sup>



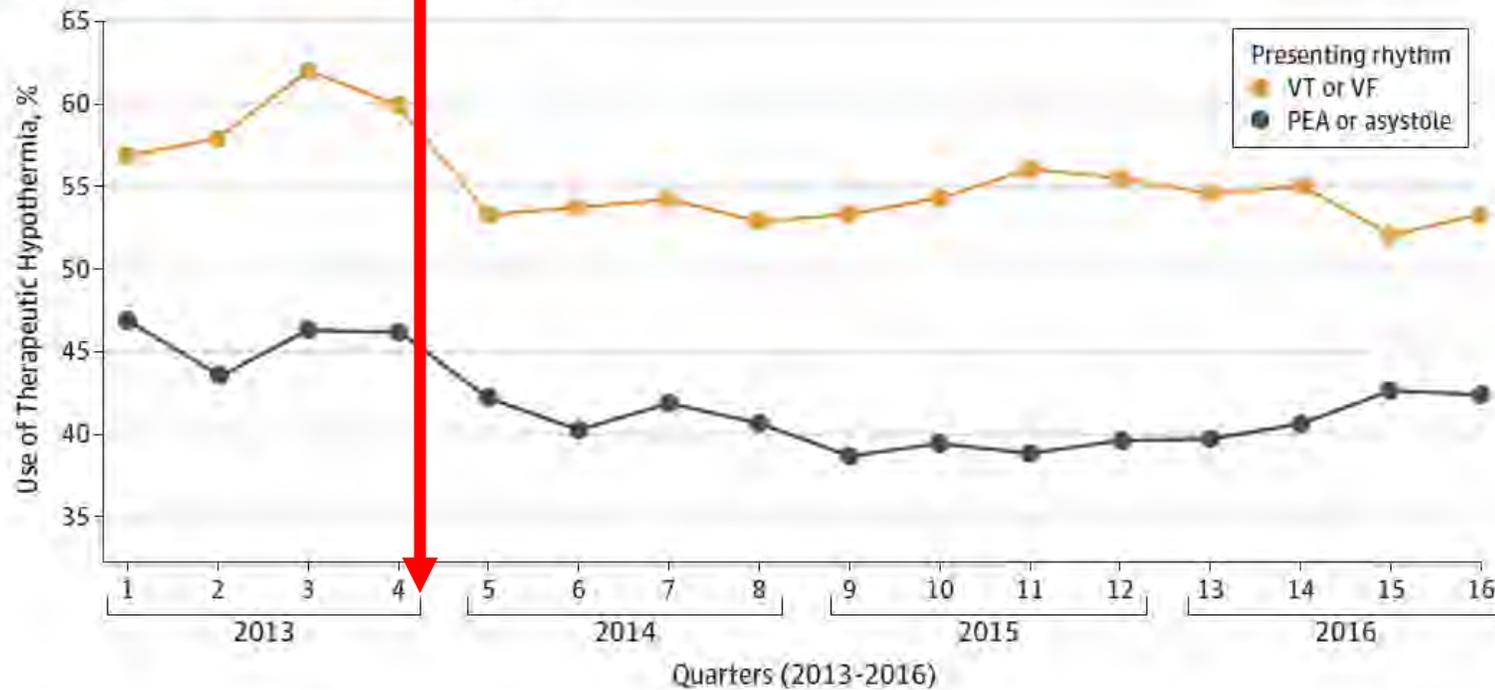
LUND UNIVERSITY

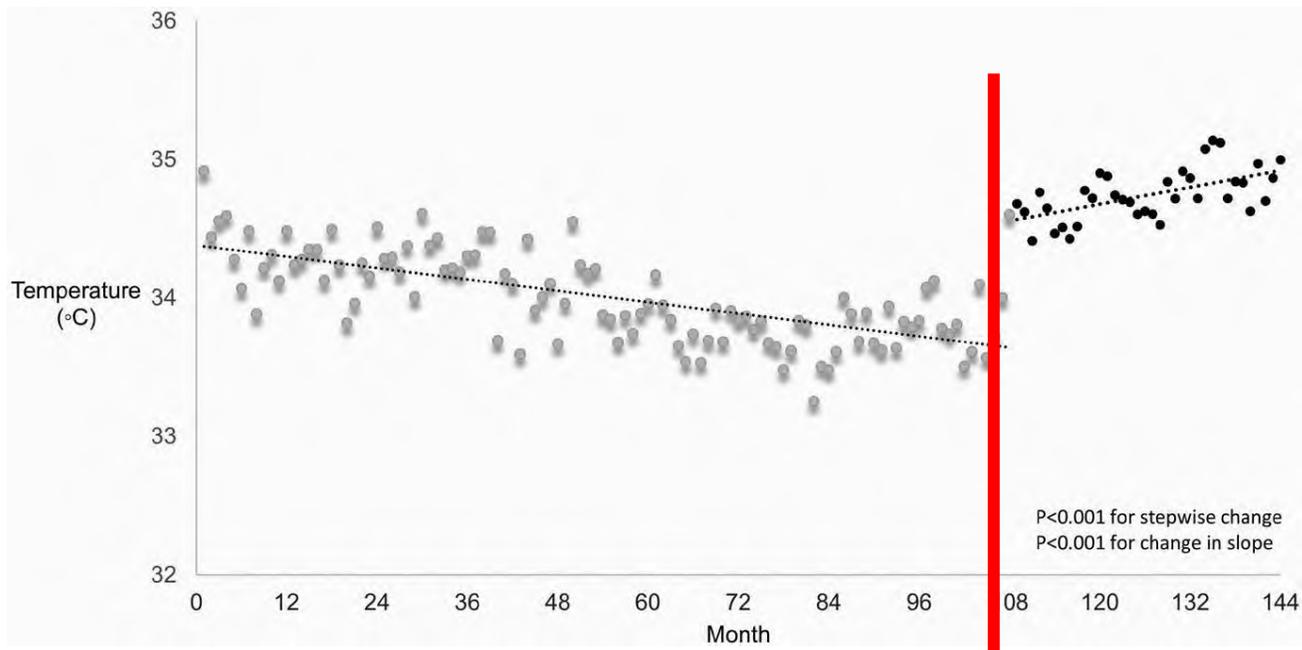
# Temporal Trends in the Use of Therapeutic Hypothermia for Out-of-Hospital Cardiac Arrest

Steven M. Bradley, MD, MPH; Wenhui Liu, MS; Bryan McNally, MD, MPH; Kimberly Vellano, MPH; Timothy D. Henry, MD; Michael R. Mooney, MD, M. Nicholas Burke, MD; Emmanouil S. Brilakis, MD, PhD; Gary L. Grunwald, PhD; Mehul Adhaduk, MD; Michael Donnino, MD; Saket Girotra, MD, SM; for the Cardiac Arrest Registry to Enhance Survival (CARES) Surveillance Group

