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Metabolically personalised dietary advice for people at risk of cardiovascular disease

Submission date
13/11/2020

Recruitment status
No longer recruiting

Registration date
04/12/2020

Overall study status
Ongoing

Last Edited
07/03/2025

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Cardiovascular disease (CVD) is a general term for conditions affecting the heart or blood vessels. It's usually associated with a build-up of fatty deposits inside the arteries (atherosclerosis) and an increased risk of blood clots. It can also be associated with damage to arteries in organs such as the brain, heart, kidneys and eyes. CVD is one of the main causes of death and disability in the UK, but it can often largely be prevented by leading a healthy lifestyle. Although genetic predisposition plays a role in CVD, diet, is known to modify disease risk. However, it is known that people respond differently to dietary changes and in order to find the best strategy for an individual it is necessary to identify objective measures of dietary adherence and dietary effect. This project aims to evaluate providing metabolically-informed personalised dietary advice to help CVD-risk people to change their dietary habits within their own environment.
In an earlier study, a group of people at risk of CVD had their response to a healthy and an unhealthy diet monitored over a 5-day period. Analysis of urine and blood was used to map the levels of many different molecules. These profiles were used to build a model for predicting whether patients are following a healthy diet, with specific molecules representing intake of individual foods.
This aim of this study is to test this model in groups of people who are given different levels of diet support and advice.

Who can participate?
Adults aged 30 - 65 years, who are at risk of CVD (i.e. have high BMI, high blood pressure, high cholesterol)

What does the study involve?
Participants will be randomly allocated to the intervention or the control group. The intervention group will receive advice for 12-weeks based on measurements of their urinary metabolic profiles and the effect of metabolically-informed personalised dietary advice on reducing CVD risk factors will be compared with a control group receiving standard dietary advice by the dietician. At the start of the study and then every 2 weeks until the end of the study, participants will attend an appointment to provide samples of blood, urine, faeces, saliva, and body measurements will be taken.

What are the possible benefits and risks of participating?
In the event that we discover something about your health that you were unaware of, for example, if your kidney tests are abnormal or if you have diabetes, we would immediately inform you of this and inform your GP so that you can be referred to an appropriate specialist. If you require a more urgent assessment we would arrange this for you immediately within the hospital.
Some of the procedures in this study, such as the recording of your weight, height and blood pressure present no risk to you. Other procedures, such as taking blood samples or the insertion of the cannula in your arm, can cause mild discomfort. The risks of taking a blood sample include slight discomfort when the needle is inserted and possible bruising and localised infection. These procedures will only be carried out by experienced health care professionals and they are also part of the research team or direct care team under aseptic conditions to minimise all these risks.

Where is the study run from?
Imperial College London (UK).

When is the study starting and how long is it expected to run for?
February 2019 to March 2026.

Who is funding the study?
National Institute for Health Research (NIHR) (UK).

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

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
237962

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 40030, IRAS 237962

Study information

Scientific Title
Assessing metabolic profiling strategies for nutritional management of cardiovascular disease risk

Study objectives
Metabolic profiling can be used to improve the accuracy of monitoring dietary intake, establishing
inter-individual variation in response to diet and provide a useful tool to improve dietary change for people at risk of CVD.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 28/02/2019, London - Dulwich Research Ethics Committee (Health Research Authority, Skipton House, 80 London Road, London, SE1 6LH, UK; +44 (0)20 7972 2561; dulwich.rec@hra.nhs.uk) ref: 18/LO/2042

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Use of nutritional advice to prevent cardiovascular disease in people with risk factors for cardiovascular disease

Interventions
The aim of this study is to validate a metabolic profiling model constructed using data from a small study carried out in the months before this study (details of this study are included at the end of this section for reference).

Pre-study visit: Two weeks before the study, volunteers will attend the NIHR/Wellcome Trust Imperial CRF at Hammersmith Hospital. The aim of this visit will be to measure height, weight and waist and hip circumference and the baseline samples. 24-h urine and faecal samples will provided by participants from the day before and blood and saliva samples upon arrival. Moreover, the resting energy expenditure of the individual by open loop indirect calorimeter will be measured.

Randomisation: Volunteers will be randomly assigned to either the control or the target group. An independent researcher (i.e. not linked to the study) will be given the task of randomisation, which will be by sealed envelopes that will reveal the group assigned for each participant. This researcher will not be directly involved in the study and will use opaque, sealed, sequentially numbered envelopes that each contained “target group” or “control group”. The envelopes will be stored securely, away from the trial site, and opened in sequence by an investigator as each participant is enrolled.

Intervention: Participants will be asked to attend the NIHR/Wellcome Trust Imperial CRF at Hammersmith Hospital for a few hours every 2 weeks during a 12-week period. Participants assigned to the target group, will follow a 12-week programme, in which a dietitian will provide personalised dietary advice based on knowledge of urine and plasma metabolic profiles from samples collected at clinic every 2 weeks in addition to 24-h food diaries. Participants assigned to the control group will mirror the intervention group but will receive standard NICE-guideline dietary recommendations. The changes in CVD-risk factors will be compared between the intervention and the control group. Furthermore, the 24-h food diaries of the intervention and the control groups will be assessed against objective measurements of their dietary habits using the metabolic profiles and the mathematical models from the in-patient study.

