

Clinical research in post cardiac arrest care

Journée de la Recherche Médicale et Translationnelle - 16th October 2024, CHL-Luxembourg

Pascal STAMMET, MD, PhD

Clinical Affiliate Professor

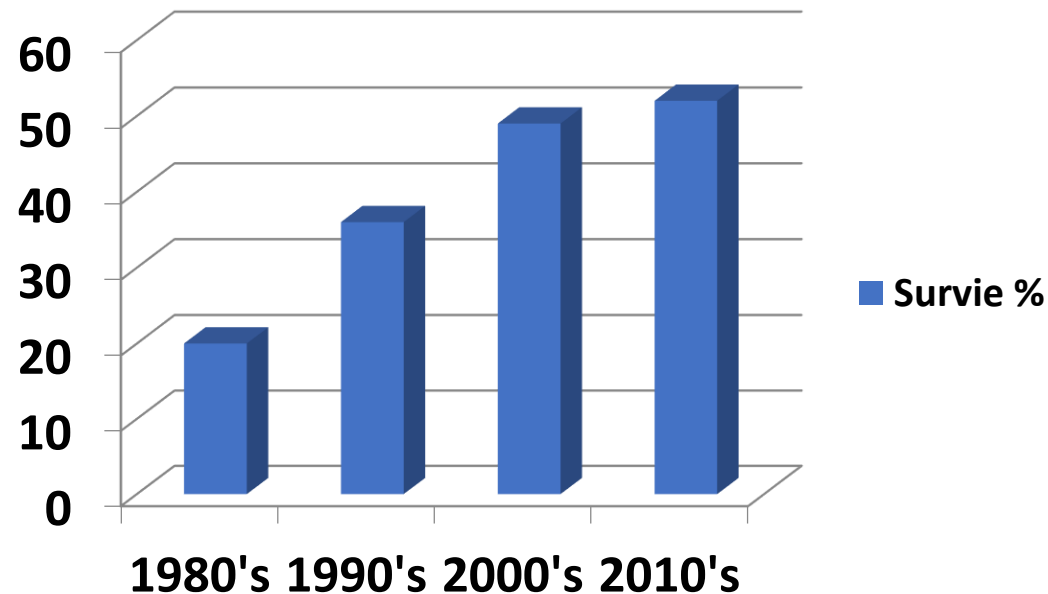
University of Luxembourg

Intensive Care Department

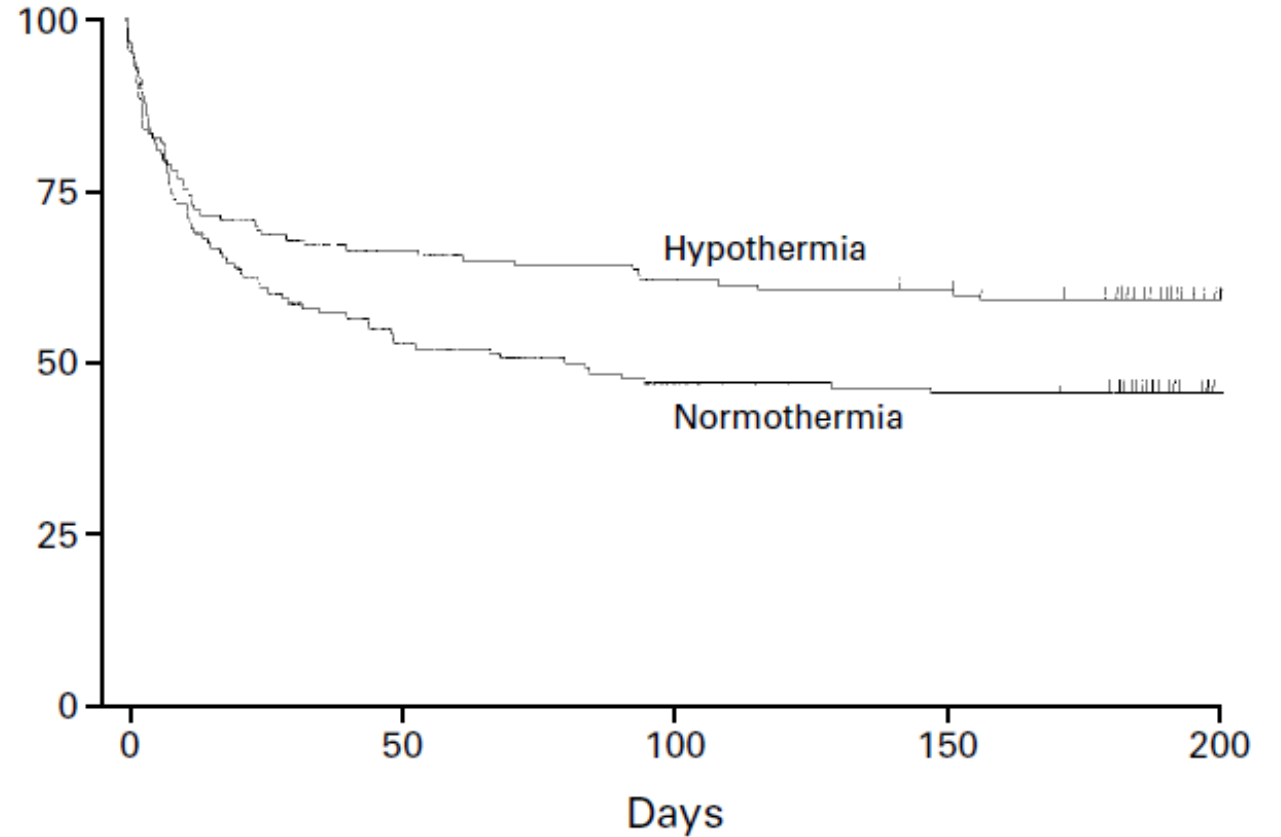
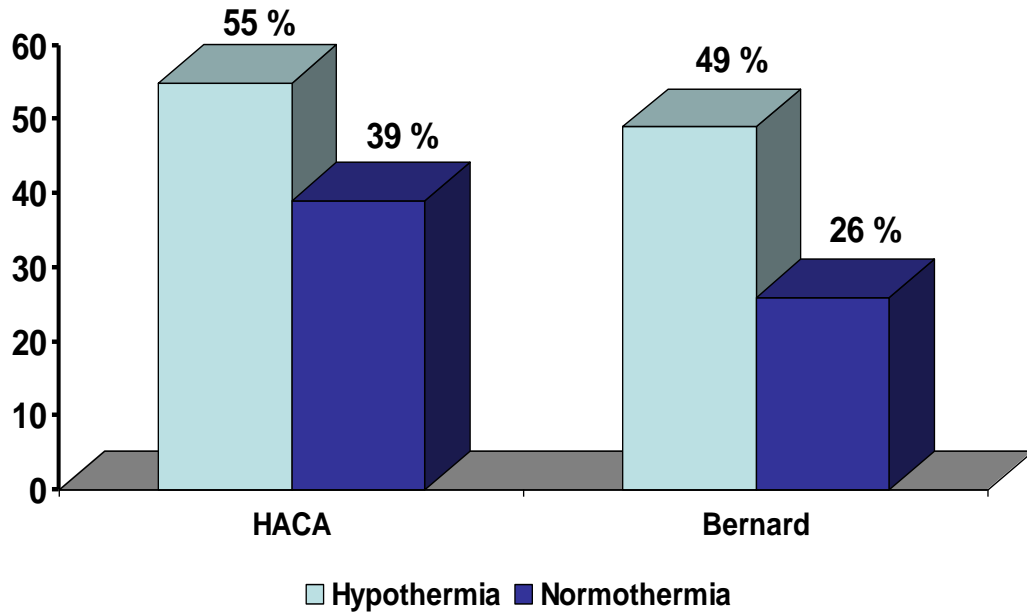
Centre Hospitalier de Luxembourg

Where do we stand now?

- Only approx. 20% of OHCA patients survive until the hospital
- Historically, very low survival: « futile » care
- Over the last 2 decades: significant improvement of outcome



The magic bullet? HACA and Bernard trial



Spectacular results! NNT = 7

NO. AT RISK

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

Collateral benefit!