Figure 3. Therapeutic Hypothermia Use Over Time by Presenting Rhythm

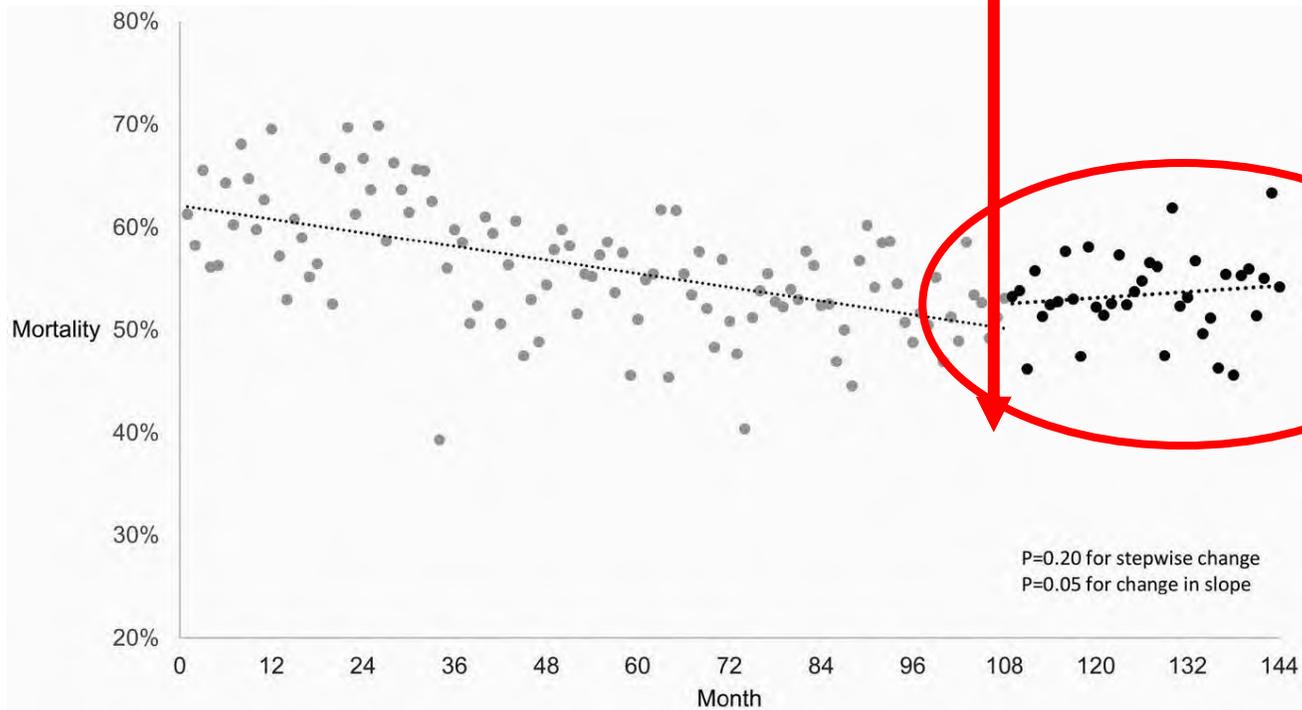
A Unadjusted rates of therapeutic hypothermia





## Changes in Temperature Management of Cardiac Arrest Patients Following Publication of the Target Temperature Management Trial\*

Ryan Salter, FANZCA<sup>1</sup>; Michael Bailey, PhD<sup>2-4</sup>; Rinaldo Bellomo, MD<sup>2,3,5</sup>; Glenn Eastwood, PhD<sup>2,5</sup>; Andrew Goodwin, BEng (Env)<sup>6</sup>; Niklas Nielsen, PhD<sup>3,5</sup>; David Pilcher, FCICM<sup>2,8,10</sup>; Alistair Nichol, PhD<sup>2,8,11</sup>; Manoj Saxena, PhD<sup>1,2-4</sup>; Yahya Shehabi, PhD<sup>4,15</sup>; Paul Young, PhD<sup>1,16</sup>; on behalf of the Australian and New Zealand Intensive Care Society Centre for Outcome and Resource Evaluation (ANZICS-CORE)



# TARGETED TEMPERATURE MANAGEMENT Tidslinje

## Bernard

77 Patients  
33°C vs. normothermia

HACA-group  
275 Patients  
33°C vs. normothermia

## TTM1

### Nielsen

939 Patients  
33° vs. 36°C

## TTH48

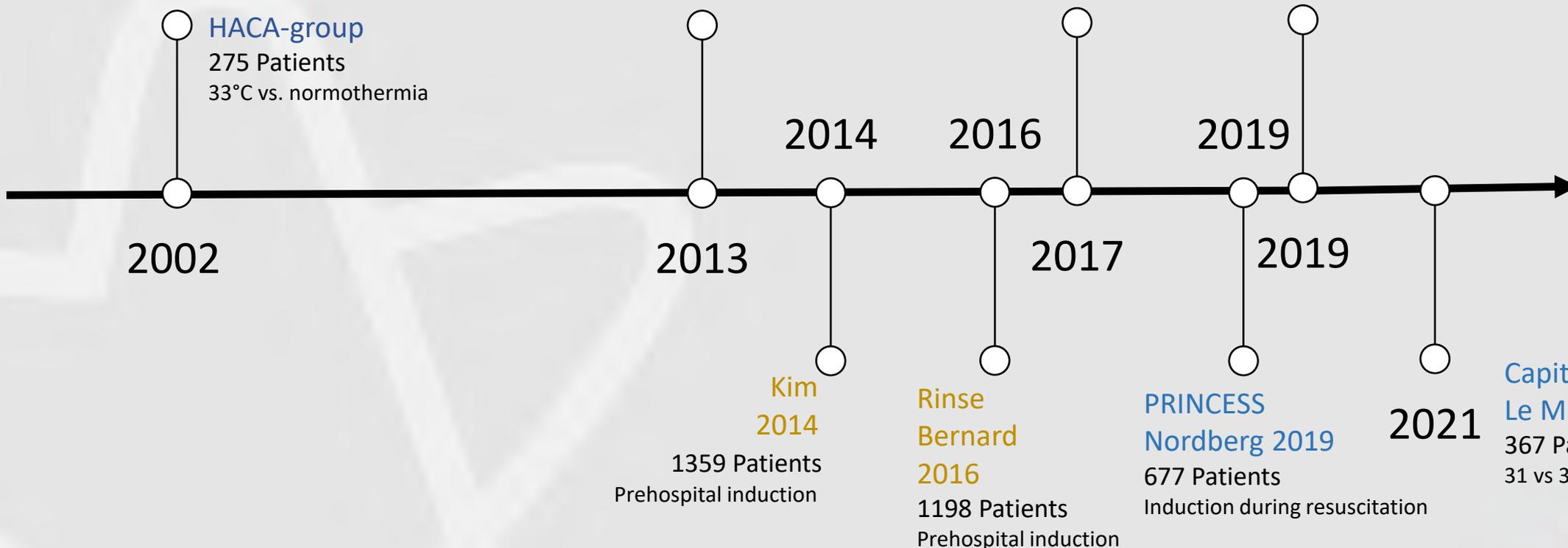
### Kirkegaard

355 Patients  
24 vs. 48 h at 33°C

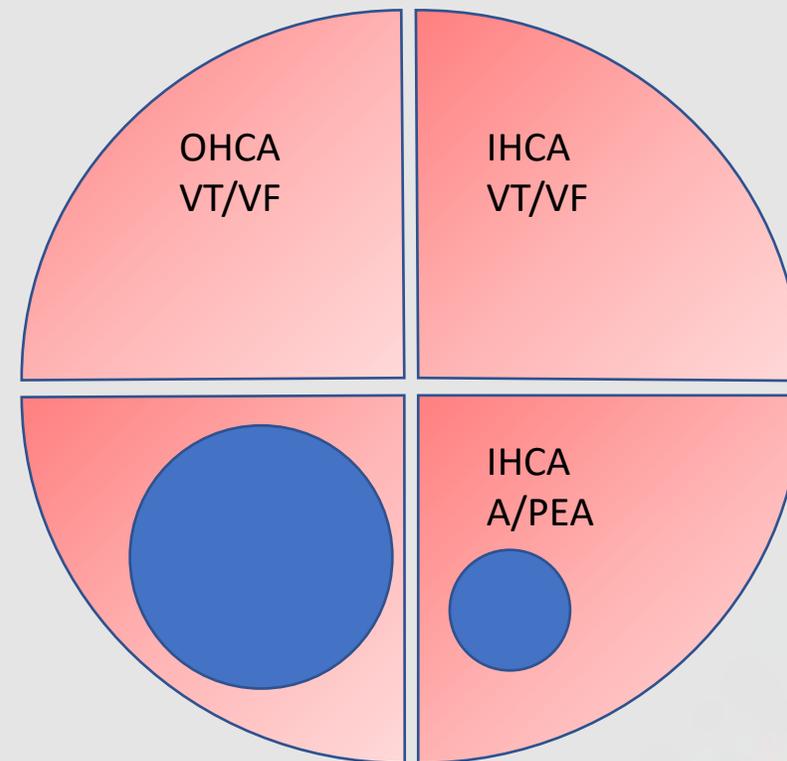
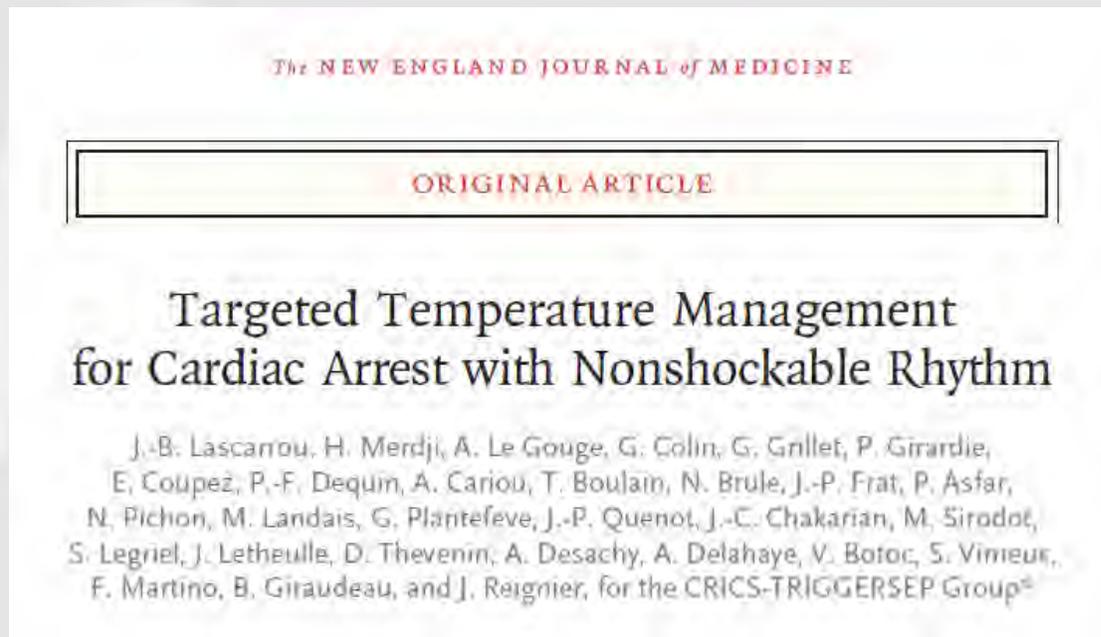
## Hyperion

