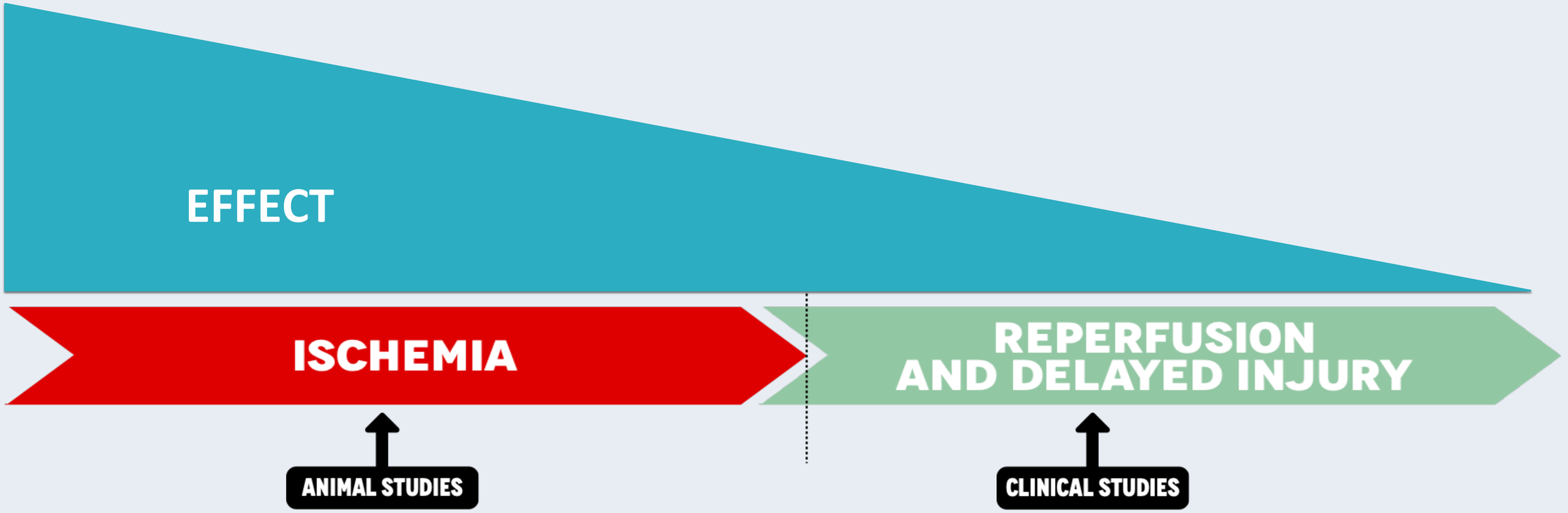
PRINCESS²

ULTRAFAST HYPOTHERMIA IN CARDIAC ARREST

Per Nordberg, PI - Fia Börjesson, Study coordinator - Thomas Hermansson, Head of training

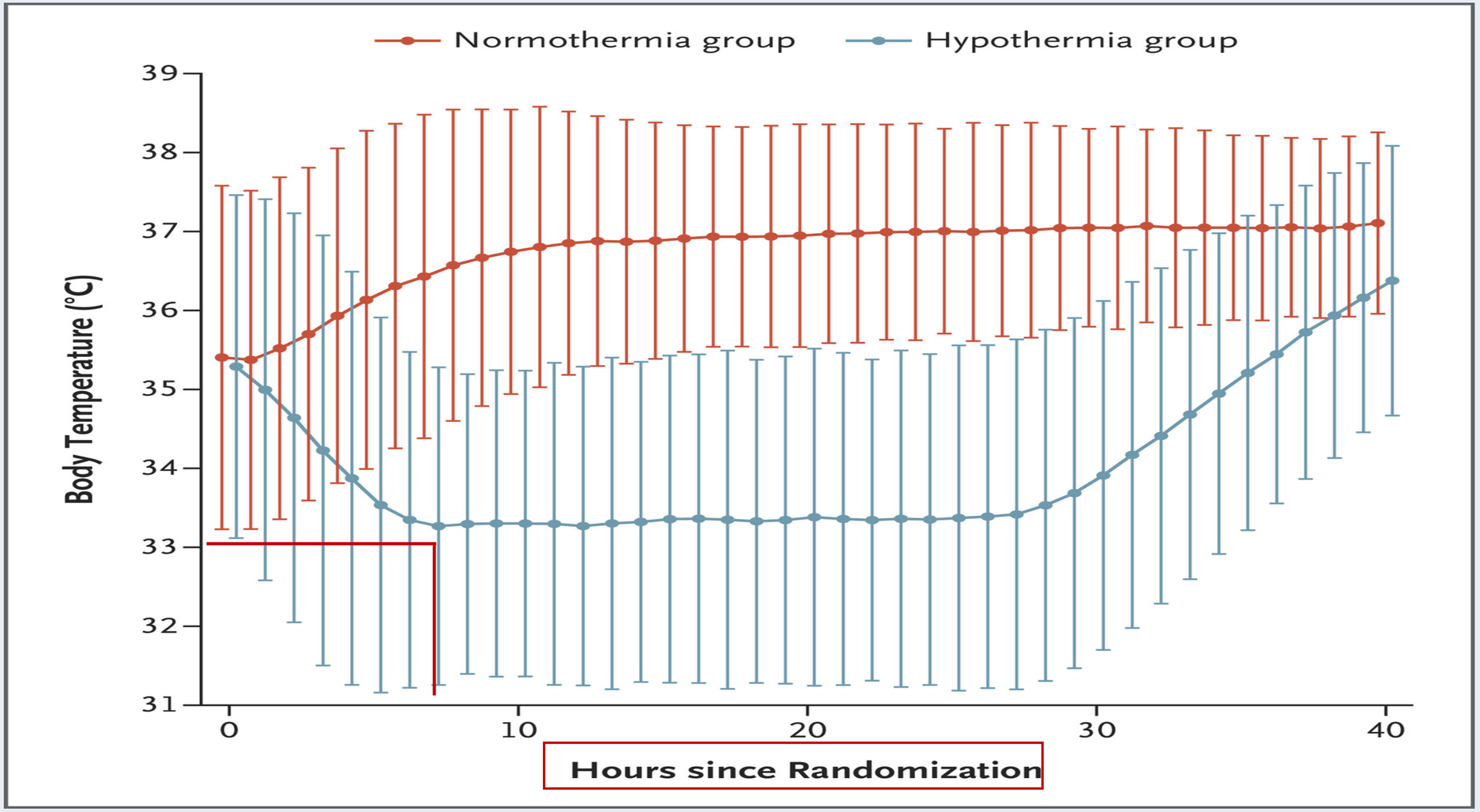
THE FACTS


EFFECT
ISCHEMIA
REPERFUSION AND DELAYED INJURY
ANIMAL STUDIES
CLINICAL STUDIES

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

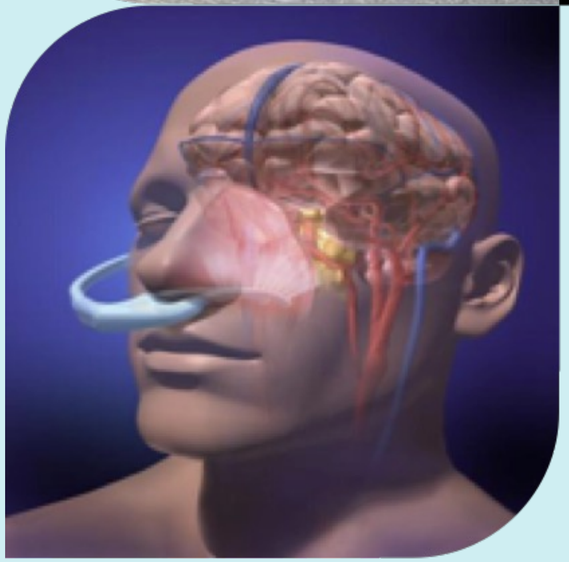
Hypothermia versus Normothermia after Out-of-Hospital Cardiac Arrest



