

PAPA Trial - Parent/Carer Information Sheet



Preventing childhood Asthma using Prophylactic house
dust mite Allergen immunotherapy

You are being invited to consider including your child in the PAPA trial. For more information please see our website: <https://papastudy.uk/>

This study is looking at whether giving babies and young children a daily dissolvable tablet containing a tiny amount of house dust mite protein could help prevent asthma.

Asthma is a common condition in children and currently there is no way to prevent it.

This study
aims to

434

babies
across the
UK

Before you decide, it is important for you to understand why the research is being done and what it will involve for your child. Please take time to read the following information carefully and discuss it with others if you wish.

Part 1 – Why is this trial being done? (page 2): This section tells you about the purpose of this trial and what will happen if your child takes part.

Part 2 – Frequently Asked Questions (page 13): This section gives you more detailed information about the conduct of the trial.

Part 3 – Contact details (page 17): This page includes contact details for the research team and out of hours emergency contacts details.

Part 4 – Glossary (page 18): This section explains some of the terms and words used in this document.

If anything is not clear and/or you require more information before you decide whether or not to take part in the study, please contact a member of the study team (details at end of

information sheet). Thank you for taking the time to consider your child taking part in our trial. If you are happy for your child to participate you will be asked to sign a consent form.

PART 1 - Why is this trial being done?

What is asthma and why is it a problem?

- Asthma is a disease which causes wheezing, coughing and/or tightening of the air passages which can be relieved with medication.
- Asthma is one of the most common long-term illnesses in children - affects more than **1 million children** in the UK. There is no cure but it may be possible to prevent asthma.
- Most children in the UK with asthma are allergic to house dust mite (HDM).

What is the purpose of the trial?

- We know that if babies are given peanut butter or egg to eat when they are young, they are less likely to develop allergy to peanut or egg.
- We want to test whether using a similar approach with HDM might stop babies developing allergy to HDM and asthma.

Previous research

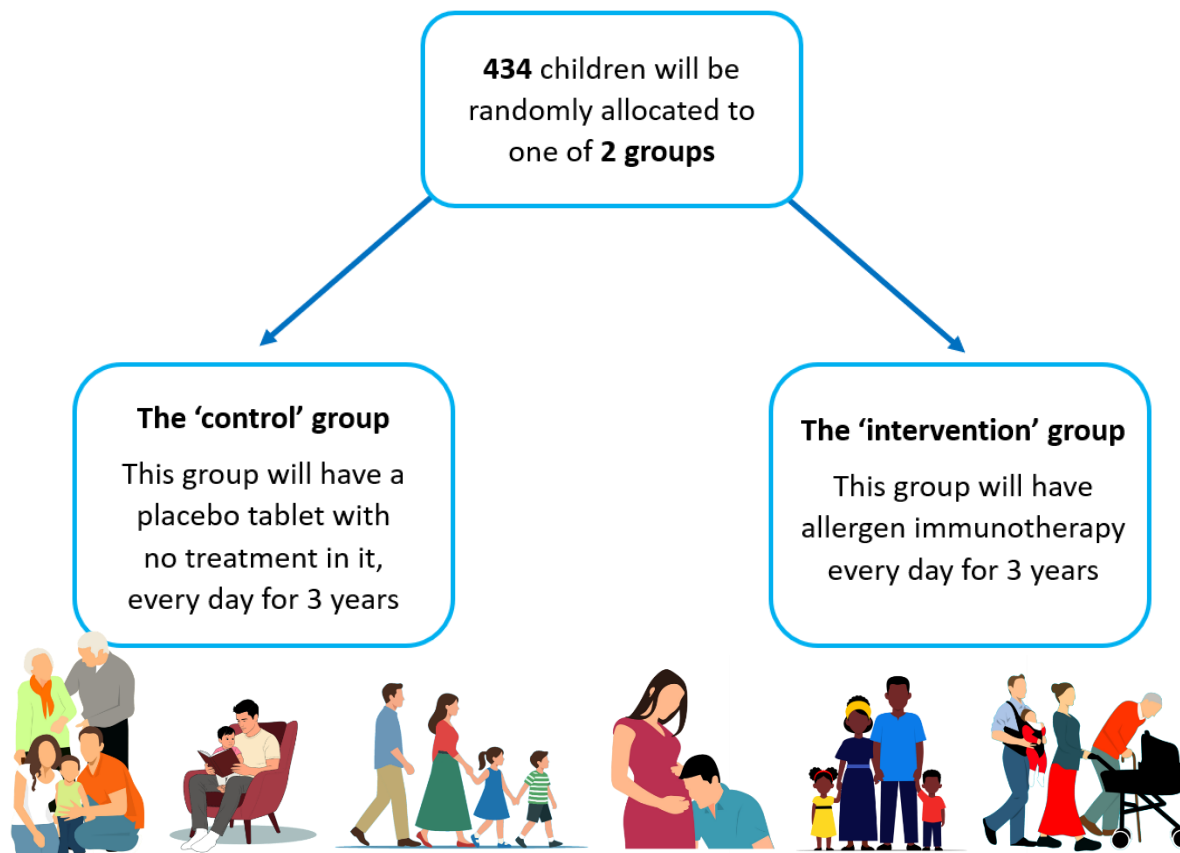
We have completed a **small trial with 111 infants less than 1 year old** which gave an indication that this treatment might prevent asthma. Also, importantly, the new treatment **did not cause any side effects** in this small group. The PAPA trial aims to find out whether asthma can be prevented through a simple daily tablet of HDM protein started in the first year of life, before HDM allergy has developed. This research study involves several NHS hospitals and a range of families whose babies are thought to be at risk of developing asthma.

