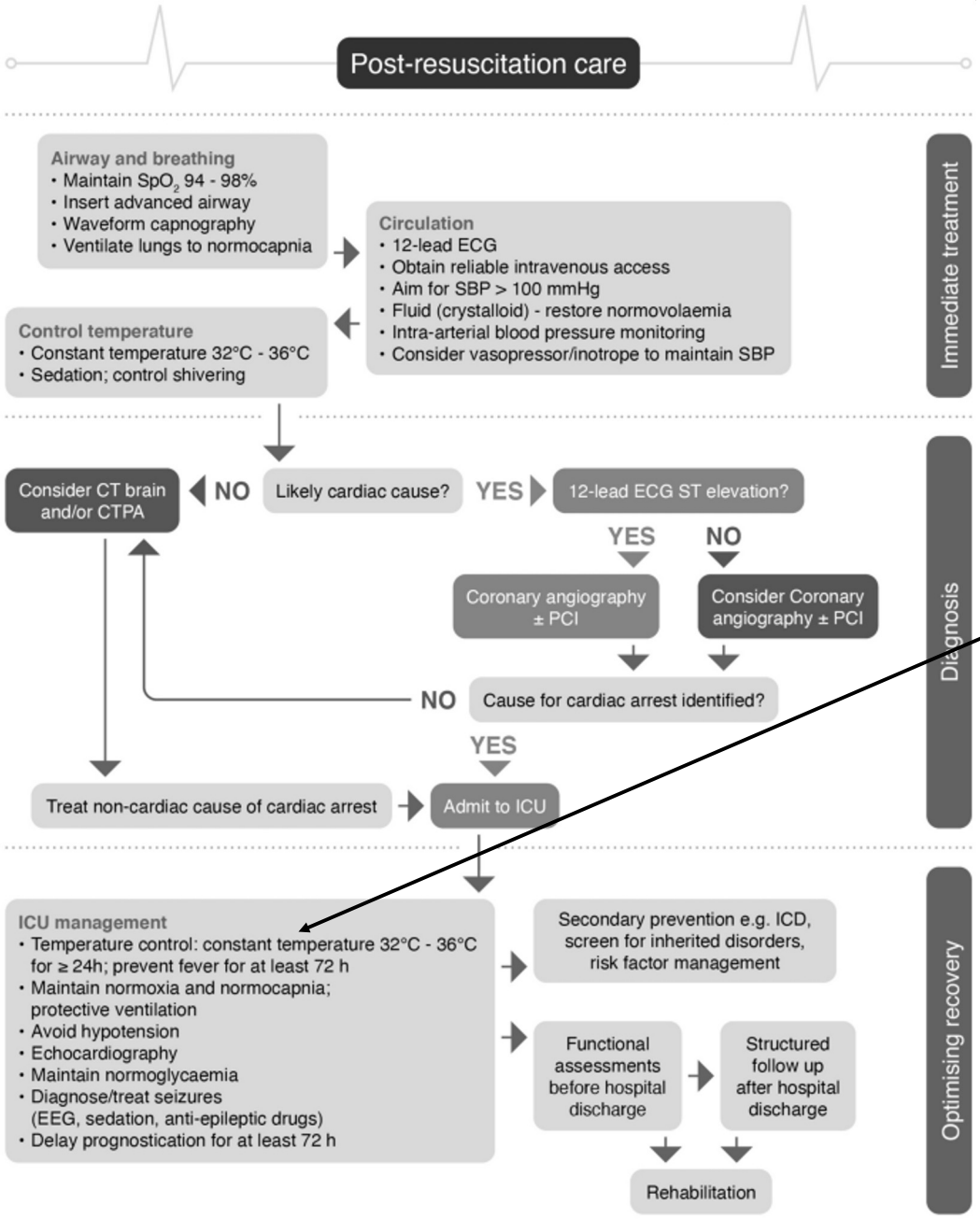
A Closer Look

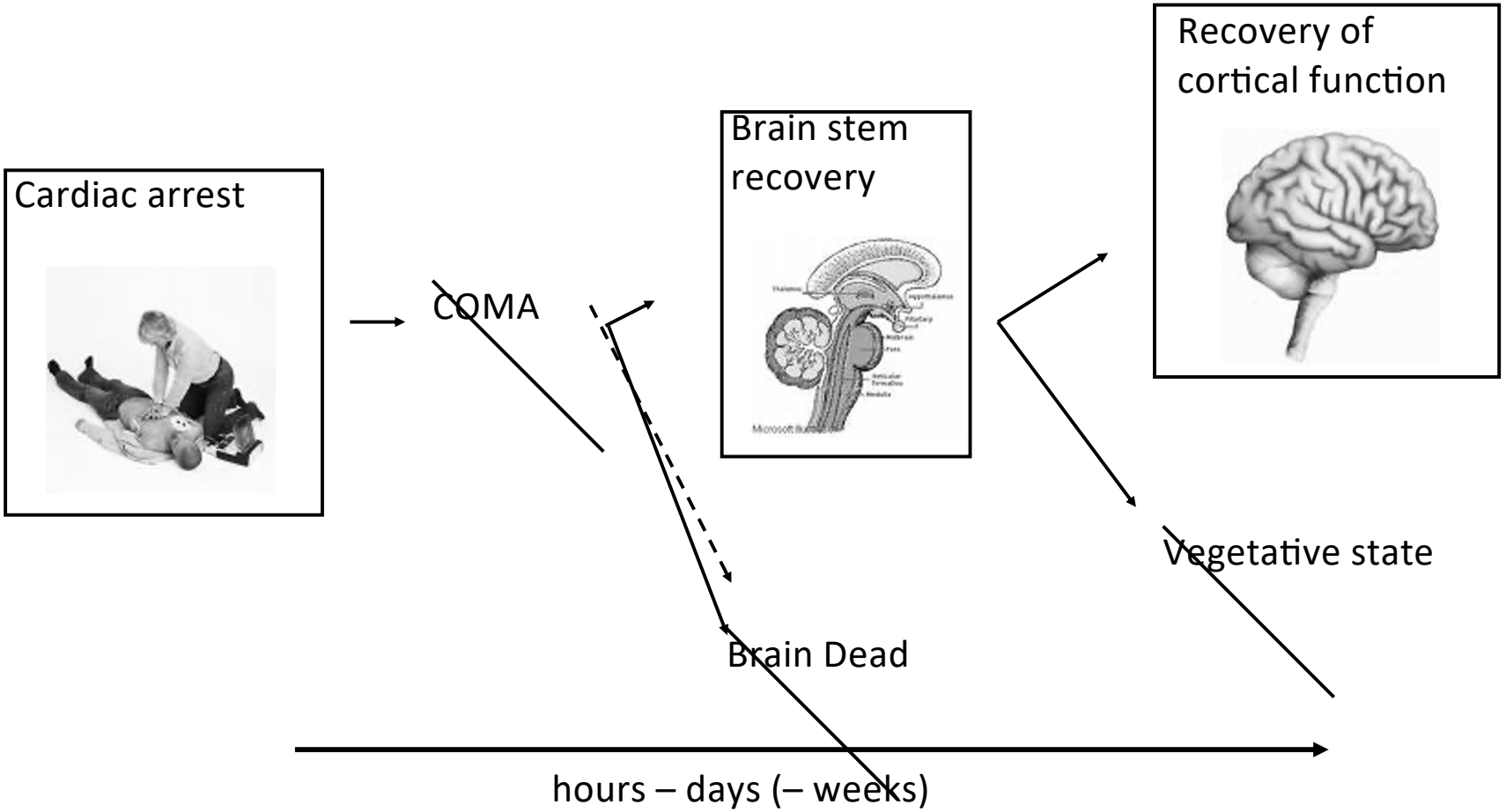
1. Statistics : 300,000 annually
2. The Challenge of ICU & Survival Rates: only 30-55% will be discharged alive.
3. Neurological Outcomes: standard scales (CPC, GOS, mRS), only 10% experiencing severe disability.



ICU MANAGEMENT

Natural course of neurological recovery following cardiac arrest

Patil KD et al. Circ Res. 2015 Jun 5;116(12):2041-9



The “Chain“ of Survival

Pekins GD et al Resuscitation 95 (2015): 81-99

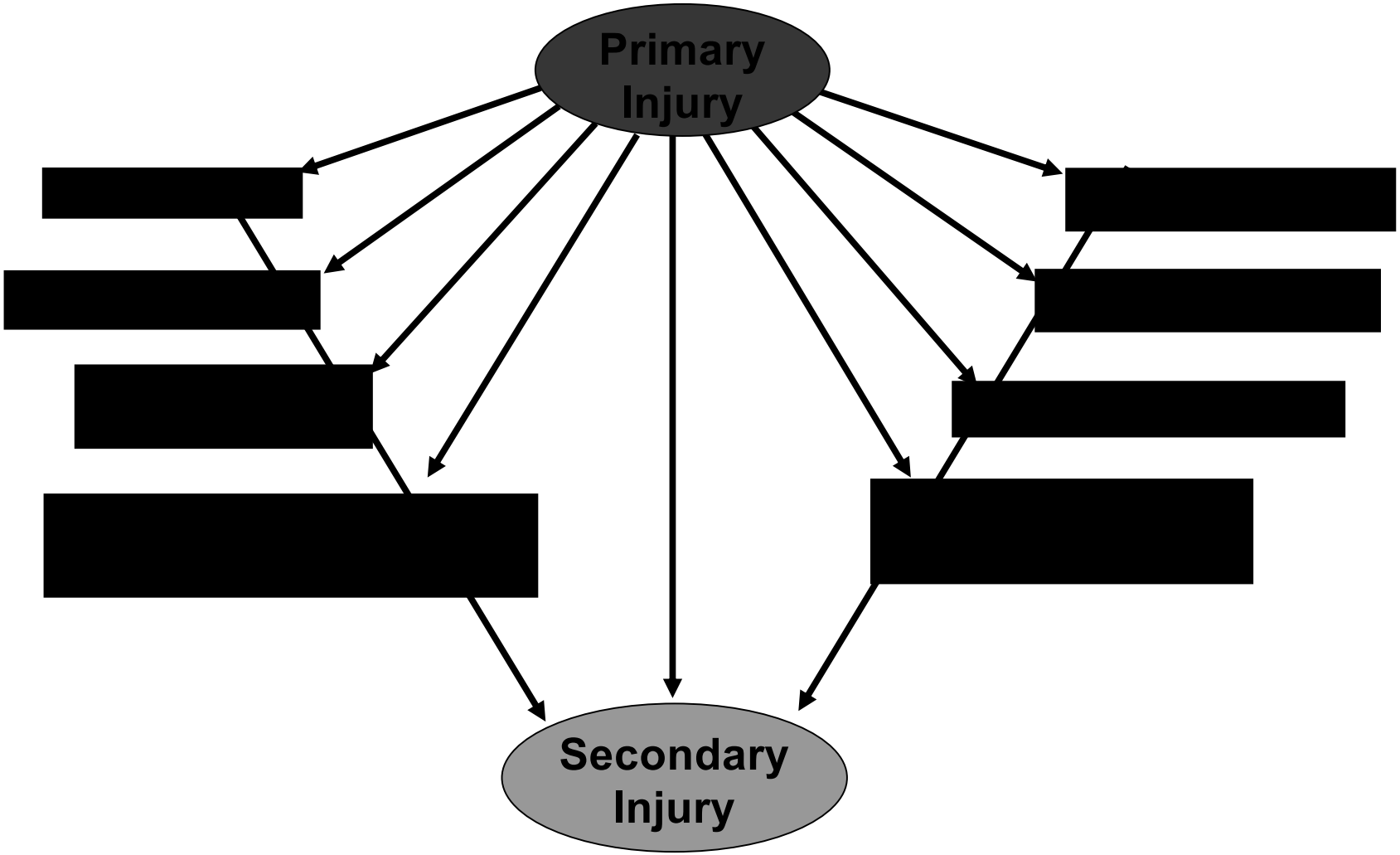
Sutherasan Y et al. Best Pract Res Clin Anaesthesiol. 2015 Dec;29(4):411-2