COOLING METHOD

TRANSNASAL EVAPORATIVE COOLING

- **Primarily brain cooling**
- **Easy to use, early initiation**
- **Non-invasive**
- **Continuous cooling**
- **No volume load**




The RhinoChill™ IntraNasal Cooling System
can be easily deployed during resuscitation efforts.
RhinoChill™ IntraNasal
Cooling System

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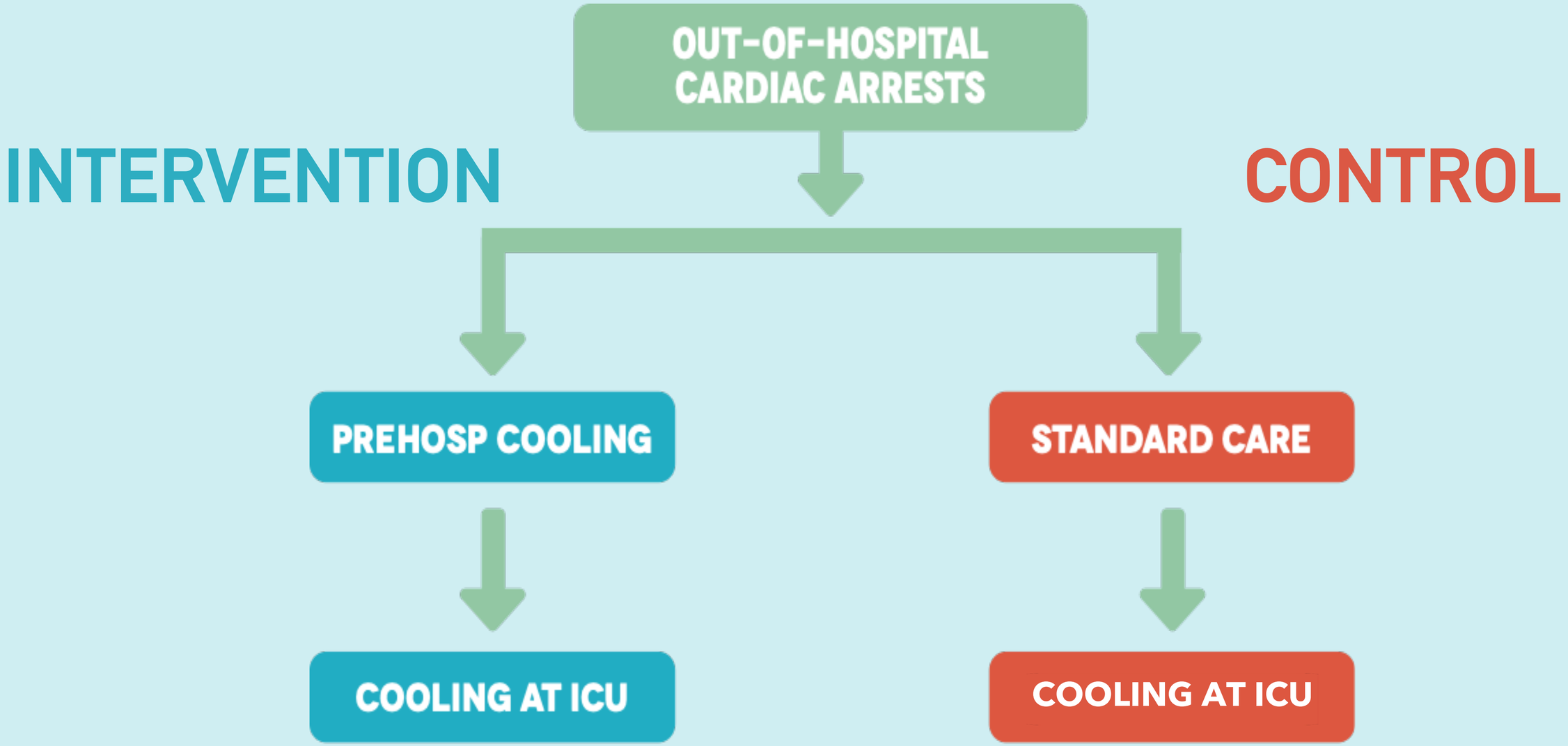
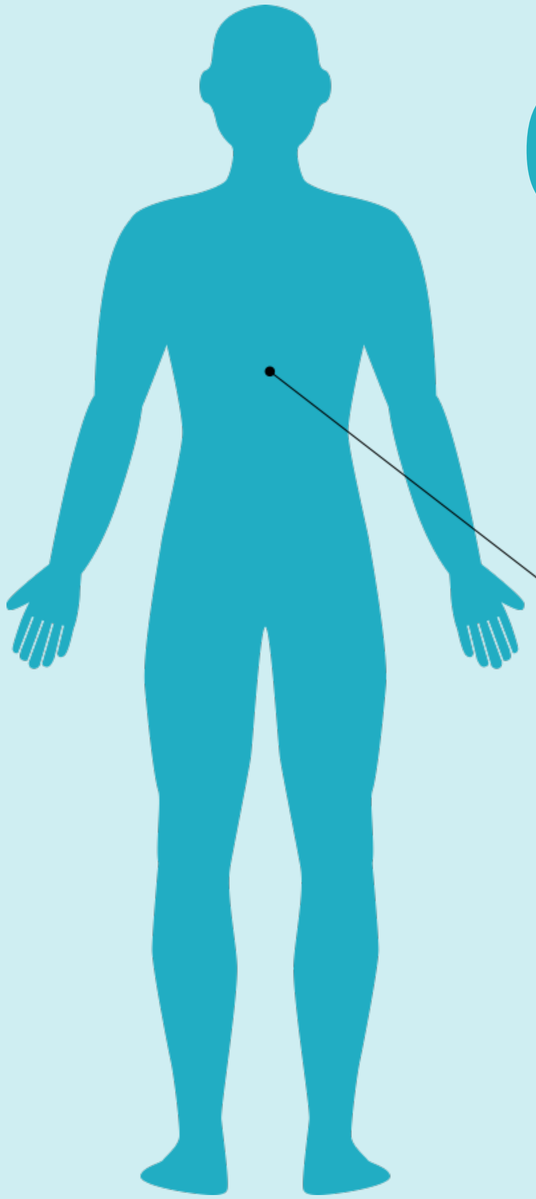
JAMA 2019





