PROTOCOL

Data-driven integration of emerging technologies to generate a Standardised and Objective Dietary Intake Assessment Tool SoDiat Study

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Sponsor

Imperial College London is the main research Sponsor for this study. For further information regarding the sponsorship conditions, please contact the Head of Regulatory Compliance at:

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Funder: Medical Research Council, UKRI

This protocol describes the Data-driven integration of emerging technologies to generate a Standardised and Objective Dietary Intake Assessment Tool study and provides information about procedures for entering participants. Every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the study. Problems relating to this study should be referred, in the first instance, to the Chief Investigator.

This study will adhere to the principles outlined in the UK Policy Framework for Health and Social Care Research. It will be conducted in compliance with the protocol, the Data Protection Act and other regulatory requirements as appropriate.

KEYWORDS

Nutrition, Health, Research, Dietary reporting, Underreporting, Misreporting

Contents

STUDY SUMMARY

TITLE Data-driven integration of emerging technologies to generate a Standardised and
Objective Dietary Intake Assessment Tool SoDiat Study

AIMS To calibrate all chosen dietary assessment tools for effectiveness to monitor exposure to foods/food groups commonly consumed in the UK in a controlled food intervention.

Objective: To explore how three dietary assessment technologies (wearable microcamera, first morning void urinary metabolomics and capillary blood sample analysis) can contribute to the measurement of nutritional intake compared to known meal plan.

DESIGN Participants will be asked to attend the Research Unit at Imperial College London or the Hugh Sinclair Unit of Human Nutrition at the University of Reading for 5-days (4 days following the menu plan with return of the samples on day 5), on two occasions, with a minimum of 1 week washout between both visits. They will receive the following 4-day isoenergetic test menu diets during each test period (5-days), delivered in a random order:

Diet 1: Diet that has an unhealthy dietary profile based on National Diet and Nutrition Survey (NDNS) data representing the highest 25% fat, sugar, and salt intake, the lowest 25% starch, fruit and vegetable and dietary fibre intake.

Diet 2: Diet based on current UK healthy dietary guidelines.
Both diets will consist of a 2-day repeated menu, delivered twice over the 4-days.

POPULATION We will be studying a population of 30, balanced in males and females, ethnicities, between two sites.

ELIGIBILITY Males and females with a BMI between 20-30kg/m^2, age 18-70 years old.
DURATION Four-day dietary intervention on two occasions with minimum one-week washout

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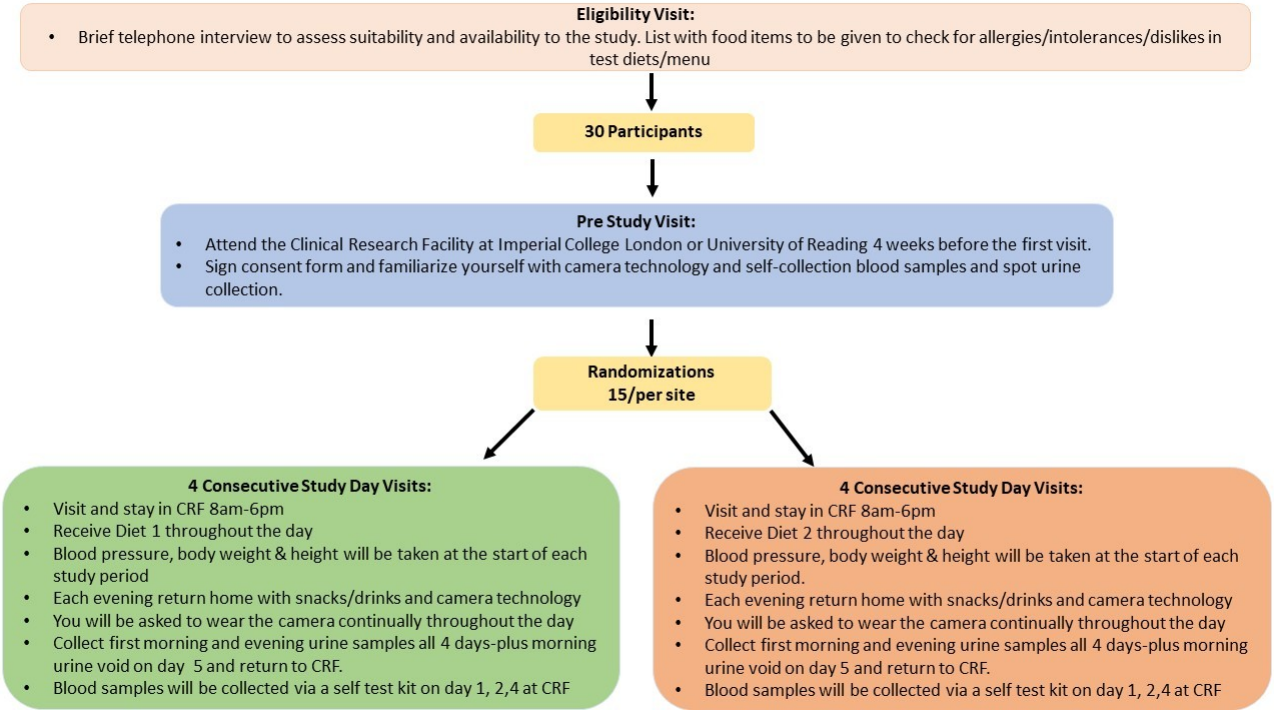
REFERENCE DIAGRAM



