ISRCTN56204499 https://doi.org/10.1186/ISRCTN56204499

# Trial of Umbilical and Foetal Flow in Europe: TRUFFLE study

| Submission date | Recruitment status | [_] Prospectively registered |
|---|---|---|
| 04/06/2009 | No longer recruiting | [_] Protocol |
| **Registration date** | **Overall study status** | [_] Statistical analysis plan |
| 27/08/2009 | Completed | [X] Results |
| **Last Edited** | **Condition category** | [_] Individual participant data |
| 11/03/2015 | Pregnancy and Childbirth | |

**Plain English summary of protocol**
Not provided at time of registration

## Contact information

**Type(s)**
Scientific

**Contact name**
Mr Christoph Lees

**Contact details**
Centre for Fetal Care
Queen Charlottes and Chelsea Hospital
Imperial College Healthcare NHS Trust
Du Cane Road
London
United Kingdom
W12 0HS
+44 (0) 20 8383 3998
Christoph.Lees@imperial.nhs.uk

## Additional identifiers

**Protocol serial number**
Lancet Protocol 02PRT/34

## Study information

**Scientific Title**

Trial of Umbilical and Foetal Flow in Europe: a multicentre three-armed randomised controlled trial

## Acronym
TRUFFLE

## Study objectives
1. That among preterm growth-restricted babies, timing delivery when the foetal ductus venosus Doppler pulsatility index reaches the 95th centile increases the rate of normal infant neurodevelopmental outcome compared with delivery timing based on foetal heart short-term variation alone.
2. That among preterm growth-restricted babies, timing delivery when the foetal ductus venosus Doppler pulsatility index reaches a late stage of abnormality (a-wave reaching the baseline) increases the rate of normal infant neurodevelopmental outcome compared with delivery timing based on foetal heart short-term variation alone.
3. That among preterm growth-restricted babies, delaying delivery until the foetal ductus venosus Doppler pulsatility index reaches a late stage of abnormality (a-wave reaching the baseline) increases the rate of normal infant neurodevelopmental outcome compared with delivering when the foetal ductus venosus Doppler pulsatility index reaches the 95th centile.

On 28/01/2011 this record was updated to include the actual end date of the trial; the previous anticipated end date of this trial was 01/01/2010.

On 28/04/2014 the anticipated end date was changed to 31/12/2013 (end of follow-up).

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
Multicentre Research Ethics Committee approved in September 2005 (ref: 05/Q0803/152). All other centres will obtain ethics approval prior to recruitment.

## Study design
Multicentre three-armed randomised controlled trial

## Primary study design
Interventional

## Study type(s)
Quality of life

## Health condition(s) or problem(s) studied
Pregnancy/foetal growth restriction

## Interventions
This is a randomised multicentre study of timing delivery in women in whom intrauterine growth restriction is found on ultrasound scan at gestations between 26 and 32 weeks. Trial entry is stratified by gestational age at enrolment. The intervention is delivery of the foetus, based on the criteria detailed below:
Group 1: control intervention, current standard of care: the timing of delivery is based on

cardiotocography criteria for delivery, namely short-term variation below preset cut-offs based on gestation
Group 2a: delivery based on early ductus venosus changes (pulsatility index greater than 95th centile)
Group 2b: delivery based on late ductus venosus changes (a-wave reaches the baseline, i.e. 0 cm /s)

### Intervention Type
Other

### Phase
Not Applicable

### Primary outcome(s)
Survival without neurodevelopmental impairment at 2 years of age corrected for prematurity. Such impairment is defined as any of the following:
1. A standardised score of 70 or less on the Cognitive Scale from the Bayley Scale of Infant Development 3rd edition (i.e., more than 2 standard deviations below the mean)
2. Severe visual loss (legally certifiable as blind or partially sighted)
3. Cerebral palsy with a score of 2 or greater on the Gross Motor Function Classification System
4. Deafness requiring hearing aids

### Key secondary outcome(s))
Long-term outcomes at 2 years age corrected for prematurity include:
1. The frequency of severe disability (Bayley score of 55 or less; severe cerebral palsy [Gross Motor Function classification systems - GMFCS] 4 or 5; blind; profound deafness)
2. Respiratory outcomes: days on home oxygen after discharge home, need for inhaled medications, hospital admissions
3. Weight, length, and head circumference (expressed as standard deviation scores)
4. Blood pressure
5. Other disability not classifiable as neurodevelopmental in origin
6. Survival analysis curves from study entry will be compared for a composite neonatal morbidity and mortality (to 28 days of life) and for mortality to 2 years, with hazard ratios and Cox's proportional model
7. Prespecified subgroup analyses include analysis by foetal sex, gestational age at delivery (less than 29 weeks; greater than 29 weeks) and indication for delivery

### Completion date
31/12/2013

## Eligibility

### Key inclusion criteria
1. The pregnancy should be singleton (i.e., not multiple pregnancy)
2. No obvious major structural abnormalities should have been identified on ultrasound
3. Certain menstrual age and/or ultrasound assessment of gestational age
4. The pregnancy should have reached at least 26 weeks gestation, but not yet 32 weeks of gestation by the time of recruitment
5. The ultrasound estimation of foetal weight should be at least 500 g at entry of the study
6. There should be ultrasound evidence of growth restriction, defined as a foetal abdominal circumference measurement under the 10th centile

7. Short term variability of the foetal heart rate after 1 hour recording should be greater than 3.5 beats per minute at 26 - 29 weeks, and greater than 4 beats per minute at 30 - 32 weeks
8. There should be evidence of abnormal umbilical artery bloodflow, manifesting as Umbilical arterial Doppler velocimetry above 95th centile
9. The foetal Ductus Venosus waveform using doppler ultrasound, should be normal defined as a venous pulsatility index under the 95th centile
10. There should be no obvious indication for immediate delivery (such as uncontrolled maternal high blood pressure)
11. The patient must be able to give informed consent to participation

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Sex
Female

### Key exclusion criteria
Does not meet inclusion criteria

### Date of first enrolment
01/01/2005

### Date of final enrolment
31/12/2013

## Locations

### Countries of recruitment
United Kingdom

England

Austria

Germany

Italy

Netherlands

### Study participating centre
**Centre for Fetal Care**
London

United Kingdom
W12 0HS

# Sponsor information

**Organisation**
Addenbrooke's Hospital (UK)

**ROR**
https://ror.org/055vbxf86

# Funder(s)

**Funder type**
Research organisation

**Funder Name**
Dutch Council for Medical Research (Netherlands) - fully funding Dutch Centres

**Funder Name**
Central trial administration is funded through small donations, awards and proceeds from educational courses

# Results and Publications

## 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 | 01/10/2013 | | Yes | No |
| Results article | results | 30/05/2015 | | Yes | No |
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |
| Study website | Study website | 11/11/2025 | 11/11/2025 | No | Yes |