

# Therapeutic hypothermia - a good example to illustrate the "Formula of Survival" concept!



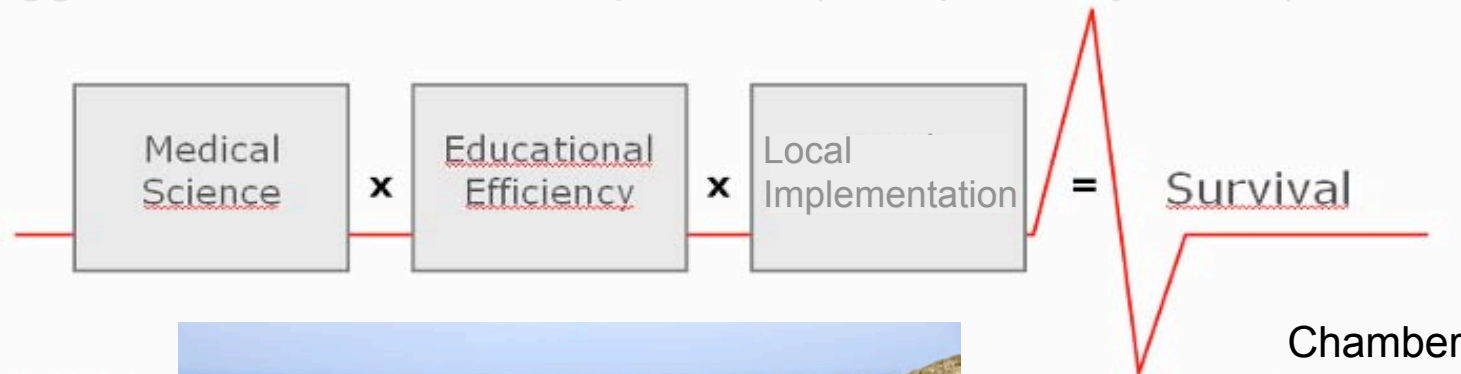
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# Formula of Survival

- suggests that outcome is a product (multiplicatory effect) of three factors:



Chamberlain et al,  
Resuscitation 2003



Utstein symposium  
- 2001  
- 2006

Science: What to do based on evidence!

Education: How to teach based on science!

Implementation: What to do and how to do it!

# Indication for therapeutic hypothermia

It has **not** been shown in randomised studies that therapeutic hypothermia improves survival after cardiac arrest

- a) if initial rhythm is asystole or PEA, or
- b) if cardiogenic shock is present

I would still treat such patients with therapeutic hypothermia

1 = Totally disagree

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# Formula of Survival and therapeutic hypothermia

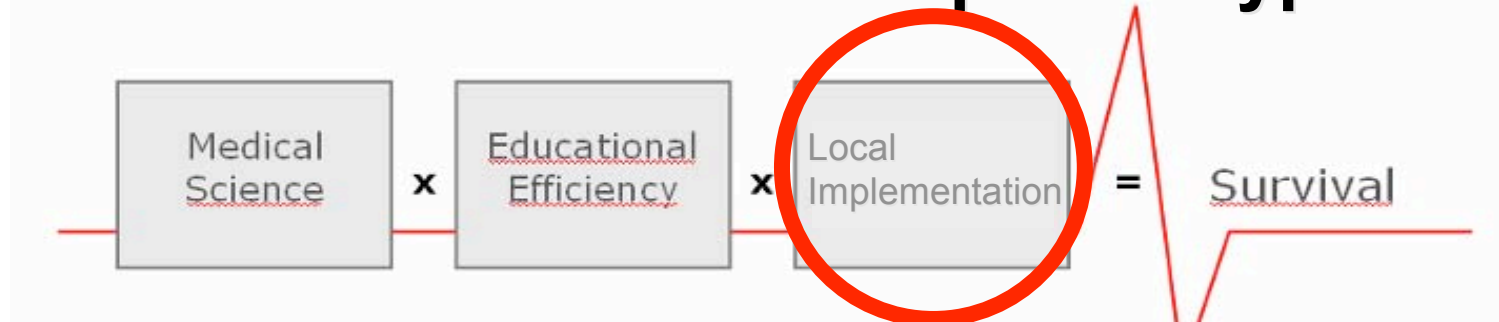
## 1. Science:

- **neuroprotective effects:** several experimental studies  
(...apoptosis, free radicals, excitatory amino acids, lactate, inflammation....)
- **three positive non-randomized studies** (from Japan, Austria, Australia)
  - Zeiner et al. Stroke 2000
  - Bernard et al. Ann Emerg Med 1997
  - Yanagawa et al. Resuscitation 1998
- **three positive randomized studies** of different size and quality
  - good survival rate in the normothermia group in the HACA trial:  
45% (39% with favourable outcome)
    - HACA-study. NEJM 2002
  - significantly better in the hypothermia group
    - Bernard et al. NEJM 2002
    - Hachimi-Idrissi et al. Resuscitation 2001

## 2. Education:

- easy to learn and to perform,
- many different methods (from simple/easy methods to more advanced systems)
  - **we are treating patients with a reperfusion syndrome and need to save the damaged brain!**

# Formula of Survival and therapeutic hypothermia



"Utopia"	1.0	x	1.0	x	1.0	=	1.0	→	40 %
Best practice	0.8	x	0.8	x	0.8	=	0.5	→	20 %
Worse practice	0.8	x	0.4	x	0.3	=	0.07	→	3 %

## Implementation of therapeutic hypothermia:

- Germany: 25% Wolfrum et al, Resuscitation 2007
- UK : 28% Laver et al, Anaesthesia 2007
- USA : 26% Merchant et al, Crit Care Med 2006

Average            0.8            x            0.6            x            0.26            =            0.12            →            5 %

