
LUND UNIVERSITY
HUS
A COLLABORATION BETWEEN
HELSINKI UNIVERSITY HOSPITAL &
UNIVERSITY OF HELSINKI
REGION SKANE
stepcare

STEP CARE

- **S**edation
- **TE**mperature
- mean arterial **P**ressure

- **CA**rdiac arrest
- **RE**suscitation

80+ hospitals?
19 countries?
500+ collaborators

Special relationships…
Copenhagen Trial Unit, Copenhagen University
The George Institute for Global Health, Sydney
University of Helsinki, Helsinki
Luxembourg Institute of Health, Luxembourg

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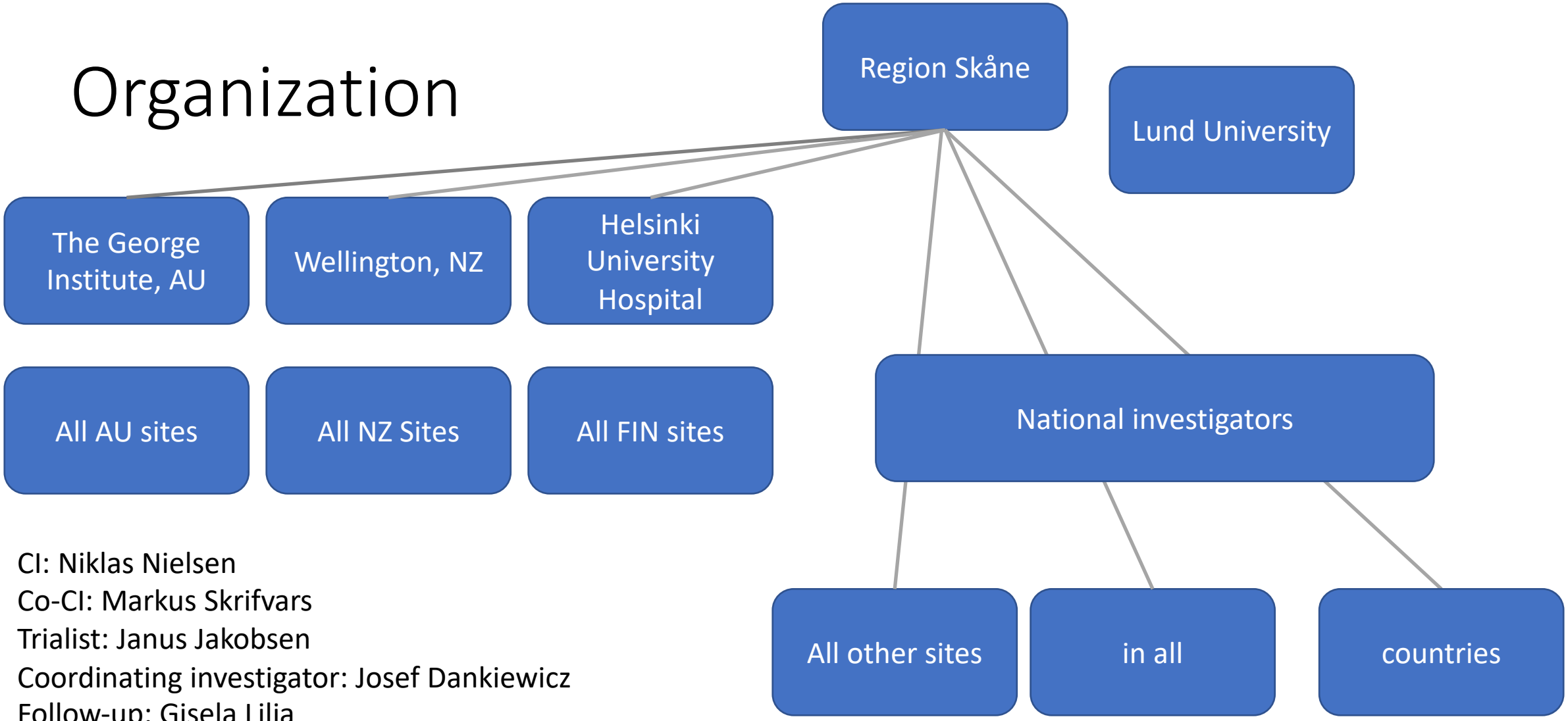
Organization



