ENDURE

Understanding beta cell disorders through the study of rare genotypes

A research study helping scientists to understand the causes and implications of making too little or too much insulin.

Could you and your child spare some time to help researchers better understand the causes and effects of genetic changes altering insulin production?

Chief Investigator: Professor Andrew Hattersley

ENDURE Study – Core Information Leaflet

Why are we doing this research?

Insulin is the only hormone in the body that lowers blood sugar levels to normal after a meal. It is produced and processed by special cells in the pancreas called beta cells. We have recently discovered that small changes in a person's genetic code (the body's instruction manual) can alter insulin production/secretion. We would like to improve understanding of how genetic changes alter the way beta cells and the body works.

Why has my child been invited?

Your child has been invited into this study because they have either been diagnosed with a genetic change that alters insulin production/secretion, or are a 'healthy control' individual. We wish to compare how people with this specific type of genetic change differ from individuals without it.

What does participation involve?

Please refer to the Core Study Flowchart describing the visit, including timings and details of the measures and tests that we would like your child to participate in. You and your child will be able to discuss the study with a member of the study team and ask any questions you have. The research visit will take place in England at the NIHR Exeter Clinical Research Facility or possibly, depending on where you live, at an alternative convenient location. You will be asked to sign a consent form to say you agree to your child taking part in the study and for their samples to be gifted to be used for research purposes (please see the back page of this leaflet for the consent statements you will be asked).

During the visit we will ask you questions about your child's health. We will measure and record their height and weight and collect blood samples. Your child's GP/clinician will be notified of their participation in the study and may be asked about aspects of their clinical care, eg, a clinical test result relevant to the study.

Some participants will also be invited to take part in the Imaging Sub-Study, designed to investigate specific genetic changes in more detail. If your child is invited for this, we will explain to you exactly what is involved and will provide the Imaging Sub-Study Flowchart.

A small number of participants may be asked to attend a return visit for more tests and will be provided with written information about them in advance.

Who is organising and funding this research?

The research will be managed through the NIHR Exeter Clinical Research Facility (Exeter CRF), which is funded by the National Institute for Health and Care Research, a part of the NHS, and a collaboration with the University of Exeter. Providers of additional funding for the study include the Wellcome Trust, Diabetes UK and JDRF International, and The Leona M. and Harry B. Helmsley Charitable Trust.

What will happen to my child's samples and data?

A unique Study ID will be allocated, under which all your child's study data and samples will be stored. Your child's samples and data will be looked after in a secure way to protect their identity. Robust procedures, in compliance with the Human Tissue Act 2004, are always followed to monitor and maintain the integrity and traceability of the samples, stored in a licensed area, including their disposal.

Some of your child's blood samples will be sent for testing at the Exeter Clinical Laboratories at the Royal Devon & Exeter (RD&E) Hospital with three forms of identifiable information (name, DOB, NHS/CHI/ hospital number), as required by UK National Health Service (NHS) laboratories for clinical sample analysis. Separately, we will conduct research tests on blood samples, including DNA, to study how genetic changes affect function and features of cells in the body. Immune system, genetic and insulin markers will be measured, and we will also record your child's other data collected from examining them and any tests performed.

Participation in the ENDURE study requires your child to donate their samples and data to the study as an absolute gift. This means you and your child will not benefit financially should there be a future discovery or invention. We may make some of their de-personalised research data and samples available to other researchers to perform further analyses and to support future ethically-approved research in and outside the UK, possibly including commercial partners.

We will also ask your permission to transfer your child's surplus samples and data collected to the Genetic Beta Cell Research Bank (https://www.diabetesgenes.org/current-research/genetic-beta-cell-research-bank/), an approved NHS tissue bank, for safe storage and use in future research. This is optional. Should you not wish to do this, their samples and data will be destroyed securely at the end of the study.

Data produced by studying your child's samples and data may be included in publications with no connection to their name or other personal identifiers. It may also be placed in electronic archives where it will only be accessible to approved researchers on application, to ensure the results are only used to advance scientific and medical understanding.

ENDURE Core Study Flowchart

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Cohort:

CORE

What will happen during my child's research appointment?

