ISRCTN15658653 https://doi.org/10.1186/ISRCTN15658653

Harnessing the potential of fermentation for healthy and sustainable foods

Submission date
26/03/2024

Recruitment status
No longer recruiting

Registration date
27/03/2024

Overall study status
Ongoing

Last Edited
05/04/2024

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Evidence suggests that the gut microbiota play an important role in host health and the development of non-communicable diseases. An increasing number of studies have shown that fermented products, particularly fermented dairy products, influence metabolic health. This study aims to demonstrate the health impacts of daily consumption of kefir on healthy and metabolic syndrome (MetS) subjects and to establish how fermented food consumption shapes the gut microbiome and provides health benefits to the consumer.

Who can participate?
Healthy volunteers aged between 18 and 60 and patients with MetS aged between 18 and 65 years old

What does the study involve?
This study is a randomised, double-blind, double arm with a parallel design trial involving three research centres: Imperial College London (IC) in the UK, Centre De Recherche en Nutrition Humaine Rhône-Alpes (CRNH-RA) in France, and the University of Naples Federico II (UNINA) in Italy. The UK site will recruit 21 healthy participants and 30 participants with MetS, while the Italian site will enrol 20 healthy participants and 30 participants with MetS. The French site will include 21 healthy participants. Participants will be randomised to consume 200 ml of intervention kefir daily, while participants from the placebo group will be asked to consume 200 ml of placebo daily. Each participant will attend the clinical research centre at their respective study site at baseline and once a month for 6 months.

What are the possible benefits and risks of participating?
The potential benefit of the study is that kefir is suggested to have a beneficial effect on gut health, although it cannot be guaranteed that this will be the case in this study, nor can participants expect direct benefits. Upon request, participants can receive results from blood, stool, and urine analysis to provide an overview of their metabolic health. Fasting blood samples and blood pressure taken throughout the visit can provide insight into aspects of chronic disease risk, such as Type 2 diabetes and cardiovascular disease.

If the study reveals any previously unknown health issues, such as abnormal kidney test results or possible type 2 diabetes, potential participants will be informed immediately, and urgent assessments will be arranged within the hospital if needed. Their GP will also be informed of their participation and any clinically significant blood test results. Procedures like recording weight and height pose no health risks. Self-collection of stool and urine samples may lead to contamination, but this risk has been minimised through the use of hygienic, easy-to-use collection kits. Blood sampling may cause mild discomfort, bruising, or localised infection, but these risks are reduced by having trained professionals perform the procedure under aseptic conditions.

Where is the study run from?
Imperial College London

When is the study starting and how long is it expected to run for?
April 2024 to March 2029

Who is funding the study?
1. UK Research and Innovation (UKRI)
2. European Horizon

Who is the main contact?
Dr Isabel Garcia Perez, i.garcia-perez@imperial.ac.uk

Study website
https://www.domino-euproject.eu/

Contact information

Type(s)
Scientific, Principal Investigator

Contact name
Dr Isabel Garcia Perez

ORCID ID
http://orcid.org/0000-0001-8398-0603

Contact details
10th Floor Commonwealth Building, Hammersmith Campus, Imperial College London
London
United Kingdom
W12 0NN
+44 (0)7704344683
i.garcia-perez@imperial.ac.uk

Type(s)
Public

Contact name
Mrs Yiwei Vally Wu

ORCID ID
https://orcid.org/0000-0001-9254-802X

Contact details
10th Floor Commonwealth Building, Hammersmith Campus, Imperial College London
London
United Kingdom
W12 0NN
+44 (0)7717000746
y.wu18@imperial.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
337740

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 337740, CPMS 61519

Study information

Scientific Title
Determination of the health impacts of milk kefir on healthy and metabolic syndrome subjects DOMINO study

Acronym
DOMINO

Study objectives
Daily consumption of milk kefir for 6 months will positively impact glucose and lipid metabolism along with inflammatory status and gut microbiome in healthy and Metabolic Syndrome volunteers.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 16/01/2024, Comitato Etico Campania 3 (Via Antonio Cardarelli, 9, Napoli, 80131, Italy; +39 081 7473312; segreteria@comitatoeticocampania3.it), ref: Protocol n.05/2024

2. Approved 05/03/2024, Comité de Protection des Personnes Nord Ouest II (Bâtiment de formation- RDC – Hôpital Nord - Place Victor Pauchet, Amiens, 80054, France; 03226685; cpp. nordouest2@chu-amiens.fr), ref: 2023-A02507-38

Study design
Multicentre interventional double-blind double-arm randomized controlled study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Home, University/medical school/dental school

Study type(s)
Other

Participant information sheet
Not available in web format

Health condition(s) or problem(s) studied
Assessing the effects of kefir consumption in both healthy subjects and those with metabolic syndrome (MetS).

