



Hjertestarterdagen

Præsentation fra
Hjertestartermødet
16. oktober 2014
Righospitalet, København

Præsentationen er venligst leveret af foredragsholderen.
Indholdet er intenderet til uddannelse og kan indeholde
holdninger som ikke nødvendigvis deles af
Dansk Råd for Genoplivning



Dansk Råd for Genoplivning

TrygFonden

Moderne hospitalsbehandling efter hjertestop

Christian Hassager, RH



CENTER FOR HJERTESTOP
I ØRESUNDSREGIONEN



DEN EUROPÆISKE
UNION
Den Europæiske
Fond for
Regionaludvikling



Interreg IVA

ØRESUND - KATTEGAT - SKAGERRAK

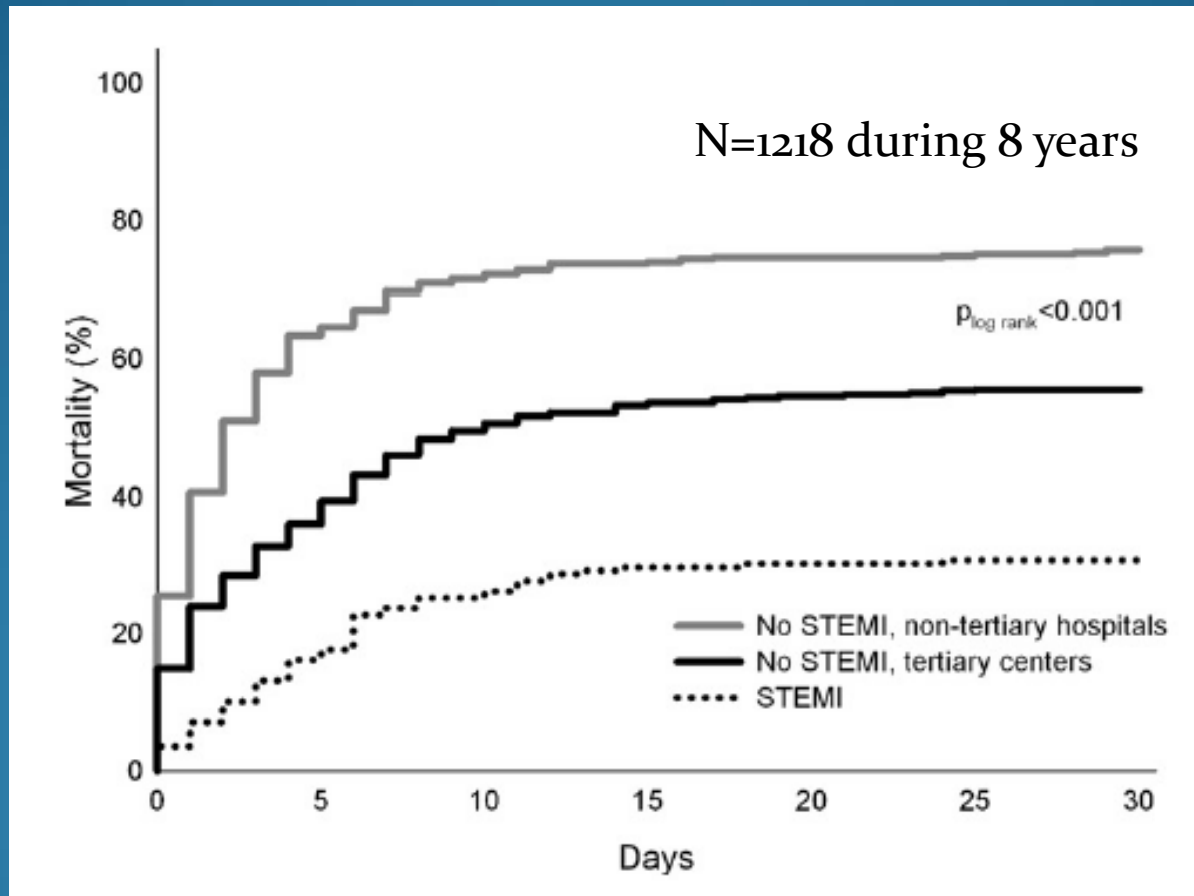
Moderne hospitalsbehandling efter hjertestop

- Evidensbaseret? Njaøee.....
- Vi ved alt for lidt

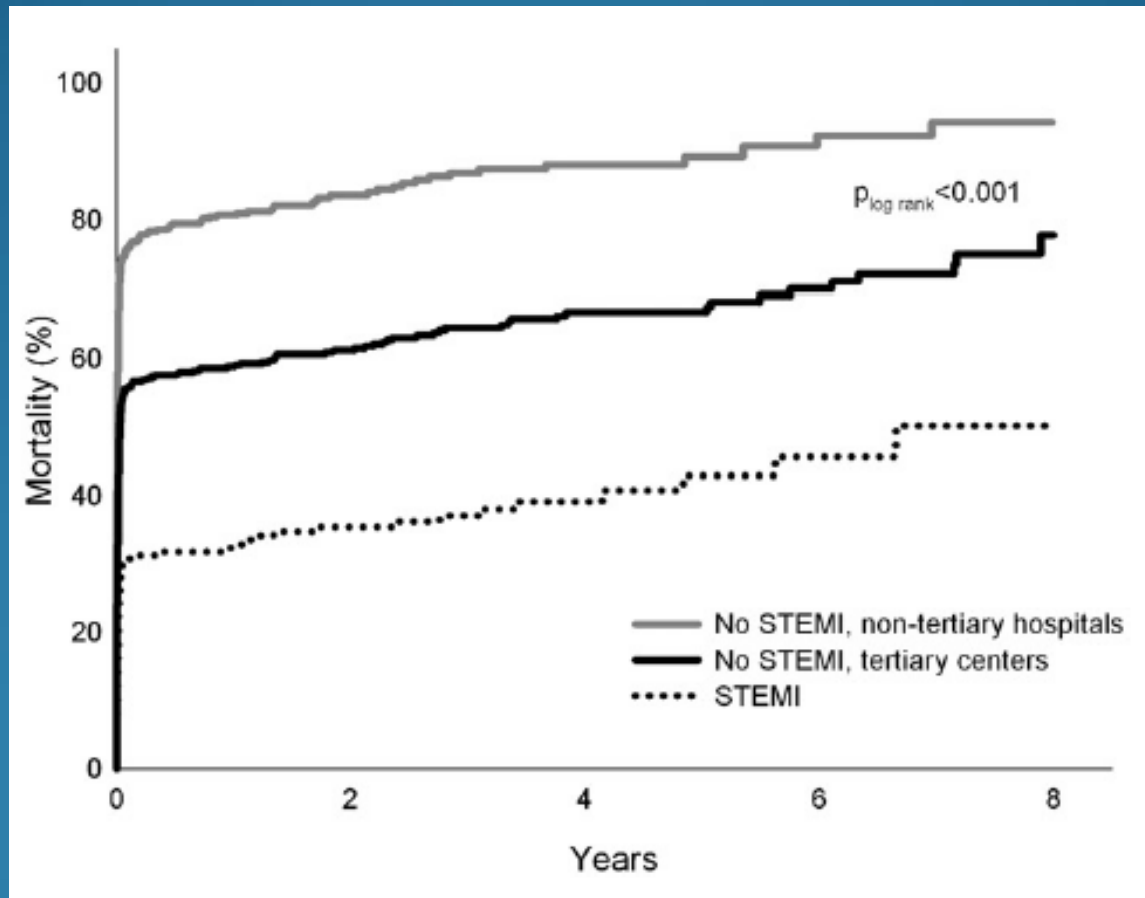
Hvad gør vi så....

- Sikre respiration
- Sikre perfusion
- Sikre homeostase iøvrigt
- Eventuelt antibiotika behandling
- Køler dem lidt ned
- Og ser hvad der sker.....

Tertiary centers or not for OHCA?

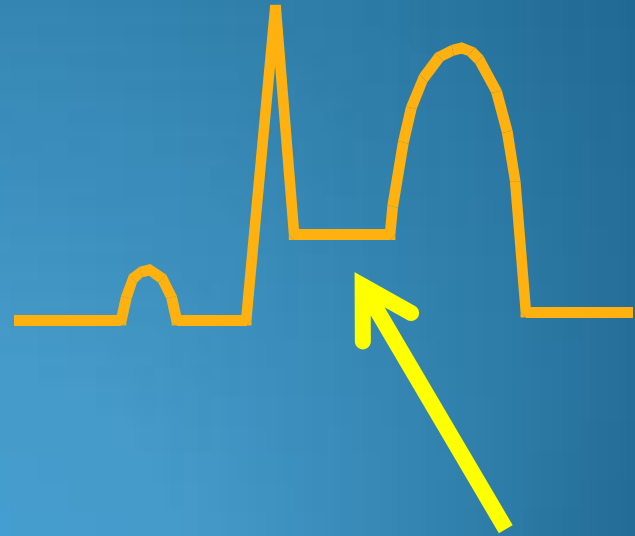


Tertiary centers or not for OHCA?

