TIGER
Trial of food allergy (IgE) tests for eczema relief

The TIGER Study Participant Information Leaflet

We would like to invite you and your child to take part in a research study

- Before you decide whether to take part, it is important for you to understand why the research is being done and what taking part will involve for you and your child.
- Please take your time. Use this leaflet and the other information to decide whether you wish to join the study.
- If you choose not to take part, this will not affect your child's care.
- Please ask us if there is anything that is unclear or if you would like more information.

The TIGER Study Office
Bristol Trials Centre
Contact: TIGER Trial Manager
☎: 0117 455 3039
✉: **tiger-study@bristol.ac.uk**
💻: www.bristol.ac.uk/tiger-study

Chief Investigator: Professor Matthew Ridd

Study summary

- You have been asked to take part because your child has eczema.
- While food allergy is more common in people with eczema, we do not know whether making changes to children's diet, based on food allergy tests, is helpful or not.
- To find out if food allergy testing can improve eczema control, we need to compare two groups in a large study. One group will receive normal care from their GP plus our "Good eczema care" leaflet. The other group will also receive the leaflet plus dietary advice based on food allergy tests.
- If your child is put in the dietary advice group, they will have a skin prick test. This is when a solution containing the study foods to test are "pricked" into the skin. A few children may also be asked to attend hospital for a day, to make sure all study foods are safe to eat at home.
- We will follow up everyone for 9 months from when they join the study.
- We may ask to talk to you in more detail about your experiences and opinions of taking part, however this bit of the study is an "optional extra".

Contents

PART A – ABOUT THE STUDY

1. Why are we doing this study?

What are we studying?

As you may be aware, eczema is common in children and causes dry, itchy and inflamed skin. Symptoms tend to come and go, and there are many reasons why a worsening or "flare" of eczema can happen. Many parents wonder whether a food allergy might be a cause, however there is currently no good research evidence to support this.

In the TIGER study, we want to find out whether making changes to the diet of children with eczema, based on the results of food allergy tests, improves eczema control or not. The foods we are looking at are cow's milk, hen's egg, wheat and soya.

Previous research into any link between food allergy and eczema symptoms is limited. This study is needed to help parents and doctors in the future know what is the best thing to do.

Is it suitable for my child to take part?

We are looking for 493 children with eczema, aged between 3 months and 2 years. Your GP surgery is supporting this study and thinks your child may be suitable.

2. What does taking part in the study involve?

What will happen if we choose to take part?

We have sent you this information because you said that you are interested in learning more about our study. In a consent appointment (see below), one of the research team will talk through what's involved. Then you can then decide whether to join.

While taking part in the study, your child will continue to be looked after by their GP as normal. You can take your child to see their GP as often as you think necessary. Taking part in the study will not stop you or your GP changing your child's treatment, if this is what you want or decide is the best thing to do. Similarly, no treatment will be withheld.

Consent appointment and pre-baseline questionnaires

At a convenient time, by telephone or video call, one of our researchers will confirm your child's eligibility and answer any questions that you have. They will ask you to confirm you understand the study and agree to take part by completing a consent form.

You do not have to enter the study unless you feel completely happy with what you are being asked to do. If you are not eligible or do not want to take part, you will continue to receive the same care that would normally be offered from your GP.

If you are eligible and consent to take part, you will be booked in for a face-to-face 'baseline' appointment with the researcher, at your own GP surgery or one nearby. Before you attend this appointment, a researcher will ask you some questions, by telephone or video call, about your child and family, including any food allergy symptoms, your child's diet and (if your child is breastfed) the diet of the breastfeeding mother. You will also be sent (by post or email) a questionnaire to complete at home before your

baseline appointment, which will ask about you and your child's wellbeing and how their eczema affects them.

Baseline appointment

Your child must be generally well and not take an antihistamine (for example chlorphenamine (Piriton), cetirizine (Zyrtec), or desloratadine (Neoclarityn)) for at least three days before this appointment. As long as they remain eligible for the study, this appointment can be delayed until they are well and/or any antihistamine is stopped.

At this appointment, you will be given a short questionnaire to complete about your child's eczema symptoms and treatments. The researcher will examine your child's skin and measure your child's weight, height and head circumference.

