The APEX Study

To better understand asthma attacks

Study information leaflet
Everything you need to know about this pioneering asthma study.

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Background to the study

Asthma is a common lung condition affecting millions of people across the globe. With your help, we can try to understand more about the triggers of asthma attacks and how to prevent the early symptoms of asthma attacks from developing into a serious event. It is the Nottingham Asthma Centre's number one priority to turn this research into potentially lifesaving treatments for the future.

Join our research study

We would like to invite you to take part in this vital study.

- Before you decide, we would like you to understand why the research that is being done is so important and what it would involve for you.
- Please be assured that one of our team will go through this information sheet with you and answer any questions you may have.
- Talk to others about the study if you wish and please ask us if there is anything that is not clear, or if you would like more information.

A big hello from the APEX research team based in Nottingham!

What is the purpose of the study?

1. Key facts about asthma attacks

- Asthma attacks lead to difficulty in breathing, which can be very frightening. Some can be treated at home with extra puffs of inhalers, but some require steroid tablets and very severe attacks can require hospital treatment.

2. The reason for doing this research

- Lots of things can cause an asthma attack and we believe different triggers may lead to different types of attacks. If we can confirm this, it may be possible to find new ways to treat asthma attacks and reduce the use of steroid tablets which may have undesirable side effects.

3. The aims of this study

- We want to study a large group of people with asthma of any severity.
- We will perform some tests when your asthma is stable and then try and repeat them if you have an attack.
- WE WILL NOT CHANGE ANY OF YOUR CURRENT TREATMENT AND WE ARE NOT TESTING ANY NEW TREATMENTS ON YOU IN THIS STUDY.

4. This will

- Help us to understand more about what causes asthma attacks and whether people have different types of attacks.

Why have I been invited?

You are being invited to take part because we believe you have asthma and you have had an asthma attack in the last two years.

Do I have to take part?

It is completely up to you to decide whether you want to take part and your decision will not affect your care in any way. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form.

If you do decide to take part, you will be joining ground-breaking research into understanding asthma attacks and the information we learn from your participation could help us to discover new, potentially lifesaving treatments for asthma patients in the future. It may also help you to better understand and cope with your asthma. Please be assured that you would be free to withdraw at any time and without giving a reason. This would not affect your legal rights.

What happens if I join the study?

1. General information

- If you decide you would like to take part in this study, we will ask you to attend for several study visits and to have tests and procedures performed.

- The total length of the study is four years and we will be recruiting participants for three years. You will take part for up to three years or up to when the study ends, whichever is the soonest.

- All the visits will take place at the Nottingham Asthma Centre, which is part of the Nottingham Respiratory Research Unit, located at Nottingham City Hospital. We will try to arrange the visits at a time and day that is convenient for you and free parking is available at the unit. You should take all your medications as usual, including your inhalers, on the day of each visit and during your involvement in the study.

An overview of the study

If you agree to take part in the study, we will ask you to:

- Attend an initial visit (Baseline) which will last about 2.5 hours.
- Attend a visit at the end of each year you are in the study (Annual Visit), which will last about 2 hours.
- If, during the study, your asthma gets worse or you start to develop an asthma attack, we would like to try and arrange another visit (attack visit) as soon as possible, to assess how bad the attack is and provide you with any additional treatment we think you need. Hopefully this may avoid you having to make an appointment with your GP.
- With your consent, the research team will also send you a monthly reminder by text, from study specific mobile phones, asking you to contact them if you feel your asthma symptoms are worsening.
- Finally, we would also like to keep in touch with you every 3 months to provide you with study updates.

The visit table below summarises the study and the procedures which are involved at each visit.

Activity	Baseline visit	Annual visit	Asthma Attack visit
Informed consent	x		
Medical history and medications	x	x	x
Inhaler technique check	x	x	x
Height/weight	x	x	x
Blood pressure	x	x	x
Questionnaires	x	x	x
Lung function tests	x	x	x
Sputum test	x	x	x
Blood tests	x	x	x
Urine tests	x	x	x
Nasal samples and throat swab	x	x	x
Skin prick (allergy) test	x		
Device training	x		

The asthma attack visit

If you feel that your asthma is getting worse and you would normally ask a healthcare professional (for example, your doctor, nurse or pharmacist) for help, we will ask you to contact the research team. If possible, we will arrange for you to come to the Clinical Trials Unit for an assessment by a unit NHS doctor, at Nottingham City Hospital.

- This assessment will last about 40 minutes and is shaded in grey on the visit table above.
- After the assessment, there will then be 3 possible outcomes:

1. **The doctor thinks that you are definitely having an asthma attack**.

