Family Information Sheet

THE BART'S-OXFORD (BOX) FAMILY STUDY OF CHILDHOOD DIABETES

Understanding the causes of type 1 diabetes:

Sub-study title: Changes to DNA (epigenetics) through the generations

- Before you decide whether you wish to continue to help, it is important for you to understand why the research is being done and what is involved.
- Please take the time to read the following information carefully, and discuss it with other members of your family.
- You are free to decide whether to take part, this will not affect the care you get from your own doctors.
- Ask us if anything is not clear or you would like further information.

Thank you for taking the time to consider helping this research.

What is epigenetics?

- Epigenetics is the study of particular chemical and structural changes to DNA that can affect how our genes work.
- These changes are a natural occurrence that happens in everyone and are influenced by many factors including age, our environment/lifestyle, and our immune response to infections.

What is the purpose of epigenetic studies?

More children today are diagnosed with type 1 diabetes and at a younger age when compared with 50 years ago.

- Studying epigenetic changes in multiple generations within the same families is important to allow us to identify genes that are susceptible to environmental influence.
- White blood cells (which are part of the immune system involved in protecting the body against both infectious disease and foreign invaders) have unique epigenetic identities which may be altered by our environment.
- In future we may be able to use this information to help delay or prevent the occurrence of type 1 diabetes.

Why have I been chosen?

You have been identified as eligible to take part because you match one of the following entry criteria:

- You have been diagnosed with type 1 diabetes.

  Or

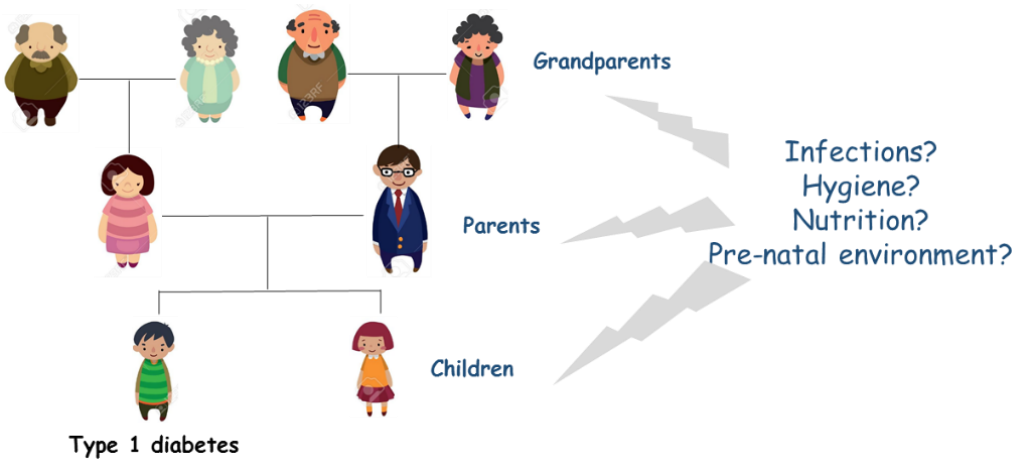
- You don't have type 1 diabetes, but are a relative of someone with type 1 diabetes.

  Or

- On previous blood sampling we have identified that you have islet autoantibody markers.

  Or

- You don't have type 1 diabetes and don't have any islet autoantibody markers (on previous blood sampling) but you are the same age and gender to someone participating in the research. This group of people are control participants.



People with type 1 diabetes (BOX Study case referral)

These are people referred to us by their diabetes care team. We will select eligible participants from the BOX study register for inclusion in this sub-study.

Relatives

- Parent(s) and (where available) grandparent(s) and sibling(s) of the above person.

Relatives **may or may not** have any type of diabetes to be eligible to take part.

Relatives with islet autoantibody risk markers

Islet autoantibodies suggest that people are at increased risk of developing type 1 diabetes sometime in the future. We wish to study whether any epigenetic changes have occurred in this participant group before the development of symptoms of type 1 diabetes.

Relatives without islet autoantibody risk markers

In order to determine differences in samples given by participants with type 1 diabetes, we need to compare with samples collected from participants who do not have type 1 diabetes and samples from participants do not have risk markers of type 1 diabetes. We call this comparison group 'control participants'.

Screening for Islet autoantibody markers

*(This information is **only applicable to grandparents** as part of this sub-study)*

Tests developed in our laboratories can detect in a small blood sample whether proteins called islet autoantibodies are present. If so, this could mean that the insulin producing cells in the pancreas may be damaged. Certain kinds of islet autoantibodies can be found in the blood many years before type 1 diabetes occurs.

- If you have islet autoantibody markers present in your blood you may be more likely to develop type 1 diabetes than other people.
- You can decide *whether you wish* to find out your islet autoantibody results.
- If you have requested to receive islet autoantibody results they will be sent to you as follows:

One islet autoantibody marker:

If we find **one** islet autoantibody (this is positive), you will receive the test results by letter. Testing positive for one islet autoantibody **does not mean that you will go on to develop type 1 diabetes** but you are at slightly increased risk when compared to the general population.

Two or more islet autoantibody markers:

If we find **two or more** islet autoantibody markers present (this is positive), we will contact you by telephone and letter to explain the results. Testing positive for two or more islet autoantibodies means that you may be more likely to develop type 1 diabetes at some time in the future, when compared with other people who do not have these markers. We will invite you to take part in stage two follow up and ask you to sign another consent form.

Do I have to take part?

Taking part is completely voluntary, it is up to you whether or not you decide to take part. If you do take part you will receive a copy of your signed consent form and this information sheet to keep. You can withdraw from the study at any time and you do not need to give a reason, the standard of your medical care or treatment you receive in the future will not be affected.