- Implementation of TTM (« hypothermia ») into 2005 guidelines
- CA care become not futile anymore!
- **Protocols in ICUs for CA care save lives**

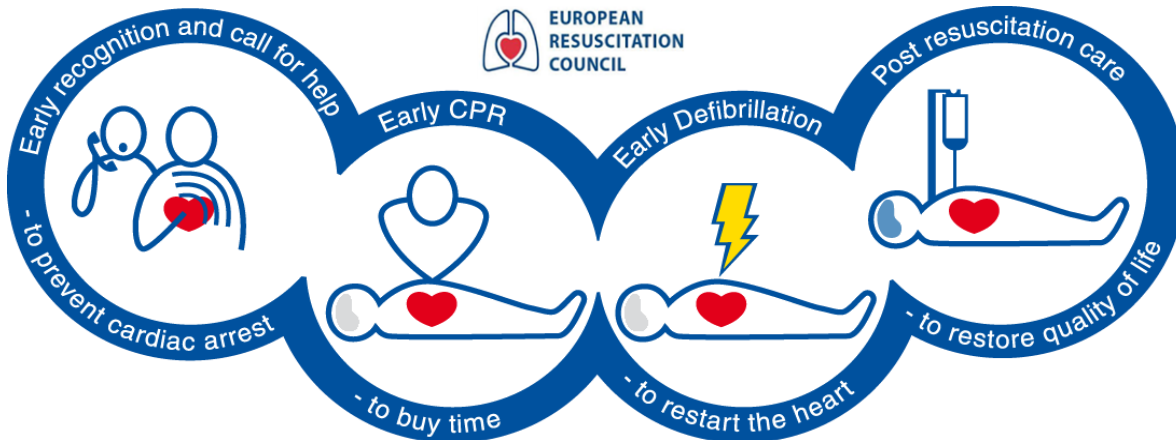
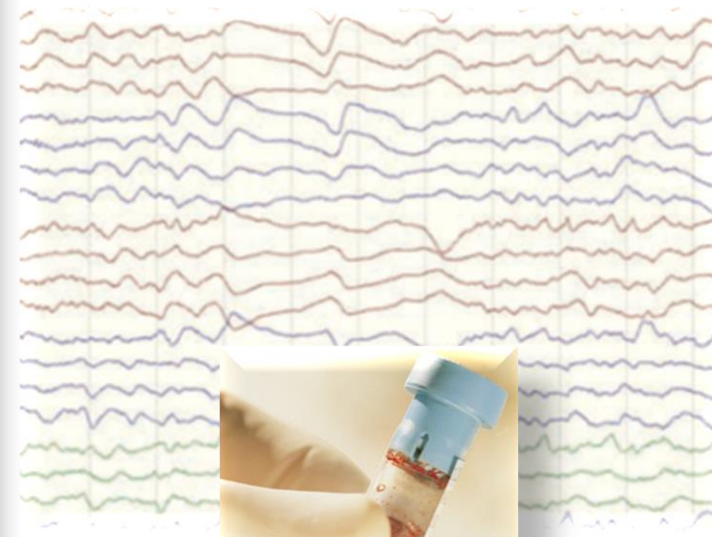
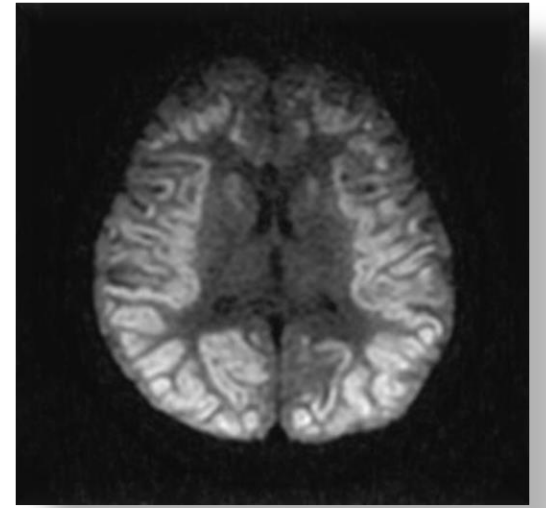


