

Evaluation of intravenous therapy (i.e. injection into the vein) in asthma

Submission date 09/07/2025	Recruitment status Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 17/09/2025	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 21/11/2025	Condition category Respiratory	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Asthma is a common lung condition that causes breathing problems. People affected may get short of breath and have a tight chest. Asthma attacks may be triggered by infections like colds or allergies such as dust mites. Many children and young people (CYP) have severe asthma attacks which do not respond to inhaled reliever medication. Hospital treatment may be needed with medication given as an intravenous (IV) injection (i.e. into a vein). Severe asthma attacks in CYP are a common medical emergency so it is important that doctors use the most effective and most acceptable IV treatments for CYP in hospital. Three IV medications are commonly given in the UK to treat severe asthma attacks: aminophylline, magnesium sulfate or salbutamol. Although all three IV medications are effective at treating asthma attacks, doctors are not sure which one works the best.

The EVITA trial aims to compare these three IV medications to determine which is best at treating severe asthma attacks in CYP. The trial will be led by experts who work in children's asthma care. They will compare the medications by looking at how well they work and how acceptable each treatment is to patients, their families and healthcare professionals.

Who can participate?

The trial aims to recruit 357 CYP (aged 2-18 years) from approximately 20 UK NHS hospitals over 2 years. All eligible CYP will have experienced a severe asthma attack which was not getting better with inhaled medications.

What does the study involve?

Participants are randomly allocated to receive one of the three medications. All the participants and their trial teams will know which treatment they have been given within the trial. The trial team will look at which CYP get better more quickly by using a validated asthma severity score, measure how long CYP stay in hospital and compare the side effects of each treatment. Participants will be asked to complete questionnaires, provide a blood sample for assessing the level of salbutamol (blue inhaler medicine) in their blood, and provide an optional saliva sample that will be for genetic analysis to see whether specific changes in their genes can predict how well the trial medication might have worked for them.

Some patients, parents and healthcare staff will be interviewed to understand how they feel about the treatment they received. Participants will be followed up for 30 or 45 days, depending on whether they take part in an optional interview.

What are the possible benefits and risks of participating?

Participants will be monitored more closely as a trial participant throughout their treatment by doctors and nurses at their hospital. If the team looking after the participant is concerned that they are not getting better, or that they are getting side effects from one of the drugs, they can change the treatment.

All medications used within the trial are commonly used in hospitals in the UK and staff are trained to monitor these for side effects. By taking part in this trial, participants will be providing doctors with valuable information about which is the best treatment for CYP having a severe asthma attack, which may lead to better future outcomes and improved care. Participants will be helping to change clinical practice so healthcare professionals can take better care of patients experiencing a severe asthma attack in the future.

As with any drug, side effects are possible but are rare, and most patients do not have any problems. Since the treatments used in this trial are routinely used for severe asthma attacks, the potential benefits of all three outweigh their potential risks.

Participants who receive IV aminophylline may also require additional blood tests to check the amount of the drug in their blood. This is a routine blood test because it is known that the amount of the drug can vary from person to person. It is therefore necessary to check that participants are getting enough of the drug to make them better but not too much as this may increase the risk of side effects.

A small disadvantage in taking part in the trial is that participants will need to give up some of their time to complete the follow-up questionnaires.

Where is the study run from?

The trial is being jointly managed by the Centre for Trials Research (CTR) at Cardiff University and the Liverpool Clinical Trial Centre (LCTC) at the University of Liverpool (UK)

When is the study starting and how long is it expected to run for?

January 2025 to December 2027

Who is funding the study?

This trial has been funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment (HTA) programme (NIHR162027) (UK)

Who is the main contact?

EVITA@cardiff.ac.uk

Contact information

Type(s)

Public, Scientific

Contact name

Dr EVITA Trial Team

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Type(s)

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Integrated Research Application System (IRAS)

1009438

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

RHM CHI1272, CPMS 60132

Study information

Scientific Title

EVALUATION of Intravenous Therapy in Asthma (EVITA): a randomised trial of aminophylline, magnesium sulfate or salbutamol intravenous therapy for acute severe asthma in children and young people

Acronym

EVITA

Study objectives

Primary objective:

To determine which of IV aminophylline, magnesium sulfate or salbutamol (interventions and comparators) is most effective at treating severe acute asthma unresponsive to maximal inhaled therapy in CYP aged 2-18 years

Primary economic objective:

To determine which IV bronchodilator is most cost-effective

Secondary objectives:

1. To determine which IV bronchodilator has the shortest time to discharge from hospital
2. To determine, using qualitative interviews, questionnaires, avoidance of escalations and adverse events, which IV bronchodilator is most acceptable to patients, parents/carers and healthcare professionals

Tertiary/exploratory objectives:

1. To determine whether the response to IV salbutamol therapy varies with the serum concentration of salbutamol immediately before IV therapy
2. To determine if specific genetic polymorphisms can predict response to individual IV bronchodilator therapies
3. To determine if specific baseline characteristics predict response to each of the three IV

bronchodilators

4. To determine whether the season of presentation affects the outcome

5. To determine whether inhaled and intravenous salbutamol can give rise to lactic acidosis

Ethics approval required

Ethics approval required

Ethics approval(s)

approved 15/09/2025, Yorkshire & The Humber - Leeds West Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, United Kingdom; +44 (0)207 1048053, +44 (0)207 104 8272, +44 (0)2071048100; leedswest.rec@hra.nhs.uk), ref: 25/YH/0152

Study design

Randomized controlled trial

Primary study design

Interventional

Study type(s)

Efficacy, Safety

Health condition(s) or problem(s) studied

Severe acute asthma

Interventions

All trial participants will be having a severe asthma attack and not getting better with inhaled medications so will be classed as a medical emergency. All eligible patients will be entered into the trial upon assessment of their condition.

Patients will be randomised using a web-based system to receive one of the following:.

1. Magnesium sulfate: single IV infusion of 40 mg/kg (max. 2 g) over 20 minutes.
2. Salbutamol: a single IV infusion of 15 micrograms/kg (max. 250 micrograms) over 5 to 10 minutes, then a continuous infusion of 1 microgram/kg/minute (max. 20 micrograms/minute), continue as clinically indicated.
3. Aminophylline: a single IV infusion of 5 mg/kg (max. 500 mg) over 20 minutes, then a continuous infusion of 1 mg/kg/hour (2–11 years) or 0.5 mg/kg/hour (≥ 12 years) and continue as clinically indicated.

Consent and assent for continuing in the trial will be sought at the earliest appropriate opportunity (i.e. on the paediatric ward once the patient is stable and they are able to give informed consent) following the medical emergency. This will ideally be prior to hospital discharge.

Participants will be followed up for 30 or 45 days, depending on whether they take part in an optional interview. The follow-up assessments will include assessment of ASS, routine blood samples, trial blood samples prior to intervention to assess salbutamol levels, adverse event monitoring, clinical reviews, vital signs, participant questionnaires, an optional saliva sample and an optional qualitative interview.

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Aminophylline, magnesium sulphate, salbutamol

Primary outcome(s)

Primary endpoint:

Assessment of wheeze, accessory muscle use and heart rate will be used to calculate the Asthma Severity Score (ASS) at 1 and 2 hours after randomisation. This will be repeated at 4, 8, 12, 24, 48 and 72 hours post randomisation.

Primary economic endpoint:

Incremental cost per quality-adjusted life year (QALY) gained based on an NHS and personal social service (PSS) perspective. The analysis will adopt the perspective of the NHS and personal social services (PSS), over a time horizon of 1-month post randomisation.

Key secondary outcome(s)

Secondary endpoints:

1. Length of stay in hospital (hours) measured from randomisation to hospital discharge
2. Number of nights in hospital measured from randomisation to hospital discharge
3. Acceptability of intervention measured using the Acceptability of Intervention Measure (AIM) participant questionnaire at 30-day follow-up
4. Intervention Appropriateness Measure (IAM) measured using the IAM participant questionnaire at 30-day follow-up
5. Feasibility of Intervention Measure (FIM) measured using the FIM participant questionnaire at 30-day follow-up
6. Escalation of therapy during the admission (e.g. additional intravenous bronchodilator, non-invasive or invasive ventilatory support) measured from randomisation to hospital discharge
7. Admission to high dependency or intensive care measured from randomisation to 30-day follow-up
8. Non-invasive ventilation measured from randomisation to 30-day follow-up
9. Invasive ventilation measured from randomisation to 30-day follow-up
10. Readmission within 30 days measured at 30-day follow-up
11. Adverse events measured from randomisation to 30-day follow-up
12. Health utility based on responses to the CHU-9D and health services utilisation measured from randomisation to 30-day follow-up

Tertiary/exploratory endpoints:

The primary care secondary end points will serve as outcome measures for the tertiary /exploratory objectives, which focus on serum salbutamol concentration pre-IMP administration, specific polymorphisms and other patient factors, and season of presentation. Blood gas results (pH, carbon dioxide, lactate) and serum potassium measured during the hospital stay will serve as the outcome for the lactic acid objective.

Completion date

31/12/2027

Eligibility

Key inclusion criteria

1. CYP aged 2-18 years (up to and including the day prior to 19th birthday).
2. Previous clinical diagnosis of asthma or presenting with acute wheeze which the assessing healthcare professional considers to relate to underlying asthma.
3. Clinically unresponsive to maximal inhaled bronchodilator therapy (this would usually include three back-to-back doses of inhaled high-dose salbutamol plus any amount of ipratropium) or is so severe (critical asthma) that IV treatment is needed immediately.

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Mixed

Lower age limit

2 years

Upper age limit

18 years

Sex

All

Total final enrolment

0

Key exclusion criteria

1. Immediate need for invasive ventilatory support
2. Co-existing long-term respiratory conditions (e.g. cystic fibrosis) or requiring long-term supplemental oxygen therapy
3. Known severe renal or liver disease
4. Uncorrected cyanotic congenital cardiac disease
5. Known neuromuscular disease
6. Participants where the use of intravenous (IV) aminophylline, magnesium sulfate or salbutamol would be contraindicated according to the relevant summary of product characteristics (SmPC), including known hypersensitivity or history of severe allergic reaction to any of the trial medications or their excipients
7. Known previous randomisation into the EVITA trial
8. Already received IV therapy for an episode of acute asthma during current hospital admission, or within the last 10 days
9. Currently receiving regular theophylline or other xanthine medication
10. Currently receiving beta-blockers
11. Involved with a trial of a medicinal product within the last 3 months
12. Participants or parents/carers request not to be included in the trial

Date of first enrolment

24/11/2025

Date of final enrolment

15/09/2027

Locations**Countries of recruitment**

United Kingdom

England

Northern Ireland

Scotland

Wales

Study participating centre

University Hospital Southampton NHS Foundation Trust

Southampton General Hospital

Tremona Road

Southampton

England

SO16 6YD

Study participating centre

University Hospitals of Leicester NHS Trust

Leicester Royal Infirmary

Infirmary Square

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LE1 5WW

Study participating centre

Royal Berkshire NHS Foundation Trust

Royal Berkshire Hospital

London Road

Reading

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RG1 5AN

Study participating centre

University College London Hospitals NHS Foundation Trust
250 Euston Road
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NW1 2PG

Study participating centre
Portsmouth Hospitals University NHS Trust
Queen Alexandra Hospital
Southwick Hill Road
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PO6 3LY

Study participating centre
University Hospitals Bristol and Weston NHS Foundation Trust
Bristol Royal Hospital for Children
Upper Maudlin Street
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Study participating centre
Leeds Teaching Hospitals NHS Trust
Paediatric Emergency Department
Leeds General Infirmary
Great George St
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LS1 3EX

Study participating centre
Birmingham Women's and Children's NHS Foundation Trust
Emergency Department
Birmingham Children's Hospital
Steelhouse Lane
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B4 6NH

Study participating centre

Royal Devon University Healthcare NHS Foundation Trust

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EX2 5DW

Study participating centre

University Hospitals of Derby and Burton NHS Foundation Trust

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Study participating centre

Alder Hey Children's Hospital NHS Foundation Trust

Alder Hey Children's Hospital
Emergency Department
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Study participating centre

Somerset NHS Foundation Trust

Trust Management
Lydeard House
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TA1 5DA

Study participating centre

Cardiff and Vale University Health Board

The University Hospital of Wales
Heath Park Way
Cardiff
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Study participating centre**King's College Hospital NHS Foundation Trust**

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Study participating centre**Imperial College Healthcare NHS Trust**

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Study participating centre**NHS Greater Glasgow and Clyde**

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Study participating centre**Belfast Health and Social Care Trust**

Royal Belfast Hospital for Sick Children

180 Falls Road

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BT12 6BE

Sponsor information**Organisation**

University Hospital Southampton NHS Foundation Trust

Funder(s)

Funder type

Government

Funder Name

National Institute for Health and Care Research

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon request from Cardiff Centre for Trials Research by contacting the trial manager (Dr Melanie Varley) at EVITA@cardiff.ac.uk. Anonymised data will be provided upon production of the requestor's trial protocol and agreement by the Centre for Trials Research and the trial sponsor (University of Southampton).

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website		28/07/2025	No	No
Study website			28/07/2025	No	No
Study website		11/11/2025	11/11/2025	No	Yes