FAMILY INFORMATION SHEET

THE BART'S OXFORD (BOX) FAMILY STUDY: Understanding the causes of Type 1 diabetes

Stage 2

- We would like to invite you to continue into the second stage of this research project that is taking place as part of the BOX study.
- Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve.
- Please take time to read the following information carefully and discuss it with others if you wish.
- Please ask us if anything is not clear or you would like further information.

Thank you for taking the time to consider taking part in stage two.

Summary of page contents:

What is the purpose of Stage 2 of the BOX family study?

- Stage 2 will give us more detailed information to allow us to study the immune system in people with and without type 1 diabetes.

- We will continue to identify and follow up people who are at increased risk of developing type 1 diabetes by the study of proteins called islet autoantibodies in the blood.

- We will continue to study type 1 diabetes genes within populations to discover why the condition is becoming more common.

- We will further our knowledge of insulin producing pancreatic beta cells in type 1 diabetes.

- We are extending our research to study gut bacteria types and pancreatic function in people with and without type 1 diabetes.

- Annual questionnaires will continue in stage 2 for data collection.

What will taking part in Stage 2 involve?

All family members with and without diabetes can take part. If you decide to take part, you will receive a copy of your signed consent form and this information sheet to keep.

- Taking part in stage 2 will involve completing an **annual questionnaire** to update the information you have provided on registration with BOX. You can participate by questionnaire alone.
- The samples we request will be on an individual participant basis. This will depend on whether you have type 1 diabetes or you are a relative (who doesn't have diabetes).

- **Control participants**: In order to determine differences in samples given by participants with type 1 diabetes and participants at risk of developing type 1 diabetes, researchers need to compare them with samples collected from participants who don't have type 1 diabetes and don't have risk markers of type 1 diabetes. We call this comparison group 'control participants' this method is commonly used in research studies to validate tests.

- We will place participants into groups based on the number of islet autoantibody markers present (0-4) in their blood, and by their age when the initial blood sample was given, (please see the sample collection chart on page 4).

- You may be asked to provide different types of samples e.g. blood, urine, and faeces (stool) for BOX research.

- **All participants that have chosen <u>not to find out</u> their islet autoantibody results will routinely be asked to provide the above samples, regardless of their islet autoantibody results.**

- All samples are optional, you can choose to give **all** samples we request, **some** of the samples, or **none**.

- We collect *where possible*, all samples by post using specialised kits. Our sample kits contain detailed instructions for people to collect the samples at home and have freepost packaging for returning them to us, using an ordinary post box. For some people, we may arrange an appointment at a local hospital to collect a blood sample, or for a study nurse to visit you at home. If we ask to see you, we will ensure that the appropriate safety measures for COVID-19 are in place.

Please let us know if you (or your child) are currently taking part in a clinical trial or if you are taking any medication which suppresses the immune system.

Stage 2

Sample Collection

Pathways	**Sample Type**	Blood		Urine		Faeces	OGTT	Questionnaire (1 per family)
	Frequency	Entry to stage 2	Yearly	6 monthly	Yearly	Yearly	Yearly	Yearly
PW0	**Do not wish to know islet autoantibody results (Research only)**		✓		✓	✓		✓
PW1	***Proband or relative with diabetes**	✓	✓	✓(less than 2years post diagnosis)	✓ (more than 2years post diagnosis)	✓		✓
PW2a	**Relative: Aab negative (over age 21)**							✓
PW2b	**Relative: Aab negative (under age 21)**		✓					✓
PW3	**Relative: Positive for 1 Aab**	✓	✓		✓	✓		✓
PW4a	**Relative: Positive for 2 or more Aab**	✓	✓		✓	✓		✓
PW4b	**Relative: Positive for 2 or more Aab, OGTT option**	✓	✓		✓	✓	✓	✓

*Proband = participant that was originally referred with type 1 diabetes to the BOX study.

Samples required and tests explained…

- Blood samples: For measuring islet autoantibodies and other factors related to type 1 diabetes - up to 1 tablespoon of blood (15ml) is required. Where a lower blood volume is needed for our tests, we will send you a finger prick blood collection kit for use at home.
- Urine samples: For measuring factors related to the function of the insulin producing cells, including urinary C-peptide creatinine ratio (UCPCR). This allows us to measure production of C-peptide, a protein that is made alongside insulin and makes it possible to tell the difference between insulin that is injected and insulin made by your own insulin-producing cells. We would post a urine collection kit to you with instructions and freepost return packaging. This sample is collected two hours after the main meal of the day on any day of your choice.
- Faecal (stool) sample: for measuring levels of gut bacteria and pancreatic function in people with and without type 1 diabetes. We would post a collection kit to you with instructions and freepost return packaging.

- Oral glucose tolerance test (OGTT): If you are positive for two or more islet autoantibodies and choose to have this test, it will measure how well your insulin producing cells are working. The test will be carried out by a research nurse either at your local hospital or (adults only) your home address. We will pay travel expenses if you travel to a local hospital for this test.

  You will be asked not to eat (to fast) after midnight the night before the test and will be given a sugary liquid (glucose) to drink. Small blood samples will be taken at various intervals throughout the test. To make taking the blood easier, we will place a needle and plastic tube (IV) in your arm. Blood samples will be drawn through the IV before you drink the glucose drink and several times after. The test will take approximately 2 ½ hours and the total amount of blood taken will be about two tablespoons (30 ml). If you choose this option, we will ensure the appropriate safety measures for COVID-19 are in place.
- HbA1c: This blood test measures average blood glucose level for the last 2-3 months before the test. This blood sample is 2.5 ml (half a teaspoon)

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

- We will continue to inform you of your islet autoantibody marker results, if you have chosen to receive them.
- OGTT test results: The research nurse will perform a blood glucose measurement on the last blood sample taken during the test to provide a preliminary diagnosis of the amount of glucose present. When the laboratory results become available, the nurse will inform participants of their results. If you are found to have blood sugar levels above the recommended levels, we will seek your permission to inform your GP and keep in touch with you for further follow up.
- The results of genetic and faecal (stool) sample analysis will not be given out to participants. This is because on an individual basis alone, they do not provide useful information, however they are extremely valuable in our research when we are looking at trends within populations.
- The results of urine C-peptide (UCPCR) will not routinely be given out, but we are happy to discuss all results on request.

Do I have to take part?

- Taking part in stage 2 is completely voluntary, it is up to you whether or not you decide to take part.
- You can choose to take part but opt out of providing some of the samples we ask you to give.
- If you decide not to take part in stage 2 (annual follow up samples) we would still like to keep in touch with you and your family via an annual questionnaire.
- You can withdraw 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 are the possible benefits of taking part in BOX?

- There is no guarantee that you will benefit from this study. If you are eligible for further testing the results may indicate that you have high sugar levels or have developed diabetes. It is possible that these changes would be found sooner, before any symptoms develop and therefore decrease the chance of sickness and hospitalisation. In the future, information obtained from BOX and similar studies may lead to ways of preventing type 1 diabetes.

What are the possible disadvantages and risks of taking part?

- You could have discomfort and/or a bruise when you get your blood drawn. Once in a while, some people may faint. It is very rare, but some people may get an infection, a small blood clot, swelling of the vein and surrounding tissue or bleeding where the needle enters the skin. There are also some risks to the OGTT, some people may feel nauseous when they have the OGTT.

- Since this research involves studying islet autoantibodies that can predict getting diabetes, there are other kinds of risks. If you learn that you are at greater risk for diabetes, it could make you worried. In order to reduce worry, at the time you are given any test results, we will explain their meaning to you.

Further Studies:

We will isolate the immune cells (white blood cells) from the blood so they can be studied in more detail in the laboratory. This provides information on the frequency of cells that activate or regulate the immune response and how well they do their job. This is important because research shows that regulation of the immune system may not function properly in people with diabetes.

A subgroup of participants will be invited to help with additional blood collections to study immune function and other markers of autoimmunity. Participants with islet autoantibody markers who have not shown symptoms of type 1 diabetes, people with type 1 diabetes and control participants (relatives without diabetes or islet autoantibodies who are the same age and gender as other participants) may be invited to take part.

Further information on this research will be available and discussed with eligible participants. If you are invited, we would ask you to sign a further consent form, you would be under no obligation to take part.

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 Professor Kathleen Gillespie, Telephone 0117 4147899 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) their web address is: http://www.ouh.nhs.uk/patient-guide/pals.aspx Telephone: 01865 221 473

How will my information be kept confidential?

- All information that is collected about you during the course of the study will be kept strictly confidential.

- Any information that leaves the co-ordinating centre will have your name and address removed so that you cannot be recognised from it.

- Some coded (anonymised) samples will be sent to our collaborator's UK and international laboratories for further measurement.

General Data Protection Regulation (GDPR) Information:

The University of Bristol is the sponsor for this study based in Bristol, United Kingdom. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that 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 in order for the research to be reliable and

accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

The only people in University of Bristol who will have access to information that identifies you will be people who need to contact you to provide study updates or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, contact details or date of birth.

The University of Bristol will keep identifiable information about you for 15 years after the study has finished.

You can find out more about how we use your information under the GDPR statement on our website:

www.bristol.ac.uk/translational-health-sciences/box-study

Who is organising and funding BOX?

BOX was initially started in 1985 by a collaboration between all the diabetes specialists in the former Oxford Regional Health Authority and a research team at St Bartholomew's Hospital, London. The research team moved to Bristol in 1997 but the name and organisational structure of the study is unchanged.

The BOX Study is supported primarily by Diabetes UK but other funding organisations have funded various aspects of the work. These include the Wellcome Trust and the Juvenile Diabetes Foundation. There are no commercial interests involved in the study.

Who has reviewed the study?

The BOX Study has been reviewed and approved by South Central Oxford C Research Ethics Committee.

Who should I talk to if I have any questions or concerns?

You are encouraged to ask any and all questions which come to your mind about the study. You may contact our Study Coordinator Mrs Isabel Wilson on Telephone: 0117 414 7915 Email: box-study@bristol.ac.uk and she will if necessary be able to put you in contact with a member of the team who can answer your enquiries.

Contact us:

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

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