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Antenatal corticosteroids for planned birth in twins

Submission date
17/03/2022

Recruitment status
No longer recruiting

Registration date
31/03/2022

Overall study status
Ongoing

Last Edited
21/02/2025

Condition category
Neonatal Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
This study aims to find out if the drug antenatal corticosteroids (ACS) given to women with a twin pregnancy prior to a planned birth of twins after 35 weeks of pregnancy reduces breathing difficulties in the twin babies.
Antenatal corticosteroids (ACS) help to mature babies' lungs and may reduce breathing difficulties and the need for high levels of respiratory (breathing) support. They are routinely used in single pregnancies that deliver early, but the use of ACS in twin births has not been studied in detail and so it is not clear if they will work in twin pregnancies. Because of the lack of evidence, there is currently no guidance on giving ACS in twin pregnancies, so whether or not women pregnant with twins receive steroids as part of routine care varies depending on their hospital. ACS may also have some unwanted side effects such as lowering babies' blood sugar and affecting their growth. We need to be certain about the benefits and risks of giving ACS before all women with twin pregnancy in the UK are offered a course of ACS prior to a planned birth.
Twin pregnancies are monitored more closely as they have a higher risk of complications than a single pregnancy, and there is a greater chance of the babies being born before 37 weeks of pregnancy. Twin births account for about 3% of live births but around 15-20% of admissions to the neonatal unit.
Current guidance recommends that twins who share a placenta (monochorionic twins) should be born from 36 weeks of pregnancy if there are no medical problems requiring earlier birth, whilst twins with a placenta each (dichorionic twins) should be born from 37 weeks of pregnancy, as evidence shows this is safer than delivering later on in the pregnancy. Being born slightly early means that twins are at higher risk of admission to neonatal units for support with their breathing, which separates mothers and babies at a crucial time.

Who can participate?
Women aged 16 years and over with a viable twin pregnancy and a planned birth scheduled between 35 and 38+6 weeks

What does the study involve?
Where possible the researchers will combine any additional visits needed for the study with routine antenatal appointments. They will carry out study procedures as close to 24 hours

before planned birth as possible. Women will be given information sheets from around 20 weeks and should discuss the trial with their care team. Women that want to take part and are eligible will be asked to sign a consent form. Data from the woman's medical records will be collected and entered into the study database. A computer system will randomise (allocate) the woman into either the corticosteroid group or the placebo (dummy drug) group. There is approximately 50:50 chance the woman is randomised into either group. The corticosteroid group will receive two doses 24 hours apart of ACS (dexamethasone) by injection (either to the thigh or buttock). The placebo group will receive two doses 24 hours apart of a visually matching placebo (saline) by injection (either to the thigh or buttock). Information on the birth and how the mother and babies are including any extra healthcare support needed after birth will then be collected from the woman's and babies' medical records until discharge or 28 days after birth, whichever comes first. The researchers will send a questionnaire by post or email to a subset of women which will ask questions on the babies' development at 2 years.

What are the possible benefits and risks of participating?
The researchers do not know if mothers and babies will directly benefit from being part of the study. Information obtained from the study will help inform the future healthcare of others. If it is found that the use of ACS improves health in twin babies, it could be used in the NHS straight away. There are very few recognised side effects of a short course of ACS. Allergic reactions are extremely rare. Headaches and short-term sleep disturbance have been reported after ACS, but not confirmed.

Where is the study run from?
University of Edinburgh and NHS Lothian (UK)

When is the study starting and how long is it expected to run for?
November 2021 to March 2027

Who is funding the study?
National Institute of Health Research (NIHR), Health Technology Assessment (HTA) (UK)

Who is the main contact?
The trial management team at the University of Edinburgh Clinical Trials Unit (ECTU)
STOPPIT.Trial@ed.ac.uk

Contact information

Type(s)
Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-002876-38

Integrated Research Application System (IRAS)
1004166

Central Portfolio Management System (CPMS)
52168

National Institute for Health and Care Research (NIHR)
131352

Protocol serial number
AC21118, HTA -

Study information

Scientific Title
A randomised placebo-controlled trial of antenatal corticosteroids for planned birth in twins