### Lascarrou

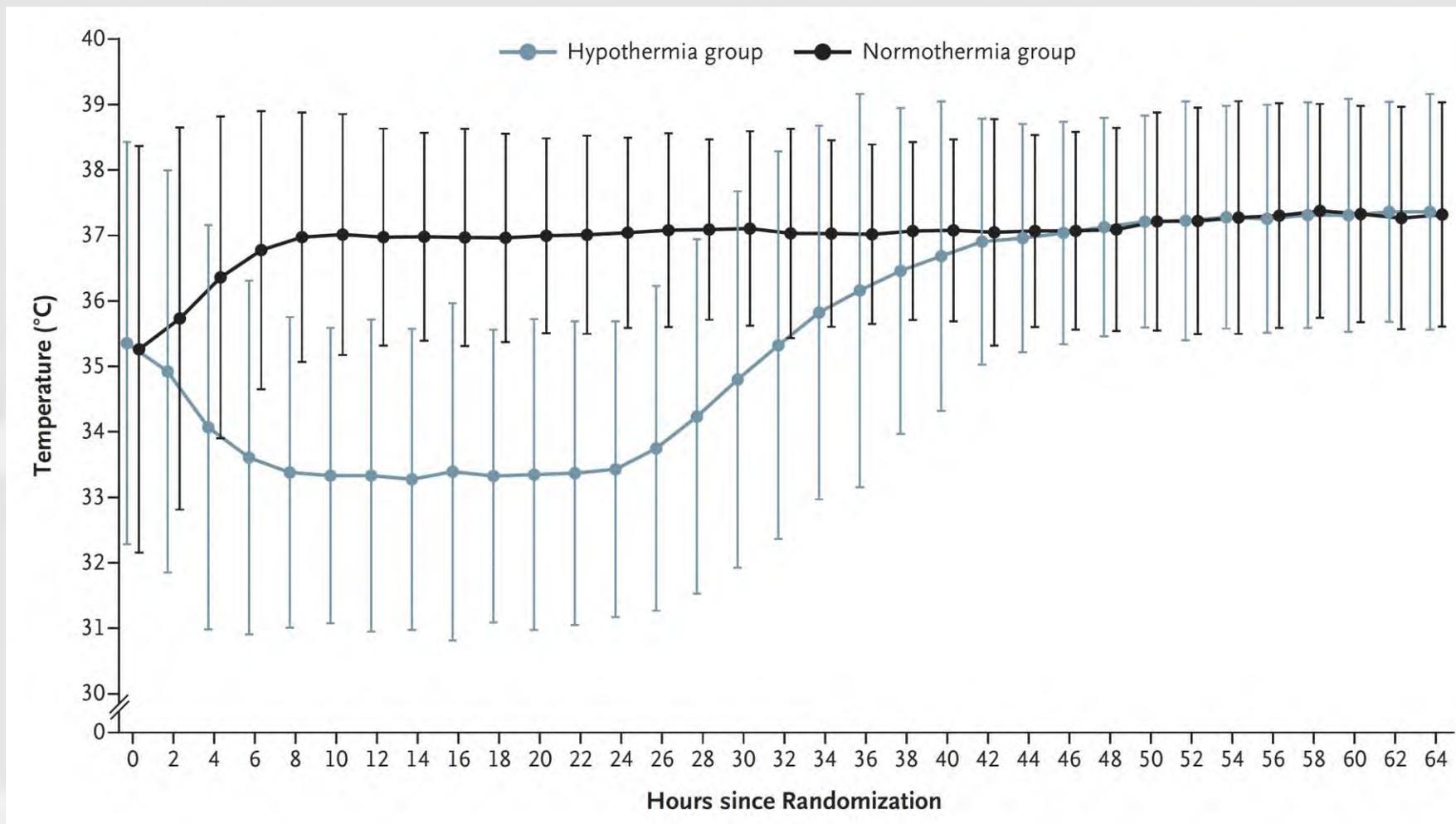
581 Patients  
33°C vs 37°C



# HYPERION 2019 – visade fördel 33°C!



# HYPERION 2019 – visade fördel 33°C!

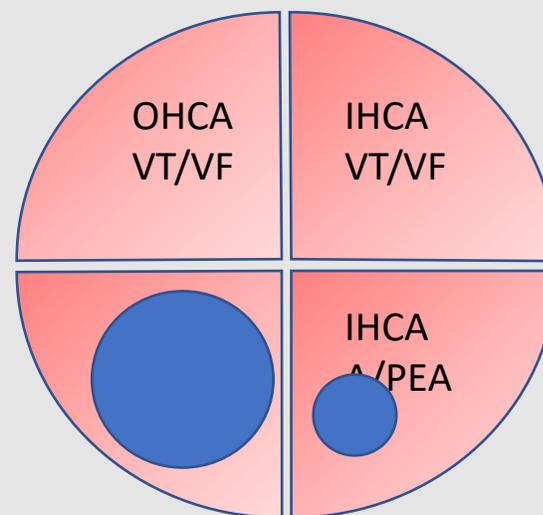
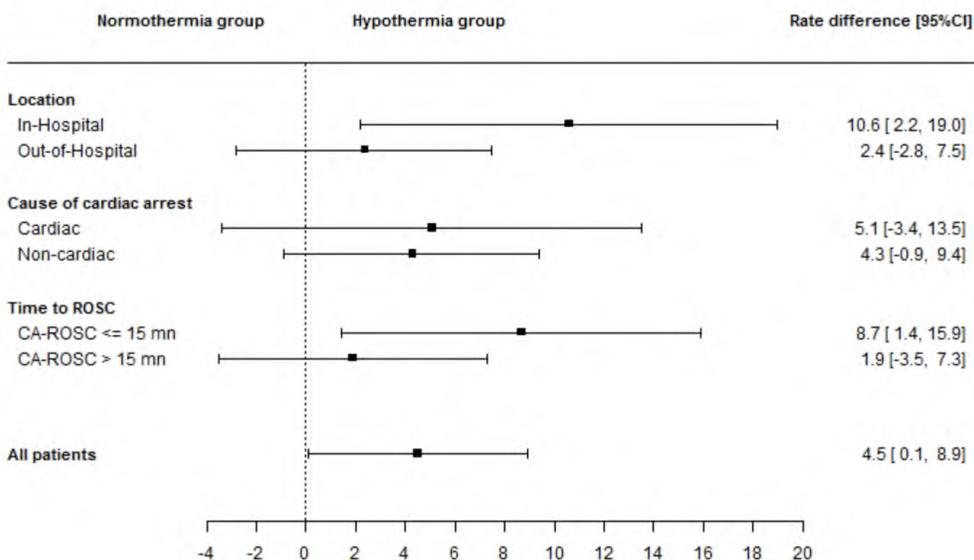


