SafeBoosC III

SAFEGUARDING THE BRAIN OF OUR SMALLEST CHILDREN

A multinational randomised clinical trial assessing treatment guided by cerebral oxygenation monitoring in extremely preterm infants

SafeBoosC

Safeguarding the brain of our smallest children – testing if monitoring of cerebral oxygenation by near-infrared spectroscopy combined with a treatment guideline can improve the chances of extremely preterm babies to survive without neurodevelopmental deficit

www.safeboosc.eu

Step 1

SafeBoosC II
Feasibility trial
Reduce burden of cerebral hypoxia/hyperoxia

Step 2

SafeBoosC III
Pragmatic trial
Increase survival without severe brain injury

Step 3

Two-year follow-up
Increase survival without neurodevelopmental impairment

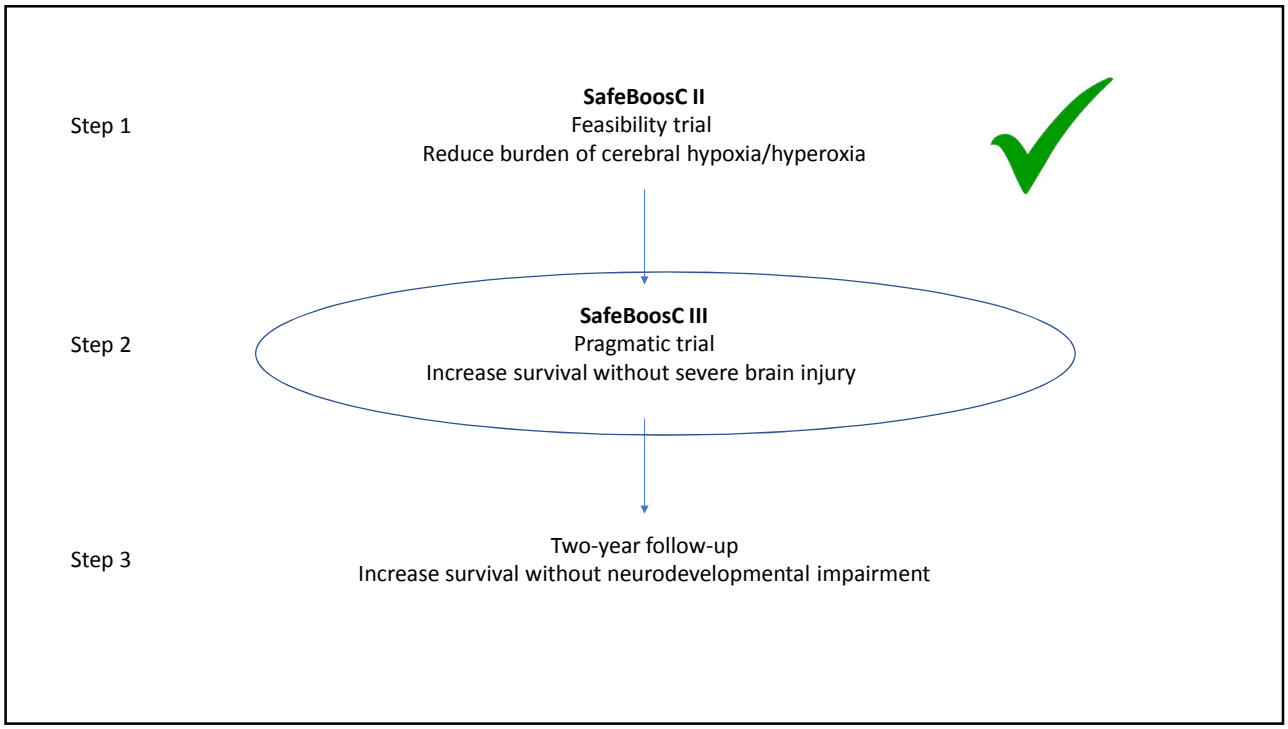
MLH6

SafeBoosC II secondary outcomes

Outcome	Experimental (n=86)	Control (n=80)	Adjusted p-value
All-cause mortality at term, %	14.0	25.0	0.10
Brain injury on cUS			
No injury, %	26.3	33.8	0.11
Mild/moderate injury, %	61.3	42.9	
Severe injury, %	12.5	23.4	

Slajd 4

MLH6 Gør tabel mere simpel, erstat med procenter i stedet for tal
Mathias Lühr Hansen; 2019-04-01



SafeBoosC III – clinical relevant effect?

