Parent / Caregiver Information Sheet

Trial title: A novel reliever strategy for children with asthma: Children's Anti-inflammatory Reliever study, United Kingdom (CARE-UK)

Chief Investigator: Dr Louise Fleming

Study Protocol Number: 23SM8661

IRAS ID: 1009041 **REC Ref:** 12/WA/0046

You are being invited to consider including your child in a research study. Before you decide whether you would like your child to be involved, it is important for you to understand why the research is being done and what it will involve for your child.

Please take the time to read the following information carefully and discuss it with others if you wish.

All backgrounds and abilities are welcome to take part!

Part 1 – Why is this study being done? (pages 2-8)

This section tells you about the purpose of this study and what will happen if your child takes part.

Part 2 – Frequently Asked Questions (pages 8-10)

This section gives you more detailed information about the study. Take time to decide whether or not you would wish for your child to take part. Please ask us if there is anything that is not clear or if you would like more information.

Part 3 – Participant Privacy Notice (pages 11-14)

This section explains how we will look after all the information collected about your child and use this information properly.

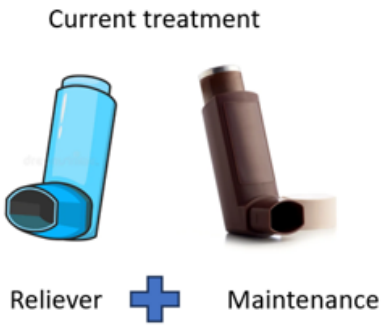
Part 4 – Glossary (page 15)

This section explains some of the terms and words used in this document.

Thank you for taking the time to consider whether your child could take part in our study.

Part 1 - Why is this study being done?

Children and young people with asthma in the United Kingdom continue to have poor control and frequent asthma attacks, despite effective therapies being available. Asthma symptoms and attacks are usually treated with a medication that briefly opens the airways (reliever medication – blue inhaler) when they become narrow. These blue inhalers act quickly but the effects wear off and don't treat the underlying problem of airway inflammation (swelling).

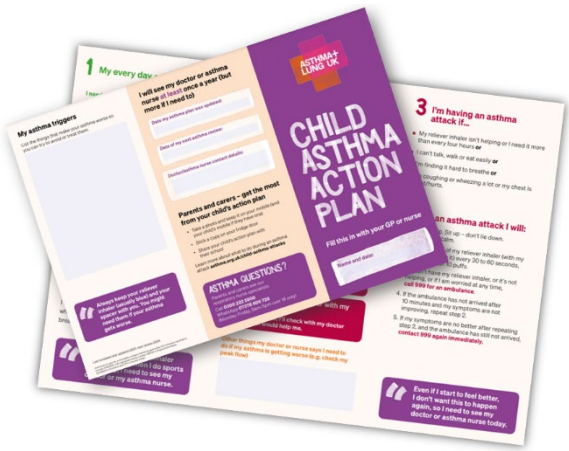


Asthma attacks can be *prevented* with an inhaled steroid treatment (usually a brown or purple inhaler) - this is called preventer or maintenance treatment. The steroid inhalers are taken regularly, usually every day, to dampen the inflammation (swelling) over time.

In adults and teenagers, there is a combination inhaler that has been shown to work well, that contains *both* a preventer steroid (budesonide) and a long-lasting reliever (formoterol) medicine (red inhaler). This is known as an anti-inflammatory reliever inhaler or AIR for short. This combination inhaler is designed to relieve the immediate symptoms whilst *also* working on the underlying airway inflammation. This combination inhaler can either be used as needed for children who have few symptoms and currently only use a blue inhaler or a low dose brown inhaler, or the combination inhaler can be used every day for both maintenance and reliever treatment for those with more frequent symptoms.

The use of anti-inflammatory reliever therapies have been shown to work very well in children over 12 years of age and adults. However, this treatment option is not currently available to younger children.