Table 1 Univariate analysis of prognostic factors and outcome data for patients admitted to ICU of Ullevål University Hospital in the control (1996–1998) or intervention (2003–2005) periods, presented as absolute numbers (percentage) or median values with interquartile range

	Control period (n = 58)	Intervention period (n = 61)	OR (95% CI)	p-Value
Male	46 (79)	50 (82)	1.2 (0.5, 2.9)	0.89
Age < 70	28 (48)	43 (71)	2.6 (1.2, 5.4)	0.022
Witnessed	55 (95)	60 (98)	3.3 (0.33, 32.4)	0.36
Bystander CPR	43 (74)	43 (71)	0.8 (0.4, 1.9)	0.81
Initial VF	49 (84)	55 (90)	1.7 (0.6, 5.1)	0.51
Ambulance response time (min)	6 (4–9)	6 (4–8)		0.70 ^a
Time to ROSC (min)	18 (13–22)	18 (10–27)		0.98 ^a
Comatose on admission	52 (90)	52 (85)	1.2 (0.5, 2.8)	0.65
Myocardial infarction	33 (57)	36 (59)	1.1 (0.5, 2.3)	0.82
Mechanical ventilation (days)	2 (1–5)	2 (1–5)		0.70 ^a
Stay at ICU (days)	4 (3–6)	5 (2–8)		0.42 ^a
Survival to discharge	18 (31)	34 (56)	2.80 (1.32, 5.93)	0.007
Favourable outcome (CPC 1–2)	15 (26)	34 (56)	3.61 (1.66, 7.84)	0.001
1-Year survival	15 (26)	34 (56)	3.61 (1.66, 7.84)	0.001

^a Two sided p-values for continuous variables from Mann–Whitney rank sum test.

Protocolized post cardiac arrest care:
this is what we talk about...



Some cardiac arrest research on prognostication and outcome



Clinical paper

Bispectral index (BIS) helps predicting bad neurological outcome in comatose survivors after cardiac arrest and induced therapeutic hypothermia^{☆,☆☆}

Pascal Stammet^{*1}, Christophe Werer¹, Luc Mertens¹, Christiane Lorang¹, Margaret Hemmer¹

Circulating microRNAs after cardiac arrest

Journal of the American College of Cardiology
© 2013 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 62, No. 9, 2013
ISSN 0735-1097/\$36.00
<http://dx.doi.org/10.1016/j.jacc.2013.04.039>

Biomarkers

Modeling Serum Level of S100 β and Bispectral Index to Predict Outcome After Cardiac Arrest

Pascal Stammet, MD,* Daniel R. Wagner, MD, PhD,^{†‡} Georges Gilson, PhD,[§] Yvan Devaux, PhD[‡]

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2015 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER INC.

VOL. 65, NO. 19, 2015
ISSN 0735-1097/\$36.00
<http://dx.doi.org/10.1016/j.jacc.2015.03.538>

Neuron-Specific Enolase as a Predictor of Death or Poor Neurological Outcome After Out-of-Hospital Cardiac Arrest and Targeted Temperature Management at 33°C and 36°C

Pascal Stammet, MD,* Olivier Collignon, PhD,[†] Christian Hassager, MD, DMSc,[‡] Matthew P. Wise, MD, DPHIL,[§] Jan Hovdenes, MD, PhD,^{||} Anders Aneman, MD, PhD,[¶] Janneke Horn, MD, PhD,[#] Yvan Devaux, PhD,^{**} David Erlinge, MD, PhD,^{††} Jesper Kjaergaard, MD, DMSc,[‡] Yvan Gasche, MD,^{‡‡} Michael Wanscher, MD, PhD,^{§§} Tobias Cronberg, MD, PhD,^{||||} Hans Friberg, MD, PhD,^{¶¶} Jørn Wetterslev, MD, PhD,^{##} Tommaso Pellis, MD,^{***} Michael Kuiper, MD, PhD,^{†††} Georges Gilson, PhD,^{‡‡‡} Niklas Nielsen, MD, PhD,^{§§§} and the TTM-Trial Investigators



