

# Children's anti-inflammatory reliever study, United Kingdom (CARE-UK)

<b>Submission date</b> 27/01/2024	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 19/11/2024	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 10/02/2026	<b>Condition category</b> 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

This study aims to see if a new type of asthma reliever inhaler reduces asthma attacks in children. Children who have asthma attacks are treated with reliever medications (blue inhalers), which act quickly to briefly open the airways when they become narrow but their effect soon wears off. These blue inhalers don't treat the underlying problem, airway inflammation (swelling). Asthma attacks can be prevented with an inhaled steroid treatment (usually brown/purple inhalers which prevents the underlying airway swelling), a maintenance treatment. This new type of combination reliever inhaler contains a fast-acting steroid working by helping to dampen inflammation and is usually taken regularly/every day. In adults and teenagers, this inhaler has been shown to work well by relieving symptoms and treating the underlying airway inflammation resulting in fewer asthma attacks. This combination inhaler can be used instead of the usual reliever medication on its own for people with infrequent asthma symptoms or as both a regular preventer and a reliever for those with more troublesome symptoms.

### Who can participate?

Children aged  $\geq 6$  to  $< 12$  years

### What does the study involve?

Children will be randomly allocated to one of 2 groups:

1. Usual care, no change in treatment
2. The new approach, using the combination inhaler on its own as a reliever when symptoms occur or for both maintenance and reliever treatment

This study will identify children through GP records, and attendance at hospital asthma clinics or they may self-refer through social media adverts. Once they have agreed to take part in the study, the study team will ask that they attend 4 visits in total, some face-to-face, some over the telephone, and some in person at their local study site. The study will see which group has the most asthma attacks requiring a course of steroid tablets. The results of the trial will change National asthma guidelines and findings may be shared by Asthma and Lung UK on their platforms.

### What are the possible benefits and risks of participating?

Children in both groups of the study will have access to the study team, who will make sure

parents and children know how to take their inhalers, have an up-to-date Personal Asthma Action Plan and know when to seek help. It is hoped that those in the intervention group will find it easier to have just one inhaler to use.

If the child is on the intervention arm, using the combination inhaler, there may be a period where the child will need to adjust to the new inhaler. The schools will have to get used to the revised Asthma Action Plan as the number of puffs of the new reliever inhaler will be different to the number of puffs of the blue reliever inhaler. Detailed directions will be sent to the schools about students who are taking part in the trial and their new Personalised Asthma Action Plan. Parents will also be encouraged to review the new Personalised Asthma Action Plan closely with the children's teachers to ensure everyone in contact with the child is aware of the change of plans.

The new combination inhaler contains steroids which can affect growth. The study will measure height at the onset of the study and the end. Some children will be given an electronic monitoring device for their inhalers so the study team can keep track of how much medicine they have taken. For all children, prescription records will be checked so that inhaled steroid doses and courses of oral steroids can be compared in each group. The risk burden is fairly low for these patients and the long-term benefits of controlled asthma, and hence reduction in asthma attacks needing a course of steroids, outweigh the potential side effects.

Where is the study run from?  
Imperial College London, UK

When is the study starting and how long is it expected to run for?  
June 2023 to February 2027

Who is funding the study?  
National Institute for Health and Care Research (NIHR), UK

Who is the main contact?  
Louise Fleming, l.fleming2@nhs.net

## Contact information

**Type(s)**  
Scientific

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**Type(s)**  
Principal investigator

**Contact name**

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## Additional identifiers

**Clinical Trials Information System (CTIS)**

Nil known

**Integrated Research Application System (IRAS)**

1009041

**ClinicalTrials.gov (NCT)**

Nil known

**Protocol serial number**

23SM8661

**Central Portfolio Management System (CPMS)**

59444

## Study information

**Scientific Title**

A novel reliever strategy for children with asthma: children's anti-inflammatory reliever study, United Kingdom (CARE-UK)

**Acronym**

CARE-UK

**Study objectives**

To determine the clinical effectiveness of budesonide-formoterol reliever therapy either alone or as part of maintenance and reliever therapy (MART) compared with SABA reliever therapy either used as monotherapy or with the child's usual maintenance treatment in children with asthma aged  $\geq 6$  years - < 12 years old.

1. To determine the clinical efficacy of budesonide-formoterol reliever therapy either AIR alone or as part of MART compared to usual care
2. To determine the safety of budesonide-formoterol reliever therapy either AIR alone or as part of MART
3. To determine the cost-effectiveness of budesonide-formoterol reliever therapy either AIR alone or as part of MART compared to usual care

## **Ethics approval required**

Ethics approval required

## **Ethics approval(s)**

approved 10/09/2024, Wales REC 5 (Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 (0)2922 940910; Wales.REC5@Wales.nhs.uk), ref: 24/WA/0046

## **Study design**

Randomized controlled open-label parallel-group study

## **Primary study design**

Interventional

## **Study type(s)**

Efficacy, Safety

## **Health condition(s) or problem(s) studied**

Paediatric asthma

## **Interventions**

Randomisation

If the child is eligible for the study they will be randomised. A computer-generated randomisation list will be created and allocation concealed using an online system (OpenClinica). Stratified block randomisation will be used. The randomisation will be stratified by:

- a. Site
- b. Current GINA treatment step (see 'Dosing Regimen' below for more details)

The study is open-label. Blinding is not being performed in order to maintain the potential real-world advantage of ICS-formoterol as a reliever.

### **Control (Standard Care) Arm**

Patients in the control arm will continue with their current standard treatment as prescribed by their usual healthcare provider. This will be one of either:

- SABA: A short-acting bronchodilator that provides immediate relief for asthma symptoms.
- ICS: An inhaled corticosteroid that can be used as maintenance therapy.
- ICS-LABA: A combination of an inhaled corticosteroid and a long-acting bronchodilator that can be used as a controller therapy or for reliever therapy.

### **Intervention Arm**

Patients in the intervention arm will be issued two budesonide-formoterol (Symbicort®) 100/3 MDIs and a compatible spacer device such as Aerochamber Plus. One for home, maintenance and reliever doses, and the other to be kept at school for reliever use.

### **Dose Regimen**

In clinical practice, treatment is stepped up and down depending on clinical control in terms of symptoms and risk of an asthma attack. Stepping up and down will be determined by the patient's usual healthcare provider. For those in the intervention arm participants will increase or decrease the number of maintenance budesonide-formoterol puffs per day. The control arm will continue as per usual clinical care whereby the ICS dose is increased or decreased and additional controllers such as LABAs are added or removed depending on clinical control.

The starting dose for budesonide-formoterol will be based on the dose of usual care inhaled corticosteroid ((ICS) low, medium or high) prescribed in the past 4 weeks as per current Global Initiative for Asthma (GINA) guidance:

For paediatric low-dose, moderate-dose and high-dose for budesonide-formoterol:

Beclomethasone dipropionate (ICS):

Standard particle CFC free inhalers: 100 - 200mcg/day; >200 - 400mcg/day; >400 - mcg/day

Extra-fine particle CFC free inhalers: 50 - 100mcg/day; >100 - 200mcg/day; >200 - mcg/day

Budesonide:

Metered dose and dry powder inhalers: 100 - 200mcg/day; >200 - 400mcg/day; >400 mcg/day

Fluticasone propionate:

Metered dose and dry powder inhalers: 100mcg/day; 150 – 200mcg/day; >200 mcg/day

## **Intervention Type**

Drug

## **Phase**

Phase III

## **Drug/device/biological/vaccine name(s)**

budesonide-formoterol (Symbicort) [budesonide, Formoterol fumarate dihydrate]

## **Primary outcome(s)**

Rate of severe asthma attacks: The rate of severe asthma attacks per patient per year, defined as worsening symptoms leading to an urgent medical review resulting in the prescription of systemic corticosteroids, measured at 52 weeks

## **Key secondary outcome(s)**

1. Rate of total asthma attacks: The rate of total asthma attacks per patient per year, defined as worsening symptoms leading to an urgent medical review, whether or not systemic corticosteroids are prescribed, measured at 52 weeks
2. Time to first severe attack: Time to first severe asthma attack measured in weeks from baseline over the 52-week study period
3. Proportion of participants with severe attacks: Proportion of participants experiencing at least one severe asthma attack, measured at 52 weeks
4. Days lost from school: Number of days lost from school due to asthma, measured annually
5. Days lost from work for childcare: Number of days lost from work due to caring for a child with asthma, measured annually
6. Change in Childhood Asthma Control Test (cACT): Change in cACT scores measured from baseline to 52 weeks
7. Change in Paediatric Asthma Quality of Life Questionnaire (PAQLQ): Change in PAQLQ scores measured from baseline to 52 weeks
8. Growth during the study period: Change in height from baseline to study completion at 52 weeks
9. Total ICS dose: Total inhaled corticosteroid (ICS) dose as measured by an electronic monitoring device or prescription records at 52 weeks
10. Total systemic corticosteroid dose: Total dose of systemic corticosteroids prescribed over 52 weeks

11. Change in Child Health Utility (CHU9D): Change in CHU9D scores measured from baseline over the course of the 52-week study
12. Quality Adjusted Life Years (QALYs): QALYs calculated as the area under the CHU9D curve over 52 weeks
13. Cost of asthma-related healthcare: Total cost of asthma-related healthcare utilization measured over 52 weeks

**Completion date**

28/02/2027

## Eligibility

**Key inclusion criteria**

Current inclusion criteria as of 10/02/2026:

1. Clinician diagnosis of asthma
2. Children aged  $\geq 6$  to  $< 12$  years
3. Washout period of 6 months post previous IMP studies
4. Prescribed asthma medication, (within license) in past 6 months (SABA (salbutamol) with or without ICS or ICS+LABA)
5. Parent or carer able to understand the study requirements and willing to provide informed consent

Previous inclusion criteria:

1. Clinician diagnosis of asthma
2. Children aged  $\geq 6$  to  $< 12$  years
3. Washout period of 6 months post previous IMP studies
4. Prescribed asthma medication in the past 6 months (SABA, ICS or ICS+LABA)
5. Parent or caregiver able to understand the study requirements and willing to provide informed consent

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Child

**Lower age limit**

6 years

**Upper age limit**

12 years

**Sex**

All

**Total final enrolment**

0

## **Key exclusion criteria**

Current exclusion criteria as of 10/02/2026:

1. Other chronic airways disease including but not limited to bronchiectasis, cystic fibrosis, sickle cell disease
2. Children prescribed non-salbutamol SABA (e.g. terbutaline) as their reliever
3. Already using ICS-formoterol as a reliever
4. Children on step 5, very high dose treatment (e.g. high dose ICS/LABA, prescription of biological therapy such as omalizumab)
5. Any known or suspected contraindications to the medications prescribed in the study or their respective excipients:
  - 5.1. Apaflurane (HFA 227)
  - 5.2. Povidone
  - 5.3. Macrogol

Previous exclusion criteria:

1. Other chronic airway diseases including but not limited to bronchiectasis, cystic fibrosis, sickle cell disease
2. Already using ICS-formoterol as a reliever
3. Children on step 5, very high dose treatment (e.g. high dose ICS/LABA, prescription of biological therapy such as omalizumab)

Added 19/06/2025:

4. Any known or suspected contraindications to the medications

## **Date of first enrolment**

01/12/2024

## **Date of final enrolment**

31/08/2026

## **Locations**

### **Countries of recruitment**

United Kingdom

England

Scotland

Wales

### **Study participating centre**

**Great Ormond Street Hospital for Children**

Great Ormond Street

London

England

WC1N 3JH

**Study participating centre**  
**The Royal London Hospital**  
Whitechapel  
London  
England  
E1 1BB

**Study participating centre**  
**Kings College Hospital**  
Mapother House  
De Crespigny Park  
Denmark Hill  
London  
England  
SE5 8AB

**Study participating centre**  
**St Georges University Hospital**  
Blackshaw Road  
London  
England  
SW17 0QT

**Study participating centre**  
**Evelina London Children's Hospital**  
Westminster Bridge Road  
London  
England  
SE1 7EH

**Study participating centre**  
**Leicester Royal Infirmary**  
Infirmary Square  
Leicester  
England  
LE1 5WW

**Study participating centre**  
**Nottingham Children's Hospital**  
Queen's Medical Centre, Derby Rd

Nottingham  
England  
NG7 2UH

**Study participating centre**

**Addenbrookes Hospital**

Hills Road  
Cambridge  
England  
CB2 0QQ

**Study participating centre**

**Jenny Lind Children's Hospital**

Norfolk and Norwich University Hospital, Colney Lane  
Norwich  
England  
NR4 7UY

**Study participating centre**

**Oxford Children's Hospital**

John Radcliffe Hospital, Headington  
Oxford  
England  
OX3 0AG

**Study participating centre**

**Birmingham Children's Hospital**

Steelhouse Ln, Queensway  
Birmingham  
England  
B4 6NH

**Study participating centre**

**Staffordshire Children's Hospital at Royal Stoke**

Royal Stoke University Hospital, Newcastle Road  
Stoke-on-Trent  
England  
ST4 6QG

**Study participating centre**  
**Royal Alexandra Children's Hospital**  
North Dr, Brighton and Hove  
Brighton  
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BN2 5BE

**Study participating centre**  
**Bristol Royal Hospital for Children**  
Paul O'Gorman Building  
Upper Maudlin Street  
St Michael's Hill  
Bristol  
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BS2 8BJ

**Study participating centre**  
**Alder Hey Children's Hospital**  
E Prescott Rd  
Liverpool  
England  
L14 5AB

**Study participating centre**  
**Royal Manchester Children's Hospital**  
Manchester Royal Infirmary, Oxford Rd  
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M13 9WL

**Study participating centre**  
**Great North Children's Hospital**  
Victoria Wing, Royal Victoria Infirmary  
Newcastle upon Tyne  
England  
NE1 4LP

**Study participating centre**  
**Leeds Children's Hospital**  
Leeds General Infirmary  
Clarendon Wing

Leeds  
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LS1 3EX

**Study participating centre**  
**Sheffield Children's Hospital**  
The University of Sheffield, Clarkson St, Broomhall  
Sheffield  
England  
S10 2TH

**Study participating centre**  
**Southampton Children's Hospital**  
Southampton General Hospital  
Tremona Road  
Southampton  
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SO16 6YD

**Study participating centre**  
**Noah's Ark Children's Hospital for Wales**  
University Hospital of Wales, Heath Park Way  
Cardiff  
Wales  
CF14 4XW

**Study participating centre**  
**Westburn Medical Group**  
Foresterhill Health Centre  
Aberdeen Royal Infirmary  
Foresterhill Road  
Aberdeen  
Scotland  
AB25 2XE

**Study participating centre**  
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1345 Govan Road  
Glasgow  
Scotland  
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# Sponsor information

## Organisation

Imperial College London

## ROR

<https://ror.org/041kmwe10>

# 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

### 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>		11/11/2025	11/11/2025	No	Yes
<a href="#">Study website</a>			13/11/2025	No	No

