

# Targeted Temperature Management Following Cardiac Arrest

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# Epidemiology of Cardiac Arrest

- An estimated 356,000 people experience out-of-hospital cardiac arrest(OHCA) annually in the US
- An estimated 292,000 patients experience in-hospital cardiac arrest(IHCA) annually

- 1) Tsao, C. W. Circulation. 2022.
- 2) Holmberg, M. J. Circulation. 2019.



# Out-of-hospital Cardiac Arrest (OHCA)

- Shockable rhythm - 37% of cases
- Survival to hospital discharge
  - VF/pVT – 32%
  - PEA – 9.2%
  - Asystole – 1.8%

- 3) Oving, I. Resuscitation. 2020.
- 4) Zive, D. M. Resuscitation.2018.



# In-hospital Cardiac Arrest (IHCA)

- Shockable rhythm – 24% of cases
- Survival to hospital discharge
  - VF/pVT – 37%
  - PEA – 12%
  - Asystole – 11%

- 5) Meaney, P. A. Crit Care Med. 2010



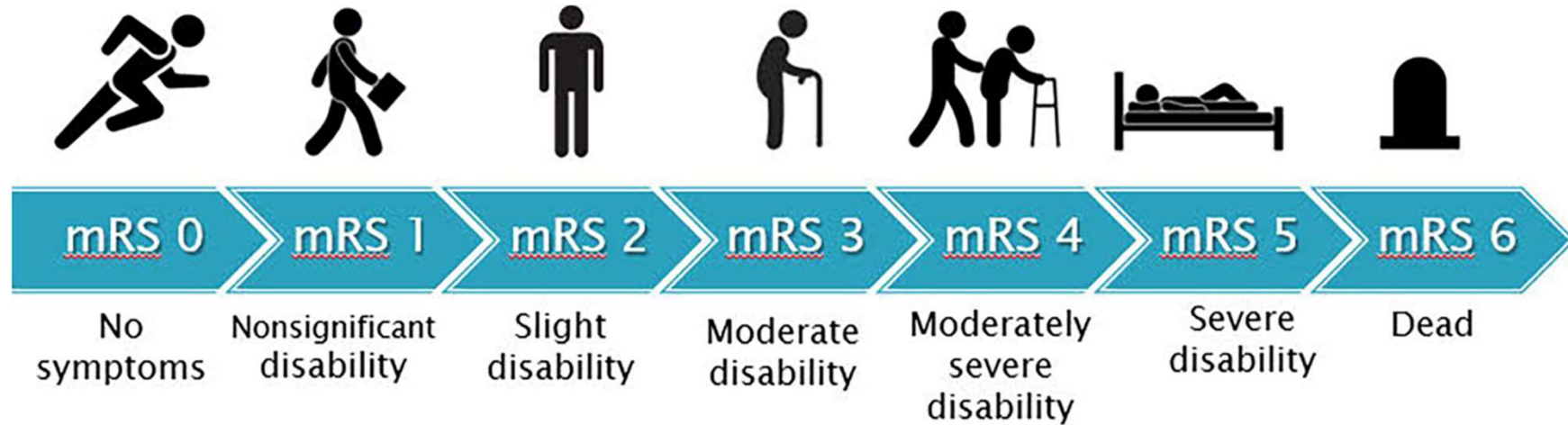
# Mortality after ROSC

- Neurological injury is the most common cause of death after achieving ROSC from cardiac arrest
- 80.5% of survivors discharged with mRS of 1 or 2

- 6) Elmer J, Torres C. Resuscitation. 2016.
- 7) Laver S, Intensive Care Med. 2004.
- 4) Zive, D. M. Resuscitation.2018.



# Modified Rankin Scale



- 13) Saver, J. L. Stroke. 2021.