CI: Niklas Nielsen
Co-CI: Markus Skrifvars
Trialist: Janus Jakobsen
Coordinating investigator: Josef Dankiewicz
Follow-up: Gisela Lilja
Neurologist: Marion Moseby Knappe
Statistician: Susann Ullén

Ethical permissions

- Sweden
- Finland
- Australia
- New Zealand
- Luxembourg
- Germany
- Kuwait

- Applications submitted: Singapore, Italy, Norway,

- Applications under way: Belgium, Czech Rep, Ireland, Saudi Arabia, UK, Austria

Main research questions

1. Is continuous deep sedation for 36 hours beneficial compared to minimal sedation (**SED-CARE**)

2. Is fever management with a feedback-controlled device for 72 hours beneficial compared to standard fever care? (**TEMP-CARE**)

3. Is a mean arterial pressure target of >85mmHg for 72 hours beneficial compared to >65mmHg. (**MAP-CARE**)

Systematic reviews, meta-analysis, trial sequential analysis, GRADE, recommendations

- One published, three underway
  - No clear answer in any direction
- No clear evidence in any direction
- Varying practice
- Recommendations are based on very low or low certainty evidence
- There is widely accepted clinical equipoise

4 Eligibility

The trial population will be adults (18 years of age or older) who experience a cardiac arrest with return of spontaneous circulation (ROSC).

Patients will be eligible for enrolment if they meet all the following inclusion criteria and none of the exclusion criteria.

4.1 Inclusion criteria

1. Out-of-hospital cardiac arrest of non-traumatic origin
2. A minimum of 20 minutes without chest compressions*
3. Unconsciousness defined as not being able to obey verbal commands (FOUR-score motor response of <4) or being intubated and sedated because of agitation after sustained ROSC
4. Eligible for intensive care without restrictions or limitations
5. Inclusion within 4 hours of ROSC **

4.2 Exclusion criteria

1. On ECMO prior to randomization
2. Pregnancy
3. Suspected or confirmed intracranial hemorrhage
4. Previously randomized in the STEPCARE trial

SEDATION

Prolonged sedation 36-40 h have been standard last 20 years

PROS

- Comfort
- Ventilator synchrony
- Brain rest
- Anti seizure effect
- Enhances glymphatic system

CONS

- Compromises circulation
- May increase delirium
- May increase VAP
- Confounds prognostication
- Prolonges ICU stay

Sedation intervention

- Short acting sedation
- Protocolized to RASS -4-5 versus only when indicated as per normal ICU care

RASS score

Richmond Agitation & Sedation Scale				CAM-ICU
Score	**Description**			
+4	Combative	Violent, immediate danger to staff		RASS ≥ -2 Proceed to CAM-ICU assessment
+3	Very agitated	Pulls at or removes tubes, aggressive		
+2	Agitated	Frequent non-purposeful movements, fights ventilator		
+1	Restless	Anxious, apprehensive but movements not aggressive or vigorous		
0	Alert & calm			
-1	Drowsy	Not fully alert, sustained awakening to voice (eye opening & contact >10 secs)	Voice	
-2	Light sedation	Briefly awakens to voice (eye opening & contact < 10 secs)		
-3	Moderate sedation	Movement or eye-opening to voice (no eye contact)		RASS < -2 STOP Recheck later
-4	Deep sedation	No response to voice, but movement or eye opening to physical stimulation	Touch	
-5	Un-rousable	No response to voice or physical stimulation		

TEMPERATURE

ERC Guidelines:

In patients who remain comatose after cardiac arrest, we recommend continuous monitoring of core temperature and actively preventing fever (defined as a temperature > 37.7 °C) for at least 72 h.

Hypothermia ☒

Treatment of fever ?

Device Group	No Device Group
Monitor temperature	Monitor temperature
Start a feedback-controlled device if the temperature is 37.8° or higher. Set it at 37.5°C.	Treat temperature the same way you would in any other general ICU patient

MAP

Higher pressure than 65 mmHg?