INTRODUCTION

Background

Habitual diet has a huge impact on the health and well-being of individuals and is a major contributor to the development of a range of chronic health conditions, such as diabetes, cardiovascular diseases, and many cancers. Many countries are facing rising levels of obesity and diet-related disease due to changes in dietary choices and eating behaviour, as well as more sedentary lifestyles. The robustness and impact of strategies aimed at addressing nutrition-related problems is consistently undermined by misreporting of dietary intake caused by our lack of an accurate tool to assess and monitor dietary intakes and nutritional exposures.

Self-reporting tools used traditionally to capture information about diet include Food Frequency Questionnaires (FFQs), 24hr dietary recalls and food diaries. At the core of the problem, we wish to address, is the reliance on such instruments, which struggle to categorise and represent accurately dietary intake and often entail costly expert researcher support, a substantial burden to study/survey participants and are subject to poor compliance, dietary change and significant reporting bias. To improve dietary reporting, we will bring together three additional technologies which have shown promise in improving accurately reporting dietary intake:

1. Urine biomarker technology measures water soluble secondary metabolites.
2. Capillary blood analysis to determine longer-term exposure to foods.
3. Camara technology with advanced image processing for food recognition and portion size estimation.

This study will compare the strengths and weakness of each technology then bring the team together to create a combined tool.

STUDY OBJECTIVES

Aims

1. Build a multiplatform model of dietary intake which report more accuracy that traditional self-report tools recommendations based on comprehensive molecular phenotyping of urine and blood plasma and camera technology.
2. To compare the individual technologies for accuracy of dietary reporting.
3. The generation of information required to inform the design of a dietary intake study protocol in a free-living population.

STUDY DESIGN

Methodology

Participants will attend to undergo two 4-day dietary interventions return the samples on the 5th day with a minimum of 1 weeks between both visits, with the administration of healthy dietary intervention, compliant with current dietary healthy guidelines and an unhealthy diet intervention. Diets will consist of a 1 day repeating menu, delivered twice over the 4-days.

Participants

30 male and female participants, aged between 18-70 years.
Potential participants will be emailed the participant information sheet; this will be followed up by a telephone call to go through the participant information sheet. All potential participants will have a brief initial telephone interview to assess their suitability and availability for the study.

Health Screening Visit

Because of the low risk of this study, on account of the intervention type and duration, there is no need for a physical examination.

Consent and Pre-Study visit

Pre-study: 4-weeks before the study, participants will attend the NIHR/ Imperial Clinical Research Facility at Hammersmith Hospital or the Hugh Sinclair Unit of Human Nutrition at the University of Reading (depending on your location), whereby informed written consent will be taken. To ensure participants are fully aware of the technology being applied they will be invited to spend 2 hours in the research facility to become familiar with the technology used prior to the study. They will be fitted with a camera and shown how to use the Onedraw self-collected capillary blood sampling method and the transfer straw and vacuum tube urine collection method. Should the volunteer want to proceed they will be invited to a two 4-day intensive studies, with a washout in between.
Additionally, a list of foods will be provided to you to ensure that you will be able to consume the food items provided. A full list of food products can also be found at the end of this document.