	What does this involve?	Are there any risks?
Arrive at Clinical Research Facility or chosen location **Give consent to participate** **15 -20 mins**	At the time of making your child's appointment, you will be asked if you require a parking permit. At the visit, a member of the study research team will discuss all aspects of the study with you. You will have the opportunity to ask questions and when you are happy that you understand what is involved, you will be asked to complete a form giving your consent for your child to participate in the study.	No. Participation is entirely voluntary and it is up to you whether your child joins the study and you can withdraw them at any time without giving a reason.
Body measurements, medical history **15 - 20 mins**	You will be asked some questions about your child's general health and any treatments, plus family history of diabetes. We will measure and record their height and weight.	No.
Blood collection **5 - 10 mins**	We will insert a small cannula (thin plastic tube) into your child's arm to make the collection of blood samples more comfortable. The blood sampling will involve a single draw of blood. The exact number of blood samples vary for different individuals so will be explained in advance. The total amount of blood we will collect during the visit will follow WHO guidelines which factor for age and weight. *Examples:* A 6-10 y child's sample will not exceed 36 millilitres (ml) (approx 2 tbsp). An 11-15 y child's sample will not exceed 44 millilitres (ml) (approx 2½ tbsp). The blood will be analysed to assess how genetic variants affect function and features of cells in the body. Immune system, genetic and insulin markers will be measured.	Blood sampling can cause some discomfort when the needle is placed in the vein to draw blood. Special spray/cream can be applied to make this painless. There is also a possibility that a small bruise may develop. These risks will be minimised by the procedures being carried out by a qualified nurse/doctor who will monitor your child closely throughout the whole procedure.
END OF STUDY	A member of the research team will make sure that your child is comfortable before they leave the research facility.	

Does my child have to take part in this study?

No, it is entirely up to you to decide whether or not your child takes part and you will have at least 24 hours to decide and can ask for more time if needed. If you decide they can take part, we will ask you to give informed consent by signing a consent form (please refer to the back page of this leaflet). You are free to withdraw your child at any time without giving a reason. Participation in the study will not affect their routine care.

Are there any risks or benefits in taking part?

There may be no direct benefit from taking part in the ENDURE study. There is no financial incentive to take part, but we will pay for or reimburse any reasonable expenses associated with you and your child attending the study visit. The study procedures are not aimed at identifying unrelated conditions so we will not routinely report results. However, should we unexpectedly identify anything that needs immediate clinical action, we will inform you and your child's usual medical provider who may then want to follow this up. Donation of blood samples can be uncomfortable but all study procedures will be carried out by an experienced nurse/doctor/researcher to minimise any discomfort.

How will my child's information be kept confidential?

We will follow current ethical and legal practice and all information about your child will be handled in confidence. The University of Exeter is the sponsor for this study. We will use information collected from your child and from their medical records to undertake this research and will act as the 'data controllers' for this study. This means that we are responsible for looking after your child's information and using it properly. All information collected in this study will be kept strictly confidential and stored at the NIHR Exeter Clinical Research Facility / Exeter Genomics Laboratory on secure password-protected databases held on an NHS server with NHS Firewall and back-up, and/or encrypted password protected computers, and/or in a locked cabinet, and can only be accessed by the research team. Your child will be allocated a unique participant number to ensure their samples and information will be protected and cannot be identified outside of the research team. Any personally identifiable information will be stored securely and will only be accessible to personnel with training in data protection who require this information to perform their study role. The University of Exeter will keep identifiable information about your child for 15 years after the study ends to link information from their medical records to their study data unless you or they ask for this information to be deleted before that time. People who do not need to know who your child is will not be able to see their name or contact details. Your child's rights to access, change or move their information are limited, as we need to manage their information in specific ways for the research to be reliable and accurate. If your child withdraws from the study, we will keep the information about them that we have already obtained. To safeguard your child's rights, we will use the minimum personally identifiable information possible. This information will include their name, date of birth, NHS number, and contact details. People will use this information to do the research or to check their records to make sure that the research is being done properly. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that your child took part in the study.

Where can I find out more?

For further information about the study, please contact a member of our study team on:

+44 (0)1392 408181 Email: lynseybeall@nhs.net

Additional information can be found on the study website:
https://www.diabetesgenes.org/current-research/endure-study/

Who has reviewed this study?