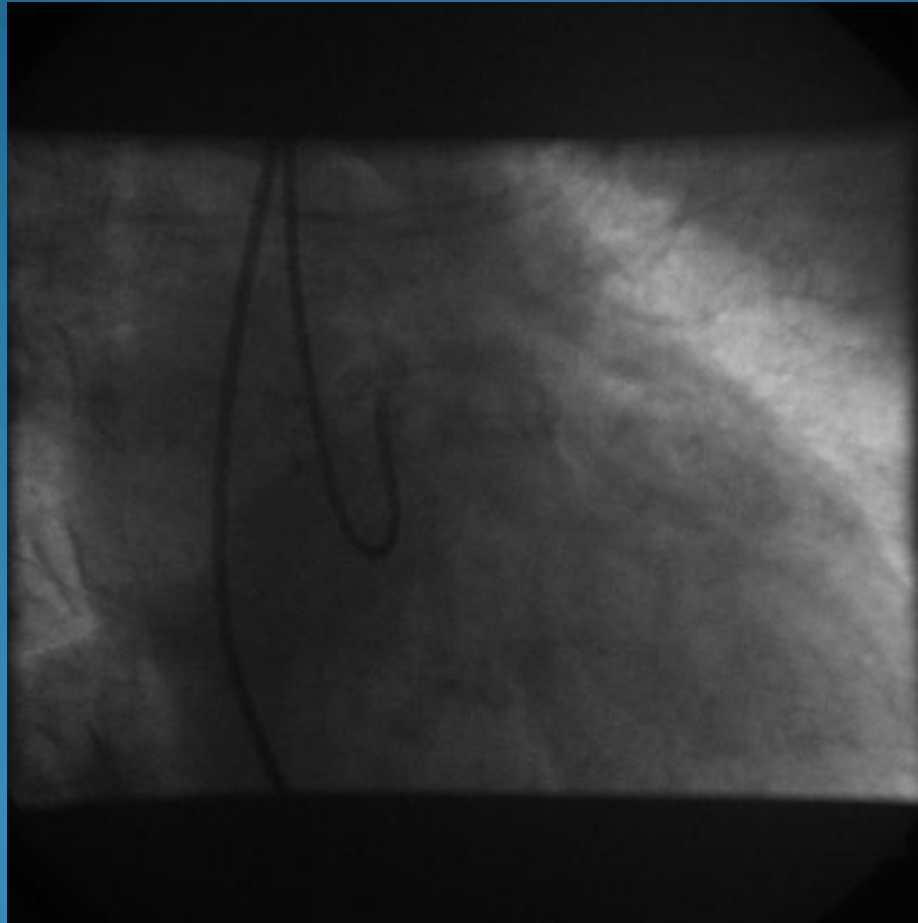


EKG lige efter hjertestop

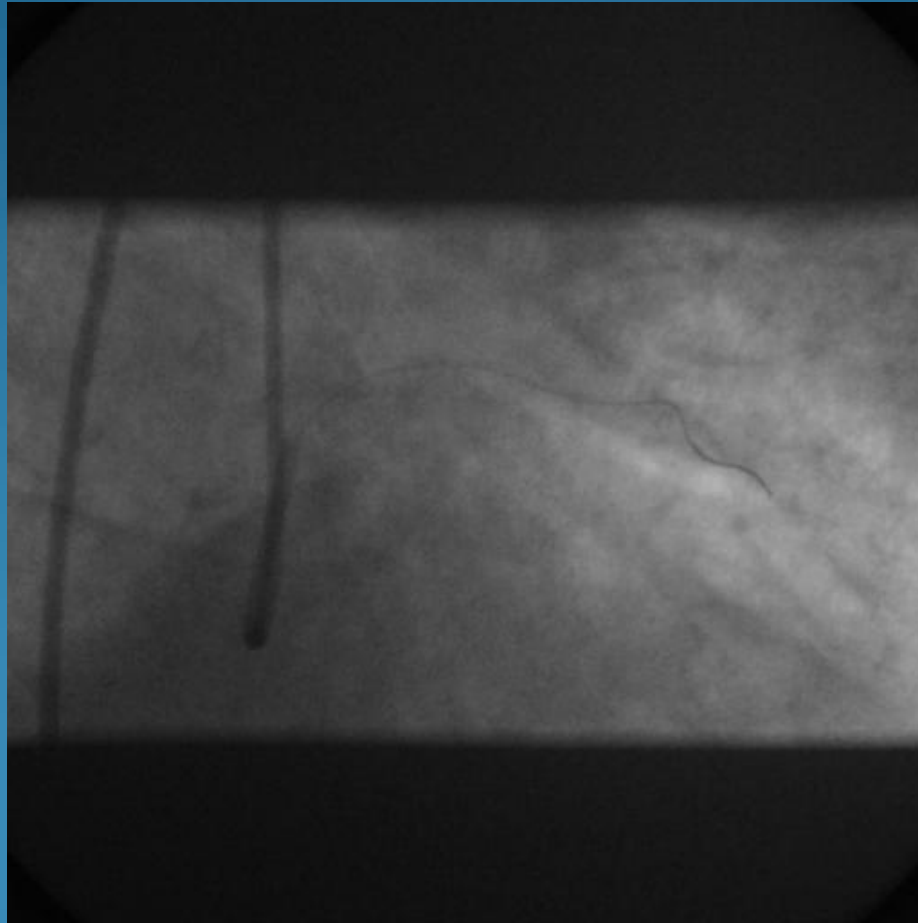
- STEMI
- NSTEMI



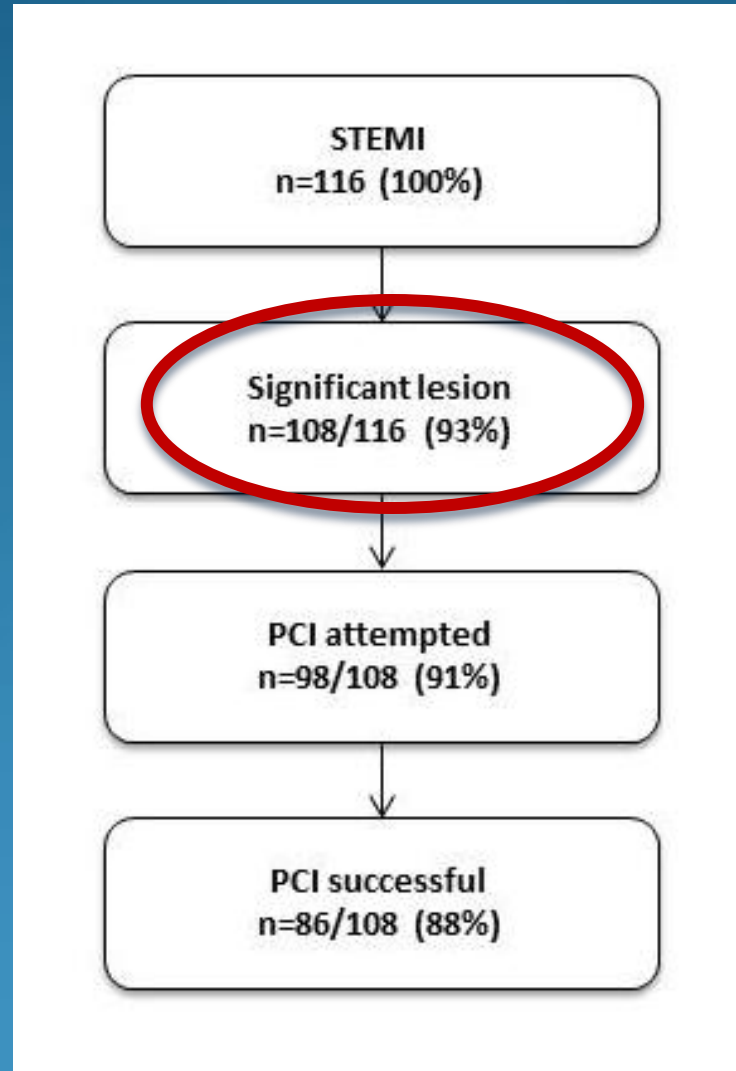
Før PCI



After PCI



CAD in OCHA – RH experience



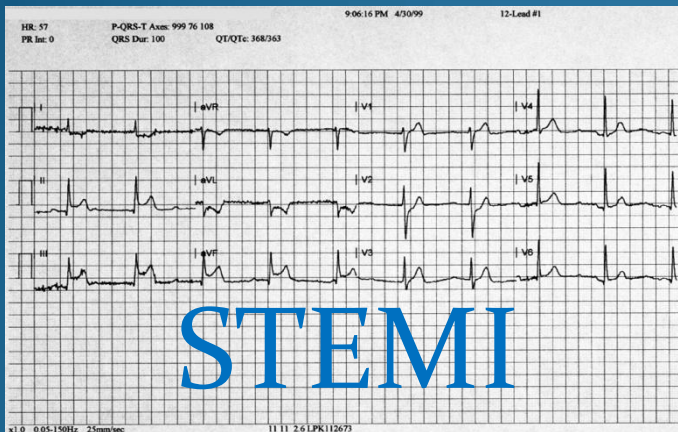
Emergency CAG
Without STEMI

$$43/82 = 52\%$$

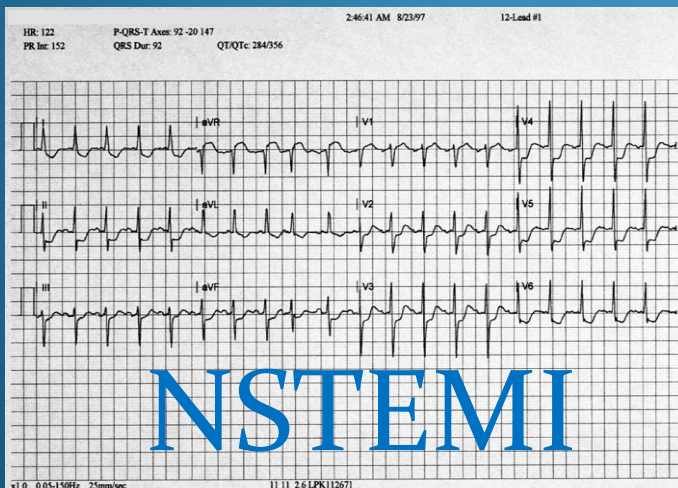
PCI successful

$$15/82 = 18\%$$

EKG gentages på hospital



Akut PCI



Subakut PCI

Dødsårsagen hos patienter der er kølebehandlet efter hjertestop

N=310
hypotermibehandlede
OHCA-patienter
Dødelighed 34%

Hjerne : 85%



Out of Hospital Cardiac Arrest (OHCA)

- Mere end 2/3 dør af hjerneskode
 - Neuron necrosis
 - Apoptosis
 - Timer til dage....

Post cardiac arrest syndrome

- “Sepsis-like syndrome”
- Øget cerebral vascular resistance
- Nedsat Cerebral Blood Flow
- Kramper øger den cerebrale metabolisme op til 3 gange

Komatøse overlevende efter hjertestop

Randomiserede placebo kontrollerede studier

Sedation/ krampe control (Thiopental, Diazepam)

NEJM 1986;31:397-403 and Neurology 2002;59:506-514

Calcium entry blocker (Lidoflazine)

NEJM 1991; 324: 1225-31

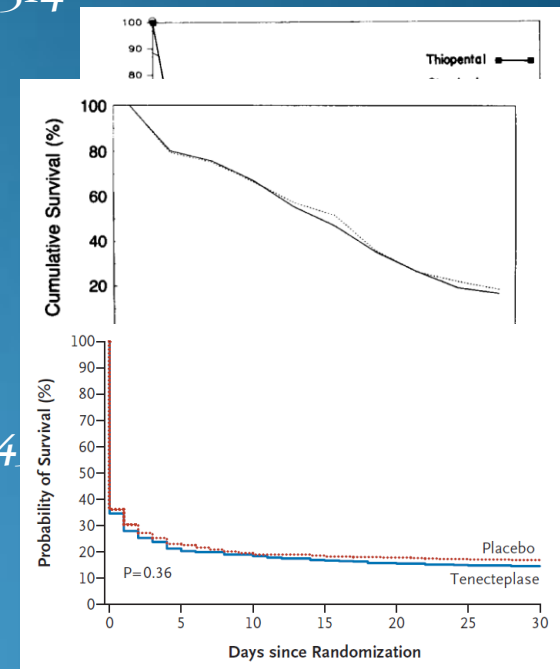
Calcium antagonist (Nimodipine)

Forsman M et al. Anesth Analg 1989; 68:4

Roine RO et al. JAMA 1990; 264:3171-3177

Trombolyse (Tenecteplase)

Böttiger BW et al. NEJM 2008;359:2651-62



ORIGINAL INVESTIGATION

Hyperthermia After Cardiac Arrest Is Associated With an Unfavorable Neurologic Outcome

Andrea Zeiner, MD; Michael Holzer, MD; Fritz Sterz, MD; Waltraud Schörkhuber, MD; Philip Eisenburger, MD; Christof Havel, MD; Andreas Kliegel, MD; Anton N. Laggner, MD

Arch Intern Med. 2001;161:2007-2012

OR = 2,3 per degree above 37° C

Accidentiel hypothermi virker!

- N=7 fundet med hjertestop i 2° C vand
- Kærne temperatur: 16-20 ° C
- Tid til EMS: 108 – 168 min
- Varighed af HLR: 56 – 125 min
- Tid til ECMO: 178 – 233 min

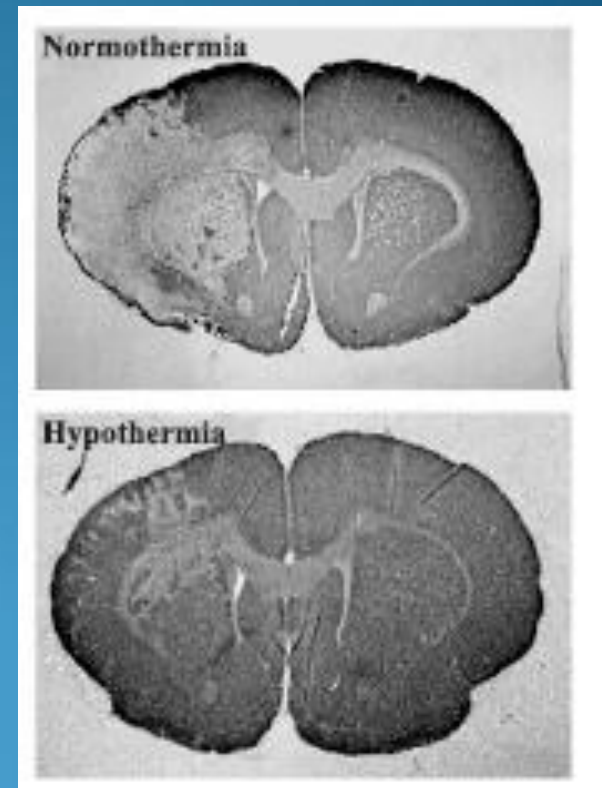


Improved Cerebral Resuscitation From Cardiac Arrest in Dogs With Mild Hypothermia Plus Blood Flow Promotion