The current challenges of cardiac arrest: Post cardiac arrest management

Mild to Moderate Hypothermia in Out-of-Hospital Cardiac Arrest

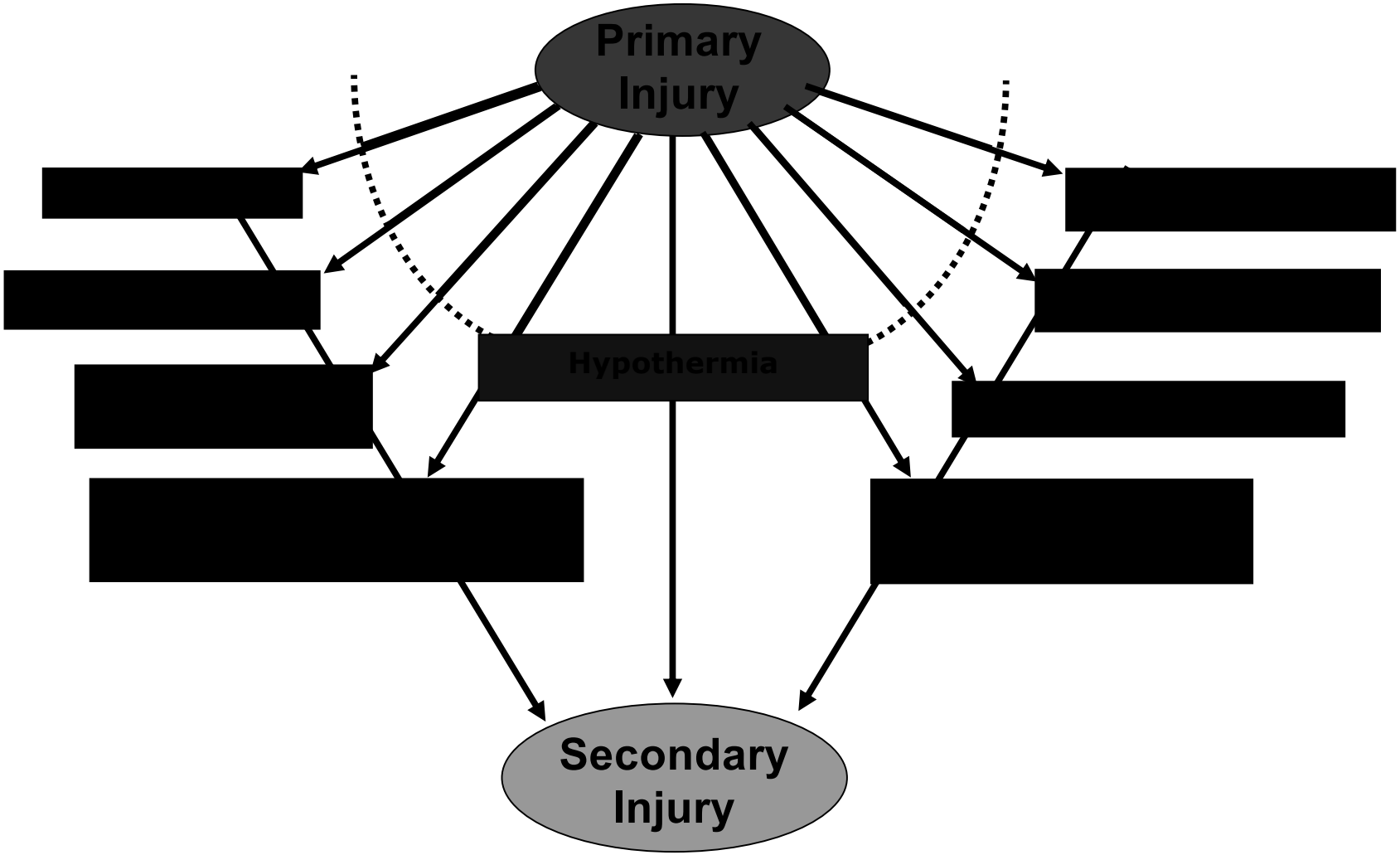
Effects of Hypothermia on Brain Damage

Fritz HG et al. Exper Toxic Pathol 2004; 56:91-102

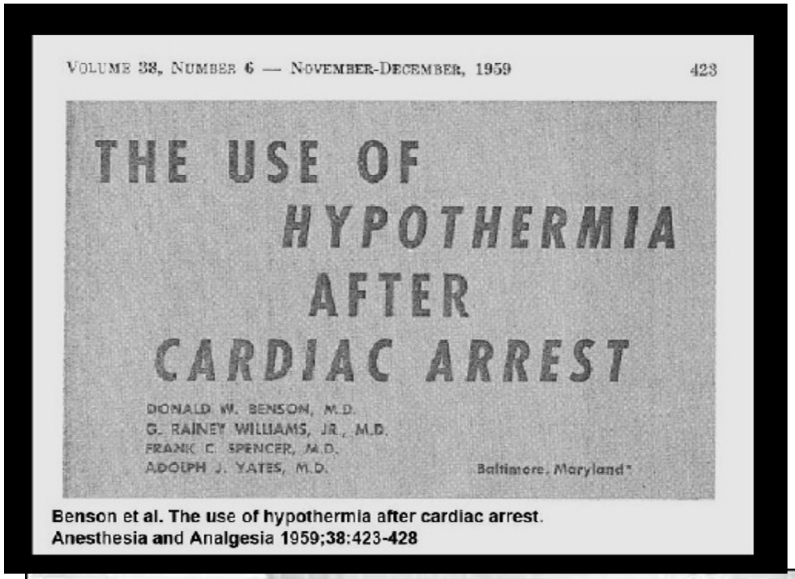


Effects of Hypothermia on Brain Damage

Fritz HG et al. Exper Toxic Pathol 2004; 56:91-102



Background

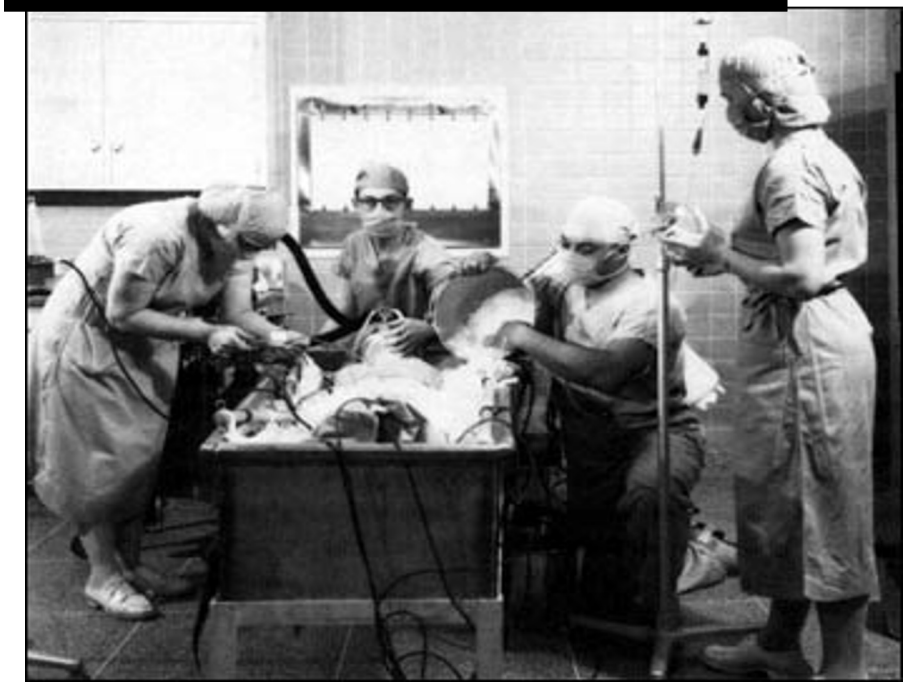


VOLUME 38, NUMBER 6 — NOVEMBER-DECEMBER, 1959 423

THE USE OF HYPOTHERMIA AFTER CARDIAC ARREST

DONALD W. BENSON, M.D.
G. RAINEY WILLIAMS, JR., M.D.
FRANK C. SPENCER, M.D.
ADOLPH J. YATES, M.D. Baltimore, Maryland*

Benson et al. The use of hypothermia after cardiac arrest. Anesthesia and Analgesia 1959;38:423-428



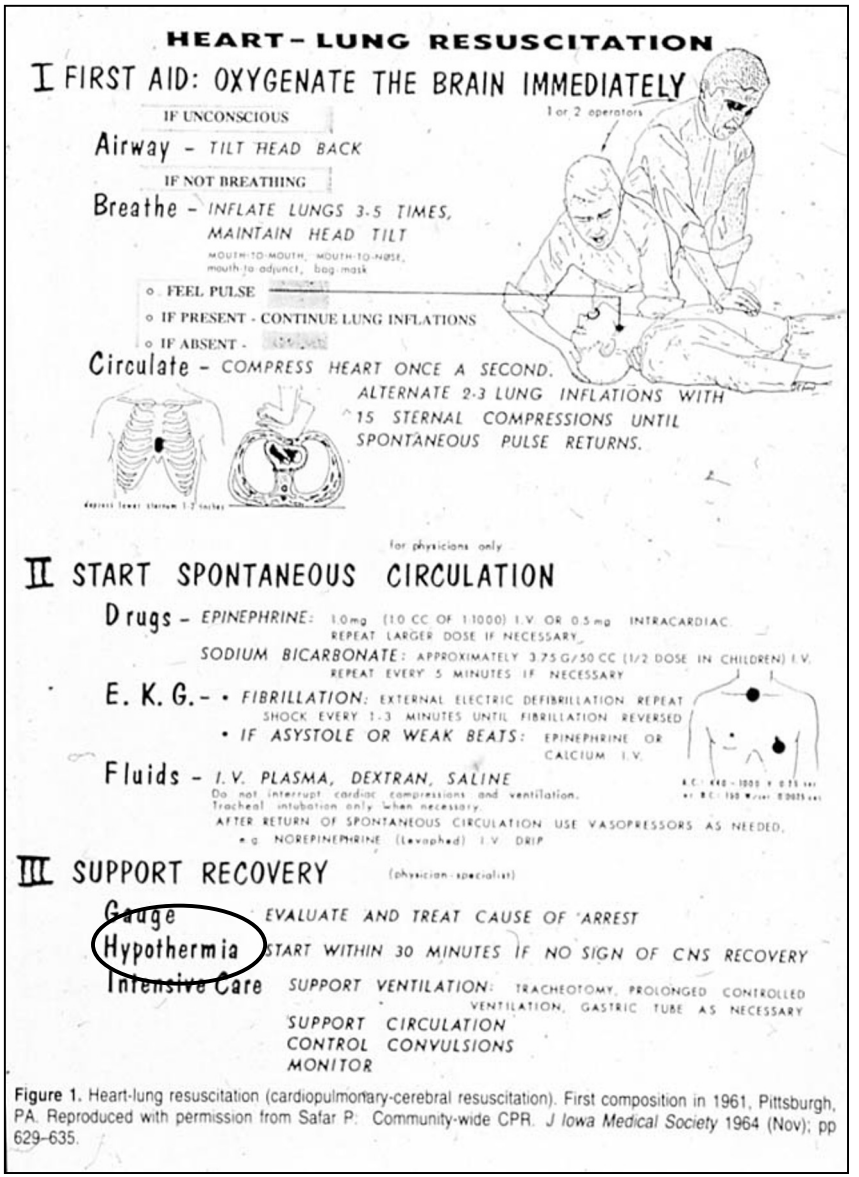
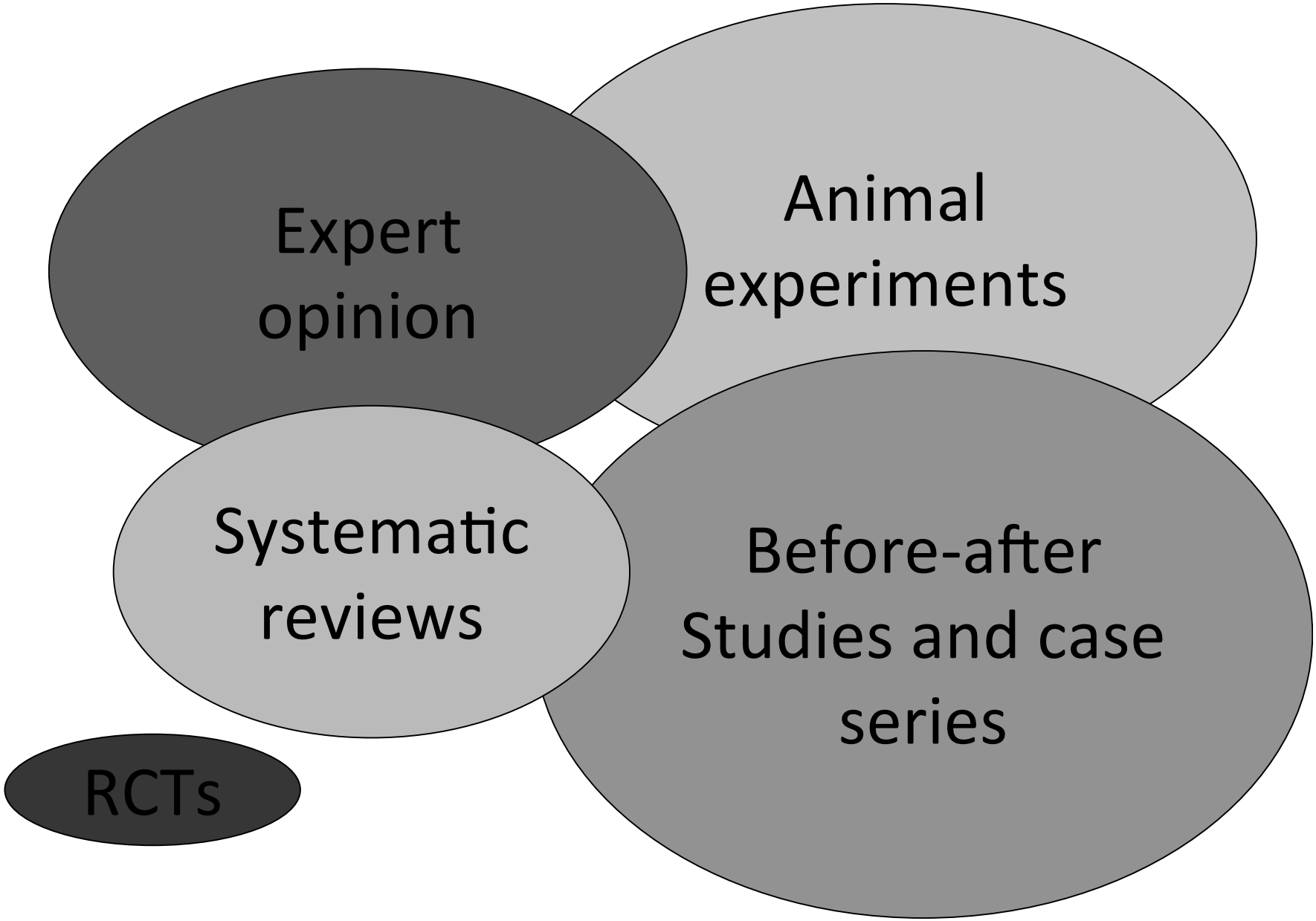


Figure 1. Heart-lung resuscitation (cardiopulmonary-cerebral resuscitation). First composition in 1961, Pittsburgh, PA. Reproduced with permission from Safar P. Community-wide CPR. *J Iowa Medical Society* 1964 (Nov); pp 629–635.

Evidence for TTM for cardiac arrest



Background

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. Buist, M.B., B.S., Bruce M. Jones, M.B., B.S., William Silvester, 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; 346:549-556 | February 21, 2002

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. BUIST, M.B., B.S.,
BRUCE M. JONES, M.B., B.S., WILLIAM SILVESTER, M.B., B.S., GEOFF GUTTERIDGE, M.B., B.S., AND KAREN SMITH, B.SC.

Bernard SA et al. N Engl J Med. 2002 Feb 21;346(8):557-63.

- Quasi-randomised, odd and even days
- 84 eligible patients, 77 included
- Unscheduled interim analysis after 62 patients
- Unusual outcome measure: *survival to hospital discharge with sufficiently good neurologic function to be discharged to home or to a rehabilitation facility.*
- Uneven groups (43 vs 34 patients)
- Temperature in control group (37.1 -37.3 °C)

Good outcome in hypothermia: normal or with minimal or moderate disability

Bernard SA et al. N Engl J Med. 2002 Feb 21;346(8):557-63.

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

The New England
Journal of Medicine

VOLUME 346 FEBRUARY 21, 2002 NUMBER 8

MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

N Engl J Med 2002;346:549-56

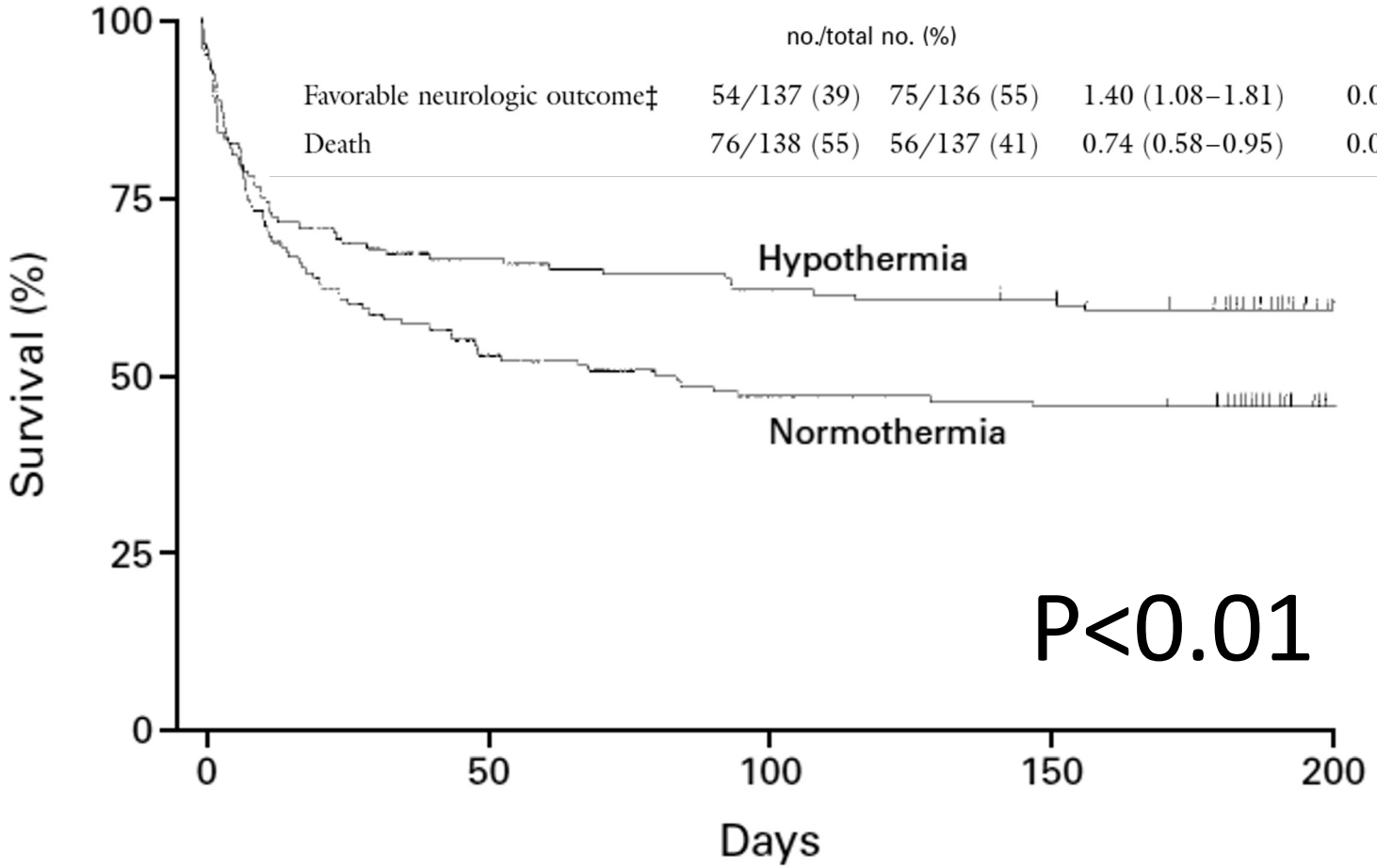
HACA-trial

- ✓ Less risk of bias/systematic errors!
- ✓ Patients after ventricular fibrillation
- ✓ Included only 8 % of patients with ROSC

HACA-trial: Hypothermia Improves Survival !