# HYPERION 2019 – var det fördel 33°C??

**Table 2.** Neurologic Outcomes and Hospitalization Characteristics.\*

| Outcome                                 | Hypothermia<br>(N = 284) | Normothermia<br>(N = 297) | Difference<br>or Hazard Ratio<br>(95% CI) |
|---|--------------------------|---------------------------|---|
| CPC score of 1 or 2 on day 90 — no. (%) | 29 (10.2)                | 17 (5.7)                  | 4.5 (0.1 to 8.9)†                         |

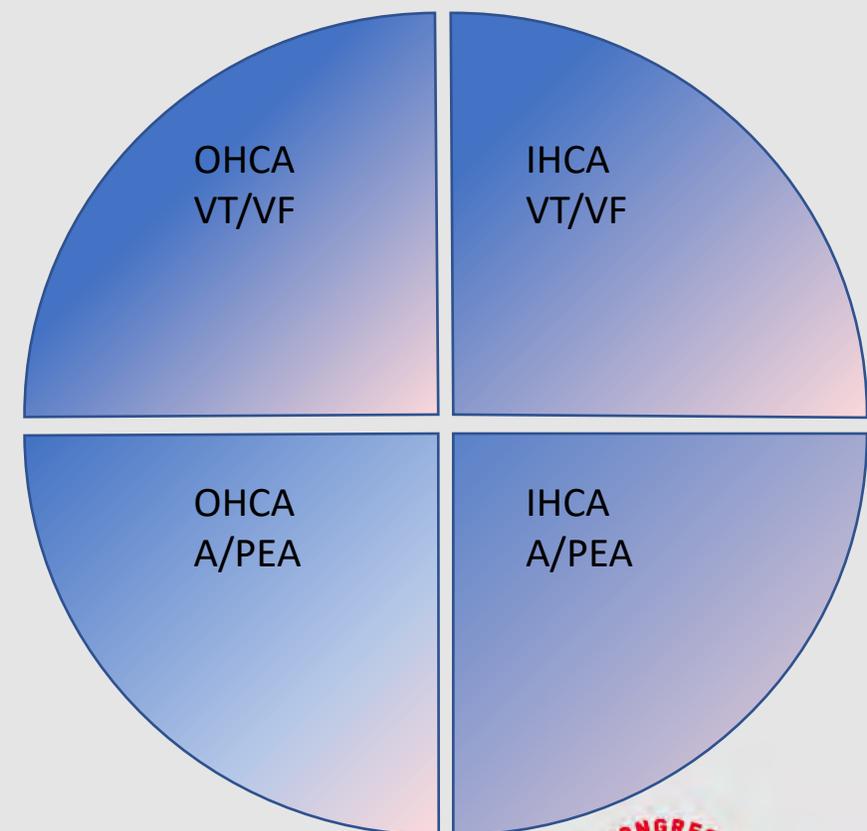
Figure S3: Sub-group analyses



# Guidelines 2020- mars 21

## **Temperature control**

- We recommend targeted temperature management (TTM) for adults after either OHCA or in-hospital cardiac arrest (IHCA) (with any initial rhythm) who remain unresponsive after ROSC.
- Maintain a constant target temperature between 32 °C and 36 °C for at least 24 h.
- Avoid fever for at least 72 h after ROSC in patients who remain in coma.
- Do not use pre-hospital intravenous cold fluids to initiate hypothermia.



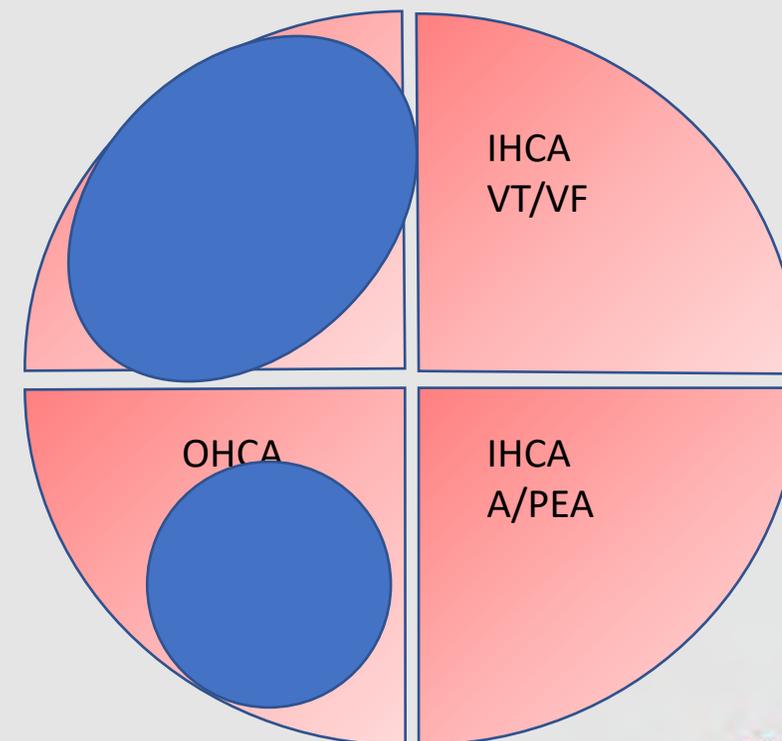
# TTM2 juni 2021

The NEW ENGLAND JOURNAL of MEDICINE

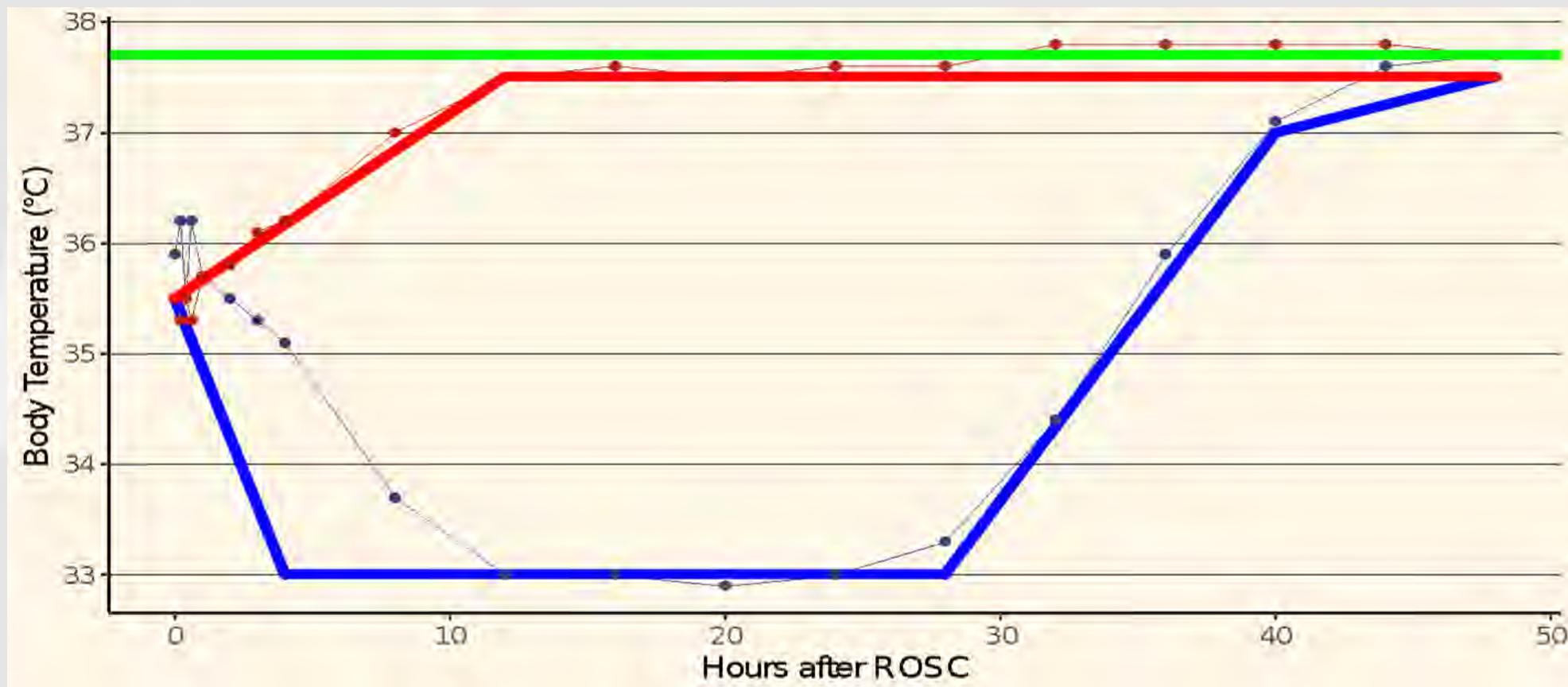
ORIGINAL ARTICLE

## Hypothermia versus Normothermia after Out-of-Hospital Cardiac Arrest

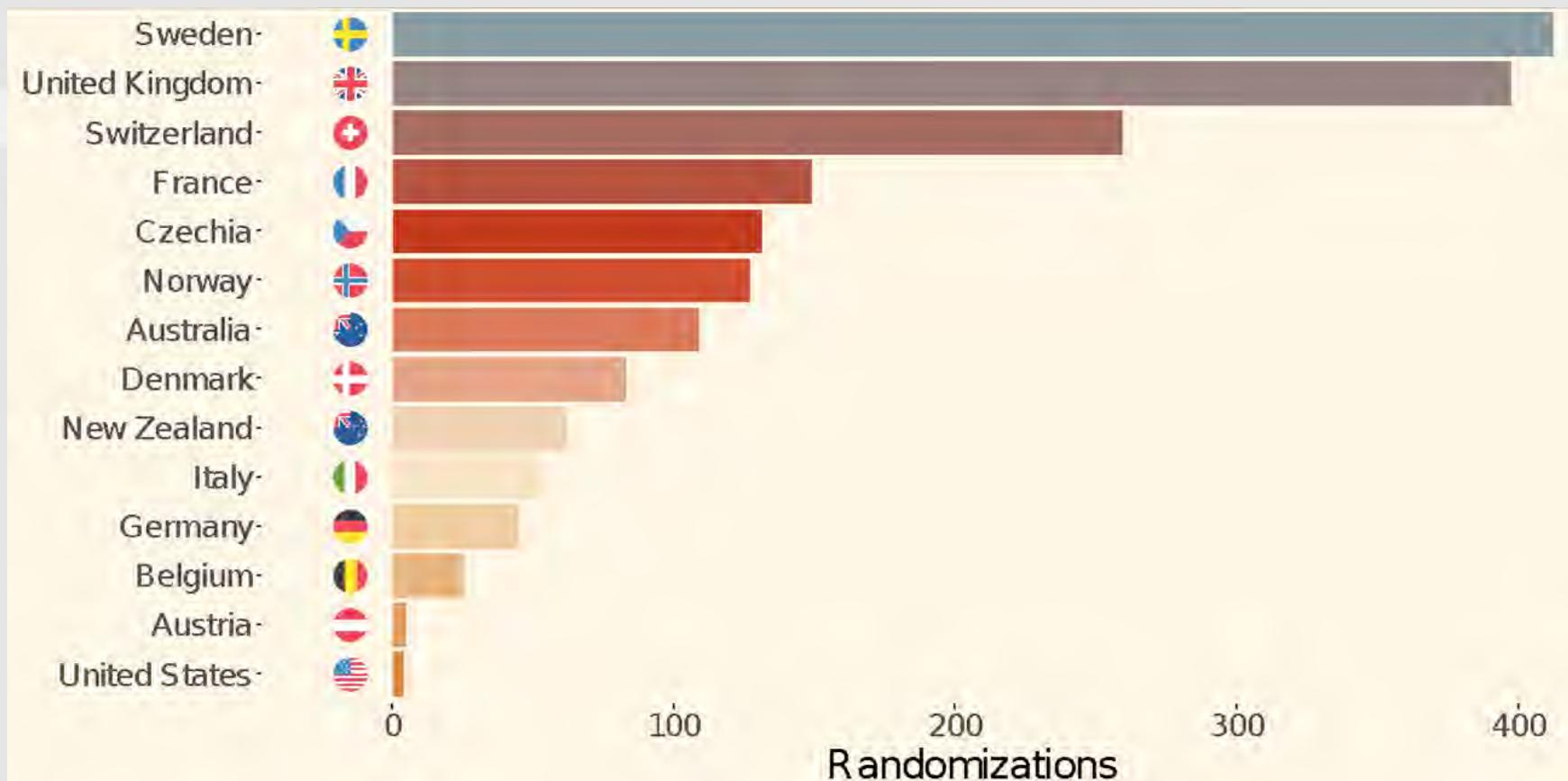
J. Dankiewicz, T. Cronberg, G. Lilja, J.C. Jakobsen, H. Levin, S. Ullén, C. Rylander, M.P. Wise, M. Oddo, A. Cariou, J. Bělohlávek, J. Hovdenes, M. Saxena, H. Kirkegaard, P.J. Young, P. Pelosi, C. Storm, F.S. Taccone, M. Joannidis, C. Callaway, G.M. Eastwood, M.P.G. Morgan, P. Nordberg, D. Erlinge, A.D. Nichol, M.S. Chew, J. Hollenberg, M. Thomas, J. Bewley, K. Sweet, A.M. Grejs, S. Christensen, M. Haenggi, A. Levis, A. Lundin, J. Düring, S. Schmidbauer, T.R. Keeble, G.V. Karamasis, C. Schrag, E. Faessler, O. Smid, M. Otáhal, M. Maggiorini, P.D. Wendel Garcia, P. Jaubert, J.M. Cole, M. Solar, O. Borgquist, C. Leithner, S. Abed-Maillard, L. Navarra, M. Annborn, J. Undén, I. Brunetti, A. Awad, P. McGuigan, R. Bjørkholt Olsen, T. Cassina, P. Vignon, H. Langeland, T. Lange, H. Friberg, and N. Nielsen, for the TTM2 Trial Investigators\*