This study has been reviewed and approved by the North West - Greater Manchester East Research Ethics Committee and the Health Research Authority (HRA).

General Data Protection Regulation ('GDPR') and your child's rights

This information sheet gives you information that you have a right to receive under changes in the law. In 2018, regulatory changes in the way that data is processed came into force, with the EU General Data Protection Regulation 2018 (GDPR) and the Data Protection Act 2018 (DPA 2018). Since the UK left the EU, the key principles of EU GDPR have been adopted in the UK GDPR (a 'UK-only' version) and the DPA 2018 still applies. The University of Exeter terms its lawful basis to process personal data for the purposes of carrying out research as being in the 'public interest' and continues to be transparent about its processing of personal data and the participant information sheet should provide a clear explanation of how your child's data will be collected, processed, stored, and destroyed.

If you have any queries about the University of Exeter's processing of your child's personal data that cannot be resolved by the research team, further information can be obtained from the University's Data Protection Officer at: https://www.exeter.ac.uk/aboutoursite/dataprotection/dpo/ . If you have any concerns about how the data is controlled and managed for this study, then please contact the Sponsor Representative, Dr Antony Walsh, Head of Research Governance, Ethics and Compliance, University of Exeter, Tel: +44 (0)1392 726621 or Email: res-sponsor@exeter.ac.uk .

What if there is a problem?

Should you have a problem, please contact the research team. If you have concerns or complaints arising from your child's experience of participating in this study which you do not wish to discuss with the research team directly, the RD&E Patient Engagement/Patient Advice & Liaison Service (PALS) team will provide independent advice: The PALS Office, Royal Devon & Exeter Hospital (Wonford), Barrack Road, Exeter EX2 5DW, +44 (0)1392 402093. In the event that something does go wrong and your child is harmed during the research due to someone's negligence, then you have grounds for compensation against The University of Exeter or Royal Devon University Healthcare NHS Foundation Trust. You may have to pay your legal costs. The University of Exeter has no fault compensation/cover in place and negligence does not have to be proved to be awarded compensation.

Thank you for reading this leaflet, which is yours to keep.

If you agree to your child participating in this study, you will be asked to sign a consent form in the presence of a member of the research team/your child's usual clinical team, a copy of which you will be given to keep. **The consent form will include the following statements:**

CONSENT STATEMENTS

I have been given the ENDURE Core study information leaflet. I have had the opportunity to ask questions and these have been answered fully.

I agree to:

- my child attending an appointment(s), as detailed in the ENDURE study information leaflet.
- provide information about my child's health for use in this study.
- allow the research team to contact my child's clinicians/GP about their clinical care now and in the future.
- my child's de-personalised samples and data being shared to support future research in and outside the UK, including with commercial partners.
- my child's samples and data being stored for the duration of the study.
- my child providing blood samples for analysis, including genetic studies using DNA, as detailed in the ENDURE study information leaflet.

I understand that:

- my child's participation is voluntary and that I may withdraw them at any time without my child's clinical care being affected.
- my child's samples and data are provided as a gift to the ENDURE study team and neither my child nor I will benefit financially should there be a future discovery or invention.
- individuals from the study team, regulatory authorities or the UK NHS Trust will have access to relevant sections of my child's medical notes and data collected during the study for research, monitoring and audit purposes.
- my child's research data and samples will be stored securely by using an ID format to protect their identity.
- my child's clinical samples will be sent for testing at the Exeter Clinical Laboratories, together with three forms of identifiable information (name, DOB, NHS/CHI/hospital number) in accordance with the NHS requirements for clinical sample analysis.
- results produced by studying my child's samples and/or data may be included in publications with no connection to their name or other personal identifiers. Results may also be placed in electronic archives only accessible to researchers on application, to ensure the results are only used to advance scientific and medical understanding.

I agree to my child taking part in the ENDURE Core study.

Optional Consent Statements:

- I agree to gift my child's samples and data from the study, for storage and future research, to the Genetic Beta Cell Research Bank, managed by The Royal Devon University Healthcare NHS Foundation Trust's Exeter Genomics Laboratory.
- I agree that information held by the Exeter Genomics Laboratory and in my child's medical records may be used to follow up on my child's future health status.
- I agree to be contacted by the research team about my child taking part in future studies.