ESC European Society of Cardiology
European Heart Journal (2019) 00, 1–11
doi:10.1093/eurheartj/ehz120

FASTTRACK CLINICAL RESEARCH
Disease management

Early goal-directed haemodynamic optimization of cerebral oxygenation in comatose survivors after cardiac arrest: the Neuroprotect post-cardiac arrest trial

Koen Ameloot[1,2,3]*, Cathy De Deyne[3,4], Ward Eertmans[3,4], Bert Ferdinande[1], Matthias Dupont[1], Pieter-Jan Palmers[1], Tibaut Petit[1,2], Philippe Nuyens[1,2], Joren Maeremans[1,3], Joris Vundelinckx[4], Maarten Vanhaverbeke[2], Ann Belmans[2], Ronald Peeters[5], Philippe Demaerel[5], Robin Lemmens[6,7,8], Jo Dens[1,3], and Stefan Janssens[2]

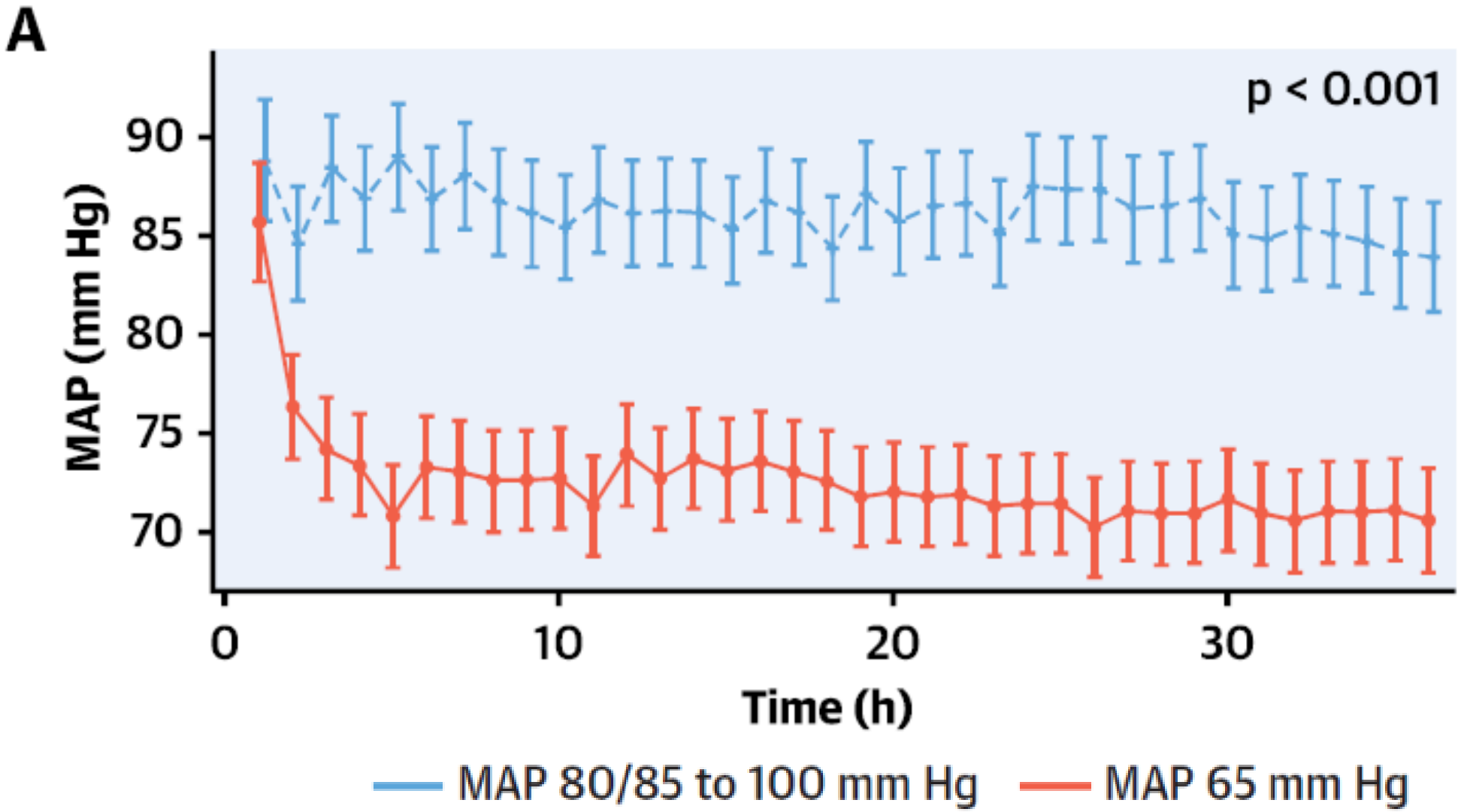
ORIGINAL

Targeting low-normal or high-normal mean arterial pressure after cardiac arrest and resuscitation: a randomised pilot trial