Clinical paper

Late heartbeat-evoked potentials are associated with survival after cardiac arrest[☆]

ORIGINAL

Quantitative versus standard pupillary light reflex for early prognostication in comatose cardiac arrest patients: an international prospective multicenter double-blinded study

JAMA Neurology | Original Investigation

Serum Neurofilament Light Chain for Prognosis of Outcome After Cardiac Arrest

RESEARCH

Open Access

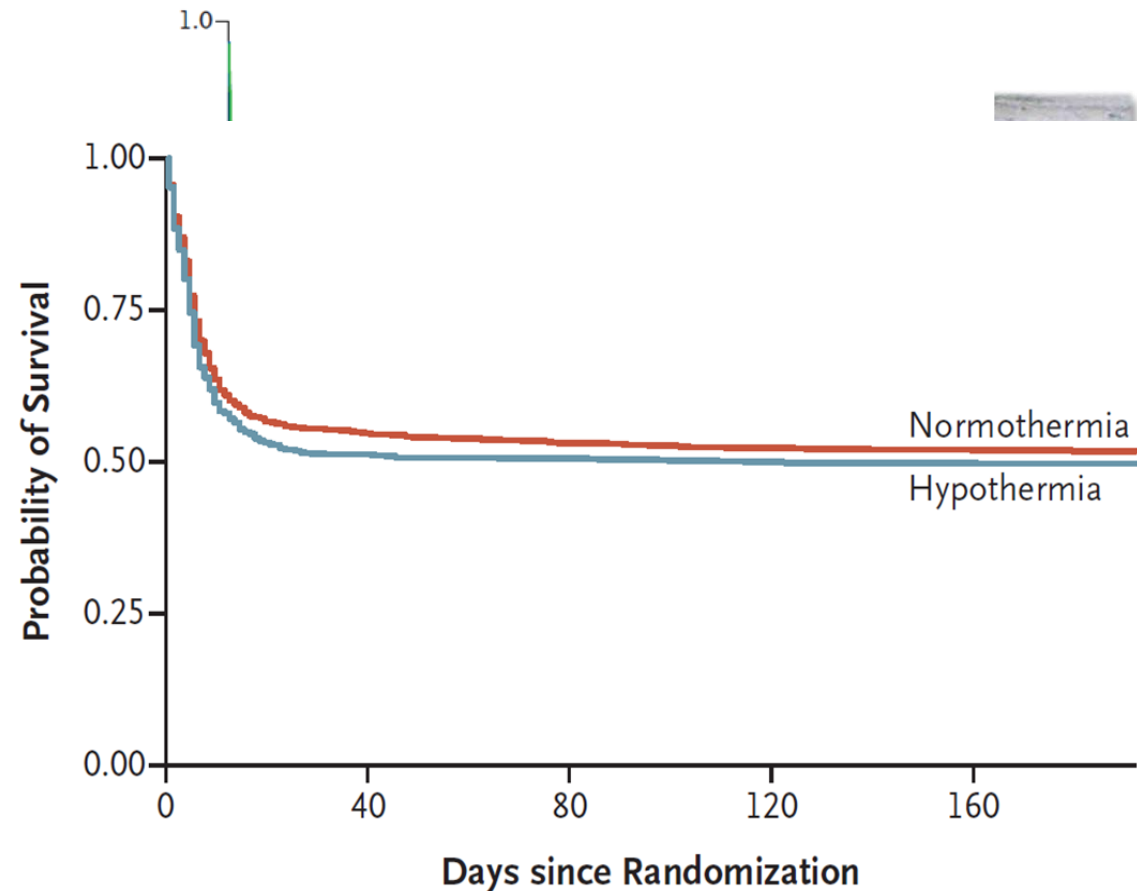
Predicting neurological outcome after out-of-hospital cardiac arrest with cumulative information; development and internal validation of an artificial neural network algorithm

