

PARTICIPANT INFORMATION SHEET

METABOLIC PHENOTYPING IN INDIVIDUALS WITH VASCULAR EHLERS-DANLOS SYNDROME (vEDS)



**UNIVERSITY OF
CAMBRIDGE**

Cambridge University Hospitals **NHS**
NHS Foundation Trust

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We are inviting individuals who have vascular Ehlers-Danlos syndrome (vEDS) to join a study aiming to understand the effect of this condition on metabolism and diabetes risk.

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 whether having vascular Ehlers-Danlos syndrome (vEDS) influences how the body handles fat and sugar. These differences might affect the risk of developing conditions such as insulin resistance, type 2 diabetes, or other metabolic health problems. The goal of this study is to answer the following two questions: 1) Do people with vEDS have differences in body fat distribution and metabolism compared with people who do not have vEDS? 2) Do these differences make people with vEDS more likely to develop diabetes or related metabolic conditions?

By answering these questions, we hope to improve understanding of vEDS and its wider effects on health. This could help doctors give better advice and management to people living with vEDS in the future.

2 Why have I been invited?

You have been invited to participate in this study because you have genetically confirmed vascular Ehlers-Danlos syndrome (vEDS) and you are between 18-85 years old. We plan to include approximately 15 participants with genetically confirmed vascular Ehlers-Danlos syndrome the greater Cambridgeshire area. All study visits will take place at the Translational Research Facility (TRF), which is part of the Addenbrooke's Hospital.

3 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 your study doctor in order 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

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participation, or leave the study, your future medical treatment and normal standard of care will not be affected in any way.

4 What will happen if we lose contact with you?

Should we be unable to contact you for over a week (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.

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-start the study. 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 at the end of this document and be given a copy of this to take away and refer to later.

We understand that people with vEDS may be at higher risk of bruising or bleeding and may experience pain, fatigue, or joint instability during procedures. All study procedures will be carried out by experienced clinical staff who are familiar with vEDS, and we will take extra care to minimise these risks. This includes using gentle techniques for blood tests and scans, applying prolonged pressure where needed to reduce bruising or bleeding, and carefully monitoring biopsy sites for swelling or haematoma.

We will adjust positioning during scans or procedures to maximise comfort, and you may request breaks or stop a procedure at any time if you feel uncomfortable, tired, or unwell.

If any unexpected or acute issue arises during your visit, the study team will assess you immediately and, if needed, escalate care to the appropriate clinical services within Addenbrooke’s Hospital. Your safety will always take priority over completing any study procedure.

First, you will be asked to attend the first visit in the TRF after given informed consent to determine your eligibility for this study. The specific screening tests and procedures are listed in **Table 1** below.

Table 1. Timeline for screening visits – All participants

Name	Week	Visit Description	Duration
First Visit	0	- Medical history and physical examination - Urine pregnancy test (females of reproductive age) - Blood tests - Oral glucose tolerance test - Vital signs - Questionnaires about food intake and physical activity - Optional fat biopsy	~3-4 hours

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Second visit	1	- Liver stiffness scan - Body composition scan	~1-1.5 hours
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Please note that there is a possibility to combine the first and second visits into one visit if you would rather minimise the number of visits.

You will be asked to fast for ~12 hours before the first visit and it will take about 3-4 hours to complete. You will be given a meal and snacks as the end of the visit. 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 and blood tests.
- A urine sample will be collected to perform a urine pregnancy test for women who are able to become pregnant. The urine pregnancy test will then be discarded.
- An oral glucose tolerance test will be completed to check for insulin resistance and diabetes
- Measure vital signs (including heart rate, respiration rate, temperature, and blood pressure)
- We will ask you about what types of food you normally eat (including food allergies and intolerances and when you eat and your physical activity)

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. 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.

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 (~8) will be collected via an IV venous catheter just before and after you consume the glucose beverage up to ~ 2 hours later.

Questionnaires. As part of the screening process, we will ask your current food intake and physical activity. You have the right to refuse to answer any questions that make you uncomfortable.

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Body composition. If you take part in this study, you will have a whole body dual energy X-ray absorptiometry (DEXA) scan. 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) which is equivalent to that received on average in the UK, from natural sources of radiation in the environment in approximately 1 week. Ionising radiation may cause cancer many years or decades after the exposure. We are all at risk of developing cancer during our lifetime. Fifty percent of the population is likely to develop one of the many forms of cancer at some stage during our lifetime. Taking part in this study will add only a very small (0.00005 - 0.00011%) chance of this happening to the participant's individual risk for cancer.

Assessment of Liver Stiffness. Liver stiffness is an index of the health of your liver. For this assessment, a probe emitting painless pulses will be placed on the skin over your liver for a few minutes. The results are recorded on the equipment and an overall liver stiffness score is generated. The assessment takes less than 15 min.

Optional Fat biopsy: At the start of the first visit, samples of fat from your abdomen (belly) or thigh will be obtained to evaluate cellular factors involved in regulating sugar and fat 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 thigh or belly 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 cut 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 for 2 visits, which we will try to schedule within 1-2 weeks. There is an option to combine both visits into one visit if that is more convenient. During the study period, you will be responsible for:

- Reporting changes in health and medication to the study team.
- Attending the scheduled study visit or visits

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

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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.

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 prior to the DEXA scan**. 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, cap or diaphragm **plus** spermicide (chemical that kills sperm)

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 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.

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Catheter insertion and blood drawing

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 series of testing sessions is about 100 ml (about 7 tablespoons) or less. The risks associated with giving this amount of blood might include headache, nausea and lightheadedness; however, most people experience none of those symptoms as it is a small amount of blood, 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 by qualified and experienced personnel, and you will be carefully monitored to decrease the risk of slipping.

Biopsies (fat)

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 sites. Pressure will be applied to the biopsy sites 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.

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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 ionising 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.

Oral glucose tolerance tests

Rare

- Blood sugar levels could change (become low or high) during the oral glucose tolerance test causing you to feel sweaty, shaky or nauseated. However, blood sugar is carefully monitored throughout these tests to decrease the risk of these problems.

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.

8. 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 with vascular Ehlers-Danlos and those at risk of developing chronic disease in the future. You will help us learn more about the effect of COL3A1 mutation (causing vascular Ehlers-Danlos) in people. This information may benefit society by leading to more effective treatment strategies for vascular Ehlers-Danlos and the cardiometabolic related diseases (type 2 diabetes, heart disease, etc.).

9. What happens when the study stops?

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

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- 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 will be paid by the sponsor of the study.

In the event a specific test needs to be repeated to ensure the scientific strength of the results, you will be compensated for the travel 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.

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.

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.

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- You become pregnant or plan to become pregnant.
- 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 cu.h.pals@nhs.net

16. How will we use information about you?

Cambridge University Hospitals NHS Foundation Trust and the University of Cambridge are the sponsors of this research.

We will need to use information from you and from your medical records and your GP for this research project. This information will include your name, contact details, date of birth, NHS number and other relevant health information. 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. Your data will have a code number instead.

Cambridge University Hospitals NHS Foundation Trust and the University of Cambridge are responsible for looking after your information. We may share your information related to this research project with the following types of organisations:

- NHS organisations involved in your care or supporting the research
- Universities and academic research institutions
- Approved research collaborators and laboratories
- Regulatory authorities and research oversight bodies
- Approved commercial research partners (where relevant)

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We will keep all information about you safe and secure by:

- Storing information on secure, password-protected systems
- Limiting access to authorised members of the research team
- Using coded or pseudonymised data wherever possible
- Following NHS and University information governance policies

International transfers

Some of your data may be shared or accessed outside the UK for research-related purposes, including future ethically approved research using coded data. If this happens, we will only share the data that is needed and will take steps to minimise the risk that you could be identified. This may not always be possible, for example if you have a rare condition.

Your data may be shared outside the UK with:

- Academic research organisations
- Approved research collaborators
- Secure research databases

We will make sure your data is protected by using appropriate legal agreements and security safeguards to ensure your data has a similar level of protection as it does under UK law. We only allow organisations outside the UK to use your data for the purposes set out in our written agreements.

How will we use information about you after the study ends?

Once we have finished the study, we will keep some of the data so we can check the results and support future research. We will write our reports in a way that no-one can work out that you took part in the study. Your identifiable information will be kept securely for the minimum period required by regulatory and research governance requirements, after which it will be anonymised or securely archived.

What are your choices about how your information is used?

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.

You have the right to ask us to access, remove, change or delete data we hold about you for the purposes of the study. You can also object to our processing of your data. We may not always be able to do this if it would prevent us from carrying out the research properly. If this applies, we will explain why.

If you agree to take part in this study, you may also be asked separately whether you agree to your data being used in future ethically approved research.

Where can you find out more about how your information is used?

You can find out more about how we use your information, including how data may be transferred outside the UK:

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- by visiting www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team
- by emailing the Data Protection Officer at Cambridge University Hospitals NHS Foundation Trust: cuh.gdpr@nhs.net
- or the University of Cambridge Information Governance team: researchgovernance@medschl.cam.ac.uk

17. 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 and samples from this study may be shared with organisations outside the study clinic for approved research purposes. These organisations may include other NHS trusts, universities, charities, and commercial research partners in the UK or overseas. Any information shared will have personal identifiers removed so that you cannot be directly identified. The information and specimens will be used for this research and may also be used for other research studies.

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.

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 measures, for example blood cholesterol, blood glucose, etc.) will be held in your Addenbrooke’s Hospital records.

A description of this clinical 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.

Any surplus samples collected during this study may be stored and used in future ethically approved research to help better understand vascular Ehlers–Danlos syndrome and/or related metabolic conditions. This may include studies examining how genetic and biological factors influence blood vessels, fat distribution, metabolism, and cardiovascular risk. These samples will be coded so that you cannot be directly identified.

If you later decide that you no longer wish your previously collected samples to be stored or used for future research, you may request that these samples are withdrawn and destroyed, where this is still possible. To do this, you should contact the research team using the details provided at the end of this information sheet.

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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. 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 don’t 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.

18. 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.

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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.

19. Who is funding the study?

The study is being funded by the Wellcome Trust.

20. 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 - Cambridgeshire and Hertfordshire Research Ethics Committee.

21. Further information and contact details

Contact details:

Additional information or questions regarding this study can be obtained by contacting the research team on 07487602584, or by email on agnieszka.jakubowska@nhs.net

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 (07487602584 or 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 through 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 07792278605 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.