34% death or severe brain injury at 36 wks
Reduction to 26%

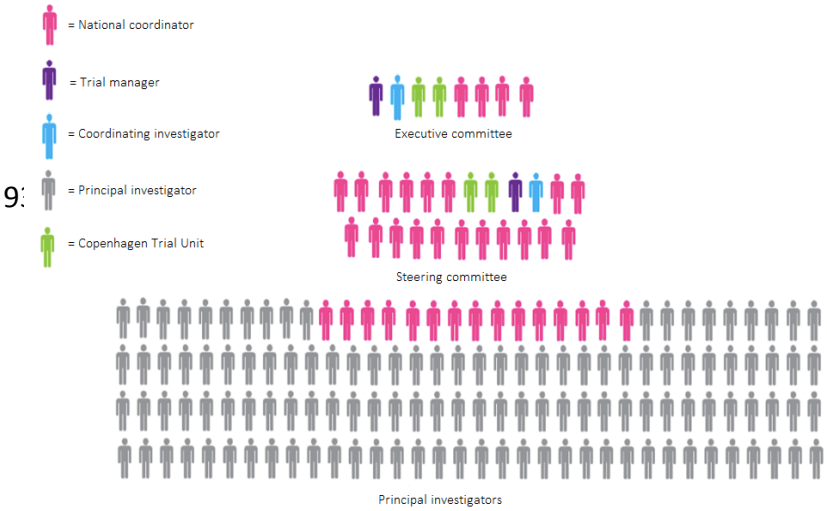
Alpha 5%, Beta 90%

N = 800 + 800

50.000 extremely preterm born infants in the world are offered intensive care every year
➔4000 more survivors without severe brain injury

NNT = 15, 1 sensor = 1000 dkk, 1 baby = 15000 dkk

How do we get this many babies?



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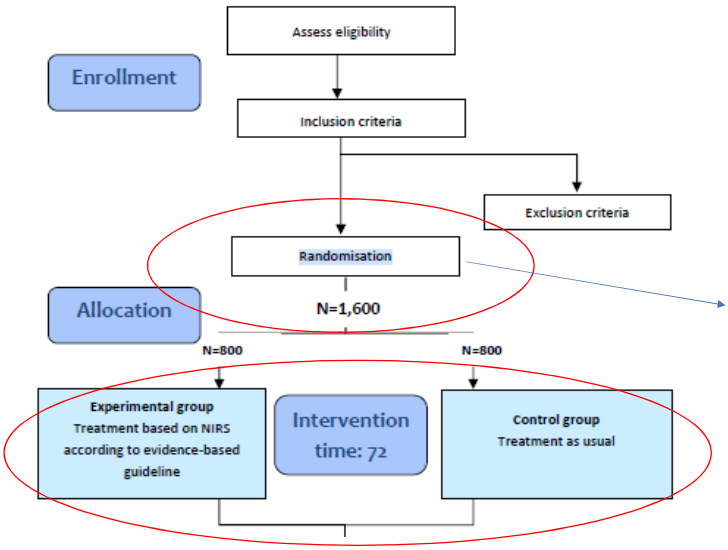
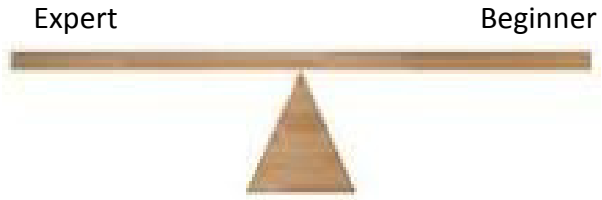
SafeBoosC phase III trial



Web-based
Copenhagen Trial Unit
Varying block size
Source verification

”Optimizing” the intervention

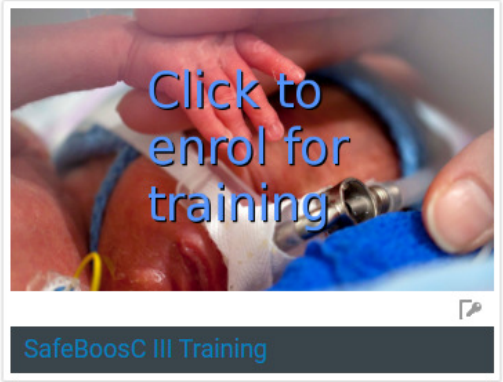


Pragmatic trial
Real-world setting

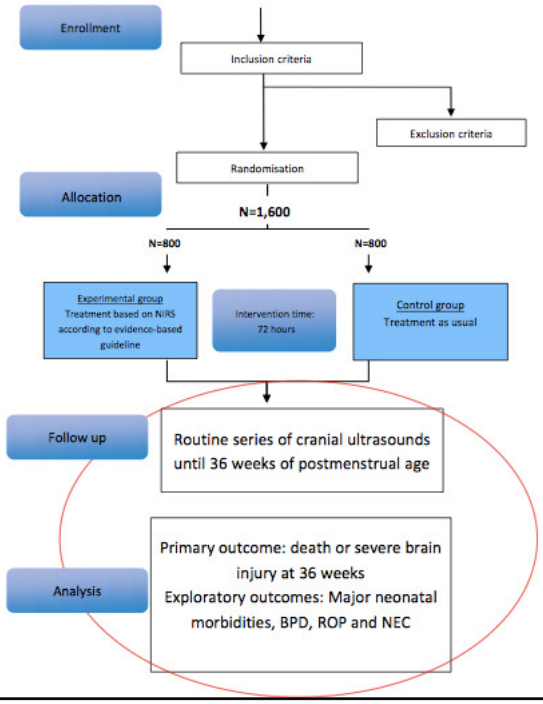
Web-based training to ”optimize” the intervention

Modules

- Introduction to SafeBoosC III
- Cerebral NIRS monitoring
- Treatment guideline
- Cranial ultrasound and brain injury
- Good Clinical Practice



Mortality
Clinical records
No blinding
Source data verification



Severe brain injury
Cranial cUS
Blinded assessment
GCP demonstration

Reliable trial results in SafeBoosC III

- Reliable sample size ✓
- Reliable randomisation ✓
- Reliable outcome assessment ✓

… But is it useful?

"Why Most Clinical Research Is Not Useful"

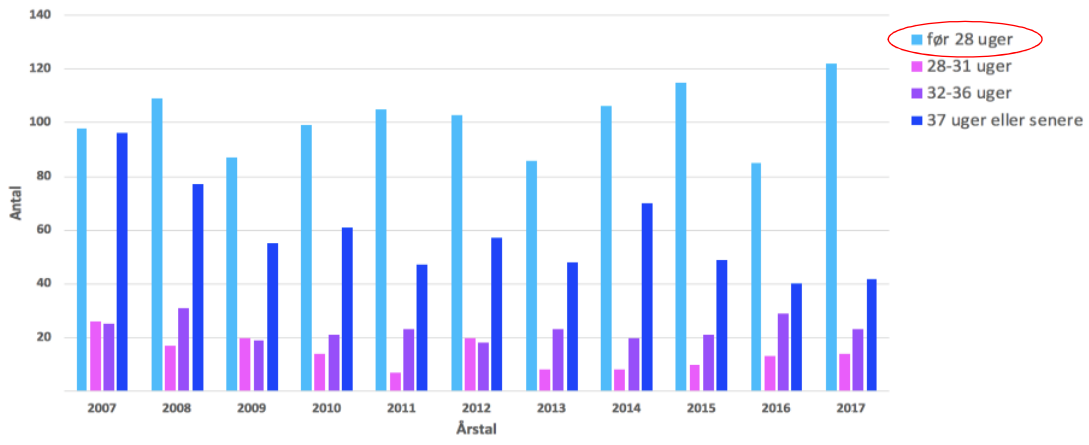
Table 1. Features to consider in appraising whether clinical research is useful.