Safar P et al. Stroke 1996;27:105-113

<i>FINAL OPC</i> at 96 hours	<i>GROUP 1</i> controls	<i>GROUP 2</i> mild hypothermia plus CBF promotion
5 BRAIN DEATH		
4 COMA	0 0 0 0 0 0	
3 SEVERE DISABILITY	0 0	0
2 MODERATE DISABILITY		0
1 NORMAL		0 0 0 0 0 0

p < 0.001



2002

The New England
Journal of Medicine

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MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC
OUTCOME AFTER CARDIAC ARREST

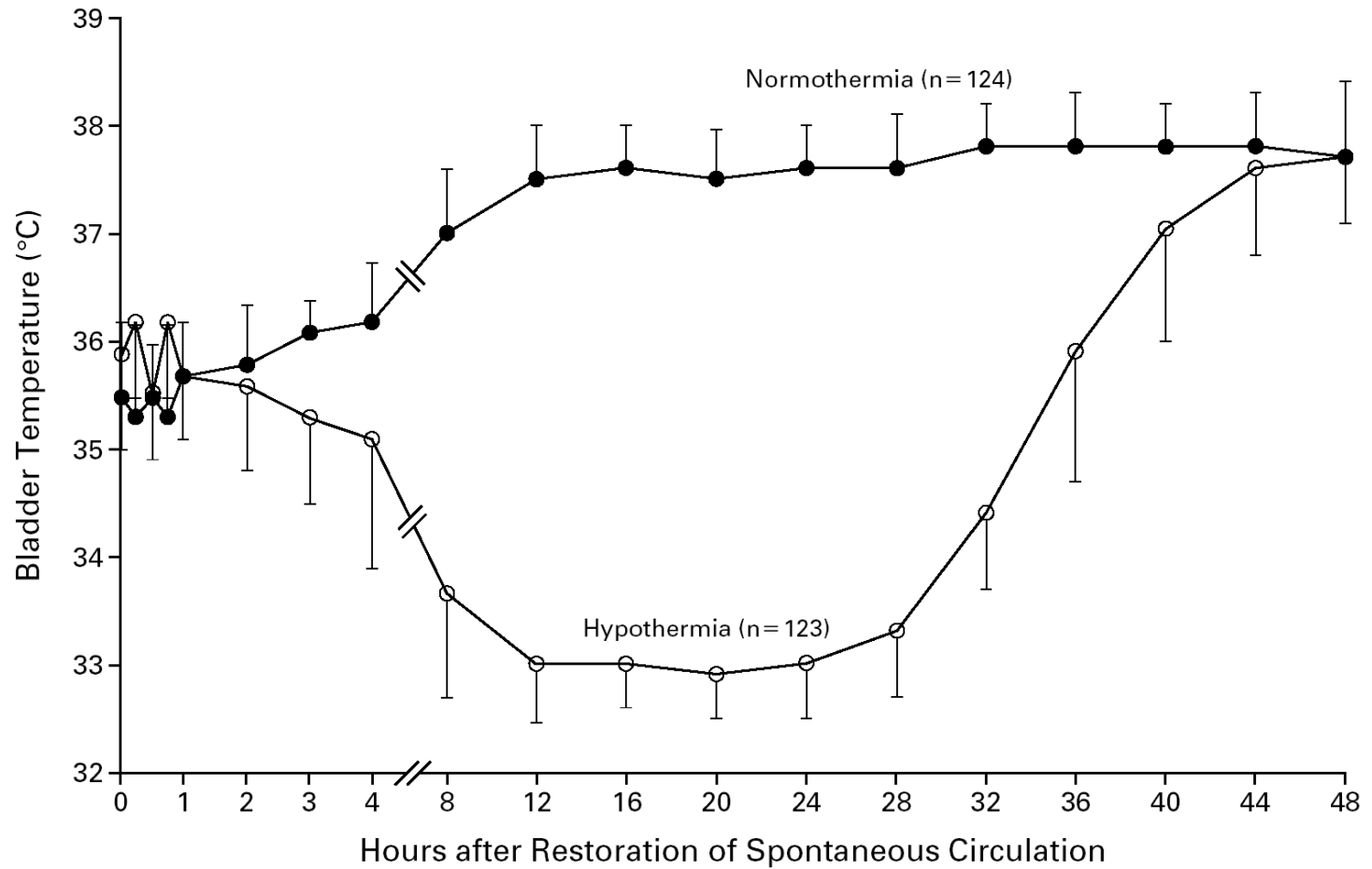
THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

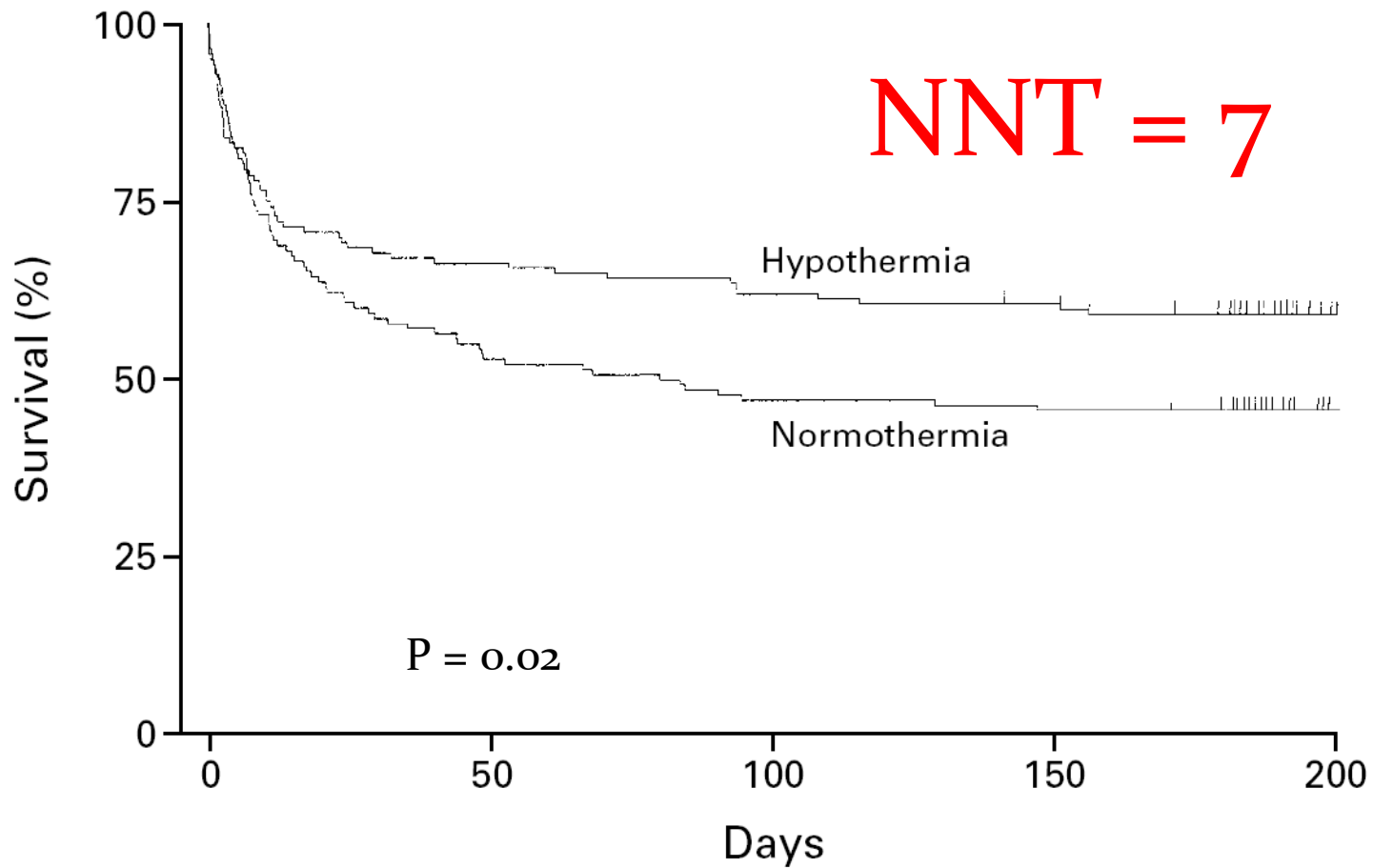
N=275

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=77

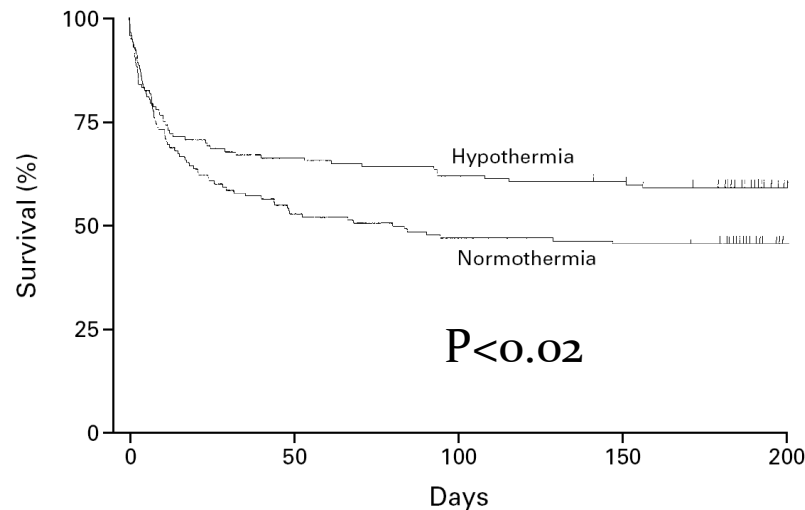




No. AT RISK

Hypothermia	137	92	86	83	11
Normothermia	138	74	66	64	9

No further discussion?



No. AT Risk

Hypothermia	137	92	86	83	11
Normothermia	138	74	66	64	9

- Åbent studie
- Stop før tid

The study was carried out between March 1996 and January 2001. Since the enrollment rate was lower than expected and funding had ended by July 2000, enrollment was stopped at this date.

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.,
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On the basis of our previous study,¹⁶ it was determined that a sample of 62 patients (31 in each group) would be required to show a change in the rate of a good outcome (discharge to home or to a rehabilitation facility) from 14 percent to 50 percent, with a power of 80 percent and a significance level of 0.05. An analysis of results from 62 eligible patients found that the outcome in the control group was better than our previously published rate,¹⁶ but that there was a strong trend toward improved outcome in the hypothermia group. The study was continued for a further 12 months, at which time 84 patients had been eligible for enrollment, 77 had been enrolled, and 72 had been treated according to the correct treatment assignment.

Ved udskrivelse...

- "Good result"

- Hypothermia 49%

- Normothermia 26%

$p < 0.05$

- Død

- Hypothermia 51%

- Normothermia 68%

NS

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

Summary: ILCOR Recommendations

On the basis of the published evidence to date, the ILCOR ALS Task Force has made the following recommendations:

- 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 VF.
- Such cooling may also be beneficial for other rhythms or in-hospital cardiac arrest.

(Circulation. 2003;108:118-121.)

Stor industri



Unparalleled Thermodynamics for Achieving Therapeutic Hypothermia

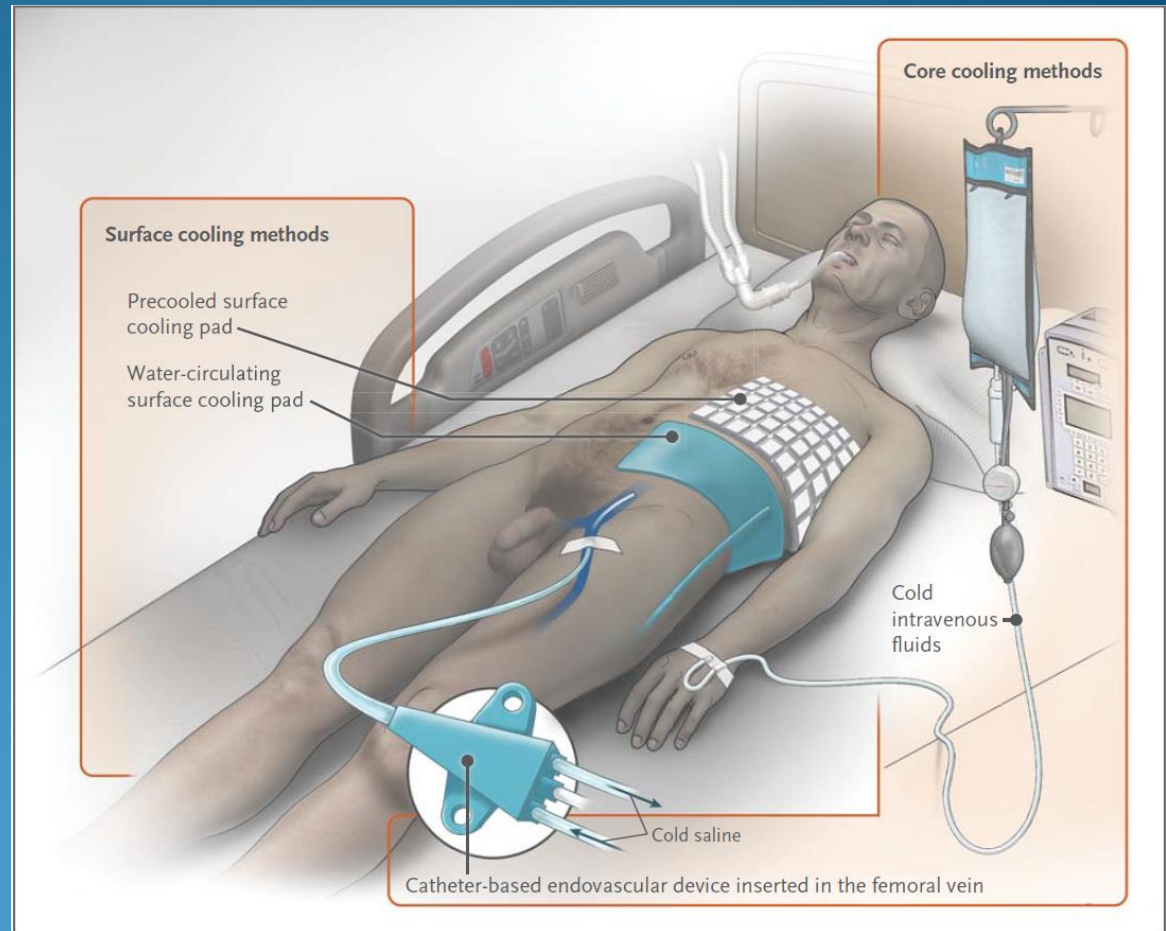
Velomedix Catheter in Peritoneal Cavity

Dialysis Catheter in Peritoneal Cavity

- Large surface area
- Access to core organs
- Access to ~50% of blood flow

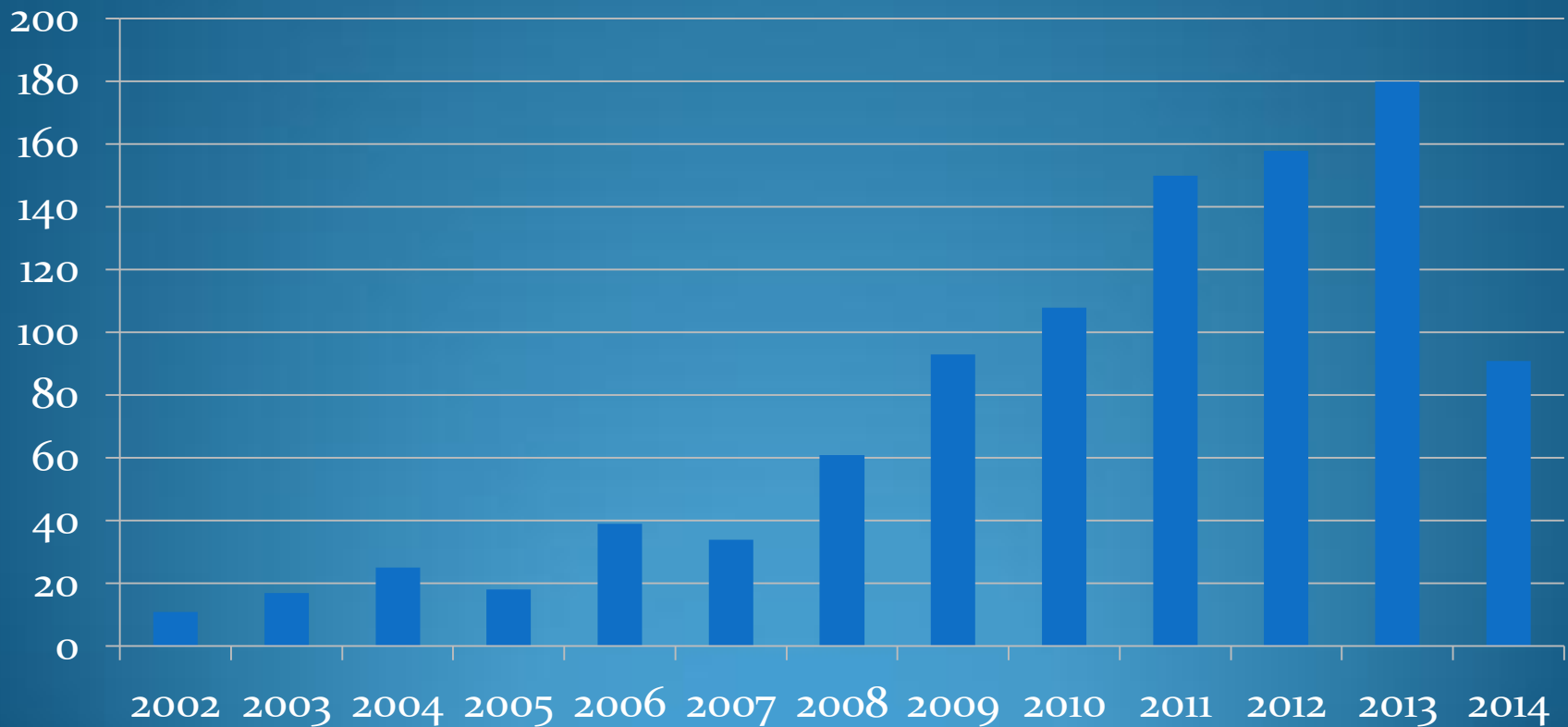
The diagram shows a cross-section of the human torso with a dialysis catheter inserted into the peritoneal cavity. Labels include: Bag containing dialysis solution, Internal organs, Disconnect tubing, Peritoneal catheter, Peritoneal cavity, and Drain line.