HACA Investigators, N Engl J Med 2002;346:549-56

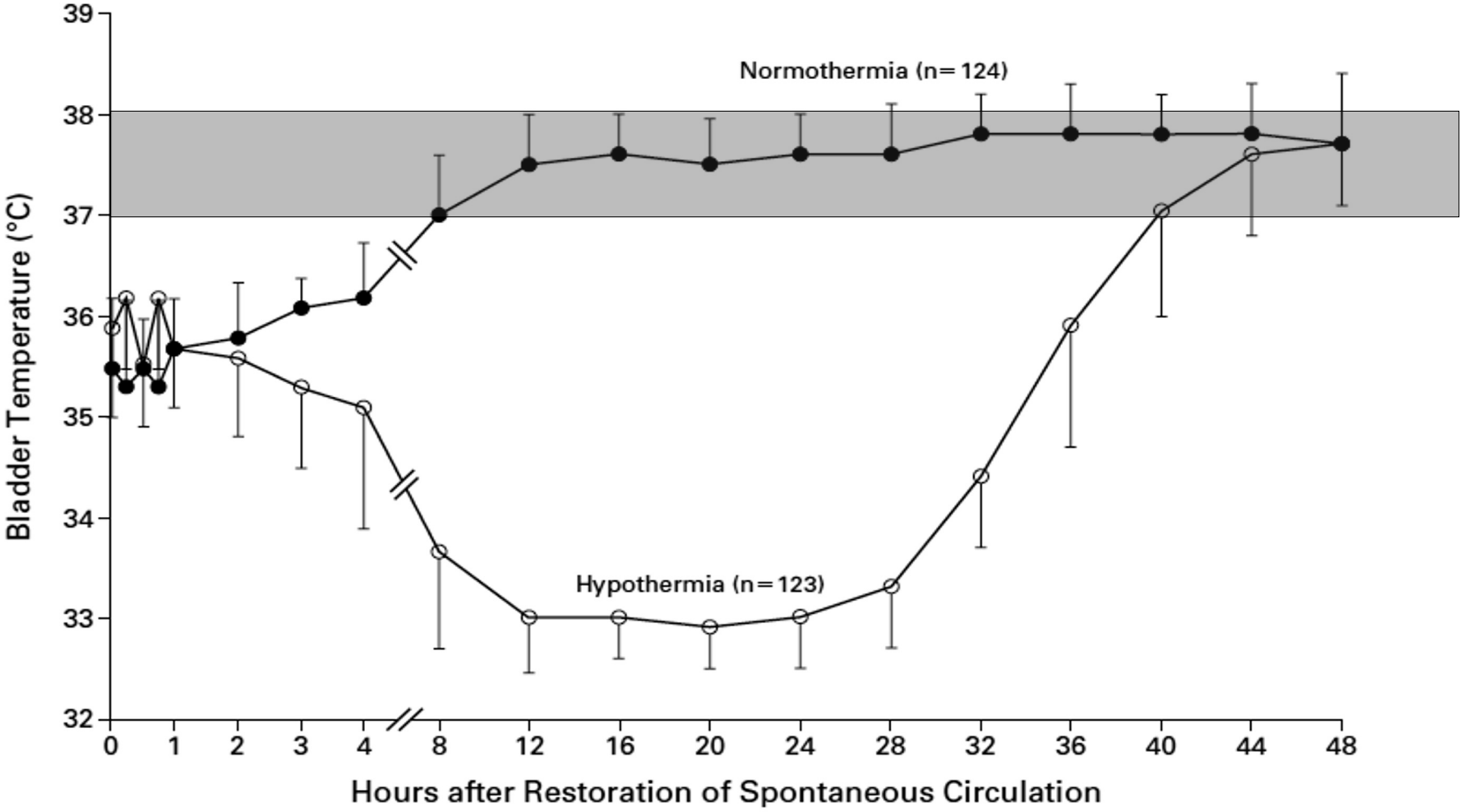
Outcome	Normothermia	Hypothermia	Risk Ratio (95% CI)*	P Value†
	no./total no. (%)			
Favorable neurologic outcome‡	54/137 (39)	75/136 (55)	1.40 (1.08–1.81)	0.009
Death	76/138 (55)	56/137 (41)	0.74 (0.58–0.95)	0.02



No. at Risk					
Hypothermia	137	92	86	83	11
Normothermia	138	74	66	64	9

HACA-trial: Hypothermia Compared with No Temperature Control = Fever!

HACA Investigators, N Engl J Med 2002;346:549-56



ELSEVIER

Resuscitation 57 (2003) 231–235

RESUSCITATION

www.elsevier.com/locate/resuscitation

Therapeutic hypothermia after cardiac arrest. An advisory statement by the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation☆

Jerry P. Nolan [a,*], Peter T. Morley [b], Terry L. Vanden Hoek [c], Robert W. Hickey [d,1], ALS Task Force [2]

- Patients after out of hospital cardiac arrest SHOULD UNDERGO HYPOTHERMIA at 32-34 °C for 12-24 h in case of VF

- Hypothermia might be useful for other type of arrest including intra hospital cardiac arrest

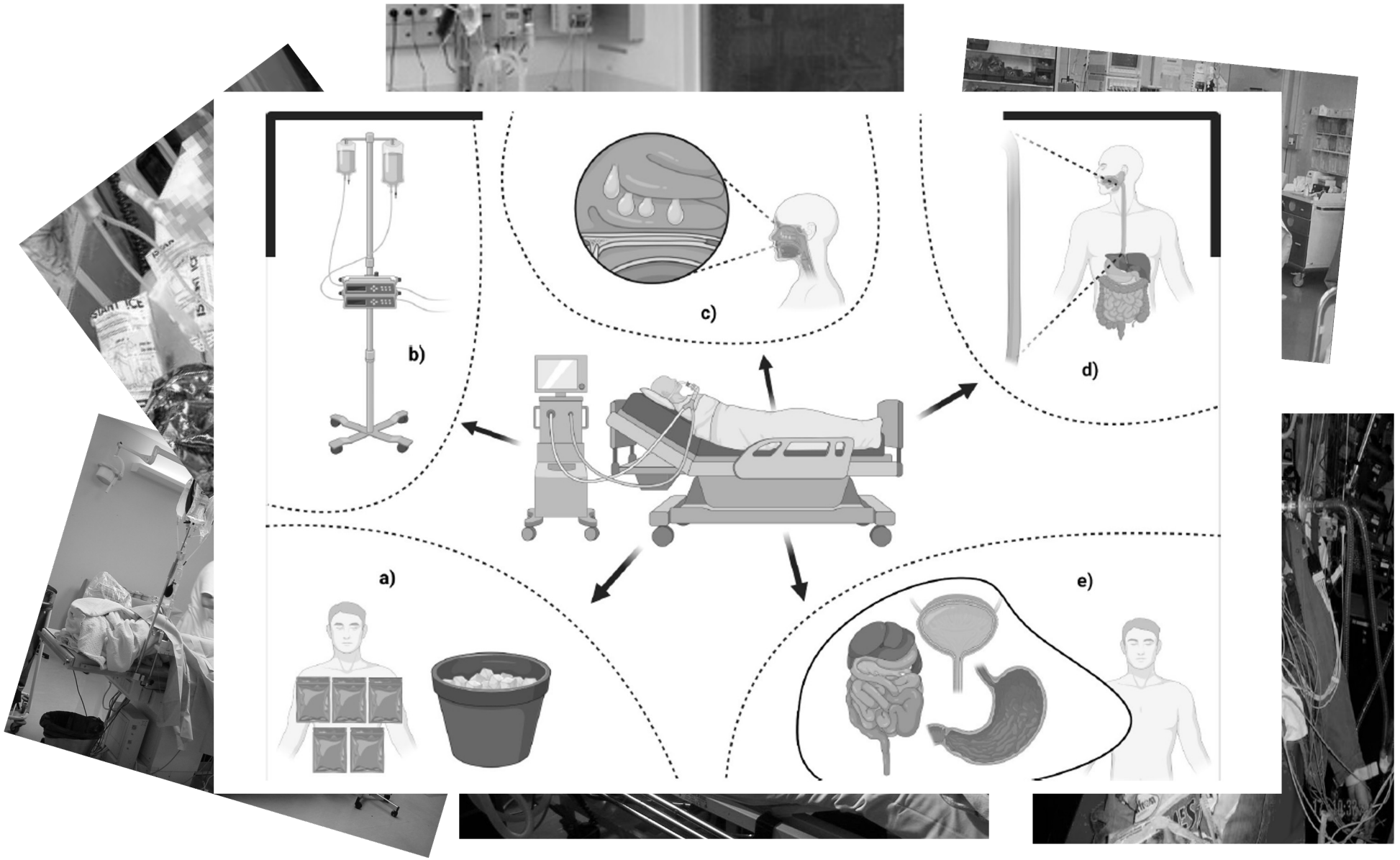
ILCOR Recommendations

On the basis of the published evidence to date, the Advanced Life Support (ALS) Task Force of the International Liaison Committee on Resuscitation (ILCOR) made the following recommendations in October 2002:

- 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.

Different cooling techniques … too many ?

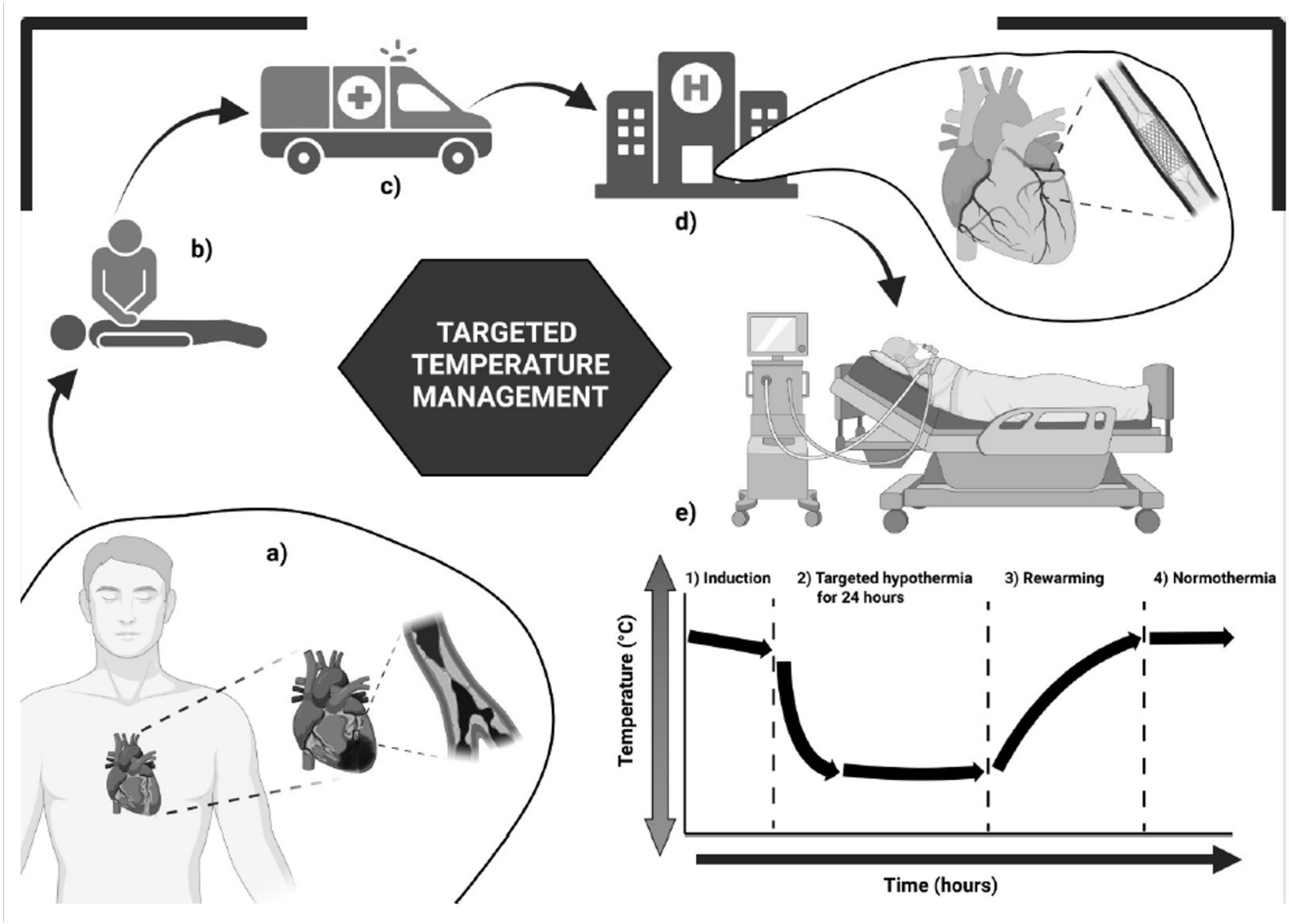
Markota A et al. Signa Vitae. 2022.doi:10.22514/sv.2021.227



Cooling Techniques save our soul & body !

TTM in OHCA: a clinical protocol

Markota A et al. Signa Vitae. 2022.doi:10.22514/sv.2021.227



Temperature Target Management is also associated with potential harm !

Increased risk of:

- ✓ infection
- ✓ arrhythmia
- ✓ hemodynamic failure
- ✓ seizures
- ✓ major bleeding
- ✓ delayed weaning

Hypothermia after Cardiac Arrest: A Metaanalysis

Nielsen et al Int J Cardiol. 2011 Sep 15;151(3):333-41

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: 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

Earlier Trials:

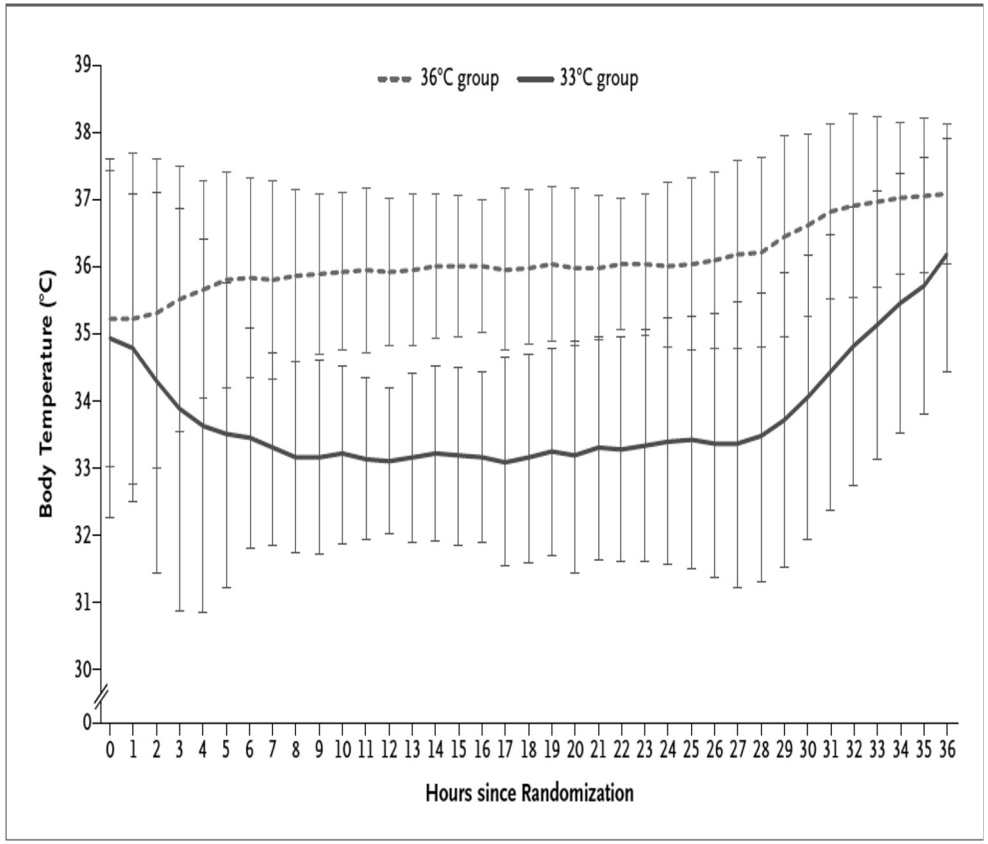
- Possible risk of systematic errors
- Possible risk of being underpowered
- Investigated a selected group

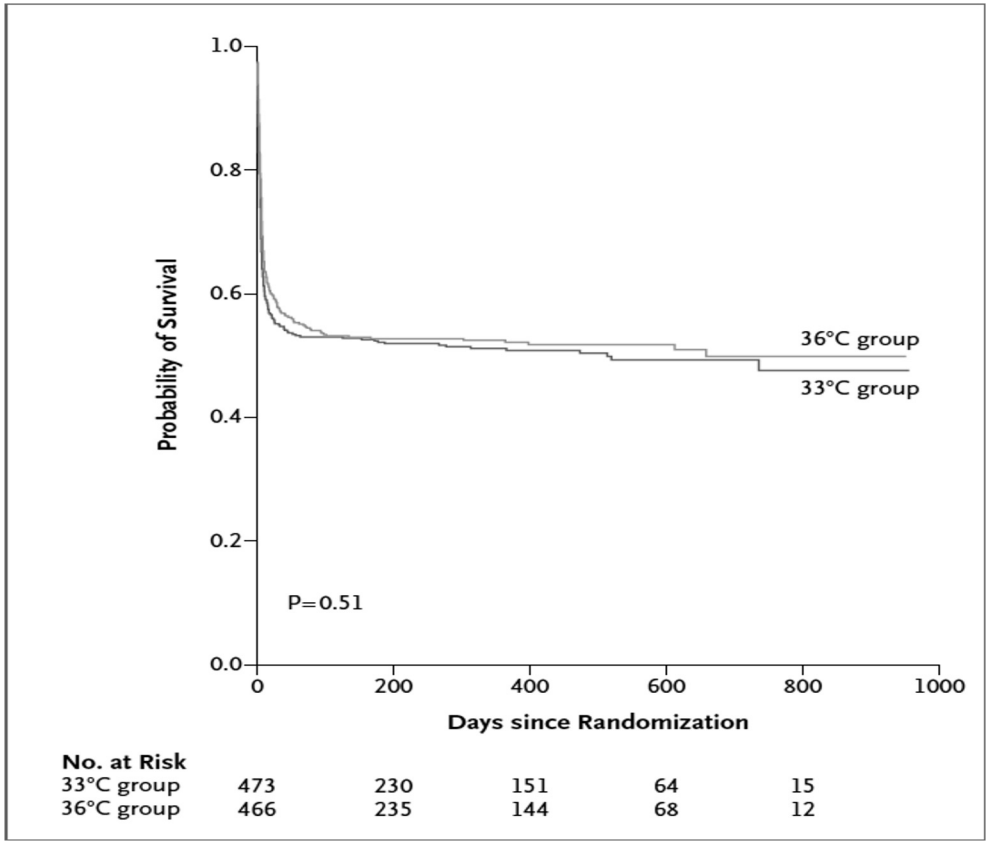
0.56 to 1.51) and for poor neurological outcome 0.92 (95% confidence interval 0.56 to 1.50). TSA indicated lack of firm evidence for a beneficial effect. The substantial risk of bias and concerns with directness rated

ORIGINAL ARTICLE

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

Nilsen N et al. Engl J Med 2013;369:2197-206

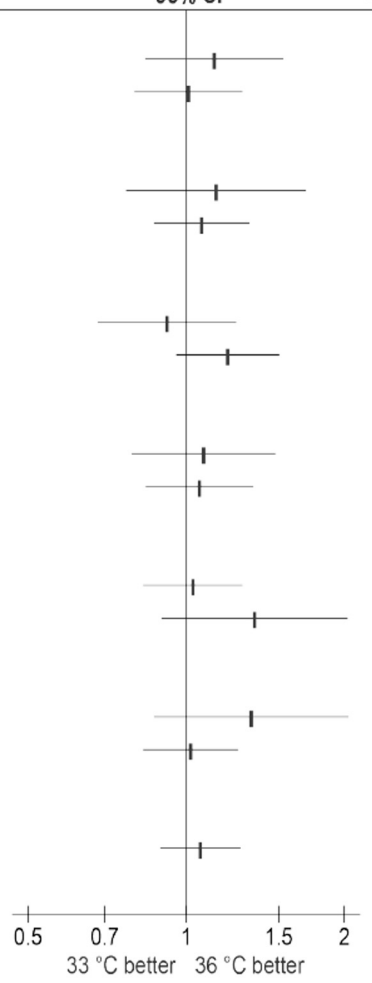




Target Temperature Management at 33 vs 36 °C after cardiac arrest

Nilsen N et al. Engl J Med 2013;369:2197-206

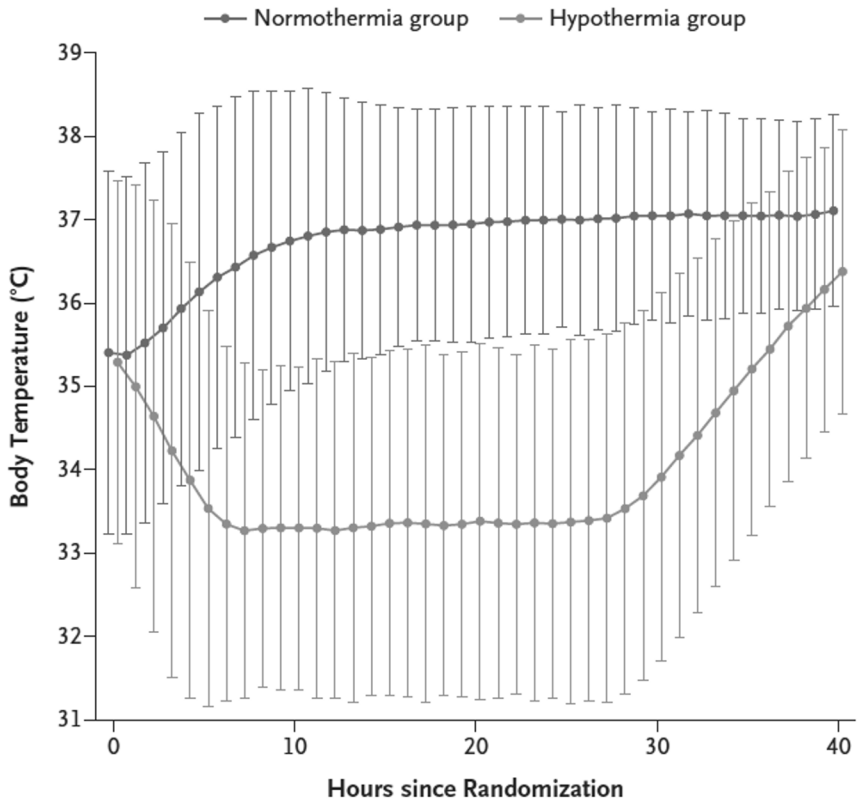
Subgroup	Target 33 °C No. of events/Total	Target 36 °C no. of patients	Hazard Ratio 95% CI	Test of interaction
Age				P = 0.52
Less than or equal to 65 years	91/238	85/250	1.13 [0.84, 1.53]	
More than 65 years	144/235	140/216	1.01 [0.80, 1.28]	
Gender				P = 0.75
Female	47/80	55/98	1.14 [0.77, 1.69]	
Male	188/393	170/368	1.07 [0.87, 1.32]	
Time from cardiac arrest to ROSC				P = 0.20
Less than or equal to 25 min	79/243	86/241	0.92 [0.68, 1.24]	
More than 25 min	156/230	138/224	1.20 [0.96, 1.50]	
Initial rhythm				P = 0.92
Non-shockable	82/98	74/88	1.08 [0.79, 1.48]	
Shockable	153/375	150/377	1.06 [0.84, 1.34]	
Shock at admission				P = 0.17
Not present	183/402	180/398	1.03 [0.83, 1.28]	
Present	52/70	44/67	1.35 [0.90, 2.03]	
Site category				P = 0.19
Two largest sites	50/110	40/108	1.33 [0.87, 2.03]	
Sites except two largest	185/363	185/358	1.02 [0.83, 1.25]	
TTM-Trial				
All patients	235/473	225/466	1.06 [0.89, 1.28]	

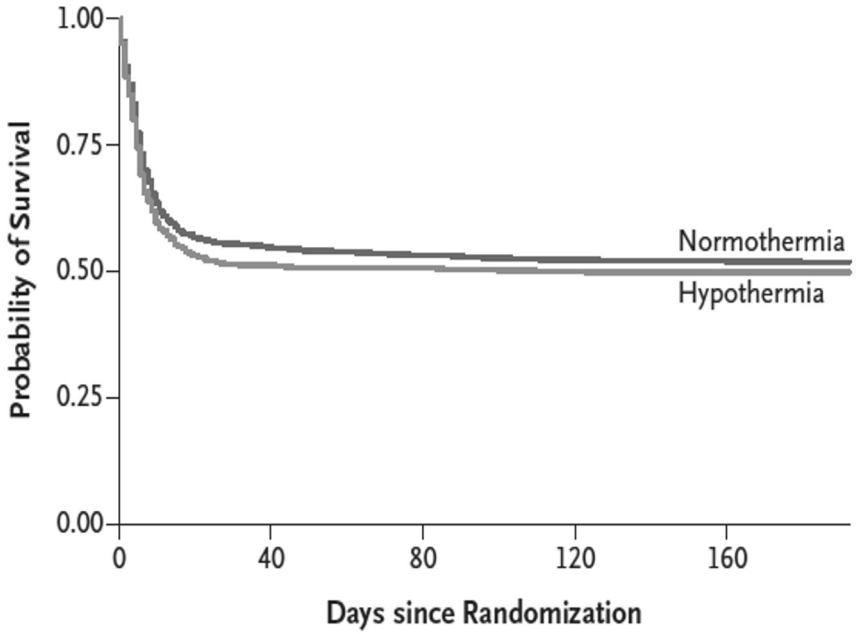


ORIGINAL ARTICLE

Hypothermia versus Normothermia after Out-of-Hospital Cardiac Arrest

Dankiewicz J N et al. Engl J Med 2021;384:2283-94



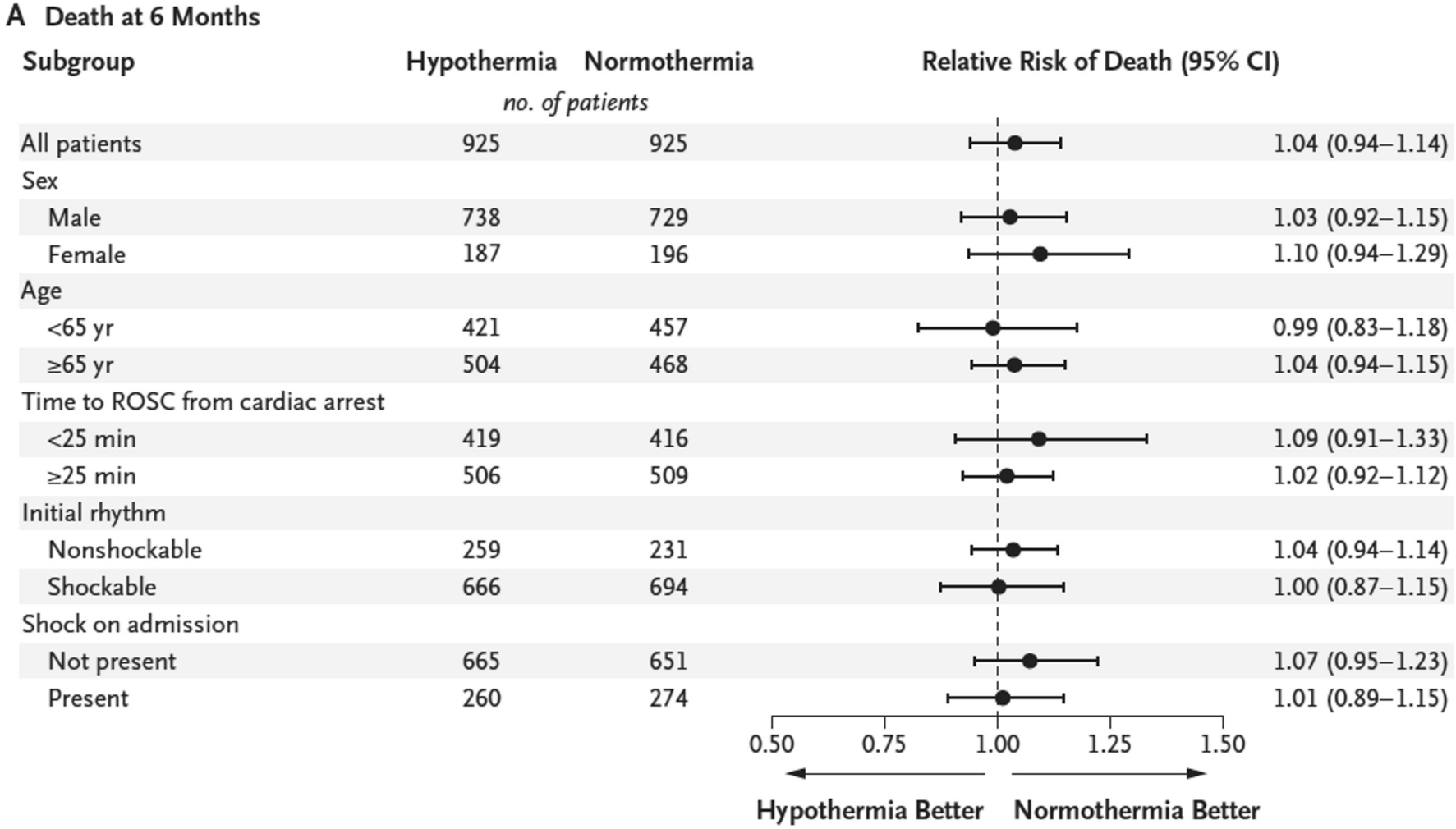


No. at Risk

Normothermia	925	506	491	484	480
Hypothermia	925	474	468	462	461

Hypothermia vs normothermia after out of hospital cardiac arrest

Dankiewicz J N et al. Engl J Med 2021;384:2283-94

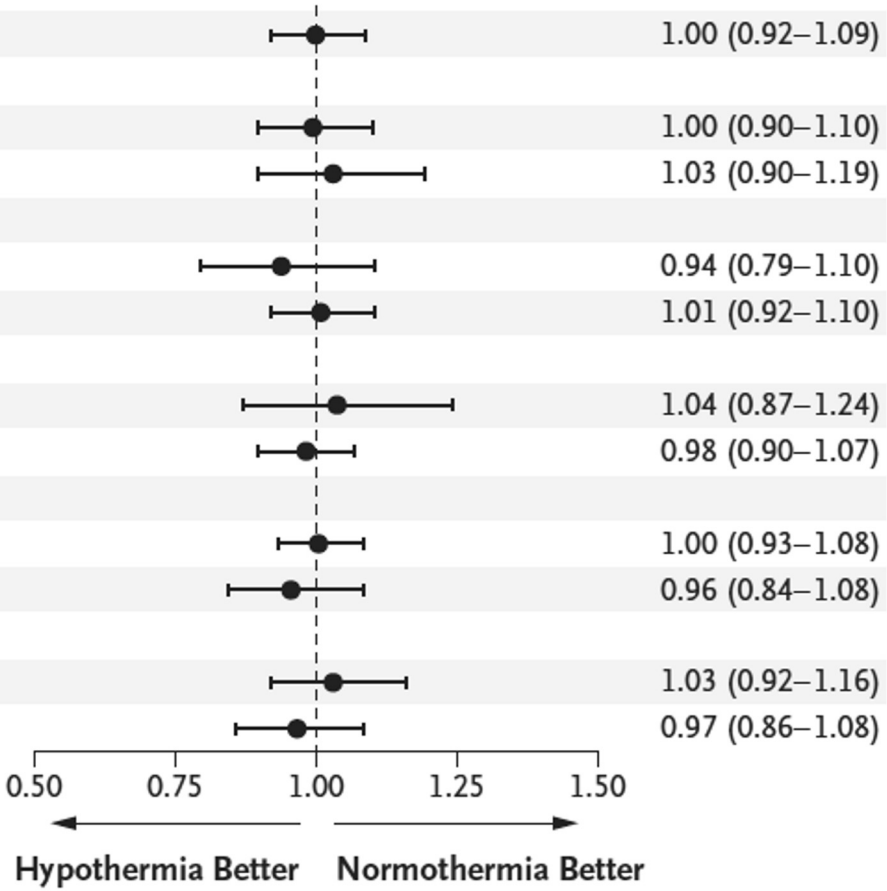


Hypothermia vs normothermia after out of hospital cardiac arrest

Dankiewicz J N et al. Engl J Med 2021;384:2283-94

B Modified Rankin Scale Score of 4–6 at 6 Months

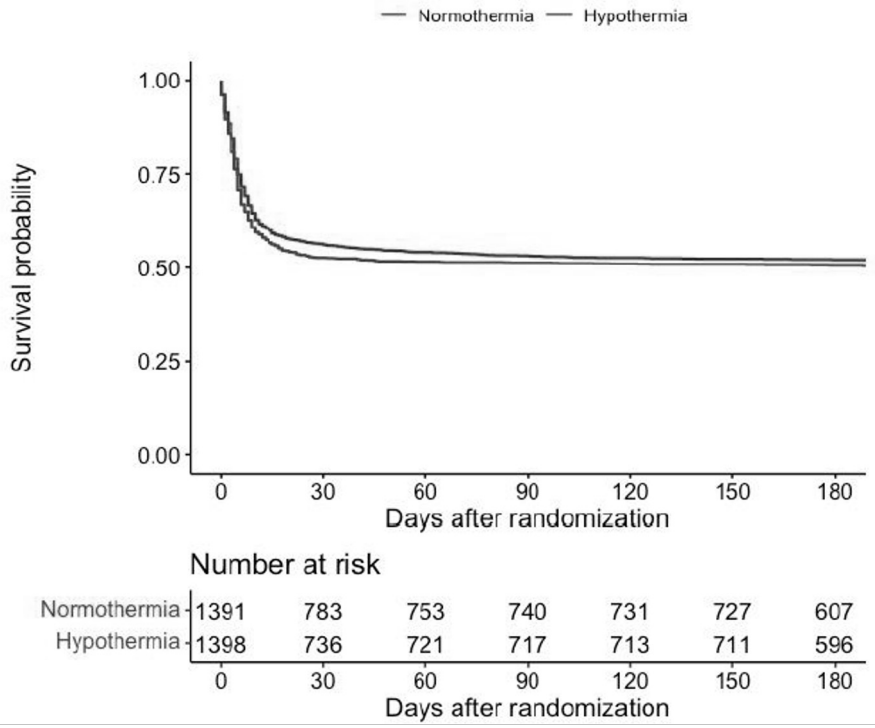
Subgroup	Hypothermia	Normothermia	Relative Risk of Score of 4–6 (95% CI)
	no. of patients		
All patients	881	866	1.00 (0.92–1.09)
Sex			
Male	701	679	1.00 (0.90–1.10)
Female	180	187	1.03 (0.90–1.19)
Age			
<65 yr	391	429	0.94 (0.79–1.10)
≥65 yr	490	437	1.01 (0.92–1.10)
Time to ROSC from cardiac arrest			
<25 min	395	389	1.04 (0.87–1.24)
≥25 min	486	477	0.98 (0.90–1.07)
Initial rhythm			
Nonshockable	252	218	1.00 (0.93–1.08)
Shockable	629	648	0.96 (0.84–1.08)
Shock on admission			
Not present	629	606	1.03 (0.92–1.16)
Present	252	260	0.97 (0.86–1.08)



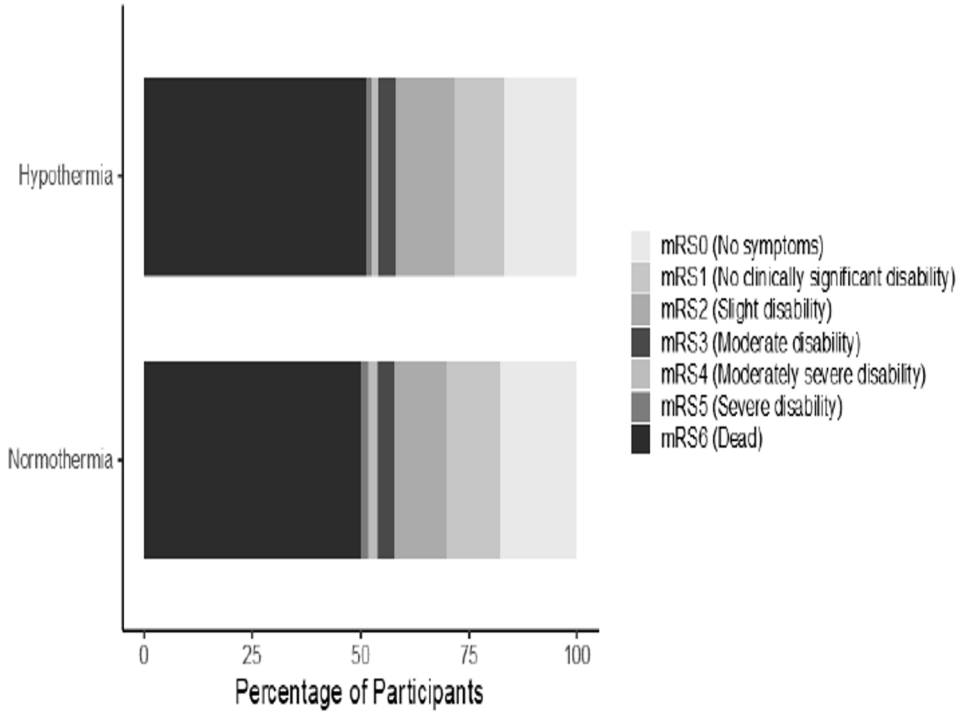
Hypothermic versus normothermic temperature control after cardiac arrest: TTM1 + TTM2

Holgersson J et al. N Engl J Med *Evidence* June 15, 2022

Effects on survival



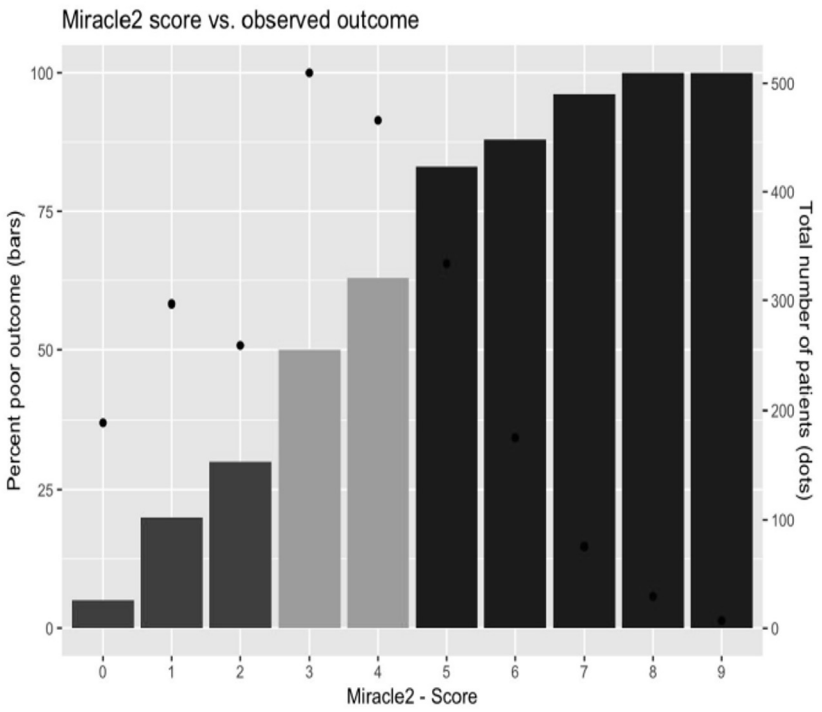
mRS at 180 d



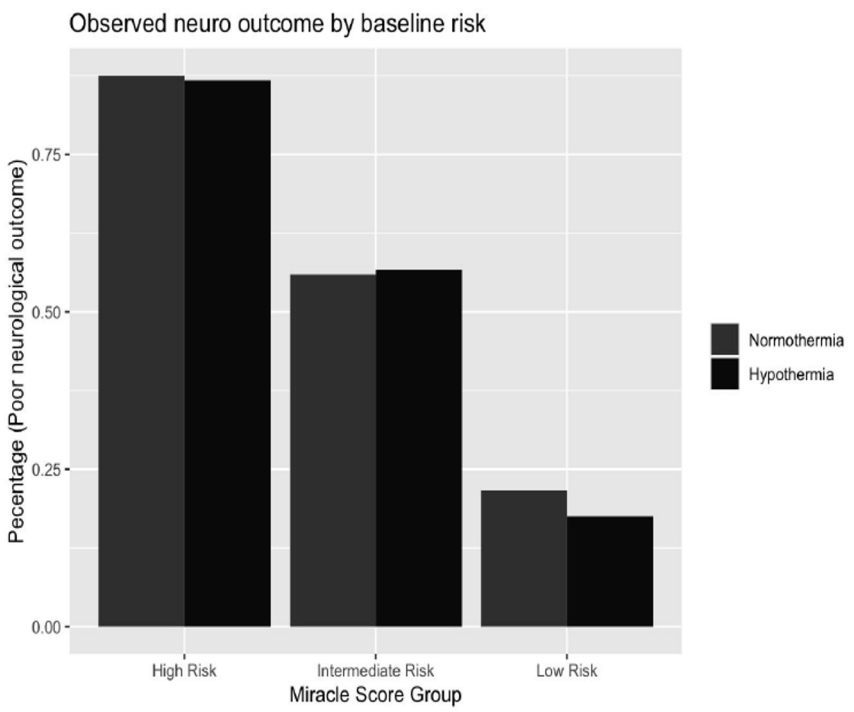
Hypothermic versus normothermic temperature control after cardiac arrest: TTM1 + TTM2