Acronym
STOPPIT-3

Study objectives
The hypothesis is that antenatal corticosteroids (ACS) reduce neonatal morbidity including the need for respiratory support within 72 hours of twin birth.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/02/2022, West Midlands - Edgbaston Research Ethics Committee (3rd Floor, Barlow House, Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8070; edgbaston.rec@hra.nhs.uk), ref: 22/WM/0018

Primary study design
Interventional

Study design
Multicentre interventional double-blind randomized placebo-controlled trial

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Assessment of neonatal morbidity and need for respiratory support for twins born by planned birth (caesarean section or induction of labour) between 35+0 and 38+6 weeks gestation

Interventions
Participants will be randomised by a simple allocation sequence with no minimisation criteria due to the large sample size (1552 women). Women will be asked to attend the hospital for administration of the IMP where it will be administered by a health care professional trained and delegated to give the IMP. Two doses of dexamethasone (corticosteroid) 6.6 mg/2 ml solution or a visually matching placebo of sodium chloride 0.9% will be administered by intramuscular injection to the thigh or buttock. The two doses will be administered 24 hours apart +/- 4 hours prior to the planned caesarean section or induction of labour. Information on the birth and how

the mother and babies are including any extra healthcare support needed after birth will then be collected from the woman's and babies' medical records until discharge or 28 days after birth whichever comes first. The researchers will send a questionnaire out to a subset of women which will ask questions on the babies' development at 2 years. This will either be posted or emailed to the woman.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Dexamethasone

Primary outcome(s)
Neonatal morbidity including the need for respiratory support within 72 hours of birth, assessed using neonatal and delivery records. This is a composite outcome encompassing a range of levels of support consisting of one or more of the following:
1. Continuous positive airway pressure (CPAP)
2. Supplemental oxygen by high-flow nasal cannulae for at least 2 consecutive hours
3. Need for supplemental oxygen by low flow nasal cannulae or incubator oxygen for at least 4 continuous hours
4. Mechanical ventilation
5. Extracorporeal membrane oxygenation (ECMO)
6. Stillbirth
7. Neonatal death within 72 hours of birth

Key secondary outcome(s)
1. Severe respiratory morbidity assessed using neonatal and delivery records, a composite outcome of one or more of the following within 72 hours of birth:
1.1. CPAP or high-flow nasal cannula for at least 12 continuous hours
1.2. Supplemental oxygen with a fraction of inspired oxygen of at least 0.30 for at least 24 continuous hours
1.3. Mechanical ventilation
1.4. ECMO
1.5. Stillbirth
1.6. Neonatal death within 72 hours of birth
2. Other perinatal morbidity assessed using neonatal and delivery records:
2.1. Any admission to NNU (i.e. admission for any reason and for any duration) between birth and 28 days
2.2. NNU admission within 72 hours of birth for 48 hours or more or any NNU admission (within 28 days of birth) or those requiring surfactant treatment or nitric oxide therapy
2.3. Apgar score at 5 minutes after birth
2.4. Umbilical arterial cord pH at birth
2.5. Umbilical arterial cord base excess at birth
2.6. The number of newborns with hypoglycaemia (defined as blood glucose of less than 2.0 mmol per litre or treatment for hypoglycaemia administered) at birth
2.7. The number of newborns with neonatal jaundice (defined as those requiring treatment with phototherapy according to the NICE threshold for gestation and postnatal age) at birth
2.8. Birthweight at birth

