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How do polyphenols, carotenoids and glucosinolates in our diets affect the diversity of our gut microbiome?

Submission date
27/01/2021

Recruitment status
No longer recruiting

Registration date
08/02/2021

Overall study status
Ongoing

Last Edited
15/04/2025

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Within the intestines there is a community of micro-organisms known as the gut microbiome. Its composition may vary from person to person, but humans depend on this community to break down some undigested food to produce essential products such as vitamin K, and to perform several other functions. Richer diversity in these communities has been linked to better health, although not all factors for this have yet been discovered. Dietary intake has a big role to play in the composition of the microbiome and studies have observed the effect of carbohydrates, fibre, proteins and fats, but little has been done on the effect of micronutrient intake and non-nutrients such as beneficial plant chemicals. Plants contain some non-nutrient compounds which might impact the diversity of the microbiome. The aim of this study is to determine if a diet high in these plant compounds; polyphenols (compounds found in foods such as blueberries), carotenoids (found in brightly coloured foods) and glucosinolates (found in foods like broccoli) will have an effect on the diversity of the gut microbiome.

Who can participate?
Non-diabetics and people with no known health conditions aged 18 to 65 with a BMI 18.5 to 35 kg/m²

What does the study involve?
Participants will be allocated to follow a diet high in dietary bioactives for 2 weeks and a diet low in dietary bioactives for 2 weeks in a random order, with a 4-week break after the first diet before crossing over to the second one. On the high bioactives weeks, they will need to consume several servings of bioactives-containing foods, while they will consume no servings or very little servings of bioactives-containing foods on the low bioactive weeks. Throughout each diet period, participants will need to record their activity and sleep levels using a Fitbit, continuously monitor glucose levels using a continuous glucose monitor worn on the back of the arm, and record their dietary intake in a smartphone dietary logging application, Libro. At the beginning and end of each diet period, participants are expected to provide stool and urine samples for analysis and they will also have blood tests and body measurements taken.

What are the possible benefits and risks of participating?
The researchers do not anticipate that the participants will experience either harm or benefit from taking part. They will help add to the body of knowledge about the gut microbiome and nutrition.

Where is the study run from?
The study is run by Quadram Institute Bioscience at Norwich Research Park, with clinical work undertaken by staff at Norfolk and Norwich University Hospitals in the Quadram Institute Clinical Research Facility (UK)

When is the study starting and how long is it expected to run for?
August 2019 to April 2026

Who is funding the study?
The study is funded by the European Commission through the Horizon 2020 research and innovation programme as part of the FNS-Cloud study (grant agreement 863059)

Who is the main contact?
Dr Jennifer Ahn-Jarvis
DIME@quadram.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Jennifer Ahn-Jarvis

ORCID ID
https://orcid.org/0000-0002-2372-5464

Contact details
Quadram Institute
Norwich Research Park
Rosalind Franklin Road
Norwich
United Kingdom
NR4 7UQ
+44 (0)1603 255052
jennifer.ahn-jarvis@quadram.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 46697

Study information

Scientific Title
The effect of dietary bioactives on gut microbiome diversity - a pilot study

Acronym
DIME

Study objectives
Consumption of a diet high in bioactive-rich foods for two weeks will increase gut microbial diversity in healthy participants compared to a 2-week diet low in bioactive-rich foods and will additionally affect markers of metabolic health.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/09/2020, Greater Manchester West Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)2071048384; gmwest.rec@hra.nhs.uk), REC ref: 20/NW/0359

Study design
Interventional randomized cross over trial

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Nutrition effects on gut microbiome

Interventions
Potential participants who express interest in the study will be contacted via telephone for the pre-study talk. This will include discussions of what the study entails in greater detail than outlined in the Participant Information Sheet which also includes a Privacy Note to ensure they are familiar with the proposed movement of data in the study. If still interested, the potential participant will be invited to attend the clinical research facility for Consent and Eligibility Screening.

The pre-study visit to the research centre will be the Consent and Eligibility Screening visit which will last for approximately 3 hours. At this visit, participants will once again have the study fully explained to them and have a chance to ask questions before giving informed consent. Eligibility screening will consist of a blood test where a 6 mL blood sample will be taken by a nurse to determine total blood count and HbA1c. The blood tests require the participant to stop eating 12 hours before the scheduled consent and eligibility visit. The nurse will also administer

questionnaires relating to general health, medication and record anthropometric measurements; weight, height, waist circumference and body mass index (BMI). At this visit participants will be given all materials and instructions required for the study. They will be contacted about their eligibility in approximately 48 hours after the results of the screening blood tests have been obtained.

Eligible participants will return to the study centre fasted at an agreed time for their first study visit. This will last for up to 3 hours and they should bring with them a 24-hour urine sample collected the day before. They should also bring a stool sample collected within the preceding 24 hours. Two days before the study visit, participants will be asked to attach a continuous glucose monitor (CGM) and a second one will be attached on the first study day which will be the day after the first study visit. They will also have been asked to begin recording their habitual diet for a 3 day period
during the preceding week.

Study visit 1: Participants will be given an oral glucose tolerance test (OGTT). Blood will also be taken to determine c-reactive protein, insulin, blood lipid profiles and some will be taken to isolate peripheral blood mononuclear cells (PBMCs) which will give an indicator of issues like inflammation. After the OGTT, participants will be given a standardised meal and a large serving of sweet corn to measure gastrointestinal transit. Menus, meal ideas and foods (or arrangements for food deliveries will be made) for the following 2 weeks will be provided, after which point they will be allowed to leave.

Intervention Phase 1: Participants will be randomised to a specific diet arm; 'high bioactives' or 'low bioactives' which will begin on the day after the study visit and last for 2 weeks. During this phase, they will record everything they eat with the Libro app, scan their CGMs every 8 hours, monitor their activity and sleep with a Fitbit and follow an approved diet plan with approved ingredients. They will also need to record their bowel habit by noting the frequency of their stools and the type according to the Bristol stool chart.

Study visit 2: Like study visit 1, they will bring with them a stool sample and a 24-hour urine sample and will arrive at the centre fasted. They will again have an OGTT. At the end of the OGTT they will be fed and allowed to leave for their 4-week washout period.

Four-week washout period: Participants will be asked to record their normal diet for 2 days midway through this period and provide a stool sample which will be collected by a researcher or delivered to the centre by the participant. The wash-out period could last for more than 4 weeks if for example the participant has existing plans preventing Phase 2 beginning immediately after 4 weeks.

Study visit 3: Will occur at the end of the washout period and will be identical to study visit 1.

Intervention Phase 2: Participants will have the other arm of the intervention but apart from this will be identical to Phase 1.

Study visit 4: Will occur at the end of intervention phase 2 and will be identical to study visit 2. This will be the end of the study.

Due to the COVID-19 pandemic, which has led to period restrictions on non-essential movement and activities, the protocol was adapted to allow the remote collection of data. Participants will be able to complete the entire study without leaving home through the use of supermarket deliveries for food, finger prick test kits for blood collection, scales and tape measure for

anthropometric measurements and home blood pressure monitors. Each study visit will proceed as planned with the face-to-face formats replaced by video conferencing apps such as Zoom, and samples will be collected by a researcher.