   You will be asked if you can complete Stage 2 of the visit immediately (shaded in blue in the table above) and afterwards, you will be given the appropriate treatment. This will be dispensed by the Nottingham City Hospital Out-Patients Pharmacy on the same day and we will contact you on Day 7 to see how you are.

2. **The doctor thinks that you may be in the early stages of an asthma attack or have a possible viral illness.**
   You will be asked if you can complete Stage 2 of the visit immediately. You will be given a prescription for the appropriate treatment, which can be dispensed by any community pharmacy, in case you get worse over the next few days. We will ask you to contact us if you have any concerns or if you feel you need to start the attack treatment. You may be asked if you can come

back to the unit to repeat Stage 2. If however, you do not get worse, we will contact you on Day 7 to check how you are.

3. **The doctor does not think you are having an asthma attack**.

   You will not need to complete Stage 2 of the visit. We will ask you to contact us if you have any concerns or you feel your symptoms are worsening. If this happens, we may ask you if you can attend the Unit for a repeat assessment. If we do not hear from you, we will contact you on Day 7.

Whatever the outcome of the Asthma Attack Visit, we hope that you will remain in the study because we want to see if people with more than one attack, have the same or different types of attacks.
You will be invited to your next annual review and we will ask you to contact us again, the next time you feel your asthma is getting worse.

IMPORTANT

If you feel you require urgent assessment by a healthcare professional, you should follow standard out-of-hours clinical practice, to ensure your safety. If you have an asthma attack and receive treatment elsewhere, then please let us know as soon as you are able to.
Please note that you will be able to contact us during office hours, which are Monday to Friday, from 9am until 5pm.

Tests and procedures

A member of the research team will be with you while you are doing any of the tests described below. We will ensure you are given full instructions on how to perform them. If you have any questions about any of these tests then please do not hesitate to ask. Any of the tests or procedures will be stopped immediately if you find them too unpleasant or develop significant side effects.

Medical History and Medications

At each visit, we will review your medical history (including respiratory and non-respiratory history, smoking and allergies) with you. We will also ask you about any treatments you are taking or have taken for asthma or other conditions.

Respiratory Questionnaires

You will be asked to complete 2 short questionnaires. These look at how asthma affects your life, what medications you use and how you use them.

Lung Function Tests

Spirometry

This is a blowing test, which is used to measure your lung function (the size of your lungs and how quickly you can empty them). Your height and weight will be recorded and then you will be asked to take a seat. You will remain seated for the test. You will be asked to take a deep breath in and then blow out as hard and fast as you can, into a mouthpiece until your lungs are empty. You may be asked to put a clip on your nose to make sure that no air escapes from your nose.

Occasionally some people can feel light-headed or faint whilst performing spirometry. It may also cause you to cough or make your chest feel tight.

Exhaled Nitric Oxide (FeNO)

Nitric Oxide is a gas present in everyone's breath. This is a blowing test which measures the amount of inflammation in the airways (breathing tubes), by measuring the concentration of exhaled nitric oxide. It involves breathing into a mouthpiece, which is connected to an analyser, for a few seconds.

FOT

This test is used to measure lung movement during normal breathing. You will be asked to breathe normally, though a mouthpiece into a tube, during which time measurements are made. This will be repeated 3 times.

Sputum Samples

Sputum is the mucus substance that is produced from the lungs and airways (breathing tubes) when a person coughs or spits. We will ask you to provide a sputum sample at every visit you attend by inhaling a salty solution through a machine called a nebuliser. This creates an aerosol of the salty water, which often helps people to produce a sputum sample. This process is usually well tolerated, however, you will experience a salty taste in your mouth and may feel nauseous or have a sore throat. The salty solution may also irritate the airways, causing chest tightness, wheeze, cough and shortness of breath, so you will be monitored closely by trained staff, before, during and after the test, as described on the next page. If, for any reason, it is not possible to use the nebuliser, we will ask you to cough some sputum into a pot

- We will measure your lung function on a spirometer.
- You will be given a dose of Salbutamol (blue inhaler), using an inhaler and spacer, to open up your airways. We will let this work for 15-20 minutes. This can sometimes make you feel a little shaky and increase your heart rate.
- We will re-measure your lung function.
- We will ask you to inhale the salty solution for 5 minutes. We may ask you to do this up to 3 times at each visit.
- After each inhalation we will ask you to blow your nose and rinse out your mouth with some water. You will then be asked to cough to see if you can produce a sputum sample.
- We will check your lung function, using the spirometer, after each inhalation period and ask you to report any symptoms you may have. Further Salbutamol can be given for relief if necessary.