In this study, we will compare the effectiveness of the (red) combination anti-inflammatory reliever inhaler (either alone or used as both maintenance and reliever) with the blue inhaler used on its own (when needed) or with your child's usual maintenance treatment. We will also determine the safety and cost effectiveness of the combination inhaler, compared to current inhalers.



All children will be given a Personal Asthma Action Plan which will clearly state the dosing plan for your child, when additional doses can be taken and the maximum number of doses to be taken in a day and when to seek medical attention.

What is the purpose of this study and who is involved?

We want to test a combination reliever inhaler (red) for children ages 6 years up to 12 years of age.

We want to determine whether using the combination inhaler will lead to fewer asthma attacks and better control than the current standard treatment.

We are looking to change and enhance the national asthma guidelines and care for children from ages 6 years up to 12 years of age the UK. This study is being undertaken in 25 clinics across the UK so that we can make sure that all children are represented throughout the country.

Why has my child been chosen to take part in this study?

We are asking your child to take part because he/she is aged between 6 and 12 years old and has asthma for which they are currently prescribed inhalers. This includes children who are only prescribed the blue inhaler as well as those prescribed a preventer inhaler containing inhaled steroids (usually a brown or purple inhaler) in addition to the blue inhaler. Potential participants will be screened from a list of all children who have asthma and who have been prescribed medication for their asthma in the past 6 months.

Does my child have to take part?

No. Your child does not have to take part in this study, it is completely voluntary. You have the right to decline your child's participation in the study for any reason and this will not affect the quality of your child's care or treatment.

What will happen if my child takes part?

If you agree for your child to take part, we will randomise your child into one of the two treatment groups of the study, the *control* group or the *intervention* group.

1,352 children will be randomly allocated to one of **2 groups**

the 'control' group

This group will have their *usual asthma care*, according to their Personal Asthma Action Plan

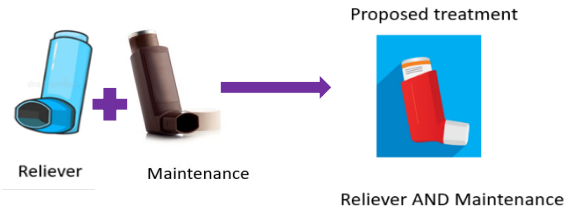
the 'intervention' group

This group will use the *combination red inhaler,* according to a new Personal Asthma Action Plan

If your child is in the control group they will stay on their current inhalers and we won't make any changes.

If your child is in the *intervention* group*,* their reliever inhaler will be changed to the anti-inflammatory combination inhaler (red).

Children currently prescribed a higher dose of the brown inhaler will use the combination inhaler for both maintenance and reliever treatment



Children currently prescribed a blue inhaler or a low dose of the brown inhaler will only take the combination (red) inhaler as needed.

If your child is in the intervention group we will let your child know how many puffs of the combination inhaler to take; this will be based on the treatment they are currently prescribed.

Over the course of the year, decisions about changes in your child's asthma treatment will be made by their usual healthcare provider (usually their GP or asthma nurse). If their asthma control has not been good, they may need to increase their asthma treatment, and if their asthma has been good their treatment may be reduced. For those in the intervention group, this will mean increasing or decreasing the number of puffs of the new combination inhaler. If any changes are made to your child's treatment, they will be given a new Personal Asthma Action Plan which will explain how many puffs of inhaler they should take.

All girls in the study we will ask questions about their periods. This is in accordance with standard clinical practice where appropriate use of all medicines needs to be considered in females of child bearing potential.

How long will the study last?

After an initial screening visit (via telephone or video call), you and your child will be invited to attend **4 visits in total**, the first one being in person at the local study site where we will ask some questions about your child's asthma and how it affects them. If they are in the intervention group they will be given the new inhaler and shown how to use it.

Your child will attend a **follow up visit at 4 months and 8 months**. These can be done over the phone or video call.

