

OptiCord Trial – Short summary

Research Question: In very preterm babies (<32 weeks' gestation at birth) requiring neonatal resuscitation, is resuscitation with the umbilical cord intact for at least 3 minutes ('intact' group) superior to resuscitation with the umbilical cord clamped up to and including 60 seconds ('clamped' group) in terms of survival without severe brain injury at 36 weeks' postmenstrual age.

Design: Multi-centre, two-arm, unmasked, cluster randomised, controlled parallel-group, superiority trial, with an internal pilot phase and alongside economic and process evaluations.

Setting: Secondary & tertiary maternity units with Level 2 or 3 neonatal intensive care units.

Population: Very preterm babies <32 weeks' gestational age requiring resuscitation at birth.

Intervention*: Bedside resuscitation with the umbilical cord intact for at least three minutes.

Comparator*: Bedside/room side resuscitation with the umbilical cord clamped up to and including 60 seconds

Primary outcome: Survival without severe brain injury at 36 weeks' postmenstrual age (PMA). Severe brain injury is defined as Grade III or IV intraventricular haemorrhage or periventricular leukomalacia.

** both the intervention and comparator groups have been designed to reflect the 2025 Newborn Life Support (NLS) guidelines on resuscitation*

Secondary outcomes: Babies

- Survival at 36 weeks' PMA, at 12- and 24-months of age corrected for prematurity (known as corrected age)
- At 36 weeks' PMA: sepsis, necrotising enterocolitis, bronchopulmonary dysplasia, retinopathy of prematurity, blood transfusions, hypotension, phototherapy, exchange transfusion
- Temperature on admission for neonatal care
- Survival without moderate or severe neurodevelopmental impairment at 24 months corrected age, measured using a validated parent-completed questionnaire
- Health-related quality of life (HRQoL) using the EQ-TIPS questionnaire measured at 12- and 24-months corrected age
- Resource use at 6 weeks after birth, 12- and 24 months corrected age

Secondary outcomes: Mother

- Survival until hospital discharge
- During hospital admission: sepsis, post-partum haemorrhage
- Post-partum infection up to 7 days after birth
- Parents' experience and satisfaction of intervention and trial (6 weeks post-partum)
- Acceptability of resuscitation and cord management (6 weeks post-partum)
- Maternal health-related quality of life (HRQoL) and wellbeing collected using the EQ-5D-5L and ICE-CAP instruments respectively at 6 weeks, 12- and 24-months post-partum

Sample size: 2422 babies from 46 UK sites. We will also target 10–16 international sites (i.e., 56–62 sites in total, to realise a total sample size of 3,198–3,420).

Analysis: Site-level and participant-level descriptive statistics will be used to illustrate balance between groups at baseline. The primary approach to between-group comparative analyses will be by intention-to-treat. The primary comparative analysis will use a generalised linear



mixed model to compare survival without severe brain injury. The comparison will be presented as a risk ratio and a risk difference along with a 95% confidence interval.

Project Timetable: Total 78 months (m): m1–12 set-up, m13–46 recruitment, m24 internal pilot, m55 primary outcome and short-term outcome report, m78 two-year outcome report.

Trial coordination: The trial is being led by co-Chief Investigators, Professor Jon Dorling (Professor of Child Health, University of Leeds) and Professor Eleanor Mitchell (Professor of Clinical Trials and Global Health, University of Nottingham). The trial is sponsored by the University of Leeds and managed by the Nottingham Clinical Trials Unit at the University of Nottingham. Funding is provided by the National Institute for Health and Care Research. Co-investigators, bringing a variety of clinical and methodological expertise, are based in institutions around the UK.