PARTICIPANT INFORMATION SHEET

THE ROLE OF PHOSPHODIESTERASE 3B IN THE REGULATION OF HUMAN ADIPOSE TISSUE BIOLOGY AND SYSTEMIC GLUCOSE AND LIPID HOMEOSTASIS

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We are inviting individuals to join this experimental medicine study aiming to understand the role an enzyme called Phosphodiesterase 3B on fat tissue and metabolism.

This document gives information about the study including the aims, risks, and benefits of taking part in this study.

In this information sheet, we use the words "I" and "you" referring to the study participant.

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You are being invited to take part in a research study. Before deciding whether to take part, you need to understand why this research is being done and what it involves. Please take time to read the following information carefully and talk to others about the study if you wish. Please ask us if anything is not clear or if you would like more information. Please take time to decide whether you wish to take part.

Section 1 tells you the purpose of this study and what will happen to you if you take part. Section 2 gives you more detailed information about the conduct of the study.

Section 1: Purpose of the study and what will happen

1. What is the purpose of the study?

The purpose of this study is to discover how an enzyme called Phosphodiesterase 3B (PDE3B) affects fat, glucose, and lipid metabolism in people.

2 What is tested?

The goal of this study is to answer the following questions:

1) What is the role of PDE3B in fat tissue function?
2) How does PDE3B influence the way one's body handles blood sugars and lipids?

3 Why have I been invited?

Because of your participation in a previous research study, your *PDE3B* gene has been characterised. We are now seeking to recruit people (21-75 years old with no major health problems) who have the typical form of that gene and an equal number of people who have a variant that reduces the function of PDE3B. We think that having the variant might be a positive thing and be associated with protection from developing metabolic disease. Having participants like you involved in our research will enable us to uncover the role of PDE3B in people and may help us build treatment strategies to prevent or tackle metabolic diseases such as diabetes and heart disease. During the study, neither you nor the study team will know whether you have the variant of interest or not. At the end of the study, we can let you know (if you are interested) which version of the gene you have.

We plan to include approximately 40 participants. All study visits will take place at the Translational Research Facility (TRF), which is part of the Addenbrooke's Hospital.

4 Do I have to take part?

Participating in this study is completely voluntary. If you decide to participate you will be asked to sign an Informed Consent Form, however you are still free to change, reduce or completely withdraw your participation after you agree to join this study. The only exception to this is where your participation must change or be stopped by the study doctor to protect your safety or well-being.

You can leave or change your participation in the study at any time without giving a reason. However, understanding your reasons for participation changes can help the study to reach more reliable conclusions when the team analyse the data at the end of the study or may

inform the design of future studies. If you choose not to participate, change your participation, or leave the study, your future medical treatment and normal standard of care will not be affected in any way.

What will happen if we lose contact with you*?*

Should we be unable to contact you for over a month (via phone, email, or text), we will consider you "lost contact". If we lose contact with you for over a week, we will pause your study and cancel the future study visits. Compensation will be provided for the visits completed to that point. Deduction in compensation may apply if the study devices are not returned (details listed in Expenses & Payments section starting on pages 10-11).

Should you need to pause your participation in this study due to unforeseen circumstances, please feel free to contact us once you are ready to re-join. We might be able to continue or re-start the whole process from the pre-screening and consent depending on the time point that we lost contact and if you had any potential changes in your health status or factors that may affect it.

5. What will happen to me if I take part?

If you agree to participate in the study, you will sign the Informed Consent Form and be given a copy of this to take away and refer to later.

The specific screening tests and procedures that will take place in the screening visit are listed in **Table 1** below.

Table 1. Assessments to be performed in the screening visit

Name	Visit Description	Duration
Screening Visit	- Medical history and physical examination - Urine pregnancy test (females of child-bearing age) - Blood tests - Oral glucose tolerance test (if needed) - Resting electrocardiogram - Vital signs - Questionnaires about current alcohol and food intake - Body composition measurements with dual X-Ray absorptiometry (DXA -if needed)	Up to 5 hours

You will be asked to fast for ~12 hours before the screening visit and it will take up to 5 hours to complete. The visit includes the following tests and procedures:

- Review the Patient Information Sheet and Informed Consent Form with the study team; once all your questions have been satisfactorily answered, you will be asked to sign the Informed Consent Form if you wish to participate in this study.
- A medical examination including an interview to review your medical history, physical examination, resting electrocardiogram and blood tests.
- A urine sample will be collected to perform a urine pregnancy test for women who are able to become pregnant.
- An oral glucose tolerance test may be completed to check for diabetes (if needed).

