DIRECT: Prediabetes glycaemic deterioration (Study WP2.1b)
Participant Information Sheet
<site name>

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Before you decide whether or not you wish to participate in this project, we need to be sure that you understand firstly why we are doing it, and secondly what it would involve if you agree. We are therefore providing you with the following information. Please read it carefully, and feel free to ask any questions you may have. If you want, discuss it further with your doctor, friends or family. We will do our best to provide further information and answer any questions you may ask for now or at a later date. You do not have to make an immediate decision.

What is the purpose of this Research?

We know that some people are at a higher risk of developing diabetes than other people. We know some of the reasons why this is – for example, risk is increased in people who are overweight or who have a family history of diabetes. However, despite these known risks there is still a lot we don't know about why people get diabetes. We are aiming to identify biological markers that will help us predict whose blood sugar levels will worsen over time and whose blood sugar levels will remain stable. This in turn will help us develop the most effective ways of preventing and treating diabetes.

Who is conducting this research?

The research is being funded by the European Union, in conjunction with funding from some leading pharmaceutical companies. Collectively, this group of European researchers and scientists is called the DIRECT Consortium. DIRECT is interested in learning about the risk factors for diabetes and how people with diabetes present or respond to treatment. The day-to-day organisation of the research in <region> is being co-ordinated by <local PI>. A number of centres are involved across Europe. Lund University is the co-ordinating centre and <insert site details> is the legal sponsor of the study (taking legal responsibility for it).

Why have I been asked to become involved?

You have been asked to participate in this research because according to measurements made on you in previous research studies and measurements taken during the screening for DIRECT, you do not have diabetes but may be at increased risk. Studying people like you in this "pre-diabetes" stage may provide new information on how diabetes develops and how to distinguish those who are likely to go on to develop the disease from those who will not. Importantly, many people with pre-diabetes remain at this stage for a long time and some will never develop the disease.

Could I choose not to take part?

Yes, of course. Participation in this study is entirely voluntary. If you chose not to participate, you wouldn't have to give a reason why and it would not affect any future medical care you may receive. It is in your and our best interests that you only participate in this study if this is something you freely decide to do.

What does the study involve?

You will at this stage already have taken part in a screening assessment for this full study. After the screening assessment you will have received some information, questionnaires and equipment for lifestyle assessment and stool sample collection; we would like you to complete these questionnaires and collect the stool sample and bring these with you to the first visit. This first visit will involve drinking a sugary drink followed by blood sampling for 2 hours (an oral glucose tolerance test) and you may be asked to undergo a body scan (MRI).

A second visit will follow 18 months later that will include some, but not all, of the things done at the first visit.

Between the two visits (the initial visit and the second visit 18 months later) you will be ask put use a special device which pricks the skin on your finger so that you can put a spot of blood on a piece of paper and mail this back to us every 4 and half months throughout the study. You will also be asked to wear a small device that measures how physically active you are, which we would like you to mail back to the study centre in a pre-paid envelope.

A small number (about one in five of those who take part) will undergo an almost identical examination to the second visit 36 months after the first visit (18 months after the second visit).

The following describes the visits in detail.

Baseline Visit (first visit).

The first visit will involve a number of assessments, which are outlined below, and returning the questionnaire/stool sample. This visit should last about 4 hrs in total. You will be asked to attend the research centre between 08:00 and 10:00am. You will be asked to attend fasting, which means you should not have eaten, smoked or drunk anything from midnight the night before, or have exercised the morning of the test. You will be allowed to drink water on the morning of the visit, but no other type of beverage.

The following will take place during the visit:

- We will measure your:
  - Height and weight.
  - Waist, hip, calf and thigh circumferences.
  - Blood pressure
  - % body fat by impedance meter
    - A bioimpedance meter is a device that passes a small electric current through your body and measures the resistance. Based on the fact that lean tissue (such as muscle) has less resistance than fat this is used to calculate your body fat %.

- A thin plastic tube (cannula) will be placed into a vein in your arm so that we can take a sample of your blood, a finger prick blood glucose test will also be carried out. We will take blood samples when you arrive and during the oral glucose tolerance test (OGTT), which is outlined below. At the end of the test, the cannula will be removed and you will be offered a drink and light snack. During the test we will take a total of just less than 100mls of blood (around a cupful).
  - During the OGTT the following will take place:
    - You will be asked to drink a sugary drink (300 mls) in 5 minutes.
    - We will then take 7 small blood samples spaced over the following 2 hours (0, 15, 30, 45, 60, 90, and 120 minutes).
- You may be taken for an MRI scan. This test will only involve about half the study's participants. It involves a scan of the tummy which takes about 30 to 40 minutes. As the MRI scanner uses a strong magnet, we will check with you before this scan that you do not have any metal inside your body, such as joint replacements or surgical clips. We will ask you to lie on the scanning table for the scan and keep still during this time. The scan takes place inside an enclosed space, but you will be able to talk to the radiographers (people who do the scan) during this time and you can listen to relaxing music. The scan is completely painless and non-invasive, and does not involve radioactivity.
- You will be given a small monitor (about half the size of a match-box) called an accelerometer, which measures how much you move around. We will ask you to wear the accelerometer on an elastic belt around your waist for 10 days. At the end of this period we will ask you to return the monitor to us in a prepaid and addressed padded envelop.
- You will have been sent two questionnaires related to your diet and quality of life which you should have completed before the first visit. We will collect these from you at the visit.
- We will have given you a special kit in which to collect a small sample of your stool. We will ask you to bring this with you to the first visit.
- A toenail clipping sample will be taken.
- We will ask you to provide us with a urine sample (a pregnancy test will also be carried if you are a woman and premenopausal).
- On completion of the study you will be given lunch.

Follow-up visit at 18 months (Second visit).

You will be sent a reminder and relevant information in the days preceding your second visit. All participants will be invited to take part in this visit; about one in five of those who take part will be asked to undergo the same measurements as at the baseline visit, whilst the remainder will undergo fewer measurements. As with the first visit, you will be asked to attend fasting (nothing but water from midnight).

The following will take place during the second visit:

- We will measure your:
  - Height and weight.
  - Waist, hip, calf and thigh circumferences.

- Blood pressure

- We will ask you to provide us with a urine sample (with pregnancy test, where relevant)
- A cannula will be placed into a vein in your arm to take blood.

If you are asked to undergo the more detailed set of measurements, we will ask you to do the following:

- OGTT (as in Visit 1).
- MRI scan (as in Visit 1).
- Diet and physical activity assessments (as in Visit 1). We will also ask a you to wear an additional physical activity monitor as in Visit 1 on your wrist.
- On completion of the study you will be given lunch.

Final visit at 36 months (third visit).

If you were asked to undergo the more detailed set of measurements during the second visit, we will also ask you to come back for a third and final visit 36 months after your first visits (18 months after your second visit). You will be sent a reminder and relevant information in the days preceding Visit 3. As before, you will be asked to attend fasting (nothing but water from midnight). The visit is similar in duration and content to the previous two visits.

The following will take place during the visit:

- We will measure your:
  - Height and weight.
  - Waist, hip, calf and thigh circumferences.
  - Blood pressure
- We will ask you to provide us with a urine sample (where relevant, a pregnancy test will be performed).
- A cannula will be placed into one of the veins in your arm for taking blood. We will take samples of blood when you arrive and during the OGTT.
- OGTT (as in Visit1).
- MRI scan (as in Visit1).
- Diet and physical activity assessments (as in Visit1). We will also ask you to wear an additional physical activity monitor as in Visit 1 on your wrist.
- On completion of the study you will be given lunch.

Are there any risks?

The insertion of the cannula into the forearm vein may cause discomfort and may result in bruising that may persist for a few days after the test.

The study does not involve a new drug or agent.

The MRI scan uses a strong magnet only, and does not use x-rays or other harmful radiation. Because the MRI uses a magnet, we will need to make sure you do not have any metal inside your body that is magnetic, and you will be asked about this. There are no known safety concerns with MRI scanning. No contrast injections, which are sometimes used with other types of scan, will be given during the MRI scan. Some people find MRI machines claustrophobic.

Can I drive before and after these visits?

There will be no problem driving to or from each visit. We will ensure that your blood sugar levels are safe before you leave the research facility.

What about travel expenses?

Your travel expenses will be reimbursed in full.

Are there any direct benefits to those taking part?

In general there is no major direct benefit to you as a participant in this study. The main benefit is that through this research, we hope to better understand the causes of diabetes, which may lead to improved prevention and treatment of the disease.

What will happen if the MRI scan shows up something abnormal?

The MRI scan is being carried out to look at the liver, pancreas. As part of this process, we will obtain images of the abdomen and lower chest. Occasionally abnormalities are seen. Often these have been there for years and are of no concern; rarely, a serious abnormality is seen that requires follow up by your doctor. The radiologist involved in this study, who is an expert in MRI scans, will study any abnormality and decide whether this needs to be followed up. In this circumstance we will tell you and your General Practitioner, and make your MRI images available to your clinical team. The MRI scans for this study are not themselves suitable for diagnosis.

What about confidentiality?

We regard the protection of your personal information (i.e., the security of any data we collect from you as part of this study) as being extremely important. We have special systems in place to make sure that once we obtain your consent and you have completed the study visits that we then separate your name, address and other information that might identify who you are from the rest of your data, which helps ensure third parties cannot link information about your health to your name, address or other information that identifies who you are.

When you have given consent to take part in the study, we assign you a code known as a “study number”. Your study number is then used in place of your name when keeping track of the remaining information or samples we collect from you. We will not write your name, address or health record number on any of your samples nor on the forms that are used to collected information from you during the study. In this way, your study data and samples are anonymised. When the information and samples we collect from you are exchanged amongst scientists working within our study, your samples and data will be identified using your study code only and we will never pass on your name or address to scientists or third parties who are not directly involved in your clinical care, such as your GP. Your name will never appear in any report or publication that arises from this study.

delete if not appropriate for site < We store the file and consent form containing your name, address, health record number and study number in a special locked database held separately from the rest of the information. This is never shared with anyone outside of the research team in <study site>. The only reason for storing this

information is to allow information from your past and future health care record to be extracted and linked anonymously to the study data for the next 10 years. >delete if not appropriate for site

What will be done with the information collected about me and blood, stool, nail and urine samples?

The anonymised data we collect from you directly and, with your permission, indirectly from your medical records will be linked to your anonymised MRI images and blood, stool, nail and urine samples. These data and samples will be stored for many years on a secure database and used as part of this study to investigate why people get diabetes. The studies to be carried out will include genetic tests on your DNA and other genetic material as well as measuring other substances in the blood, stool, nails and urine.

Who will have access to my anonymised data and samples and how will this be controlled?

This study is being conducted by a large group of European doctors and scientists at universities and hospitals as part of a consortium that includes a number of companies from the pharmaceutical industry. None of these groups will ever have access to your name, date of birth or address. Your anonymised data will be stored on secure computers at the research centre and at the central DIRECT data facility in Denmark. These data will be accessible by members of the consortium and by approved members of the scientific research community, but access to the data and your blood, stool, nail and urine samples will require approval by a data access committee which will ensure that all use of the data and samples is for justified scientific research and that these data and samples are handled in a secure way that safegaurds your confidentiality. Your samples and data will only be used for research involving diabetes, its treatment and related conditions. Where necessary, permission will be sought from an ethics committee to use your samples or data for future studies into diabetes, its treatment and related conditions. We may also invite you to take part in future studies based on the results from the DIRECT study.

Where commercial companies conduct research or provide financial assistance to non-commercial researchers to do the research, they could require the commercial rights to benefits arising from the discoveries. To allow potential collaborators to proceed, you are asked to waive any future claim to financial benefit through participation in the study. So for example, if a company discovered the basis of a new diabetes drug by using your blood sample (as one of thousands of blood samples), and went on to profit from this discovery, you would have no future claim on this profit.

Could I withdraw from the study?

Yes. You would be free to withdraw from the study at any time by contacting your local diabetes study team (contact details are at the end of this document). You would then carry on with your diabetes treatment as planned by your health care team. We would still store and utilise your samples and data collected up until that point unless you specifically ask us not to by formally withdrawing your consent. If you decided to withdraw your consent, we would destroy any of your samples held by us and from then on any anonymised data collected from you would not be included in the analyses we perform as part of this study. Importantly, if your anonymised data had already been included by researchers in an analysis from which results had been derived and reported, this could not be changed.

What about insurance companies?

Sometimes insurance companies ask people if they've ever had any genetic tests. However participation in this study does NOT constitute a "genetic test" as defined by insurance companies. The fact that you are taking part in this study will not affect your ability to get insurance. Data will never be released by us to a third party unless we are legally required to do so.

Will there be any further contact?

At the time of participation we will ask you to indicate if you are willing to be re-contacted by the study team in the future to be invited to participate in any ethically approved research related to this project.

Will my GP be informed that I am taking part in the study?

Yes, if you agree, your GP will receive a copy of the results that we provide for you.

Who has reviewed this study?

The <insert relevant ethics committee details here>, which has responsibility for scrutinising all proposals for medical research, has reviewed the proposal. It is a requirement that the research records are made available to monitors from Lund University in Sweden, whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

What if I have a complaint?

If you are harmed as a result of taking part in this study, then compensation can be sought from the study sponsor. A copy of the guidelines is available on request. However, the sponsor will not compensate you where harm results from any procedure that is not in accordance with the study protocol. Under these circumstances, your right at law to claim compensation for harm where you can prove negligence is not affected.

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

If you have any questions regarding this study you can phone the study team.

<Contact details of study team>

Or if you wish to seek independent advice then please contact <details of local contact> who is a clinician with an interest in diabetes and is independent of the research team