Why might my child be suitable for this study?

Your child:

- Is between 5 and 12 months old.
- Is at higher chance of developing asthma. This is because there is a family history or your child has eczema.

- This trial is **randomised, double blind** trial
- This means **neither you or your doctor will know what treatment your child is getting.**
- This helps keep the results fair and unbiased.
- One group will receive Acarizax®, which is a small dissolvable tablet containing a tiny amount of house dust mite protein, and the other will receive a placebo, which looks the same but has no active ingredient. Your child has a 50/50 chance of being in either group, and you cannot choose the group.
- All children will have **the same number of visits.** The same checks will be done at each visit.



Do I have to take part?

- No, it is your choice.
- 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 decide to take part, you are still free to withdraw at any time and without giving a reason.
- A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care your child receives.

What will happen if we take part?

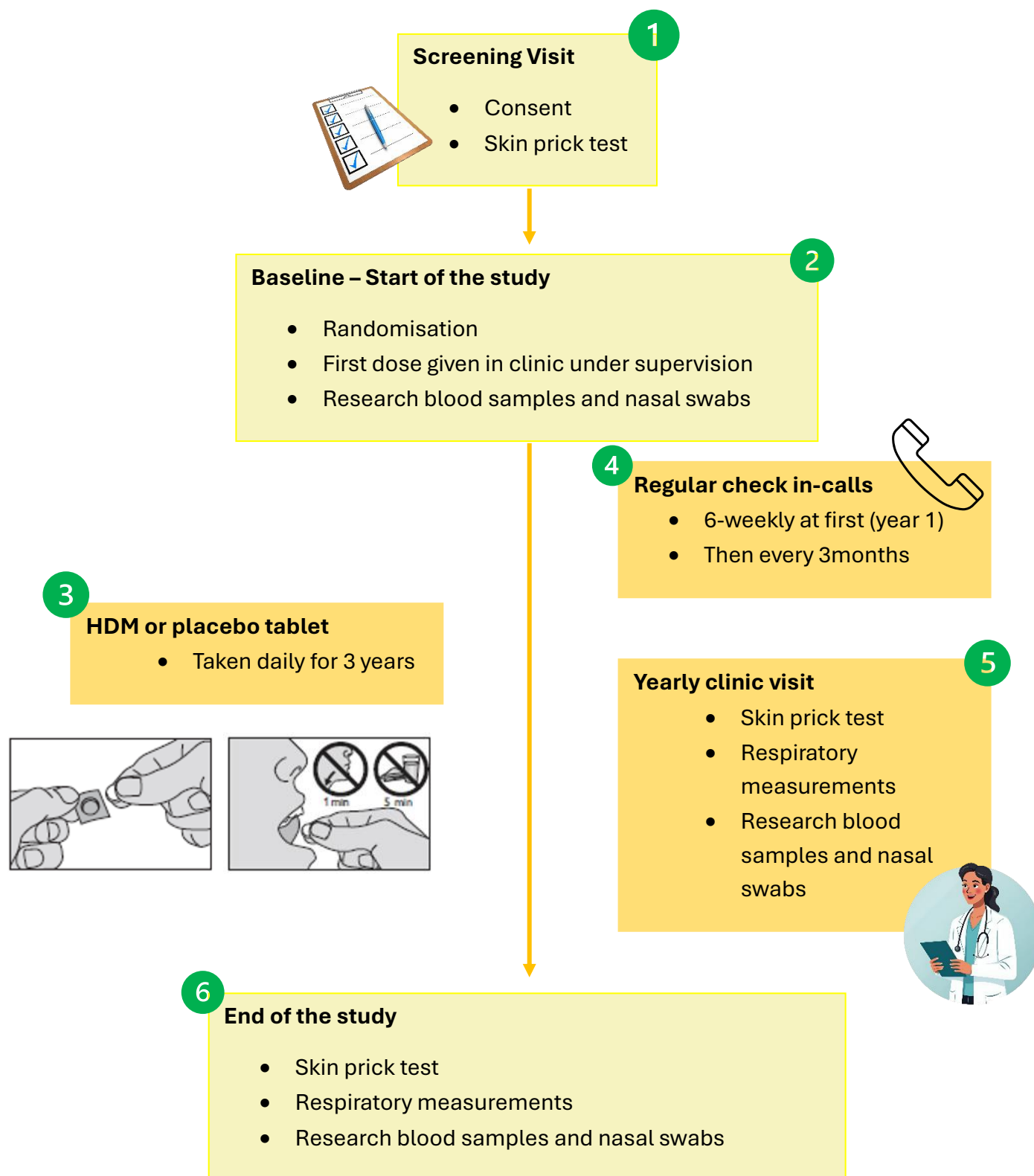
Your child will be in the research for about 3 years. There are no additional visits after this time.

- We will ask that your child takes the trial medication for three years to give the best chance of success.

Before any trial procedures are completed you will be asked to sign a consent form and a copy will be given to you to keep.



On the next page is a schedule of the visits and appointments your child will need to attend with each visit explained in more detail.



Screening Visit (completed at your local hospital, will last around 1 hour)

1

The screening visit will include:

- review your child's medical history of asthma and allergies.
- If your child has not been seen in the clinic, we may ask for permission to contact your child's doctor to get a copy of any medical records about their allergies.

At the visit we will do the following:

1. **Skin Prick Test:** We will test your child for allergies to 9 things (grass pollen mix, tree pollen mix, dog, cat, house dust mite (2 kinds), cow's milk, egg, peanut). We do this on both arms by putting drops on the skin and lightly scratching the skin. This takes about 20 minutes.

Baseline Visit (completed at your local hospital, will last around 2 hours)

2

You will be invited to a baseline visit, which may be combined with the first check-up if possible.

Your child will be placed into 1 of 2 groups by chance. To keep the study fair, neither you nor the research doctor will know which group your child is in until the study ends, unless there is an emergency and this information is needed for your child's safety. After the study finishes, expected in **2031**, you can find out which treatment group your child was in.