The final visit will be at your local study site in person at **1 year**. At all visits, you will receive an updated Personalised Asthma Action Plan for your child, and we will check to ensure your child has remembered how to use their inhalers. We will ask you to return all used and unused inhalers at the end of the study to your study centre. We will dispose of the inhalers responsibly using an inhaler recycling scheme.
If your child is part of the sub-study we will ask you to please return the electronic monitoring device to your study centre.

Your child will be in the study for up to 12 months with 5 visits in total, as follows:

- Initial screening visit: telephone or video call
- Baseline visit: in person
- Month 4 visit: telephone or video call
- Month 8 visit: telephone or video call
- 1 Year visit: in person

Visits / Month		0	1	2	3	4	5	6	7	8	9	10	11	12
Screening visit (telephone)	Telephone													
Baseline (in person)		In person												
Follow up 1 & 2 (telephone)						Telephone				Telephone				
1 Year (in person)														In person
Text message	Monthly text messages to see if your child has had any asthma attacks													

- **Screening Visit (telephone):** **~ 20 Minutes**
  - Information about your child's asthma
  - Asthma History
    - Current Medications

Participants who meet the requirements of the study will be invited to join and will be provided further information about the study.

- **Baseline (in person):** **~ 45 Minutes**
  - Asthma History/ Review
    - Medication history
    - Medical history
  - Height & Vitals
  - Menstrual History (female patients only)
  - Saliva Collection
  - Asthma & Child Health Questionnaires
  - Asthma Plan
  - Inhaler Check
  - Inhaler given

*monthly text messages to see if your child has had any asthma attacks

- **Month 4 & 8 (telephone):** **~ 15 Minutes**
  - Side Effects
  - Menstrual History (female patients only)
  - Asthma History/ Review
    - Current medication
  - Asthma & Child Health Questionnaires
  - Asthma Plan
  - Inhaler Check
  - Inhaler given

*monthly text messages to see if your child has had any asthma attacks

- **Year 1 (in person):** **~ 45 Minutes**
  - Side Effects
  - Menstrual History (female patients only)
  - Asthma History/ Review
    - Current medication
  - Height & Vitals
  - Saliva Collection
  - Asthma & Child Health Questionnaires
  - Asthma Plan
  - Inhaler Check

What if my child becomes unwell while in the study?

If your child becomes unwell, you should follow your child's asthma management plan, and take them to their GP or A&E as you would normally do. Their treatment when they have an asthma attack will not change.

We do ask that you inform us if your child becomes unwell - we will give you the name of the person in the study team to contact if this happens. If you think your child is unwell because of the treatment they are receiving, this can be discussed with your doctor and your child can be withdrawn from the study at any time. However, they should not stop taking their asthma treatment. If your child has any side effects (such as oral thrush) that may be related to the treatment, these will be monitored and recorded by the study team.

What are the possible disadvantages or risks of my child taking part?

If your child is allocated to the 'intervention group' then they will be changed to the combination red inhaler. Some children might not like having a different inhaler. The number of puffs of the combination red inhaler may be different to the number of puffs of their current blue inhaler. We will go through this carefully so that both you and your child understand the new plan, including when to seek help.

The combination inhaler contains an inhaled steroid and Long term use of inhaled steroids can result in unwanted side effects, therefore we will monitor closely how much extra steroid your child receives and whether they have any side effects (such as oral thrush) or if there is any effect on your child's growth. This is why we will be measuring their height at the beginning and end of the study. High doses of inhaled steroids can also reduce the body's own production of steroid hormones from the adrenal glands (also known as cortisol). For children in the intervention arm prescribed the combination inhaler for both maintenance and reliever treatment and children in the control arm prescribed higher doses of steroid (the brown inhaler) we will also measure the body's own steroid production. We will do this by collecting a saliva sample at the first and last visits and measuring the level of cortisol (steroid) in the saliva. If it is found to be very low your child will be referred for further testing in accordance with current clinical practice.

There is a sub-study, which is a mini study, that we are doing within this study. Some children will also be eligible for this sub-study. Children who choose to be in the sub-study will be given an electronic monitoring device for their inhaler so that we can work out exactly how much inhaled steroid they have received. This sub-study is optional and if you do not wish for your child to take part they do not have to.

For children who will be in the sub-study, you will have to download an app from the electronic monitoring device's website or app store (Adherium (NZ) Limited). Having the app will allow the study teams to understand your child's inhaler use. The downloaded data will not have any of your child's personal identifying information attached to it. The data from your child's inhaler use will be stored on the Adherium (NZ) Limited servers. The monitoring devices should be returned at the final visit.

For all study groups we will also be checking the children's prescriptions to check the amount of inhaled steroids they have been prescribed and to see the number of courses of oral steroids (such as prednisolone or dexamethasone) children are given for asthma attacks while they are enrolled in the study. The dose of these oral steroids is much higher than inhaled steroids, so we hope that the new combination inhaler will reduce the number of oral steroid courses that your child is prescribed for an asthma attack, as well as improving their day-to-day symptoms.

What are the advantages of my child taking part?

Children in both groups of the study will have access to the study team, who will make sure you and your child know how to take their inhalers, have an up-to-date Personal Asthma Action Plan and know when to seek help. We hope that those in the intervention group will find it easier having just one inhaler to use.

What will happen if I do not agree to my child taking part?

Your child's treatment will not be affected in any way if they do not take part. They will continue with their current asthma management, whether that is with their GP or at a hospital clinic.

Part 2 – Frequently Asked Questions

What if new information becomes available?

Sometimes during the course of a research study, new information becomes available about the treatment that is being studied. If this happens, your research doctor will tell you and your child about it and discuss with you whether you want your child to continue in the study. If you decide your child can continue in the study you will be asked to sign an updated consent form. It is also possible that on receiving new information your research doctor might consider it to be in your child's best interest to withdraw your child from the study.

Can I stop my child from being part of the study even if I initially agree?

Yes. You can decide to withdraw your child from the study at any time. This will not affect your child's treatment in any way and they will continue to receive their usual asthma care. If you do decide for your child to stop taking part in the study, we will ask whether you will allow us to use the information collected until that point in the study. If you do not want anything relating to your child to be included, we will destroy all information.

Can the study be stopped for other reasons?

Your child may be withdrawn from the treatment if the research doctor thinks that their health will be compromised due to any side effects or illness that develop while they are in the study. In this case your child will no longer take the treatment but if you agree, we will still use their information collected until that point.

An Ethics Committee has approved the study and a Trial Steering Committee is overseeing the study and may stop the study if there are any serious issues.

What if I lose capacity to consent at some point during the study?

Your child would be withdrawn from the study. Unidentifiable data already collected with your initial consent would be retained and used in the study. However, no further data would be collected or any other research procedures carried out on your child.

Will my child's details and information be confidential?

Yes. All of your child's personal details will be kept de-identifiable and confidential. Any results from the study will not allow your child to be identified in any way. Your child's GP will be informed of their participation in this study. We would also like to send some information to your child's school so that they understand about the new reliever inhaler and asthma plan.

What will happen to the samples taken during the study?

We are planning on taking saliva samples from some children as part of this study. All activities (storage, use and disposal) concerning the saliva samples will be carried out in accordance with the Human Tissue Act 2004. We will ask for 2 saliva samples taken in the morning (or earliest time of day possible) at the first in person visit and the last visit.

Will I get paid for participating?

You and your child will not receive any payment for your child taking part in the research but you are able to claim back expenses for your travel for face to face study visits.

What if something goes wrong?

Imperial College London holds insurance policies which apply to this study. If your child experiences harm or injury as a result of taking part in this study, you and your child will be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation. If your child is harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you and your child have been treated during the course of this study then you should immediately inform the Investigator at your hospital using the contact details below. The normal National Health Service complaints mechanisms are also available to you. If for any reason you are not satisfied with the response, you may contact the Research Governance and Integrity Team (RGIT).

Study Investigators Contact details

Study Investigator:
Study Nurse:
Day time Telephone:
Emergency Telephone:

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given a favourable opinion by NRES Committee Wales REC 5.

What happens when the research study stops?

After the study ends your child's asthma management and treatment decisions will be overseen by their usual caregiver.

What will happen to the results of the study?

The results will be presented at national and international medical conferences. They will also be published in a medical journal so that we can let all other doctors worldwide that are treating children with asthma know whether the new inhaler is better than the current inhalers we are using.

Yours and your child's confidentiality will be ensured at all times and you will not be identified in any publication. Only group information and no personal information will be presented. At the end of the study, the results of the study can be made available to you/your child and/or your GP should you wish.

Who is organising and funding the study?

The study is being organised by researchers at Imperial College London. The main Investigator of the study is Dr Louise Fleming. The study is funded by the National Institute for Health Research (Health technology Assessment programme) and sponsored by Imperial College London. The sponsors of this study will pay (name of hospital department or research fund) for including your child in this study.

Who has reviewed the study?

This study was given a favourable ethical opinion for conduct in the NHS (or private sector) by Wales REC 5.

Who can I contact for independent research information?

If you have any questions about your child being in a research study, you can contact the Trust's Patient Advice Liaison Service (PALS). They will give you advice about who you can talk to for independent advice.

Patient Advisory Liaison Service (PALS):

Nearest PALS office can be found on the NHS website

You can also ask your GP surgery, hospital or phone NHS111 for details of your nearest PALS

Part 3 - Participant Privacy Notice

Further information

Thank you in advance for considering your child's participation in this study. If you have any questions about this research, the study staff will be more than happy to answer them.

Imperial College London is the sponsor for this study based in the United Kingdom. We will be using information from your child and their medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your child's information and using it properly. Imperial College London will keep identifiable information about your child for:

- 10 years after the study has finished in relation to data subject consent forms.
- 10 years after the study has completed in relation to primary research data.

Further information on Imperial College London's retention periods may be found at https://www.imperial.ac.uk/media/imperial-college/administration-and-support-services/records-and-archives/public/RetentionSchedule.pdf.

A link to Imperial College London's data protection webpage may be found at https://www.imperial.ac.uk/admin-services/legal-services-office/data-protection/ but this is the notice most applicable to the information provided by participants and therefore takes precedence for all purposes described hereunder.

Your Rights

You/your child's usual statutory rights to access, change or move your child's information are limited, because of exceptions applicable to some types of research, and also because we need to manage your child's information in specific, lawful ways in order for the research to be reliable and accurateyou're your child withdraws from the study, we will keep the information about your child that we have already obtained. To safeguard your child's rights, we will use the minimum personally-identifiable information possible.

Legal Basis

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree for your child to take part in a research study, we will use your child's data in the ways needed to conduct and analyse the research study. Our legal basis for using your child's information under the General Data Protection Regulation (GDPR) and the Data Protection Act 2018, is as follows:

• Imperial College London - "performance of a task carried out in the public interest" (Article 6(1)(e) in the GDPR); Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research.

- Where special category personal information is involved (most commonly health data, biometric data and genetic data, racial and ethnic data etc.), Imperial College London relies

on "scientific or historical research purposes or statistical purposes (Article 9(2)(j) in accordance with Article 89(1)in the GDPR)".

International Transfers of Information

There may be a requirement to transfer information to countries outside the United Kingdom (for example, to a research partner, either within the European Economic Area (EEA) or to other countries outside the EEA). Where this information contains your child's personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a UK adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient research partner that incorporates UK approved standard contractual clauses or utilise another transfer mechanism that safeguards how your child's personal data is processed.