Kølestrategier

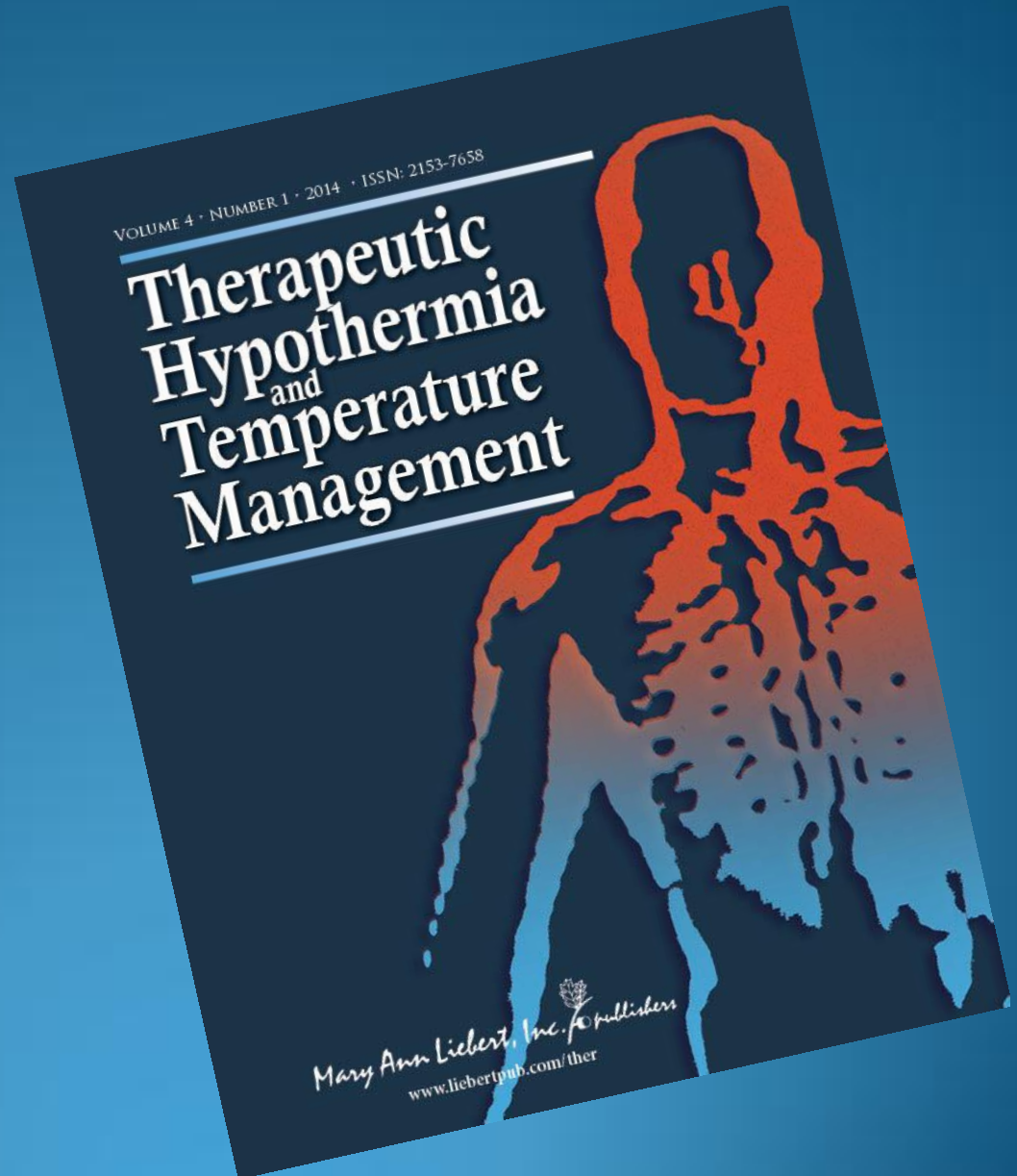


Publikationer med "Therapeutic Hypothermia" I titlen - PUBMED

Antal



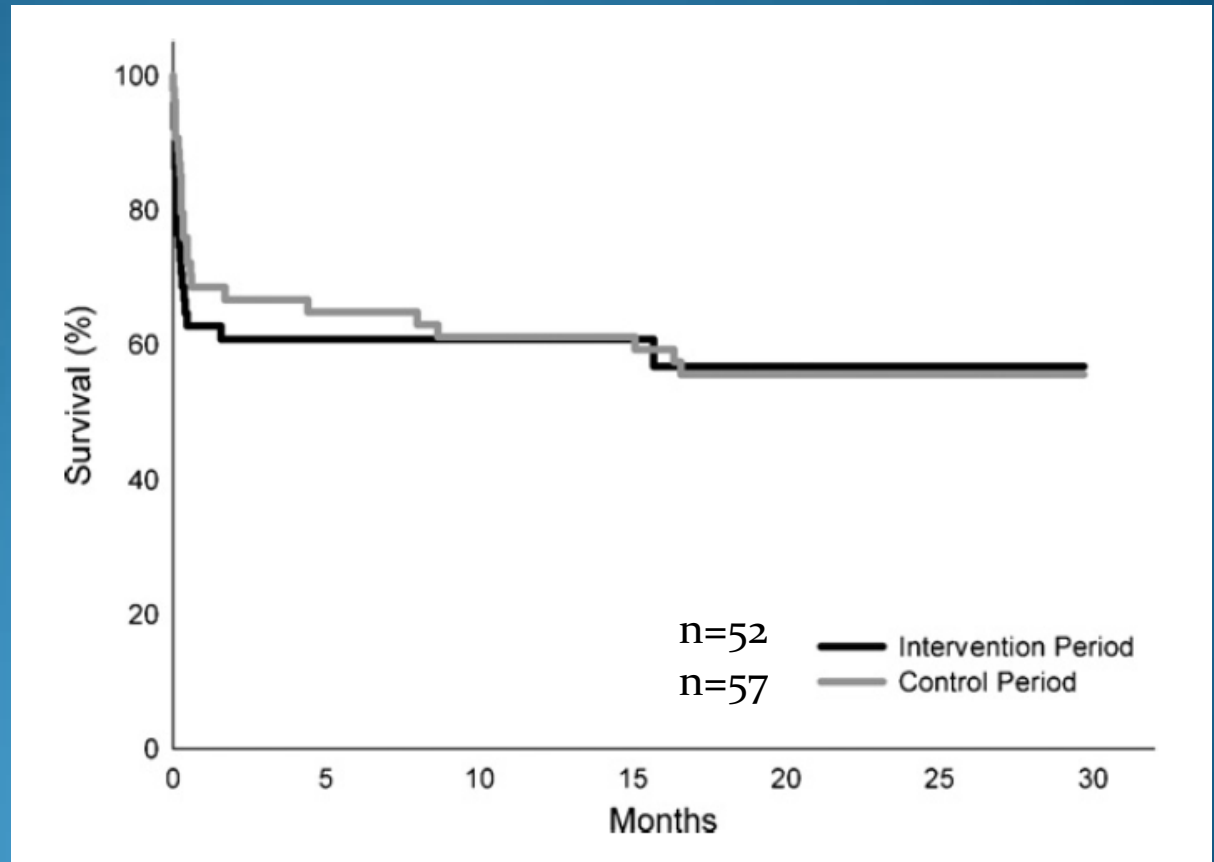
Tidskrift



*“Når du først har anekdoten,
kan du smide data ud”*

Psykologiprofessor Richard Nisbett , University of Michigan

Første RH erfaring

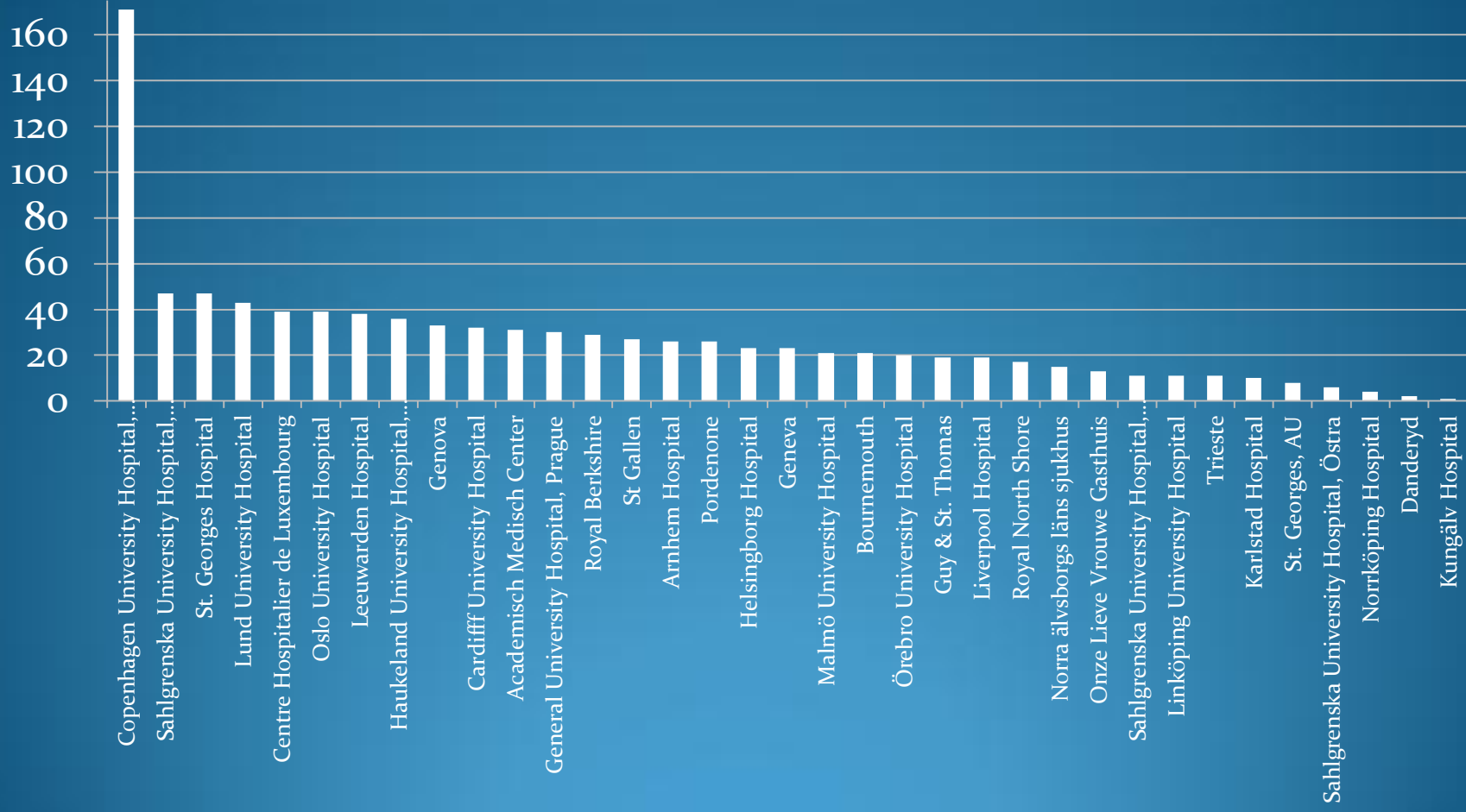


- Hypotermi anbefales i guidelines
- Evidensen er tynd
- Optimal target temperatur er ukendt

ORIGINAL ARTICLE

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

Niklas Nielsen, M.D., Ph.D., Jørn Wetterslev, M.D., Ph.D., Tobias Cronberg, M.D., Ph.D.,
David Erlinge, M.D., Ph.D., Yvan Gasche, M.D., Christian Hassager, M.D., D.M.Sci.,
Janneke Horn, M.D., Ph.D., Jan Hovdenes, M.D., Ph.D.,
Jesper Kjaergaard, M.D., D.M.Sci., Michael Kuiper, M.D., Ph.D., Tommaso Pellis, M.D.,
Pascal Stammer, M.D., Michael Wanscher, M.D., Ph.D., Matt P. Wise, M.D., D.Phil.,
Anders Åneman, M.D., Ph.D., Nawaf Al-Subaie, M.D.,
Søren Boesgaard, M.D., D.M.Sci., John Bro-Jeppesen, M.D., Iole Brunetti, M.D.,
Jan Frederik Bugge, M.D., Ph.D., Christopher D. Hingston, M.D.,
Nicole P. Juffermans, M.D., Ph.D., Matty Koopmans, R.N., M.Sc.,
Lars Køber, M.D., D.M.Sci., Jørund Langørgen, M.D., Gisela Lilja, O.T.,
Jacob Eifer Møller, M.D., D.M.Sci., Malin Rundgren, M.D., Ph.D.,
Christian Rylander, M.D., Ph.D., Ondrej Smid, M.D., Christophe Werer, M.D.,
Per Winkel, M.D., D.M.Sci., and Hans Friberg, M.D., Ph.D.,
for the TTM Trial Investigators*



Main objective

- To assess the benefits and harms of a targeted temperature management at 33°C versus 36°C
- Avoiding fever in post-cardiac arrest patients in both groups

TTM-trial – 2010-2013

- 950 patienter blev randomiseret
- 36 hospitals
- 10 countries
- Europe and Australia



Funded by:

Swedish Heart Lung Foundation

AFA-insurance Foundation, Sweden

Swedish Research Council

Governmental and Regional funding within the Swedish National Health System

Tryg Foundation, Denmark

Zoega, Krapperup, Thure Carlsson, Trolle-Wachtmeister foundations, Sweden

Inklussions kriterier

- Hjertestop opstået uden for hospital
- ≥ 18 år
- Formodet kardiell årsag
- Alle hjerterytmier
- Bevidstløs (GCS <8)
- Stabil ROSC

Ekklussions kriterier

- Ubevidnet asystoli
- >240 minutter fra ROSC
- $T_p < 30^{\circ}\text{C}$
- Kendt eller mistænkt intracranial blødning og apoplexi