Pekka Jakkula[1*], Ville Pettilä[1], Markus B. Skrifvars[1,2], Johanna Hästbacka[1], Pekka Loisa[3], Marjaana Tiainen[4], Erika Wilkman[1], Jussi Toppila[5], Talvikki Koskue[1], Stepani Bendel[6], Thomas Birkelund[7], Raili Laru-Sompa[8], Miia Valkonen[1], Matti Reinikainen[9] and COMACARE study group

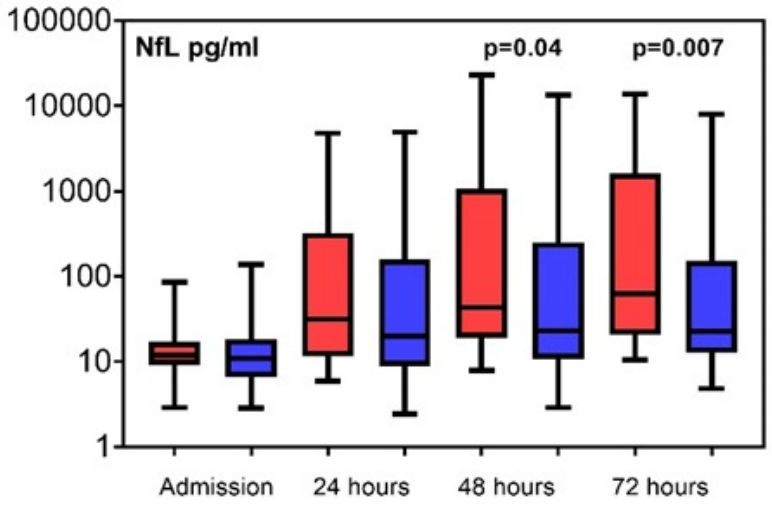
- Comparison of 65-70 mmHg to 80-100 mmHg
- 240 patients all in total
- 120 with myocardial infarction verified on angiography

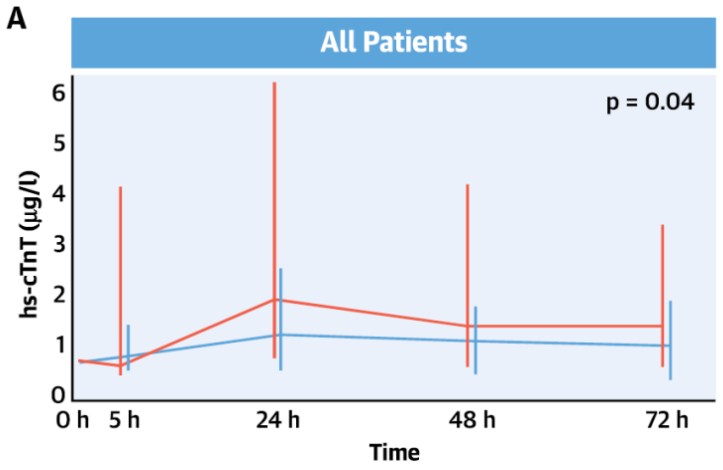
Separation between MAP groups



Ameloot et al. JACC 2020

Signals of benefit in biomarkers Neurofilament and Troponin





MAP 80/85 to 100 mm Hg MAP 65 mm Hg

Need for larger trials!

