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Imperial College London

INFORMATION SHEET FOR RESEARCH PARTICIPANTS

You will be given a copy of this information sheet and a signed copy of your consent form to keep, should you decide to participate in the study.

What is the impact of a modified Roux-en-Y-gastric bypass operation on people with type 2 diabetes mellitus?
The LONG LIMB-2 double-blinded randomised controlled clinical trial

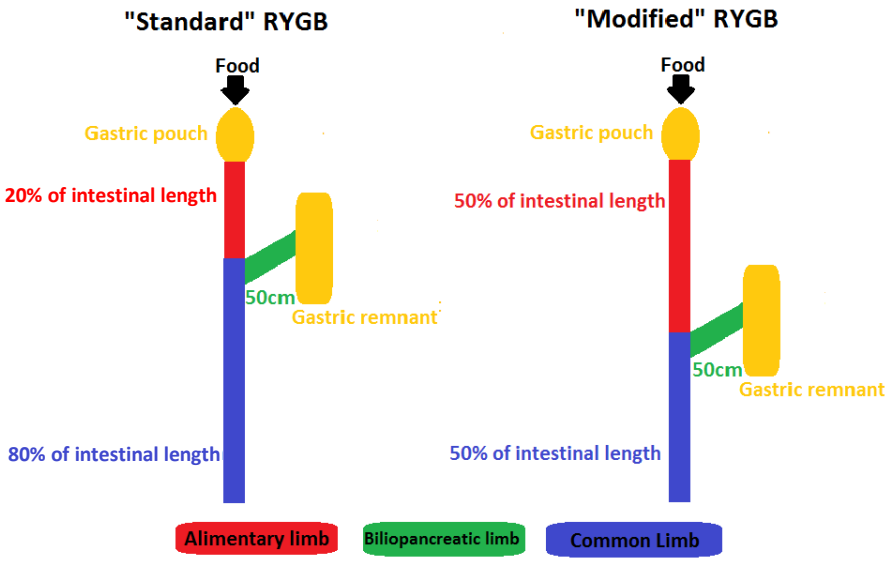
You are being invited to take part in a research study which forms part of a PhD. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. If you do decide to take part, please let us know beforehand if you have been involved in any other study during the last year. You are free to withdraw at any time without explanation. **Please be assured that if you decide not to take part this will not affect your clinical care in any way.**

WHAT IS THE PURPOSE OF THE STUDY?

You have been invited to participate in this research study because you have type 2 diabetes mellitus (T2DM), Body Mass Index (BMI) >30 kg/m^2 and are on the waiting list for bariatric surgery at Imperial College Healthcare NHS Trust, London. Obesity is the most potent risk factor for T2DM and it accounts for 80-85% of the overall risk of developing the disease. Modern laparoscopic bariatric surgery and in particular Roux-en-Y bypass (RYGB) is one of the safest operations in the field of surgery. In RYGB surgery, there are three intestinal segments or "limbs": the "alimentary limb" through which food enters through a much smaller portion of stomach (the gastric pouch) to the small intestine, the "biliopancreatic limb" which includes the bypassed segment of duodenum and jejunum (parts of the small intestine) and through which digestive juices from the bile duct and pancreas flow, and the "common limb" which is where food and juices mix together.

For this study we will be comparing the safety and efficacy of a "standard" RYGB surgery with a short alimentary and long common limb to the "modified" RYGB with a long alimentary and short common limb. The purpose of this study is to assess whether "modified" RYGB achieves better glucose (glycaemic) control. Of note, the "modified" RYGB is **not** a new or experimental procedure and is currently performed around the world. Therefore we expect that it carries the same risks as the standard RYGB.

Design of the "standard" and "modified" RYGB in the proposed LONG LIMB-2 trial.



WHY HAVE I BEEN INVITED?

You have been invited because you are 18 years of age (and over), have a BMI >35 kg/m^2 and a diagnosis of T2DM.

You should not take part in this study if you:

- Currently use or need insulin
- Have an unacceptably high risk of anaesthesia or surgery
- Are pregnant of breastfeeding

DO I HAVE TO TAKE PART?

No, it is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and will be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without providing a reason.

WHAT ARE THE TREATMENTS BEING TESTED?

We are testing the effectiveness and safety of "standard" RYGB surgery to "modified" RYGB surgery in patients with T2DM and obesity.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART?

The main benefit we hope for is significant weight loss leading to improved glycaemic (sugar) control and the possibility of remission of T2DM. There are other benefits to weight loss such as improvement in overall physical health and quality of life. You will also benefit from regular contact with a specialist.

WHAT ARE THE RISKS OF TAKING PART?

Risks of the clinical trial

For both "standard" and "modified" RYGB surgery: **these will be explained to you in greater detail by the surgical team.** The total risk for any complication is approximately 2%.

Common risks: chest infection, wound infection/haematoma, scars

Less common risks are blood clots in the lung or leg/s, bleeding intraoperative/postoperatively, anastomotic leak, port site hernia, injury of intra-abdominal viscera, internal hernia /small bowel obstruction, postprandial pain, dumping syndrome, severe malabsorption/excessive weight loss, conversion to open operation due to bleeding/visceral injury difficult anatomy, risk of not being able to do the bypass due to difficult anatomy (large liver, short mesentery, no space due to excessive intra-abdominal fat)

Very rare risk of death

During the study, experienced doctors will be available at any time should you have any concerns. You will be provided with a mobile number that you can call 24 hours a day 7 days a week in case you develop any unusual severe symptoms and want to speak urgently to a member of the team. If you suffer from any ill effects during the study you should report these to the doctors immediately. You may withdraw from the study at any time, without providing any explanation and this will not affect your future care in any way. If there are any unexpected side effects, the study will be stopped.

WHAT WILL HAPPEN TO ME IF I TAKE PART?

Screening visit
If you agree to participate in this study you will have an initial consultation with a medical doctor to check that you meet the inclusion criteria stated above. They will take a medical history, examine you and ensure that you have had all routine investigations as part of your NHS weight-loss treatment. They will also take additional blood tests to check your glycaemic control and lipid (cholesterol) levels. Females will be asked to provide a urine sample for a pregnancy test. The importance of effective contraceptive use for the duration of the trial will be emphasized in this patient.

Baseline visit
At this visit, we will measure your blood pressure and other vitals, perform a body composition scan, make a record of current medications and request any outstanding blood tests. If you meet the eligibility criteria, you will need to sign a consent form to say that you have understood what the study involves and are happy to take part. You will be randomly allocated (randomisation) to either arm of the trial – **this will take place intra-operatively (during the surgery**) following measurement of your total intestinal length (only patients with a total intestinal length of greater than 5.5 metres will be eligible for randomisation). If during the surgery your total intestinal length is less than 5.5 metres and you cannot be randomised, you will have the standard RYGB surgery and will not be recruited to the study. You will be informed of this once the surgery is over.

Interventions
The interventions will take place at Imperial College London NHS Trust. Both types of surgery will be performed by skilled bariatric surgeons.

Clinical trial follow-up
In addition to your routine NHS care follow-up you will be asked to attend follow-up for this clinical trial for 12 months. During these visits the following parameters will be measured/assessed:

- On day 10 post operatively: arterial blood pressure, body weight, waist circumference, body composition, blood tests, urine pregnancy test, number of glucose lowering medications, adverse events.
- At 3, 6 and 12 months: arterial blood pressure, body weight, waist circumference, body composition, blood tests, urine pregnancy test, number of glucose lowering medications, adverse events.

Female participants who are pre-menopausal and using the oral contraceptive pill (OCP) will be asked to stop it one month pre- and post-operatively (due to the risk of blood clots in the leg/s) and use alternative contraception which include:

- Barrier methods
- intrauterine device (non-hormone releasing)
- vasectomised partner: this is a highly effective birth control method provided that partner is the sole sexual partner of the trial participant and that the vasectomised partner has received medical assessment of the surgical success.
- sexual abstinence: sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments and when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods), declaration of abstinence for the duration of a trial, and withdrawal are not acceptable methods of contraception.

Following the surgery, this group of women can resume the OCP (one month after surgery) but there may be a chance of unplanned pregnancy as the surgery can theoretically affect drug absorption. **For this reason, we recommend the use of an alternative method of contraception (above) for the first 18 months post-operatively.**

Depending on the results of the study, we may ask you to be followed-up for longer than 12 months.

With your consent, any findings of clinical significance will be fed back to you and your GP.

Optional sub-study

The aim of this sub-study is to evaluate the effect of RYGB on intestinal absorption of ingested glucose. If you agree to take part you will be asked to attend the NIHR Imperial Clinical Research Facility (CRF) at Hammersmith Hospital after an overnight fast. Your glucose-lowering medications will be adjusted for 5 days before the visit using blood sugar readings obtained from finger-prick testing (these medications can affect results). You will be asked to refrain from alcohol and vigorous exercise for 24 hours before the visit. Each participant will have two visits – one pre-operatively and one post-operatively.

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A feeding tube will be placed by a trained medical professional using the CORTRAK system that tracks the position of the tube during placement. The tube will be inserted through the nose into the duodenum (first part of the small intestine) during the first visit and in the alimentary limb (jejunum – second part of the small intestine) after the operation (second visit). The position of the tube will be confirmed by testing the acid concentration of the fluid in the intestine. A solution containing glucose and a marker of glucose absorption will be infused through the feeding tube. An intravenous cannula will be inserted for blood sampling at various time points (seven in total). Once the last blood test is taken, both the feeding tube and cannula will be removed and you will be free to leave the facility. Potential risks of the feeding tube are local irritation to the nose, misplacement in the lung (CORTRAK system and pH testing are designed to pick up on this and correct it promptly) and a rare complication of causing a hole/tear in your oesophagus (called perforation; less than 1 in 5000).

As the first visit is scheduled to take place before the surgery, if you are not randomised during surgery, then you will be withdrawn from both aspects of the research study.

As this is an **optional** sub-study, participants can partake in the main study without opting into the sub-study.

CAN I TAKE PART IF I AM PREGNANT?

Pregnant women must not take part in this study because of potential risk to the women and the foetus. Women who plan to become pregnant in the 12 months immediately after surgery will also be excluded. All female participants will be asked to have a pregnancy test at the beginning of each study visit in order to ensure that they are not pregnant before the study visit commences. You should use contraception for the

duration of the study. If you find out that you are pregnant during the study, please inform the research doctor immediately.

WHAT IF NEW INFORMATION BECOMES AVAILABLE?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to continue in the study you will be asked to sign an updated consent form. Alternatively, on receiving new information your research doctor might consider it to be in your best interests to withdraw you from the study.

WHAT WOULD HAPPEN IF I LOST THE ABILITY TO CONSENT DURING THE COURSE OF THE STUDY?

In the unlikely event that during the course of the study you were no longer able to give your consent because you had lost the capacity to do so, the research team would withdraw you from the study and not perform any further testing on you. However, they would retain body fluid samples and personal data collected previously and would continue to use it for the purposes which you had already consented.

WHAT HAPPENS WHEN THE RESEARCH STUDY STOPS?

Once the study has finished, the results of the study will be made available to you and/or your GP should you wish. If you have any problems immediately following the study, then you should contact one of the research doctors.

With your consent, any samples taken during the sub-studies will be stored for up to 10 years in freezers located in the Department of Metabolism, Digestion and Reproduction at Imperial College London. After this time, samples will be destroyed but during the 10 years we may use the samples from the sub-studies in future research studies, send them to other organisations including outside of the EEA.

WHAT IF SOMETHING GOES WRONG?

Imperial College London holds insurance policies which apply to this study. If you experience serious and enduring harm or injury as a result of taking part in this study, you may be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation. Complainants may have to be pay their own legal fees.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Chief Investigator or the study team (07710067018). You can also contact the Patient Advice and Liaison Service (PALS) at whichever site your intervention for this study is being delivered. The normal National Health Service complaints mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial AHSC Joint Research Compliance Office (email: jrco@ic.ac.uk).

WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

Imperial College London is the sponsor for this study and will act as the data controlled for this study. This means that we are responsible for looking after your information and using it properly. Imperial College London will keep your personal date for:

• 10 years after the study has finished in relation to data subject consent forms.

• 10 after the study has completed in relation to primary research data.

We will need to use information from you, from your medical records and your GP for this research project.

This information will include your initials, NHS number, name and contact details. 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 are will not be able to see your name or contact details. 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 took part in the study.

LEGAL BASIS

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research

INTERNATIONAL TRANSFERS

There may be a requirement to transfer information to countries outside the European Economic Area (for example, to a research partner). Where this information contains your personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a European Commission (EC) adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient organisation that incorporates EC approved standard contractual clauses that safeguard how your personal data is processed.

For the purposes referred to in this privacy notice and relying on the bases for processing as set out above, we will share your personal data with certain third parties.

- Other College employees, agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third party service providers are required to enter into data processing agreements with us. We only permit them to process your personal data for specified purposes and in accordance with our policies.

WHAT ARE YOU 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.

- If you choose to stop taking part in the study, we would like to continue collecting information about your health from central NHS records, your hospital and your GP. If you do not want this to happen, tell us and we will stop.
- 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.

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-patients/
- by asking one of the research team

- by sending an email to suhaniya.samarasinghe@nhs.net, or
- by ringing us on 07710067018 .

CONTACT US

If you wish to raise a complaint on how we have handled your personal data or if you want to find out more about how we use your information, please contact Imperial College London's Data Protection Officer via email at dpo@imperial.ac.uk, via telephone on 020 7594 3502 and via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO). The ICO does recommend that you seek to resolve matters with the data controller (us) first before involving the regulator.

Imperial College Healthcare NHS Trust will collect information from you and your medical records for this research study in accordance with our instructions.

Imperial College Healthcare NHS Trust will keep your name, NHS number and contact details confidential and will not pass this information to Imperial College London. Imperial College Healthcare NHS Trust will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from Imperial College London and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Imperial College London will only receive information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

Imperial College Healthcare NHS Trust will keep identifiable information about you from this study for 10 years after the study has finished.

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research. Your information could be used for research in any aspect of health or care, and could be combined with information about you from other sources held by researchers, the NHS or government. Where this information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of health and care research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you, such as insurance. Where there is a risk that you can be identified your data will only be used in research that has been independently reviewed by an ethics committee.

With your consent, your GP will be informed of your involvement in the study.

WHAT WILL HAPPEN TO THE RESULTS OF THE RESEARCH STUDY?

The results are likely to be published within the 12 months following the study in peer-reviewed journals and websites as well as presented at medical conferences. Your confidentiality will be ensured at all times and you will not be identified in any publication as these are anonymised. A lay summary of the key results from the study will be written and sent and/or presented to you.

WHO IS ORGANISING AND FUNDING THE RESEARCH?

This study is being organised by the Department of Investigative Medicine, Imperial College London and funded by the J P Moulton Charitable Foundation. The doctor conducting the research will not be paid for including and looking after the subject in the study.

WHO HAS REVIEWED THE STUDY?

This study has been peer reviewed by the Imperial College Peer Review Office (Imperial College Healthcare NHS Trust) and reviewed and approved by the London-Westminster Health Research Authority.

CONTACT FOR FURTHER INFORMATION

If you experience any problems during the study, you may withdraw at any stage. You will also have direct emergency access, 24 hours a day, to one of the doctors involved in the study through mobile number 07710067018. The doctors may also be contacted through Dr. Alexander Miras secretary (0207 594 9048) during office hours. The hospital switchboard (020 8383 1000) holds the home and mobile phone numbers for all the doctors involved in the study and can contact them at any time outside normal working hours if necessary.

PAYMENT

You will receive £200 for your participation in the optional sub-study as reimbursement for your time and your travel expenses (assessable for tax and benefits).