Feature	Questions to Ask
Problem base	Is there a health problem that is big/important enough to fix?
Context placement	Has prior evidence been systematically assessed to inform (the need for) new studies?
Information gain	Is the proposed study large and long enough to be sufficiently informative?
Pragmatism	Does the research reflect real life? If it deviates, does this matter?
Patient centeredness	Does the research reflect top patient priorities?
Value for money	Is the research worth the money?
Feasibility	Can this research be done?
Transparency	Are methods, data, and analyses verifiable and unbiased?

doi:10.1371/journal.pmed.1002049.t001

John P. A. Ioannidis, PLOS Medicine, June 21, 2016

Deaths in Denmark before 1 year of age by year and gestational age



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doi:10.1371/journal.pmed.1002049.t001

John P. A. Ioannidis, PLOS Medicine, June 21, 2016

[Intervention Review]

Cerebral near-infrared spectroscopy monitoring for prevention of brain injury in very preterm infants

Simon Hyttel-Sorensen[1], Gorm Greisen[1], Bodil Als-Nielsen[2], Christian Gluud[3]

[1]Department of Neonatology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark. [2]Department of Paediatric Haematology/Oncology (5054), The Child and Youth Clinic, Copenhagen, Denmark. [3]The Cochrane Hepato-Biliary Group, Copen-

Authors' conclusions

The only eligible randomised clinical trial did not demonstrate any consistent effects of NIRS plus a guideline on the assessed clinical outcomes. The trial was, however, only powered to detect difference in cerebral oxygenation, not morbidities or mortality. Our systematic review did not reach sufficient power to prove or disprove effects on clinical outcomes. Further randomised clinical trials with low risks of bias and low risks of random errors are needed.

tion of brain injury in very preterm infants. *Cochrane Database of Systematic Reviews* 2017, Issue 9. Art. No.: CD011506. DOI: 10.1002/14651858.CD011506.pub2.

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414 former patients, parents, healthcare professionals and researchers
Core outcomes

Table 2 Highest scoring outcomes in round 3 by stakeholder group (outcomes ranked by mean score)

Patients and parents	Nurses and therapists	Doctors	Researchers
Survival	Survival	Survival	Survival
Necrotising enterocolitis	Necrotising enterocolitis	Necrotising enterocolitis	Necrotising enterocolitis
Sepsis	Harm due to treatment*	Sepsis	Sepsis
Brain injury on imaging	Sepsis	Brain injury on imaging	Visual impairment
Harm due to treatment*	Brain injury on imaging	Hearing impairment	Hearing impairment
Parental bonding with baby	Quality of life	Retinopathy of prematurity	General cognitive ability
Pain	Visual impairment	General cognitive ability	Quality of life
Suffering	Pain	Harm due to treatment*	Brain injury on imaging
Parental involvement	Suffering	Ability to walk	Breast feeding
Retinopathy of prematurity	Parental bonding with baby	General gross motor ability	General gross motor ability

*At the consensus meeting 'Harm from medical treatment' was redefined as 'Adverse events'.

Webbe JWH, Duffy JMN, Afonso E, *et al.* Core outcomes in neonatology: development of a core outcome set for neonatal research. *Archives of Disease in Childhood - Fetal and Neonatal Edition*

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Reliable trial results

- Reliable sample size ✓
- Reliable randomisation ✓
- Reliable outcome assessment ✓

… But is it useful? ✓

Recruitment has started!

First baby randomised June-19

15 sites are enrolling babies
(Czech Republic, Denmark, Greece, Italy, Spain, Switzerland, Turkey)

40 additional sites have ethics approval

If you want to read more: www.safeboosc.eu