Faecal samples and fasting urine and blood samples will be collected at the beginning and at the end of the 12 week period. Moreover, the C-reactive protein (CRP) and the HbA1c will be also measured at the beginning and at the end of the study. To monitor changes over time, all volunteers will attend the Clinical Unit 3 h after lunch, once every 2 weeks, for 12 weeks. Blood pressure, BMI and waist circumference will be measured at each visit. All the volunteers will provide from the day before 24-h urine, faecal samples and corresponding 24-h food diaries. Finally, spot urine and blood samples will be collected at each visit upon arrival at the unit. Blood samples will be collected at the beginning and at the end of the study and at each visit), via

venepuncture. The urine, feces, saliva and blood samples will be subjected to metabolic profiling analysis and other methodologies (e.g. whole genome genetics and epigenetics, transcriptomics, targeted proteomics) for the measurements of blood hormones and metabolites.

Dietary Counselling: All volunteers will receive the same high quality dietary counselling aimed at supporting good compliance to the diet in both the control and the intervention group. This will include face-to-face meetings at weeks 1, 2, 4 and 8, which will set and review dietary progress. This will be undertaken by Prof Frost's team who have 25 years of experience on clinical dietetic intervention. The methodology will reflect current dietetic counselling using individualised targets based on risk factor profile and dietary assessment. In addition, volunteers from the intervention group will receive enhanced personalised dietary advice using urinary and plasma metabolic profiles taken at each visit after obtaining patient consent. Prior to each visit, the dietitian will receive information on each participant's adherence to diet and changes in the level of biomarkers according to the "metabotracker" report. For example, if the metabolic profile indicates low prolinebetaine levels, which is related to low citrus fruit intake, then increasing citrus fruit intake will become a key dietary target. At the review visits, in weeks 4 and 8, annotated metabolic profiles from week 2 and 6 will be used to encourage change. The dietitian will also be able to assess adherence to the diet based on the mathematical model and to use this information to engage and educate participants.

STUDY CARRIED OUT TO COLLECT DATA TO DESIGN METABOLIC PROFILING MODEL
Participants underwent a 10 days study period. Participants were asked to attend the NIHR /Wellcome Trust Imperial CRF at Hammersmith Hospital for 5-days (and 4 nights) on two occasions, with a minimum of 2 weeks between both visits and in a randomized order, participants received a diet with different levels of compliance with NICE-guidelines for the management of CVD-Risk:
Week 1: 25% compliance to dietary guidelines ('unhealthy' diet)
Week 2: 100% compliance to dietary guidelines ('healthy' diet)

Blood pressure, BMI and waist circumference were measured at the start and end of each diet. 24 hour urine and spots urine samples and feces were be collected during each 5-day study period. Saliva samples were collected at the beginning of the first visit. Blood samples were collected at the beginning and at the end of each visit and on the 4th day of each study. The urine, faeces, saliva and blood samples were subjected to metabolic profiling analysis and other methodologies (e.g. whole genome genetics and epigenetics, transcriptomics, targeted proteomics) for the measurements of blood hormones and metabolites to:
1. Build a multiplatform mathematical model to establish the level of adherence of individuals at risk of CVD to dietary recommendations based on urine and blood composition
2. Investigate variability of individual's responses to both dietary interventions
3. Identify metabolic patterns at baseline that are predictive of an individual's response to diet in terms of changes in metabolism

Intervention Type
Other

Primary outcome(s)
Urinary and blood metabolic profiles measured from urine and blood samples using Nuclear Magnetic Resonance and Mass Spectrometry at baseline and then once every 2 weeks, for 12 weeks

Key secondary outcome(s))

1. Dietary biomarkers present in urine, blood, faeces, and saliva samples measured at baseline and then once every 2 weeks, for 12 weeks using metabolic profiling analysis
2. Participants eating behaviour measured using 24-h food diary measured once every 2 weeks, for 12 weeks
3. C-reactive protein (CRP) measured at baseline and 12 weeks
4. HbA1c measured at baseline and 12 weeks
5. Blood pressure (mmHg) measured using a sphygmomanometer at baseline and then once every 2 weeks, for 12 weeks
6. BMI (kg/m²) at baseline and then once every 2 weeks, for 12 weeks
7. Waist circumference (cm) at baseline and then once every 2 weeks, for 12 weeks

Completion date
31/03/2026

Eligibility

Key inclusion criteria
1. Aged between 30 and 65 years
2. At risk of CVD with at least three of the below criteria:
2.1. Body mass index of 20 - 35 kg/m²
2.2. Systolic BP >=140 mmHg or diastolic BP >=90 mmHg, or taking antihypertensive medication
2.3. LDL-cholesterol >= 4.14 mmol/l and HDL-cholesterol <=1.03 mmol/l (men) or <=1.29 mmol/l (women)
2.4. Family history of premature CHD
2.5. Waist circumference >102cm in men or > 88cm in women

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Have been involved in any other study during the 12 weeks
2. Weight change of >=3kg in the preceding 3 months
3. Substance abuse
4. Excess alcohol intake
5. Taken any dietary supplements in the last 6 months
6. Pregnancy
7. Diabetes
8. Cancer
9. Gastrointestinal disease e.g. inflammatory bowel disease or irritable bowel syndrome
10. Kidney disease
11. Liver disease
12. Pancreatitis

13. Any other chronic illness or being diagnosed with HIV
14. Use of medications likely to interfere with energy metabolism, appetite regulation and hormonal balance, including: anti inflammatory drugs or steroids, antibiotics, androgens, phenytoin, erythromycin or thyroid hormones

Subjects with the above conditions would have an altered pattern of hormones and inflammatory molecules because of their disease process and would therefore give us confounding or misleading results.

Date of first enrolment
01/07/2021

Date of final enrolment
31/01/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St. Mary's Hospital
Imperial College Healthcare NHS Trust
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W2 1NY

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
NIHR Academy; Grant Codes: CDF-2017-10-032

Funder Name
National Institute for Health Research (NIHR) (UK)

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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

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

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
Protocol file	version 3	11/11/2020	09/06/2023	No	No