Next, to make sure the study is fair, a computer will put you into a group by chance (at random). You will have an equal chance of being in either group:

Standard care group: Children in the "standard care" group will have normal care for their eczema from their GP plus our "Good eczema care" leaflet.

Dietary advice group: Children in the "dietary advice" group will receive our "Good eczema care" leaflet plus dietary advice based on food allergy tests (skin prick tests). If your child's skin prick tests or symptoms are unclear, an Oral Food Challenge may be required. For more information, see section 6 below (blue section).

How is it decided who gets an allergy test and who doesn't?

In this kind of study (a randomised controlled trial), nobody involved (you, your GP or the research team) decides or can predict which group your child gets put in. It is done using a computer, by a process called 'randomisation'. It's a bit like rolling dice and ensures the comparison between 'standard care' and 'dietary advice based on food allergy testing' is fair by keeping both the groups the same, apart from what we are comparing.

3. What else is involved in the study?

Questionnaires

We will ask you to record your child's eczema symptoms, treatment use and diet every month for 9 months. It is important to collect this information regularly because eczema can change quite a lot over time. We would like the same person to complete the questionnaires throughout the study.

The questionnaire at 3, 6 and 9 months include some extra questions about you and your child's health-related quality of life, your well-being and any care your child has received due to their eczema.

The questionnaires will be online, but if needed you can complete them on paper or by telephone. Whatever method you use, the research team will send you a reminder when the next questionnaire is due and may get in touch if we don't hear back from you.

Follow up appointment

We will arrange to meet with you and your child again at 6 months to re-assess their skin and measure their weight, height and head circumference. This appointment will be at a time and place convenient for you (usually your home). At the appointment, we will ask you to share your child's birth weight to enable us to complete a growth assessment, using measurements from the baseline appointment and this appointment. If there are any signs of faltering growth from our assessment, we will inform you and your child's GP so this can be monitored.

Electronic medical record review

On the consent form, we will ask for your permission for us to review your child's medical records history at the end of the study so that we can fully understand the impact of allergy testing. We will look at a history of your child's illnesses, healthcare appointments and medications prescribed. These will only be accessed at the end of the study.

4. Optional extras

In addition to the main study, you can sign-up to have a saliva sample collected from your child for genetic analysis; and be interviewed about your experience about taking part generally, and in particular about the healthcare use questionnaire. Taking part in any of these 'extras' (described below) is optional, and you can still take part in the rest of the study if you choose not to do these.

Saliva sample for genetic analysis

We know that some genes are linked with eczema and/or food allergy. If you agree to a saliva sample being collected from your child, it will be sent to a laboratory at the University of Edinburgh who will oversee the analysis for any genes related to these specific conditions. This is purely for research purposes.

The results will not be shared with you for two reasons:

▪ Tests done in a research laboratory are not validated in the same way as they are in an NHS laboratory (where tests are done for clinical rather than research reasons)

▪ Any differences we find cannot help you or your child at an individual level. That is, the results will not help inform your child's healthcare.

The findings may be used later in research which combines information from multiple studies to see if differences can be detected that cannot be seen in single, individual studies. Any remaining sample will be destroyed within six months of the study results being published.

Interviews about your experiences

We are also interested in finding out your views on:

- Taking part in this study and your experience of allergy testing, if your child has it.
- The questionnaires that we use to collect data on the healthcare services your child has used (e.g., the number of times they have seen a GP) and anything you have paid for due to your child's eczema or any food allergy (e.g., over-the-counter medications).

Interviews will be by telephone or video call (e.g. Zoom or Microsoft Teams) and will be audio-recorded and transcribed.

If you are willing to be invited and we contact you, we will talk to you about what this would involve and ask for your additional consent before doing the interview.

Audio recording and observation of study appointments

The researcher may ask you if you are happy for your appointment to be observed by another study researcher, or audio recorded, and the recording may be transcribed. If you are happy for this to happen, you will be asked to provide verbal consent and your consent will be audio recorded.

Transcription will be done by a University of Bristol-approved transcriber with a confidentiality agreement in place. Direct quotes will be used in study reports but it will not be possible to identify anyone from them. Audio recordings will be deleted upon completion of the study, but transcripts will be retained until the youngest participant's 25th birthday.

