

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Shankaran S, Pappas A, McDonald SA, et al. Childhood outcomes after hypothermia for neonatal encephalopathy. *N Engl J Med* 2012;366:2085-92.

Supplementary Appendix

Supplement to: Shankaran S, Pappas A, McDonald SA., et al. Childhood Outcomes Following Encephalopathy Treated with Hypothermia

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Supplemental Table 1. Characteristics of children with and without data available at 6-7 years ≠

Characteristics	6-7 year outcome (N = 190)	6-7 year outcome unavailable (N = 18)
Maternal		
Race ---no. (%)*		
Black	66 (35)	6 (33)
White	70 (37)	2 (11)
Other	54 (28)	10 (56)
Maternal age--- yr	27.3 ± 6.1	26.8 ± 6.4
Married---no. (%)*	110 (59)	5 (29)
Gravida ---median no.	2	2
Parity---median no.	2	1
Complications of pregnancy---no. (%)		
Chronic hypertension	23 (12)	3 (17)
Antepartum hemorrhage	28 (15)	2 (11)
Thyroid disease	2 (1)	0
Diabetes	16 (8)	1 (6)

Intrapartum complications---no. (%)		
Fetal heart rate decelerations	137 (72)	16 (89)
Cord prolapse	35 (18)	2 (11)
Uterine rupture	27 (14)	2 (11)
Maternal pyrexia	19 (10)	2 (11)
Shoulder dystocia	18 (10)	2 (11)
Maternal hemorrhage	14 (7)	0
Labor--- hr	12 ± 9	12 ± 10
Rupture of membranes--- hr	6 ± 10	6 ± 8
Emergency cesarean delivery---no. (%)	140 (74)	12 (67)
Characteristic		
Neonatal		
Age at randomization--- hr	4.3 ± 1.2	4.5 ± 1.1
Transferred from birth hospital---no. (%)	87 (46)	6 (33)
Male sex---no. (%)	106 (56)	11 (61)
Apgar score at 5 min ≤ 5---no. (%)	173 (92)	16 (89)

Apgar score at 10 min ≤ 5---no. (%)	142 (82)	12 (71)
Birth weight--- g	3375 ± 603	3401 ± 890
Intubation in delivery room---no. (%)	179 (94)	16 (89)
Continued resuscitation at 10 min---no. (%)	178 (94)	17 (94)
Time to spontaneous respiration ≥ 10 min ---no. (%)	132 (73)	8 (50)
Cord blood pH*	6.8 ± 0.2	7.0 ± 0.2
Base deficit mmol/liter	19.5 ± 7.8	15.6 ± 6.8
Seizures---no. (%)	89 (47)	5 (28)
Moderate encephalopathy---no. (%)	120 (63)	14 (82)
Severe encephalopathy---no. (%)	70 (37)	3 (18)
Inotropic support---no. (%)	53 (28)	6 (33)
Anticonvulsants---no. (%)	78 (45)	5 (29)

±Plus-minus values are means ± SD. Percentages are based on the number of mothers or children for whom data was available. Because of rounding, not all percentages sum to 100. * P Values ≤ 0.05 from Fisher's exact test, T-Test, or Median Test.

Supplemental Table 2. Parent assessment outcomes at 6-7 years of age

Variable	Hypothermia Group (N = 97) No. (%)	Control Group (N = 93) No. (%)	Relative Risk (95% CI)	P Value
Physical Health+				0.08
Excellent	36 (54)	18 (36)		
Very Good	15 (22)	14 (28)		
Good	14 (21)	12 (24)		
Fair	1 (1)	6 (12)		
Poor	1 (1)	0		
Child's self esteem++				0.42•
Very satisfied	49 (75)	35 (76)		
Somewhat satisfied	11 (17)	11 (24)		
Neither satisfied nor dissatisfied	5 (8)	0		
Emotional Impact on parents+++				0.08
None at all	33 (49)	17 (34)		
A little bit	13 (19)	10 (20)		

Some	8 (12)	8 (16)	
Quite a bit	4 (6)	7 (14)	
A lot	9 (13)	8 (16)	

+ Parental assessment of child health. Data were unavailable for 3 hypothermia and 2 control group children. P-value from multinomial cumulative logistic regression, adjusted for center.

++ Parental assessment of child's satisfaction with his/her life. Data were unavailable for 5 hypothermia and 6 control children. P-value from Cochran-Armitage trend test.

+++ Parental assessment of worry caused by child's emotional well-being or behavior. Data were unavailable for 3 hypothermia and 2 control children. P-value from multinomial cumulative logistic regression, adjusted for center.

Supplemental Table 3: Concordance of outcome between 18 months and 6-7 years of age (N=140)

Hypothermia			Control		
Moderate-severe disability	6-7 years – Yes	6-7 years – No	Moderate-severe disability	6-7 years – Yes	6-7 years – No
18 months – Yes	15	2	18 months – Yes	18	1
18 months – No	9	44	18 months – No	1	32
Moderate-severe CP	6-7 years – Yes	6-7 years – No	Moderate-severe CP	6-7 years – Yes	6-7 years – No
18 months – Yes	12	0	18 months – Yes	14	0
18 months – No	0	56	18 months – No	1	35
Blindness	6-7 years – Yes	6-7 years – No	Blindness	6-7 years – Yes	6-7 years – No
18 months – Yes	1	1	18 months – Yes	2	3
18 months – No	0	63	18 months – No	0	44
Hearing impairment (with aids)	6-7 years – Yes	6-7 years – No	Hearing impairment (with aids)	6-7 years – Yes	6-7 years – No
18 months – Yes	1	0	18 months – Yes	1	2
18 months – No	2	59	18 months – No	0	46
Seizure disorder	6-7 years – Yes	6-7 years – No	Seizure disorder	6-7 years – Yes	6-7 years – No
18 months – Yes	4	6	18 months – Yes	5	5
18 months – No	3	54	18 months – No	3	34

Hypothermia group: sensitivity: 63%, specificity 96%, positive predictive value 88% and negative predictive value 83% for moderate/severe disability at 6 to 7 years of age for children disabled at 18 months of age.

Control group: sensitivity: 95%, specificity 97%, positive predictive value 95% and negative predictive value 97% for moderate/severe disability at 6 to 7 years of age for children disabled at 18 months of age.

Hypothermia group: sensitivity: 100%, specificity 100%, positive predictive value 100% and negative predictive value 100% for moderate-severe cerebral palsy at 6 to 7 years of age for children with moderate-severe CP at 18 months of age.

Control group: sensitivity: 93%, specificity 100%, positive predictive value 100% and negative predictive value 97% for moderate-severe cerebral palsy at 6 to 7 years of age for children with moderate-severe CP at 18 months of age.

The odds of disability at 6 to 7 years for an infant disabled at the earlier age, compared to an infant who was not disabled was 37 times higher (95 percent confidence interval 7-189) in the hypothermia group and 576 times higher (95 percent confidence interval 34-9774) in the control group.

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