# Metabolically personalised dietary advice for people at risk of cardiovascular disease

Submission date 13/11/2020	<b>Recruitment status</b> Recruiting	<ul><li>[X] Prospectively registered</li><li>[X] Protocol</li></ul>
<b>Registration date</b> 04/12/2020	<b>Overall study status</b> Ongoing	<ul> <li>Statistical analysis plan</li> <li>Results</li> </ul>
Last Edited 07/03/2025	<b>Condition category</b> Circulatory System	<ul> <li>Individual participant data</li> <li>[X] Record updated in last year</li> </ul>

## 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

**Contact name** Dr Isabel Garcia-Perez

#### **Contact details**

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**Type(s)** Scientific

**Contact name** Prof Gary Frost

ORCID ID

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## **Contact details**

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# Additional identifiers

EudraCT/CTIS number Nil known

IRAS number 237962

**ClinicalTrials.gov number** Nil known

Secondary identifying numbers 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

#### Secondary study design Randomised controlled trial

**Study setting(s)** Hospital

**Study type(s)** Prevention

#### Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

#### 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 measure

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

#### Secondary outcome measures

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

## Overall study start date

28/02/2019

## **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

#### Age group

Adult

**Sex** Both

**Target number of participants** Planned Sample Size: 154; UK Sample Size: 154

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** England

United Kingdom

Study participating centre

**St. Mary's Hospital** Imperial College Healthcare NHS Trust Praed Street London United Kingdom W2 1NY

## Sponsor information

Organisation Imperial College London

#### **Sponsor details**

Joint Research and Compliance Office Imperial College London and Imperial College Healthcare NHS Trust Norfolk Place London England United Kingdom W2 1PG +44 (0)2075949459 becky.ward@imperial.ac.uk

**Sponsor type** University/education

Website http://www3.imperial.ac.uk/

**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**

#### Publication and dissemination plan

Planned publication in a high-impact peer-reviewed journal. Data will be shared with the scientific community by presenting findings from the project on an on-going basis via speaking engagements at conferences and workshops attended by diverse user groups including practitioners and regulators (Department of Health and Food Standards Agency, etc). Specifically, I will work with the nutrition public health research communities and submit presentations and workshops at the British Nutrition Society and the British Dietetic Associations.

Moreover, I will work in partnership with my local Patients and Public Involvement (PPI) representatives to disseminate the results of the research to a wider audience through patient and support groups and I will additionally circulate the research outcomes in LinkedIn's nutritional groups. I will continue to actively participate in outreach activities.

#### Intention to publish date

01/10/2024

#### 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?
<u>Protocol file</u>	version 3	11/11/2020	09/06/2023	No	No
HRA research summary			28/06/2023	No	No