5. Possible benefits and disadvantages of taking part

Most people find it rewarding to take part in medical research and appreciate the additional contact with the research team. The findings from the study will help doctors and parents in the future to decide if food allergy testing should be recommended for children with eczema.

If you are in the dietary advice group, the food allergy tests may provide reassurance or reveal undiagnosed problems. However, we are only testing four foods and the dietary advice based on the skin prick test results may not make any difference to your child's eczema. In addition, your child may have a reaction to either the skin prick tests or the Oral Food Challenges. Usually any reaction is localised and mild. The risk of a serious ("anaphylaxis") reaction to skin prick tests is estimated to be less than 1 in a million. In the unlikely event of an emergency, there will be medical help on hand.

6. "Dietary advice" group only

If your child is allocated to the "Dietary advice" group, you will be offered skin prick tests for your child.

Skin Prick Test

Skin prick tests will be offered for cow's milk, hen's egg, wheat, and soya.

During the test, a researcher will place a drop of the relevant food on your child's skin, usually their forearm, outer upper arm or back. The skin under the drop is then 'pricked' with a lancet, which is a sterile metal stick with a small point on the end that scratches the top layer of the skin. This helps the food to get under the skin surface. The skin prick test may be slightly uncomfortable when the skin is pricked, but it should not hurt. The researcher will then wipe away the drop and repeat the same process for each food. With a washable pen, the researcher will make a mark on your child's skin to identify each test. After 15 minutes, the researcher will check your child's skin for a reaction.

If your child has no reaction, the skin under the drop will remain normal. If your child is sensitised , the skin under the drop will become red and itchy – usually a white, raised swelling surrounded by a red area ("wheal"). This will fade after a few hours.

If the test is positive, the wheal may feel itchy but will usually start to settle after 20 minutes. A cold compress/ice pack can be used on the area to help relieve the itching if your child is upset. You can also give your child some antihistamine medicine after the test is finished.

Depending on the results of each skin prick test and any symptoms your child has, you will be given advice to:

• follow an unrestricted diet; or

• have a trial period (of up to 4 weeks) of including or excluding the study food; or

• avoid that study food in your child's diet.

If the findings are unclear, you will be offered an appointment for an Oral Food Challenge (see next page).

We will write to your GP to let them know the results of the food allergy testing, dietitian assessment and of any actions that need to be taken.

Follow-up after the study

If a food allergy is diagnosed, some children may require follow-up after the study has finished. This may be either from a dietitian or the local allergy team. We will let you know if we think this is necessary and ask your GP to arrange it for you.

Oral Food Challenge

An Oral Food Challenge is a "gold standard" test, done in hospital to find out if your child is immediately allergic to a particular food.

In the TIGER study, you will only be offered an appointment for an Oral Food Challenge if your child's skin prick tests or symptoms are unclear. The Oral Food Challenge will take place at your nearest allergy centre, in Bristol, Manchester, Oxford or Southampton. If your child has not started eating solid foods yet, we will delay arranging the Oral Food Challenge until after solid foods have been introduced.

We aim to offer an appointment within two weeks of your first study visit. However, only one food can be assessed at each appointment, so it is possible you may need more than one appointment if your child's results were unclear for more than one food.

What is a Food Challenge?

An Oral food challenge is when a single food is fed to your child under close medical supervision. Over the course of a morning your child will be gradually given bigger doses of the food, until the "top dose" is eaten without any symptoms, or a reaction occurs. The top dose is what a child would be expected to eat as a normal portion. Oral Food Challenges can take up to 6 hours.

It is important that your child is well at the time of their challenge and that they have not taken any antihistamines before the challenge.

What happens during the food challenge or supervised feed?

First, a doctor or nurse will check that you understand the test, including the risks and benefits, and answer any questions that you have.

Next, a nurse will take your child's temperature, pulse and blood pressure. They will continue to monitor these throughout the test. Then, over the course of the morning your child will be given increasing amounts of the challenge food every 20 minutes or so.

The amount of food given varies according to the food being tested. We often hide the challenge food in a familiar food to make sure that the required amount is eaten.