677 PATIENTS

343 INTERVENTION vs 334 CONTROLS
138 INTERVENTION vs 135 CONTROLS

Inclusion criteria

Bystander witnessed OHCA

Age ≥18 years

Predefined subgroup
Ventricular fibrillation

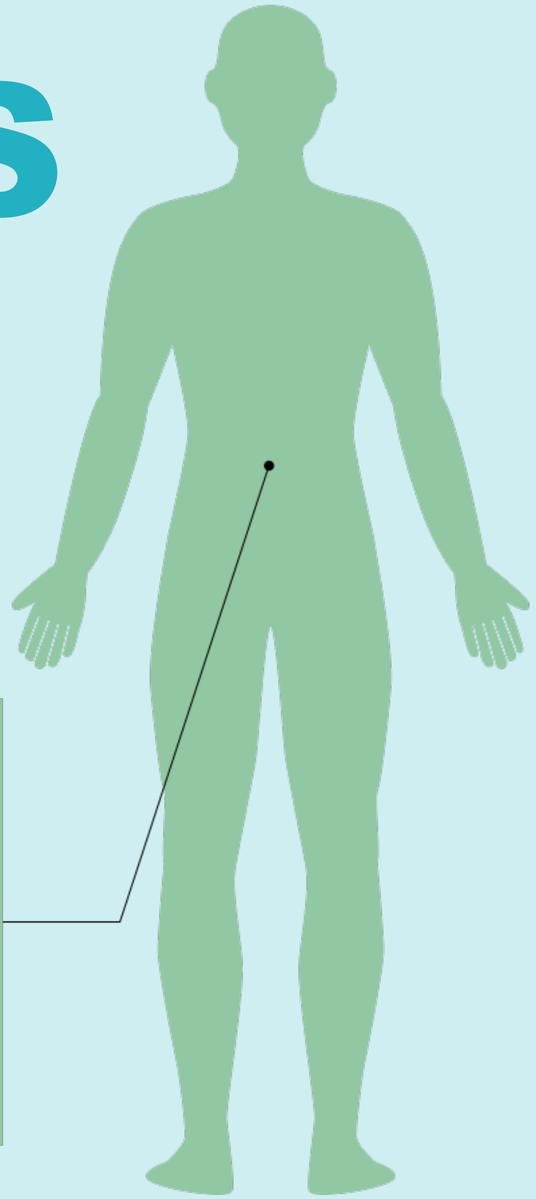
Exclusion criteria

Age ≥80 years

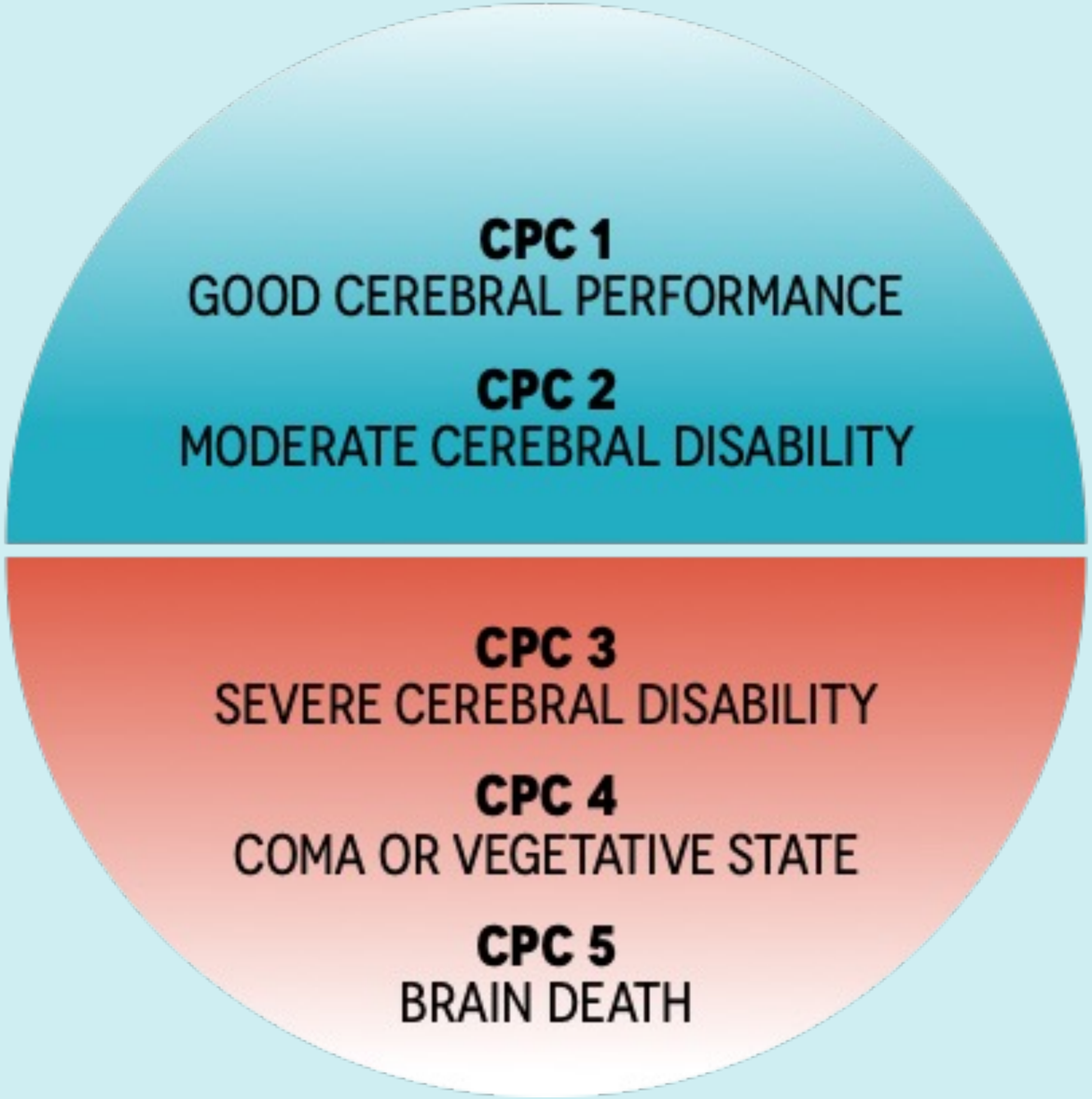
Obvious non-cardiac cause

ROSC prior to randomization

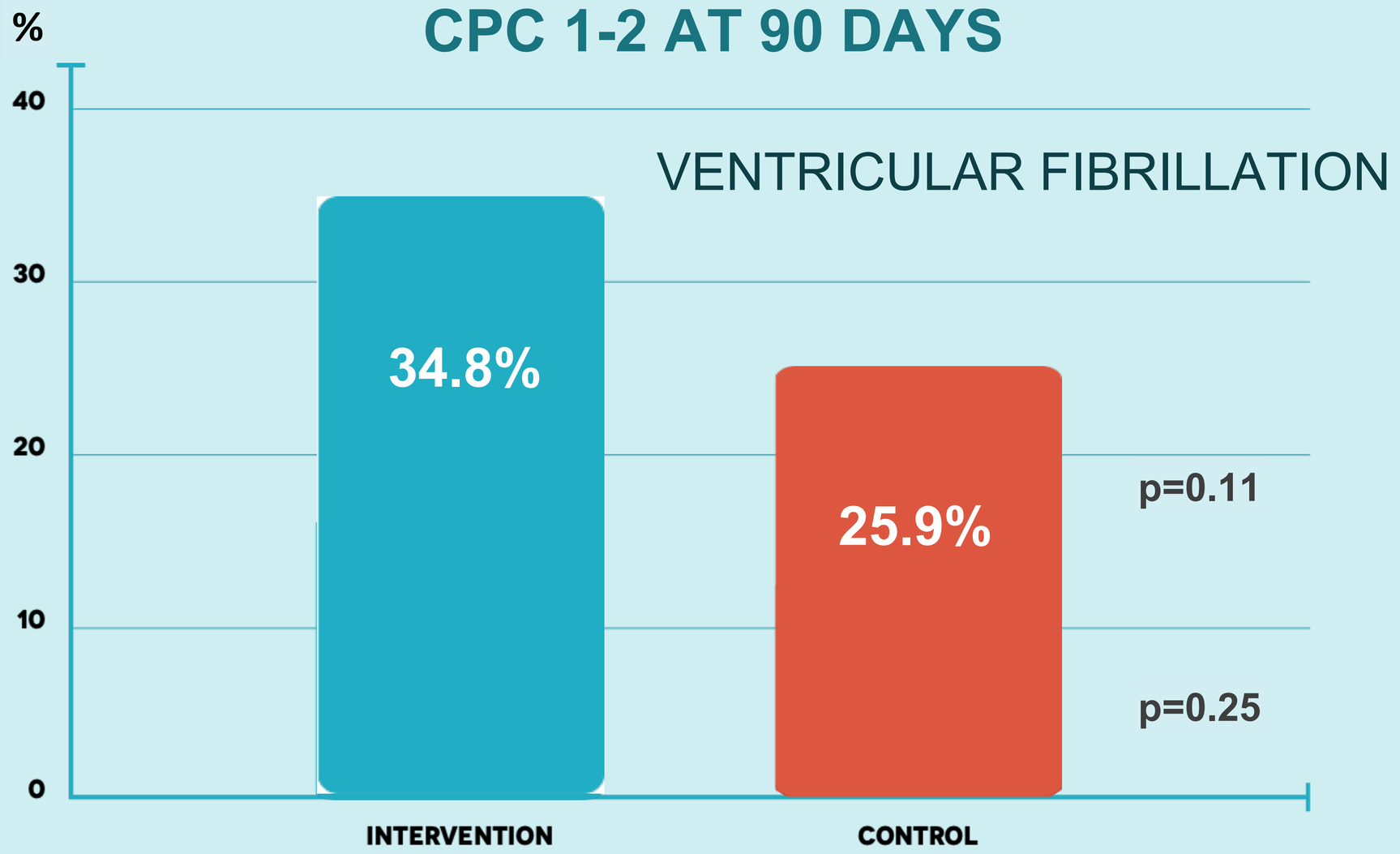
EMS time > 15 minutes



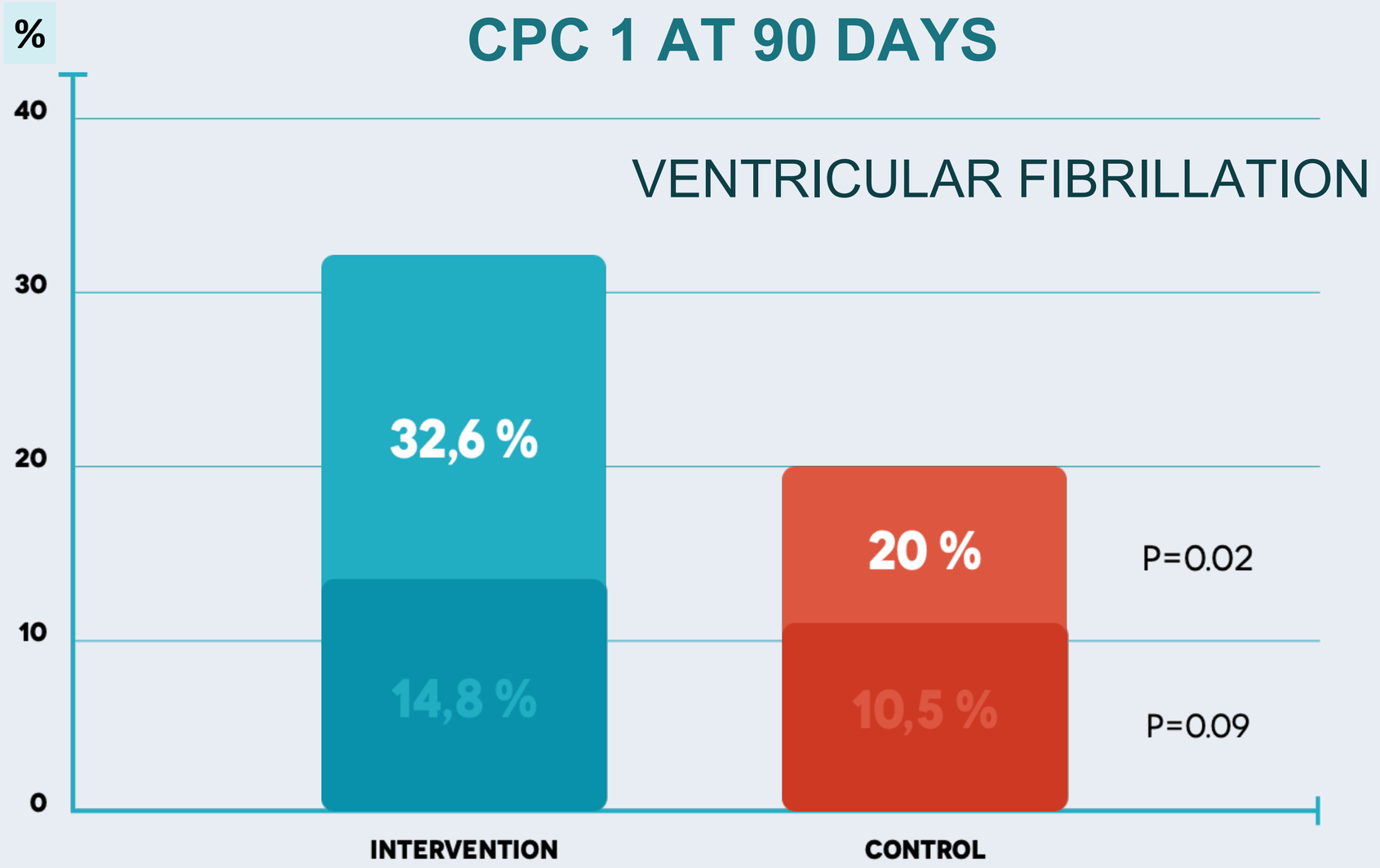