Randomization

Randomisation will be undertaken using an online provider, sealed envelope.com (**https://www.sealedenvelope.com/**).

Study visits

The study visits will take place at the NIHR/ Imperial Clinical Research Facility at Hammersmith Hospital or the Hugh Sinclair Unit of Human Nutrition at the University of Reading and will include two 4-day study periods as follows:

- Study period 1: 4 full day visits then return to the unit on the 5th day to return samples/equipment.
- Wash out: there will be a gap of at least 1 week between study periods (this will be longer for menstruating women who will attend study visits at the same phase of their menstrual cycle).
- Study period 2: another 4 full day visits then return to the unit on the 5th day to return samples/equipment.

Participants will be asked to attend the research unit at 8am every morning of the 8 study days, following a 12 hour overnight fast (not consuming any food or drink, except water) and remain in the unit until 6pm. Blood pressure, height and body weight will be measured when you arrive on the first day of each study period.

In a randomised order, they will receive a test diet during each study period that has a different level of compliance with UK healthy eating guidelines:

- Diet 1: far from meeting healthy eating dietary guidelines (e.g., high in fat, sugar, and salt and low in starch, fruit, vegetables, and fibre)

- Diet 2: fully compliant with healthy eating dietary guidelines (e.g., high in fruits and vegetables as well as good quality protein and fat, and complex carbohydrate sources).

Participants will be served meals and snacks throughout the 8 study days (8am – 6pm) according to the diet they have been randomly assigned during each study period. Diets will consist of a 2-day repeating menu (e.g., menu 1 on days 1 and 3, and menu 2 on days 2 and 4). At 6pm of the 4 study days, they will return home with a snack and drinks (coffee, tea, or soft drinks) to be consumed in the evening. They will be instructed not to eat or drink anything, except for the evening snack and drinks provided between each 4-day study period.

Micro camera

You will be given a micro camera which can be attached to the frame of eyeglasses or a broach or a pendant for the two 4-day study periods to video record everything that you eat and drink. The camera will have to be worn continuously for the 4-day study period (it can be removed when having a shower, sleeping etc.).
Full instructions on how to wear and activate the camera will be given as well as instructions on how to plug the cameras into the chargers at night. The camera technology will capture everything in its vision, which includes food, drink, and potentially other people. Additionally, although you will eat separately to other participants in the research unit, there is a chance of being filmed by another study participant. To ensure everyone’s anonymity any footage of people recorded by the cameras, including you and other people who live with you, will be blurred. When the video data is being downloaded and analysed to assess your food intake this is

achieved via an artificial intelligence methodology which only considers the food and drink images and not face recognition.

Spot urine samples

For each study period, they will be asked to collect first morning urine and evening urine samples on all study days plus first morning urine on day 5. These will be returned to the research facility daily. They will be provided with detailed instructions and a kit to collect, store, and transport your urine samples.

Self-collection blood samples

Additionally, they will be asked to provide the team with a self-collected capillary blood sample on days 1, 2 and 4 to be taken by you in the unit (a researcher will be present if assistance is required but they will not take the blood samples). 'OneDraw' is a single-use system that simplifies the collection, stabilisation, and transport of blood samples. A researcher will provide guidance on how to use the equipment and clear instructions will be given. In summary, the OneDraw device attaches to your upper arm via a vacuum mechanism and two small lancets (retractable needles) pierce the skin. The device then collects approximately 3 drops of blood on a strip of filter paper. The whole process, including reading the instructions, takes about 20 minutes.

Online dietary assessments: Intake24 and eNutri

Intake24 and eNutri are easy-to-use, self-reporting online tools that records what a person eats and drink. They can be used on any device (tablet, laptop, smartphone) via a web browser (e.g., Chrome, Safari, Edge). Participants will be provided with login details. Each tool also has a tutorial video for participants to watch before starting.

Intake24 is a 24-hour multi-pass dietary recall. Participants will record what they have been eating and drinking during the 8 study visits by using Intake24 the following day (for example, on day 2 they will recall what they ate and drank during day 1, etc.). Intake24 guides you through the process that starts by listing what you ate/drank the previous day, then asking how much you had using portion size photos as well as recording extra details (e.g., if you had a cup of tea, did you add milk and, if so, what type?). This takes around 15 minutes to complete.

Participants will also complete the eNutri food frequency questionnaire. they will be presented with a detailed list of food and drink items and asked to report how often they had each during the previous 4 weeks and how much they typically ate/drank by selecting from one of the portion size photos/buttons. This takes around 25 minutes to complete. It will be used at the start of day 1 of the first diet period only to record habitual diet. It will then be used again towards the end of day 4 for both diet periods to record intake during study visits.

Usability of the study tools/techniques

For each of the tools/techniques listed above, they will be asked how easy/difficult you found each to use by answering a short questionnaire on one occasion.

PARTICIPANT ENTRY

Pre randomization evaluations

Potential participants will first have a short telephone interview to assess their suitability for the study.

Inclusion criteria

Male and female participants of all ethnicities (aged 18 to 70 years old)
Normal to overweight individuals (body mass index (BMI) 20-30 kg/m2)

Exclusion criteria

- Have been involved in any other study during the 12 weeks, are not able to commit to the study (e.g travel commitments), unwilling to collect urine and blood samples.
- Had a weight change of ≥ 3kg in the preceding 3 months or are currently following a weight-loss diet.
- Have excess alcohol intake (>21 units per week) (E.g., a medium glass of wine = 2.3 units).
- Are unwilling to abstain from drinking alcohol during the 5-day test periods.
- Are unwilling to follow the study menus (e.g., dislike of food items, following a restrictive/specialised diet, such as vegan, or receiving specialised dietary advice for a medical condition).
- Are not able to eat fish or meat. Are vegan or vegetarian.
- Have an allergy/intolerance to food items menu.
- Have taken any dietary supplements in the last 3 months.
- Are pregnant or lactating.
- Currently, suffer from any of the following: eating disorders, diabetes, cancer, gastrointestinal disorders (e.g., inflammatory bowel disease or irritable bowel syndrome), kidney disease, liver disease, pancreatitis, or any other chronic illness.
- Have being diagnosed with HIV or AIDS
- Are taking any of the following medications: anti-inflammatory drugs or steroids, antibiotics, androgens, phenytoin, erythromycin or thyroid hormones, statins and blood pressure medications, antidepressants.
- Use illicite substances.
- Have been diagnosed with dementia or other conditions affecting memory.
- Have difficulty using laptops/tablets (e.g., cannot use these devices without assistance, are blind or have other conditions affecting sight, or have physical disabilities/conditions that affect ability to press buttons).
- Cannot read and understand English.

Withdrawal criteria

- The safety of the study participants takes priority. Any significant adverse event (as assessed by the researchers) will halt the study and the ethics committee and sponsor will be informed as per standard protocol. All adverse events will be recorded, and investigators will review each adverse event as it arises. In addition, participants will be free to withdraw at any time and are not required to give a reason. Finally, if participant's lose capacity to consent, they and their data will be immediately excluded from the study.

ADVERSE EVENTS

Definitions

Adverse event (AE):

Any untoward medical occurrence in a patient or clinical study subject.

Serious/serious Adverse Event (SAE):

Any untoward and unexpected medical occurrence that:

- results in death
- is life- threatening – refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it was more severe
- requires hospitalisation.
- results in persistent or significant disability or incapacity
- is a congenital abnormality or birth defect

Medical judgement should be exercised in deciding whether an AE is serious in other situations. Important AEs that are not immediately life threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

REPORTING PROCEDURES

All adverse events should be reported. Depending on the nature of the event the reporting procedures below should be followed. Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance.

Non-serious AEs

All such events, whether expected or not, should be recorded.

Serious AEs (SEAs)

An SAE form should be completed and emailed to the Chief Investigator within 24 h. However, relapse, death, and hospitalisations for elective treatment of a pre-existing condition do not need reporting as SAEs.