Holgersson J et al. N Engl J Med *Evidence* June 15, 2022

Severity & survival



TTM & survival

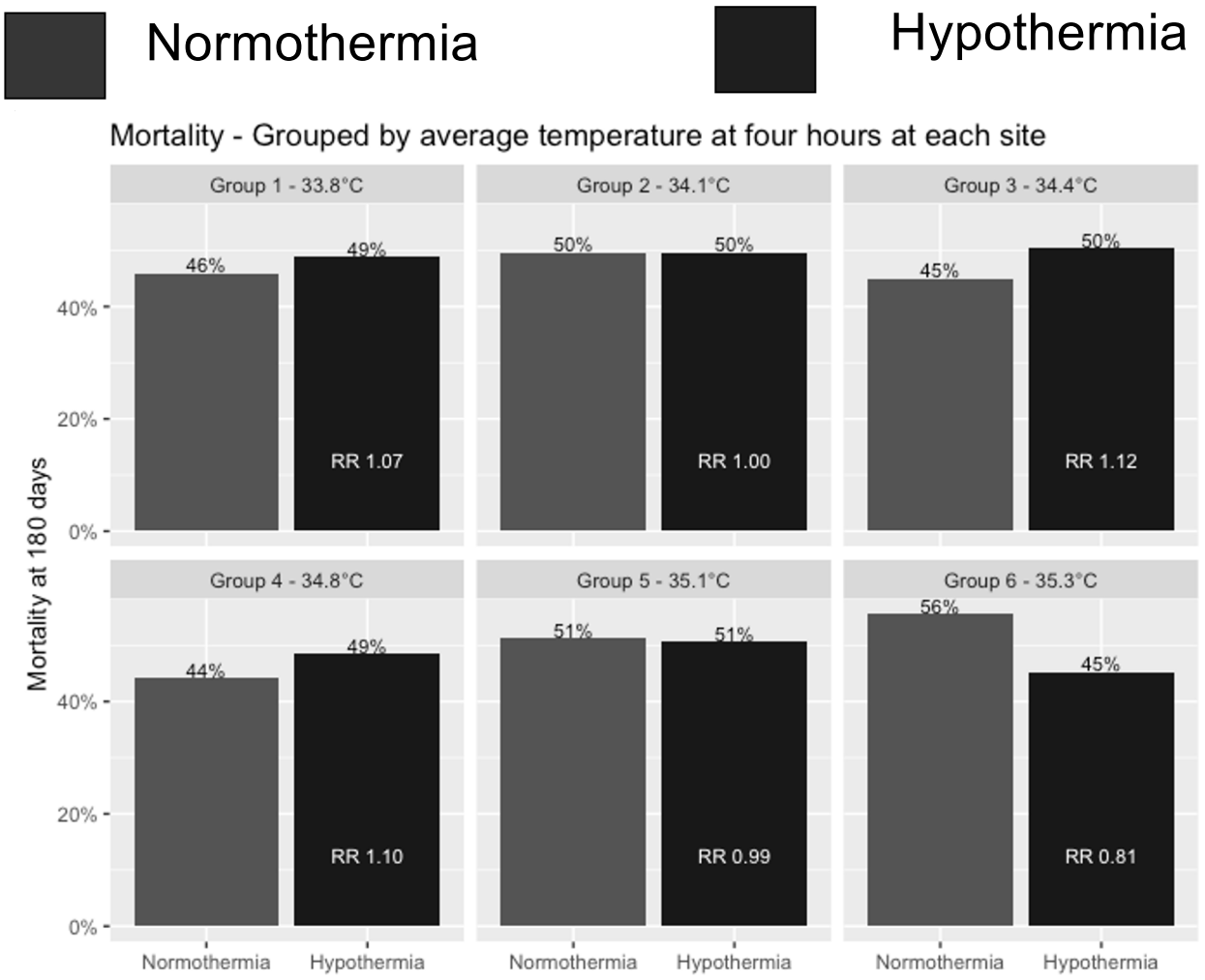


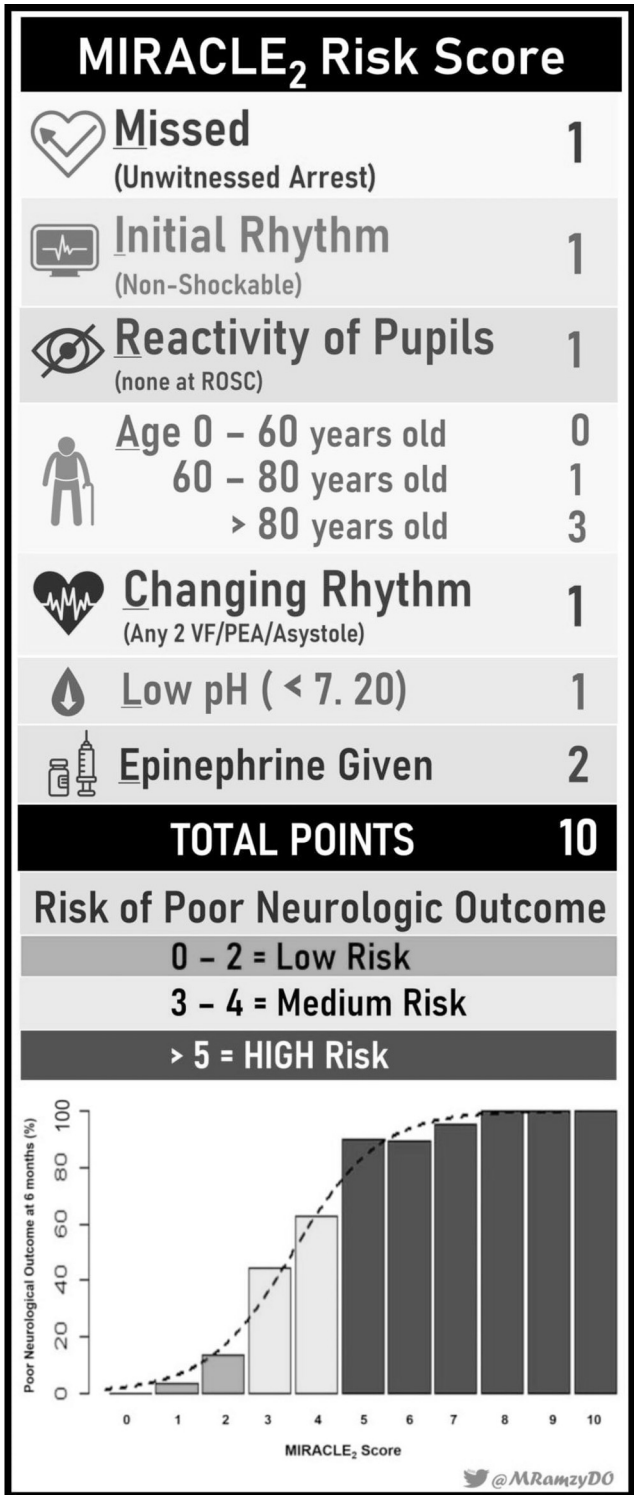
Hypothermia improved good functional outcome
in patients who had not received bystander cardiopulmonary resuscitation

Speed of cooling after cardiac arrest in relation to the intervention effect: a TTM2 trial sub-study

Simpson RFG et al. Crit Care. 2022 Nov 15;26(1):356

Average temperature at 4 hours (240 min) after for each participating sites





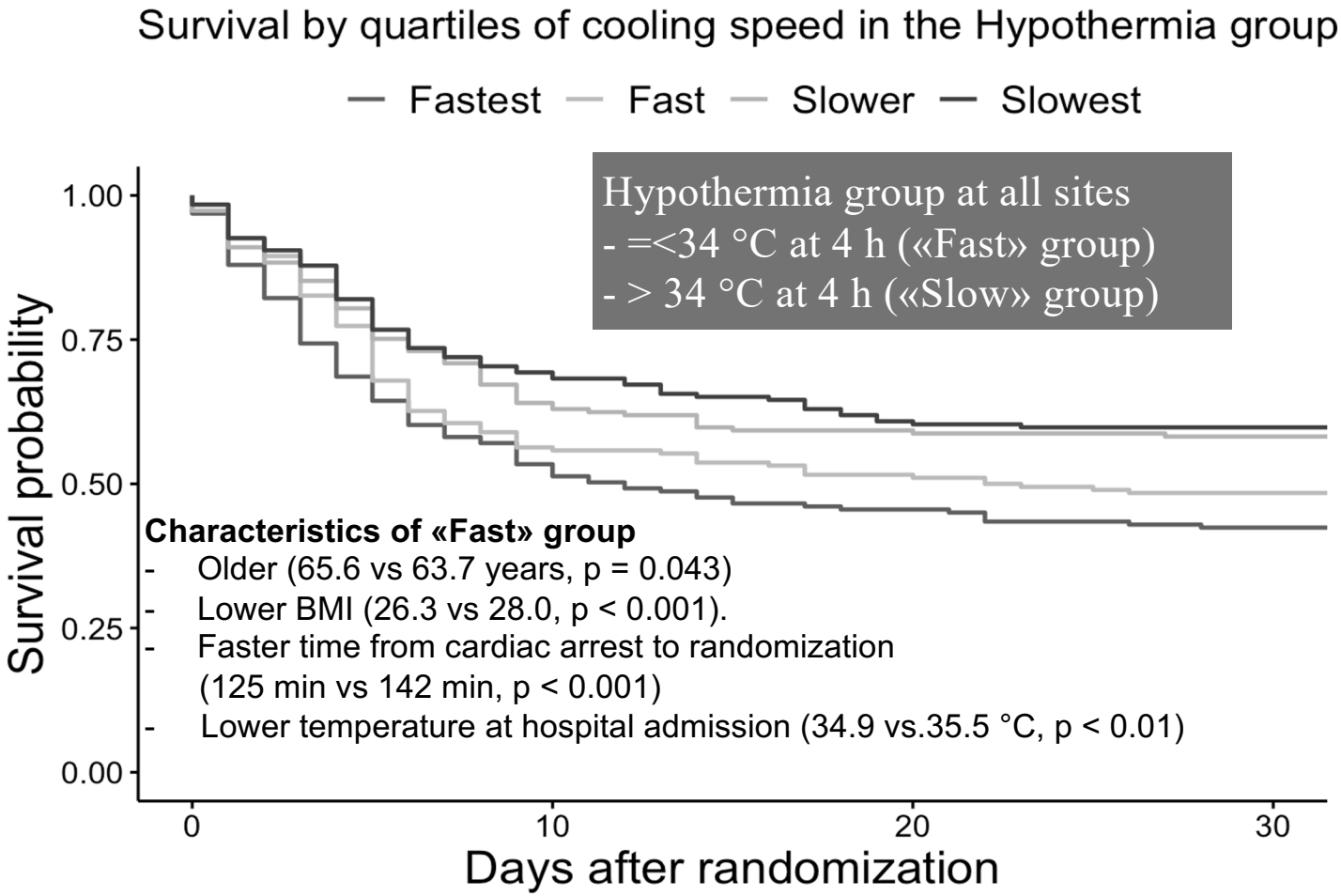
Seven predictor variables resulting in a final score ranging from 0 to 10 were used in the final model and it was named MIRACLE2

- 0 – 2 = **LOW** risk of poor neurologic outcome
- 3 – 4 = **INTERMEDIATE** risk of poor neurologic outcome
- ≥ 5 = **HIGH** risk of poor neurologic outcome

Speed of cooling after cardiac arrest in relation to the intervention effect: a TTM2 trial sub-study

Simpson RFG et al. Crit Care 2022 (accepted, in press)

Average temperature at 4 hours (240 min) after for each participating sites



What TTM 1 & TTM2 trials did show ?

- Strictly controlled TTM regiments (32 °C vs 36 °C & 33 °C vs 36.5-37.7 °C) do not give different results

- Target temperature management works and it is necessary (with data available)

- The importance of avoiding fever in cardiac arrest

Limitations of TTM 1 & TTM 2 trials

- OHCA patients (generazibility to in hospital?)

- High patients' heterogeneity
  - ✓ shockable and non-shockable rhythms
  - ✓ no age limit

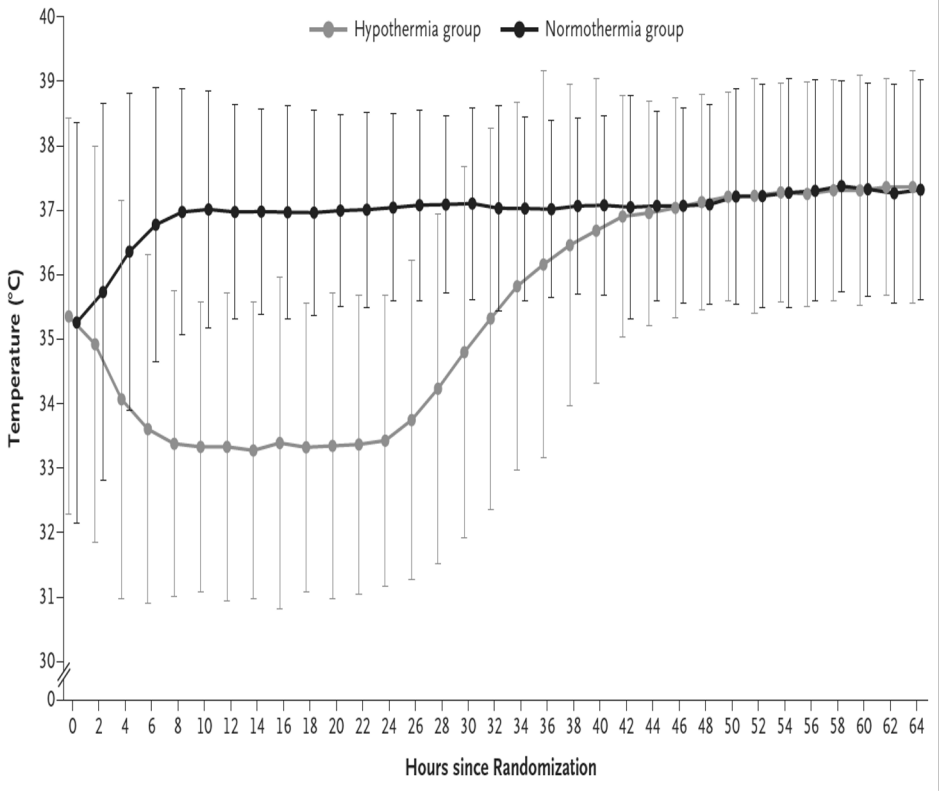
- Very short no-flow time and a large number of bystander-initiated resuscitation (implying a limited brain injury)

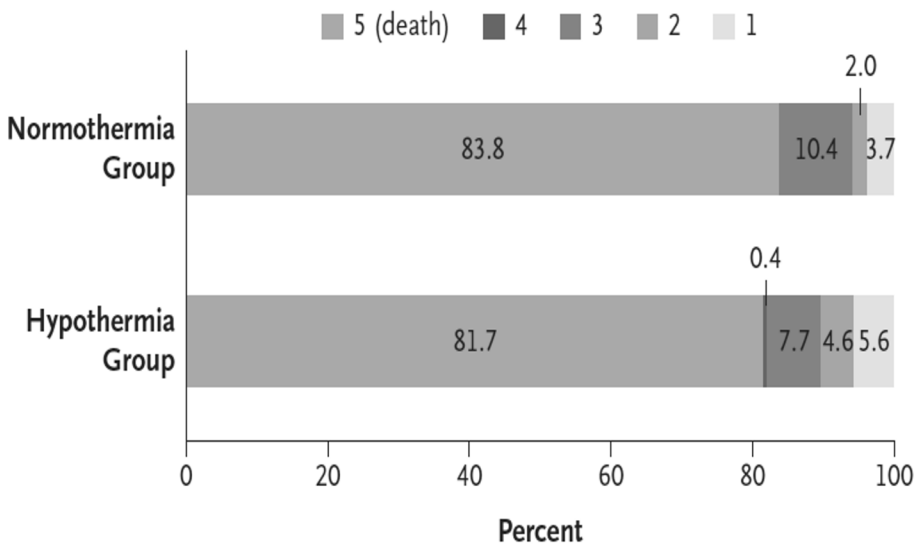
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Targeted Temperature Management for Cardiac Arrest with Nonshockable Rhythm

Lescarrou JB et al. N Engl J Med 2019;381:2327-37.





No differences in Survival

Targeted temperature management and cardiac arrest after the TTM-1 &2 and HYPERION trials

Taccone FS et al. Crit Care (2021) 25:275

All the randomized studies on TTM after cardiac arrest are not entirely comparable !

	Bernard et al. [1]	HACA group [2]	Nielsen et al. [7]	Dankiewicz et al. [5]	Lascarrou et al. [4]
Design	Single-Centre	Multicentric	Multicentric	Multicentric	Multicentric
N (HT group)	79 (43)**	275 (138)*	939 (473)	1861 (930)	584 (284)
Age, years	67 (49–89)	59 (49–67)	64 ± 12	64 ± 13	67 (57–76)
Male gender	58%	77%	83%	80%	65%
OHCA	100%	100%	100%	100%	74%
Bystander CPR	49%	49%	73%	82%	70%
Shockable rhythm	100%	96%	79%	72%	0%
Time to ROSC, min	27 ± 13	22 (17–33)*	25 (18–40)	25 (16–40)	18 (10–25)
Cause of Arrest	Cardiac	Cardiac	Cardiac/UNK	Cardiac/UNK	All**
Shock on Admission	NR	49*	15%	28%	56%
STEMI on Admission	NR	NR	40%	41%	16%
Lactate, mmol/L	8.3 (2.2–14.9)	NR	6.7 ± 4.5	5.9 ± 4.4	5.8 (3.2–9.0)
Outcome Assessment	Hospital Discharge	6 months	6 months	6 months	3 months
Mortality, %*	51%	41%	50%	50%	81%
UO Assessment Scale	CPC 3–5	CPC 3–5	CPC 3–5	mRS 4–6	CPC 3–5
UO, %	51	45	54	55	90
Prognostication Rules	Absent	Absent	Present	Present	Present
Generalisability/Bias	Low/high	Low/high	High/low	High/low	High/moderate

Targeted temperature management and cardiac arrest after the TTM-1 &2 and HYPERION trials

Taccone FS et al. Crit Care (2021) 25:275

All the randomized studies on TTM after cardiac arrest are not entirely comparable

❖ **The TTM-2 study findings would be applicable:**

✓ OHCA of cardiac causes

✓ Bystander CPR (i.e., short no-flow time and less severe initial anoxic injury)

✓ Patients with acute myocardial infarction and a low occurrence of shock on admission

❖ **In patients with an initial non-shockable rhythm due to respiratory/hypoxic causes and hemodynamic instability:**

✓ The use of hypothermia at 33 °C could be considered more effective than normothermia, in particular for in-hospital cardiac arrest (?)