# Terminology

- Therapeutic hypothermia - temperature goal of 33°C (32°C - 34°C)
- Targeted temperature management - temp goal of 32°C - 36°C
- Targeted normothermia - avoid fever with goal temp < 37.5 - 37.8



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

**TABLE 2.** NEUROLOGIC OUTCOME AND MORTALITY AT SIX MONTHS.

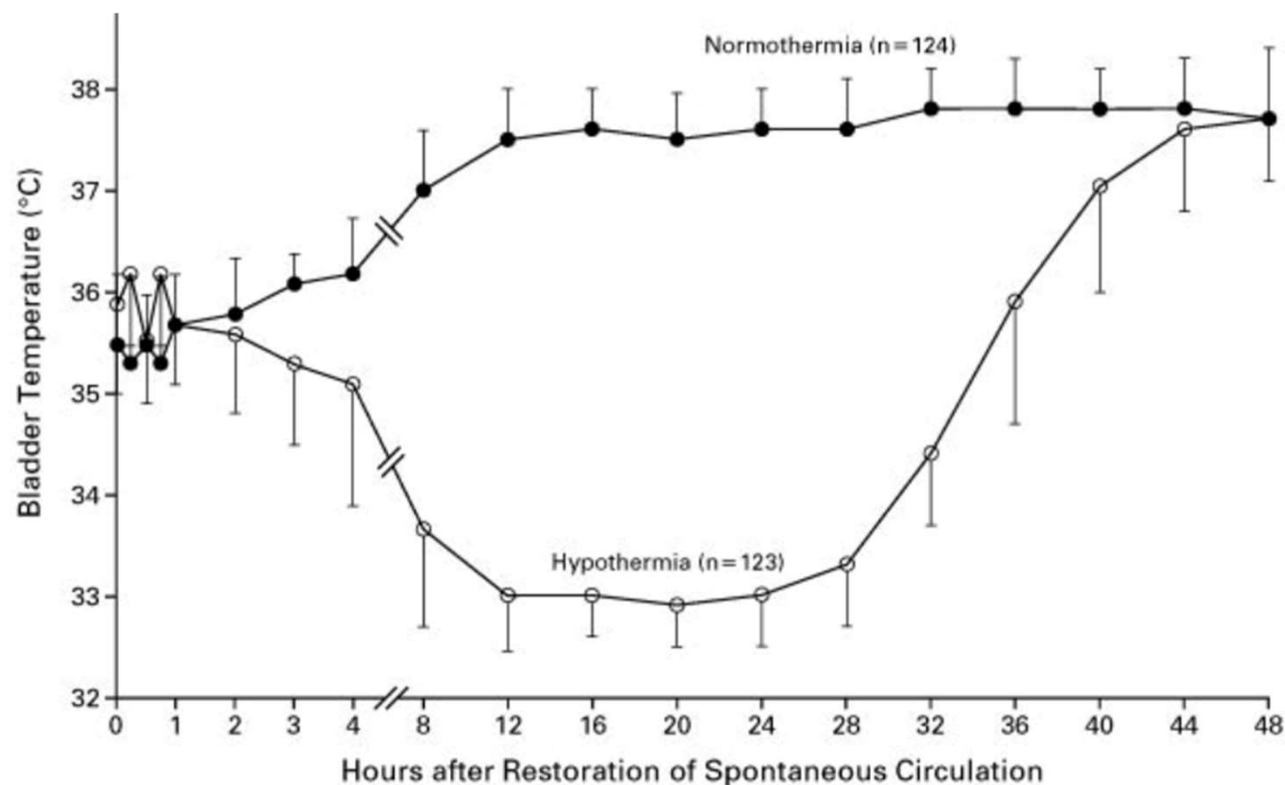
OUTCOME	NORMOTHERMIA	HYPOTHERMIA	RISK RATIO (95% CI)*	P VALUE†
	no./total no. (%)			
Favorable neurologic outcome‡	54/137 (39)	75/136 (55)	1.40 (1.08–1.81)	0.009
Death	76/138 (55)	56/137 (41)	0.74 (0.58–0.95)	0.02

- 14) The Hypothermia after Cardiac Arrest Study Group. N Engl J Med. 2002.