CPC 1-2 at 90 days



PRIMARY OUTCOME



COMPLETE RECOVERY



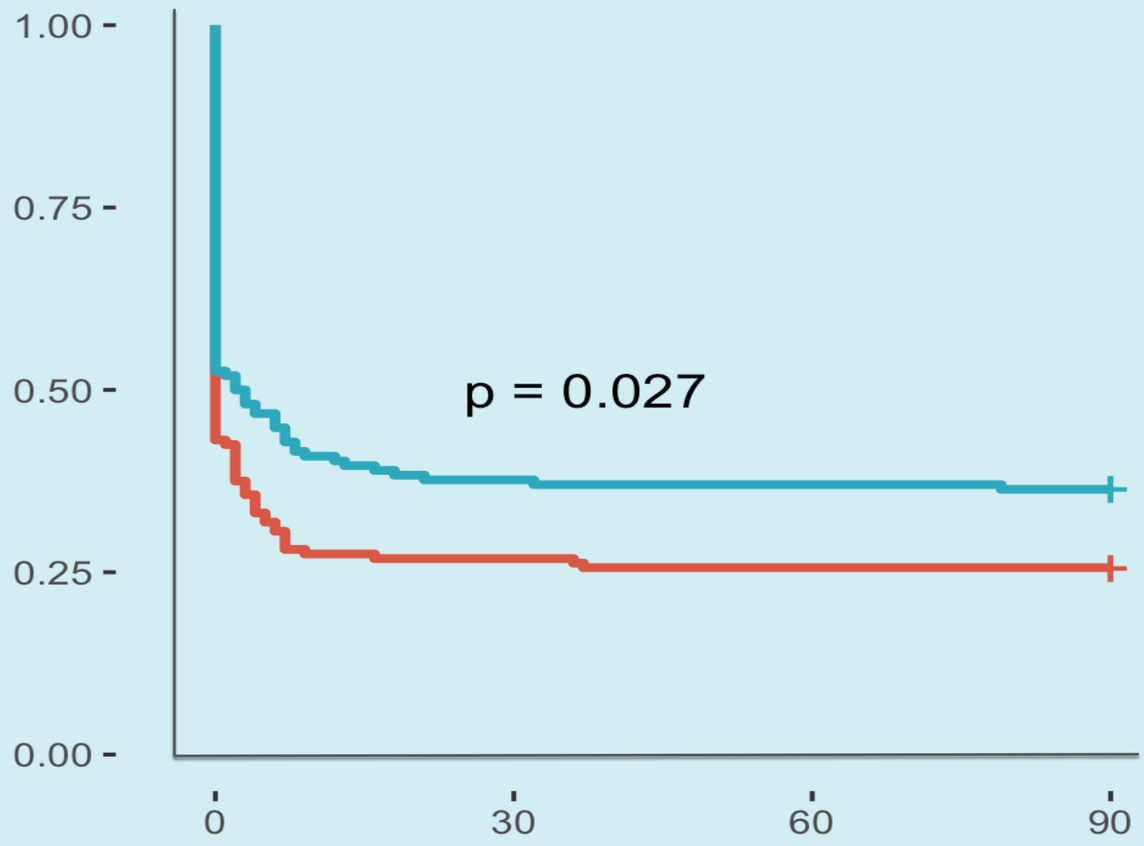
PRINCE AND PRINCESS TRIALS, 858 PATIENTS

Pooled analysis by initial rhythm

KAPLAN MEIER CURVE

SURVIVAL WITH CPC 1-2 AT 90 DAYS

SHOCKABLE RHYTHMS



Control -	160	43	41	41
Intervention -	154	58	57	56

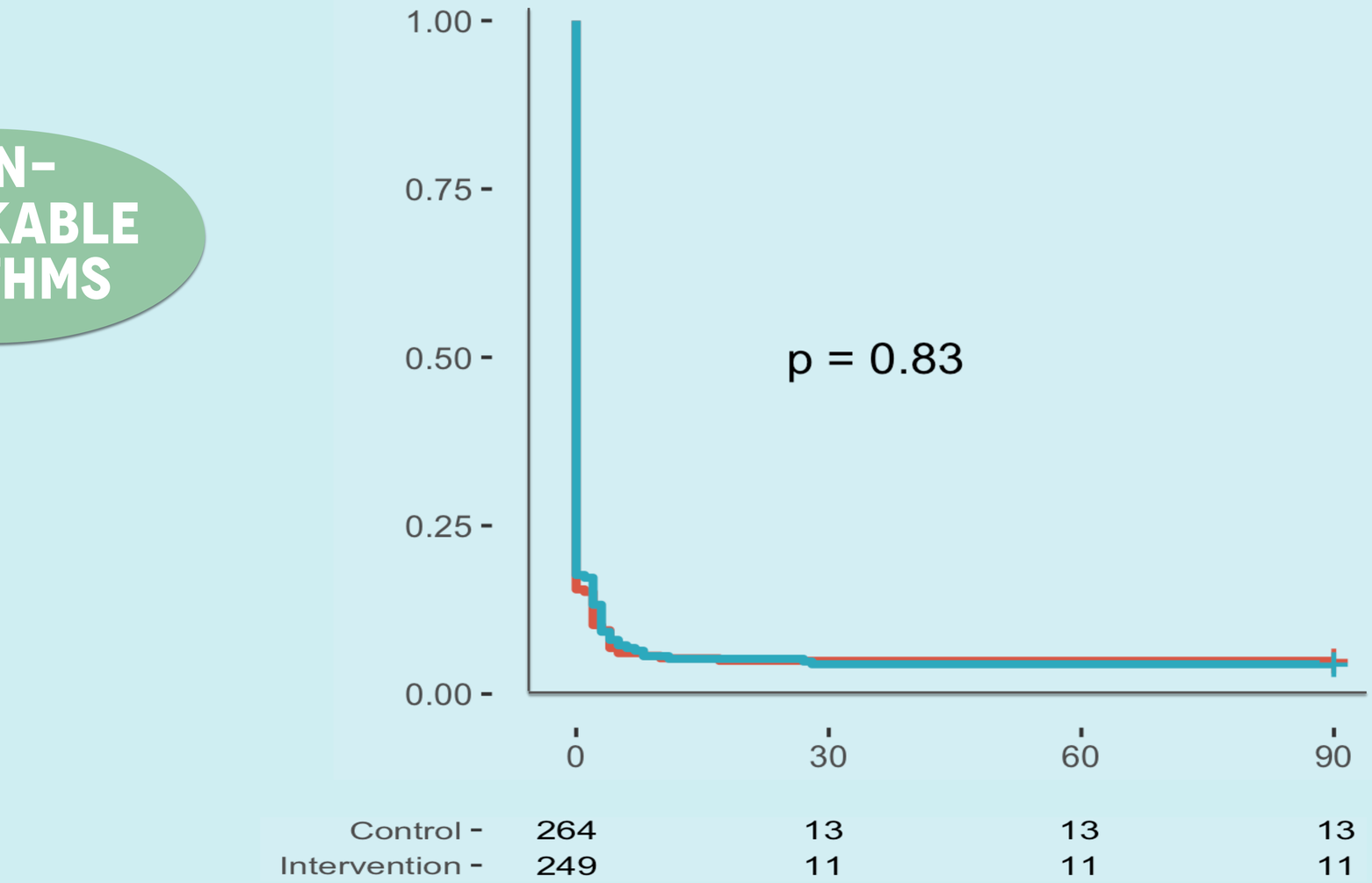
36.4%, intervention

25.6%, control

KAPLAN MEIER CURVE

SURVIVAL WITH CPC 1-2 AT 90 DAYS

NON-SHOCKABLE RHYTHMS



4.4%, intervention

4.9%, control

HYPOTHESIS:

Ultrafast hypothermia in cardiac arrest with shockable rhythms increase survival with complete recovery compared to normothermia.

DESIGN:

Multicenter RCT

1000 patients with VF

Intra-arrest and early post-ROSC

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STUDY SITES

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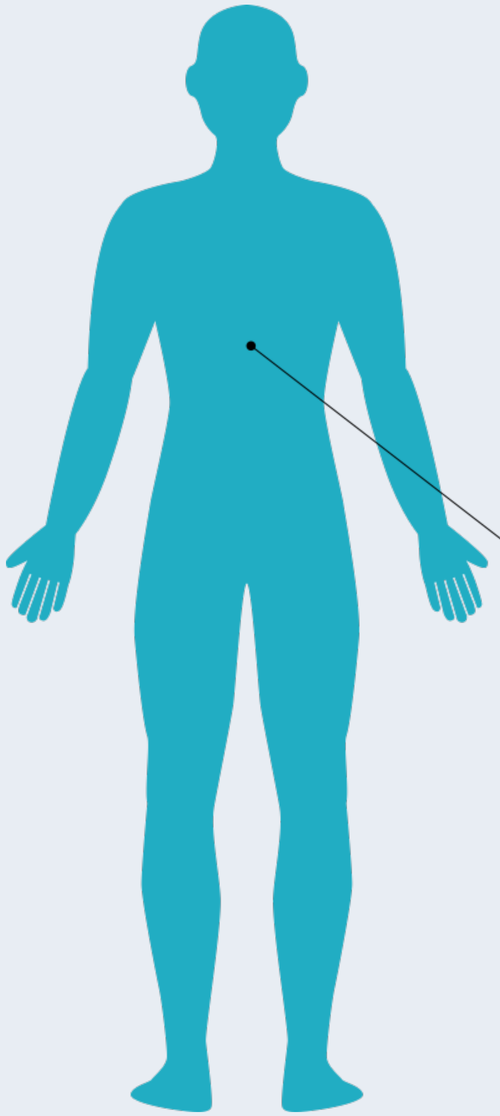
POPULATION