What will taking part in this epigenetic study involve?

- We discuss this information with you and answer any questions you may have. We will ask you to sign a consent form if you agree to take part.
- All members of your immediate family plus grandparents that agree to take part will be visited at home *(preferably by visit to one home address if grandparent(s) live locally to their family members)* by our study nurse. Alternatively, we may ask families to attend an appointment at a local hospital, if so we will pay your travel expenses
- At this visit our nurse will collect a blood sample from each family member. It will be taken in a similar way to that used for any standard blood test.
- You will also be asked to provide general health/lifestyle information as well as your weight and height for BMI (body mass index) calculation.

Important please let us know:

If you (*or if parent* your child/children*)*

- Have developed diabetes since we last contacted you.
- Are currently taking part in a clinical trial
- Are taking or have taken any medication which suppresses the immune system.
- Have had any vaccination or immunisation within the last four weeks as this would affect this blood sample and we may need to delay your appointment.
- Women will not be able to take part while pregnant or breast-feeding.

What are the tests and what are they for?

The blood sample(s) you and others who take part will be used to study epigenetic patterns in white blood cells, to measure diabetes related autoantibodies, and to test average blood glucose levels.

The amount of blood taken from adults in this research will depend on your BMI (your weight in relation to your height).

The maximum amounts of blood we will ask adults and children to give are shown in the following table:

For Adults:	Usually: 70mls (max 150mls)
Children (Under age 16)	3ml per kilogram (body weight)
Please note: In some cases we may need a repeat sample	

Will I find out the results on any samples that I give?

The results of epigenetic tests will not be reported to you. These tests provide very important information for research but the results are not helpful when considered on an individual basis.

We will inform you of your islet autoantibody markers, if you have chosen to receive them. We will only tell you the result of the HbA1c test if we consider that it may affect your healthcare. We will ask your permission to contact your GP or diabetes specialist.

Will anything else happen to my samples?

- All information that is collected about you during the study will be kept strictly confidential. The samples that you give will only be labelled with your BOX study barcode. All tests are performed on anonymised samples are identified only by this unique number.
- Your BOX study number and name are kept by the study administrators and are not supplied to the laboratory or to anyone analysing the results. It is not therefore possible for researchers to identify or link results back to personal data. It is however possible for us to link the results with the health information that you have previously provided us with.
- Some barcoded samples will be sent to our collaborator's UK and international laboratories for further measurement.

Storage of blood samples

Your blood samples could be stored for a number of years, but we can't say for how long. As long as the BOX study continues, your anonymised samples could be used by BOX researchers and other researchers working with them. They will be used to help us learn more about the causes of type 1 diabetes. Even if you do not want to have your samples stored, you can still participate in the rest of the study.

What are the risks of taking part in this study?

Some discomfort can occur when blood is taken from a vein and there may be some bruising around the site where the sample is taken. Occasionally, some people may faint. It is rare, but some people may get an infection, form a small blood clot, get swelling of the vein and surrounding tissue or bleeding at the needle puncture site.

If you wish, we can post you some local anaesthetic cream for you to apply before the blood sample is taken. This helps to numb the area.

Are there any benefits?

There is no guarantee that you will benefit from taking part in this study. This research might eventually increase knowledge about the process underlying type 1 diabetes and may contribute to the development of therapies that help preserve insulin-making beta cells in the future.

What's the alternative?

There are no proven alternative routine tests or treatments available for protecting insulin-making cells in type 1 diabetes.

Will payment be available?

No payment will be given for being in this study, but you will be offered reimbursement for your travel expenses. By signing the consent form, you acknowledge and agree that, in the event that this research project results in the development of any marketable product, you will have no ownership interest in the product and no right to share in any profits from its sale or commercialisation.

What if there is a problem?

It is highly unlikely that anything will go wrong. If taking part in this research project harms you, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action, but you may have to pay your legal costs.

Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study please contact Dr Kathleen Gillespie telephone 0117 414 7899 /0117 414 7915 or by writing to our freepost address given at the end of this leaflet.

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure: Patient Advice and Liaison Services (PALS). The web address is: http://www.ouh.nhs.uk/patient-guide/pals.aspx and telephone number is: 01865 221473

What would happen to my data?

- You must give your consent in order to participate in this study. Your consent gives the research permission to collect personal details and study data about you, and to record this information on paper and in a computer database. These study records will be used only as needed for the purposes of this study.
- Personal details are information such as your name that directly identifies you. This personal information will be kept in a secure database help by the study administrator at the University of Bristol.
- The study data (results from samples analysed) will be entered into a separate database that will be used for statistical analysis. The results of this study may be published for scientific purposes but individual records and results will not be identified in any publication.

Can I withdraw from the study?

You can withdraw from the study at any time and you do not need to give a reason, the standard of your medical care or treatment you receive in the future will not be affected

Should you wish to do so, you can request that your samples be destroyed at any time.

Who has reviewed this study?

The BOX study was given favourable ethical opinion for conduct in the NHS South Oxford C Research Ethics committee. The sponsor of the study is the University of Bristol.

Who can I ask for more information?

You are encouraged to ask any and all questions which come to your mind about the study. The research staff below will be happy to discuss any questions with you.

Contact us:

Chief Investigator: Dr Kathleen Gillespie PhD
Study Administrator: Mrs Isabel Wilson
Research Technician: Mrs Rachel Aitken

Telephone: 0117 414 7915 or 0117 414 7905

Box Study Nurse: 01865 234905

Email: box-study@bristol.ac.uk

Web: bristol.ac.uk/clinical-sciences/box-study

Address: Freepost RTKH-ASKE-GSBX
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