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



- 14) The Hypothermia after Cardiac Arrest Study Group. N Engl J Med. 2002



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

**TABLE 5. OUTCOME OF PATIENTS AT DISCHARGE FROM THE HOSPITAL.**

OUTCOME*	HYPOTHERMIA (N=43)	NORMOTHERMIA (N=34)
	number of patients	
Normal or minimal disability (able to care for self, discharged directly to home)	15	7
Moderate disability (discharged to a rehabilitation facility)	6	2
Severe disability, awake but completely dependent (discharged to a long-term nursing facility)	0	1
Severe disability, unconscious (discharged to a long-term nursing facility)	0	1
Death	22	23

- 15) Bernard SA. N Engl J Med. 2002.



# Updates to the Standard of Care

- International Liaison Committee on Resuscitation (ILCOR)
  - 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

- 16) Nolan, J. P. Circulation. 2003.



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

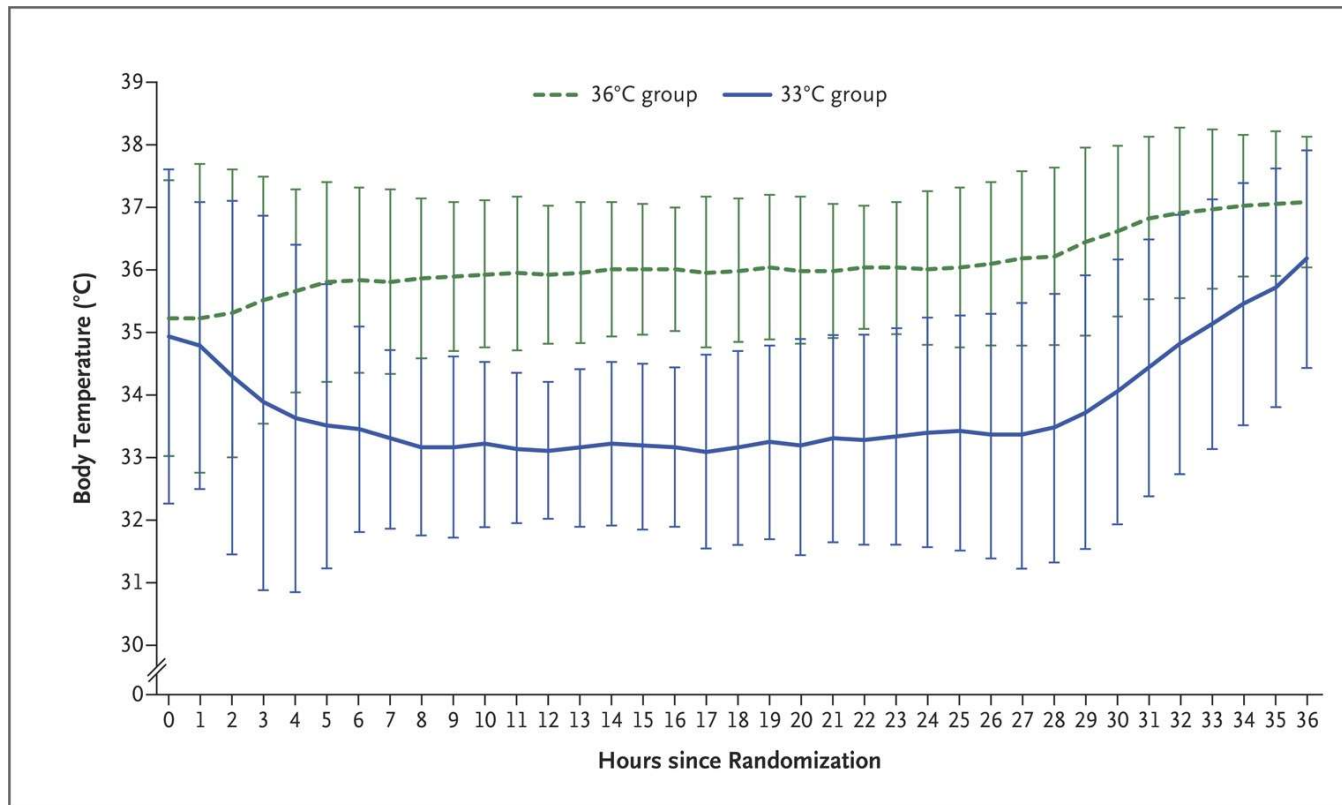
**Table 2. Outcomes.**

Outcome	33°C Group	36°C Group	Hazard Ratio or Risk Ratio (95% CI)*	P Value
	<i>no./total no. (%)</i>			
Primary outcome: deaths at end of trial	235/473 (50)	225/466 (48)	1.06 (0.89–1.28)	0.51
Secondary outcomes				
Neurologic function at follow-up†				
CPC of 3–5	251/469 (54)	242/464 (52)	1.02 (0.88–1.16)	0.78
Modified Rankin scale score of 4–6	245/469 (52)	239/464 (52)	1.01 (0.89–1.14)	0.87
Deaths at 180 days	226/473 (48)	220/466 (47)	1.01 (0.87–1.15)	0.92

- 17) Nielsen, N. N Engl J Med. 2013.



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



- 17) Nielsen, N. N Engl J Med. 2013



# Effects of TTM 1

- Use of therapeutic hypothermia in OHCA dropped 18% after TTM-1 was published, but most notably in non-shockable rhythm

- 18) Bradley SM. JAMA. 2018.

