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

Submission date 09/07/2025	**Recruitment status** Not yet recruiting	[X] Prospectively registered [_] Protocol
Registration date 17/09/2025	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 03/10/2025	**Condition category** Respiratory	[_] Individual participant data [X] 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

Study website
https://evita.org.uk/

Contact information

Type(s)
Public, Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1009438

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
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

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

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

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacogenetic, Pharmacogenomic, Pharmacoeconomic

Phase
Phase III

Drug/device/biological/vaccine name(s)
Aminophylline, magnesium sulphate, salbutamol

Primary outcome measure
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.

Secondary outcome measures
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.

Overall study start date
07/07/2025

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

Age group
Child

Lower age limit
2 Years

Upper age limit
18 Years

Sex
Both

Target number of participants
357

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
06/10/2025

Date of final enrolment
15/09/2027

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
University Hospital Southampton NHS Foundation Trust
Southampton General Hospital
Tremona Road
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SO16 6YD

Study participating centre

University Hospitals of Leicester NHS Trust
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Study participating centre
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Study participating centre
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Study participating centre

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Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre
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Sponsor type
Hospital/treatment centre

Website
https://www.uhs.nhs.uk/

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

Publication and dissemination plan
Peer-reviewed scientific journals
Conference presentation
Publication on website
Submission to regulatory authorities

Data release will require approval by the Trial Management Group (TMG) and the Trial Steering Committee (TSC) and will involve pseudo-anonymised data only.

Intention to publish date
31/12/2028

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?
Study website			28/07/2025	No	No
Study website			28/07/2025	No	No