Quadram Institute

Science Health Food Innovation

The REST Study

Glycaemic response to high REsistant STarch bread

NHS

Norfolk and Norwich University Hospitals

NHS Foundation Trust

REST Participant Information Sheet
Version 3
Date 25 September 2019
Investigator: Marina Corrado
IRAS 262271

CONTACT DETAILS

This booklet contains information about the REST study (Measuring the Effects of High Resistant Starch bread on glycaemic response).
Please read it carefully. If you would like to know more, please get in touch with the study team.

Marina Corrado is QIB Principal investigator of the REST study

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https://quadram.ac.uk/reststudy/

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The mission of the Quadram Institute is to understand how food and the gut are linked and to promote health and the prevention of disease. We aim to fine-tune the impact of foods on health, from early life to the extension of a healthy lifespan in old age and reduce the economic and societal costs of chronic diseases. The Quadram Institute is an interdisciplinary institute founded on a cluster of academic and clinical expertise at the Norwich Research Park, working alongside the food and pharmaceutical industries

What is REST

REST is about white bread made from wheat with high **RE**sistant **ST**arch, a type of fibre. Wheat bread made from white flour is one of the UK's favourite foods but normally, it has very low levels of fibre, which is an essential part of a healthy diet. Fibre exerts a protective role in reducing the risk of developing many common diseases that are diet related. However, in the UK, 91% of the adult population does not meet the recommended fibre intake of 30g per day1. A correct fibre intake helps to control blood sugar levels and body weight, reducing the risk of developing type II diabetes and obesity.

We have developed a type of white wheat flour that appears similar to conventional white flour but has higher resistant starch content. In this study, we want to compare body sugar levels (called glucose) after eating a high resistant starch bread with eating a conventional bread, low in resistant starch. This will help us understand whether high resistant starch bread can help to boost fibre intake of healthy people. In the long term, we might be able to determine whether high resistant starch bread can help reduce the risk of common chronic diseases such as type II diabetes and obesity

We are looking for:

- **Healthy** people
- Between **18 and 65** years of age
- Living within 40 miles from the **Norwich Research Park**

[1]The average fibre intake of adults in the UK is 19g per day. The recommended average intake for adults is 30g per day. From National Diet and Nutrition Survey (NDNS) from 2014 to 2016 by Public Health England

Meet the REST team

The study is led by Miss Marina Corrado, a PhD student at Quadram Institute Bioscience (QIB).

Dr. Jennifer Ahn-Jarvis and Mr Brendan Fahy are the study co- investigators helping the study to run.

Dr. Cathrina Edwards and Dr. Brittany Hazard are the study advisors.

The QI Clinical Research Facility (QI CRF) is managed by the Norfolk and Norwich University Hospital.

The study team is supported by a Medical Advisor and a Research Nurse.

Our Clinical Research Facility is equipped with Wifi and TV.

The Quadram Café is open from 8am to 6pm and parking is free of charge for REST study participants during study visits

Why am I invited?

We are inviting you because you showed an interest in the study. In this booklet, we will explain what participating in this study involves. Please read it carefully and discuss with others if you wish.

If, after reading it you would like to participate, or you would like to know more about the REST study, please let us know. We will contact you by phone to talk you through the details of the study and answer any questions you may have.

At the end of the talk, we will leave you some time to think about whether you want to book an appointment for eligibility screening at the QI Clinical Research Facility (QI CRF).

We will then ask you to sign a consent form, once you have understood what you are being asked to do for the study.

If you would like more information or have any concerns, please get in touch with us.

About the REST Study

REST happens during the week! Visits are scheduled according to your availability during week days, usually in the morning. We aim to complete the study within 2 weeks.

Screening visit
Sign consent, measure blood pressure, height, weight, do a blood test and health questionnaire

Calibration visit
Wear 2 glucose sensors until the end of the study
Training on how to complete a food and activity diary

Prepare for intervention day - at home
Eat a standard dinner provided by the study team then fast for 10h

Intervention visit 1
Breakfast: bread with Flora diary free spread and water
Finger prick blood tests
Fill in Questionnaire about your hunger and about the bread
Lunch is served!