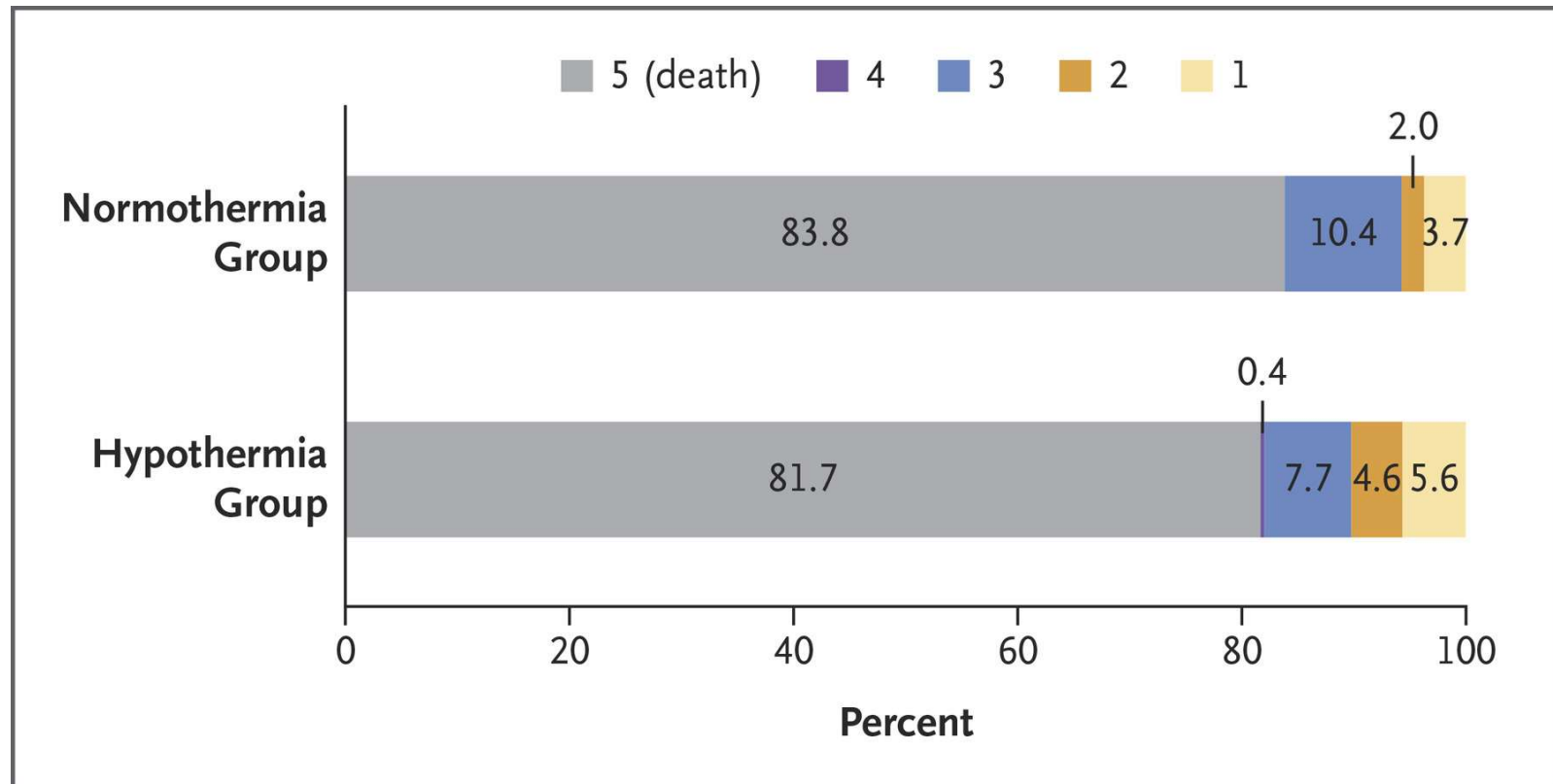


# AHA 2015 Guidelines

- Recommended TTM for adults with out-of-hospital cardiac arrest with an initial shockable rhythm
  - Similar suggestions are made for out-of-hospital cardiac arrest with a non-shockable rhythm and in-hospital cardiac arrest
  - Recommend against pre-hospital cooling with rapid infusion of large volumes of cold intravenous fluid



# Targeted Temperature Management for Cardiac Arrest with Non-shockable Rhythm



- 20) Lascarrou JB. NEJM. 2019.



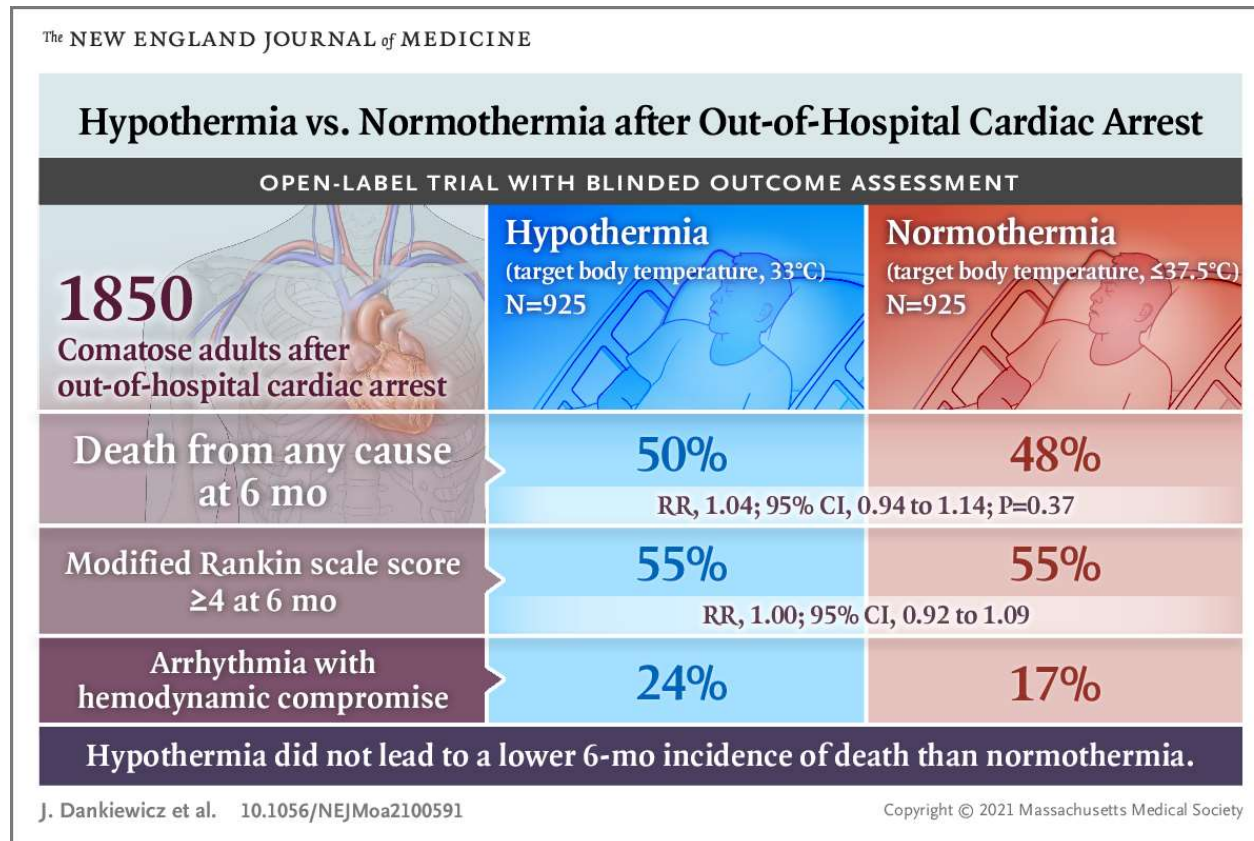


# AHA 2020 Guidelines

- If ROSC achieved and patient not following commands, initiate TTM as soon as possible
- 32°C – 36°C for at least 24 hours for cardiac arrest associated with all rhythms in both in-hospital and out-of-hospital cardiac arrest



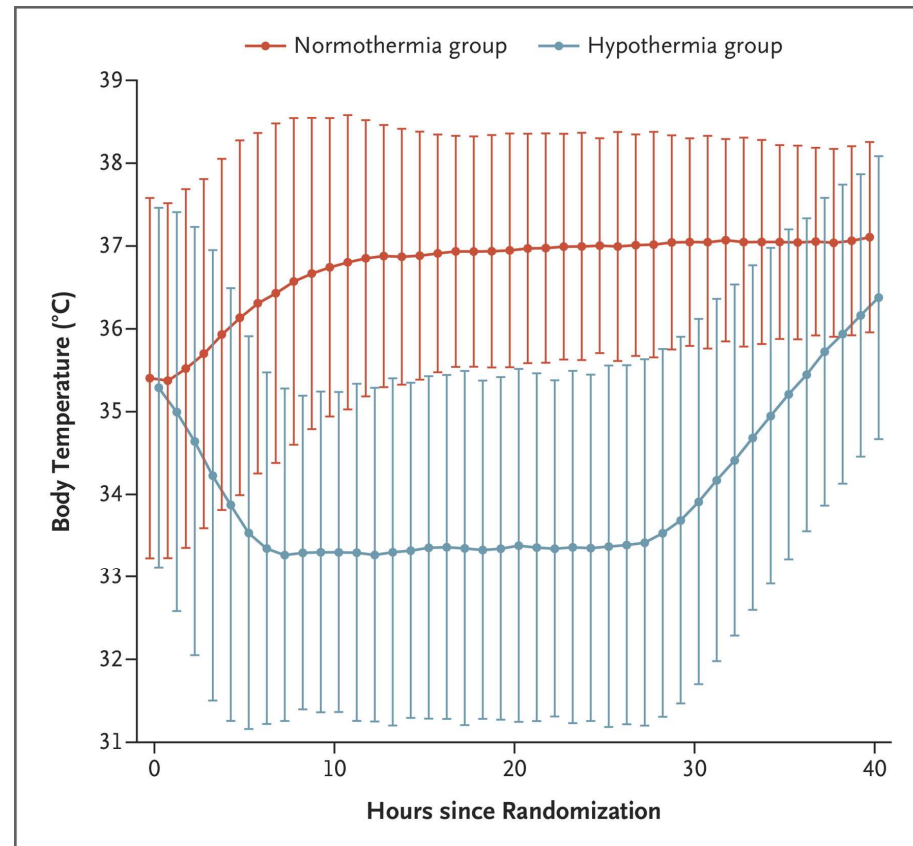
# Hypothermia versus Normothermia after Out-of-Hospital Cardiac Arrest



- 22) Dankiewicz J. NEJM. 2021



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



- 22) Dankiewicz J. NEJM. 2021



# Adverse Effects of Therapeutic Hypothermia

- Based on systematic review no significantly increased risk of:
  - Bradycardia
  - Ventricular dysrhythmia
  - Pneumonia
  - Thrombocytopenia
  - Coagulopathy
  - Hypokalemia
  - Hypomagnesemia
  - Reduced hepatic drug metabolism

- 23) Karcioglu, O. Am. J. Emerg. Med. 2018.



# ILCOR Guidelines 2021

- TTM in adult cardiac arrest: systematic review and meta-analysis
  - 6 trials of acceptable quality and included
  - 32°C – 34°C vs normothermia (often included active cooling)
  - No difference in survival or favorable neurological outcome
- Pre-hospital cooling vs no pre-hospital cooling
  - 10 trials, no difference in survival or favorable neurological outcome at discharge



# ILCOR CoSTR 2021

- CoSTR Publication Oct 2021
  - Recommend against pre-hospital cooling
  - Recommend preventing fever by targeting temp  $\leq 37.5^{\circ}\text{C}$  x 72 hours
  - Recommend continuous temperature monitoring technique
  - Uncertain if sub-populations would benefit from targeting temp of  $32^{\circ}\text{C} - 34^{\circ}\text{C}$

- 25) Wyckoff T. International Consensus on Cardiopulmonary Resuscitation and Emergency Care Science with Treatment Recommendations. 2022.
- 26) Nolan, J. P. Resuscitation. 2022.



# ILCOR CoSTR Terminology

- Temperature control with hypothermia:
  - Active temperature control with the target temperature below the normal range
  - Temperature control with normothermia: Active temperature control with the target temperature in the normal range
  - Temperature control with fever prevention: Monitoring temperature and actively preventing and treating temperature above the normal range
  - No temperature control: No protocolized active temperature control strategy



# ILCOR CoSTR Knowledge Gaps 2021

- CoSTR Publication
  - Effect of temperature control after extracorporeal resuscitation
  - Effect of temperature control after in-hospital cardiac arrest (IHCA)
  - Is there a treatment window at which temperature control is effective
  - If so is there a mechanism for achieving hypothermic temperatures in this window
  - Is duration of temperature control important

- 26) Nolan, J. P. Resuscitation. 2022.





# The Influence of Cooling Duration on Efficacy in Cardiac Arrest Patients

- Multicenter, randomized trial to assess duration effect of induced hypothermia post out-of-hospital cardiac arrest
  - Targeted for 1800 patients
  - OHCA with shockable or non-shockable rhythm
  - Anywhere from 6 to 72 hours of cooling at 33°C
  - Primary endpoint is mRankin score at 90 days
- Results pending



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- 3) Oving, I., de Graaf, C., Karlsson, L., Jonsson, M., Kramer-Johansen, J., Berglund, E., ... & Blom, M. T. (2020). Occurrence of shockable rhythm in out-of-hospital cardiac arrest over time: A report from the COSTA group. *Resuscitation*, 151, 67-74.
- 4) Zive, D. M., Schmicker, R., Daya, M., Kudenchuk, P., Nichol, G., Rittenberger, J. C., ... & ROC Investigators. (2018). Survival and variability over time from out of hospital cardiac arrest across large geographically diverse communities participating in the Resuscitation Outcomes Consortium. *Resuscitation*, 131, 74-82.
- 5) Meaney, P. A., Nadkarni, V. M., Kern, K. B., Indik, J. H., Halperin, H. R., & Berg, R. A. (2010). Rhythms and outcomes of adult in-hospital cardiac arrest. *Critical care medicine*, 38(1), 101-108.



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- 7) Laver S, Farrow C, Turner D, Nolan J. Mode of death after admission to an intensive care unit following cardiac arrest. *Intensive Care Med*. 2004 Nov;30(11):2126-8
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- 13) Bradley SM, Liu W, McNally B, et al. Temporal Trends in the Use of Therapeutic Hypothermia for Out-of-Hospital Cardiac Arrest. *JAMA Netw Open*. 2018;1(7):e184511. doi:10.1001/jamanetworkopen.2018.4511.
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