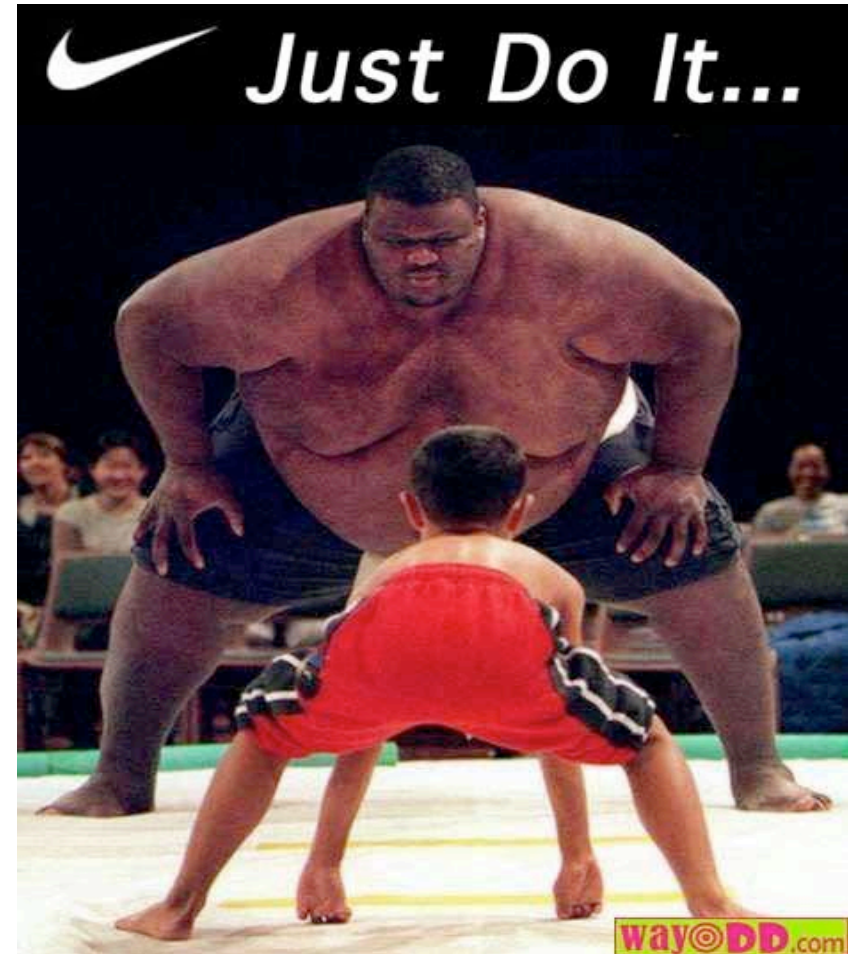
# Implementation



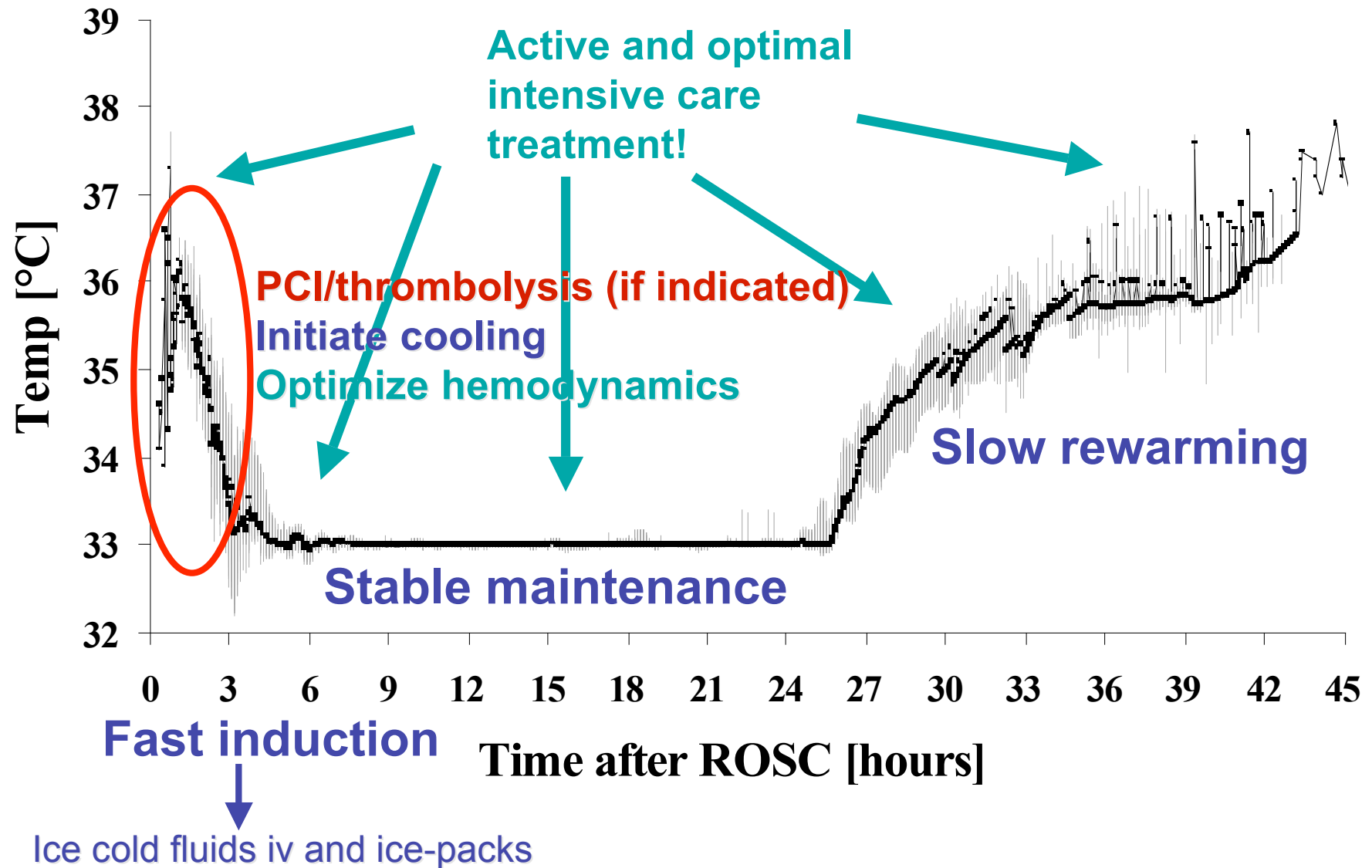
# Main challenge: Implementation

Carefully plan a well-defined implementation plan:

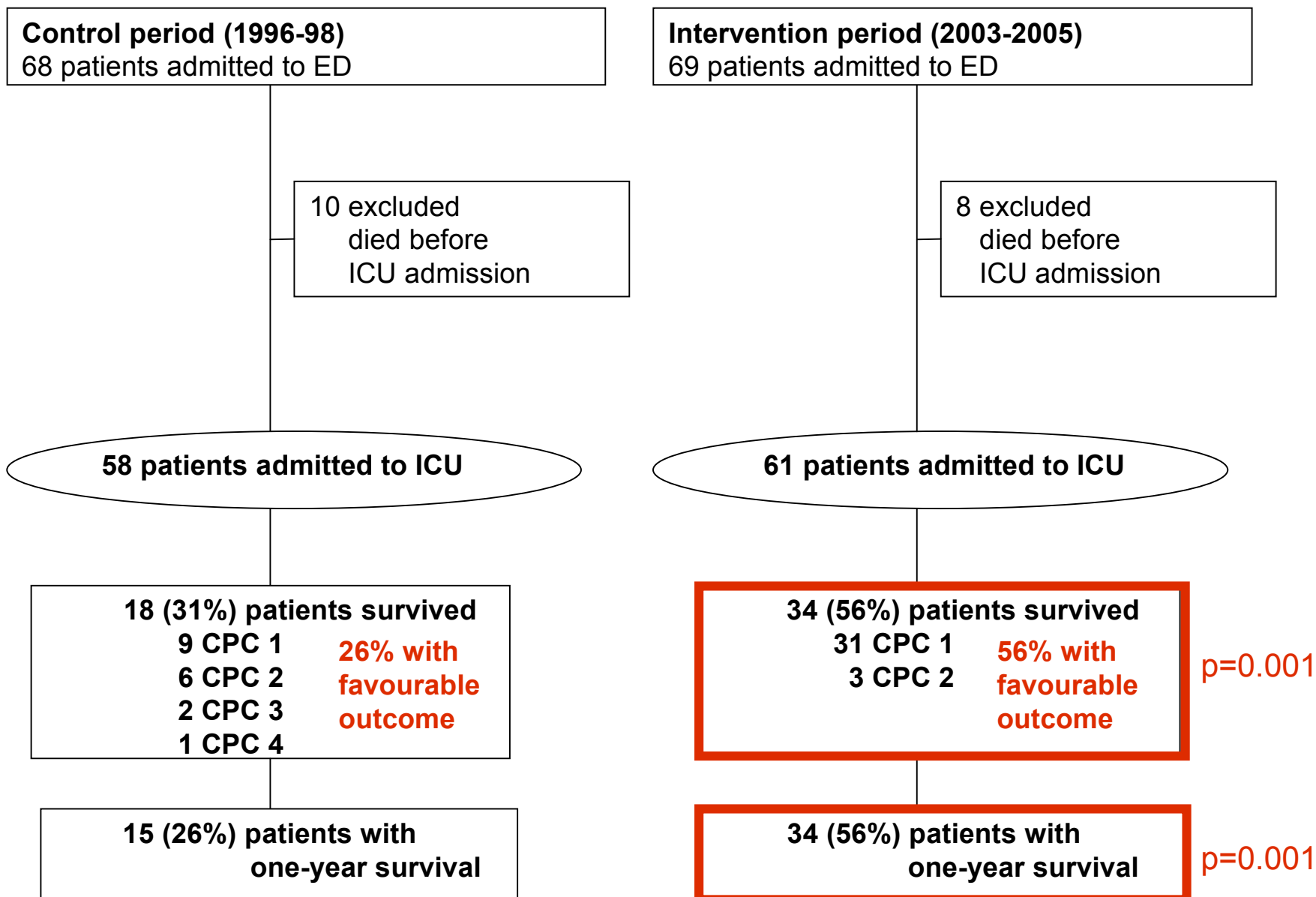
- chaired by a charismatic strong leader with accessibility and skills to change
- identify the weak links in the local infra-structure
- define a simple, goaldirected protocol
- define and select important collaborators from different fields (doctors, nurses)
- financial and institutional support
- a continuous process evaluation with feedback and research



# Optimal treatment during reperfusion



# Patients from Oslo EMS admitted to Ullevål UH



# Complications

	Control period (n=58)	Intervention period (n=61)	OR (95% CI)	P value
<b>General complications</b>	<b>37 (64)</b>	<b>44 (72)</b>	<b>1.47 (0.68 – 3.19)</b>	<b>0.44</b>
<b>Pneumonia</b>	<b>33 (57)</b>	<b>29 (48)</b>	<b>1.28 (0.69 – 2.40)</b>	<b>0.43</b>
<b>Sepsis</b>	<b>1 (1)</b>	<b>2 (3)</b>	<b>2.33 (0.21 – 26.21)</b>	<b>0.60</b>
<b>Severe arrhythmias</b>	<b>9 (16)</b>	<b>15 (25)</b>	<b>1.90 (0.80 – 4.53)</b>	<b>0.14</b>
<b>Bleeding</b>	<b>n.a</b>	<b>5 (9)</b>		
<b>Seizures</b>	<b>16 (28)</b>	<b>11 (18)</b>	<b>0.63 (0.28 – 1.39)</b>	<b>0.34</b>
<b>Status epilepticus</b>	<b>3 (5)</b>	<b>5 (8)</b>	<b>1.98 (0.46 – 8.56)</b>	<b>0.47</b>

Sunde et al, Resuscitation 2007

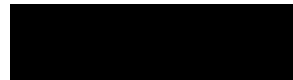
## Results UUH: from 1.9.03 – 30.06.06

All patients treated after  
OHCA at Ulleval University  
Hospital with cardiac aetiology

135 patients admitted to ICU

82 (61%) patients survived  
71 CPC 1  
9 CPC 2  
2 CPC 3

- 59% of all patients survive with favourable outcome
- 25 patients admitted after asystoli/PEA, 19 cooled (76%)  
(both cardiac and non-cardiac aetiology)
  - 8 survivors (4 CPC 1, 2 CPC 2, 1 CPC 3, 1 CPC 4)  
→ **6 survivors (24%) with favourable survival**



# Therapeutic hypothermia: more clinical data

- **Lausanne (Switzerland): before and after implementation of TH**

- favourable outcome (CPC 1 and 2), all initial rhythms included

- **26/55 (47%) vs 11/54 (20%)**,  $p=0.005$  (chi-square)

Oddo et al, Crit Care Med 2006

- **Stavanger (Norway): before and after implementation of TH**

- CPC 1 and 2, all comatose patients with cardiac origin admitted to ICU

- **16/27 (59%) vs 11/34 (32%)**,  $p<0.05$  (chi-square)

Busch et al, Acta Anesthesiol Scand 2006

- **ERCHACA Registry** (owned by ERC, supported by Alsius Corp.)

