

# Antenatal corticosteroids for planned birth in twins

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<b>Registration date</b> 31/03/2022	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 21/02/2025	<b>Condition category</b> Neonatal Diseases	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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

**Study website**

<https://www.stoppitstudy.co.uk>

## Contact information

**Type(s)**

Scientific, Principal Investigator

**Contact name**

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**Additional identifiers**

**EudraCT/CTIS number**

2021-002876-38

**IRAS number**

1004166

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

AC21118, HTA - NIHR131352, IRAS 1004166, CPMS 52168

## **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

**Study design**

Multicentre interventional double-blind randomized placebo-controlled trial

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Prevention

**Participant information sheet**

See study outputs table

**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 measure**

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

## **Secondary outcome measures**

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

**Overall study start date**

01/11/2021

**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  $\leq 16$  weeks according to NICE guidelines and known chorionicity
4.  $\geq 24$  hours and  $< 7$  days until planned birth

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

16 Years

**Sex**

Female

**Target number of participants**

1552

**Total final enrolment**

116

**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

England

Scotland

United Kingdom

Wales

## Study participating centre

**NHS Lothian**

Waverley Gate

2-4 Waterloo Place

Edinburgh

United Kingdom

EH1 3EG

# Sponsor information

## Organisation

University of Edinburgh

## Sponsor details

ACCORD, QMRI

47 Little France Crescent

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## Sponsor type

University/education

## Website

<https://www.accord.scot>

## ROR

<https://ror.org/01nrxf90>

**Organisation**

NHS Lothian

**Sponsor details**

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United Kingdom  
EH1 3EG  
+44 (0)845 424 2424  
accord@nhslothian.scot.nhs.uk

**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.nhslothian.scot.nhs.uk/Pages/default.aspx>

**ROR**

<https://ror.org/03q82t418>

**Funder(s)****Funder type**

Government

**Funder Name**

Health Technology Assessment Programme

**Alternative Name(s)**

NIHR Health Technology Assessment Programme, HTA

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

**Results and Publications**

Publication and dissemination plan

It is expected that the study findings will be published as soon as possible in a peer-reviewed open access journal. The final report for NIHR HTA Journals Library will be submitted within 24 months of the end of the study

## Intention to publish date

01/05/2026

## 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?
<a href="#">Participant information sheet</a>	version 2.0	25/01/2022	17/03/2022	No	Yes
<a href="#">Protocol file</a>	version 2.0	27/01/2022	17/03/2022	No	No
<a href="#">Participant information sheet</a>	version 3.0	08/03/2022	12/05/2022	No	Yes
<a href="#">Protocol file</a>	version 3.0	09/03/2022	12/05/2022	No	No
<a href="#">Protocol file</a>	version 4.0	27/04/2022	09/08/2022	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Protocol article</a>		18/01/2024	19/01/2024	Yes	No
<a href="#">Participant information sheet</a>	version 12.0	30/09/2024	14/01/2025	No	Yes
<a href="#">Protocol file</a>	version 12.0	02/08/2024	14/01/2025	No	No