Peder Andersson^{1,16*}, Jesper Johnsson², Ola Björnsson^{3,4}, Tobias Cronberg⁵, Christian Hassager⁶, Henrik Zetterberg^{7,8,9,10}, Pascal Stammet¹¹, Johan Undén¹², Jesper Kjaergaard⁶, Hans Friberg¹³, Kaj Blennow^{7,8}, Gisela Lilja⁵, Matt P. Wise¹⁴, Josef Dankiewicz¹⁵, Niklas Nielsen^{2†} and Attila Frigyesi^{1,4†}



The challenges of cardiac arrest

- Methodological flaws of initial trials
(no true randomisation, small sample sizes, statistical significance at the limit, no clear separation between groups regarding temperature, withdrawal criteria not reported, ...)
- Need for new trials
- **TTM(1) trial : 33°C vs 36°C** with a strict separation of temperature groups, clear withdrawal criteria, blinded outcome assessment
- **TTM2: hypothermia (33°C) vs normothermia ($\leq 37.8^\circ\text{C}$)**



No. at Risk						
Normothermia	925	506	491	484	480	
Hypothermia	925	474	468	462	461	

What do the guidelines 2021 tell us?



- **Temperature management:** In patients who remain comatose after cardiac arrest, continuous monitoring of core temperature should be practiced, and active measures should be undertaken to **prevent fever** (defined as >37.7 °C) for at least 72 hours.
- **Hemodynamics :** **Avoid hypotension (<65 mmHg).** Target MAP to achieve adequate urine output (>0.5 mL/kg/h) and normal or decreasing lactate.
- **Sedation:** Use short acting sedatives and opioid.
- And not much more...





**Sedation, Temperature and Pressure after
Cardiac Arrest and REsuscitation**

Main research questions

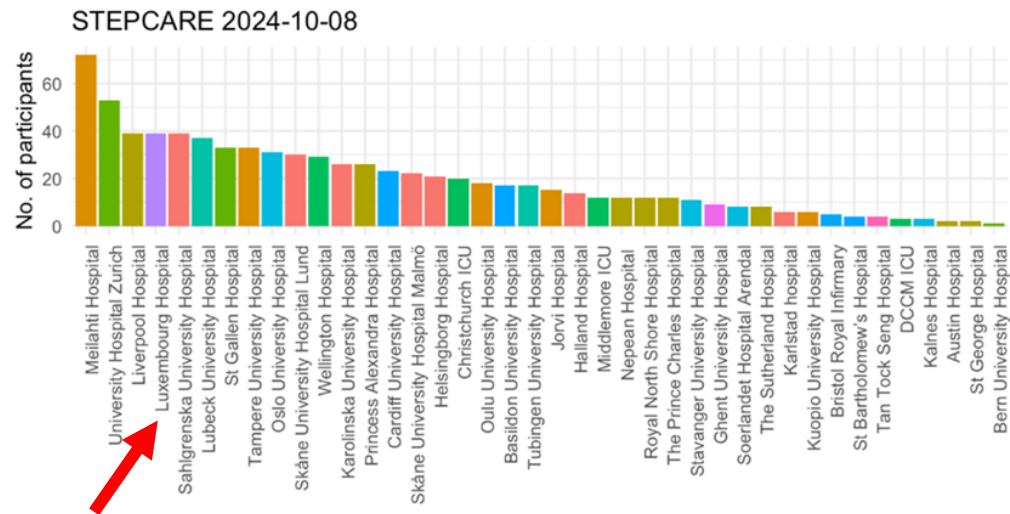
1. Is continuous **deep sedation** for 36 hours beneficial compared to minimal sedation? (SED-CARE)
2. Is **fever management** with a feedback-controlled device for 72 hours beneficial compared to standard fever care? (TEMP-CARE)
3. Is a mean **arterial pressure target of >85mmHg** for 72 hours beneficial compared to >65mmHg? (MAP-CARE)

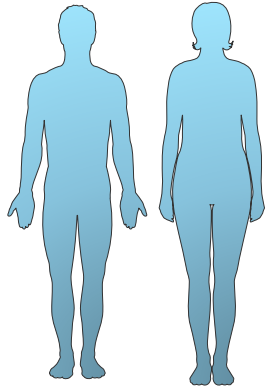
Inclusion criteria: adult, non traumatic out-of-hospital-cardiac arrest with stable ROSC for at least 20 min, unconscious or intubated

Exclusion criteria: ECMO, pregnancy, neurological cause, randomized before



- 2x2x2 factorial design, multi center, randomized clinical trial
- 3500 patients
- Started end of 2023
- CHL started 11/2023
- 795 patients included





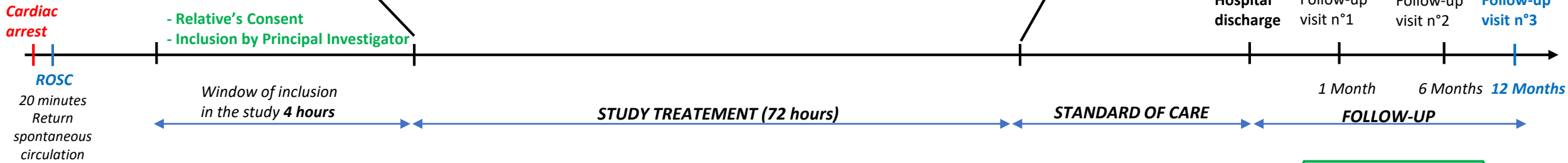
- ≥ 18 years
- Cardiac arrest
- Return of spontaneous blood circulation
- Unconscious



	Sedation	Temperature	Arterial pressure
1	Deep (36 h)	Fever control with MD	mean AP > 85 mmHg
2	Deep (36 h)	Fever control with MD	mean AP > 65 mmHg
3	Deep		mean AP > 85 mmHg
4	Deep		mean AP > 65 mmHg
5	Light (36h)		mean AP > 85 mmHg
6	Light (36h)	Fever control with MD	mean AP > 65 mmHg
7	Light (36h)	Fever control without MD	mean AP > 85 mmHg
8	Light (36h)	Fever control without MD	mean AP > 65 mmHg

8 possible interventions

Primary outcome: 6 month-survival



- Relative's Consent
- Inclusion by Principal Investigator

Unconscious patient taken to the hospital

Patient's return to a conscious state : Collection of patient's deferred consent

Continue participation
OR
Stop participation

3 substudies

1. Substudy «Biomarkers»
 2 x 6 ml { additional samples : at 12h, 24h, 48h (+ 1 tube 2,5 ml), 72h

2. Substudy «Early neurological pronostication »
 • Early prognosis based on standard examinations performed 24h after cardiac arrest

3. Substudy «Extended follow-up» at 6 months and 12 months
 • Questionnaires and tests for the patient
 • Questionnaires for the carer/caregiver

MD : medical device
AP : arterial pressure

STEP CARE substudies and perspectives

- Follow-up substudy
 - Follow-up of patients at 1, 6 and 12 months
 - Including caregivers and partners of CA patients
- Early prognostication sub-study
 - Can we already predict outcome at 24 hours (actual guidelines >72hours)?
- Biomarker substudy
 - 12, 24, 48 and 72 hours blood sampling for « biomarkers »
 - in STEP CARE, IBBL is the biobank (collaboration started in 2010 with the TTM(1) trial, continued for TTM2 and now STEPACRE)
- Close collaboration ICU of CHL with Cardiovascular Research Unit of LIH (Dr Yvan Devaux) since more than 15 years

Don't forget, today is October 16th!

JIDDEREEN
op dëser Welt
— kann e Liewe **RETTEN** —



16 OKTOBER
World Restart a Heart Day

En Häerz an **3** einfache Schrëtt erëm
un d'Schloe bréngen!

Méi Info
WWW.ILCOR.ORG/WRAH
[#WORLDRESTARTAHEART](https://twitter.com/WORLDRESTARTAHEART)
eng Initiative vun

1 Präiwen **2** Uruffen **3** Drécken

ILCOR EUROPEAN RESUSCITATION COUNCIL LUXEMBOURG RESUSCITATION COUNCIL



Thank you for your attention!
And don't forget to push hard
and fast!