The SafeBoosC hybrid Investigator Meeting
19-20th of May 2022

SafeBoosC II 2y outcome

Anne Mette Plomgaard, MD, Ph.D.

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Cerebral near infrared spectroscopy oximetry in extremely preterm infants: phase II randomised clinical trial

Simon Hyttel-Sorensen *research fellow*[1], Adelina Pellicer *associate professor*[2], Thomas Alderliesten *research fellow*[3], Topun Austin *consultant neonatologist*[4], Frank van Bel *professor of Neonatology*[3], Manon Benders *consultant neonatologist*[3,5], Olivier Claris *professor*[6], Eugene Dempsey *professor*[7], Axel R Franz *associate professor*[8], Monica Fumagalli *consultant neonatologist*[9], Christian Gluud *head of department*[10], Berit Grevstad *trial manager*[11], Cornelia Hagmann *consultant neonatologist*[12], Petra Lemmers *consultant neonatologist*[3], Wim van Oeveren *managing director*[13], Gerhard Pichler *associate professor*[14], Anne Mette Plomgaard *research fellow*[1], Joan Riera *biomedical engineer*[2,15], Laura Sanchez *consultant neonatologist*[2], Per Winkel *senior researcher*[10], Martin Wolf *professor*[16], Gorm Greisen *professor*[1]

Additional result Composite outcome

	Experimental group (n/n)	Control group (n/n)
Death before TEA	12/86	20/80
Severe brain injury *	10/80	18/77
Death or severe brain injury*	19/82	30/78

P = 0,04

Table 2| **Outcome measures. Values are number affected/number in group (percentage) unless stated otherwise**

Outcomes	NIRS (n=86)	Blinded NIRS (control) (n=80)	Relative change in % (95% CI)	Adjusted relative risk (95% CI)	Adjusted P value (unadjusted)
Primary					
Median (interquartile range) burden of hypoxia and hyperoxia (%hours)	36.1 (9.2-79.5)	81.3 (38.5-181.3) (n=78)	−58 (−35 to −74)	NA	<0.001*
Secondary					
All cause mortality at term	12/86 (14)	20/80 (25)	NA	0.50 (0.29 to 1.00)	0.10 (0.049)
Brain injury on cerebral ultrasonography:					
None	21/80 (26)	26/77 (34)	NA	—	0.11 (0.053)
Mild-moderate	49/80 (61)	33/77 (43)	NA	—	
Severe	10/80 (13)	18/77 (23)	NA	—	

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Brain injury in the international multicenter randomized SafeBoosC phase II feasibility trial: cranial ultrasound and magnetic resonance imaging assessments

Anne M Plomgaard[1], Cornelia Hagmann[2], Thomas Alderliesten[3], Topun Austin[4], Frank van Bel[3], Olivier Claris[5], Eugene Dempsey[6], Axel Franz[7], Monica Fumagalli[8], Christian Gluud[9], Gorm Greisen[1], Simon Hyttel-Sorensen[1], Petra Lemmers[3], Adelina Pellicer[10], Gerhard Pichler[11] and Manon Benders[3]

Table 2. Brain injury severity for each of the sequential and the overall cUS score as assessed by central reading

	Day 1	Day 4	Day 7	Day 14	Day 35	TEA	Overall cUS score
Experimental group ($n = 80$)							
No injury (n)	54	42	44	30	32	10	21
Mild/moderate injury (n)	19	22	22	27	29	31	49
Severe injury (n)	1	7	7	8	6	5	10
Control group ($n = 77$)							
No injury (n)	55	41	36	26	23	23	26
Mild/moderate injury (n)	10	18	18	24	19	17	33
Severe injury (n)	6	12	11	10	10	6	18
χ^2 test, P value[a]	0.043	0.42	0.44	0.78	0.26	0.01	0.053
Severe vs. no severe brain injury[b]							
Odds ratio (95% confidence interval)	0.15 (0.02–1.27)	0.54 (0.20–1.46)	0.52 (0.19–1.44)	0.70 (0.26–1.92)	0.41 (0.14–1.22)	0.81 (0.23–2.88)	0.47 (0.20–1.09)

cUS, cranial ultrasound; TEA, term-equivalent age.
[a]χ^2 analysis of the between-group distribution of brain injuries in the three categories: no injury, mild/moderate injury, and severe injury. [b]Odds ratio for severe vs. no severe (no/mild/moderate) brain injury.

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The SafeBoosC II randomized trial: treatment guided by near-infrared spectroscopy reduces cerebral hypoxia without changing early biomarkers of brain injury

Anne M. Plomgaard[1], Wim van Oeveren[2], Tue H. Petersen[3], Thomas Alderliesten[4], Topun Austin[5], Frank van Bel[4], Manon Benders[4], Olivier Claris[6], Eugene Dempsey[7], Axel Franz[8], Monica Fumagalli[9], Christian Gluud[10], Cornelia Hagmann[11], Simon Hyttel-Sorensen[1], Petra Lemmers[4], Adelina Pellicer[12], Gerhard Pichler[13], Per Winkel[10] and Gorm Greisen[1]

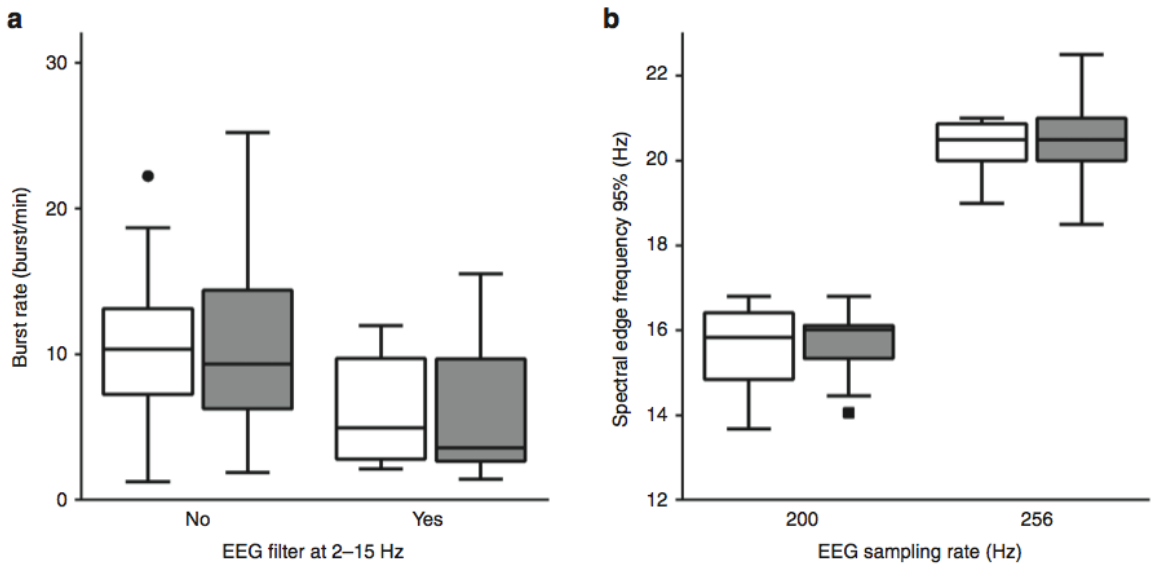

Figure 1. Intervention effects on EEG outcomes. (**a**) Intervention effect on burst rates, according to EEG filter of the device. (**b**) Intervention effect on spectral edge frequency 95%, according to the EEG sampling rate of the device. □ = control group, ■ = experimental group.

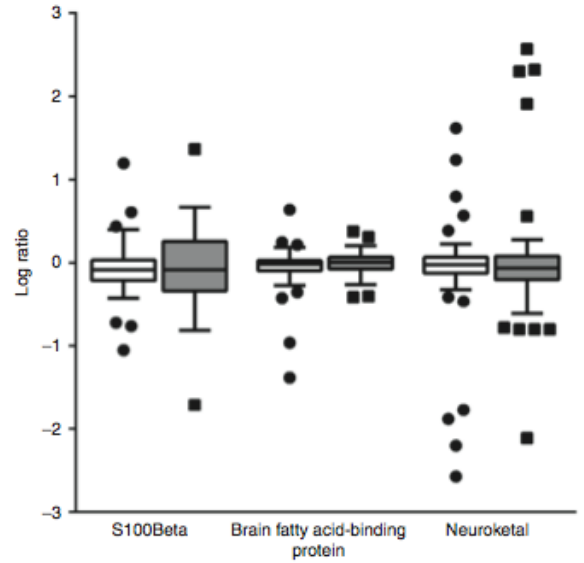

Figure 2. Intervention effect on the blood biomarkers illustrated as log ratio for the change in the concentration of the blood biomarkers from 6 to 64 h of age. □ = control group, ■ = experimental group.

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RESEARCH ARTICLE

Early biomarkers of brain injury and cerebral hypo- and hyperoxia in the SafeBoosC II trial

Anne M. Plomgaard, Thomas Alderliesten, Topun Austin, Frank van Bel, Manon Benders, Olivier Claris, Eugene Dempsey, Monica Fumagalli, Christian Gluud, Cornelia Hagmann, Simon Hyttel-Sorensen, Petra Lemmers, Wim van Oeveren, [...], Gorm Greisen [view all]

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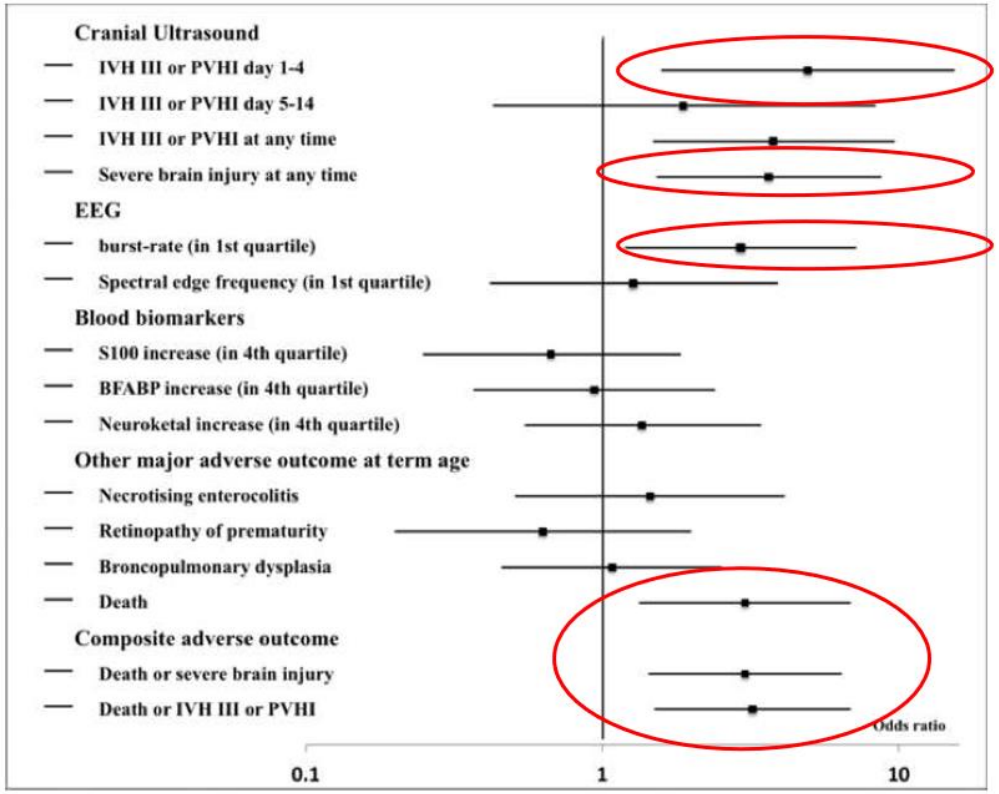
Explorative analyses, not planned pr. protocol

Fig 1. Risk for adverse outcomes for infants with a *burden of cerebral hypoxia* within the highest quartile versus infants with a burden in the three lower quartiles.

Odds ratio (OR) and 95% confidence interval.



ACTA PÆDIATRICA
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REGULAR ARTICLE

No neurodevelopmental benefit of cerebral oximetry in the first randomised trial (SafeBoosC II) in preterm infants during the first days of life

Anne M. Plomgaard (amplomgaard@gmail.com)[1], Thomas Alderliesten[2], Frank van Bel[2], Manon Benders[2], Olivier Claris[3], Malaika Cordeiro[4], Eugene Dempsey[5], Monica Fumagalli[6], Christian Gluud[7], Simon Hyttel-Sorensen[1], Petra Lemmers[2], Adelina Pellicer[4], Gerhard Pichler[8], Gorm Greisen[1]

Aim: Cerebral hypoxia has been associated with neurodevelopmental impairment. We studied whether reducing cerebral hypoxia in extremely preterm infants during the first 72 hours of life affected neurological outcomes at two years of corrected age.

2y assessment methods

- ASQ
- Bayley II/III
- Hearing
- Vision
- CP

Neurodevelopmental impairment – British Association of Perinatal Medicine
Moderate to severe neurodevelopmental disability if any of the following conditions were present: CP; a cognitive function score below -2 standard deviations scores (MDI below 70); hearing impairment; no meaningful words or signs; and impaired vision.

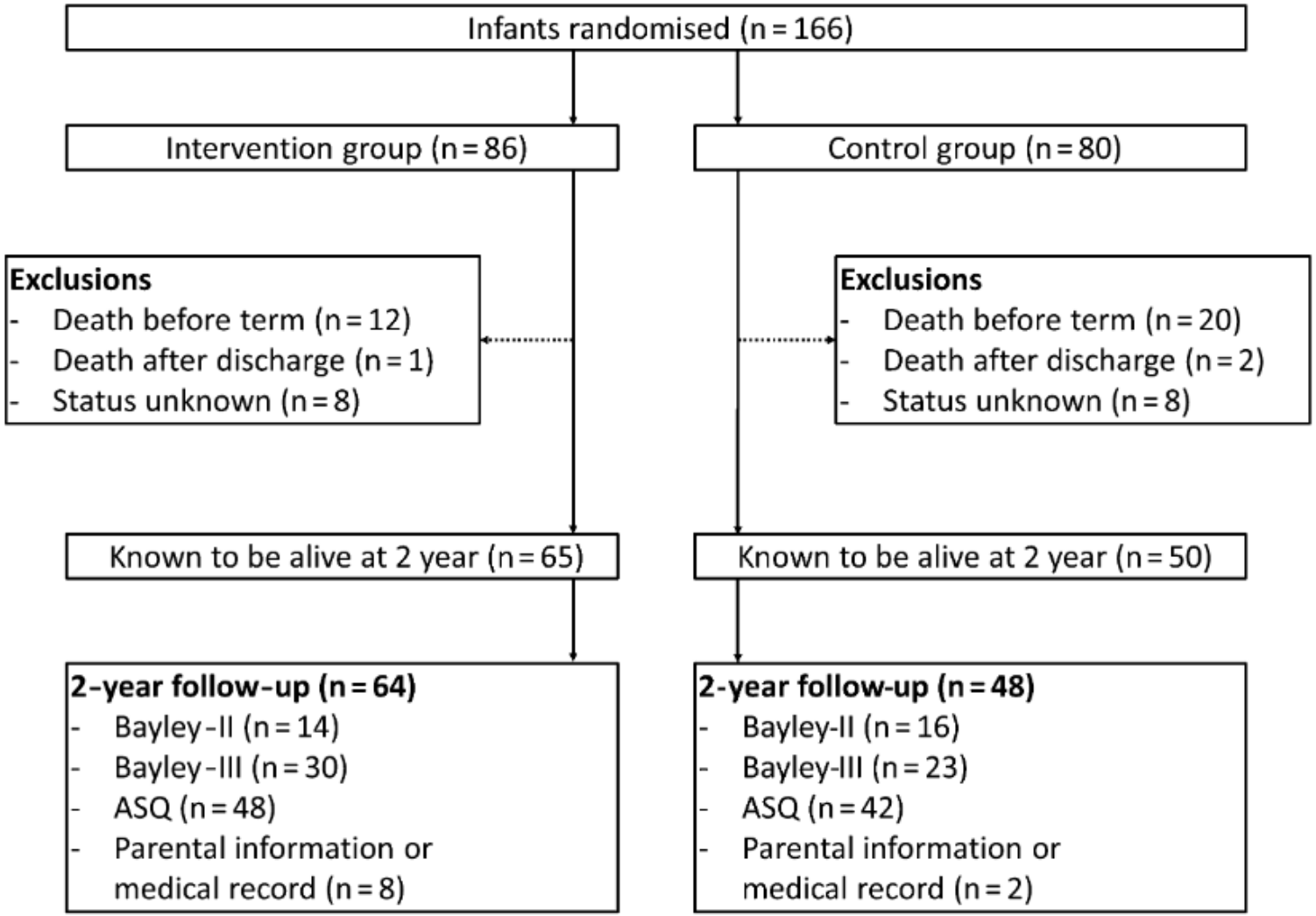

Figure 1 Trial participant flow in the SafeBoosC II clinical trial from randomisation within three hours of birth to follow-up at two years of corrected age.