TTM after Cardiac Arrest: A Systematic Review & Meta-Analysis with Trial Sequential Analysis

Sanfilippo F et al. J. Clin. Med. 2021, 10, 3943

Journal of *Clinical Medicine*

MDPI

Review

Targeted Temperature Management after Cardiac Arrest: A Systematic Review and Meta-Analysis with Trial Sequential Analysis

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TTM after Cardiac Arrest: A Systematic Review & Meta-Analysis with Trial Sequential Analysis

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❖ **Effects on survival & neurologic outcome**

➢ **TTM** (Temperature range of 32-34 °C)
➢ **Controls:**
- "actively" controlled (avoiding fever)
- "uncontrolled" normothermia (may hesitate in hyperthermia/fever)

❖ **Serious adverse events**

PICOS CRITERIA

Population	Patients experiencing CA both in and out-of-hospital, independently from the initially detected rhythm (shockable or not), with TTM performed after hospital arrival
Intervention	TTM with temperature range set at 32–34 °C
Comparison	TTM with either actively controlled or uncontrolled normothermia
Outcome(s)	Survival and neurological outcome at longest follow-up (primary); adverse effects (secondary)
Study design	Randomized controlled trial only

CA: cardiac arrest; TTM: target temperature management.

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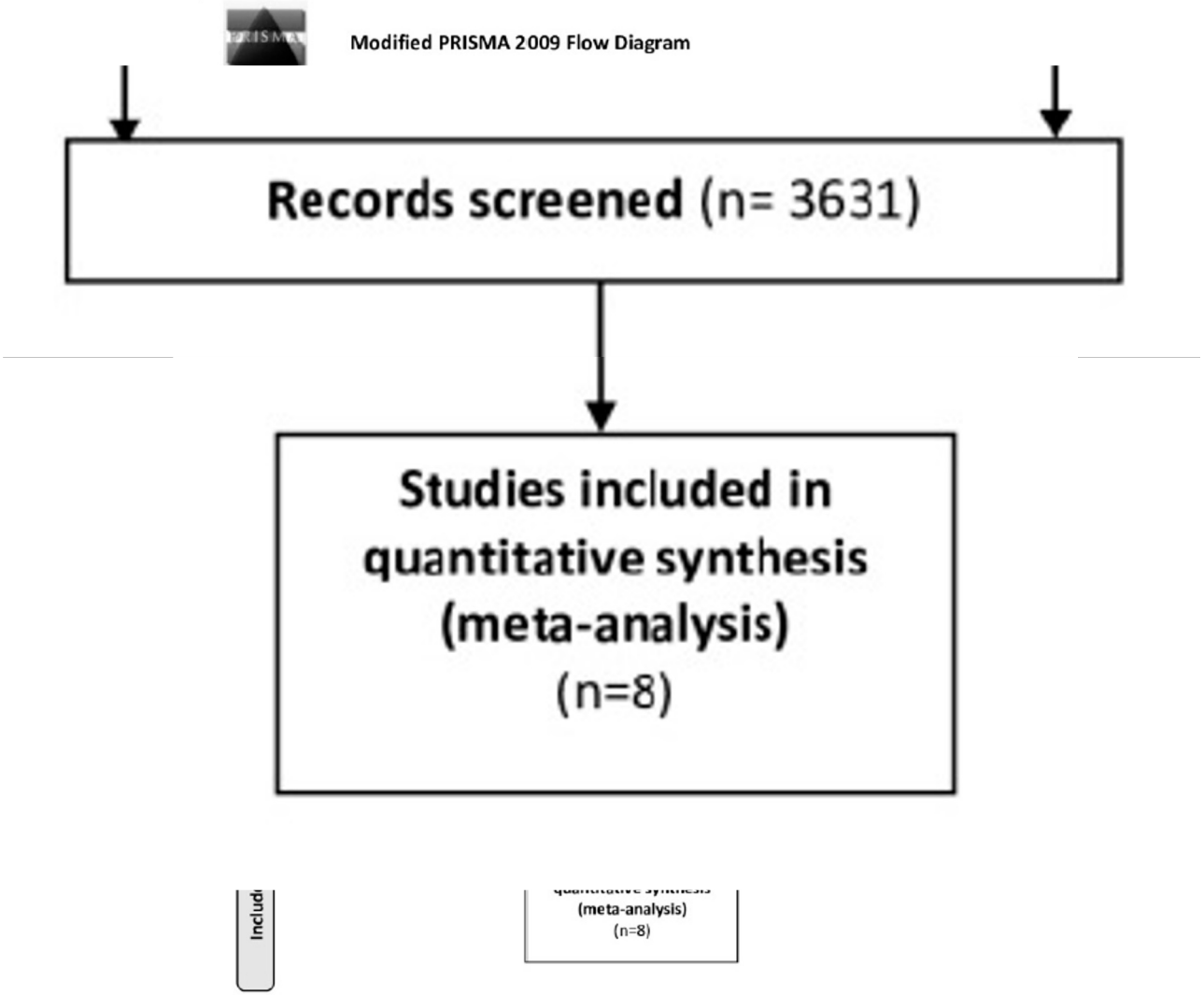

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First Author Year	Location of Arrest	First Rhythm Detected	Treatment in the Intervention Group Treatment in the Control Group	Longest Follow Up GNO Assessment
Dankiewicz 2021 *N* = 1861	OHCA	Shockable 74% Non-shockable 26%	TTM (surface/ iv, 33 °C, 28 h) + active RW (12 h) Normothermia (≤37.5 °C + surface/iv if ≥37.8 °C)	6-months mRS
Nielsen 2013 *N* = 939	OHCA	Shockable 80% Non-shockable 20%	TTM (any method, 33 °C, 28 h) + active RW (8 h) TTM (any method, 36 °C, 28 h) + active RW (2 h)	6-months—End trial CPC—mRS
Lascarrou 2019 *N* = 548	Mixed (73% OHCA)	Non-shockable 100%	TTM (any method, 33 °C, 24 h) + active RW (8–16 h, 36 °C, 24 h) TTM (any method, 37 °C, 48 h)	90-days CPC
Holzer 2002 *N* = 136	OHCA	Shockable 96% Other 4%	TTM (mattress, 32–34 °C, 24 h) + passive RW Normothermia (no target)	6-months CPC
Bernard 2002 *N* = 77	OHCA	Shockable 100%	TTM (ice-packs, 33 °C, 12 h) + active RW (6 h) Normothermia (37 °C)	Hospital discharge Home/short term rehab
Hachimi-idrissi 2005 *N* = 61	OHCA	Non-shockable 54% Shockable 46%	TTM (Helmet, 33 °C, brief *) + passive RW Normothermia (37 °C) TTM (mattress, 33 °C, 24 h) + passive RW Normothermia (37 °C)	6-months CPC
Laurent 2005 * *N* = 42	OHCA	Shockable 74% Non-shockable 26%	TTM (HF + ice-packs, 32 °C, 24 h) + passive RW Normothermia + HF 8 h (37 °C)	6-months CPC
Hachimi-idrissi 2001 *N* = 30	OHCA	Non-shockable 100%	TTM (Helmet, 34 °C, brief *) + passive RW Normothermia + treatment of fever (38 °C)	2-weeks CPC

HF: hemofiltration; OHCA: out-of-hospital cardiac arrest; RW: rewarming; TTM: target temperature management; mRS: modified rankin scale; CPC: cerebral performance category. * The control group not treated with HF was not considered (n = 19)

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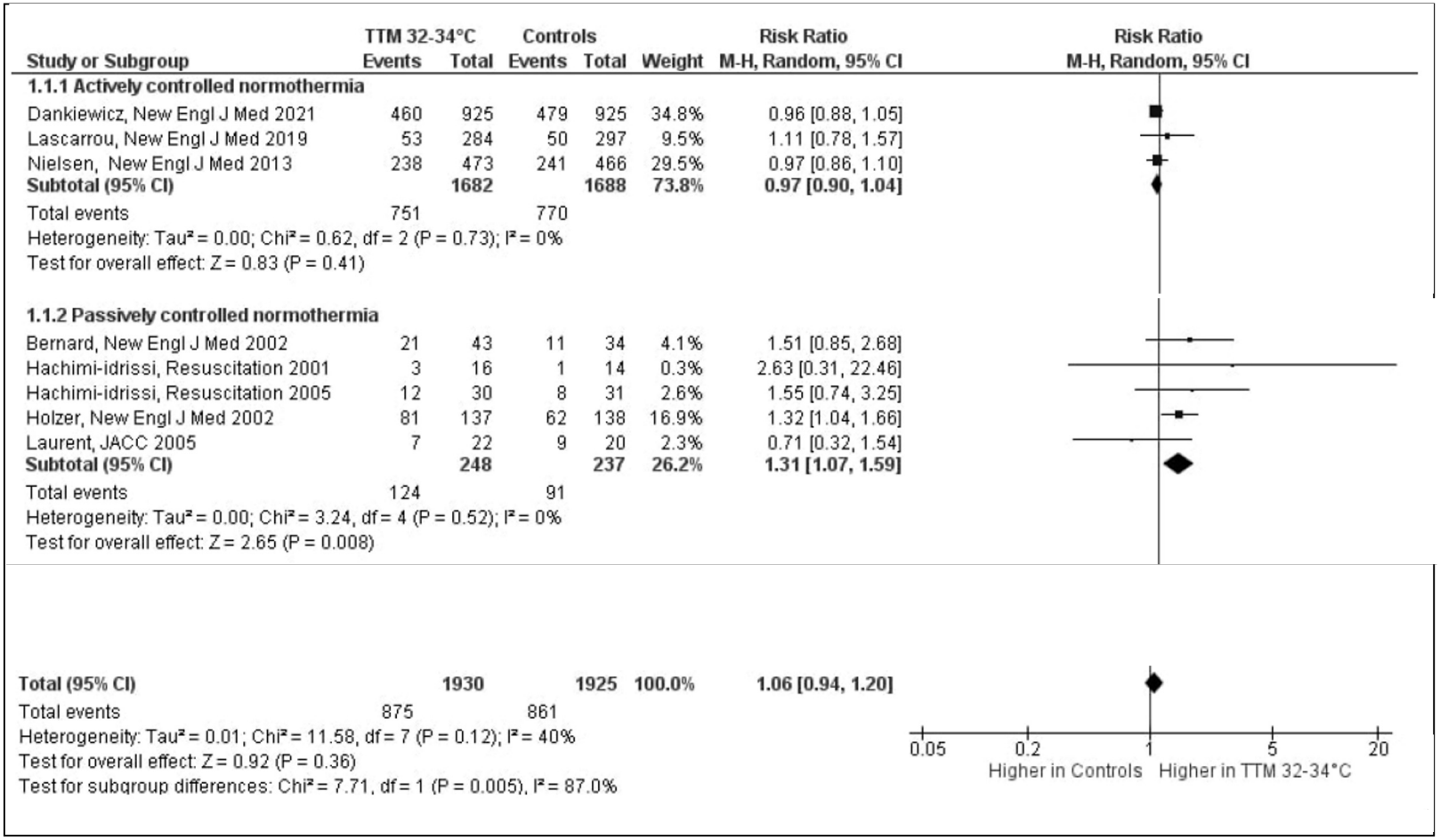
Effects on survival



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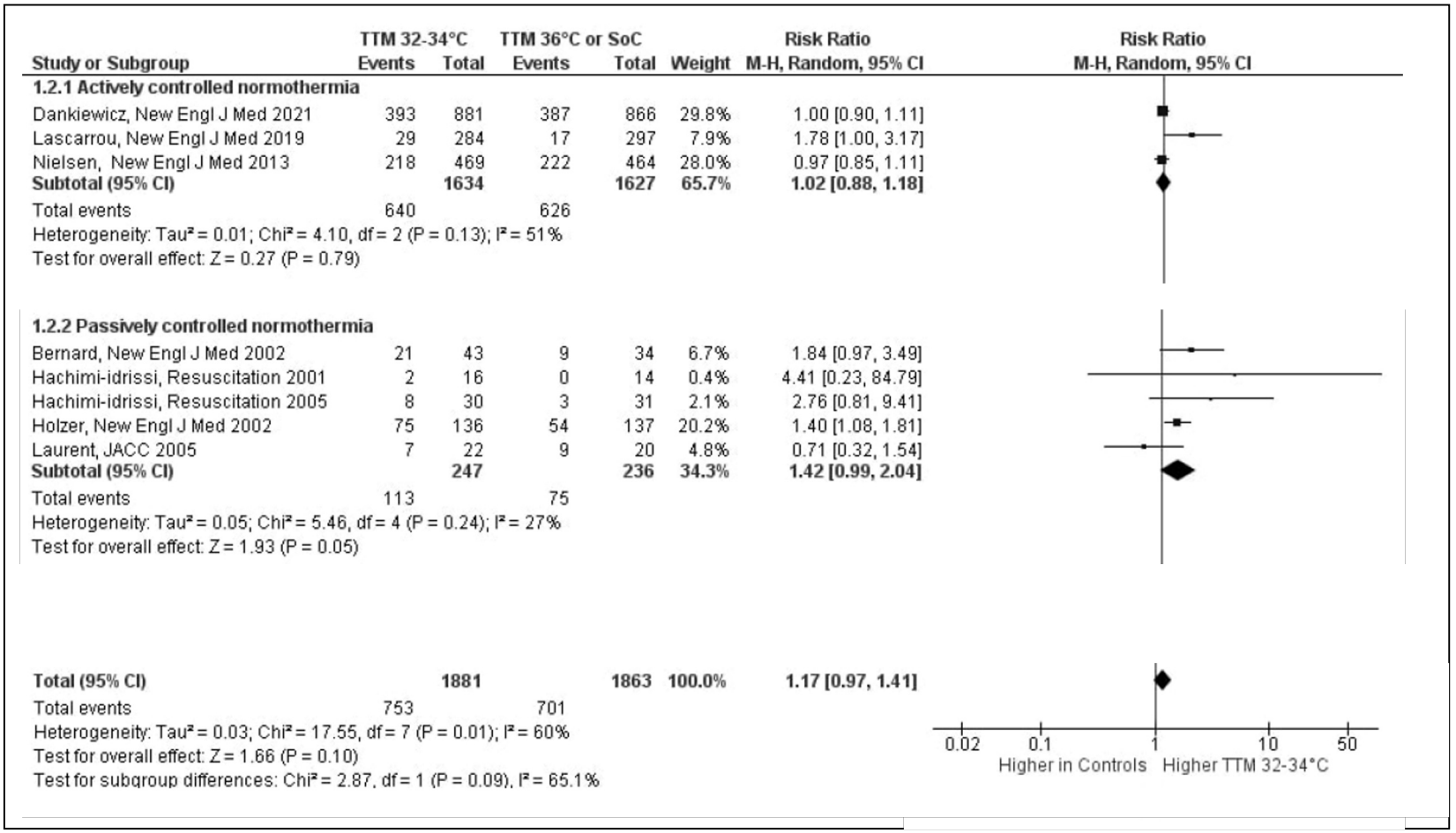
Effects on neurologic outcome