Food diary - at home
Log ALL you eat and drink for 3 days in the app or paper (eat as you would normally do)

Prepare for intervention day - at home
Eat a standard dinner provided by the study team then fast for 10h

Intervention visit 2
Breakfast: bread with Flora dairy free spread and water
Finger prick blood tests
Fill in Questionnaire about your hunger and about the bread
Lunch is served!

Follow up
Remove glucose sensors, complete follow up questionnaire. Return them to the study team

How does it work?

We will invite you for a screening visit for a health assessment **(visit 1)**. We will ask you to sign a consent form to join the study and we will then measure your blood pressure, weight and height. We will also ask you some questions about your general health and collect a blood sample.
We will ask you for your contact details and the contact details of your GP.

Once you are enrolled, there are 3 visits to complete at the QI Clinical Research Facility, in Norwich. During two of the three visits, you will be served breakfast bread, one with low resistant starch and one with high resistant starch.
You will not be told which bread you are eating on each day, but you will have both bread types, if you complete the study.

After eating the bread portion, you will be asked to measure your blood glucose level with a "finger-prick test" and to complete some questionnaires.

At calibration (visit 2) you will be asked to complete a general health assessment after which you will be given 2 glucose sensors to wear for the whole duration of the study. These automatically record your body sugar levels. We would like you to scan the devices every 6 to 8h to collect body glucose readings. Because we would like you to eat and drink as you would do normally, you will not be able to see your readings.

The sensors should not interfere with your daily routine. While the sensors warm up, we will also show you how to record your food and drink intake while at home. This visit will last approx. 3h.

Before the intervention, we will give you instructions on how to prepare at home for the intervention day. You will be asked to avoid caffeine, alcohol and very calorific meals[2], as well as intense exercise (such as hiking, jogging at 6mph, basketball or football game). You will be provided with a standard dinner to consume the night before each intervention, you will need to fast for 10h before your next visit.

On intervention day (visit 3), you will be at the QI CRF from approx. 8.30am until 1.30pm. You will be provided with breakfast and lunch. Between breakfast and lunch, you will be asked to collect a series of blood drops from the tip of your fingers to measure blood sugar level and complete a series of questionnaires. A member of the study team will be there to support you with this.

Between visit 3 and 4, we would like you to complete a non-consecutive 3-day food diary at home. This means recording everything you eat and drink for 3 days (2-week days and 1 weekend day) using an app or paper-based diary.

Before the intervention, you will be asked to prepare as you did for your previous visit (No caffeine, alcohol, very calorific meals[2]). As before you will be provided with a standard dinner.

The second and last intervention visit (visit 4) will proceed exactly as visit 3.

The day after visit 4, you will be asked to remove the glucose sensors and return them to the study team together with a follow up questionnaire as soon as possible.Once the study is completed, we will summarise the results and let you know the outcome of REST.

[2] a very calorific meal is a meal 1000kcal (4184 kj) or more

Expenses refund

We will refund you for travel expenses and for taking the time to take part in the study.
See **EXPENSES AND PAYMENTS** for more details.

Are you eligible?

Please read the statements below. If you answer YES to all of them, you might be eligible to take part in this study.

- [ ] I am between 18 and 65 years of age
- [ ] I do not smoke
- [ ] I am not pregnant
- [ ] I do not have type I or II diabetes
- [ ] I do not have allergies or intolerances to gluten, yeast
- [ ] I am not allergic to adhesives which could prevent the attachment of the glucose monitor
- [ ] I am not suffering from an eating disorder
- [ ] I do not have Inflammatory bowel disease (IBD), or other inflammatory diseases like rheumatoid arthritis, polymyalgia rheumatica or other connective tissues diseases
- [ ] I have not donated blood or taken part in another dietary intervention in the last 16 weeks or I am willing to wait until 16 weeks have elapsed
- [ ] I have not had cancer in the last 3 years
- [ ] I am not suffering from a gastrointestinal disease or disorders including regular diarrhoea and constipation
- [ ] I have not had a heart attack (myocardial infarction) or stroke in the last 6 months
- [ ] I have not taken antibiotics in the last 4 weeks or I am willing to wait until 4 weeks after the treatment is completed
- [ ] I am able/willing to consume one of the lunch choices and one of the dinner choices provided (see REST day-lunch)
- [ ] I am not or do not plan to start a diet programme that cannot be postponed
- [ ] I do not take dietary supplements, or I am willing to stop taking them during the study period if required
- [ ] I am willing to wear the glucose sensors for the duration of the study
- [ ] I will be able to fast for 10h the night before the interventions

