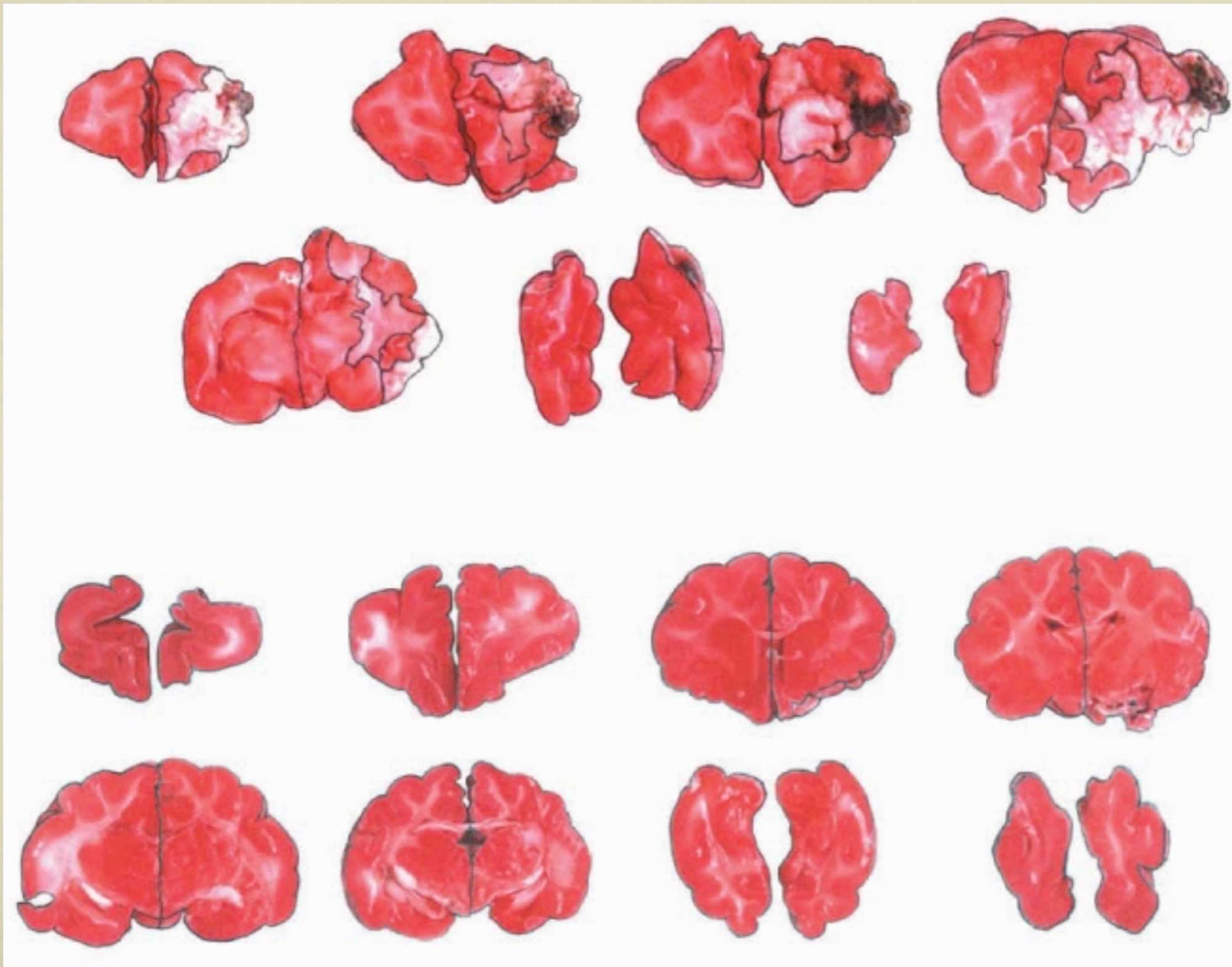


THERAPEUTIC HYPOTHERMIA

**ALEXANDER FLINT, M.D., PH.D.
NEUROCRITICAL CARE AND STROKE
KAISER REDWOOD CITY**



HYPOTHERMIA AS NEUROPROTECTION



HUMAN STUDIES

The Clinical Use of Hypothermia Following Cardiac Arrest *

G. RAINEY WILLIAMS, JR., M.D., FRANK C. SPENCER, M.D.

*From the Department of Surgery, The Johns Hopkins University School of Medicine
and Hospital, Baltimore, Maryland*

Ann Surg. 1958 September; 148(3): 462.

VOLUME 38, NUMBER 6 — NOVEMBER-DECEMBER, 1959

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THE USE OF HYPOTHERMIA AFTER CARDIAC ARREST

DONALD W. BENSON, M.D.
G. RAINEY WILLIAMS, JR., M.D.
FRANK C. SPENCER, M.D.
ADOLPH J. YATES, M.D.

Baltimore, Maryland*

Anesth Analg 1959 November; 38(6): 423.

BETTER HUMAN STUDIES

The New England Journal of Medicine

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VOLUME 346

FEBRUARY 21, 2002

NUMBER 8



MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

INDUCED HYPOTHERMIA AFTER OUT-OF-HOSPITAL CARDIAC ARREST

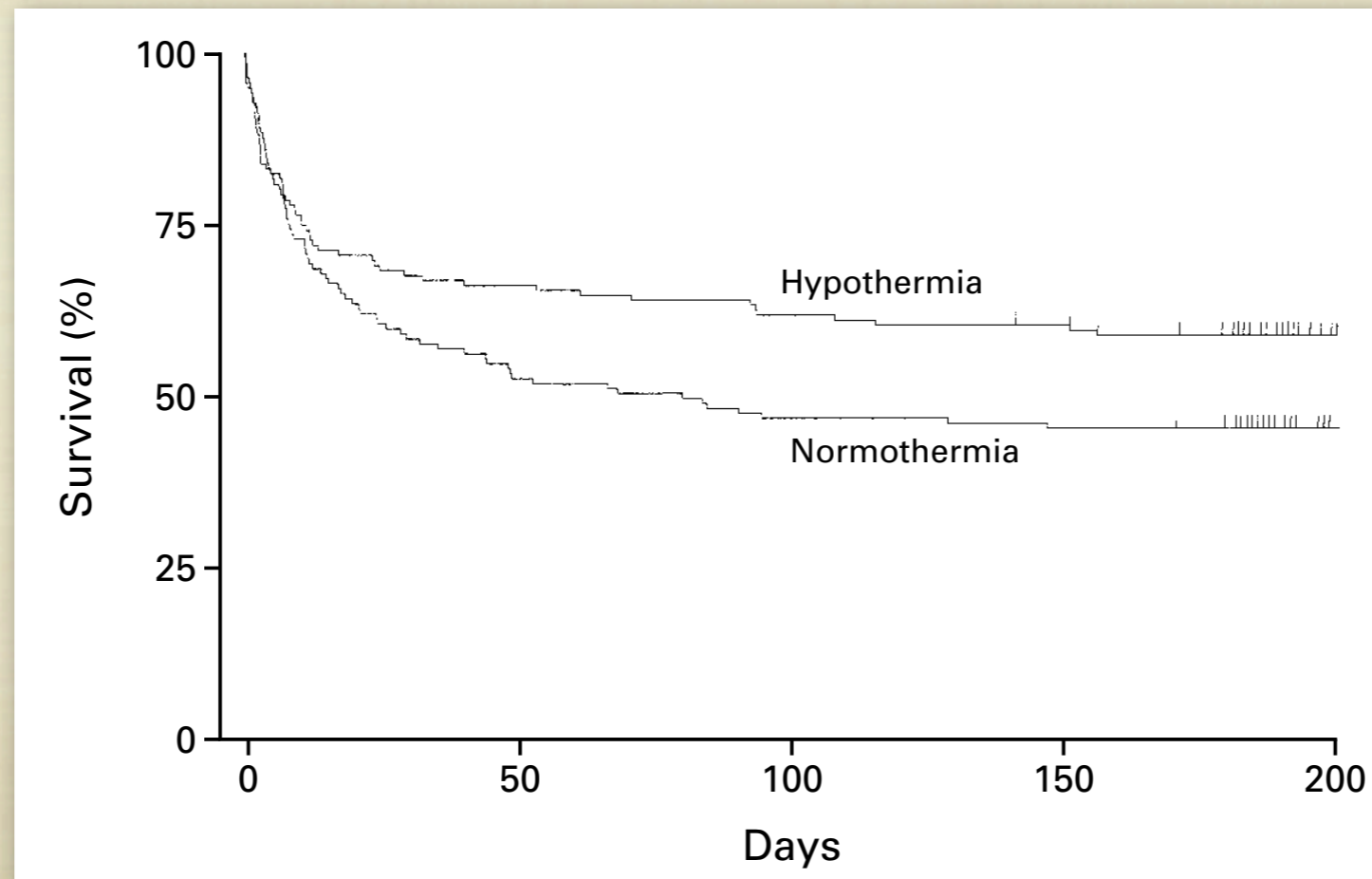
TREATMENT OF COMATOSE SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST WITH INDUCED HYPOTHERMIA

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.

BETTER HUMAN STUDIES

TABLE 2. NEUROLOGIC OUTCOME AND MORTALITY AT SIX MONTHS.

OUTCOME	NORMOTHERMIA	HYPOTHERMIA	RISK RATIO (95% CI)*	P VALUE†
	no./total no. (%)			
Favorable neurologic outcome‡	54/137 (39)	75/136 (55)	1.40 (1.08–1.81)	0.009
Death	76/138 (55)	56/137 (41)	0.74 (0.58–0.95)	0.02



BETTER HUMAN STUDIES

TABLE 5. OUTCOME OF PATIENTS AT DISCHARGE FROM THE HOSPITAL.

OUTCOME*	HYPOTHERMIA (N=43)	NORMOTHERMIA (N=34)
	number of patients	
Normal or minimal disability (able to care for self, discharged directly to home)	15	7
Moderate disability (discharged to a rehabilitation facility)	6	2
Severe disability, awake but completely dependent (discharged to a long-term nursing facility)	0	1
Severe disability, unconscious (discharged to a long-term nursing facility)	0	1
Death	22	23

*The difference between the rates of a good outcome (normal or with minimal or moderate disability) in the hypothermia and the normothermia groups (49 percent and 26 percent, respectively) was 23 percentage points (95 percent confidence interval, 13 to 43 percentage points; $P=0.046$). The unadjusted odds ratio for a good outcome in the hypothermia group as compared with the normothermia group was 2.65 (95 percent confidence interval, 1.02 to 6.88; $P=0.046$). The odds ratio for a good outcome in the hypothermia group as compared with the normothermia group, after adjustment by logistic regression for age and time from collapse to return of spontaneous circulation, was 5.25 (95 percent confidence interval, 1.47 to 18.76; $P=0.011$).

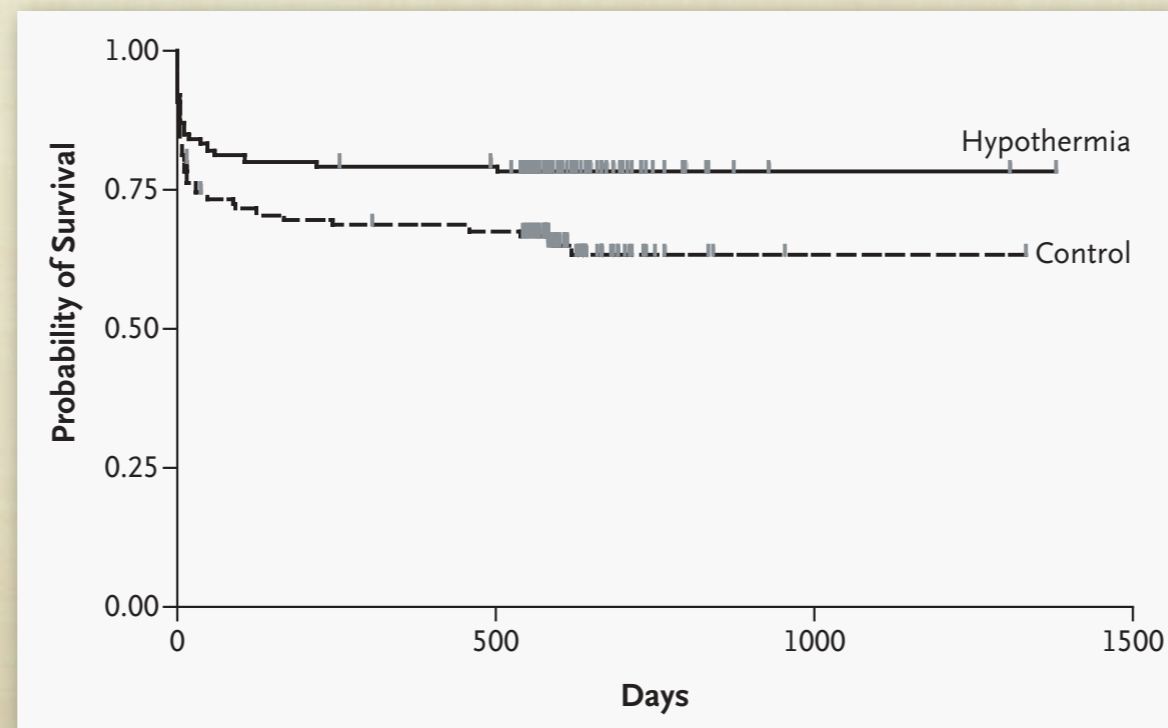
BETTER HUMAN STUDIES

The NEW ENGLAND JOURNAL of MEDICINE

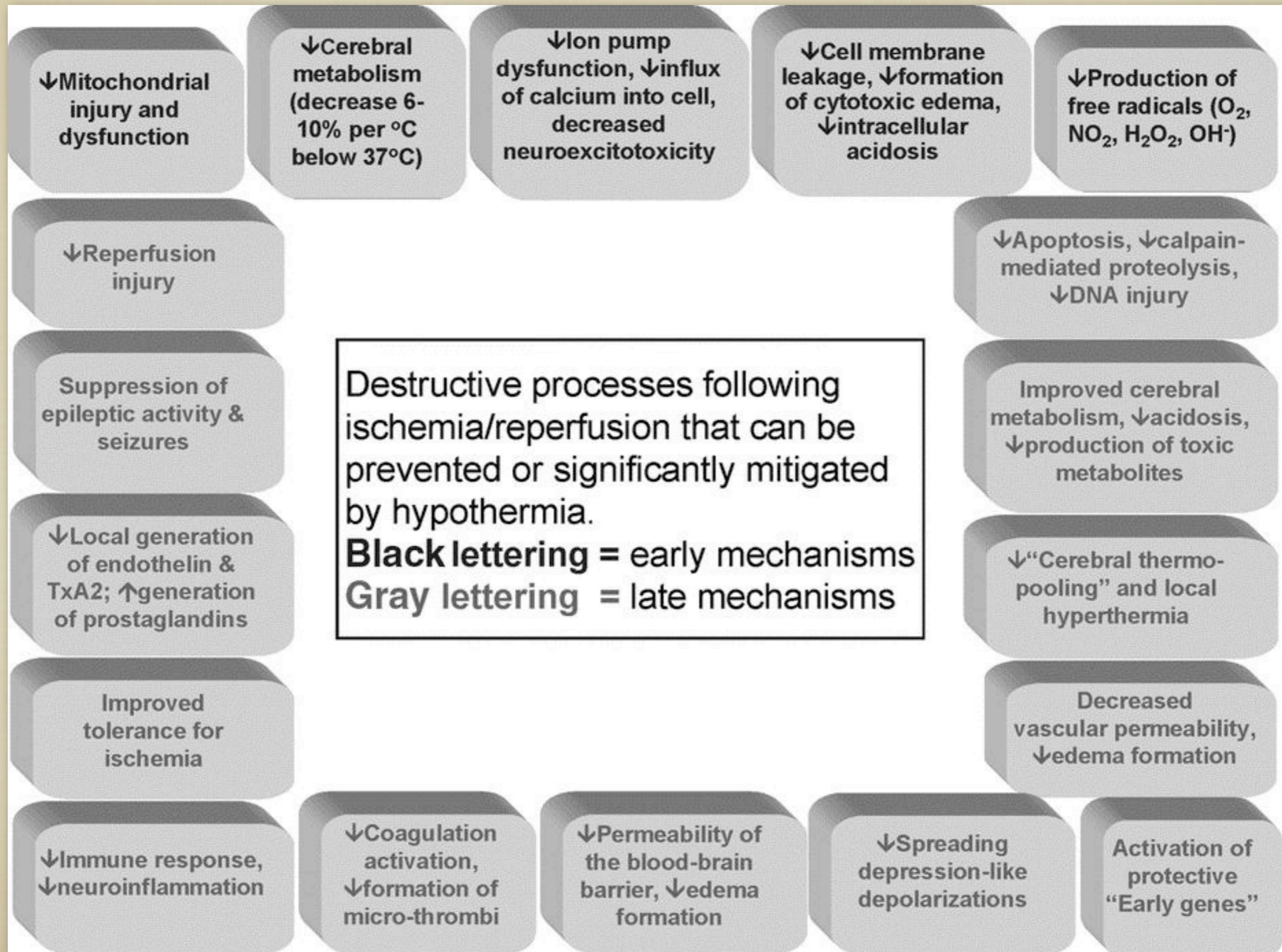
ORIGINAL ARTICLE

Whole-Body Hypothermia for Neonates with Hypoxic–Ischemic Encephalopathy

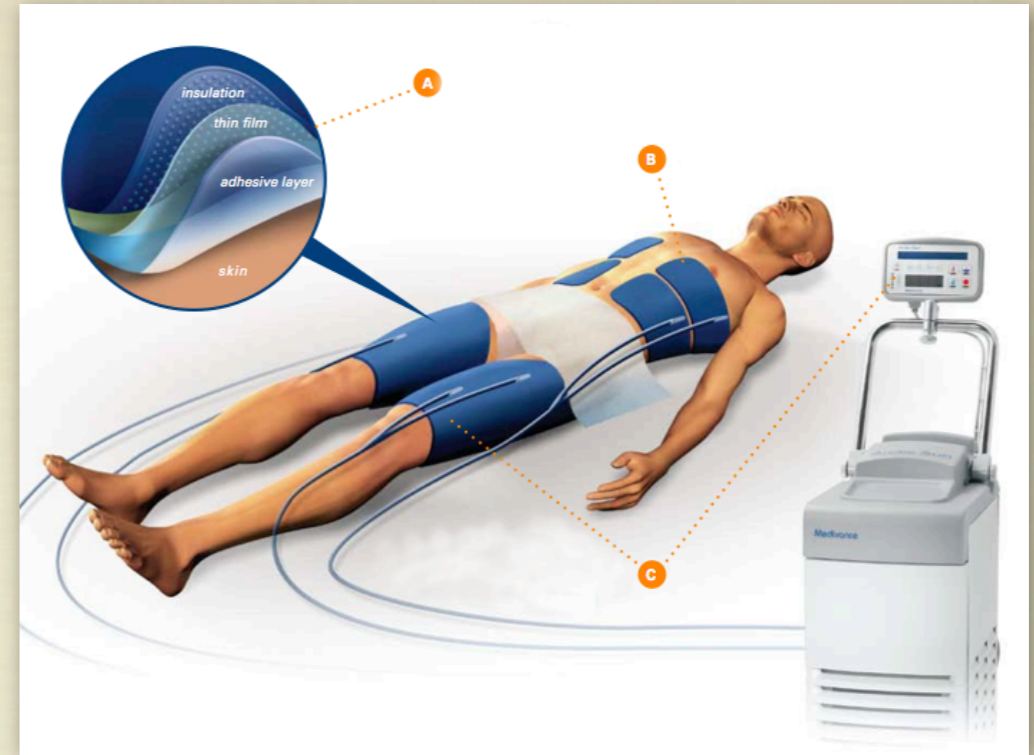
Seetha Shankaran, M.D., Abbot R. Laptook, M.D., Richard A. Ehrenkranz, M.D., Jon E. Tyson, M.D., M.P.H., Scott A. McDonald, B.S., Edward F. Donovan, M.D., Avroy A. Fanaroff, M.D., W. Kenneth Poole, Ph.D., Linda L. Wright, M.D., Rosemary D. Higgins, M.D., Neil N. Finer, M.D., Waldemar A. Carlo, M.D., Shahnaz Duara, M.D., William Oh, M.D., C. Michael Cotten, M.D., David K. Stevenson, M.D., Barbara J. Stoll, M.D., James A. Lemons, M.D., Ronnie Guillet, M.D., Ph.D., and Alan H. Jobe, M.D., Ph.D., for the National Institute of Child Health and Human Development Neonatal Research Network*



HYPOTHERMIA MECHANISMS

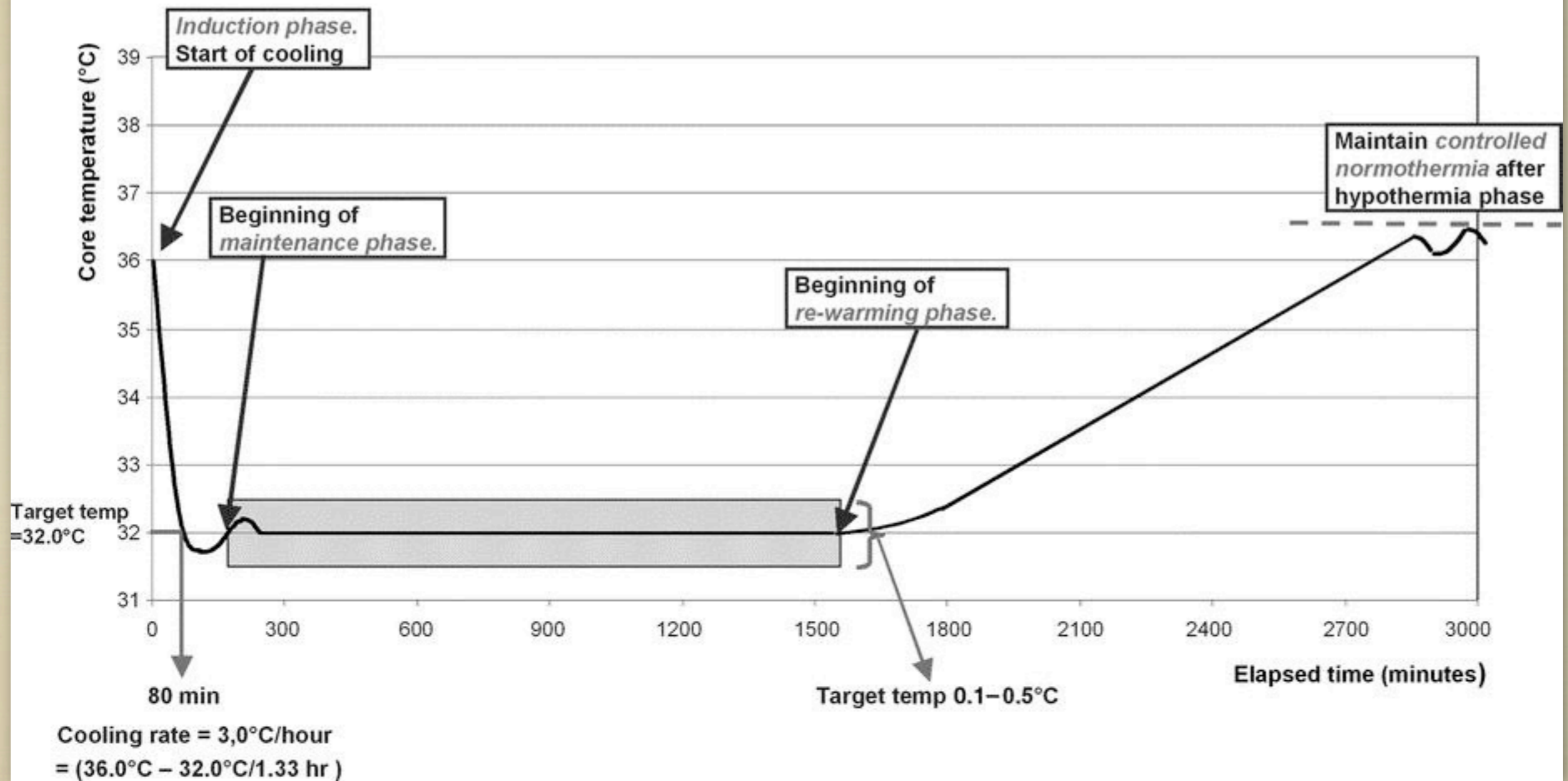


HOW TO COOL



HOW TO COOL

The three phases of hypothermia treatment



HOW TO COOL

- INDUCE HYPOTHERMIA TO 33 °C AS QUICKLY AS POSSIBLE
- MAINTAIN 33 °C WITH MINIMAL OVERSHOOT AND UNDERSHOOT
- SLOWLY REWARM BACK TO 37 °C OVER 18-24 HOURS
- MINIMIZE AND TREAT COMPLICATIONS

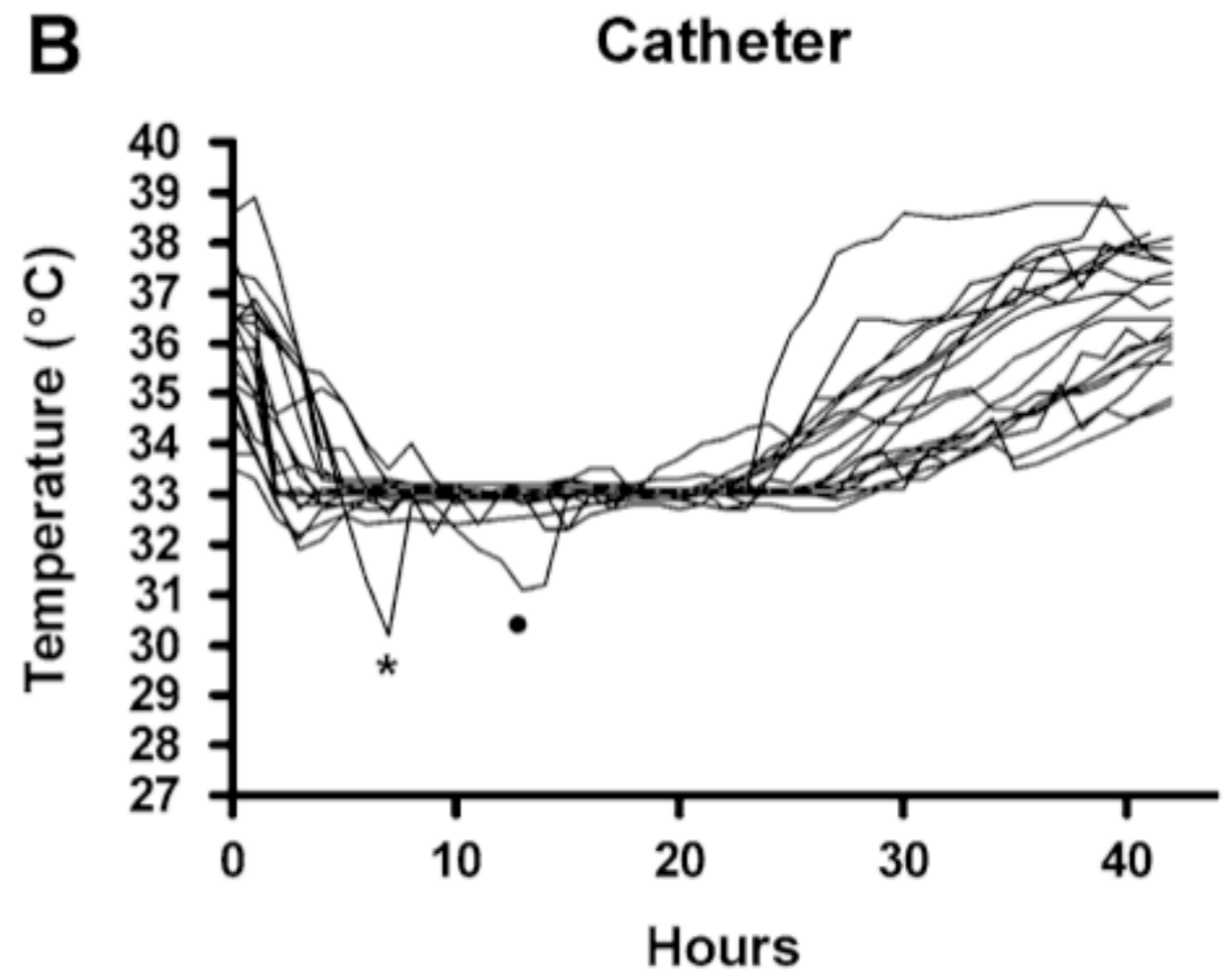
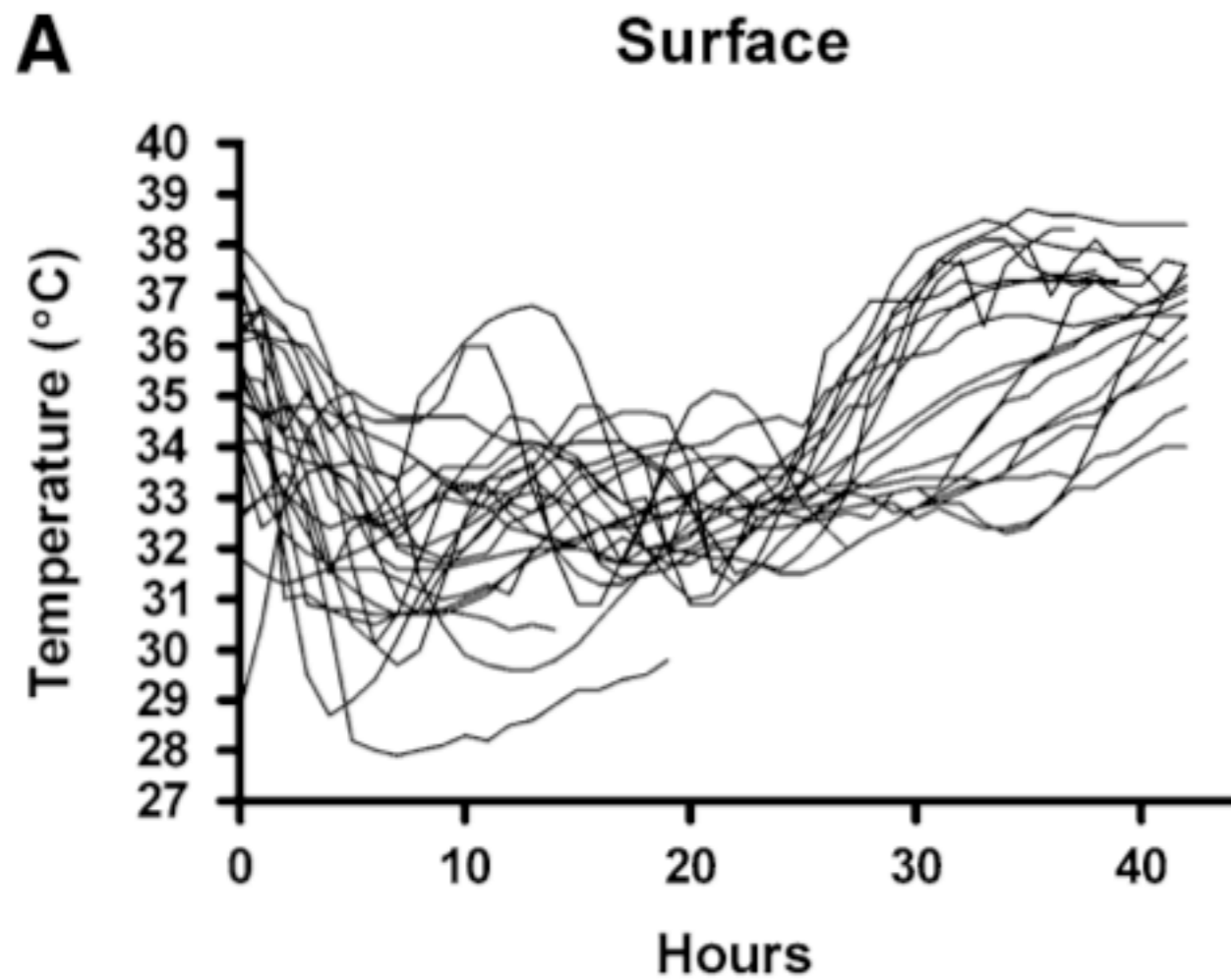
TIPS AND TRICKS

- INDUCE HYPOTHERMIA TO 33 °C AS QUICKLY AS POSSIBLE



TIPS AND TRICKS

- MAINTAIN 33 °C WITH MINIMAL OVERTHOOT AND UNDERSHOOT



TIPS AND TRICKS

- **SLOWLY REWARM BACK TO 37 °C OVER 18-24 HOURS**

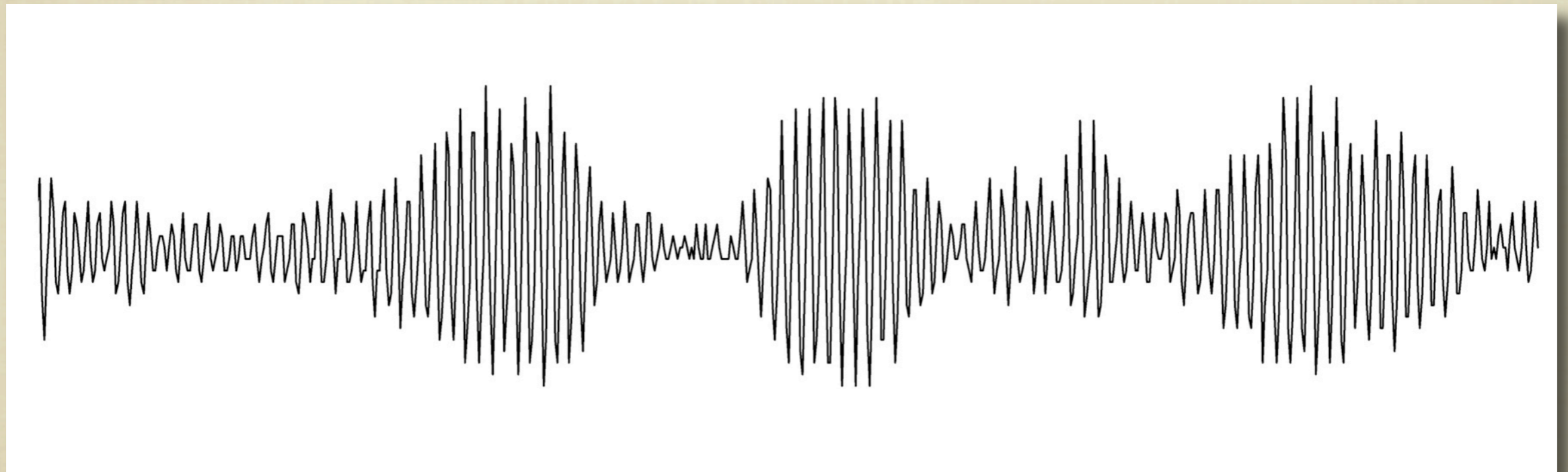


RAPID REWARMING CAN CAUSE RECURRENCE OF ARRHYTHMIAS



TIPS AND TRICKS

■ MINIMIZE AND TREAT COMPLICATIONS



SHIVERING

LAB ADJUSTMENTS

- PREFERABLY, ANALYZE ABGs AT PATIENT TEMPERATURE AT THE POINT OF CARE
- ALTERNATIVELY, CORRECT 37 °C SPECIMENS:
 - FOR EVERY °C, SUBTRACT 5 MMHG PO₂
 - FOR EVERY °C, SUBTRACT 2 MMHG PCO₂
 - FOR EVERY °C, ADD 0.012 PH UNITS

THE THERAPEUTIC HYPOTHERMIA

- IMPROVES NEUROLOGICAL OUTCOMES AND SURVIVAL AFTER CARDIAC ARREST
- ONCE PROTOCOLS AND EQUIPMENT ARE IN PLACE, IT IS EASY AND SAFE TO ADMINISTER
- MAY WORK IN OTHER SETTINGS (E.G., STROKE) BUT NOT YET PROVEN