At the baseline visit we will do the following:

1. **Questionnaires:** We will ask about your child's allergies, asthma, diet and environment. These can be completed online or on paper.
2. **Measurements:** Record your child's height, weight, heart rate and blood pressure.
3. **Physical Examination:** Check for wheezing or itchy skin, including assessment of any atopic dermatitis if needed.
4. **Review of symptoms and medications:** Ask about any symptoms, confirm current medicines, and review medical records for anything relevant to the trial.
5. **Blood sample:** Take up to 15 ml of blood for research to better understand how this treatment might work in preventing asthma and further to investigate into other ways asthma can be prevented. At some hospitals, an **extra optional sample of up to 10 ml** may also be collected for additional research.

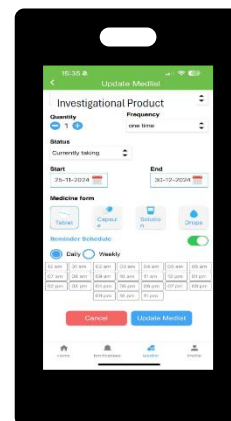
- As your child is young we may only be able to collect a smaller amount. This sample will be used to assess what type of allergic and protective antibodies are present in your child.
 - **The extra sample is optional** and if you do not agree for your child to take part this will not affect your child taking part in the rest of the trial. This additional sample will be used to see how immune cells react to house dust mite allergen.
- 6. Nasal swab:** Take a sample from your child's nose to help understand responses to the intervention.
 - 7. First Dose:** The first dose (Acarizax® HDM/placebo tablets) will be **given at the baseline visit**, followed by 60 minutes of observation and checks of heart rate, blood pressure and breathing. This is to ensure your child does not have any unexpected reactions to the trial medication and is in the presence of medically trained staff if anything was to happen.
 - 8. Follow up after the baseline visit:** A research nurse will contact you the next day, after 1 week, and after 2 weeks to check for side effects. If needed, your child will be seen at the clinic.

Treatment Phase with trial medication (3 years)

3

Your child will take trial medication, Acarizax® or placebo, every day for 3 years, with a mix of phone calls and clinic visits during this time.

The **PAPA app** on your smartphone or tablet will help you remember daily doses, takes less than a minute to use, and uses only your child's unique ID number. You can also use it to report concerns to the research team. If you do not have a smartphone or tablet, or if you have problems with the app, you can use a paper diary instead, which should be posted to the research team in pre-paid envelopes ahead of each phone call.



Phone contact

4

We will keep in touch to see how your child is doing and answer any questions or concerns. These calls will last about **30 minutes** and will take place **every 6 weeks in Year 1**, and **3 times a year in Years 2 and 3**.

During these calls, we will ask you to complete the Allergy and Environment questionnaire to record any changes and review your child's trial medication, any new symptoms, and any new medicines using the data in the PAPA app.

Annual in-person visits (completed at the hospital, will last around 1.5 hours)

5

In addition to the research nurse phone calls, you will be asked to attend **1 clinic visit each year for 3 years**. You may also need to come to the hospital approximately once between annual visits to pick up more trial medication, if needed.

At the visit we will do the following:

1. **Allergy and Environment questionnaire**
2. **Review of symptoms and medications**
3. **Height, weight, blood pressure measurements & Physical Examination**
4. **Allergy Skin Testing**
5. **Nasal Swab**

At the final visit (year 3, aged 3½ to 4 years) only we will also:

6

1. **Blood Sample:** about 1 tablespoon (max.15 ml) of blood and an **optional 10ml** if this was collected at the baseline visit.
2. **Lung Function Test:** Your child will breathe normally through a tube for about 30 seconds while airflow in the lungs is measured. This may be repeated and takes about 20 minutes.
3. **Peak Flow Test:** Your child will blow hard into a handheld device to measure how fast they can breathe out. This takes about 5 minutes.
4. **Exhaled Nitric Oxide Measurement:** Your child will blow slowly into a machine to measure nitric oxide in their breath, which can show airway swelling linked to asthma. This only takes a few minutes.