- Perform resting electrocardiogram and measure vital signs (including heart rate, respiration rate, temperature, and blood pressure).
- The Alcohol Use Disorders Identification Test (AUDIT) will be completed to learn about your alcohol intake. Alcohol affects blood sugar and lipid metabolism, which is being examined in this study. The AUDIT includes sensitive information. If your score excludes you from participating in the study, the questionnaire will be destroyed to protect your privacy.
- We will ask you about what types of food you normally eat (including food allergies and intolerances), when you eat, and your sleeping habits.
- A whole-body dual X-Ray absorptiometry (DXA -if needed)
- You will be provided with a wrist-worn activity monitoring sensor (if needed).

If you pass the screening visit, you will be asked to return for a second overnight visit where we plan to perform further metabolic testing assessments. The measurements performed in the metabolic assessment visit are detailed in **Table 2.**

Table 2. Investigations in the metabolic assessment visit

Name	Visit Description	Duration
Metabolic assessment visit	- Insulin infusion procedure - Adipose tissue biopsies - Vital signs - Pregnancy test (if you are a woman of childbearing potential)	~24 hours

Detailed Description of All Study Procedures

Medical History & Physical Exam. A study physician will review your medical history, medication history, and perform a brief physical exam.

Urine Pregnancy Test. If you are a woman of childbearing potential, you will be required to provide urine for a pregnancy test. Additional urine pregnancy tests will occur at metabolic testing visit. If you are pregnant, you will be withdrawn from the study and no further testing will be performed.

Vital Signs & Body Measurements. Measurements of resting blood pressure, temperature, heart rate, respiration rate, height, and weight will be taken. Shoulder, hip, and waist circumference measurements may be also taken.

Electrocardiogram (ECG). The ECG measures your heart rhythm painlessly. It involves putting sticky tabs on your chest, arms, and legs, then connecting the tabs to a wire from the machine that reads your heart rhythm. This test takes about 10 minutes.

Blood Tests. You will have blood drawn for routine lab analyses and outcome measurements. Using a small needle, blood will be collected from a vein in your arm.

Oral Glucose Tolerance Test (OGTT). An oral glucose tolerance test measures your body's response to a glucose (sugar) beverage. This test provides information regarding your risk for diabetes. After fasting for ~ 12 hours, you will drink a glucose beverage that

tastes like a soft drink. Blood samples (~12 samples in total) will be collected via an IV catheter just before and after you consume the glucose beverage up to ~ 3 hours later.

Questionnaires. As part of the screening process, we will ask your current alcohol and food intake and sleep habits, and any barriers that could interfere with your ability to complete all study requirements. You have the right to refuse to answer any questions that make you uncomfortable.

Body composition. If you take part in this study, you will have a whole-body dual energy X-ray absorptiometry (DXA) scan, unless you recently had one as part of your participation in another study. This would be additional to that you would have if you did not take part. You may be asked to change into clothing that is free of metal such as zippers. This measurement involves a very low dose of x-rays (ionising radiation). Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. We are all at risk of developing cancer during our lifetime. The normal risk is that this will happen to about 50% of people at some point in their life. Taking part in this study will add only a very small (0.00001 - 0.0001%) chance of this happening to you.

Activity Monitor. You will be asked to wear a monitor on your wrist for about 1 week after the initial screening visit, unless you recently had one as part of your participation in another study. The monitor will record your activity level. Once you have completed the 7 days monitoring period you will be asked to post the monitor back to us using the pre-paid packaging that we will provide.

Resting Energy Expenditure (REE). Your REE is a method used to access the number of calories you burn at rest. This test may be performed for about ~30-45 minutes during your 24-hour metabolic study, and insulin infusion visit. The REE measurement involves lying quietly in bed, while breathing normally with a clear canopy (a large plastic hood) placed over your head; the hood is ventilated with fresh room air. This test measures how much oxygen you breathe in and how much carbon dioxide you breathe out.

Insulin Infusion Procedure and Biopsy (Metabolic Assessment) Visit. This visit will allow the study team to thoroughly test: 1) how your body controls your glucose and fat levels and 2) how your muscles and fat contribute to the removal of sugars and lipids from your blood. Three days before the visit, you will be instructed not to exercise and will be given specific dietary guidance to follow (e.g., avoiding caffeine and alcohol). You will be asked to arrive at the TRF at about 7 pm the evening before insulin infusion and biopsy procedures. Dinner will be provided at about 8.00 pm.