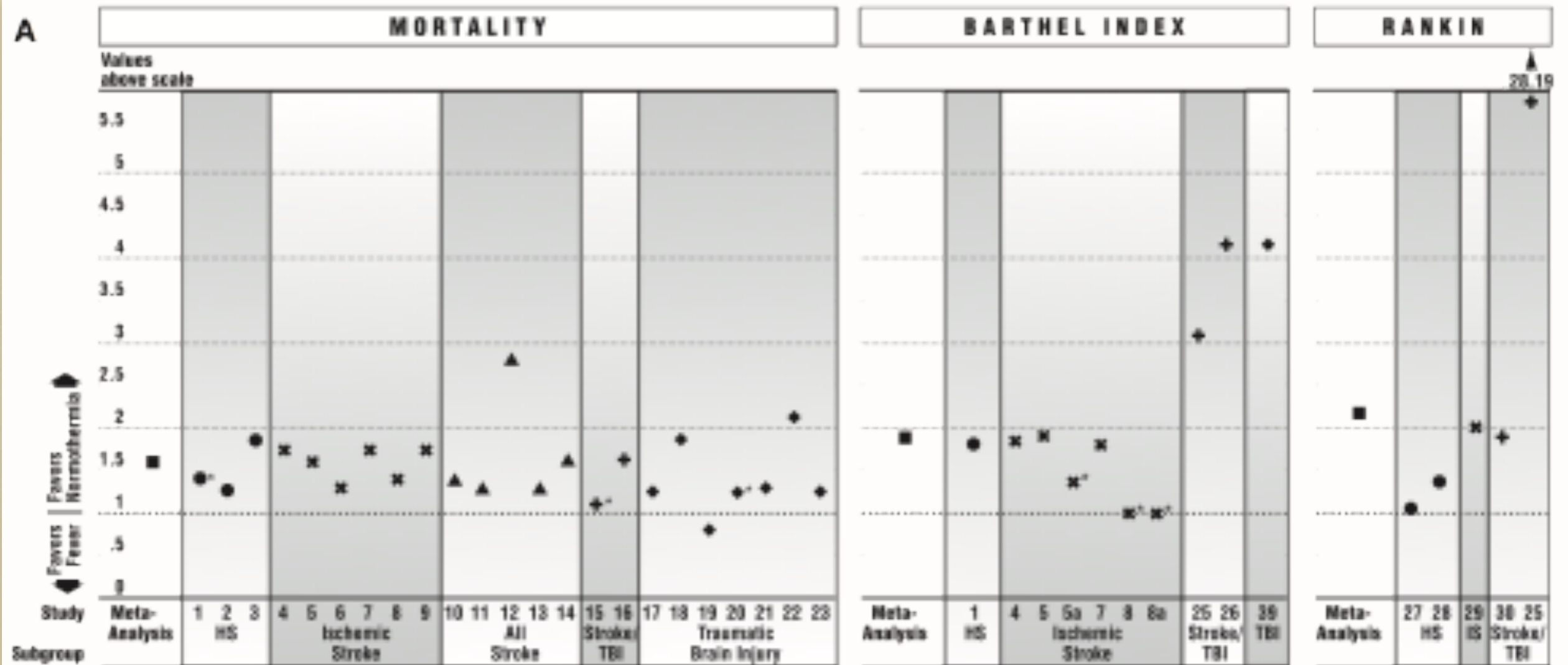
CONTROLLED NORMOTHERMIA

- PREVENTION OF CENTRAL FEVERS
- MAY REDUCE NEGATIVE IMPACT OF FEVERS ON NEUROLOGICAL OUTCOMES

Impact of Fever on Outcome in Patients With Stroke and Neurologic Injury

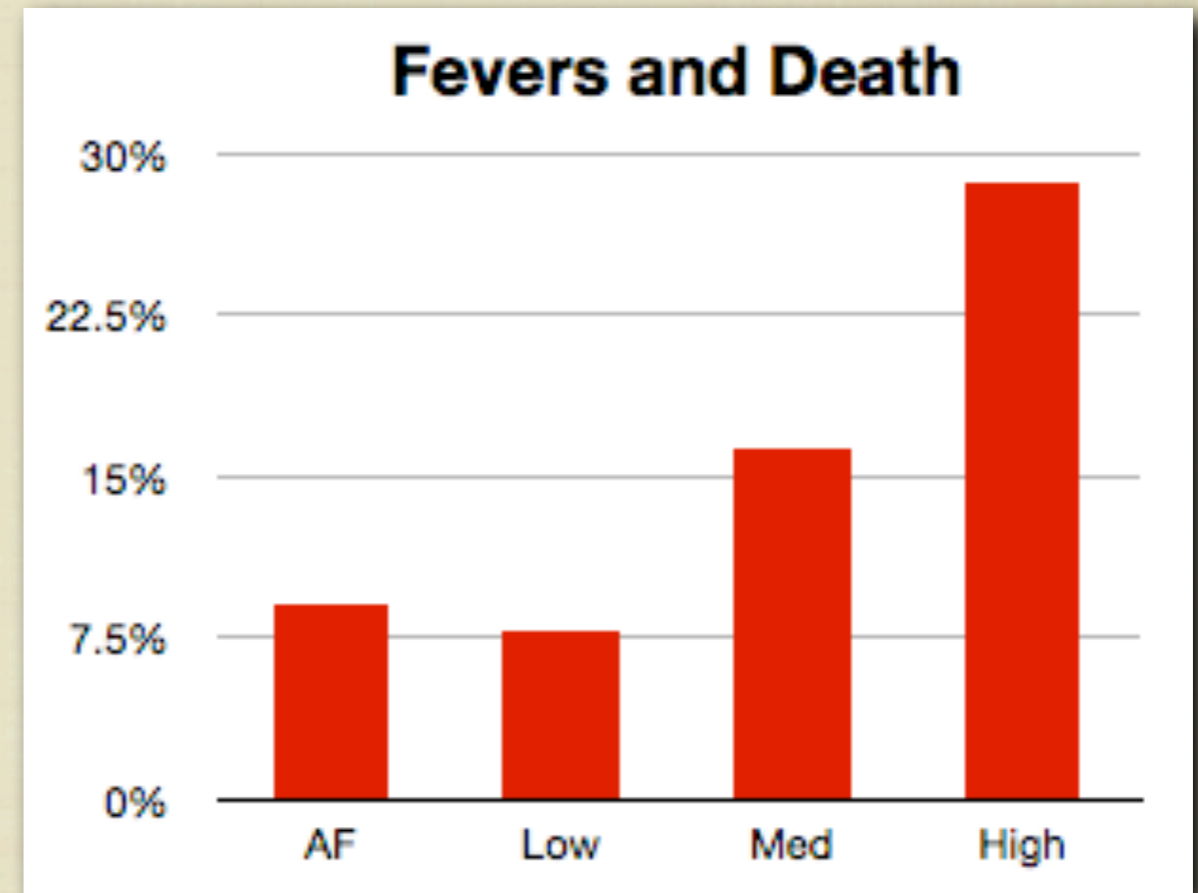
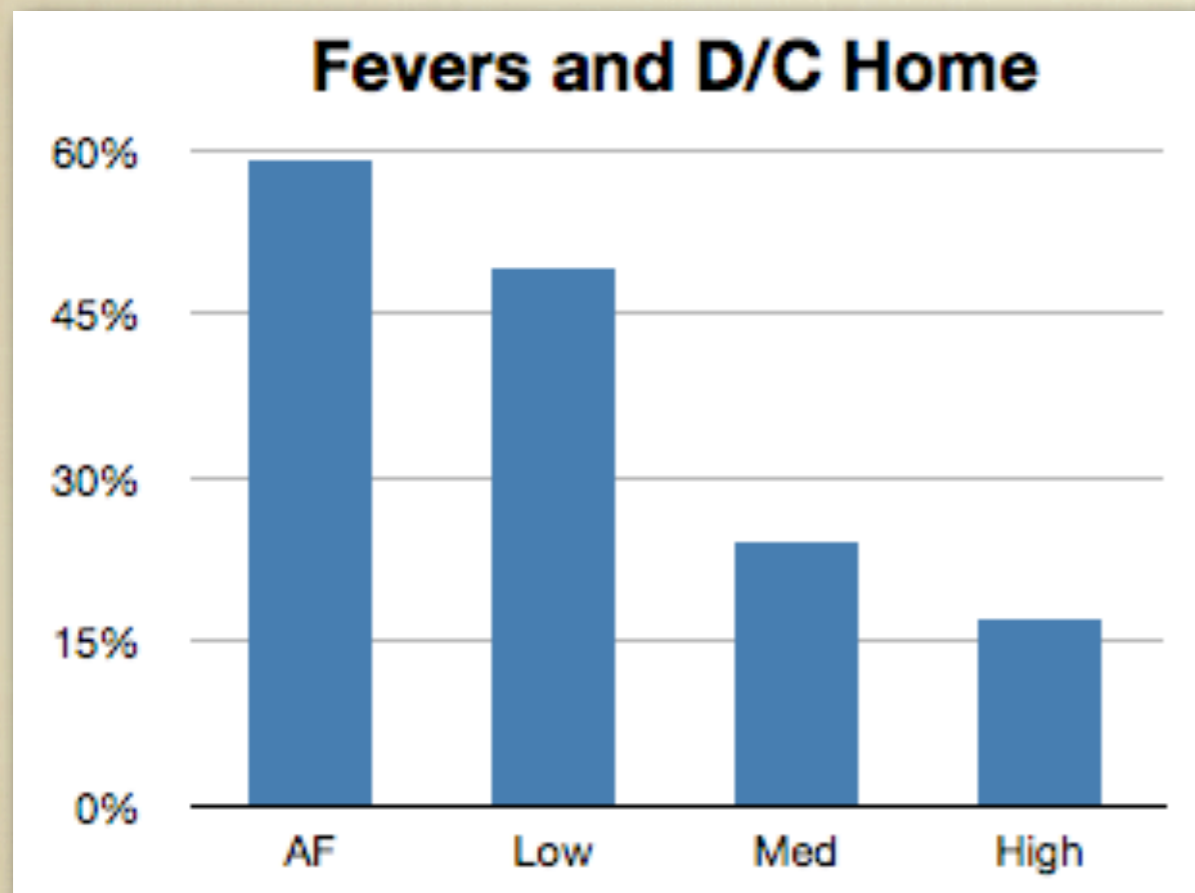
A Comprehensive Meta-Analysis

David M. Greer, MD, MA; Susan E. Funk, MBA; Nancy L. Reaven, MA;
Myrsini Ouzounelli, MD; Gwen C. Uman, RN, PhD



Elevated body temperature independently contributes to increased length of stay in neurologic intensive care unit patients*

Michael N. Diringer, MD, FCCM; Nancy L. Reaven, MA; Susan E. Funk, MBA; Gwen C. Uman, RN, PhD



No Fever
<37.5 °C
(n = 1268)

Low
37.5–38.4 °C
(n = 1591)

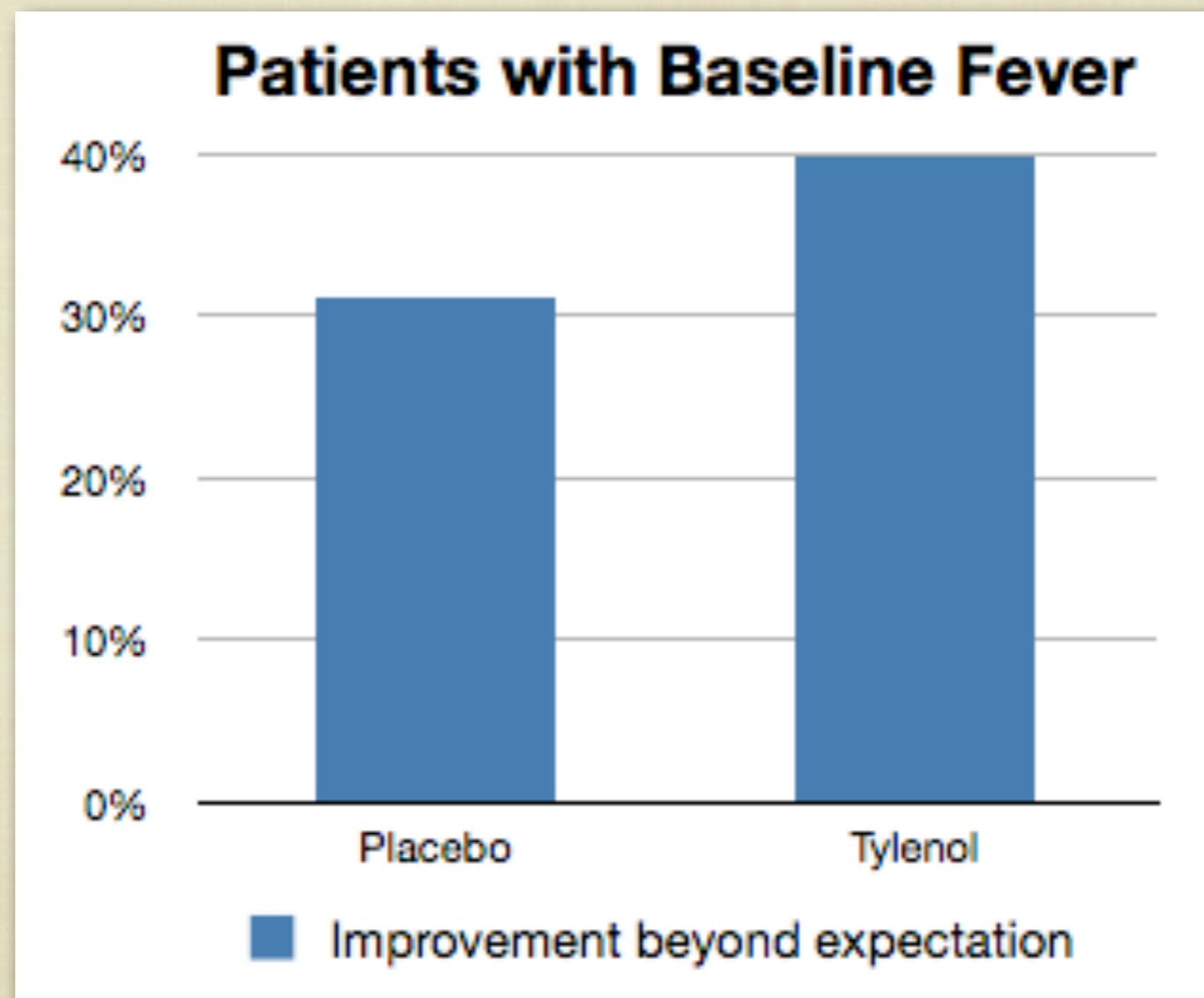
Medium
38.5–39.0 °C
(n = 719)

High
>39.0 °C
(n = 717)

The Paracetamol (Acetaminophen) In Stroke (PAIS) trial: a multicentre, randomised, placebo-controlled, phase III trial