2.9. Head circumference at birth
2.10. All-cause early-onset sepsis within 72 hours of birth (defined as culture positive [pure growth from blood or CSF of a known bacterial pathogen] or culture-negative [acute onset of illness with three or more predefined clinical signs])
3. Perinatal mortality assessed using neonatal and delivery records:
3.1. Extended perinatal mortality (stillbirth or neonatal death up to 28 days)
3.2. Stillbirth (death in utero)
3.3. Neonatal death (death within 28 days of birth)
4. Maternal outcomes assessed using maternity records:
4.1. Exclusive breastmilk nutrition at discharge
4.2. Confirmed or suspected postpartum infection during hospital admission (defined by a new prescription of antibiotics, confirmed systemic infection on culture, or endometritis as defined by the US Centers for Disease Control and Prevention)
5. The cost-effectiveness of treatment with ACS compared to placebo, reported as incremental cost per reduction in respiratory support over a 28-day time horizon
6. Childhood cognitive and language development in a subset of twins determined by the Parent Report of Children's Abilities-Revised (PARCA-R) score at 2 years of age
7. Sample size, recruitment and outcome frequency estimates determined by analysing the internal pilot data at 10 months after the trial starts to recruit

Completion date
31/03/2027

Eligibility

Key inclusion criteria
1. Women aged 16 years or older and able to provide electronic or written consent
2. Women presenting with a viable twin pregnancy (monochorionic or dichorionic) with a planned birth (caesarean section or induction of labour) scheduled between 35+0 and 38+6 weeks gestation including women who have a planned birth due to logistic reasons (e.g. availability of beds or staff), parental preference or other maternal or fetal indications.
3. Women with gestation established by scan at ≤16 weeks according to NICE guidelines and known chorionicity
4. ≥24 hours and <7 days until planned birth

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
16 Years

Sex
Female

Total final enrolment

Key exclusion criteria
Current exclusion criteria as of 14/01/2025:
1. Women who are unable to give informed consent
2. Women who have a known or suspected major congenital fetal anomaly at the time of inclusion (defined as any structural or chromosomal anomaly that would influence management at or around birth or in the immediate postnatal period. Suspected isolated minor anomalies with lesser medical, functional or cosmetic consequences; or isolated limb abnormalities such as talipes can be included).
3. Women who have received ACS within the seven days prior to randomisation
4. Women who have a sensitivity, contraindication or intolerance to any of the ACS or any of its excipients
5. Women in whom chorionicity or gestational age are unknown
6. Women with other serious pregnancy morbidities which indicate either birth before 35 weeks or urgent birth within 24 hours
7. Women involved in a clinical trial of an investigational medicinal product (CTIMP) in pregnancy

Previous exclusion criteria:
1. Women who are unable to give informed consent
2. Women who have a known or suspected major congenital fetal anomaly at the time of inclusion (defined as any structural or chromosomal anomaly that would influence management at or around birth or in the immediate postnatal period. Suspected isolated minor anomalies with lesser medical, functional or cosmetic consequences; or isolated limb abnormalities such as talipes can be included).
3. Diabetes (pre-existing or gestational)
4. Women who have received ACS within the seven days prior to randomisation
5. Women who have a sensitivity, contraindication or intolerance to any of the ACS or any of its excipients
6. Women in whom chorionicity or gestational age are unknown
7. Women with other serious pregnancy morbidities which indicate either birth before 35 weeks or urgent birth within 24 hours
8. Women involved in a clinical trial of an investigational medicinal product (CTIMP) in pregnancy

Date of first enrolment
22/08/2022

Date of final enrolment
25/11/2024

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place
Edinburgh
United Kingdom
EH1 3EG

Sponsor information

Organisation
University of Edinburgh

ROR
https://ror.org/01nrxwf90

Organisation
NHS Lothian

ROR
https://ror.org/03q82t418

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		18/01/2024	19/01/2024	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version 2.0	25/01/2022	17/03/2022	No	Yes
Participant information sheet	version 3.0	08/03/2022	12/05/2022	No	Yes
Participant information sheet	version 12.0	30/09/2024	14/01/2025	No	Yes
Protocol file	version 2.0	27/01/2022	17/03/2022	No	No
Protocol file	version 3.0	09/03/2022	12/05/2022	No	No
Protocol file	version 4.0	27/04/2022	09/08/2022	No	No
Protocol file	version 12.0	02/08/2024	14/01/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes