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

Submission date 27/01/2024	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 19/11/2024	**Overall study status** Ongoing	
Last Edited 19/06/2025	**Condition category** Respiratory	

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 ≥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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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1009041

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
23SM8661, IRAS 1009041, 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 ≥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

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice, Home, Hospital, Medical and other records, School

Study type(s)
Safety, Efficacy

Participant information sheet
https://careukstudy.uk/

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

Pharmaceutical study type(s)
Dose response, Pharmacoeconomic, Prophylaxis, Therapy

Phase
Phase III

Drug/device/biological/vaccine name(s)
budesonide-formoterol (Symbicort) [budesonide, Formoterol fumarate dihydrate]

Primary outcome measure
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

Secondary outcome measures
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

Overall study start date
01/06/2023

Completion date
28/02/2027

Eligibility

Key inclusion criteria
1. Clinician diagnosis of asthma
2. Children aged ≥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

Age group
Child

Lower age limit
6 Years

Upper age limit
12 Years

Sex
Both

Target number of participants
1352

Key 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
01/08/2025

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
Great Ormond Street Hospital for Children
Great Ormond Street
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WC1N 3JH

Study participating centre
The Royal London Hospital
Whitechapel
London
United Kingdom
E1 1BB

Study participating centre
Kings College Hospital
Mapother House
De Crespigny Park

Denmark Hill
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SE5 8AB

Study participating centre
St Georges University Hospital
Blackshaw Road
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United Kingdom
SW17 0QT

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

Study participating centre
Leicester Royal Infirmary
Infirmary Square
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LE1 5WW

Study participating centre
Nottingham Children's Hospital
Queen's Medical Centre, Derby Rd
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Addenbrookes Hospital
Hills Road
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CB2 0QQ

Study participating centre
Jenny Lind Children's Hospital
Norfolk and Norwich University Hospital, Colney Lane
Norwich
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NR4 7UY

Study participating centre
Oxford Children's Hospital
John Radcliffe Hospital, Headington
Oxford
United Kingdom
OX3 0AG

Study participating centre
Birmingham Children's Hospital
Steelhouse Ln, Queensway
Birmingham
United Kingdom
B4 6NH

Study participating centre
Staffordshire Children's Hospital at Royal Stoke
Royal Stoke University Hospital, Newcastle Road
Stoke-on-Trent
United Kingdom
ST4 6QG

Study participating centre
Royal Alexandra Children's Hospital
North Dr, Brighton and Hove
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United Kingdom
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 Prescot Rd
Liverpool
United Kingdom
L14 5AB

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

Study participating centre
Great North Children's Hospital
Victoria Wing, Royal Victoria Infirmary
Newcastle upon Tyne
United Kingdom
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
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S10 2TH

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

Study participating centre
Noah's Ark Children's Hospital for Wales
University Hospital of Wales, Heath Park Way
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Study participating centre
Westburn Medical Group
Foresterhill Health Centre
Aberdeen Royal Infirmary
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AB25 2XE

Study participating centre
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Sponsor type
University/education

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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

Publication and dissemination plan
1. Peer reviewed scientific journals
2. Internal report
3. Conference presentation
4. Publication on website
5. Other publication

We will ensure the data is disseminated as widely as possible, both via scientific publications and at conferences, but also via our patient and public representatives who are co-applicants

(Asthma and Lung-UK). We will disseminate the results using Asthma and Lung UK's website and social media platforms and also via Imperial College website and social media platforms.

Intention to publish date
28/02/2028

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