Intervention Type
Behavioural

Primary outcome(s)
1. Gut microbiota diversity and composition and described by the Shannon index, a measure of alpha diversity. This will be measured at baseline and 2 weeks for each intervention
2. Adherence to diets based on self-reported logging in a dietary app throughout and compliance as measured by metabolite signatures in urine at baseline and 2 weeks for each intervention

Key secondary outcome(s))
1. Gut microbial function through assessment of faecal metabolomics and total gene content of the microbiome of each host measured at baseline and 2 weeks for each intervention period
2. Urine metabolomics measured through liquid chromatography-mass spectrometry on 24-hour urine samples produced at baseline and 2 weeks of each intervention period
3. Vascular health as measured by blood pressure (in mmHg), blood levels of triglycerides and cholesterol (in mmol/L) at baseline and 2 weeks for each intervention period
4. Inflammation as measured by hsCRP (in mg/L) at baseline and 2 weeks for each intervention
5. Estimates of postprandial glycaemic metabolism measured by continuous glucose monitoring (measured in mmol/L) throughout both intervention periods, and glycaemic response to standardised meals at the end of each intervention period

Completion date
30/04/2026

Eligibility

Key inclusion criteria
1. Males and females aged 18 - 65 years old
2. BMI between 18.5 and 35 kg/m²
3. HbA1c below 42 mmol/mol
4. Access to a personal smart mobile phone enabled with near field communication (NFC) technology (this technology allows contactless card payments)
5. Living in an area which can receive a supermarket delivery

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Total final enrolment
27

Key exclusion criteria
1. Smokers (or stopped smoking for less than 3 months)
2. Having diabetes, defined as HbA1c ≥48 mmol/mol or pre-diabetes, defined as HbA1c 42 – 47 mmol/mol
3. Prescribed and non-prescribed medications that may affect the outcome measures for this study e.g. statins, laxatives
4. Dietary supplements judged to affect the study data unless the participant is willing to discontinue them 4 weeks before the start of the study and for the duration of the study
5. Use of antibiotics in the 6 months prior to the study
6. Regular/recent use of colonic irrigation or other bowel cleansing techniques
7. Use of pre/probiotics or fermented foods such as Yakult, Kefir products, unless the participant is willing to discontinue use 4 weeks before the start of the study and for the duration of the study
8. Bowel movements ≤3 times per week
9. Gastrointestinal diseases (excluding hiatus hernia unless symptomatic or study intervention /procedure is contraindicated)
10. History of inflamed bowel (ulcerative colitis, Crohn's disease or diverticulitis)
11. Immune-related conditions associated with altered microbiome – lupus, type 1 diabetes, multiple sclerosis, poorly controlled thyroid disorders (Greaves disease, Hashimoto's disease), rheumatoid arthritis
12. Parallel participation in another research project
13. Unwillingness to adhere to the dietary guidelines for the study
14. Participation in another research project which has involved blood sampling within the last 4 months unless the total amount of combined blood from both studies does not exceed 470 ml
15. Has donated or intends to donate blood within 16 weeks prior to or during the study period
16. Any person related to or living with any member of the study team
17. Those who are part of the line management or supervisory structure of the Chief Investigator
18. Lack of capacity to provide written informed consent
19. Are pregnant or have been pregnant within the last 12 months
20. Participants following a vegetarian or vegan diet, as restrictions to bioactive-rich foods (fruits and vegetables) during the study may be too limiting
21. Clinical eligibility test results deemed by the CRF medical advisor to be indicative of a health problem which may compromise the well-being of the participant or which could affect the study outcome
22. Being susceptible to food allergies and intolerances
23. Active infection with COVID-19

Date of first enrolment
04/01/2021

Date of final enrolment
01/01/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Norfolk & Norwich University Hospital
Norfolk And Norwich University Hospitals NHS Foundation Trust
Colney Lane
Norwich
United Kingdom
NR4 7UY

Sponsor information

Organisation
Quadram Institute

ROR
https://ror.org/04td3ys19

Funder(s)

Funder type
Government

Funder Name
European Commission; Grant Codes: 863059

Alternative Name(s)
European Union, Comisión Europea, Europäische Kommission, EU-Kommissionen, Euroopa Komisjoni, EC, EU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a publically available repository. (FNS-Cloud, to be shared with data fully anonymised after the end of the study. Participants will be asked to consent to this before they can be enrolled.)

IPD sharing plan summary

Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes