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Which oxygen saturation level should we use for very premature infants? A randomised controlled trial

Submission date 07/02/2006	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 23/03/2006	**Overall study status** Completed	
Last Edited 08/03/2016	**Condition category** Neonatal Diseases	

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.npeu.ox.ac.uk/boost

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
G0400415

Study information

Scientific Title
Which oxygen saturation level should we use for very premature infants? A randomised controlled trial

Acronym
BOOST-II UK

Study objectives
Does varying the concentration of inspired oxygen so as to target a low (85-89%) versus a high (91-95%) functional arterial oxygen saturation (SpO2), from the day of birth until the baby is breathing air (or until the baby has reached a postmenstrual age of at least 36 weeks) affect the incidence of:
1. Retinopathy of prematurity (plus disease or Grade 3 and 4) and its two year outcome?
2. Other surgery (for conditions such as patent ductus arteriosus, post-haemorrhagic ventriculomegaly or necrotising enterocolitis)?
3. Chronic lung disease?
4. Death or severe neurosensory disability on assessment 2 years after the child was due to be born?
5. Poor weight gain and head growth between birth and 36 weeks postmenstrual age, and between birth and 2 years of age?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Trent Multi-Centre Ethics Committee, 02/05/2007, ref: 06/MRE04/91

Study design
Double-blind randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Information leaflet for parents: http://www.npeu.ox.ac.uk/boost/downloads/boost_pil.pdf

Health condition(s) or problem(s) studied
Prematurity

Interventions
The intervention is to maintain functional oxygen saturations in the range 85-89% or 91-95%. Masimo radical oximeters (Irvine, CA) will be used to monitor oxygen saturation levels. The oximeters will be modified to display and store a figure that is either 3% above or 3% below the 'true' oxygen saturation between 85% and 95% as computed by the machines' internal algorithm. Outside of these limits the oximeter will display the true value. Staff will aim for an oximeter reading of between 88 and 92%. This will, therefore, generate two trial groups: one for which oxygen saturation is maintained at 85-89%, and one for which it is maintained at 91-95%.

Added 30/11/2015:
The Masimo oximeters used in the trial were revised on 08/12/2008 to correct an artefact in their calibration algorithm. Achieved oxygen saturation distributions were clearly different with the revised oximeters. On 02/11/2009 the Data Monitoring Committee recommended that the Trial Steering Committee should consider whether the data from the two oximeter types should be considered separately. On 01/12/2010, blind to any outcome data, the Trial Steering Committee recommended to the Chief Investigator to change the protocol and to enrol the originally intended target sample size of 1,200 infants using the revised oximeters and to make this the primary analysis outcome population for the trial. A secondary analysis was planned to include the results of the infants treated with the original oximeters.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Death or serious neurosensory disability at 2 years corrected for prematurity

Added 30/11/2015:
Serious neurosensory disability was defined before recruitment commenced as: a cognitive score of <70 (i.e. more than 2 standard deviations below the mean) using the Bayley Scale of Infant Development (BSID-3); severe visual loss (certifiable as legally blind or partially sighted); severe cerebral palsy (unable to walk without help at 2 years); deafness requiring (or too severe to benefit from) a hearing aid.

Before the neurodevelopmental assessments even began, a cut-off score <85 on the cognitive or language component of the Bayley-III was decided because this matched a cognitive score <70 on the BSID-II that was used from the outset in some of the NeOProM trials. Bayley-III assessments could not always be arranged. To minimize the risk of bias from post-randomization exclusions, alternative corroborative measures of cognition and language were therefore pre-specified in the Statistical Analysis Plan (SAP) on 27/11/2013 and in the final version of the SAP that was signed off on 31/03/2014 prior to unblinding or analysis of the results. Serious neurosensory disability was assessed blind to trial group assessment. Paediatricians completed a follow-up assessment including information about visual function, hearing, gross motor function, the results of the Bayley-III test or any other test of cognitive function, an assessment

of language skills, an assessment of the degree of any developmental delay and information about general health. Parents were asked to fill in a parental questionnaire including information about general health, strengths and difficulties and Parent Report of Children's Abilities–Revised (PARCA-R). If a Paediatrician report could not be obtained or was incomplete the missing information was sought from the family General Practitioner (GP). Tests reported on the Paediatrician form included the Wechsler Preschool and Primary Scales of Intelligence (WPPSI-III), the Denver Developmental Screening Test, the Griffiths Mental Development Scales, and the Schedule of Growing Skills. The primary outcome of death or serious neurosensory disability was first defined by death, severe visual loss, deafness or cerebral palsy. In the remaining infants the cognitive measure of serious neurosensory disability was first defined as a cognitive or language score <85 on the Bayley-III. If this was not available the outcome was classified using the Paediatrician's assessment of developmental delay or language delay and then by the GP assessment. Free text on the forms returned by health professionals and parents was assessed independently by two assessors masked to group assignment to adjudicate cognitive outcome in a small number of cases. A secondary analysis of the results was pre-specified, excluding the alternative measures of disability.

Secondary outcome measures
1. Respiratory outcomes:
1.1. Days of endotracheal intubation
1.2. Days of nasal continuous positive airway pressure
1.3. Supplemental oxygen at a postmenstrual age of 36 weeks
1.4. Days of oxygen prior to home discharge
1.5. Days in oxygen after home discharge
2. Retinopathy of prematurity (ROP), plus disease, stage 3 and 4 disease
3. Patent ductus arteriosus requiring medical or surgical treatment
4. Necrotising enterocolitis, Bell stage 3 or 4
5. Changes in weight and head circumference from birth to 36 weeks postmenstrual age, and 2 years after delivery was due
6. Retinal structure when last seen for ophthalmic review; outcomes at age 2 years
7. Re-admissions to hospital until 2 years after delivery was due (and their cause)
8. Cerebral palsy (and its severity)
9. Visual disability
10. Deafness
11. Developmental delay using the Bayley Test Mental Developmental Index (MDI)
12. Other disability not classifiable as neurosensory in origin
13. All postneonatal (>27 days) deaths, together with their immediate and underlying cause

Overall study start date
01/04/2005

Completion date
31/05/2014

Eligibility

Key inclusion criteria
Infants are eligible if they are:
1. Less than 28 weeks gestation at birth
2. Less than 12 h old (24 h if the baby is outborn)
3. The clinician and parents are substantially uncertain which SpO2 is better

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
1200 (973 recruited by end of recruitment)

Key exclusion criteria
Recruitment is not appropriate if there is no realistic prospect of survival, or follow-up is unlikely to be possible

Date of first enrolment
29/09/2007

Date of final enrolment
24/12/2010

Locations

Countries of recruitment
England

Ireland

United Kingdom

Study participating centre
University of Oxford
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Sponsor information

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Sponsor type
University/education

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Medical Research Council (UK)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	30/05/2013		Yes	No
Results article	results	25/02/2016		Yes	No