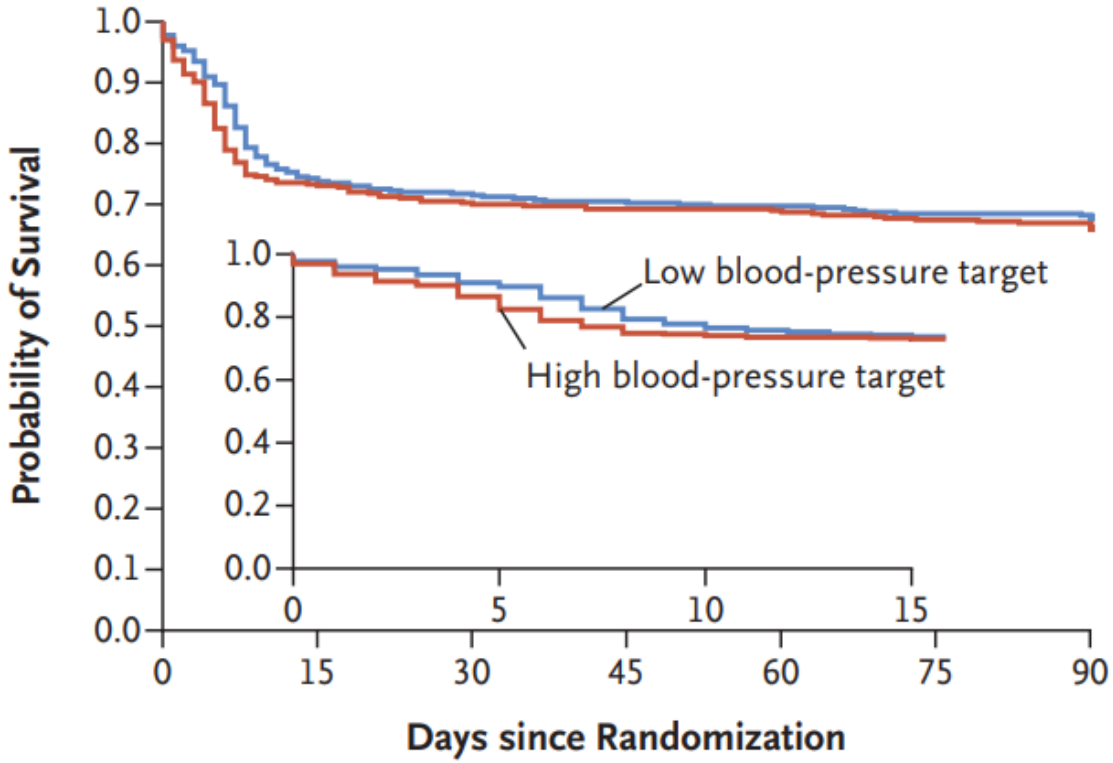
ORIGINAL ARTICLE

Blood-Pressure Targets in Comatose Survivors of Cardiac Arrest

J. Kjaergaard, J.E. Møller, H. Schmidt, J. Grand, S. Mølstrøm, B. Borregaard, S. Venø, L. Sarkisian, D. Mamaev, L.O. Jensen, B. Nyholm, D.E. Høfsten, J. Josiassen, J.H. Thomsen, J.J. Thune, L.E.R. Obling, M.G. Lindholm, M. Frydland, M.A.S. Meyer, M. Winther-Jensen, R.P. Beske, R. Frikke-Schmidt, S. Wiberg, S. Boesgaard, S.A. Madsen, V.L. Jørgensen, and C. Hassager

- 802 comatose patients resuscitated from a presumed cardiac reason for the arrest
- Blinded study with regards to blood pressure!

No difference in outcome



No. at Risk

Low blood-pressure target	396	294	284	279	276	271	270
High blood-pressure target	393	288	276	272	271	265	263

Kjaergaard et al. NEJM 2022

MAP-intervention

- Target arterial line MAP
- Fluids
- Vasopressors

Outcomes

- Primary: Mortality at 6 months
- Secondary: Modified Rankin Scale/Functional Outcome and HR QoL and proportion of predefined safety events
- Exploratory: Vent free days, hospital free days; within 30 days

- Additional outcomes in sub-study.

Safety events

SED-CARE: sepsis or septic shock (Sepsis III criteria), arrhythmia requiring defibrillation, cardioversion or chest compressions, venous thromboembolism, reintubation, non-planned extubation

TEMP-CARE: sepsis or septic shock (Sepsis III criteria), arrhythmia requiring defibrillation, cardioversion or chest compressions, venous thromboembolism, moderate or severe bleeding (GUSTO criteria)

MAP-CARE: arrhythmia requiring defibrillation, cardioversion or chest compressions, moderate or severe bleeding (GUSTO criteria), acute kidney injury with renal replacement therapy, limb ischemia requiring radiological or surgical intervention, or gut ischemia demonstrated at laparotomy/laparoscopy or clinically suspected based on abdominal CT-scan or in the context of palliative management.