Sharing your information with others

We will only share your child's personal data with certain third parties for the purposes referred to in this participant information sheet and by relying on the legal basis for processing your data as set out above.

- Other Imperial College London employees (including staff involved directly with the research study or as part of certain secondary activities which may include support functions, internal audits, ensuring accuracy of contact details etc.), Imperial College London agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third party service providers are required to enter into data processing agreements with us. We only permit them to process your child's personal data for specified purposes and in accordance with our policies.

Potential use of the study data for future research

When you agree for your child to take part in a research study, the information collected either as part of the study or in preparation for the study (such as contact details) may, if you both consent, be provided to researchers running other research studies at Imperial College London and in other organisations which may be universities or organisations involved in research in this country or abroad. Your child's information will only be used to conduct research in accordance with legislation including the GDPR and the UK Policy Framework for Health and Social Care Research.

This information will not identify your child and will not be combined with other information in a way that could identify your child, used against your child or used to make decisions about your child.

Commercialisation

Data from the study may also be provided to organisations not named in this participant information sheet, e.g. commercial organisations or non-commercial organisations for the purposes of undertaking the current study, future research studies or commercial purposes such as development by a company of a new test, product or treatment. We will ensure your child's name and any identifying details will NOT be given to these third parties, instead your child will be identified by a unique study number with any data analysis having the potential to generate 'personal data'.

Aggregated (combined) or anonymised data sets (all identifying information is removed) may also be

created using your child's data (in a way which does not identify your child individually) and be used for such research or commercial purposes where the purposes align to relevant legislation (including the GDPR) and wider aims of the study. Your child's data will not be shared with a commercial organisation for marketing purposes.

What are your choices about how your information is used?
You can stop your child being part of the study at any time, without giving a reason, but we will keep information about your child that we already have. Because some research using your child's data may have already taken place and this cannot be undone.

- **OPTION if follow up data will be collected after withdrawal:** If you choose for your child to stop taking part in the study, we would like to continue collecting information about your child's health from central NHS records/ your GP. If you do not want this to happen, tell us and we will stop. This will not affect any healthcare or support your child may be receiving separately.
- We need to manage your child's records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about your child. If this could affect the wider study or the accuracy of data collected.
- **OPTION if data will be used for future research:** If you agree for your child to take part in this study, you will have the option for your child to take part in future research using your data saved from this study.

Where can you find out more about how your information is used

You can find out more about how we use your child's information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by sending an email to [**email**], or
- by ringing us on [**phone number**].
- **OPTION** Link to Research website – if there is one

Complaint

If you wish to raise a complaint about how we have handled your child's personal data, please contact the research team first by sending an email to [**email**], or by ringing us on [**phone number**].

Following our response, if you are not satisfied please contact Imperial College London's Data Protection Officer via email at dpo@imperial.ac.uk, via telephone on 020 7594 3502 and/or via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you remain unsatisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO)- via www.ico.org.uk. Please note the ICO does recommend that you seek to resolve matters with the data controller (us) first before involving them.

Contact for Further Information

Please contact the Chief Investigator of the study, Dr Louise Fleming on the following 24-hour contact details:

Name: Dr Louise Fleming
Telephone: 079 177 73771
Email (if applicable): L.Fleming@rbht.nhs.uk

A copy of this patient information sheet and the signed consent form will be given to you for your records.
Thank you for taking part in our study!

Glossary

Randomisation

- Randomisation means that a group of people are split into two groups at random; one group is kept on their normal intervention (blue inhaler) and the other is given a different intervention (red inhaler).
- For this trial, we will measure how each group is doing and see if one group has achieved its supposed outcome any better.

Inflammation

- Your body's reaction to something irritating, swelling.

Intervention group

- A group of participants is split in two groups; one half gets one study treatment we are testing for, whilst the other half stays on their regular treatment.

Control group

A group of participants is split in two groups; this half does not get the study treatment, they will have usual care or usual medicines to provide a comparison for the other treatment or medicine.