Skin Prick Test

This test is used to assess how allergic you are to up to 10 different substances, such as grass or pollen, which will be dissolved in liquid to make a solution. A small drop of the solution is placed on the forearm, which is scratched slightly with a needle, to see whether a reaction such as a red itchy bump occurs.
A skin prick test may cause mild discomfort from the scratch of the needle. In extremely rare cases, you may have a whole body allergic reaction that might cause a rash, swelling of the tongue or skin, shortness of breath or a fall in blood pressure. Emergency care is always available if this rare reaction occurs.
This test will usually be performed once during the study, at the Baseline Visit. However, if this is not possible for any reason, we can do this at any subsequent visit.

Blood Tests

You will be asked to provide up to 50mls (about 10 teaspoons) of blood at each visit. This will include samples for routine clinical screening and for future research into asthma and lung diseases.
Taking blood may cause pain where the needle is inserted and there is a small risk of bruising and infection at the needle site. Some people experience dizziness or fainting during a blood test, so it will be done with you sitting down.

Urine Sample

We will ask you to provide a urine sample of approximately 20mls. This will be stored in a freezer and we will look at inflammation molecules related to asthma.

Nasal Samples

To detect viruses and inflammation, we will take a sample of secretions from your nose. Firstly, we will insert a small piece of paper up one nostril to abosrob any mucus. Following this we will then squirt salty water into your nose and then immediately draw the fluid back into a syringe.

If you agree, we will also take cell samples from your nose for genetic analysis. These will be obtained by using a small brush. This will be optional and you will be asked to consent specifically to this.

Throat Swab

This will also be taken to detect viruses. A sterile cotton swab will be rubbed across the back of your throat for a few seconds. This may make you gag slightly, but it should not be painful.

Study Devices

Albus Home RD (Passive Bedside Monitoring Device)

Albus Home RD is an automated non-contact monitoring device that is plugged into the mains and placed by your bedside at home. Each night it monitors symptoms and signs relevant to asthma using different sensors. A wireless motion sensor (similar to those used in automatic lights) monitors breathing rate, a microphone records sounds of coughing and an environmental sensor measures temperature and humidity. The microphone captures all room sounds, but an automatic computer program identifies any recorded speech and scrambles it so it cannot be heard or identified by the research team. The audio recording function of the device can also be turned off or paused at any time.

The device uses minimal electricity (<1p per day) and is safe for long-term home use. All data is stored on a secure USB stick which we will occasionally ask you to bring with you to study visits for the data to be downloaded. If you agree, the device may be connected to your home wireless internet (WiFi) to allow the company (Albus Health) to check that the device is working properly, but the company would have no access to the data stored on the device. If you do have home internet or do not wish it to be used, pre-paid internet dongles, which connect to the device, can be provided.

If you use this device during the study, training on its use will be provided. Any technical support you require, will be provided by the research team. The devices will need to be returned to the research team at the end of your involvement with the study.

Expenses and payment

Unfortunately you will not be paid to take part in this study, but we can cover any travelling expenses or arrange a taxi if necessary. Please note that the costs of any prescribed treatment arising from attendance at study visits, will be met by yourself, according to your existing circumstances. For example, you may usually pay for prescriptions, have a pre-payment certificate or qualify for free prescriptions.

What are the benefits of taking part?

We cannot promise the study will help you, but we hope the information we obtain from this study will help us to understand more about the nature of asthma attacks, which could lead to the development of more targeted treatments. We also hope that you may gain a better personal understanding of your asthma and asthma attacks and that by seeing us we can avoid you having to make an appointment with your GP.

What are the risks?

As with all tests and procedures, some people experience side effects, some of which are detailed in the “Tests and Procedures” section. However, we believe the risks of this study are very small.

What happens when the study ends?

The study will end 4 years after the first participant is entered. The day-to-day care of your asthma will remain with your GP throughout your involvement in the study and with your permission, we will provide them with updates as detailed on Page 12.

What happens if there’s a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers, who will do their best to answer your questions. The researchers’ contact details are given at the end of this information sheet. If you remain unhappy and wish to complain formally, you can do this by contacting the Patients Advice and Liaison Service (PALS) office.

PALS Telephone: 0800 1830204 (free from a landline) or 0115 9249924 Extension 65412.

Email: pals@nuh.nhs.uk

Post: NUH NHS Trust, c/o PALS, Freepost, NEA 14614, Nottingham NG7 1BR or via www.pals.nhs.uk

In the event that something does go wrong and you are harmed during the research and this is due to

someone's negligence, then you may have grounds for a legal action for compensation against the University of Nottingham, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

Will my taking part in the study be kept confidential?

We will follow ethical and legal practice and all information about you will be handled in confidence. If you join the study, we will use information collected from you (and your medical records) during the course of the research. This information will be kept strictly confidential, stored in a secure and locked office, and on a password protected database at the University of Nottingham. Under UK Data Protection laws the University is the data controller (legally responsible for the data security) and the Chief Investigator of this study (named in this information sheet) is the Data Custodian (manages access to the data). This means we are responsible for looking after your information and using it properly. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways to comply with certain laws and for the research to be reliable and accurate. To safeguard your rights, we will use the minimum personally identifiable information possible.

You can find out more about how we use your information and to read our privacy notice at:

https://www.nottingham.ac.uk/utilities/privacy.aspx.

The data collected for the study will be looked at and stored by authorised persons from the University of Nottingham who are organising the research. They may also be looked at by authorised people from regulatory organisations to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

Information about you which leaves the research site will have your name and address removed and a unique code will be used, so that you cannot be recognised from it. However, sometimes we need to ensure that we can recognise you, to link the research data with your medical records, so in these instances, we will need to know your name and date of birth.

If you use the Albus Home RD bedside monitoring device during the study, to monitor the signs and symptoms of asthma, your speech will be scrambled by a computer so it will not be understood. All other data (breathing rate, coughing, room temperature and humidity will be transferred from a secure USB stick to Albus Health via secure servers, for analysis. All the data will be anonymised and identity code numbers, rather than your personal details will be used.

Your contact information will be kept by the University of Nottingham for one year after the end of the study, so that we are able to contact you about the findings of the study and possible follow up studies (unless you advise us that you do not wish to be contacted). This information will be kept separately from the research data and only those who need to, will have access to it. If you consent to the collection of your home and work addresses with postcodes, for the analysis of your exposure to pollen and air pollutants, this will be kept for two years after the end of the study. All other data (research data), will be kept securely for seven years. After this time, your data will be disposed of securely. During this time all

precautions will be taken by all those involved, to maintain your confidentiality. Only members of the research team given permission by the data custodian will have access to your personal data.

In accordance with the University of Nottingham's, the Government's and our funder's policies, we may share our research data with researchers in other universities and organisations, including those in other countries, for research in health and social care. Sharing research data is important to allow peer scrutiny, re-use (and therefore avoiding duplication of research) and to understand the bigger picture in particular areas of research. Data sharing in this way will be anonymised (so that you cannot be identified).

Although what you say during the study visits is confidential, should you disclose anything to us which we feel puts you or anyone else at any risk, we may feel it necessary to report this to the appropriate persons.

What happens if I don't want to carry on with the study?

Your participation is voluntary and you are free to withdraw at any time, without giving any reason, and without your legal or medical treatment rights being affected. If you withdraw, we will no longer collect any information about you or from you, but we will keep the information about you that we have already obtained, as we are not allowed to tamper with study records and this information may have already been used in some analyses and may still be used in the final study analyses. To safeguard your rights, we will use the minimum personally identifiable information possible.

What involvement will my General Practitioner (GP) have?

With your permission, your GP will be notified that you are taking part in this study.
If you attend the Asthma Attack visit, we will send a letter to your GP, informing them of the outcome of the visit. We will also, with your permission, notify you and your GP of any findings that are of clinical concern. This will be discussed with you in the first instance. Please note that the results of the genetic analysis will not be given to your GP.

What happens to the samples I give?

We would also like to seek your consent, so that samples may be stored and used in possible future research (please indicate you agree to this on the consent form). These samples will be stored with a code unique to you and securely at the University of Nottingham, under the University's Human Tissue Research Licence (No. 12265).

Some of these future studies may be carried out by researchers other the current team of Professor Tim Harrison and Dr Matthew Martin, who ran the first study, including researchers working for commercial companies. Any samples or data used will be anonymised and you will not be identified in any way. If you do not agree to this, any remaining samples will be disposed of in accordance with the Human Tissue Authority's codes of practice.

Will any genetic tests be done?

Yes. The samples we collect using the nasal brushes and whole blood will undergo genetic analysis. Please note that this part of the study is optional. If you agree to these samples being collected and analysed, you will be asked to sign an optional clause on the consent form. Please note that the results of this analysis will not be given to you.

What happens to the results of the research study?

We anticipate that the results of this study will be published in scientific journals and will be presented at scientific meetings and conferences. Copies of these can be sent to you on request. We may also publish a summary of the research on relevant websites and social media and in our newsletters. You will not be identified in any reports or publications as all data used is anonymous.

Who is organising and funding of research?

This research is being organised by the University of Nottingham and is being funded by AstraZeneca.

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 checked and approved by the Health and Social Care Research Ethics Committee A (HSC REC A).

Who can I contact for more information?

For further information please contact the APEX Team

Email Karen.Shaw@nottingham.ac.uk
Rob.Needham@nottingham.ac.uk

Telephone 07967327345 or 07970224153

We look forward to hearing from you.

The Nottingham Asthma Centre Team.