Please note: some medications may preclude you from taking part in the study. This will be assessed on an individual basis

Eligibility Screening

When you arrive at the Quadram Institute we will welcome you and walk you through the study and answer any questions. To join the study, you will be required to provide written consent.
We will ask you whether you have fasted for at least 10 hours. If you have not, we might have to reschedule the screening visit to another day.
We will ask you a series of questions about your health, similar to those we listed on page 5 under 'Why am I invited?' but in more detail. We will ask you details about any medications you are taking, please bring the details of this with you.

If you meet the study criteria, we will measure your blood pressure, height and weight and calculate your BMI

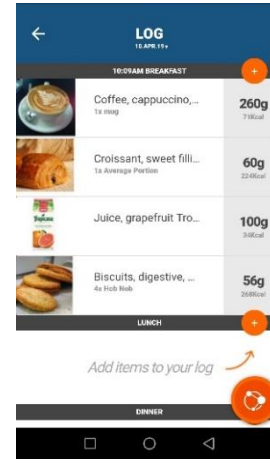
If these measurements are within the study criteria, we will proceed to draw blood samples from a superficial vein in your forearm. We will collect a maximum of 20mL of blood (about 2 tablespoons) to check your glucose metabolism, fat levels in the blood and general health status.
Once we have your blood test results, we will let you and your GP know if you are eligible or not to participate in the REST study. Your GP will have access to your test results, we may advise you to discuss these results with your GP.
Because **you have to be fasted** for the blood test (nothing to eat or drink apart from water since the night before), at the end of the visit, we will accompany you to the QI café for a complimentary breakfast.
This visit will last approximately 3 hours.

Calibration

During this study we would like to measure your body glucose levels in two different ways: using a glucose sensor applied to the back of your arm (see picture below) and by collecting finger prick blood samples.

The sensor that you will wear measures your sugar level every 15 min for the duration of the study. This device is currently used by diabetic patients to monitor their sugar level.

After you arrive at the CRF on the calibration day, you will be given two *FreeStyle Libre* (www.freestylelibre.co.uk) sensors to apply to the back of your upper arm. The sensors are waterproof and should not interfere with your daily activities. However, you should avoid strenuous activities for the duration of the study. We would like you to wear the sensors day and night and you will scan them every 8h with a reader device to store the measurements collected by the sensors. Once applied, the device takes one hour to warm up.



Meanwhile we will introduce you to the *Libro* app or form that is used to record your food intake. The *Libro* app is based in the UK and is GDPR compliant (see **WHAT WILL HAPPEN TO MY DATA AND SAMPLES)**

We would like you to record what you eat and drink accurately for 3 non-consecutive days during the study. This can be done between visits and preferably on two-week days and one weekend day. This information will be used by the research team to characterise your normal diet.
We will also match what you eat and drink with your glucose levels measured by the sensor you will be wearing. We do not want you to change your dietary habits. You should feel free to consume any food or drink as you would normally do. We will demo the app and practice recording your intake while your sensor warms up.

On the intervention day, you will be asked to measure your blood sugar level using a blood drop from your finger. During the calibration visit, we will show you how to do this and answer any questions you may have at this stage.

This visit will last approx. 3 hours.

Preparing to a study day

The day before your intervention days (visits 3 and 4), we would like you to avoid caffeine, alcohol and strenuous exercise.

You will be given a standard meal to consume the night before your visit.

You should consume this meal at least 10h before your morning visit (not later than 9pm).

On the morning of your visit we will ask you to arrive fasted for at least 10h. You can drink water during this period but no other drink such as coffee or tea.
You will be sent reminders during the study on how to prepare for a visit.
If you have queries during the study, you can contact the study team at +44 (0)1603 255101 or email us at REST@quadram.ac.uk.

ReSt day - Intervention

There are two intervention visits. The only difference between the two visits is the type of bread you consume.

On arrival at the QI CRF, we will go through the plan for the day. We will provide a study bundle explaining the tasks of the day. A member of the study team will be with you during the visit.

We will ask you to arrive at the QI CRF having fasted for at least 10h and we will give you breakfast: a serving of bread with Flora diary free spread with a glass of water.

- You will be asked to scan the sensor on your upper arm.
- You will also be asked to complete a series of questionnaires on satiety. Satiety is the feeling of fullness and we want to determine how long before you feel hungry after breakfast. We will ask you to write on a scale between 0 and 10 how hungry, full, thirsty etc. you feel during the visit.
- We would also like you to complete a questionnaire about how the bread taste to you.
- After this You will be asked to collect a series of blood drops from your fingers tip to measure blood sugar levels.
- Four hours after breakfast, you will be served lunch. We would like you to eat lunch within 1.5/2h.

The intervention visits will last approx. 5 hours.

REST day- Lunch

During the intervention day, you will be given two options for lunch. You will be asked to consume the same lunch option on both intervention visits.

Additional helpings will be served until you let us know that you feel 'comfortably satisfied'.

Option A is white rice with tomato and basil sauce[2] and parmesan cheese.

Allergens recipe A: Milk, Parmesan cheese

Option B is white rice with beef bolognese sauce[3].

Allergens recipe B: Celery

[2]Tomato and Basil ingredients are Tomato (88%), Tomato Puree, Rapeseed Oil, Demerara Sugar, Garlic Puree, Basil (0.5%), Salt, Balsamic Vinegar (Red Wine Vinegar, Grape Must Concentrate), Black Pepper.

[3]Bolognese sauce ingredients are Minced British Beef (26%), Tomato Concentrate, Water, Tomato, Carrot, Onion, Tomato Puree, Celery, Red Wine (3%), Rapeseed Oil, Cornflour, Salt, Garlic Puree, Oregano, Sugar, Black Pepper.

Follow up

The day after the final visit (visit 4), you will be asked to remove the sensor from the back of the arm and return both the sensor and reader to us in a pre-paid envelope supplied.

We would also like you to complete a follow up questionnaire, which can be returned along with the sensor.

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FAQs

DO I HAVE TO TAKE PART IN THIS STUDY?

No, taking part in this study is your choice. To help you decide, we will give you detailed information about the study over the phone or in an email, and in person during your first visit.

If you decide to take part, we will ask you to sign a consent form agreeing to take part.

CAN I WITHDRAW FROM THE STUDY?

Yes, you are free to withdraw from the study at any time without giving a reason. This will not preclude you from taking part in future QI studies. Data collected up to the point of withdrawal will be kept and, if possible, used in our data analyses to answer the study aims. Study data is analysed as a group and not by individual, so it will not be possible to identify you personally.
To withdraw, please contact the study team. We will send you a confirmation of your withdrawal from the study by email or mail.

WILL I BE GIVEN ANY MEDICATIONS DURING THE STUDY?

No, this is not a drug trial. We will not ask you to take any medicine.

WHO WILL CARRY OUT THE MEDICAL PROCEDURES?

The study will be carried out in the QI CRF. The QI CRF is an NHS-governed facility and all clinical procedures for this study will be carried out by the QI CRF team following NNUH

standard operating procedures. Clinical assessments and procedures will be performed by the QI CRF research nurse supported by a REST study team member. Non-clinical assessments or interventions (for example during intervention days) will be conducted by either the QI CRF research nurse or QI CRF Healthcare professional who is trained in NNUH emergency procedures, or a REST study team member.

WILL I GET MY TEST RESULTS?

As a volunteer you are valuable to us, but we are unable to tell you any of your individual results. However, the general findings of the study will be given to you in the form of talk or letter once the study is complete. Your GP will have access to your blood test results from the eligibility visit and will discuss any clinically relevant result with you directly.

WHY SHOULD I TAKE PART IN THIS STUDY?

You will be able to taste a high fibre white bread made from wheat grown in Norwich and baked at the Quadram Institute. This bread is not commercially available at the moment.