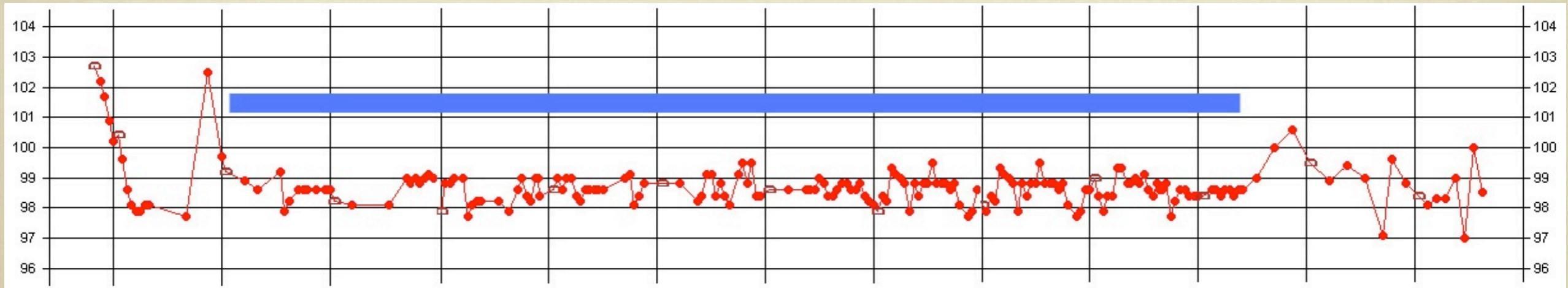
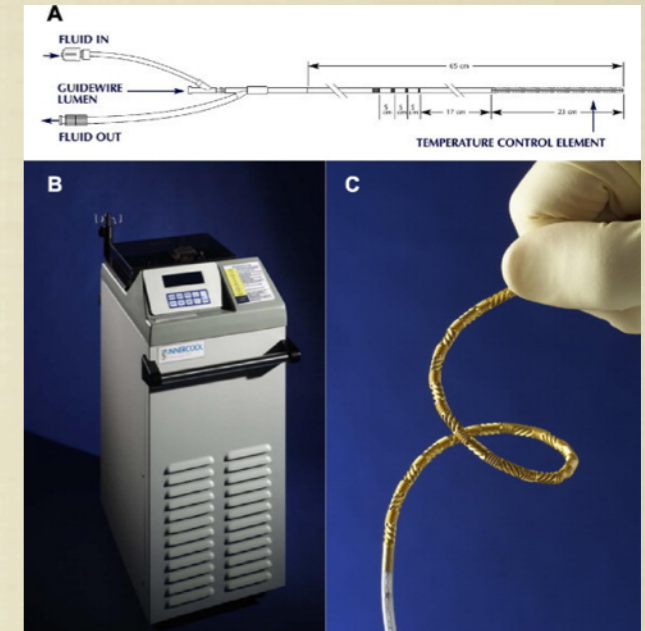
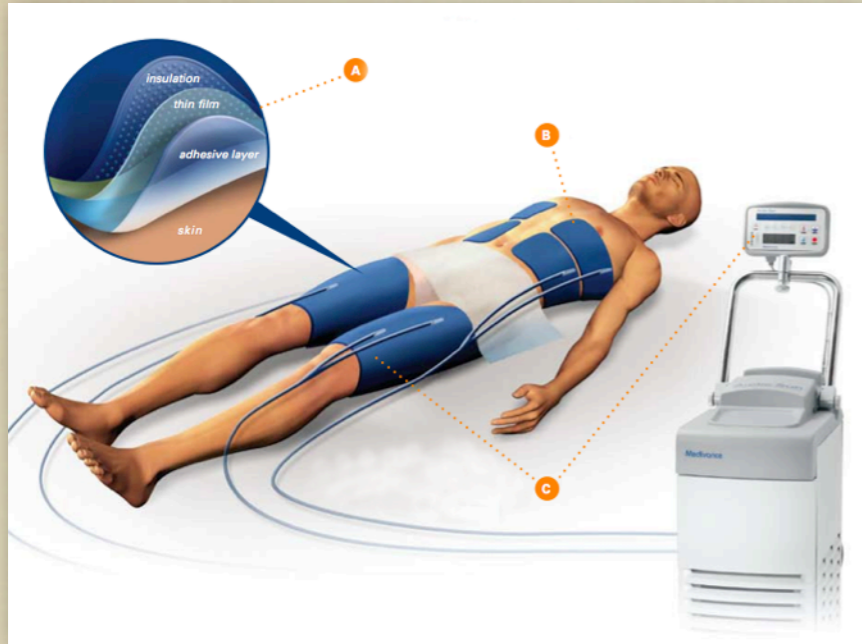
Heleen M den Hertog, H Bart van der Worp, H Maarten A van Gemert, Ale Algra, L Jaap Kappelle, Jan van Gijn, Peter J Koudstaal, Diederik W J Dippel; on behalf of the PAIS investigators

Mean
temp
difference
at 24h =
0.26 °C

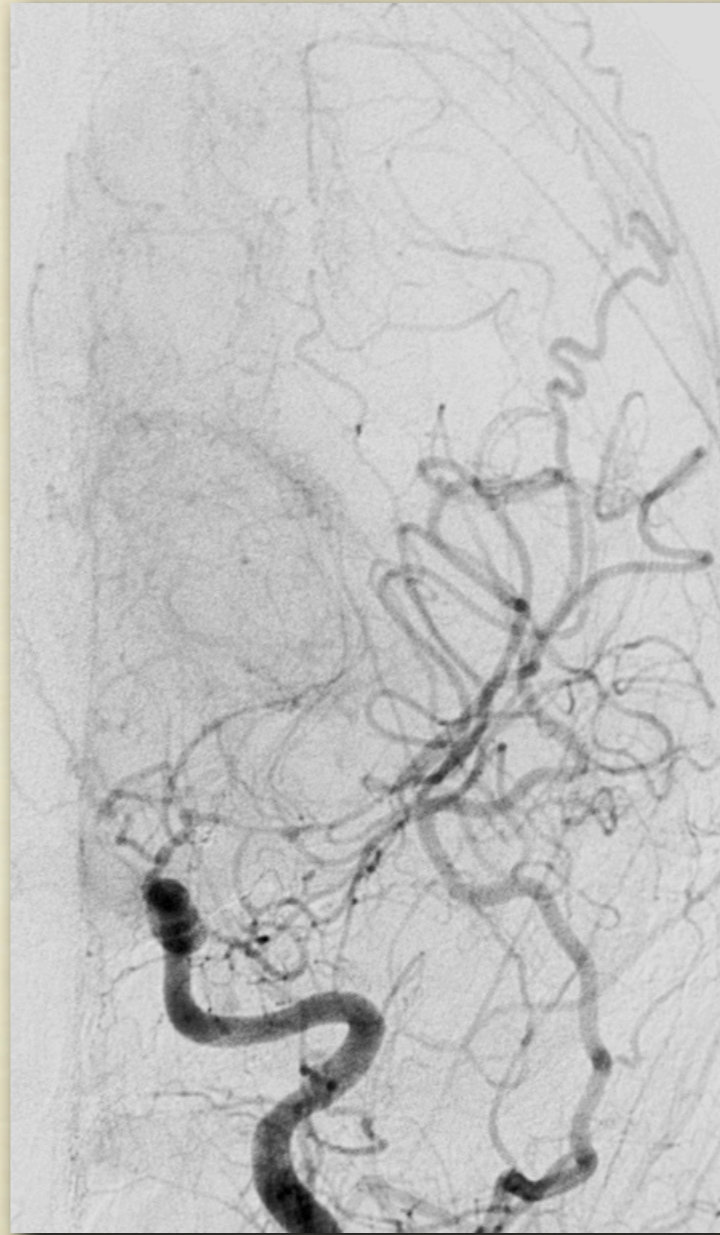


**NNT
= 11**

CONTROLLED NORMOTHERMIA



GRADE V SAH



GRADE V SAH

- Outcome:
 - At 3 month follow-up, neurologically normal.

CONTROLLED NORMOTHERMIA

- PREVENTION OF CENTRAL FEVERS IS POSSIBLE WITH FEEDBACK DEVICES
- MAY REDUCE NEGATIVE IMPACT OF FEVERS ON NEUROLOGICAL OUTCOMES
- REMAINS TO BE PROVEN