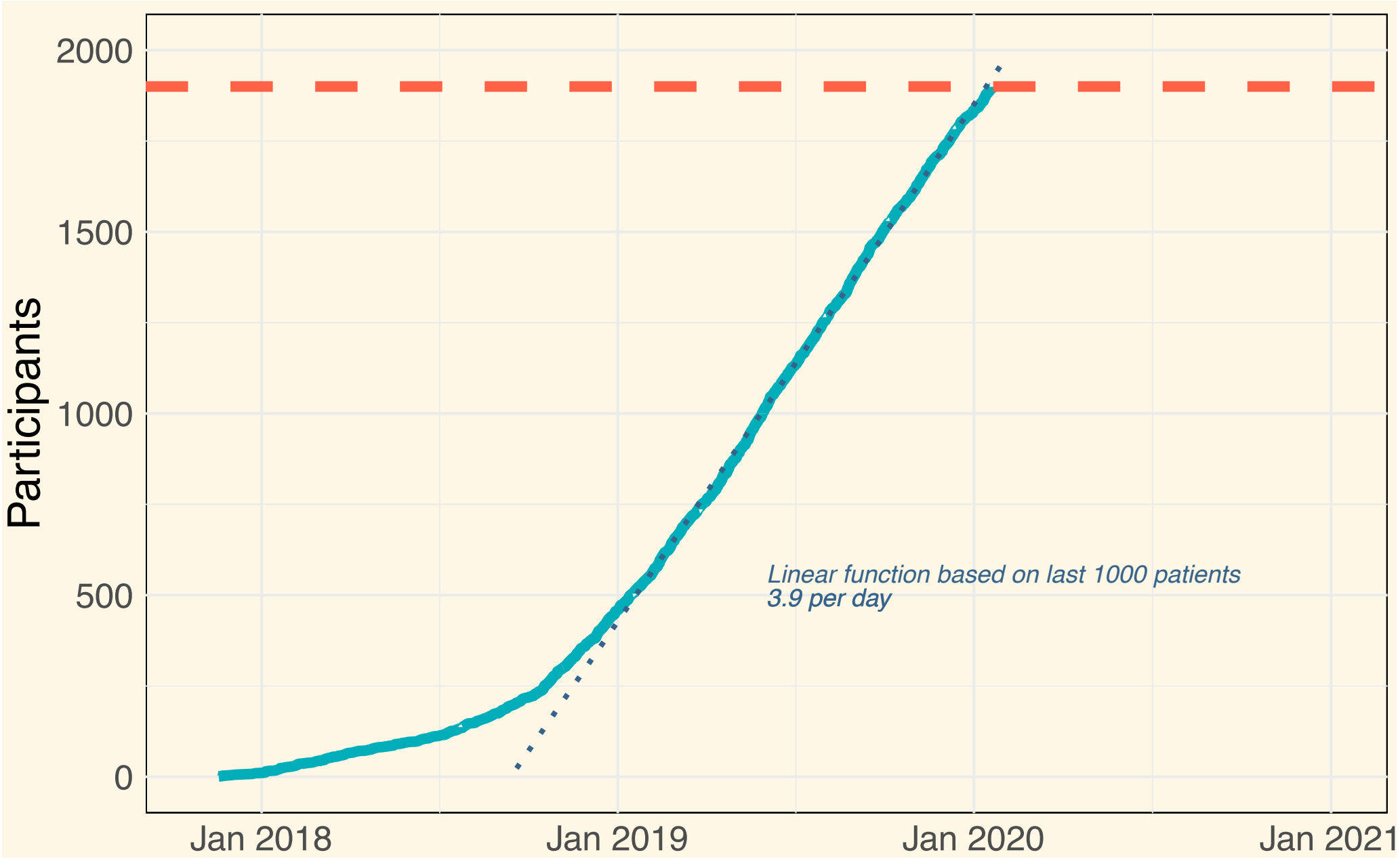
Unexpected serious safety events

Unexpected serious complications

Events which might reasonably occur as a consequence of the trial intervention and which are not part of the natural history of critical illness, the process which caused the cardiac arrest, or the cardiac arrest itself. These events should only be reported if they are life-threatening, prolong hospitalization or result in meaningful harm to the participant.

Sample size and power

- Test used: Power calculation for two proportions
- Probability of death in the control group: 60%
- Probability of death in the intervention group: 54.4%
- Power 90%
- Effect size: 2*asin(sqrt(p1))-2*asin(sqrt(p2)) = 0.113
- Required sample size: 3278
- Final sample size: Required sample size + 6.8% =**3500**


2000
1500
1000
500
0
Participants
Jan 2018
Jan 2019
Jan 2020
Jan 2021
Linear function based on last 1000 patients
3.9 per day

www.stepcare.org

https://clinicaltrials.gov/ct2/show/NCT05564754?term=stepcare&cond=Cardiac+Arrest&draw=2&rank=1