At the end of the study you will receive a report about the study outcome.

Your results will contribute to advancing nutritional research and the search for foods that can have a positive impact on

our health. This study will contribute to understanding whether white flour with resistant starch helps prevent blood sugar levels from spiking and delay the return of hunger. By controlling blood sugar and the return of hunger, we hope to help reduce the risk of chronic diseases such as type II diabetes and obesity.

ARE THERE ANY DISADVANTAGES OR RISKS?

You should not experience any side effects by taking part in this study. You may feel a slight discomfort when giving a blood sample or when pricking your finger to take a blood drop. This area may be slightly tender, sore or bruised after the procedure but these should fade within a few weeks.
The continuous glucose monitoring device (the sensor) will be applied to the back of your upper arm using an applicator. Applying the sensor should not be more painful than a finger prick. As with a finger prick, you may feel a slight discomfort when applying the sensor and the application area may be slightly tender or sore after the procedure.

The sensor is kept in place by an adhesive that sticks to your skin. You may experience some irritation when removing the sensor which should fade with time.

Our test bread is a white bread with higher resistant starch content (a type of fibre). The resistant starch content of the bread is higher than in normal white bread but not higher than in a whole-wheat bread. If you are not used to consuming fibre, you may experience wind or bloating due to the change in diet.

WHAT IF THERE IS A PROBLEM?

If you have any concerns about the study, you should ask to speak to the QIB Principal investigator, Marina Corrado on 01603 255101 who will do her best to answer your questions.

If you are still unhappy, and wish to complain formally, you can do this through the chairperson of the QI Human Research Governance Committee (HRGC) – Dr Antonietta Melchini on 01603 255030.

QIB accepts responsibility for carrying out trials and as such will give consideration to claims from participants for any harm suffered by them as a result of participating in the trial, with the exception of those claims arising out of negligence by the participant. QIB has liability insurance in respect of research work involving human volunteers. Please note that the Institute will not fund any legal costs arising from any action unless awarded by a court.

If you wish to complain or have any concerns about the way you have been treated whilst taking part in this study at the QI CRF, there will be a local hospital complaints procedure that you can follow. If you wish to complain you should contact the Patient Advice and Liaison Service (PALS) at the NNUH on 01603 289036 (email: pals@nnuh.nhs.uk). Their offices are located next to Kimberley Ward, East Block Level 2 or please ask at the main reception desks at the Inpatient and Outpatient NNUH hospital entrances. The office has an answerphone which is available 24 hours a day and messages will be responded to as quickly as possible. As this study involves the QI CRF, which is an NHS facility, indemnity is provided through NHS schemes.

KEEP IN TOUCH!

For your safety and the success of the study, it is important that you let us know if your health changes.
Please tell us if you

- Have any episodes of illness, even if it is just a headache
- Are injured in any way
- Feel unwell during or after a visit to the unit
- Become pregnant

Some medicines affect the information we are collecting. Please tell us if you take any medication including over-the-counter medicines and those you purchase at the chemist or supermarket (e.g. acetaminophen, also known as paracetamol).
You should bring details of any medication (i.e. name of the medicine and the dose taken) you are taking when you come for your screening visit (visit 1).

EXPENSES AND PAYMENTS

Participation in this study is on a voluntary basis. However, we do recognise that taking part can cause some inconvenience and there are associated travel costs. Thus, you will receive £162.50 as an inconvenience payment upon completion of the study; if you withdraw or are excluded from the study, *payment will be pro-rata*. This means that you will be paid up until the point of withdrawal/exclusion from study. Travelling expenses to and from the QI CRF will be reimbursed on presentation of a receipt for buses or trains, or at the current QIB mileage rate for private cars. QI parking fees will be lifted. If you require transport to and from the QI CRF, please let us know and we will arrange and pay for a taxi.

All payments are liable to tax and you are responsible for declaring your own payments for tax purposes. Members of staff at QIB are free to participate in this study provided they meet the study criteria. However, we would like to point out that their inconvenience payment will be taxed at source in accordance with Biotechnology and Biological Science Research Council (BBSRC) and QIB rules and HM Revenue and Customs (HMRC). If you are in receipt of benefits this payment may affect your benefits.

HOW WILL YOU CONTACT ME?

We will contact you by phone, email or mail, depending on your preference. We will ask you how we should reach you during the first visit at QI.

WHO ORGANISES AND FUNDS THIS PROJECT?

This study is led by Miss Marina Corrado, based at QIB in the Food Innovation and Health Programme. The study is funded by the BBSRC and Norwich Research Park through the Biosciences Doctoral Training Partnership (grant number BB/M011216/1) and the BBSRC QIB Institute Strategic Programme Food Innovation and Health BB/R012512/1 and its constituent projects BBS/E/F/000PR10343 (Theme 1, Food Innovation) and BBS/E/F/000PR10345 (Theme 2, Digestion in the Upper GI Tract).

WHAT WILL HAPPEN TO MY DATA AND SAMPLES?

We will store your clinical data and diet information anonymously in an electronic database at QIB. All information collected about you during the course of the study will be kept strictly confidential.
Hard copies of the clinical data will be archived separately from your personal information. Access to your personal records is restricted to the study team, the QI CRF research nurse and your GP.

Your biological samples collected during the screening visit will be processed at QI Clinical Research facility and sent to the Norwich and Norfolk University Hospital for analysis. These blood tests results will be logged on the hospital electronic system where your GP can access them if needed.

Your personal information is confidential! We follow Good Clinical Practice (GCP) and strict ethical and research governance rules. All information about you will be handled in
confidence. Data will be managed by the study team in compliance with EU General Data Protection Regulation (GPDR) and the UK Data Protection Act (DPA; 2018).

Any information that could show who you are will be held safely with strict limits on who can access it. We will store all your data using a unique a code number (ID) to protect your privacy and we work with trustworthy services (Libro app for dietary intake and/or the SMS reminder service) to ensure your personal information are safe. QIB acts as data controller of the information collected during the study. This means that at the end of the study the information stored by the service providers will be returned to the data controller (QIB) and deleted from the Libro and SMS reminder service platforms.

The research team will record the study data and combine it with the information from everyone else in the study. The group data will be published in scientific journals and/or presented to the scientific community to share the outcome of the study. We will make sure that any other information that could show who you are is removed so you will not have a claim on the material collected or the data resulting from this study.

QIB is the sponsor of this study. We will be using information from you in order to complete this study and will act as the data controller for the study. This means that we are responsible for looking after your information and using it correctly. QIB will keep identifiable information about you for 15 years after the study has finished. Any archived identifiable data will not be used to contact you after the end of the study.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.
The only people at QIB who will have access to information that identifies you personally, will be people who need to contact you under emergency unblinding procedures or audit the data collection process. Other researchers won't be able to contact you to ask you about future research.

All research is subject to inspection and audit. Although your records may be accessed for this purpose, any personal information remains confidential. Please note, QI has CCTV cameras in use for security purposes.

You can find out more about how we use your information by contacting the QIB Data Protection Officer [Mr Mohamed Imran; mohamed.imran@nbi.ac.uk] or the QIB Human Studies coordinator (Dr Antonietta Melchini; antonietta.melchini@quadram.ac.uk).

WHO HAS REVIEWED AND APPROVED THE STUDY?

At QIB this research project has been reviewed by the QIB Human Research Governance Committee (HRGC), as well as an external Local Research Ethics Committee (REC). These are groups of independent people who review research to protect your safety, rights, well-being and dignity. This study has been reviewed by all committees and given a favourable opinion. Following ethical approval, the study protocol will also be registered at Clinicaltrials.gov, a publicly available database. It is good practice for all research projects to be registered in a publicly-accessible database and this supports our duties to promote research transparency.

REST Study reply slip

Please check the box if you are interested in taking part in this study or if you would like to know about it

I am interested in taking part in this study

Please provide your contact details.

We will contact you to give you more information

Name ……..

Address ……..

……..

Telephone number ……..

Email ……..

Get in touch

If you have any questions or concerns, please speak to a member of the REST study team during your visit or contact the Principal Investigator, Marina Corrado.

01603 255101

REST@quadram.ac.uk

https://quadram.ac.uk/reststudy/

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