What are the benefits of having an oral food challenge?

An Oral Food Challenge will confirm whether your child has an immediate-type allergy to a particular food. If your child completes the food challenge without a reaction, they should be able to reintroduce that food into their normal diet. If your child is found to be allergic, then we will ensure that they are given a management plan and appropriate medications. You can then share this information with anyone involved in your child's care.

Are there any risks associated with having a food challenge?

There is a potential risk that your child will have a reaction to the food they are being challenged to. This is why the test will be done in hospital where all emergency medications for an allergic reaction are on hand. Your child will be closely monitored by a nurse who will watch for any signs of an allergic reaction, such as an itchy rash or breathing difficulties. If your child does have an allergic reaction the test will be stopped, and appropriate medication will be given to relieve the symptoms and to stop the reaction getting any worse. This is most likely to be an antihistamine, but in the case of a more severe reaction, may include adrenaline (e.g. EpiPen) or a salbutamol (asthma) nebuliser.

What are the alternatives to my child having a food challenge or supervised feed?

You may choose for your child not to have an oral food challenge and just avoid the food they may be allergic to. However, a food challenge is the only safe way to definitively find out whether your child has a specific food allergy or not.

What should I do to prepare my child for the food challenge?

Appropriate to the age of your child, it is important to prepare your child for their challenge, so that they understand what is happening to them. This can help with their willingness to cooperate. You should give your child truthful information. Explain that your child will meet nurses and doctors and that they will be there for about half a day.

Please feel free to bring familiar toys with you to help your child feel at ease. They can eat normally when the test is completed.

In some cases, you will be asked to bring the test food with you. This will be clearly explained in your appointment letter. We will offer reimbursement of expenses incurred for any foods you need to bring for the challenge and to cover your travel to attend the appointment.

7. More information about taking part

Do we have to take part?

No, it is up to you to decide whether to take part. Invitation letters have been sent to all children who might be able to take part from your GP surgery. If you choose to the join the study, you are free to withdraw from it at any time, without giving a reason. This would not affect the quality or type of care your child will receive.

Will I receive any payment for taking part?

Although it is not appropriate for us to offer you payment for taking part in this study, to part compensate you for potential loss of earnings, we are able to offer you: a £10 voucher at the beginning and another £10 voucher part-way through the study. If you take part in the optional interviews, we will offer an additional £20 voucher.

What happens if new information becomes available during the study?

During a study, sometimes new information becomes available about the treatment being studied. If this happens, the research team will tell you and discuss whether you want to continue in the study.

If you decide to stop taking part in the study, your usual care with your GP will continue. If we think your child should withdraw from the study, we will explain the reasons and arrange for their normal care to continue.

What happens when the study stops?

Very occasionally, a study is stopped early. If this happens, the reasons will be explained to you and your GP care would continue as usual. Following completion of the study at the expected time, your normal GP care will continue as usual.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researcher or trial manager who will do their best to answer your questions. Alternatively, you could speak to the Chief Investigator, Professor Matthew Ridd (email: m.ridd@bristol.ac.uk).

You can also get independent advice from the Patient Advice and Liaison Service (PALS). You can find your local service via the NHS website: https://www.nhs.uk/nhs-services/hospitals/what-is-pals-patient-advice-and-liaison-service/

If you remain unhappy and wish to complain formally, the normal NHS complaints process is available to you.

What will happen if my child or I don't want to carry on with the study?

You can stop taking part in the study at any stage without giving a reason, your medical care and legal rights will not be affected. If possible, we would still like you to complete the follow-up questionnaires so that we can monitor your progress. However, if you no longer want to complete the questionnaires (or other optional elements of the study) that is OK. In this situation we will continue to collect relevant information from your medical notes, without bothering you, unless you tell us you don't want us to.

If you wish to stop participation completely, we will confidentially keep any information (data) collected about you up to the point of withdrawal to include in our analysis of the study results.

Will my GP be informed?

Your GP is supporting this research. If you join the study, we will tell your child's GP that they are taking part. Your child may be offered food allergy test(s) depending on their allocation. Otherwise, your child will receive the same care as they are currently getting from your GP practice. We will also inform your child's GP if we suspect any signs of faltering growth from the growth assessment we complete after the follow up appointment.