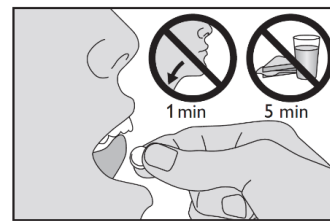
If there is any indication that your child may have developed sensitisation e.g. if they had a reproducible rash or swelling following administration of the tablet, they will be seen at the hospital for an additional visit.

Will I get paid for my child participating?

- You will not receive any payment for your child taking part in the research however we do offer a gift for your time of £15 per visit to the hospital (up to 5 visits, £75 maximum).
- You may claim back expenses for your travel for the study visits up to a maximum of £250.
- You will be required to share receipts or travel distance with your hospital to claim expenses.
- It may also be necessary to share your bank details with your hospital in order to process payments. Your research nurse will explain this to you.

What do I have to do?

- You will receive **detailed instructions** on how to give the tablets including **training and practical demonstration**
- If possible, swallowing should be avoided for 1 minute to minimise side effects.
- Food and drink should not be taken for 5 minutes after intake of the tablet.



What is the treatment or intervention that is being tested?

- House Dust Mite protein or placebo - placebo tablets are identical to the active tablet but contain no active ingredients.
- This is given in a small dissolvable tablet placed under the tongue.
- The tablets contain gelatine (from fish source). If you have any concerns, please speak with your research team.
- No need to stop eating any foods, taking any medications or change their lifestyle.
- You will be given a card with details of the trial. You should carry it at all times. You could take a photo on your phone to help with this.

What are the alternatives?

1. Getting no treatment to prevent your child developing asthma.
2. Getting standard treatment for your child if they do go on to develop asthma - Currently there is no medication available to stop asthma symptoms from getting worse as your child grows older.

Your child does not have to take part in this trial, it is **completely voluntary**. You have the right to decline your child's participation in the trial for any reason and this **will not affect the quality of your child's care or treatment**.

What are the side effects?

HDM is safe for both children and adults, with only a **few mild side effects**, when used to treat allergies like asthma and rhinitis caused by HDM in people who have encountered HDM before (“are sensitised”).

We plan to give HDM allergen to infants who are not known to be sensitised and hence the risk of adverse effects is very low.

The safety of the HDM tablet has been tested in **21 completed trials** with people of all ages, including children, with more than **7500 participants**.

We completed a small trial with **111 infants less than 1 years old using HDM liquid extract and saw no differences in the amount or type of side effects** between the 2 groups (active and dummy treatment).

There is a **very small chance** your child will experience an **allergic reaction**. Even in those who are sensitised to HDM, severe reactions are rare (less than 0.1%). As your child is not sensitised, the risk of any reaction is even less. **Your child will be observed closely for 60 minutes** after the first administration of HDM and the team is skilled on treating an allergic reaction if that happens.

Rarely (in less than 0.1%), those undergoing allergen immunotherapy experience a condition called Eosinophilic Esophagitis (EoE). In EoE oesophagus (the tube that carries food to the stomach) becomes inflamed. Although rare, it is more common in people with allergies and can be triggered by sensitisation to certain foods or airborne allergens. While EoE can be uncomfortable, it’s usually not dangerous and can be improved by stopping the trial treatment and using the right treatments. If this happens, **the trial treatment can be stopped for up to 14 days and your child can then restart the trial**.

If you experience any side effects and are concerned, please contact your trial team. Their contact details can be found at the end of this information sheet. Alternatively, you can contact the 24 hour PAPA helpline.



The side effects that have been reported, in those who are allergic to HDM, are summarised below.