# TTM2 temperaturprofil



# Länder



# Svenska sjukhus

Sahlgrenska

Skövde

NÄL/Trollhättan

St Göran

Södersjukhuset

Akademiska

Halmstad

Varberg

Karlstad

Linköping

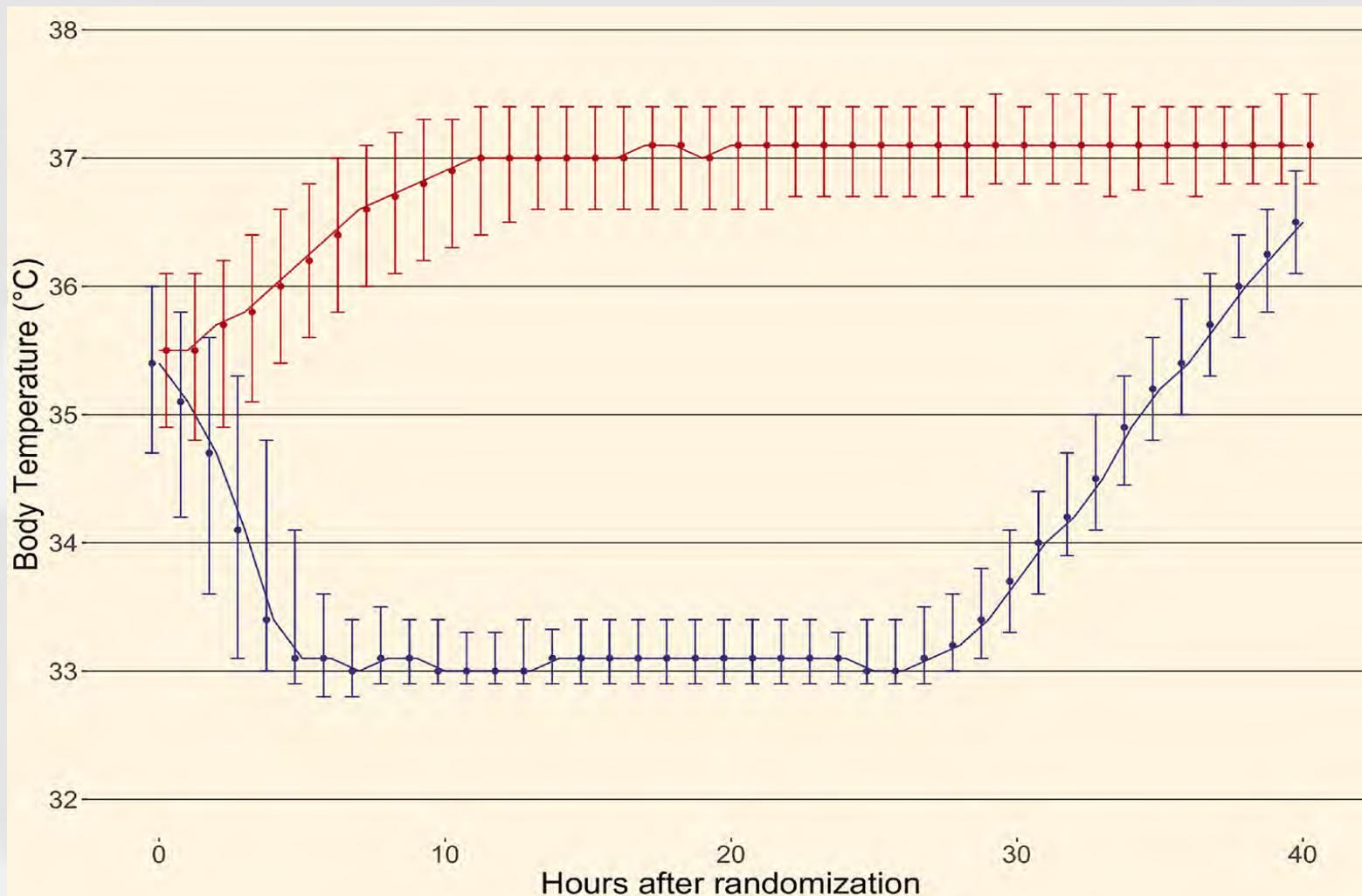
Örebro

SUS Malmö/Lund

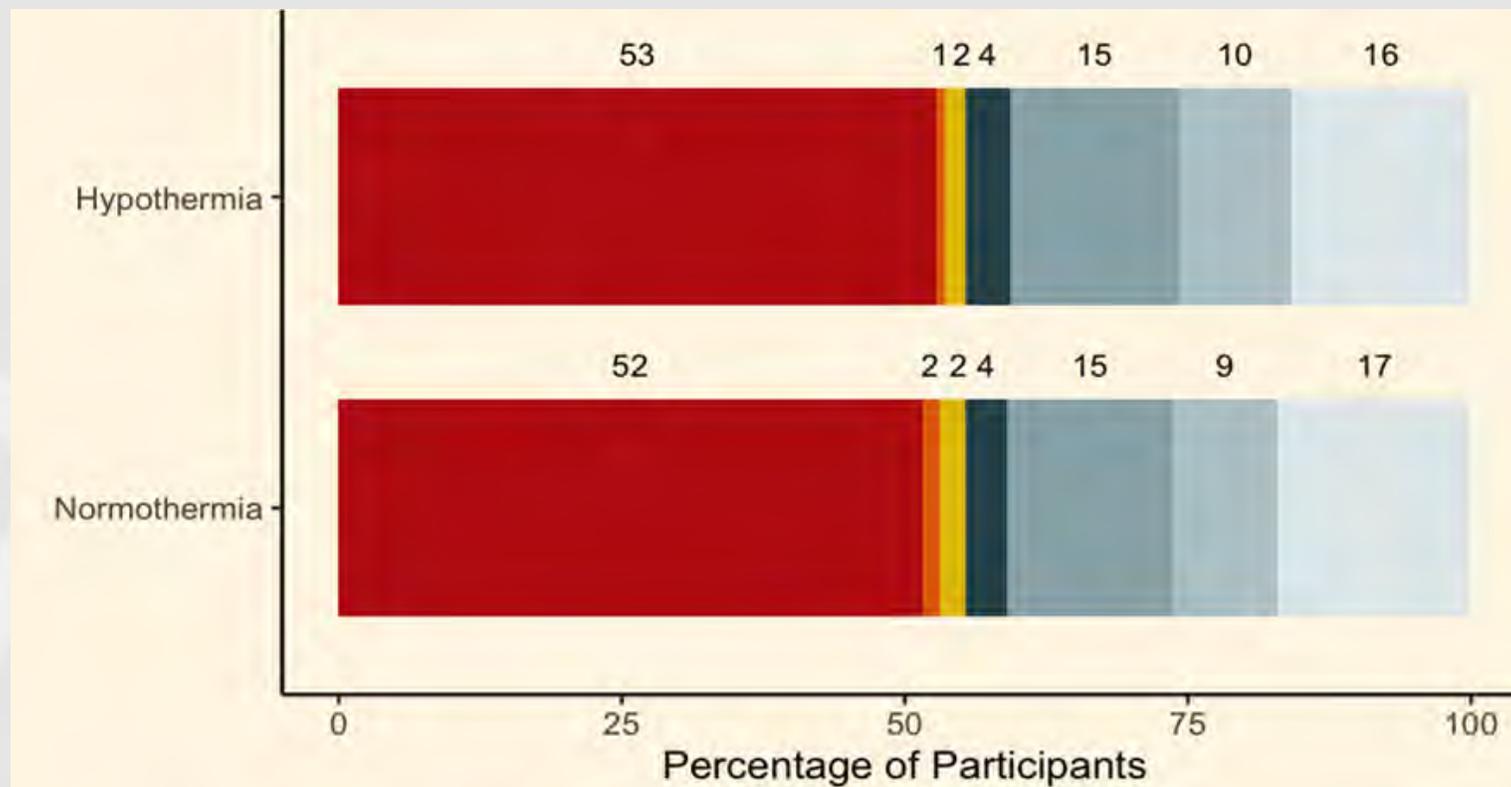
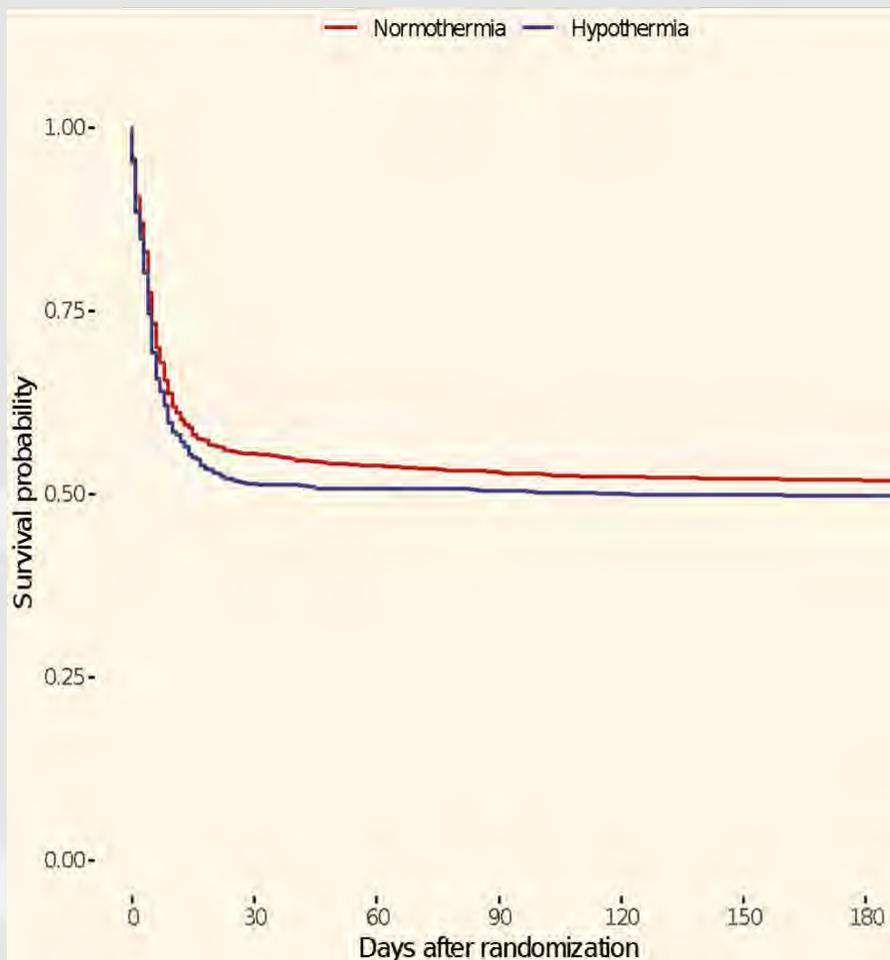
Helsingborg



# TTM2 - temperaturkurva



# Resultaten TTM2



# Biverkningar TTM2

|             |           |           |         |
|-------------|-----------|-----------|---------|
| Pneumoni    | 330 (36%) | 322 (35%) | p=0.75  |
| Sepsis      | 99 (11%)  | 83 (9%)   | p=0.23  |
| Blödning    | 44 (5%)   | 46 (5%)   | p=0.81  |
| Arytmi      | 222 (24%) | 152 (16%) | p<0.001 |
| Hudpåverkan | 10 (<1%)  | 5 (<1%)   | p=0.21  |

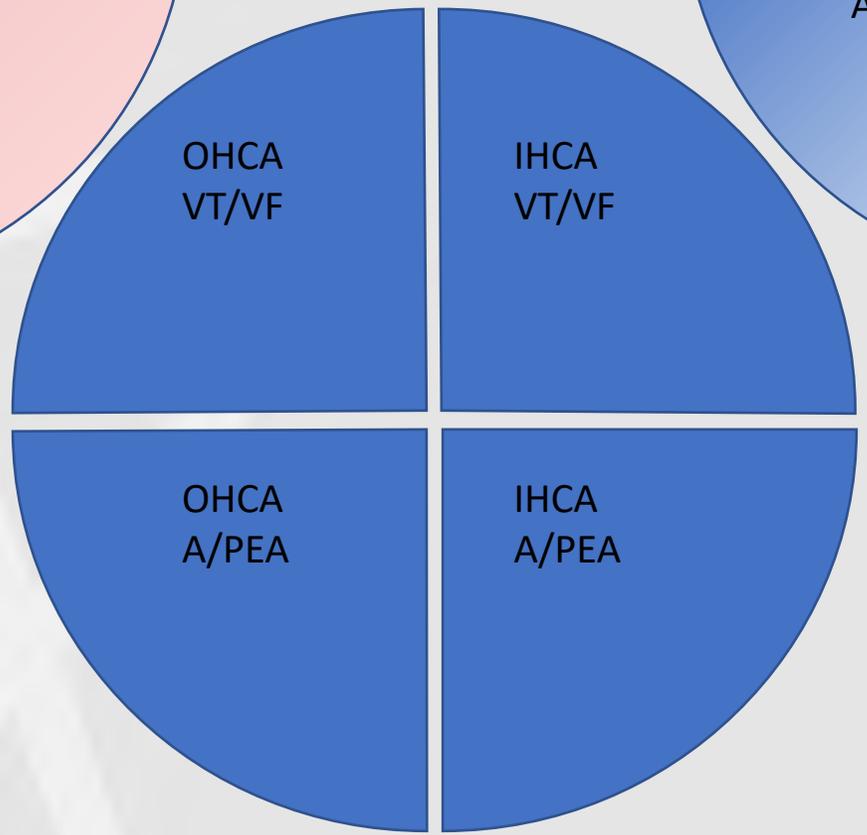
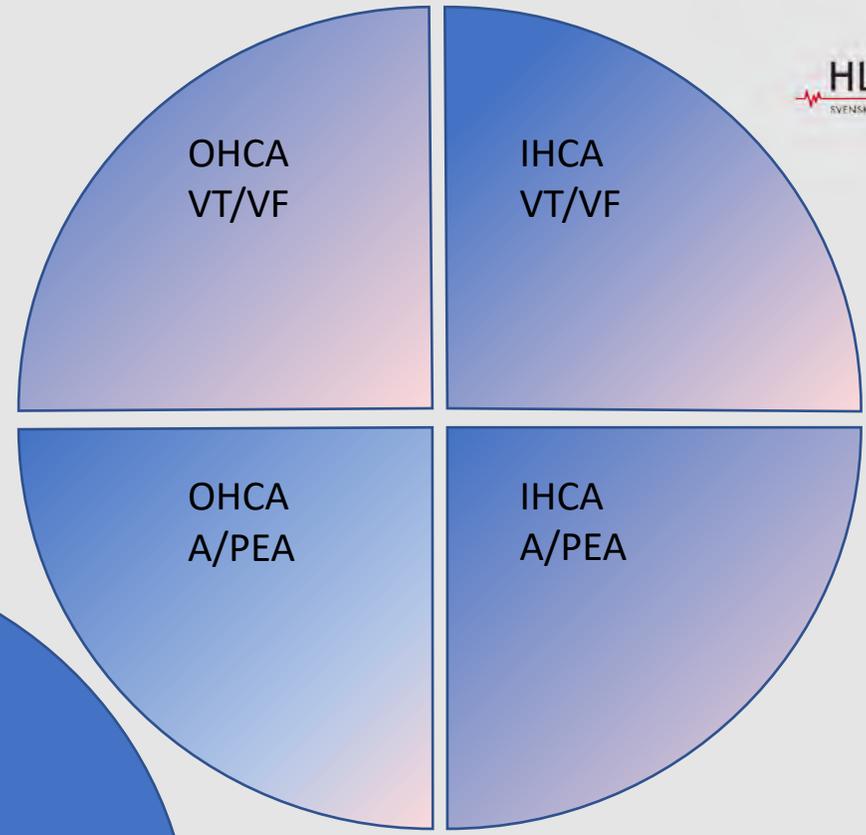
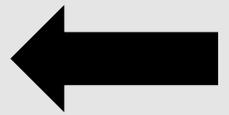
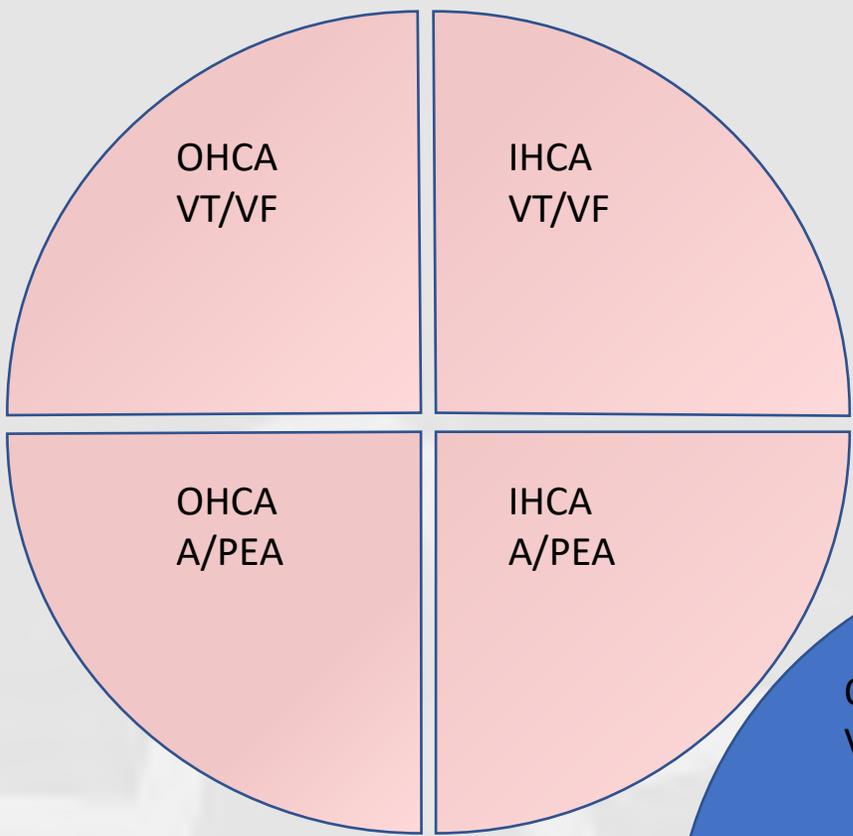
# Systematic reviews and guidelines

**Conclusions:** Mild, moderate, or deep hypothermia may not improve survival or functional outcome after OHCA, as compared to normothermia. Moderate and deep hypothermia were associated with higher incidence of arrhythmia.

(RR: 0.97 (95%CI 0.90, 1.04),  $p = 0.41$ ). TTM at 32–34 °C does not improve neurological outcome as compared to normothermia (RR: 1.17 (95%CI 0.97, 1.41),  $p = 0.10$ ;  $I^2 = 60\%$ ). TTM at 32–34 °C increases the risk of arrhythmias (RR: 1.35 (95%CI 1.16, 1.57),  $p = 0.0001$ ,  $I^2 = 0\%$ ). TTM at 32–34 °C does not improve survival nor neurological outcome after CA and increases the risk of arrhythmias.

**Conclusions:** Among adult patients with cardiac arrest, the use of targeted temperature management at 32–34 °C, when compared to normothermia, did not result in improved outcomes in this meta-analysis. There was no effect of initiating targeted temperature management prior to hospital arrival. These findings warrant an update of international cardiac arrest guidelines.

We suggest actively preventing fever by targeting a temperature  $\leq 37.5$  for those patients who remain comatose after ROSC from cardiac arrest (weak recommendation, low certainty evidence).