- ***Insulin Infusion Procedure:*** The insulin sensitivity test provides an evaluation of how well your body responds to insulin to control blood sugar and lipids. The insulin sensitivity test will start at about 8 am and will last about 10 hours. A catheter will be inserted into a vein in your arm or hand and stable isotope labelled tracers of glucose (a sugar), glycerol and palmitate (component of fats and oils), insulin, and dextrose (another type of sugar) will be slowly infused. Another catheter will be placed into a vein in your hand to obtain blood samples throughout the infusion study. One third catheter may be also inserted into an arm or hand vein to draw blood in case the previous catheter fails. You will be asked to place your hand into a plastic box that

will warm your hand up before blood samples**.** You will be able to drink water but cannot eat any food during the insulin sensitivity test. A total of about 90 ml (about 6 tablespoons) of blood will be collected during the insulin sensitivity test. You will be asked to lie in bed quietly and remain in bed during the entire duration of the insulin infusion study. If you need to use the toilet during the procedure, you will be provided with a bedside commode. At the end of the study, you will be provided with food before being discharged from the research unit.

- ***Fat biopsy:*** During the insulin infusion test, samples of fat from your abdomen (belly) will be obtained to evaluate cellular factors involved in regulating glucose and lipid metabolism. The procedures will be performed by a Study Doctor or Study Nurse or Principal Investigator. All steps of the procedure will be described to you by team member who performs the procedure, and you will be able to ask any questions you may have. To obtain samples of fat tissue from your abdomen we will numb the area by injecting a numbing medication called lidocaine. The physician or Principal Investigator or Study Nurse performing the biopsies will perform a small incision of your skin and will remove a small piece of fat (~10 ml which is about 2 teaspoons). The incision is then closed with a piece of sterile tape/suture and a bandage, and an ice pack will be put on the biopsy site. Due to the sensitivity of some people during surgical procedures, a drape will be placed to block you from seeing the procedure and the instruments used. However, you will still be able to see the environment and watch TV if you wish. Before your discharge (after the biopsy) you will receive printed instructions and supplies for wound care. Some of the tests we run on your tissue samples are considered “genetic tests” because they measure how your genes affect your metabolism. The tests in this protocol are not the kind that may reveal that you are a carrier of a genetic disorder.

6. What will I have to do?

Participation in this study will last about 1-2 months (depending on scheduling). During the study period, you will be responsible for:

- Attending the two study visits
- Maintaining a stable body weight
- Wearing activity and sleep monitor as requested from the study team.
- Reporting changes in health and medication to the study team.

The researchers may take you out of the study, even if you want to continue, if you do not follow the study rules mentioned above.

Women Capable of Becoming Pregnant

You may not participate in this study if you are pregnant. If you are a woman capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study and before each study visit, especially before exposing you to research-related radiation. You must use effective birth control methods and try not to become pregnant while participating in this study. Please see the next page for a list of effective birth control methods.

If you become pregnant, there may be unknown risks to your unborn child, or risks to your unborn child that we did not anticipate. There may be long-term effects of some of the study procedures that could increase the risk of harm to an unborn child. You must tell the doctor if your birth control method fails while you are in the study. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

If you believe or know you have become pregnant while participating in this research study, please contact the research team member identified at the end of this document as soon as possible. Also, please discuss with the research team before participating in this study on how long you need to wait before becoming pregnant after completing the treatment or procedures in this study.

Contraception Requirements for Women

Some of the study ***procedures*** may harm a foetus or a breastfeeding baby. If you are pregnant or breastfeeding, you cannot take part in this study. If you think you may be pregnant, you should not volunteer for this study. If you can become pregnant, you must have a pregnancy test before you begin the study ***and while you are in the study.*** You must not get pregnant or breastfeed while you are in this study. If you are a woman who can become pregnant, you must take measures to avoid becoming pregnant while you are in this study. The following are acceptable measures to avoid becoming pregnant:

One of the following forms of birth control should be used:

- Abstinence (not having sexual relations with a person of the opposite sex) where this reflects your usual and preferred lifestyle.
- Implantable hormone
- Intrauterine Device (IUD, coil or intrauterine system)
- Female sterilization
- Hormonal injection or patches
- Oral contraceptives
- Vaginal ring
- Condom **and** cap or diaphragm **plus** spermicide (chemical that kills sperm)

You must use contraception, at least ***one month*** before starting study treatment unless you abstain from sexual intercourse. You must use contraception during your participation in the study.

You do not need to use contraception if:

- you have only one partner, and the man has had an operation to cut the tubes that carry sperm (vasectomy)
- you (or your partner) are a woman who cannot become pregnant.

You should tell the study team if you feel unwell or different in any way. If you have any major concerns or are feeling very unwell, please contact the study team using the contact numbers at the end of this information sheet.

7. What are the side effects of the intervention being tested?

There is no intervention tested in this study.

8. What are the possible disadvantages and risks of taking part?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study. If new risks become known, you will be informed of these risks. The physician or the Principal Investigator of the study will inform you of any new discoveries that could make you change your mind about whether you want to continue in the study.

Catheter insertion, blood drawing and intravenous infusions

Common (less than 10% of participants)

- It is likely that the intravenous catheter insertion will cause discomfort, bruising, and/or bleeding.

Uncommon (less than 1% of participants)

- Occasionally some people experience dizziness or feel faint during catheter insertion and/or blood drawing.

Rare

- The total amount of blood that will be collected during the testing sessions is about 300 ml (about 18 tablespoons). The risks associated with giving this amount of blood include headache, nausea, and lightheadedness; however, this amount is spread out between the two study visits, so it is very unlikely to cause a problem.
- An infection can occur at the catheter insertion sites. Careful techniques are used when inserting the catheters, and when obtaining blood samples to decrease the risk of infection.
- If the IV catheter slips out of the vein, fluid could collect in your arm and cause swelling and discomfort. Catheters will be placed and secured by qualified and experienced personnel, and you will be carefully monitored to decrease the risk of slipping.
- Infusion of insulin can cause an allergic reaction (including rash, swelling of the tongue or throat, and/or difficulty breathing).
- Rarely, an infection can occur from the infusions. However, careful sterile technique will be always used in preparing the solutions to decrease the risk of this complication.

Fat biopsy

Common (less than 10% of participants)

- Possible side effects of the biopsy procedures are pain during and for some time after the procedure. The biopsy site may also be tender or sore for two to three days after the biopsy.
- Swelling, bleeding and/or bruising may occur at the biopsy site. Pressure will be applied to the biopsy site after the tissue has been collected to minimize these risks.
- Lidocaine injection may be painful during the injection followed by numbness in the area injected (see lidocaine risks below).

Uncommon (less than 1% of participants)

A biopsy can cause temporary numbness or loss of sensation in the skin in the region of the biopsy site.

Rare

- An infection can occur at the biopsy sites. Careful aseptic techniques are used when obtaining biopsy samples to decrease the risk of infection.
- Light-headedness, dizziness, fainting, pain, and/or nausea may occur during the biopsies.

Lidocaine: Please inform the doctor or nurse if you have a known allergy to lidocaine.

Common (less than 10% of participants)

- Numbness and tingling at lidocaine application site.
- It is common to feel some mild discomfort when the lidocaine is first administered.

Rare

- An allergic reaction may occur that would result in minor swelling or irritation at the injection site.

Very Rare

- People may feel light-headed and nauseated or even faint due to the pain at the injection site.
- An allergic reaction may be severe and cause itching, swelling of the face or extremely low blood pressure or difficulty breathing may occur. Severe cases of generalized allergy may be life threatening. All these symptoms will be treated should they develop.

Dual energy x-ray absorptiometry (DEXA)

This study involves a radiation exposure that is typical of other diagnostic tests for ionizing radiation. The amount of radiation exposure received in this study is below the levels that are thought to result in a significant risk of harmful effects.

Electrocardiogram

Common (less than 10% of participants)

- Redness or skin irritation from electrodes (sticky tabs).

Oral glucose tolerance tests

Rare

- Blood sugar levels during the oral glucose tolerance test are expected to increase but occasionally they could become low causing you to feel sweaty, shaky, or nauseated. However, blood sugar is carefully monitored throughout these tests to decrease the risk of these problems and if you develop these symptoms, we may have to stop the test and correct the dropping blood sugar (called hypoglycaemia).

Insulin

Rare

- Allergic reaction (including rash, swelling of the tongue or throat, and difficulty breathing). Severe cases of generalized allergy may be life threatening. All these symptoms will be treated should they develop.
- Low or high blood sugar causing you to feel sweaty, shaky or nauseated. Your blood sugar will be carefully monitored to avoid this risk.

Interviews/Questionnaires

Rare

- You may experience emotional discomfort when answering some questions in the questionnaires. You may choose not to answer any questions that make you feel uncomfortable.

Travel for study visits

Common (less than 10% of participants)

- Frequent travel for study visits may be inconvenient and require missing work.

9. What are the possible benefits of taking part?

There is no guarantee that you will benefit from taking part in this study. You may obtain information regarding body composition and receive a medical examination and the results of some of your blood tests. Information collected as part of your participation in this study may benefit people at risk of developing chronic disease in the future. You will help us learn more about the role of PDE3B in people. This information may benefit the society by leading to more effective treatment strategies for the obesity-related diseases (type 2 diabetes, heart disease, etc.).

10. What are the alternatives for treatment?

This study is an observational study which cannot substitute your regular medical care. You should continue to see your regular medical providers and follow their advice on prescribed medications (if needed). If you decide not to participate, you have other choices. For example, you may choose to take part in a different study if one is available or opt to make other lifestyle changes that are more suitable for you.

11. What happens when the study stops?

The researchers may stop you from participating in this study, even if you want to continue, if:

- Your health changes and staying on the study is no longer in your best interests.
- You do not follow the study rules, or you no longer meet the requirements to be in the study.
- The study is stopped by the sponsor or researchers.

When the study stops, we will inform you via phone/text/email and cancel all your future study visits. Compensation will be provided for the visits completed to that point.

12. Expenses & Payment

There will be no cost to you for any of the study activities or procedures. Neither you nor your insurance carrier will be charged for taking part in the research. All costs associated with the study including travel costs (except the cost of your daily meals) will be paid by the sponsor of the study. If you agree to take part in this research study, we will compensate you up to £350 for your time and effort. If you do not complete the study, you will receive prorated payment based on the number of study visits completed. The payment is considered to constitute income and it may affect eligibility for means-tested benefits. Payment forms will be processed when your participation in the study has ended and upon return of any study supplies and materials, including the physical activity monitor. If unreturned, the cost of the physical activity monitor, may be deducted from your total compensation, with a maximum deduction of £100 (the cost of the device).

Table 3. *Study compensation.*

Study Visit	Amount
Metabolic and biopsy study visit	£290
Screening visit	£60
Total for completing both visits	£350

In the event a specific test needs to be repeated to ensure the scientific strength of the results, you will be compensated for the time and inconvenience of repeating that specific test. The additional compensation would be the same as the compensation provided for the original test.

Section 2: Study Conduct

13. What if new information becomes available?

Sometimes during a study, new information becomes available which might affect your decision to continue participating in this study. Your study doctor will contact you to discuss the new information and whether you wish to continue participating in the study. If you still wish to continue the study, you may be asked to sign a new Informed Consent Form.

The study sponsor, the regulatory authority or the study doctor may decide to stop the study at any time. If that happens, we will tell you why the study has been stopped and arrange for appropriate care and treatment for you.

14. What if I decide to change or stop my participation in the study?

You are free to change your participation or withdraw from this study at any time without giving a reason and without affecting your future care or medical treatment.

If you decide not to participate any further, no further tests will be performed on you and no further research samples will be collected. Any data or samples already collected or results from tests already performed on you, or your samples will continue to be used in the study analysis, unless you explicitly request otherwise.

You do not have to be in this research study. If you decide not to take part in this study, you have other choices. For example, you may choose to take part in a different study if one is available or opt to make other lifestyle changes.

The study doctor may also choose to withdraw you from the study if they feel it is in your best interests or if you have been unable to comply with the requirements of the study. Reasons for study withdrawal could include:

- You have experienced a serious side effect.
- You are unable to complete the visits, intervention or study documentation as required.
- You become pregnant or plan to become pregnant.
- The study doctor feels you no longer appear to benefit from the treatment.
- The study is stopped by the sponsor or researchers.

If you have experienced any serious side effects during the study which requires you to change your participation in this study, your study doctor will follow-up with you regarding your progress until the side effect has stabilised or resolved.

15. What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. If you have any concerns about any aspect of this study, you should speak to your study doctor or Principal Investigator who will do their best to answer your questions.

If something does go wrong, and you are harmed by taking part in the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against Cambridge University Hospitals National Health Service (NHS) Foundation Trust or the University of Cambridge. The normal NHS complaints mechanisms will still be available to you (if appropriate). The University has obtained insurance which provides no-fault compensation i.e., for non-negligent harm, you may be entitled to make a claim for this.

If you wish to complain or have any concerns about any aspect of the way you have been approached or treated during this study, you can do this through the NHS complaints procedure. In the first instance it may be helpful to contact the Patient Advice and Liaison Service (PALS) at Addenbrooke's Hospital, telephone no 01223 516756 or email cuh.pals@nhs.net

16. How will we use information about you?

Cambridge University Hospitals NHS Foundation Trust (CUH) and The University of Cambridge are the Sponsors for this clinical study based in the United Kingdom.

We will need to use information *from* your medical records and/or your GP for this research project. This information will include your:

- Initials
- NHS number
- Name
- Contact details
- Date of birth

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. We will keep all information about you safe and secure. Your data will have a code number instead. We will keep all information about you safe and secure. 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 you took part in the study.

You 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.

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.

You can find out more about how we use your information:

- At one of following links
  - www.hra.nhs.uk/information-about-patients/
  - https://www.cuh.nhs.uk/corporate-information/about-us/our-responsibilities/looking-after-your-information
  - https://www.medschl.cam.ac.uk/research/information-governance/
- by asking one of the research team
- by sending an email to the Cambridge University Hospitals NHS Foundation Trust Data Protection Officer (cuh.gdpr@nhs.net) or the University of Cambridge, Information Governance team at: researchgovernance@medschl.cam.ac.uk

17. What are your choices about how your information is used if you withdraw from the study?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we have already collected. Data and specimens collected up to the point of withdrawal will be used by the investigators to perform the previously specified assessments. If you do not want this to happen, tell us and we will destroy your samples. 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.

18. 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-participants/
- our leaflet available from www.hra.nhs.uk/participantdataandresearch. Or please visit, for Cambridge University Hospitals NHS Foundation Trust: https://www.cuh.nhs.uk/participant-privacy/. For University of Cambridge: https://www.medschl.cam.ac.uk/research/information-governance or email The Information Governance team at: researchgovernance@medschl.cam.ac.uk
- by asking one of the research team members. Please see page 19, section 23
- by sending an email to cuh.gdpr@nhs.net mailto:or
- by ringing us on 01223 762634

19. What will happen to my samples/data?

During this research, the study team will obtain information about you. They will also collect biological specimens from you such as blood and tissue samples. The information and specimens will be used for this research and may also be used for other research studies. De-identified information about your health and care or biospecimens (such as blood and tissue) may be made available for other research studies run by CUH and/or the University of Cambridge or other organisations. These organisations may be NHS or other public sector organisations, academic institutions, charities, and commercial companies in the UK or abroad. Before your data is shared with other organisations, all personal identifiers, such as names, addresses and dates of birth, will be removed. Making information from studies available for further research helps maximise the benefit of conducting studies and allows other researchers to verify results and avoid duplicating research. To facilitate this, some study datasets are made available to researchers via a public online database and become "open data". Data are thoroughly de-identified before they are submitted to an open data platform and once the data are uploaded, we do not have control over how they are used. We will not ask for additional consent from you to use your information and specimens for the additional research.

We cannot promise complete confidentiality. If you agree to be in this study, existing laws may permit or require us to show information to university or government officials responsible for monitoring this study. We may also show your medical records to study monitors, auditors, and the local ethics and other regulatory committees responsible for the oversight of research. These groups are obligated to maintain your confidentiality. The following is a list of individuals who may access your records:

- Members of the research team
- Offices and committees responsible for the oversight of research
- Personnel who schedule or perform medical tests or procedures, handle accounting and billing, or do other tasks related to this study
- The Medicines and Health care products Regulatory Agency (MHRA)

If you agree to participate in this research study, a signed copy of this consent document may be filed in your electronic medical record (EMR) and your study participation may be added to your EMR. Details of your participation and some of the study results (standard clinical measureless, for example blood cholesterol, blood glucose, etc.) will be held in your Addenbrooke's Hospital records.

A description of this study will be available on http://www.ClinicalTrials.gov, as required by U.K. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this web site at any time.

Cambridge University Hospitals NHS Foundation Trust (CUHNFT) and the University of Cambridge are joint sponsors for this study based in the United Kingdom. CUHNFT and the University of Cambridge will be using information from you and/or your medical records to undertake this study and will act as joint data controllers. This means that both organisations are responsible for looking after your information and using it properly. The University of Cambridge and CUHNFT will keep identifiable information about you for 5 years after the

study all primary outcomes of study have been published. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways 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.

We will keep the data we collect about you, and we ***keep*** your data and samples for an indefinite period. Keeping data or samples for future research is called "banking." The banked data and samples will be kept in a secure location for use by researchers.

This is what will happen with your banked data and samples:

- We will use the data and samples in other research projects ***in nutrition and metabolism.***
- The data and samples may be shared with other researchers at the University of Cambridge and with researchers outside of the University.
- The banked data and samples will be labeled with a code instead of your name.
- When we give your data and samples to other investigators for research projects, they will not be able to use the code to figure out which data and samples are yours.
- The research team will maintain a link between your data and samples and your identifiable information kept by the study team.
- You can request to have your data and samples removed from the bank by contacting the research team at any time.
- You will not be given the results of any of the studies done using your banked data and samples. Also, banked data and samples will not be shared with your health care providers or used in your treatment outside this study.

At the end of the current study, the research team will analyse the results of all the study participants together to address the main questions of this investigation.

Genetics

Some of the tests we may perform on your blood and tissue samples may be genetic testing, which is done on your DNA. DNA, or deoxyribonucleic acid, carries the genetic instructions for the cells that make up your body. Genes tell your body how to do things like form your spine, or what colour your eyes should be. We may do whole genome testing for this study. Your "genome" is the complete DNA instruction book. "Whole genome testing" means making a list of the entire order, or sequence, of the DNA in your genome. The DNA samples and information may be sent to other researchers and will not include personal information like your name or your birthdate. However, even without your name or other identifiers, your genetic information is unique to you, like a fingerprint. Scientists expect that over the next few years, researchers will be able to look at your genetic information and be able to trace the data back to you (and potentially also to your blood relatives). Performing this assessment is optional for your participation in this study.

Samples containing genetic material will be frozen and stored in Addenbrooke's Hospital for potential future testing. We do not have immediate plans to perform genetic testing in the samples of this study, but we may do so in the future. Unless explicitly told otherwise by you,

any samples already collected will continue to be used in the study analysis should you decide to withdraw from this study early. Should you opt out from the genetic analysis part of this study, your samples will be excluded from the genetic testing. Hence, we will use them only to perform the other planned analysis.

At the end of this study, cellular material (whole blood, tissue samples, paraffin blocks) will be retained by the study team in a Human Authority's (HTA) licenced facility pending Ethical Approval for use in another project. The non-cellular material (e.g., serum, plasma, DNA extracted) samples will be kept by the study team until results are published and then disposed in accordance with the HTA's code of Practice or will be used for future research.

20. What will happen to the results of the study?

When the results of this study are available, they may be published in peer reviewed medical/nutrition journals and used for medical presentations and conferences. They may also be published on the ClinicalTrials.gov. The results of the study will be thoroughly anonymised, and you will not be able to be identified from any of the data published.

If you would like to obtain a copy of the published results, please contact your study doctor directly who will be able to arrange this for you.

Upon completion of participation, the results that will be shared with you include copies of your clinical blood tests which are generated from the blood samples collected during screenings and/or other metabolic study visits, and body composition information. Other study results will not be shared with you, as they will generally be unavailable until the end of the study.

21. Who is funding the study?

The study is being funded by the Wellcome Trust, the European Association for the Study of Diabetes, and the Novo Nordisk Foundation.

22. Who has reviewed this study?

All research within the NHS is reviewed by an independent group of people called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the East of England - Cambridge Central Research Ethics Committee.

23. Further information and contact details

Contact details:

Additional information or questions regarding this study can be obtained by contacting the research team on 01223 762634 or by email on mc2425@medschl.cam.ac.uk

Who should you contact if you have any concerns about the study:

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (01223 762634). The Addenbrooke's Hospital Patients Advice and Liaison Service (PALS) is also available to offer advice or support and to listen to any concerns (01223 216756 or cuh.pals@nhs.net). If you remain unhappy and wish to complain formally you can do this though the NHS Complaints Procedure (University of Cambridge), details of which can be obtained from the hospital.

In the event of an emergency please contact:

In case of emergency, please contact the PI of the study at 07522186464 or your GP. You can alternatively also contact the following study related numbers at 01223 762634 (office hours only) or 01223 245151 via hospital switchboard for out of office hours.