Study or Subgroup	TTM 32-34°C Events	Total	TTM 36°C or SoC Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 Actively controlled normothermia						
Dankiewicz, New Engl J Med 2021	393	881	387	866	29.8%	1.00 [0.90, 1.11]
Lascarrou, New Engl J Med 2019	29	284	17	297	7.9%	1.78 [1.00, 3.17]
Nielsen, New Engl J Med 2013	218	469	222	464	28.0%	0.97 [0.85, 1.11]
Subtotal (95% CI)		**1634**		**1627**	**65.7%**	**1.02 [0.88, 1.18]**
Total events	640		626			
Heterogeneity: Tau² = 0.01; Chi² = 4.10, df = 2 (P = 0.13); I² = 51%						
Test for overall effect: Z = 0.27 (P = 0.79)						
1.2.2 Passively controlled normothermia						
Bernard, New Engl J Med 2002	21	43	9	34	6.7%	1.84 [0.97, 3.49]
Hachimi-idrissi, Resuscitation 2001	2	16	0	14	0.4%	4.41 [0.23, 84.79]
Hachimi-idrissi, Resuscitation 2005	8	30	3	31	2.1%	2.76 [0.81, 9.41]
Holzer, New Engl J Med 2002	75	136	54	137	20.2%	1.40 [1.08, 1.81]
Laurent, JACC 2005	7	22	9	20	4.8%	0.71 [0.32, 1.54]
Subtotal (95% CI)		**247**		**236**	**34.3%**	**1.42 [0.99, 2.04]**
Total events	113		75			
Heterogeneity: Tau² = 0.05; Chi² = 5.46, df = 4 (P = 0.24); I² = 27%						
Test for overall effect: Z = 1.93 (P = 0.05)						
Total (95% CI)		**1881**		**1863**	**100.0%**	**1.17 [0.97, 1.41]**
Total events	753		701			
Heterogeneity: Tau² = 0.03; Chi² = 17.55, df = 7 (P = 0.01); I² = 60%						
Test for overall effect: Z = 1.66 (P = 0.10)						
Test for subgroup differences: Chi² = 2.87, df = 1 (P = 0.09), I² = 65.1%						

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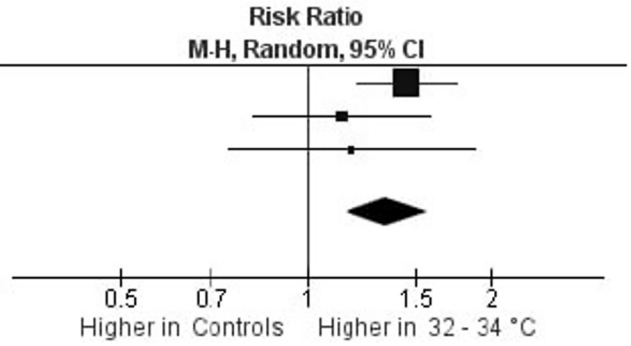
Adverse events

Arrhythmias

Study or Subgroup	TTM 32 - 34 °C Events	Total	TTM Controls Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Dankiewicz, New Engl J Med 2021	222	927	152	921	67.6%	1.45 [1.21, 1.75]
Holzer, New Engl J Med 2002	49	135	44	138	21.2%	1.14 [0.82, 1.58]
Lascarrou, New Engl J Med 2019	35	284	31	297	11.2%	1.18 [0.75, 1.86]
Total (95% CI)		**1346**		**1356**	**100.0%**	**1.35 [1.16, 1.57]**
Total events	306		227			

Heterogeneity: Tau² = 0.00; Chi² = 1.94, df = 2 (P = 0.38); I² = 0%
Test for overall effect: Z = 3.83 (P = 0.0001)



No differences in the incidence of:
✓ bleeding (RR 1.10 (95%CI 0.83, 1.44))
✓ pneumonia (RR 1.11 (95%CI 0.96, 1.29))

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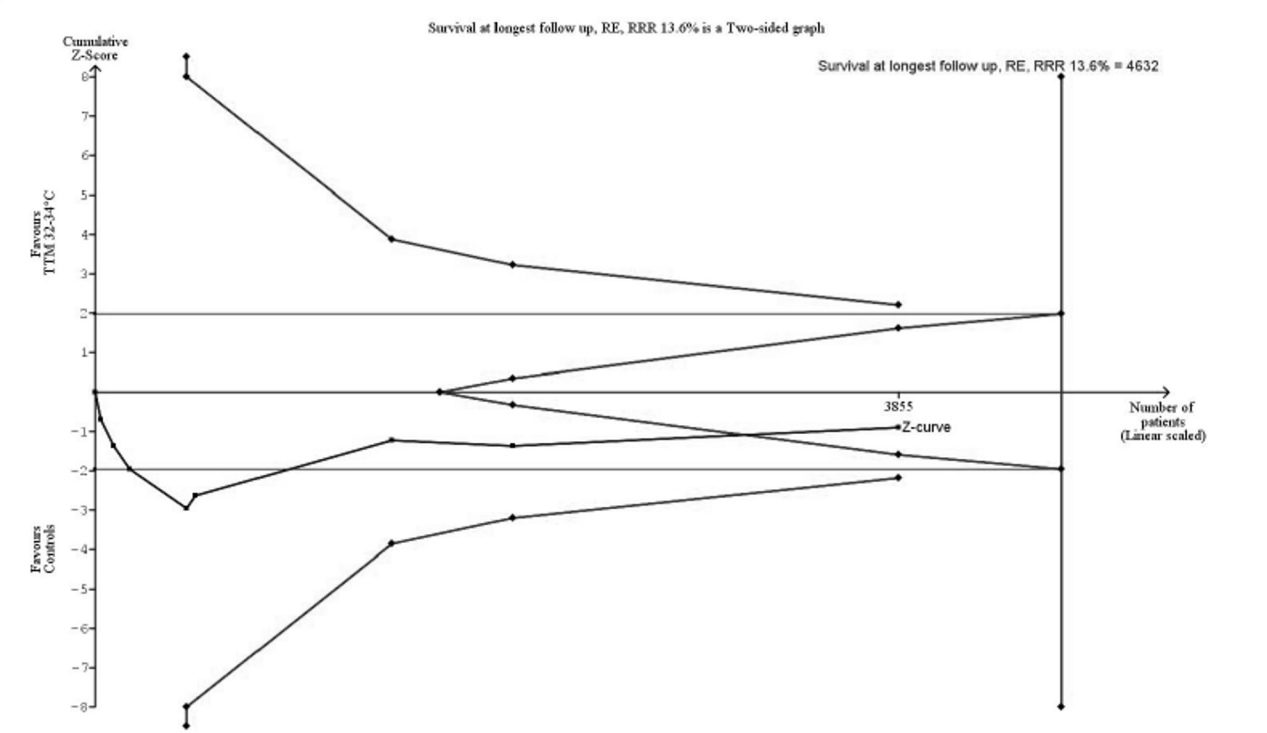
Trials sequential analysis

Survival at longest follow-up



RE=random effect, RRR=Relative risk reduction.

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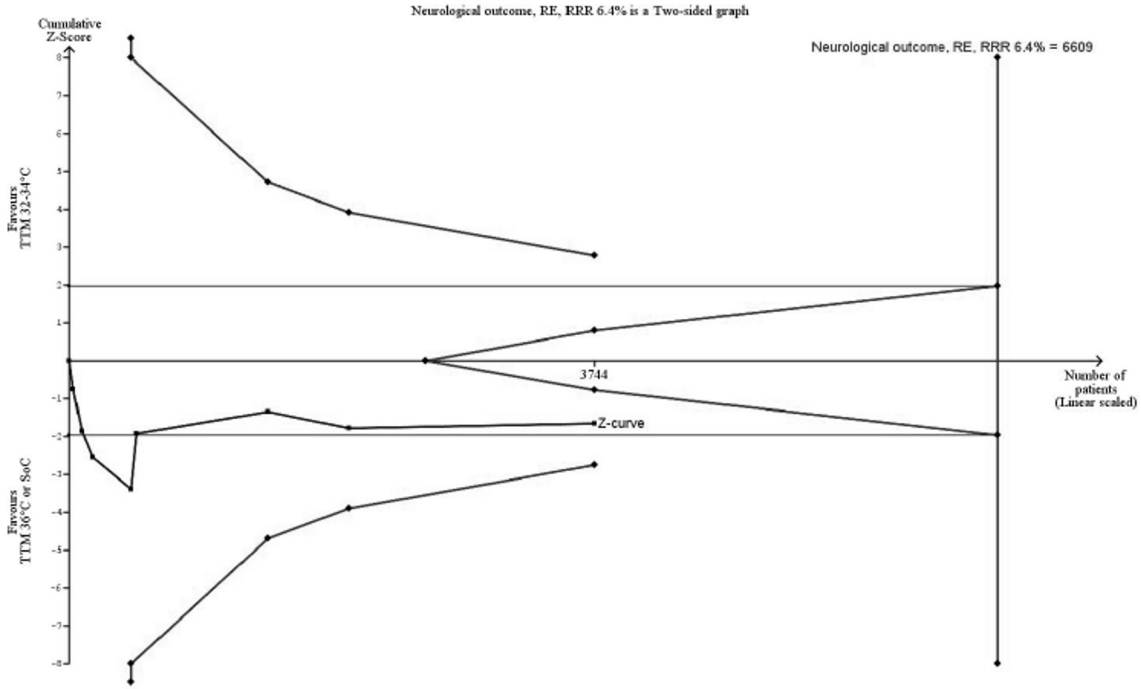
Trials sequential analysis

Neurological outcome



RE=random effect, RRR=Relative risk reduction.

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Conclusions

- ❖ In CA survivors admitted to hospital, the implementation of TTM with a target temperature of 32 - 34 °C:
- ✓ does not improve survival nor neurological outcome
- ✓ it increases the risk of arrhythmias

- ❖ For survival, robust evidence and no more studies are needed.
- ❖ For neurological outcome current evidence is not robust enough - thus new research is needed.

- ❖ Approaching temperature management with“uncontrolled” normothermia may be associated with worse outcomes and this should not be considered an option nowadays.

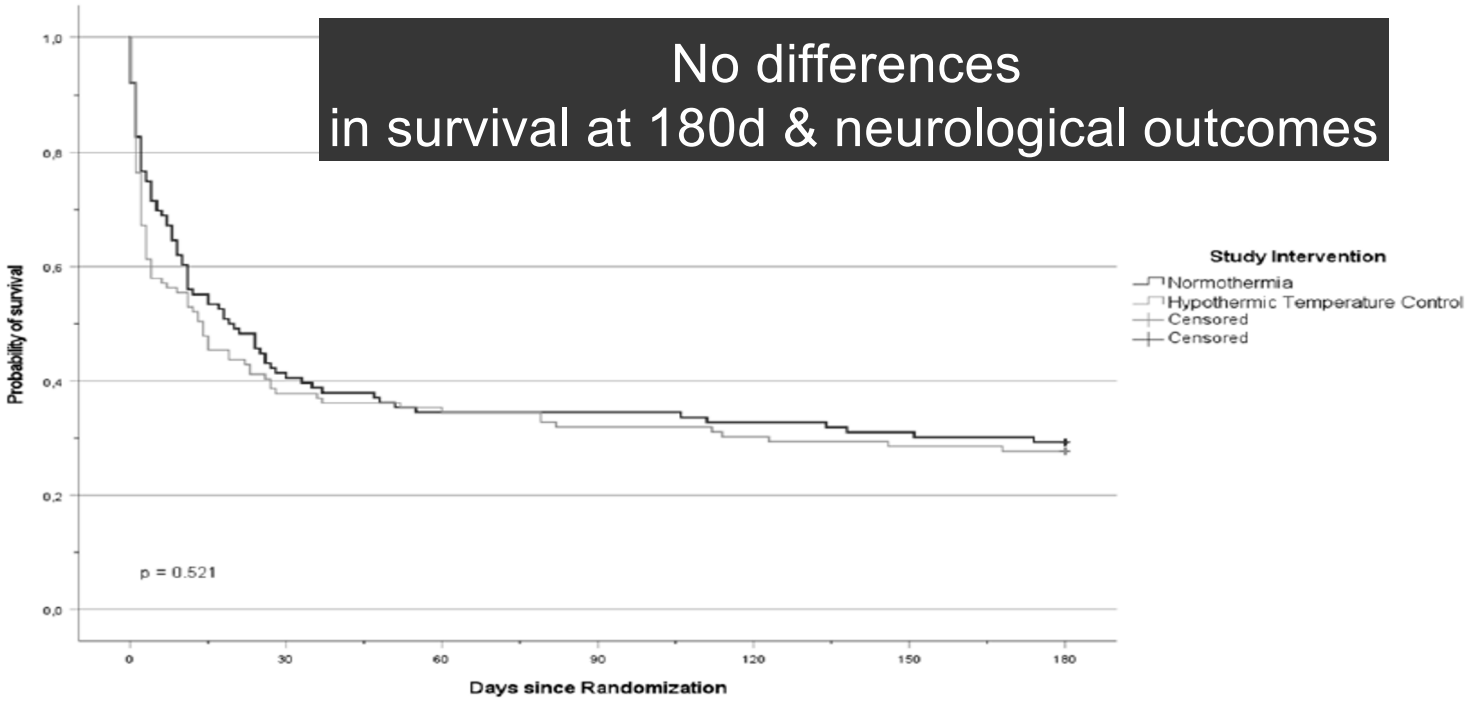
ORIGINAL RESEARCH ARTICLE

Temperature Control After In-Hospital Cardiac Arrest: A Randomized Clinical Trial

Sebastian Wolfrum, MD*; Kevin Roedl, MD*; Alexia Hanebutte, MD; Rüdiger Pfeifer, MD; Volkhard Kurowski, MD; Reimer Riessen, MD; Anne Daubmann, MSc; Stephan Braune, MD; Gerold Söffker, MD; Eric Bibiza-Freiwald, MSc; Karl Wegscheider, PhD; Heribert Schunkert, MD; Holger Thiele, MD*; Stefan Kluge, MD*; for the Hypothermia After In-Hospital Cardiac Arrest Study Group

Wolfrum S et al. Circulation 2022; 146:000-000

No differences
in survival at 180d & neurological outcomes



Patients at risk

Days	0	30	60	90	120	150	180
Hypothermic Temperature Control	120	45	32	38	36	34	33
Normothermia	118	48	40	40	38	36	34

The Care Consortium & STEPCARE trial

The STEPCARE trial is an international, multicenter, parallel group, noncommercial, randomized, factorial, superiority trial to include 3100 patients

1. Continuous sedation for 36 h or minimal sedation (SEDCARE)
2. Fever management with or without a TTM device for 72 h (TEMPCARE)
3. A mean arterial pressure target of > 85mmHg or > 65mmHg for 36 hours (MAPCARE)

Follow-up will be performed at 30 days and 6 months after cardiac arrest including mortality, functional outcome and quality of life

1. Detailed cognitive outcome with focus on patients and caregivers
2. Prognostication to identify and validate early and accurate instruments and algorithm
3. Biobank with blood samples at 0, 24, 48, and 72 hours after the cardiac arrest