Inclusion criteria

OHCA with shockable rhythms

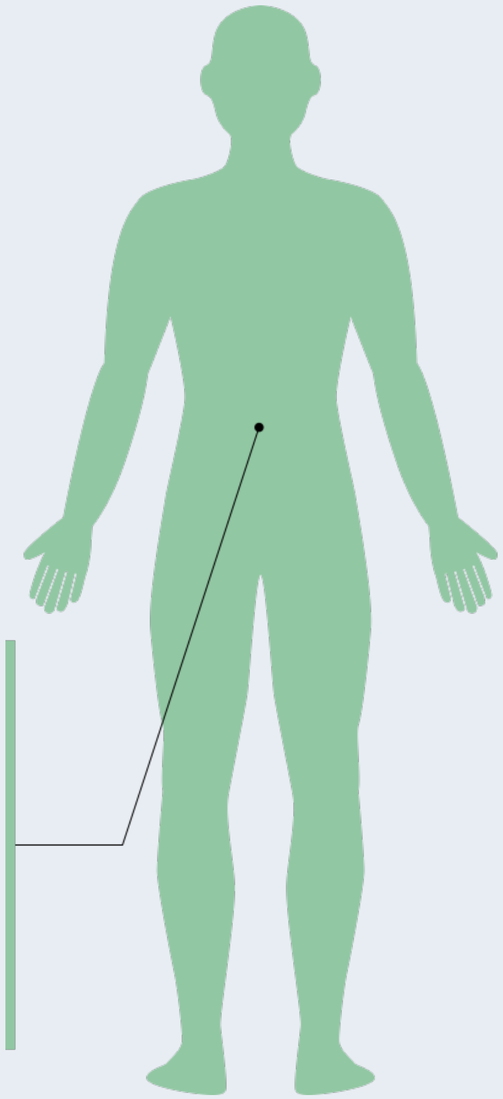
Age ≥18 years

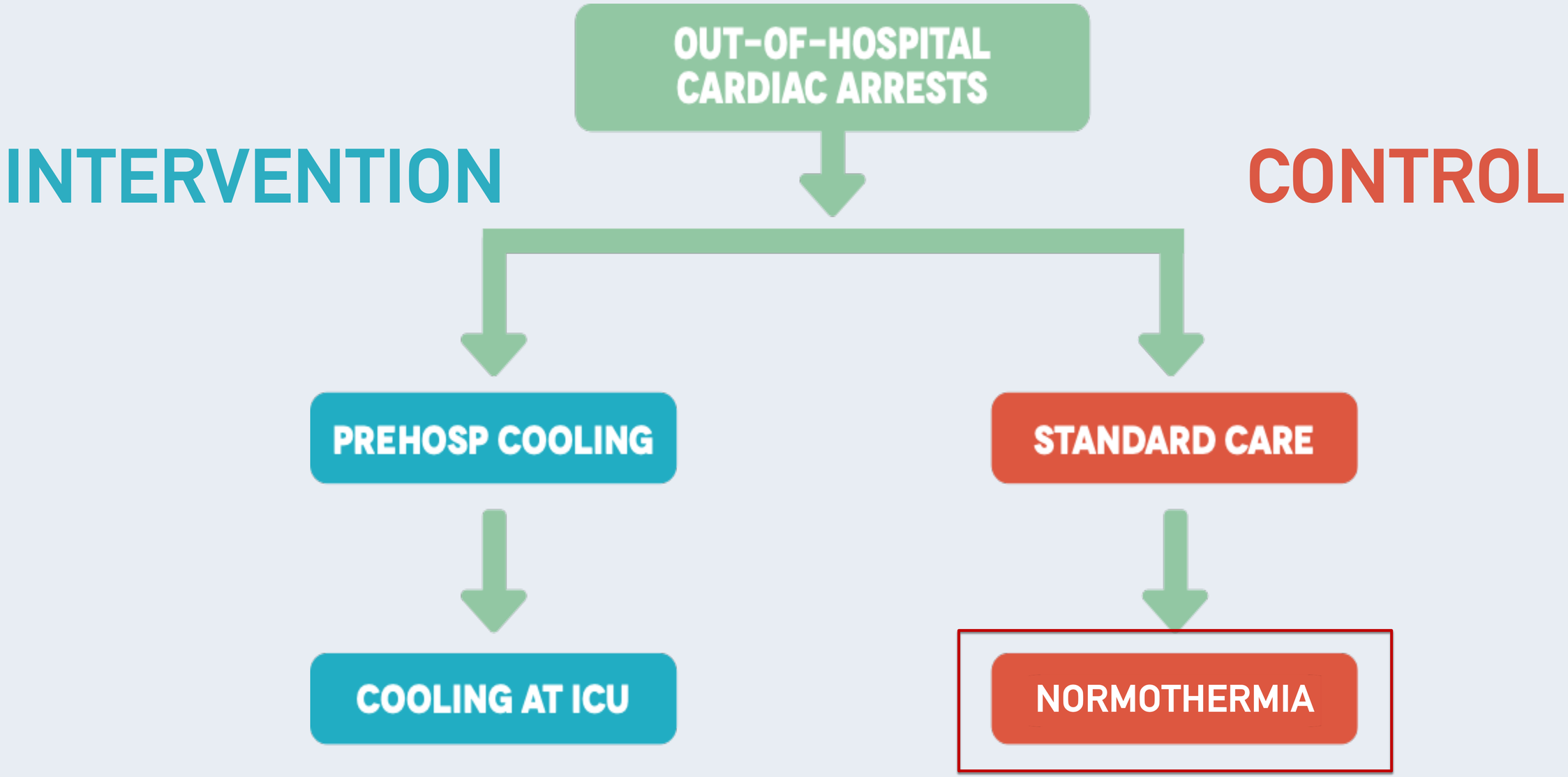
Within 20 min from EMS arrival

Exclusion criteria

Age ≥80 years

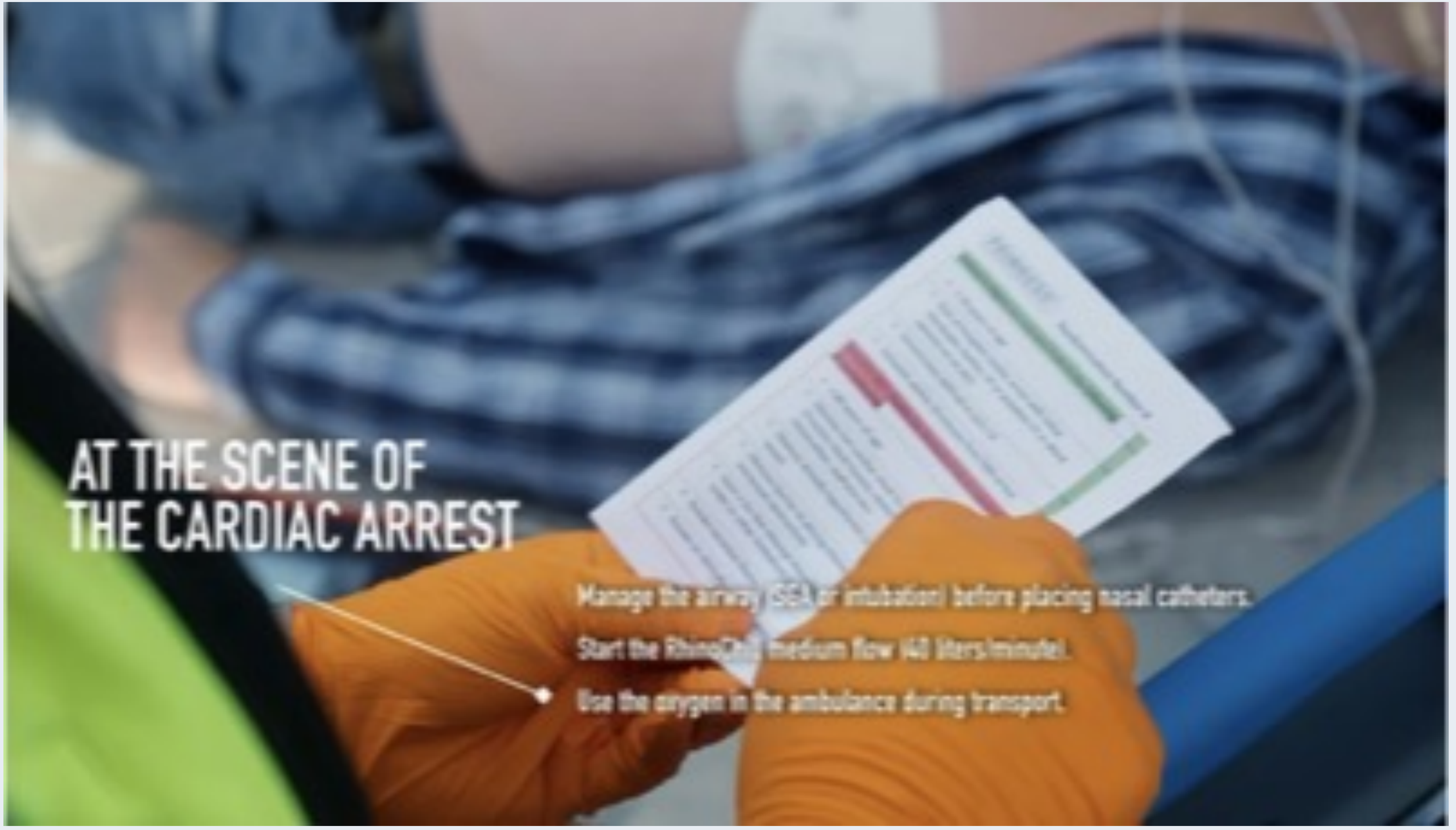
Obvious non-cardiac cause




OUT-OF-HOSPITAL CARDIAC ARRESTS
INTERVENTION
CONTROL
PREHOSP COOLING
STANDARD CARE
COOLING AT ICU
NORMOTHERMIA

For the EMS

- Equipment in a complete bag including oxygen cylinder
- Randomize after airway (SGA or intubation), within 20 minutes from EMS arrival on scene
- Randomization envelopes with patient study criteria (i.e. adult VF-patients) are in the bag
- Initiate cooling immediately if allocated to intervention (control group standard care)
- During transfer, use oxygen supply in the ambulance
- At ED arrival, switch to hospital RhinoChill Device
- Digital CRF with the most important variables


AT THE SCENE OF
THE CARDIAC ARREST
Manage the airway (SGA or intubation) before placing nasal catheters.
Start the RhinoChiq medium flow (40 liters/minute).
Use the oxygen in the ambulance during transport.

Inclusion and exclusion criteria

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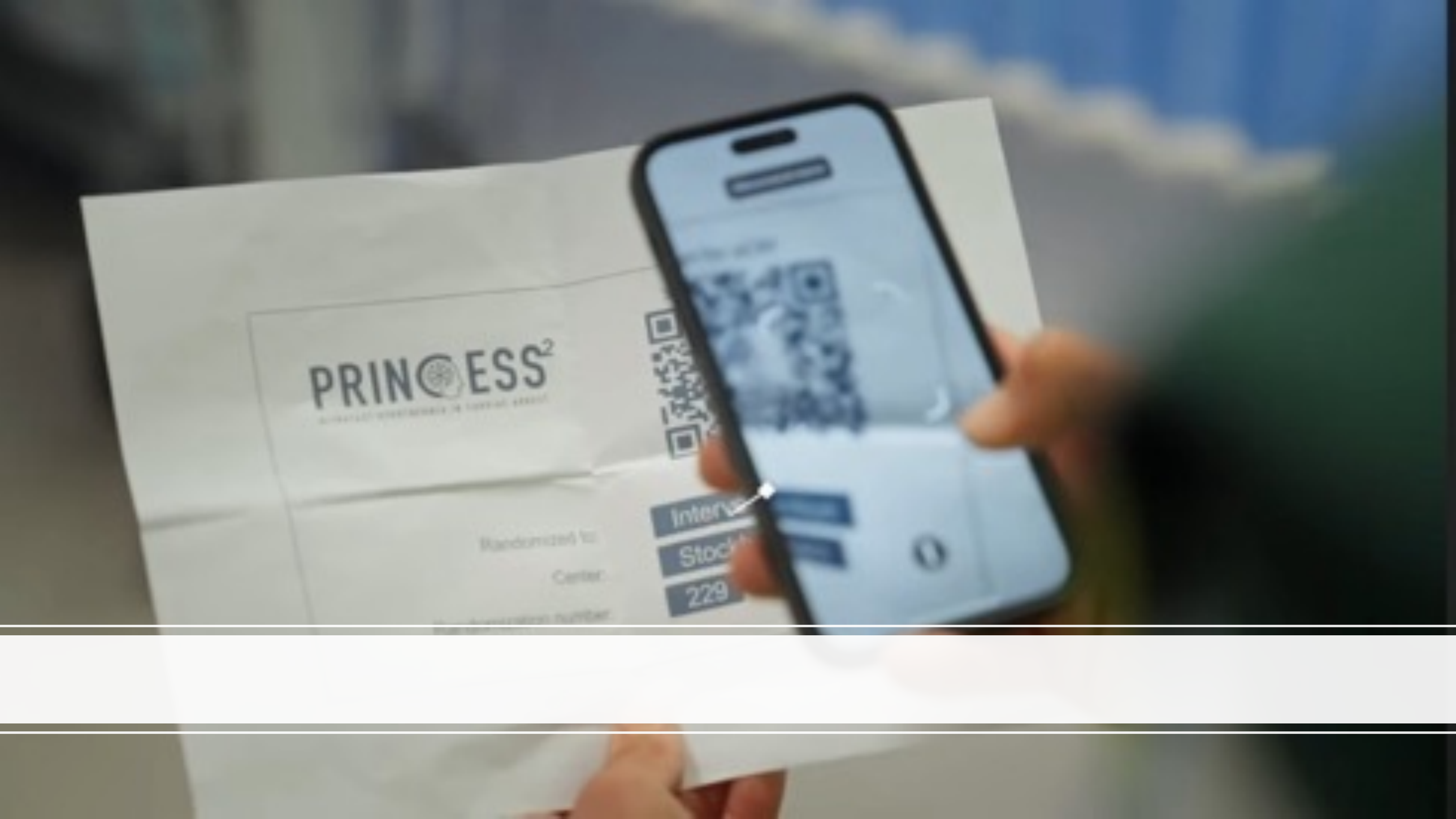
Patienten är lämplig för inklusion om ”JA” till följande	
• ≥ 18 års ålder	
• Initialt defibrillerbar rytm	
• Medvetslös (GCS ≤8)	
• Inklusion inom 20 min från ambulansens ankomst (första enheten)	
Inklusion kan göras både intra-arrest och efter ROSC	