What will happen to the results of the study?

When the study is completed, the results will be published in a journal, so healthcare professionals can learn about the main findings. If published, the identity of you and your child and all personal details will be kept confidential. No named information about you or your child will be published in any report about this study. We will also provide you with a summary of our findings from the study, if you wish.

Who is organising and funding the study?

This trial is organised by the University of Bristol and the host institution is NHS Bristol, North Somerset and South Gloucestershire Integrated Care Board. The funder is the National Institute for Health and Care Research (NIHR) Health Technology Assessment (HTA) (Reference: NIHR133464). The trial has not received any funding, samples or promotional materials from the pharmaceutical industry.

Who has reviewed the study?

This trial has been reviewed by an independent group of people, called a Research Ethics Committee, to protect your safety, rights, well-being and dignity. The study has been reviewed by the Health Research Authority and given a favourable opinion by North West – Greater Manchester Central Research Ethics Committee.

What insurance is in place for the study?

The University of Bristol has arranged insurance to cover the legal liability of the University as Research Sponsor in the event of harm to a research participant as a result of the management of the research by the University.

The University of Bristol holds Professional Negligence insurance to cover the legal liability of the University, for harm to participants arising from the design of the research.

This does not affect the responsibility of the NHS or the participant's GP practice for clinical patient care.

PART B - ABOUT DATA USAGE

If you are interested, these pages tell you more about how we process, store and share any information that you give us

How will we use information about you?

We will need to use information from you and your child, from your child's medical records and their GP for this research project.

This information will include their:

- Initials
- NHS number
- Name
- Contact details

People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number ('Study ID') instead.

Some of your information will be sent to "Sealed Envelope™". This is the company that provides the computer software that randomly decides which treatment group your child is allocated to. Your local researcher will provide this company with the minimum relevant information about you/your child to enable the randomisation process. They must follow our rules about keeping your information safe.

Once we have finished the study, we may keep identifiable data about you and your child up until the youngest participant's 25th birthday for audit, inspection, insurance and governance purposes only. Data will be held confidentially and securely by the research team. We will write our reports in a way that no-one can work out that you took part in the study.

Will mine/my child's taking part in in this study be kept confidential?

Yes, all information collected about you/your child during the study will be kept strictly confidential. Your data will be stored and used in compliance with the current data protection laws; Data Protection Act 2018 and General Data Protection Regulation 2018 (GDPR).

Relevant sections of your child's medical records and information collected during the study may be looked at by authorised individuals from regulatory authorities, participating NHS sites, the University of Bristol (as Sponsor) or its representatives, and the TIGER central research team, where it is relevant to you taking part in this research. University of Bristol will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Personal information such as your name, email address and phone number will be stored on a secure database with the central research team (University of Bristol). Any identifiable data from your child may be kept until the youngest participant's 25th birthday for audit, inspection, insurance and governance purposes only.

What are your choices about how your information is used?

- You and your child can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- If you and your child choose to stop taking part in the study, we would like to continue collecting information about your child's health from central NHS records, their hospital and/or their GP. If you do not want this to happen, tell us and we will stop.
- We need to manage your 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 you.
- If you agree to take part in this study, you will have the option 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 information

- at www.hra.nhs.uk/information-about-patients/
- at www.hra.nhs.uk/patientdataandresearch
- at www.bristol.ac.uk/secretary/data-protection/
- by asking a member of the research team
- by sending an email to tiger-study@bristol.ac.uk, or
- by telephoning us on 0117 455 3039.

Contact details for further information

If you have any questions regarding the study or how you might be involved further, please contact one of the research team below:

TIGER study Trial Manager
University of Bristol
1-5 Whiteladies Road
Clifton
Bristol, BS8 1NU
0117 455 3039
tiger-study@bristol.ac.uk
www.bristol.ac.uk/tiger-study

Professor Matthew Ridd
TIGER study Chief Investigator
University of Bristol
Canynge Hall
39 Whatley Road
Bristol, BS8 2PS
m.ridd@bristol.ac.uk

Thank you for taking the time to read this leaflet and for considering whether to take part in this study

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