All SAEs should be reported to the xxxx Research Ethics Committee where in the opinion of the Chief Investigator the event was:

- 'related', i.e., resulted from the administration of any of the research procedures; and
- 'unexpected', i.e., an event that is not listed in the protocol as an expected occurrence.

Reports of related and unexpected SAEs should be submitted within 15 days of the Chief Investigator becoming aware of the event, using the NRES SAE form.

Local investigators should report any SAEs to the sponsor and their Local Research Ethics Committee and/ or Research and Development Office.

Contact details for reporting SAEs
RGIT@imperial.ac.uk
Prof. Gary Frost
Fax 020 8383 8320
Please send SAE forms to: g.frost@imperial.ac.uk

Tel: 020 7594 0959 (Mon to Fri 09.00 – 17.00)

ASSESSMENT AND FOLLOW-UP:

No follow up visit or monitoring of the participant will be needed after participation in the study.

STATISTICS AND DATA ANALYSIS

Data from Pettitt et al, 2016 was used. The misreporting rate of total energy expenditure between self-reported diet records compared to the 'gold standard' of double labelled water was 35%, with a standard deviation of 33 %. Passive food intake determination, using egocentric camera technology alongside web-based food records (Intake24) reduced the misreporting rate to less than 10 %, in controlled conditions. To achieve a power at 80 % with a Type 1 error (alpha) of 5.0 %, and a delta of 25 %, a total of 27 participants are required. Accounting for a potential drop-out rate of up to 10 %, a further 3 participants are required, to give a total sample size of 30. Two separate clinical research centres (Imperial and Reading) will be used, with both centres recruiting participants to ensure consistent demographics between sites (gender, age, BMI). Additionally, other appropriate statistical tests may also be performed if needed (e.g Cohen Kappa coefficients and Bland-Altman).

REGULATORY ISSUES

Ethics Approval

The Study Coordination Centre will obtain approval from the Research Ethics Committee (REC) and Health Regulator Authority (HRA) and approval will also be sought from the University of Reading REC. The study must also receive confirmation of capacity and capability from each participating NHS Trust before accepting participants into the study or any research activity is carried out. The study will be conducted in accordance with the recommendations for physicians/researchers involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

Consent

Consent to enter the study must be sought from each participant only after a full explanation has been given, an information leaflet offered, and time allowed for consideration. Signed and initialled participant consent, which is countersigned by the researcher taking consent. should be obtained. The right of the participant to refuse to participate without giving reasons must be respected. After the participant has entered the study, the clinician remains free to give alternative treatment to that

specified in the protocol at any stage if he/she feels it is in the participant's best interest, but the reasons for doing so should be recorded. In such cases, the participants remain within the study for the purposes of follow-up and data analyses. All participants are free to withdraw at any time from the study without giving reasons and without prejudicing further treatment.

Confidentiality

Pseudonymised data is data that can be linked back to a person (e.g., coded data). It is considered both personal and identifiable data. Anonymised data is data that has no code and cannot be linked back to a person (e.g., aggregated data for publication, data without a code that cannot be linked back to a person).

The Chief Investigator will preserve the confidentiality of participants taking part in the study and is registered under the Data Protection Act.

Data will be both anonymized and pseudonymised.

Pseudonymised data will be transferred between researcher partners, including University of Cambridge and Aberystwyth University.

Indemnity

Imperial College holds negligent harm and non-negligent harm insurance policies, which apply to both research sites in this study.

Sponsor

Imperial College London will act as the main sponsor for this study. Delegated responsibilities will be assigned to the NHS trusts taking part in this study.

Funding

This research project is part of a grant funded by the MRC/BBSRC Programme grant.
Participants will be reimbursed for their time and for any inconvenience caused due to attending the study periods. They will receive £400 for successful completion of the study.

Audits and Inspections

The study may be subject to inspection and audit by Imperial College London under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the NHS Research Governance Framework for Health and Social Care.

Study Management

The day-to-day management of the study will be co-ordinated through the research teams at Imperial College London and University of Reading.

Publication Policy

The findings of the research will be published in an open-access, peer-reviewed journal. In addition, we will be collaborating with patient groups and professional groups to disseminate the findings via multiple media channels such as patient association publications, print and broadcast media.

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