Patienten är *INTE* lämplig för inklusion om ”JA” till en eller fler av följande;	
• ≥ 80 års ålder	
• Uppenbart icke-kardiellt hjärtstopp	
• Uppenbart redan hypoterm	
• Uppenbart hinder att placera intranasal kateter (ex intranasal obstruktion)	
• Behandlingsbegränsningar (tex EJ HLR)	
• Känd terminal sjukdom	
• Graviditet	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INTERVENTION

ACLS and Cooling at the scene of the arrest.

Standardized post-resuscitation protocol

- Hypothermia to 33°C for 24 hours
- Fever control for 72 hours
- Standardized prognostication

CONTROL

ACLS at the scene of the arrest

Standardized post-resuscitation protocol

- Fever control for 72 hours
- Standardized prognostication

OUTCOME

Primary Outcome measure:

- Survival with complete neurologic function at 90 days defined as mRs 0-1.

Main secondary outcomes:

- Survival at hospital discharge
- Survival at 90 days.
- mRs 0-3 at 90 days

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TIME LINE

- Study start Q1 in Sweden, Austria, Germany, Slovenia
- Assessment of sites (ongoing), goal 20-25 sites
- Expected full inclusion rate Q3-4 2024

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Support for next step

Website with study documents (ethical approval, consent forms etc) and instruction film:

www.princess2.org

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ULTRAFAST HYPOTHERMIA IN CARDIAC ARREST

per.nordberg@ki.se

the Staff

Princess 2 – trial

Anna-Sofia Hallberg Börjesson | 2023-11-30

international steering committee

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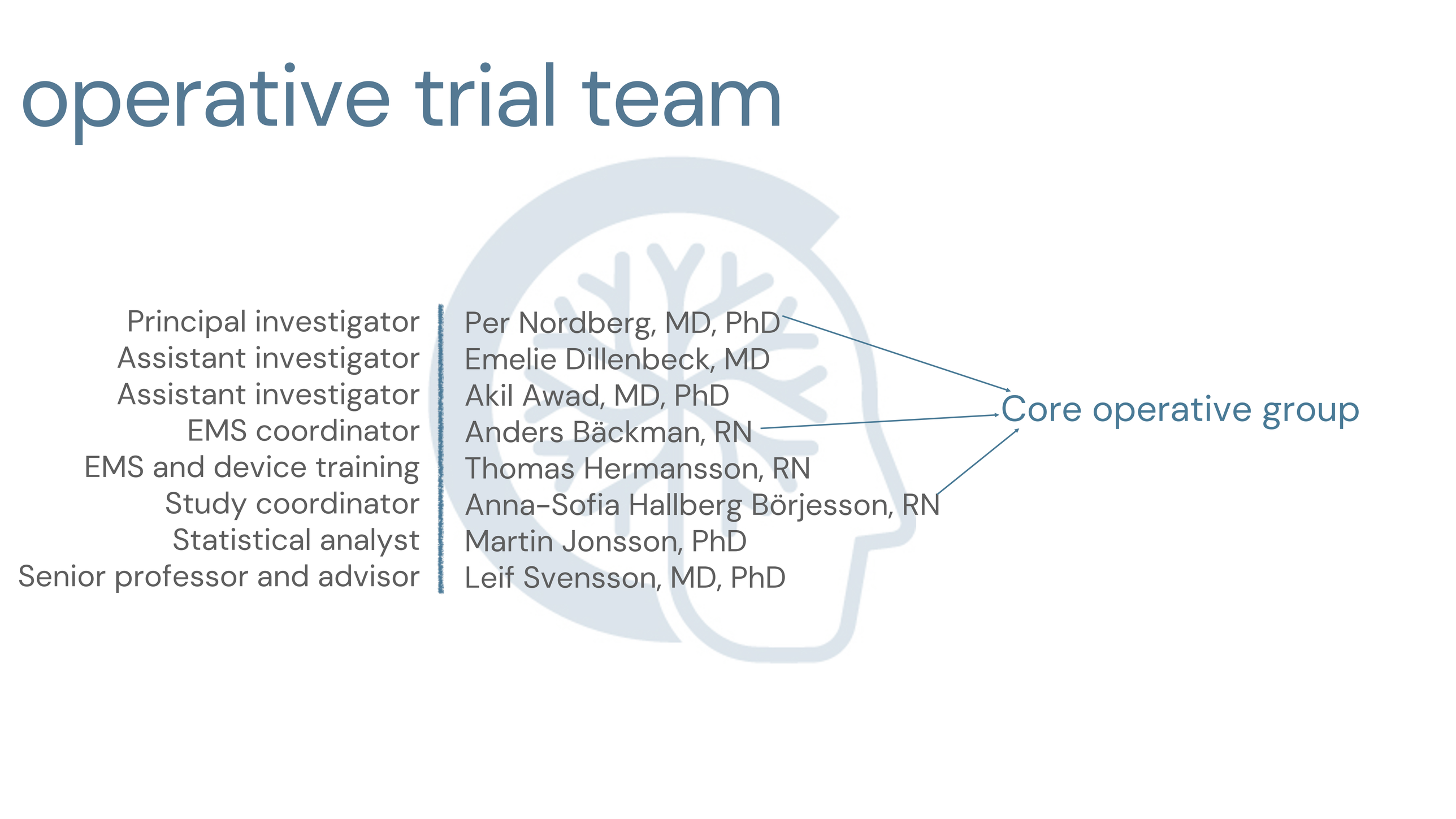
Michael Holzer - MD, PhD
Graham Nichols - MD, PhD
Jacob Hollenberg - MD, PhD
Sune Forsberg - MD, PhD

Fabio Taccone, MD, PhD
Peter Radsel, MD, PhD
Giuseppe Ristagno, MD, PhD
Esteban Lopez de Sa Areses, MD, PhD

operative trial team

Principal investigator	Per Nordberg, MD, PhD
Assistant investigator	Emelie Dillenbeck, MD
Assistant investigator	Akil Awad, MD, PhD
EMS coordinator	Anders Bäckman, RN
EMS and device training	Thomas Hermansson, RN
Study coordinator	Anna-Sofia Hallberg Börjesson, RN
Statistical analyst	Martin Jonsson, PhD
Senior professor and advisor	Leif Svensson, MD, PhD



operative trial team

trainings and logistics

inhospital	prehospital
emelie dillenbeck	anders bäckman
akil awad	thomas hermansson
anna-sofia hallberg börjesson	

operative trial team

database and eCRF – support

martin jonsson
emelie dillenbeck
anna-sofia hallberg börjesson

meetings, startup–, monitoring visits, trial documents, assistance

anna-sofia hallberg börjesson

Thank You

www.princess2.org

trial@princess2.org

AT THE SCENE OF THE CARDIAC ARREST

Patients with shockable rhythms can be included.

Randomize as soon as possible, preferably intra-arrest.