Very common (more than 1 in 10)

Irritating sensation in the throat,
Swelling of the mouth and lips,
Itching of the mouth and ears

Common (up to 1 in 10)

Prickling sensation or numbness of the mouth or tongue, Itching of the eyes, Itching of the tongue and lips, Swelling of the tongue or throat, Inflammation, discomfort or burning sensation in the mouth, Redness in the mouth or mouth ulcers, Pain in the mouth, Altered taste, Stomach pain or discomfort, Diarrhoea, Feeling sick (nausea) and vomiting, Pain when swallowing or difficulty in swallowing, Symptoms of asthma, Cough, Shortness of breath, Chest discomfort, Indigestion and heartburn, Hoarseness, Tiredness, Hives and itching of the skin

Uncommon (up to 1 in 100)

Inflammation of the eyes, Sensation of rapid forceful or irregular beating of the heart, Ear discomfort, Tightness in the throat, Nasal discomfort, stuffy or runny nose, sneezing, Blisters in the mouth, Irritation of the oesophagus, Sensation of something stuck in the throat, Dizziness, General discomfort, Dry mouth, Prickling sensation of the skin, Red throat, Tonsil enlargement, Pain in the lip, Lip ulcer, Salivary gland enlargement, Increased production of saliva, Redness of the skin

Rare (up to 1 in 1000)

Rapid swelling of face or skin, Allergic inflammation of the oesophagus (eosinophilic oesophagitis) which may present as heartburn or difficulty in swallowing that is severe or does not go away

What are the possible disadvantages of this research trial?

The skin tests, blood samples and breathing tests are part of routine clinical care. Your child doctor will tell you about these risks.

- **Blood Sample:** side effects may include minor discomfort, bruising and infection. When possible, we will take research blood samples at the same time as a other routine samples or procedures.
- **Breathing Tests:** Your child may become short of breath or experience chest tightness while performing the breathing tests. Treatment will be made available if this occurs. This treatment (albuterol) may cause an increase in your child's heart rate.
- **Nasal Sample:** there may be some minor discomfort involved. However, the sample collection is simple and our staff are fully trained.

What are the possible benefits of taking part?

- **Regular health checkup/assessment:** you over the phone every 6 weeks in the first year and every 3 monthly in years 2 and 3, by health care professionals who are experts in asthma and allergy.
- **Access to allergy asthma experts:** access to an out of hours phone line to discuss any issues with the consultant paediatrician.
- **Asthma prevention:** We cannot be certain if this new treatment will work but it may be possible to reduce the risk of your child developing asthma and/or allergic diseases. The trial may not help your child but the knowledge gained from this trial may aid in the advancement and understanding of asthma and allergic disease and help in the development of new approaches for its treatment and most importantly, prevention.

PART 2 - Frequently Asked Questions

What if new information becomes available?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied.

- Your research doctor will tell you about it and discuss with you whether you want your child to continue in the trial.
- If you decide to withdraw, your research doctor will make arrangements for your care to continue.
- If you decide to continue in the trial, you will be asked to sign an updated consent form.
- Your research doctor might consider it to be in your child's best interests to withdraw them from the trial.
- Your child may also be withdrawn from the trial if you are not able to attend the research visits required or you fail to follow the research requirements.
- If any unexpected other findings are found while your child is participating, the information will be sent to your child's GP so they can take any necessary action.

What happens when the research stops?



- Once your child has completed 3 years of the HDM tablets/placebo they will stop taking this.
- For participants in the **placebo group** who develop symptomatic house dust mite allergy, there would be an opportunity to receive the PAPA trial medication (Acarizax®) **from 5 years of age in the NHS allergy service.**
- An independent Data and Safety Monitoring Committee and independent Trial Steering Committee are overseeing the trial and may stop the trial if there are any serious issues.

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



- Your child would be withdrawn from the trial.
- Identifiable data or tissue already collected with your initial consent would be retained and used in the trial.
- No further data or samples would be collected or any other research procedures carried out on your child.

What if something goes wrong?

The **University of Southampton holds insurance policies** which apply to this trial. If your child experiences harm or injury as a result of taking part in this trial, you and your child will be eligible to claim compensation without having to prove that University of Southampton 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 trial 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 university's Head of Research Ethics and Governance, **details can be located in Part 3.**

Will my child's details and information be confidential?

- All of your child's personal details will be kept in a **pseudonymised format**.
- This means a **code number** will be used instead of their name and only your care team can link the code with their details.
- Any results from the trial will not allow your child to be identified in any way.
- Your child's **GP will be informed** of their participation in this trial.
- We may collect your contact details (name, address, email, telephone number) in order to ship the trial medication to your home address if a telephone visit occurs. This will only be shared with third party organisations such as the medication couriers where you are unable to collect your medication in person at the hospital.

If you consent, we will also collect **your child's NHS number** (CHI number for Scottish hospitals) and **date of birth** so we can **track their progress and if they go on to develop asthma in the future**. We will track their progress until they are around aged 9 (5 years after they stop taking part in the PAPA trial).

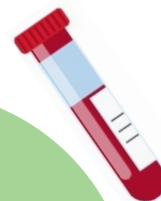
- We will store this data securely and ensure it is not shared with anyone other than NHS Digital (or their collaborators and subsequent organisations) to obtain this long term data.
- Once the research is completed this data will be archived along with all other trial data. **This is optional** and will not affect your child's participation in the rest of the PAPA trial.

Who is organising and funding this trial?

- Run by researchers at the University of Southampton and Imperial College London.
- The main Investigator - Dr Syed Hasan Arshad.
- Funded by the National Institute for Health Research .
- Sponsored by University of Southampton. The sponsors of this trial will pay your hospital the costs associated for including your child in this trial.



What will happen to the samples taken during the trial?



- All activities (storage, use and disposal) will be carried out in accordance with the [Human Tissue Act 2004](#).
- Your child's samples will be used to **help researchers understand how the treatment works**.
- Researchers will study the immune system responds to the treatment.
- The samples are tested in a **research lab**, not a certified clinical lab. Because of this, individual results cannot be given directly to you.
- The results will **not identify your child** and will **not affect normal medical care**.
- If you agree, researchers will share the overall study results and any general findings from the samples.
- Your child's sample will be labelled with their **code number**, not their name. Only the investigator can link the sample to your child. This information will be kept secure and confidential.
- If there are **extra samples left over**, you will be asked whether they can be:
 - stored for future tests related to this trial, or used in future research, even if it is not about allergy or asthma.
 - If you do not want extra samples stored, they will be destroyed.
- **Other research teams may ask to use the samples** or data from the trial. If you agree, the samples or data may be shared for future research.
- All requests are checked by the Trial Management Group to make sure the research is meaningful.
- Any shared samples will **only have the unique code number**, not names or medical record numbers.
- **You can ask at any time for the sample to be removed from storage and destroyed**. However, it may not always be possible to remove or get back samples that have already been sent to other researchers.



What will happen to the results of the trial?

Regular updates on the trial including recruitment and progress can be found on the trial website <https://papastudy.uk/>

- Results presented at **national and international medical conferences**.
- **Published in a medical journal** so that we can let all other doctors worldwide that are treating children with asthma know whether the treatment works at preventing asthma.
- 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.
- The results of the trial including if the treatment helps to prevent asthma, in the form of a **newsletter summary** can be made available to you/your child and/or your GP should you wish. We will collect your contact details in order to provide this to you.

Who can I contact for independent research information?

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.

The 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.

Who has reviewed the trial?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests.

This trial has been reviewed and given a favourable opinion by Nottingham Research Ethics Committee.

Research involving medications is also reviewed by the Medicines and Healthcare Products Regulatory Agency (MHRA). This trial has been given a notice of no objection by the MHRA.



PART 3 – Contact Details

Contact for Further Information

If you wish to ask any questions or speak to a member of the hospital research team, please, use any of the following contact details:

Name: [name of doctor and/or nurse]

Telephone number: [phone number]

Email: [email]

In an emergency, please follow your usual care pathway, NHS 111 or 999.

For non-urgent queries, you can contact the PAPA out-of-hours phoneline which is covered by consultant paediatricians on the following 24-hour contact details:

Telephone: 0800 654 6368

If you are unhappy or have a complaint about any aspect of this study, please contact:

University of Southampton Head of Research Ethics and Governance details:

Telephone: 023 8059 5058

Email: rgoinfo@soton.ac.uk

PART 4 - Glossary

<u>Term</u>	<u>Explanation</u>
Allergen immunotherapy	Allergen immunotherapy is a medical treatment for allergies. The idea is that a person's immune system can be 'trained' to tolerate the allergen and therefore not cause allergic symptoms.
Allergy	Allergy occurs when a person's immune system reacts in an inappropriate or exaggerated way to a food or substance that, in the majority of people, causes no symptoms. A food or substance that causes an allergic reaction is called an allergen.
Asthma	Asthma is a long-term lung condition. It affects the airways (breathing tubes) that carry air in and out of your lungs, causing them to become swollen (inflamed). This makes the airways narrower so less air gets into and out of the lungs. People with asthma can get symptoms like wheezing, breathlessness, a cough or a tight chest. Sometimes symptoms can get worse quickly. This is an asthma attack. Symptoms can be triggered by things like exercise, allergens or changes in weather. There are lots of potential triggers and everyone with asthma will have their own set of triggers. At the moment there is no cure for asthma.
Atopic Dermatitis	Atopic dermatitis is the most common and chronic type of eczema. Eczema is a broad umbrella term for any group of skin conditions that cause inflammation, dryness, and itching.
Consent Form	A trial consent form, also known as an informed consent form, is a document used in research studies, especially clinical trials, to ensure that potential participants understand the study and agree to participate voluntarily. By signing the form, participants confirm they understand the information and are agreeing to participate.
Control group	A group of participants is split in two groups; this half does not get the trial treatment, they will have usual care or usual medicines to provide a comparison for the other treatment or medicine.
Exhaled nitric oxide test	FeNO (fractional exhaled nitric oxide) is a test that measures the levels of nitric oxide in your breath. A high level of nitric oxide when you breathe out can be a sign that you have inflamed airways, and could be a sign that you have asthma.

House dust mite allergen (HDM)	Found in household dust known to cause allergic reactions in some people
Immune cells	Protect our body from harmful invaders like germs, viruses and bacteria
Immune response	How your body defends itself against harmful invaders like bacteria and viruses
Impulse oscillometry	Impulse oscillometry is a test that uses sound waves to measure how much resistance there is to the normal movement of air in and out of your lungs when you are breathing at rest. The test is performed for either diagnostic or monitoring purposes.
Intervention group	A group of participants is split in two groups; one half gets one trial treatment we are testing for (the intervention), whilst the other half stays on their regular treatment.
Peak flow test	Peak flow is a simple measurement of how quickly you can blow air out of your lungs. It's often used to help diagnose and monitor asthma.
Placebo	An inactive substance or other intervention that looks the same as, and is given the same way as, an active drug or treatment being tested.
Protective antibodies	Made by the immune system to protect you from substances that the body identifies as “foreign” such as bacteria and viruses
Randomisation	Randomisation means that a group of people are split into different groups at random, like flipping a coin; one group is kept on their normal care the others are given a different treatment. For this trial, we will split into 2 groups and measure how each group is doing. We will see if one group has experienced less episodes of wheezing.
Screening	Clinical trial screening is the process of determining a potential participant's eligibility for a trial by assessing their characteristics against the trial's inclusion and exclusion criteria. This process can be done via pre-screening (online or phone) and a more comprehensive screening visit at the hospital clinic. The goal is to ensure the trial is safe and the research is valid by enrolling participants who are most likely to benefit from the investigational drug or intervention.
Skin Prick Test	A skin prick test is a common allergy test that identifies substances causing allergic reactions. It involves applying small amounts of potential

allergens to the skin, then pricking the skin to introduce the allergen. If allergic, a small, raised, and itchy bump appears, indicating a reaction.