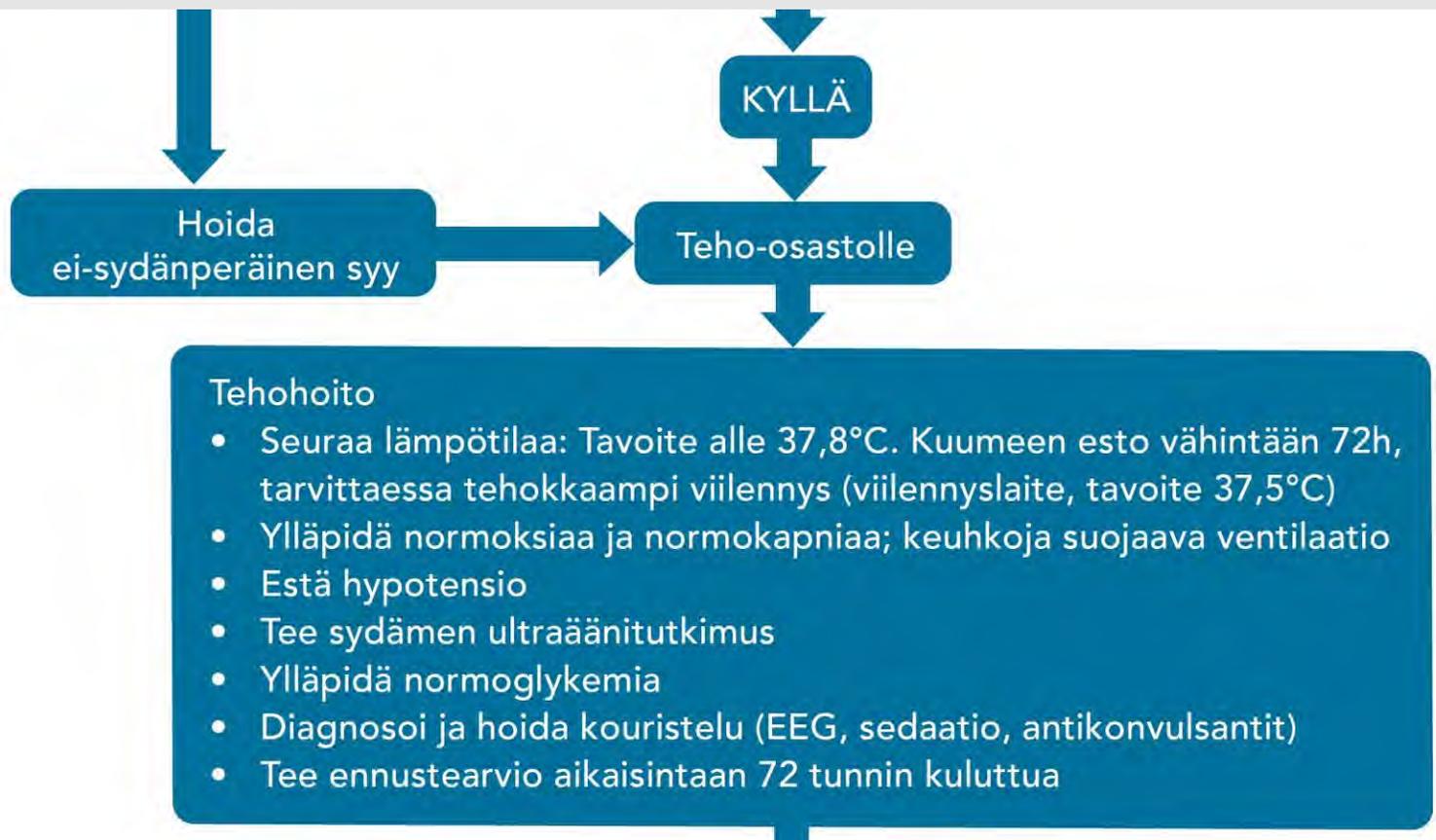
## The American Academy of Neurology affirms the revival of cooling for the revived

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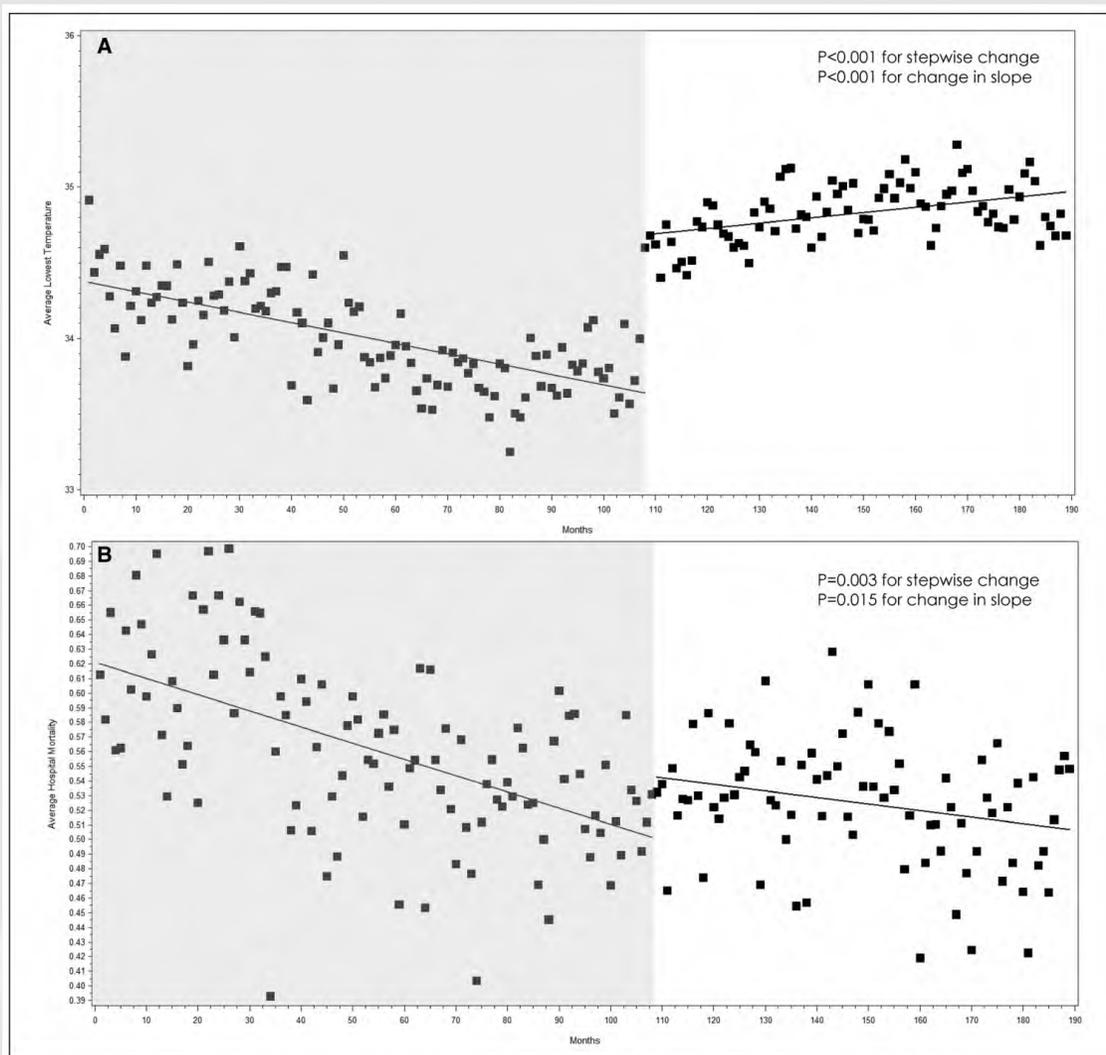
*Neurology*® 2017;88:2076–2077

We concur with the AAN experts that less is not more and cooling should be *harder, better, faster, stronger*, in the sense that neurologists should be hard-liners who embrace cooling as a default mode for nearly all cardiac arrest survivors, making it harder to exclude patients, while using cooling techniques that are the better ones, starting as quickly as possible after ROSC, and that 33°C is stronger than 36°C.



- Monitorera temperaturen och behandla feber  $\geq 37,8^{\circ}\text{C}$
- Om inte konservativa metoder räcker till, använd en apparat för temperaturkontroll och sträva efter  $\leq 37,5^{\circ}\text{C}$
- Fortsätt med detta fram till 72 timmar från hjärtstoppet, om inte patienten vaknar

# Uppdaterade data från Australien



# Men nedkylning då....?



# Chain of survival





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