- 650 patients from 19 sites, 2003-2005

- 462 (79%) received TH

- **45% vs 32%** in good outcome,

- cooled patients were less likely to have an unfavourable outcome

- (OR 0.32 (95 CI 0.38-0.89,  $p=0.01$ )) ERCHACAR, Crit Care Med 2007

- **The Hypothermia Network** ([www.hypothermianetwork.com](http://www.hypothermianetwork.com), independent)

- 900 patients from 32 sites, 2004-2006

- Data from 500 patients 6 months after arrest:

- 54% alive, 92% with good outcome** (VF: 64% alive, Asystoli/PEA: 21%)

Nielsen et al, Abstract ESICM 2006

→ **few complications, few adverse events**

# Case report 1: Indication 1

- Healthy male, approx. 50 years
- Witnessed VF cardiac arrest
- Immediate good BLS for 5 min before EMS arrival
- During resuscitation spastic, still breathing, not possible to intubate, 30:2
- 7 min ALS before ROSC (2 shocks)  
= 12 min of CPR

What would you do after ROSC?

- 1= Immediate anaesthesia and intubation, stabilise circulation
- 2 = Same as in 1, but in addition start cooling
- 3 = Check if breathing is still adequate, wait for 5-10 min to see if he awakes before further decision, stabilise circulation

# Case report 1: Indication 2

- Woman, 30 years, 14 days post partum, chest pain for one day
- 3 years earlier a critical stroke, requiring hemicranectomy, minimal sequele
- Witnessed VF cardiac arrest
- Immediate good BLS
- Prolonged ALS for approx. 30 min before unstable ROSC, BP↓

## *In hospital:*

- *Coronary angiography: LAD dissection → PCI*
- *AMI with EF: 15-20% → Cardiogenic shock*
- *She moves and breaths (but not yet adequate awake)*

What would you do now?

- 1= Try to stabilise circulation, IABP, full intensive care treatment including therapeutic hypothermia
- 2 = Same as in 1, but due to low blood pressure and cardiogenic shock **no** therapeutic hypothermia
- 3 = Try to extubate and awake her → BP↑, and give further full heart stabilising intensive care treatment

# Case report 3: Prognostication

Healthy male, 50 years  
Witnessed VF cardiac arrest  
Prolonged arrest, > 30 shocks  
45 min ALS before ROSC

*Initial hospital treatment:*

- PCI
- TH
- Standardised intensive care

*First days in ICU:*

- No adequate reactions
- seizures, grimacing
- sepsis

*After one week:*

- Status epilepticus not responding to traditional treatment
- New sepsis
- Hemodynamic unstable

What would you do know?

- 1= Because of his bad prognosis stop further active treatment (no antibiotics, pressors, barbiturates)
- 2 = Continue full intensive care treatment with antibiotics, pressors and start a barbiturate infusion

# Prognostication is difficult!

- no clinical absolute predictive clinical signs the first two days after the arrest! Edgren et al, Lancet 1993 Madl et al, Crit Care Med 2000
- EEG should be performed during induced hypothermia.  
Hovland et al, Resuscitation 2006; 68:143-6
- Determination of prognosis after cardiac arrest may be more difficult after introduction of therapeutic hypothermia.  
Sunde et al, Resuscitation 2006; 69: 29-32
  - Amplitude-integrated EEG (aEEG) predicts outcome after cardiac arrest and induced hypothermia.  
Rundgren et al, Intensive Care Med 2006; 32: 836-42.
  - Other cerebral monitoring: SEP, BIS/CSM, S100/NSE....?

# Conclusion

## TH is part of standardised post resuscitation care

- decide as early as possible, “yes” or “no” to **active treatment**
  - ethics, co-morbidity and general condition, total anoxia time
- ☞ If active treatment, do everything, be **goaldirected**
  - optimise haemodynamics and normalise oxygenation
  - treat the cause (revascularisation if indicated)
  - mechanical ventilation and therapeutic hypothermia
  - standardised general post resuscitation intensive care
- ◆ If the patients are awake and adequate: keep them awake!
- ◆ Keep comatose patients sedated and cold at the respirator for 24 h
  - rewarm
  - prognostication after 36-72 hours
    - ◆ no clinical absolute predictive clinical signs the first two days after the arrest

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