Follow-up 88% of survivors

Table 3 Follow-up at two years of corrected age

	Intervention	Control	p value
Combined outcome (n)	45	38	
Moderate neurodevelopmental impairment[§](number)	8	3	0.21
Severe neurodevelopmental impairment[§§] (number)	2	3	>0.99

In conclusion, cerebral oxygenation monitoring was not associated with adverse long-term outcomes in extremely preterm infants

The SafeBoosC II trial was a feasibility trial that was powered to prove only the possibility of reducing the burden of cerebral hypoxia and hyperoxia. Larger randomized clinical trials are needed……. SafeBoosC III

Challenges

- The primary outcome is known

- Routine follow up?
- New methods – ASQ - Bayley
- Standard test – Bayley II or III

- SOPs

- Data collection

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Post hoc analysis

PLOS ONE

RESEARCH ARTICLE

Early cerebral hypoxia in extremely preterm infants and neurodevelopmental impairment at 2 year of age: A post hoc analysis of the SafeBoosC II trial

Anne Mette Plomgaard[1]*, Christoph E. Schwarz[2,3], Olivier Claris[4], Eugene M. Dempsey[3], Monica Fumagalli[5,6], Simon Hyttel-Sorensen[1], Petra Lemmers[7], Adelina Pellicer[8], Gerhard Pichler[9], Gorm Greisen[1]

1 Department of Neonatology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, **2** Department of Neonatology, University Children's Hospital, Tuebingen, Germany, **3** INFANT Centre, University College Cork, Cork, Ireland, **4** Department of Neonatology, Hospices Civils de Lyon, Claude Bernard University, Lyon, France, **5** NICU, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, **6** Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy, **7** Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, The Netherlands, **8** Department of Neonatology, La Paz University Hospital, Madrid, Spain, **9** Department of Pediatrics, Medical University of Graz, Graz, Austria

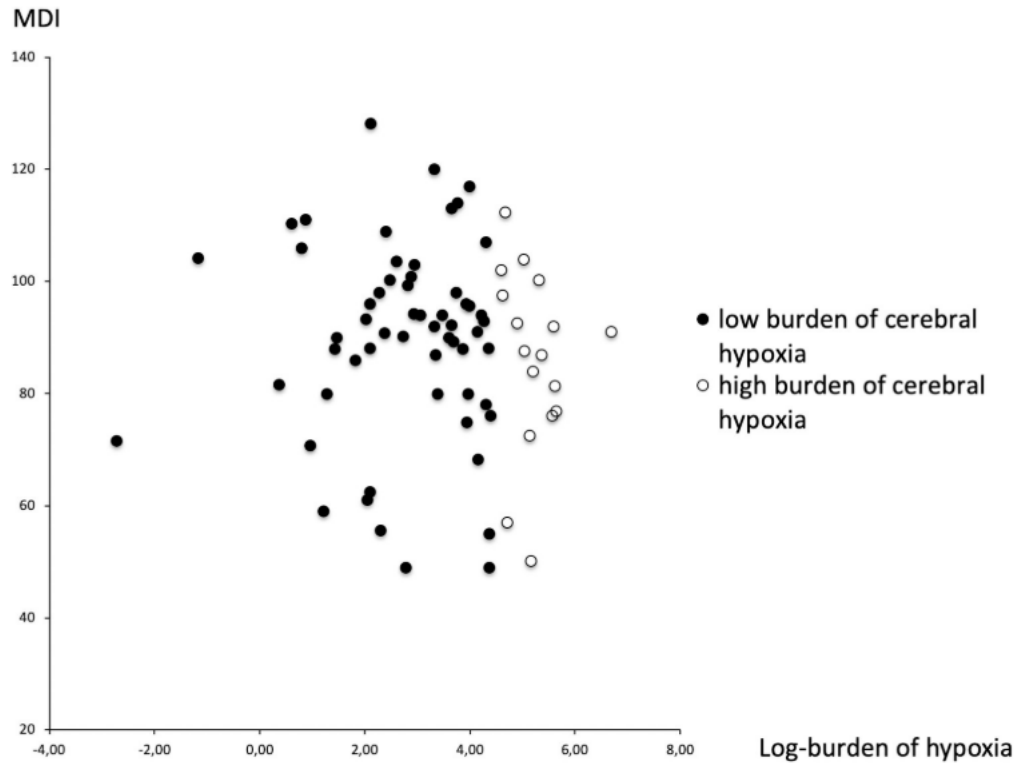

Fig 2. Burden of cerebral hypoxia and mental development index at 2 year. Log-burden of hypoxia and Mental Development Index (MDI) combined of Bayley II and III at 2 year corrected age. The X-axis is a logarithmic scale (base2), i.e. one unit corresponds to a doubling of the hypoxic burden, and the limit between the two groups is at 78% hours. There is no suggestion of a different threshold of hypoxic burden, nor of a correlation across the scales.