Interventions
The study aims to investigate the effects of kefir consumption in both healthy subjects and those with metabolic syndrome. Participants will be randomised using randomisation software to a kefir group that is asked to consume 200 ml of kefir daily and a placebo group that is asked to consume 200 ml of placebo daily. Each participant will attend the clinical research centre at their respective study site at baseline and once a month for 6 months. The study sites include Imperial College London (IC) in the UK, Centre De Recherche en Nutrition Humaine Rhône-Alpes (CRNH-RA) in France, and the University of Naples Federico II (UNINA) in Italy. At each time point, anthropometric measurements will be taken, and urine, stool, and blood samples will be collected.

Intervention Type
Supplement

Primary outcome measure
The effects of daily kefir consumption on markers of glucose metabolism in healthy volunteers are measured using fasting blood glucose (FG), glycated haemoglobin (HbA1C), and homeostasis model assessment-insulin resistance (HOMA-IR); and, in subjects with metabolic syndrome (MetS) are measured using insulin and homeostasis model assessment-insulin resistance (HOMA-IR), as follows:

1. Fasting blood glucose (FG) is measured using the PAP peroxidase method at baseline and months 1, 2, 3, 4, 5, and 6
2. Glycated haemoglobin (HbA1C) is measured using capillary electrophoresis at baseline and months 3 and 6
3. Homeostasis model assessment-insulin resistance HOMA-IR, calculated using formula HOMA-IR = Fasting insulin (μU/mL) x fasting glucose (mg/dL)/405, is measured using Enzyme-Linked Immunosorbent Assay (ELISA) at baseline and months 1, 2, 3, 4, 5, 6

Secondary outcome measures
1. Measures of lipid metabolism (blood cholesterol, triglyceride, HDL cholesterol and LDL cholesterol) are measured by Nuclear Magnetic Resonance at baseline and month 6
2. Inflammatory status (CRP, IL-6, IL-8, TNF-alpha and leptin) is measured using Enzyme-Linked Immunosorbent Assay (ELISA) at baseline and month 6
3. Gut permeability and changes to the gut microbiome (microbial diversity, microbial composition) measured by metagenomics at baseline and months 1, 2, 3, 4, 5, and 6

Overall study start date
05/04/2024

Completion date
01/03/2029

Eligibility

Key inclusion criteria
Healthy participants inclusion criteria:
1. General good health
2. Both gender
3. BMI between 20 and 29.9 kg/m2
4. Aged between 18 and 60 years old
5. Willing to take one daily portion of kefir or placebo and to follow the procedures as well as a 2-3h metabolic exploration day every month of follow-up
6. Written informed consent

Metabolic syndrome participants inclusion criteria:
1. Aged between 18 and 65 years old
2. Subjects diagnosed with metabolic syndrome according to the International Diabetes Federation (IDF) criteria
3. Low consumption (max intake 3 servings/week) of kefir or supplements/foods labelled as having probiotic effect during the prior 3 months
4. Consumption of fruits and vegetables ≤ 3 servings per day
5. Willing to take one daily portion of kefir or placebo and to follow the procedures as well as a 2-3h metabolic exploration day every month of follow-up
6. Written informed consent

Participant type(s)
Healthy volunteer, Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex

Both

Target number of participants
122

Key exclusion criteria
Healthy participants exclusion criteria:
1. BMI ≥30 kg/m2
2. Gastrointestinal disorders of any kind
3. Previous abdominal surgery
4. Lactose intolerance or intolerance to the study products
5. Blood triglyceride > 150 mg/dL
6. Blood total cholesterol > 240 mg/dL or HDL-cholesterol <40 mg/dl (men) or < 50 mg/dl (women)
7. Blood pressure ≥140/90 mm Hg or taking blood pressure medications
8. Fasting blood glucose >105 mg/dL
9. Pharmacological treatments of any type at enrolment and in the 2 months before the study
10. Consumption of supplements or foods labelled as having a probiotic effect prior 3 months
11. Consumption of Kefir > 3 servings/week during the prior 3 months
12. Menopause women
13. Alcohol consumption exceeding 30g of alcohol/day (1 alcoholic beverage dose = 10g of alcohol) or proven abuse or dependence on another drug. Consumption of more than 3 alcoholic beverages per day is considered abusive. An alcoholic beverage corresponds, for example, to 30 ml of spirits, 120 ml of wine or 330 ml of beer
14. Consumption of fruits and vegetables > 5 servings per day
15. Dietary fibre intake > 30g/1000 kcal per day
16. Pregnant, parturient or breast-feeding woman; for women of childbearing age: positive urine pregnancy test
17. Antibiotics consumption over the prior 1 month before the trial
18. Daily use of laxatives in the 3 months before explorations, or use of drugs that may strongly interfere with the composition of the intestinal microbiota
19. Contemporary participation in other studies
20. Blood donors in the last 2 months
21. Use of lipid-lowering drugs
22. Under antidiabetic treatment
23. Individuals who have lost/ gained ≥ 3 kg in the last 3 months
24. Individuals with unstable medical or psychological conditions which, in the investigator's opinion, could lead the volunteer to be non-compliant or uncooperative during the study, or which could compromise the volunteer's safety or participation in the study
25. Pre-diabetes, type 1 or 2 diabetes
26. Cancer
27. Infectious diseases
28. Cardiovascular disease
29. Hypertension
30. Severe eating disorders (anorexia/bulimia, binge eating disorder, noctophagia, etc.)
31. Severe chronic renal failure (GFR<60mL/min)
32. Hepatocellular insufficiency
33. Exocrine pancreatic insufficiency
34. Known endocrine pathology inducing hyperglycaemia (uncontrolled dysthyroid, acromegaly, hypercorticism, etc.)
35. Previous intestinal or abdominal surgery, bariatric surgery, gallbladder surgery, polyp

removal, known gastroparesis, total gastrectomy or colectomy
36. Pathology detectable on clinical examination and medical questioning that may interfere with the study's evaluation criteria
37. Adult subject to a legal protection measure (guardianship, curatorship)
38. Person deprived of liberty by judicial or administrative decision

Metabolic syndrome participants exclusion criteria:
1. Lactose intolerance
2. Type 1 diabetes
3. Abnormal thyroid hormone levels
4. Chronic gastrointestinal system disease
5. Cancer
6. Severe liver disease
7. Kidney insufficiency
8. Immunodeficiency
9. Taking medication to regulate blood glucose (except metformin) or lipid levels
10. Taking antibiotics prior to one month of the study
11. Taking supplement which may affect the metabolic outcomes such as prebiotic or omega-3
12. Dieting for weight loss or for another disease
13. Pregnant, parturient, or breast-feeding woman; for women of childbearing age: positive urine pregnancy test
14. Alcohol consumption exceeding 30g of alcohol/day (1 alcoholic beverage dose = 10g of alcohol) or proven abuse or dependence on another drug. Consumption of more than 3 alcoholic beverages per day is considered abusive. An alcoholic beverage corresponds, for example, to 30 ml of spirits, 120 ml of wine or 330 ml of beer
15. Contemporary participation in other studies
16. Blood donors in the last 2 months
17. Pathology detectable on clinical examination and medical questioning that may interfere with the study's evaluation criteria
18. Adult subject to a legal protection measure (guardianship, curatorship)
19. Person deprived of liberty by judicial or administrative decision

Date of first enrolment
05/04/2024

Date of final enrolment
01/01/2025

Locations

Countries of recruitment
England

France

Italy

United Kingdom

Study participating centre
NIHR Imperial Clinical Research Facility
Hammersmith Hospital
Du Cane Rd
Shepherd's Bush
London
United Kingdom
W12 0HS

Study participating centre
Dipartimento di Agraria, Università degli Studi di Napoli Federico II
Via Università, 100
Portici
Italy
80055

Study participating centre
Centre de Recherche en Nutrition humaine Rhône-Alpes
Centre Hospitalier Lyon Sud - Bâtiment 2D CENS ELI
165 chemin du Grand Revoyet
Pierre-Bénite
France
69310

Sponsor information

Organisation
Imperial College London

Sponsor details
Imperial College London and Imperial College Healthcare NHS Trust 217, 2nd Floor, Medical School, St Mary's Campus, Norfolk Place
London
England
United Kingdom
W2 1PG
+44 (0)20 7594 9832
cheuk-fung.wong@imperial.ac.uk

Sponsor type
University/education

Website

https://www.imperial.ac.uk/

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
HORIZON EUROPE European Research Council

Alternative Name(s)
European Research Council, Horizon Europe - European Research Council, EU - Horizon Europe - ERC, ERC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Funder Name
UK Research and Innovation

Alternative Name(s)
UKRI

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

We plan to disseminate our findings through peer-reviewed manuscripts, public engagement activities, and our project website at https://www.domino-euproject.eu/

Intention to publish date
10/05/2025

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date