Inclusion 240 min

Prognostication

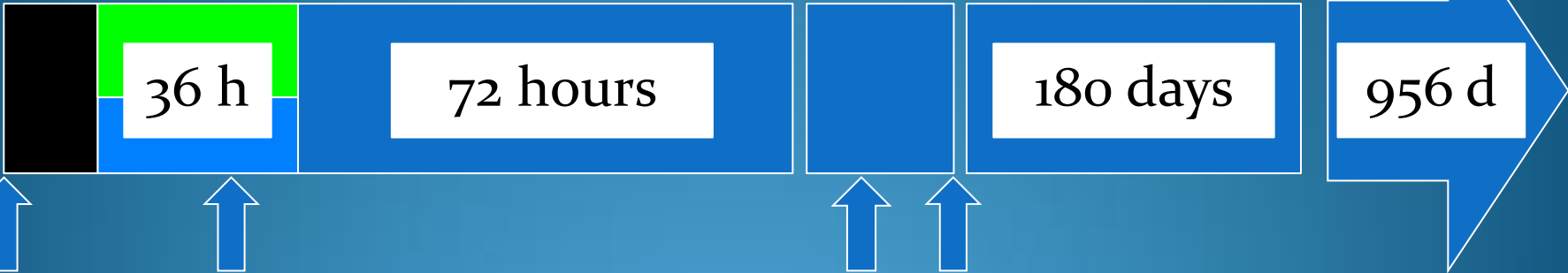
Half year follow up



ROSC

Intervention

ICU, hospital discharge

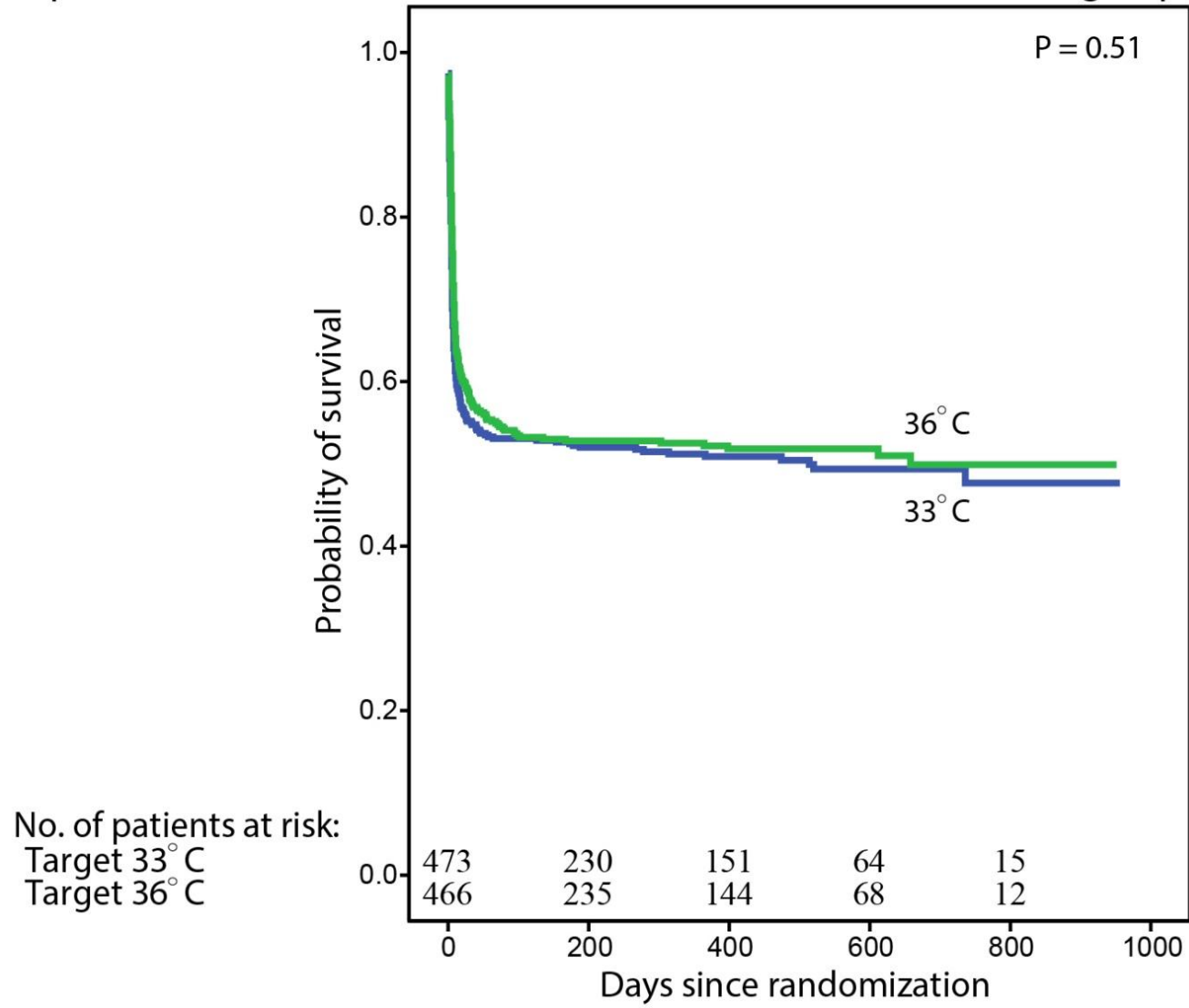


- **Primært outcome:** Overlevelse
- **Sekundært outcomes:** Død og neurologisk status ved 180 dage
 - ✓ Cerebral Performance Category
 - ✓ Modified Rankin Scale
- Serious adverse events

Baseline data

	33°C	36°C
No.	473	466
Age	64+/-12	64+/-13
Male sex	83 %	79 %
Arrest in place of residence	52 %	55 %
Arrest in public place	42 %	40 %
Bystander witnessed	89 %	90 %
Bystander CPR	73 %	73 %
Shockable rhythm	79 %	81 %
Arrest to ROSC (min)	25 [18-40]	25 [16-40]
Lactate mmol/L	6.7±4.5	6.7±4.5
ST-elevation infarction	40 %	42 %
GCS	3 [3-4]	3 [3-4]

Kaplan-Meier estimates for time to death in TTM-trial intervention groups



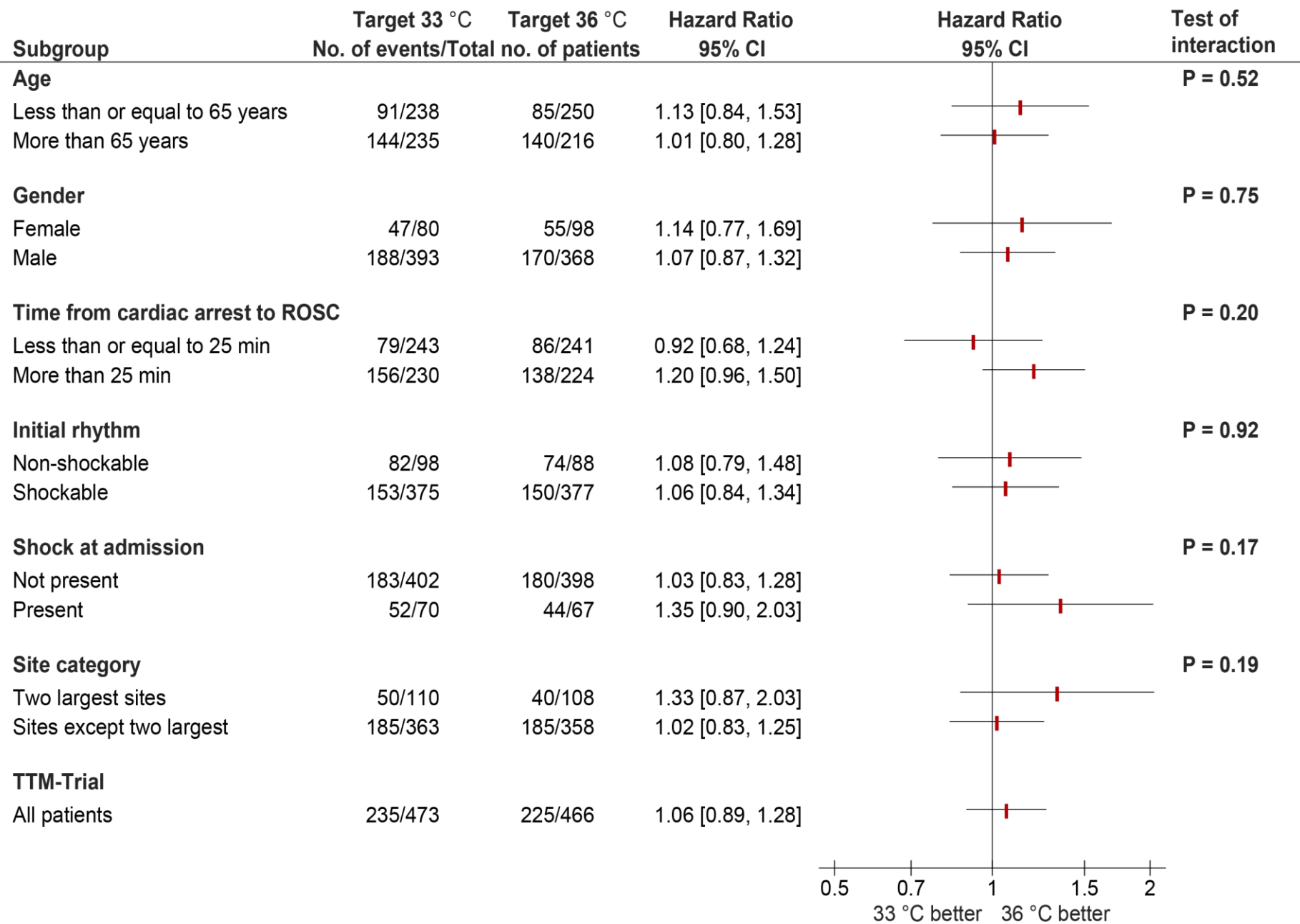
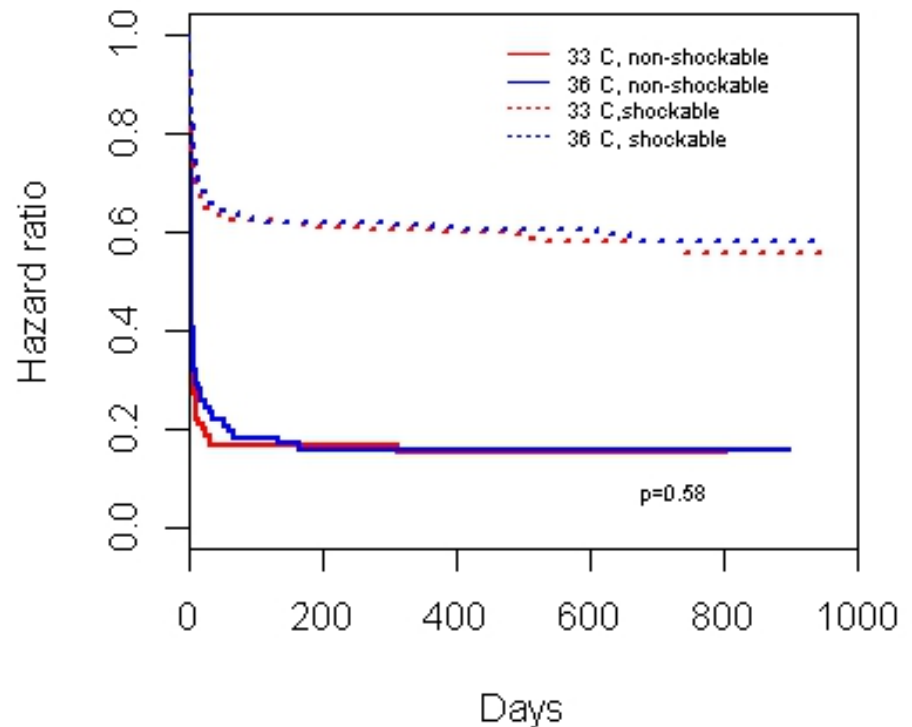
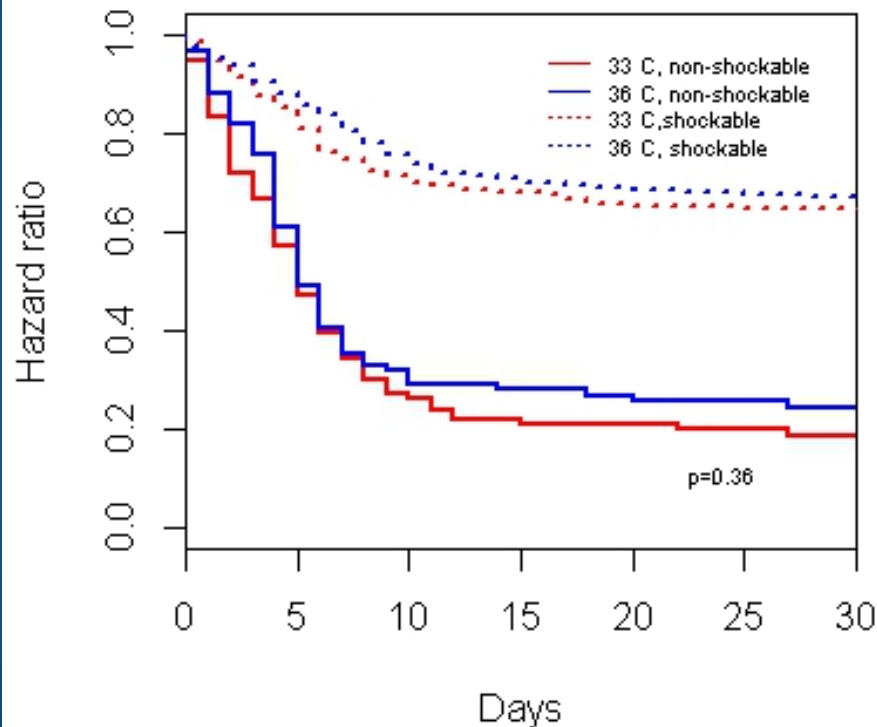


Figure 3

Stødbar vs ikke-stødbar rytme

A

B

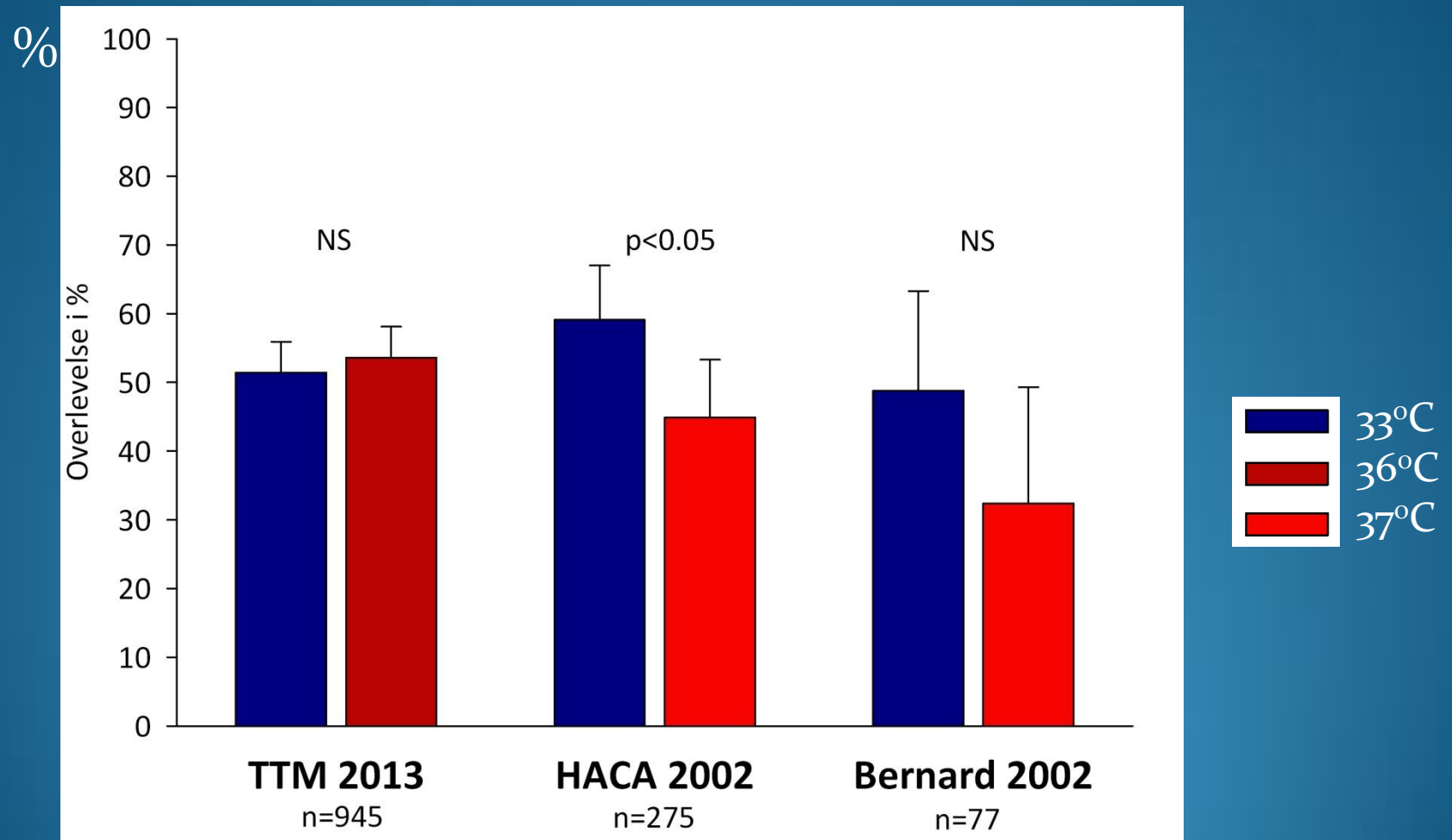


Outcome	TTM33	TTM36	HR or RR (95% CI)	P Value
PRIMARY OUTCOME				
Mortality at the end of trial			100% follow-up	
Dead no./total no. (%)	235/473 (50)	225/466 (48)	HR=1.06 (0.89-1.28)	0.51
SECONDARY OUTCOMES				
Neurological function at follow-up			99% follow-up	
CPC 3-5–no./total no. (%)	252/469 (54)	242/464 (52)	RR=1.02 (0.88-1.16)	0.78
mRS 4-6–no./total no. (%)	245/469 (52)	239/464 (52)	RR=1.01 (0.89-1.14)	0.87
Serious adverse events				
Any event–no./total no. (%)	439/472 (93)	417/464 (90)	RR=1.03 (1.00-1.08)	0.09

Konklussion fra TTM studiet

$$33^{\circ}\text{C} = 36^{\circ}\text{C}$$

Overlevelse

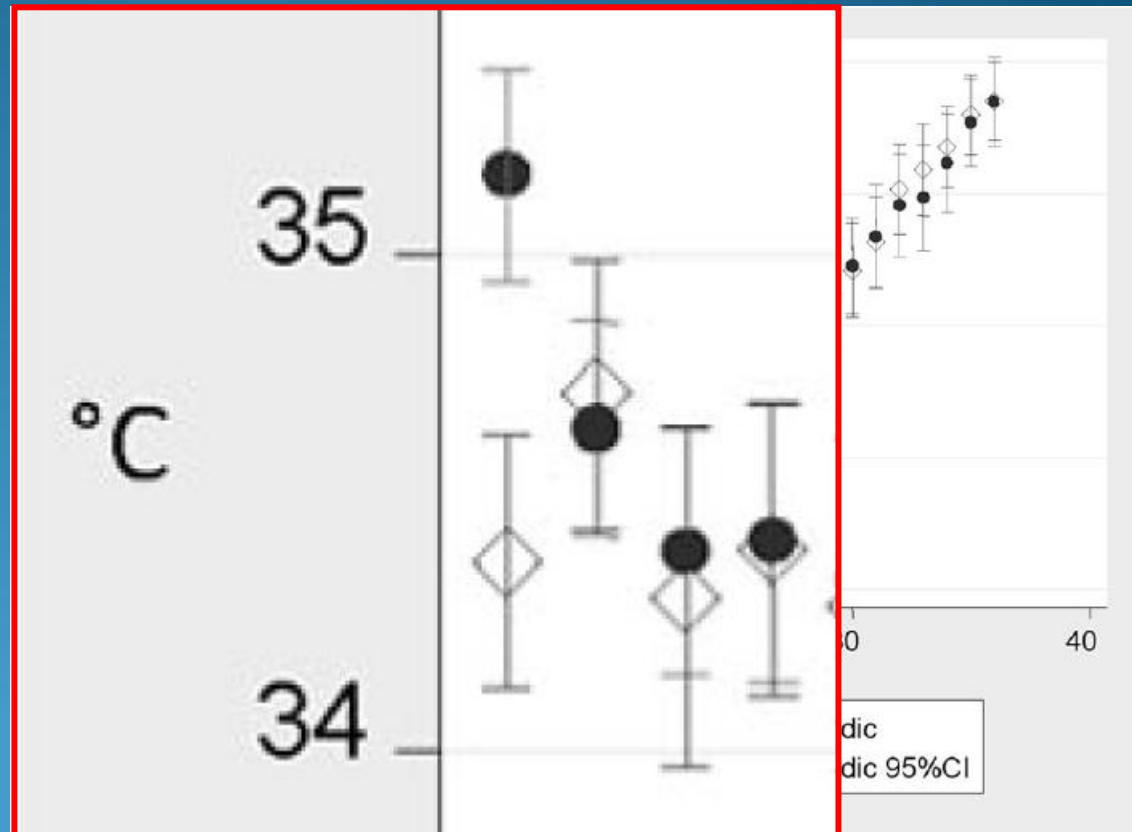


Præhospita Kølning?

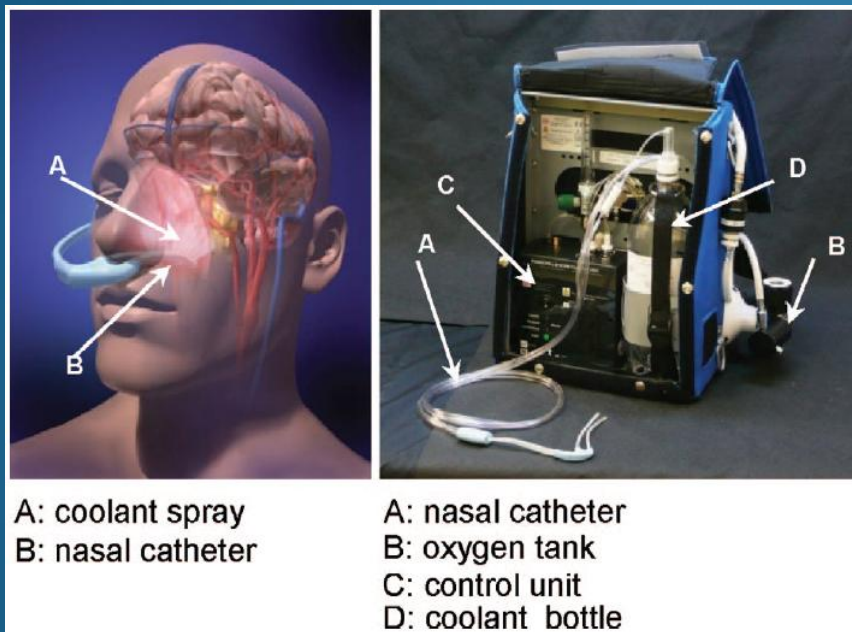
Mortalitet

Præhospita køling
 $62/118=53\%$

Hospita køling
 $54/116=47\%$



Intra-arrest cooling (RhinoChill)



N=200

Overlevelse til
udskrivelse:

Normotermia 13%

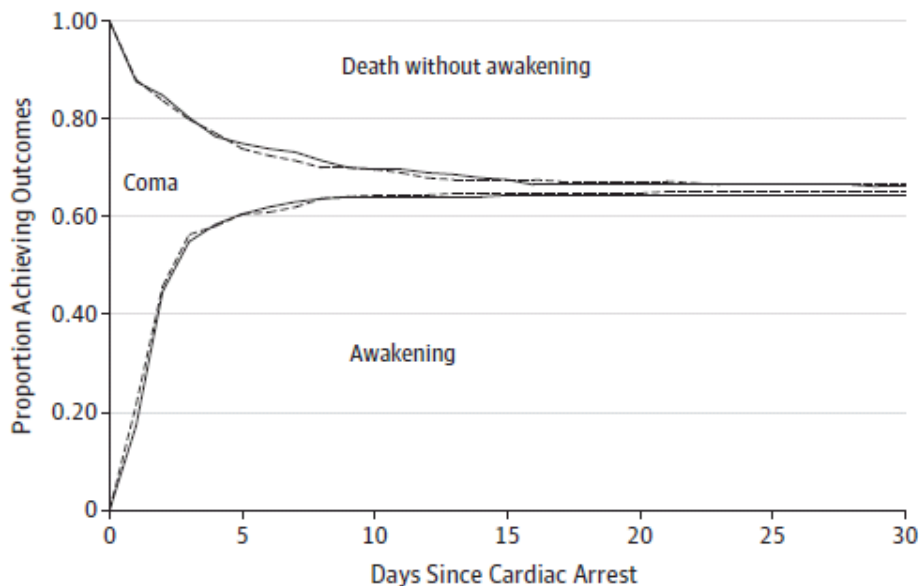
Hypotermia 15%

Effect of Prehospital Induction of Mild Hypothermia on Survival and Neurological Status Among Adults With Cardiac Arrest

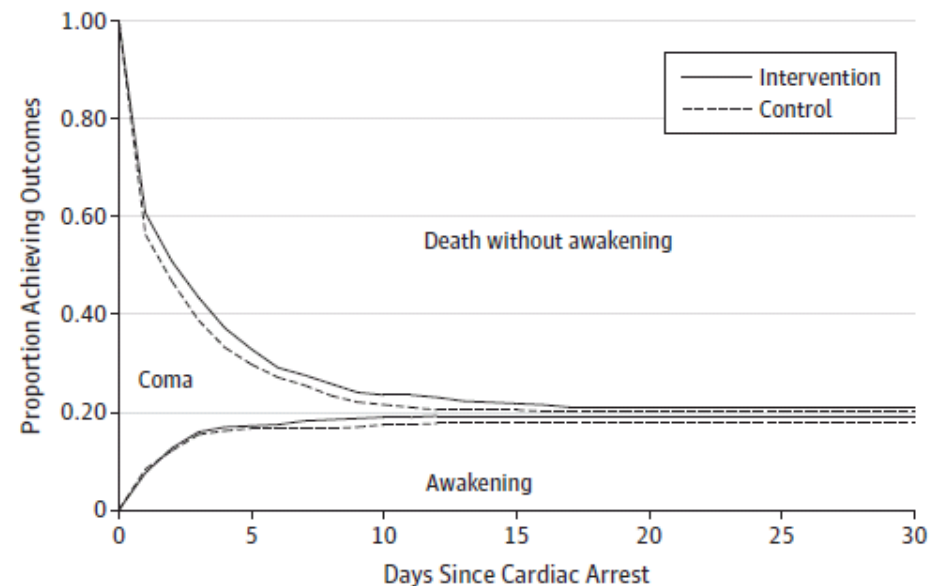
A Randomized Clinical Trial

Francis Kim, MD; Graham Nichol, MD, MPH; Charles Maynard, PhD; Al Hallstrom, PhD; Peter J. Kudenchuk, MD; Thomas Rea, MD, MPH; Michael K. Copass, MD; David Carlborn, MD; Steven Deem, MD; W. T. Longstreth Jr, MD; Michele Olsufka, RN; Leonard A. Cobb, MD

A With ventricular fibrillation



B Without ventricular fibrillation



N=1359.

Temp ved ankomst til hospital- 1.2° C

Table 3. Prehospital, Emergency Department, and In-Hospital Safety Data

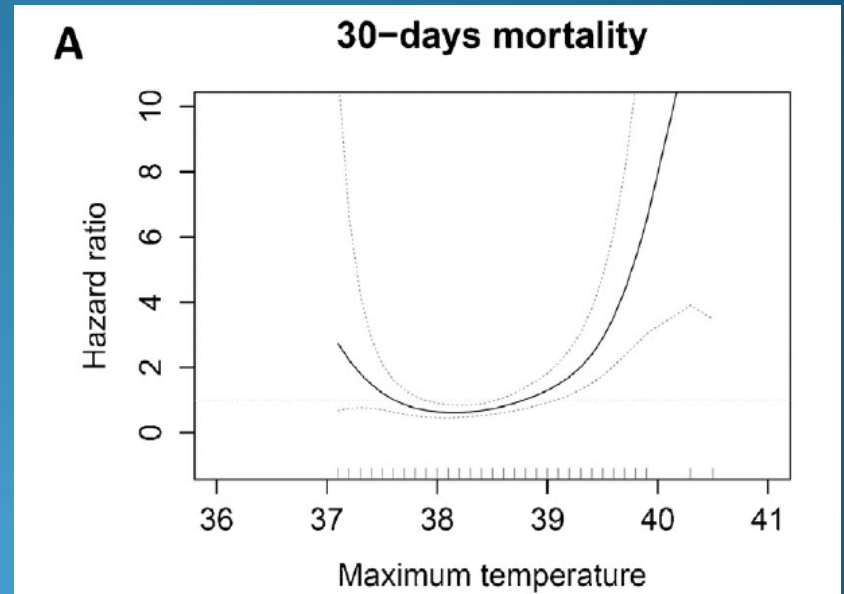
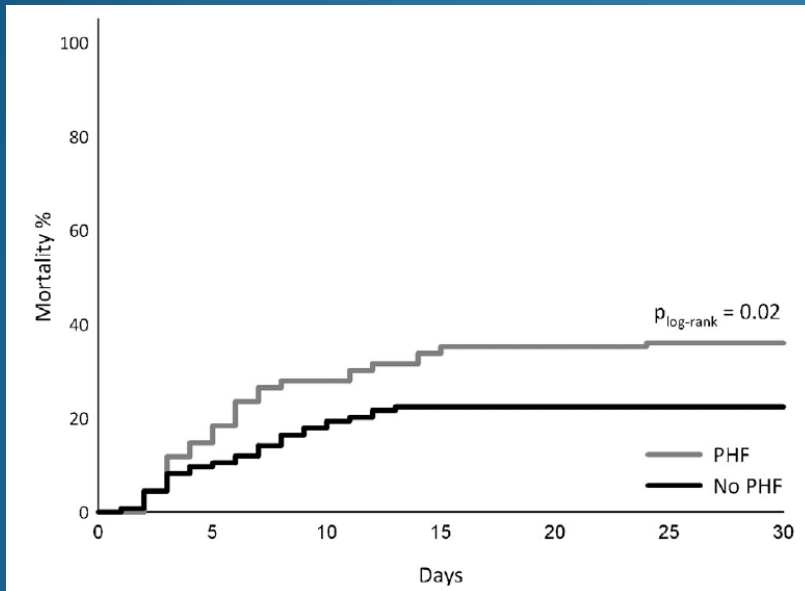
	Intervention	Control	P Value
Rearrest postrandomization ^a	(n = 686) 176 (26) [22 to 29]	(n = 671) 138 (21) [18 to 24]	.008
Use of pressors postrandomization ^a	(n = 686) 62 (9) [7 to 11]	(n = 671) 59 (9) [7 to 11]	.82
Prehospital deaths ^a	(n = 688) 9 (1.3) [0.7 to 2.5]	(n = 671) 11 (1.6) [0.9 to 2.5]	.61
Time from first dispatch to hospital arrival, min ^b	(n = 654) 51 (50 to 52) [13]	(n = 629) 49 (48 to 50) [14]	.006
First arterial blood gas			
pH ^b	(n = 612) 7.16 (7.14 to 7.18) [0.23]	(n = 590) 7.20 (7.18 to 7.22) [0.29]	.005
PaO ₂ , mm Hg ^b	(n = 609) 189 (178 to 200) [135]	(n = 585) 218 (206 to 230) [144]	<.001
Pulmonary edema			
First chest film ^a	(n = 631) 256 (41) [37 to 44]	(n = 609) 184 (30) [27 to 34]	<.001

CONCLUSION AND RELEVANCE Although use of prehospital cooling reduced core temperature by hospital arrival and reduced the time to reach a temperature of 34°C, it did not improve survival or neurological status among patients resuscitated from prehospital VF or those without VF.

Fortolknings muligheder

- 2002-studierne var forkerte. Køling virker ikke.
- TTM underpowered?
- TTM forkerte patienter?
- TTM for langsom nedkøling?
- TTM for hurtig opvarmning?
- Det at undgå feber er nok

Feber efter hypotermibeh



Fortolknings muligheder

- 2002-studierne var forkerte. Køling virker ikke.
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- TTM for langsom nedkøling?
- TTM for hurtig opvarmning?
- Det at undgå feber er nok
- Hawthorne effekt?.....

Hawthorne effekten

Western Electric's
samlefabrikker for
telefoncentraler
(Hawthorne Works)

Udenfor Chicago

Data fra 1924-32



ILCOR og NBV

“We accept that some clinicians may make a local decision to use a target temperature of 36°C pending this further guidance”

NBVen anbefaler ‘terapeutisk hypotermi’ uden angivelse af target temperatur

Thus, the TTM trial should change practice immediately. The compelling evidence from the TTM trial is that patients who have been resuscitated from an out of hospital cardiac arrest and who remain comatose should not receive therapeutic hypothermia (32-34°C) after admission to hospital. Instead, a temperature target of 36°C is appropriate and much more easily achieved. Importantly, prognostication in such patients should be delayed for at least 72 hours after sedation is stopped, except in cases of brain death or early myoclonus with bilaterally absent somatosensory evoked responses. In addition, there seems to be no supportive evidence for active cooling using ice cold intravenous fluid bolus in the prehospital setting.

Prognostisering af cerebralt udkomme hos patienter med manglende opvågning efter hjertestop

-udarbejdet af en arbejdsgruppe nedsat af
Dansk Selskab for Anæstesiologi og Intensiv Medicin (DASAIM)
og Dansk Selskab for Intensiv Terapi (DSIT)
2013



DASAIM

Dansk Selskab
for Anæstesiologi
og Intensiv Medicin

Dansk Selskab for Intensiv Terapi
Danish Society of Intensive Care Medicine



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Christian Hassager, Overlæge, dr.med., Kardiologisk Klinik B, Rigshospitalet
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Ditte Gry Strange, Overlæge, Intensiv afdeling ZIT, Bispebjerg Hospital
Sven Weber, Overlæge, Thoraxintensiv Afsnit, Aalborg Universitetshospital

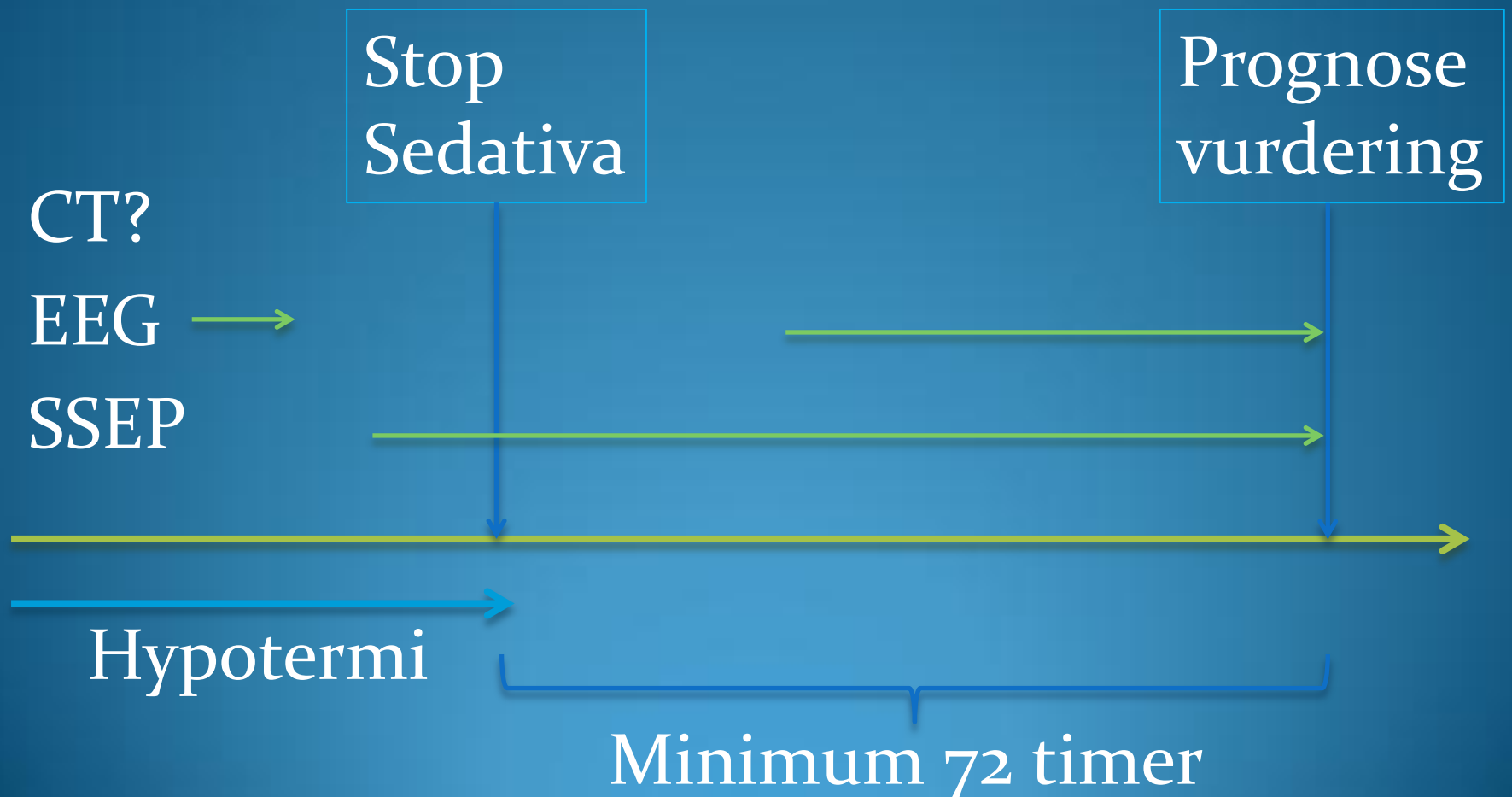
Repræsentanter fra øvrige selskaber:

Dansk Cardiologisk Selskab:	Christian Hassager, Overlæge, dr.med.
Dansk Neurologisk Selskab:	Niels Sanderhoff Degn
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Routine flow



Hvad så nu?

- Hold patienten på 36° C de første 24 timer
- Forebyg feber de næste 24 timer
- Vent med prognostisering til efter 5 døgn

- Vi må igang med at undersøge
 - Om 'feber er farligt'
 - Hvad er den bedste rehabilisering efter institio?
 - Akut KAG og revaskularisering ved NSTEMI+Institio?
 - Er temperatur management overhoved nødvendig?
 - Farmako terapi