STARCHy staples: a randomised controlled trial on Cardiometabolic Health.

Clinical Trials ref: NCT05994313

REC: HR/DP-22/23-35587

Version number: 5.1
31 August 2025

Short title/ Acronym: The STARCHy study.

Abbreviations

CGM - Continuous Glucose Monitor
ECG – Electrocardiogram
HRV – Heart Rate Variability
BP- Blood pressure
FMD – Flow mediated dilation
VAS – Visual analogue scale

1. Trial summary

Responsible Individuals

Principal Investigators

Professor Wendy Hall
Reader in Nutritional Sciences
Franklin Wilkins Building
Faculty of Life Sciences and Medicine
Department of Nutritional Sciences
150 Stamford Street, London, SE1 9NH
Email: wendy.hall.ac.uk

Professor Sarah Berry
Reader in Nutritional Sciences
Franklin Wilkins Building
Faculty of Life Sciences and Medicine
Department of Nutritional Sciences
150 Stamford Street, London, SE1 9NH
Email: sarah.e.berry@kcl.ac.uk

PhD researcher and trial coordinator

Anya Klarner, ANutr
Franklin Wilkins Building, Room 4.46
Faculty of Life Sciences and Medicine
Department of Nutritional Sciences
150 Stamford Street, London, SE1 9NH
Email: anya.klarner@kcl.ac.uk

Collaborators

Dr Peter Joris
Universiteitssingel 50, room 0.314
P.O. Box 616, 6200 MD Maastricht, The Netherlands
Phone: +31 (0)43 388 1311
E-mail: p.joris@maastrichtuniversity.nl

V5.1 31/08/2025
NON-CTIMP randomised trial
Clinical Trials ref: NCT05994313
REC: HR/DP-22/23-35587

Nihat Baysal
Chemical and Biological Engineering
Rensselaer Polytechnic Institute, Troy, New York 12180-3590
E-mail: baysan@rpi.edu

Study Synopsis

Title	STARCHy staples: a randomised controlled trial on Cardiometabolic Health
Protocol Short Title/Acronym	The STARCHy study
Protocol Version number and Date	Version 5: 20/08/2025
Study Phase if not mentioned in title	n/a
Is the study a Pilot?	No
Study Site	In-person visits: Metabolic Research Unit, Corridor A, 4th floor, Franklin Wilkins Building, SE1 9NH Remote video calls via Teams
Study Duration	24-months
Official study start date	09/09/2023
Estimated Primary Completion	01/05/2025
Methodology	A randomised, two-parallel arm, in clinic and remote, 12-week dietary intervention, with a 2-week run in period. Participants with either receive 230g of potatoes in their evening meal (intervention) or isocaloric amounts of other refined starchy staples, such as rice, pasta, or cous cous (control). Participants will make their own meals based on dietary guidance and resources (meal plans), given from a registered nutritionist, to match UK recommendations.
Sponsor name	King's College London

Chief Investigator	Dr Wendy Hall and Dr Sarah Berry
REC number	22/23-35587
Medical condition or disease under investigation	Cardio-metabolic health
Purpose of clinical trial	To investigate the cardio-metabolic health effects of consuming potatoes in place of other refined carbohydrate (pasta and rice), in healthy adults.
Primary objective	The primary objective of this proposal is to investigate whether consuming a portion of potatoes in the evening meal, in place of other refined carbohydrates, can improve sleep quality (measurable as the ratio of total sleep time in bed: "sleep efficiency"), and improve mean nocturnal glucose, both risk factors for cardiometabolic diseases.
Secondary objective (s)	To investigate the effects of regular white potato consumption on endothelium-dependent vasodilation (measured by flow-mediated dilatation) and other related biomarkers of cardio-metabolic disease risk, when compared to regular refined carbohydrate consumption.
Number of Participants	The study aims to recruit a total of 80 participants (allowing ~15% drop out rate), for an allocation of 1:1 intervention to control, to reach 80% power at a significance level of 0.025 (based on two outcomes).
Trial Design	A randomised, two-parallel arm, in clinic and remote, 12-week dietary intervention study.
Study arms	1. Experimental: Habitual potato consumption. At minimum of 230g white potatoes, including fresh and frozen, baked, boiled and mashed potatoes, will be consumed in the evening meal, in replacement of other starches. 2. Active Comparator: Habitual non-nutrient dense starch consumption.

	Isocaloric amount of non-nutrient dense starchy staples, such as white rice, white pasta, and white couscous, will be consume din the evening meal.

Endpoints	**Primary**
	• 7-day Sleep efficiency, at baseline and endline
	• 12-day nocturnal mean glucose (using Continuous Glucose Monitors (CGM) during sleep), at baseline (0 weeks) and endline (12 weeks)
	Secondary
	• Endothelium-dependent vasodilation (measured by ultrasound image analysis as Flow-Mediated Dilation (FMD)), at baseline and endline.
	• 12-day daytime and 24-hour glucose metabolism (CGM outcomes, glycaemic variability, time in range).
	• 48hrs nocturnal, daytime and stress-related heart rate variability (measure of autonomic function; higher range the more autonomic function)
	• 12-week daytime and night-time continuous blood pressure (Aktiia blood pressure bracelet)
	• Blood parameters
	  ○ Glucose control (fasting HbA1C, fasting glucose and insulin)
	  ○ Lipids
	• Body composition
	  ○ weight and waist circumference
	  ○ % body fat and lean body mass (Tanita scales)
	• Visual Analogue Scale (VAS) assessments of satiety, included in 4-day diet diaries.
	• Urinary potassium and sodium
	• Urinary alkaloids (calystegines)
	Compliance
	• Urinary potassium and sodium
	• Dietary assessments
	  ○ 24-hour recall (Wk 2, 4, 8)
	  ○ 4-day food diary (Wk 0, 6, 12)
	  ○ Self-reported adherence: checklist of evening meal

Main Inclusion Criteria	Participants will be healthy male or females, aged between 40-80 years who consume ≤4 fruits and vegetables a day (excluding potatoes), with a less favourable sleep efficiency score of <85%

Statistical Methodology and Analysis	Differences between groups (minimized for age, gender, BMI) will be analysed using Linear mixed models for outcomes with 3 timepoints (urinary outcomes, dietary intake data), with change being the dependent factor, participant ID as random effect, treatment and season as fixed effects, and baseline outcome and BMI as covariates. Variables with 2 timepoints will be assessed with an ANCOVA regression model. A 2 -sided P value <0.05 will be considered as showing statistical significance. For more details of statistical analysis plan, see section 4.2.
Data monitoring and sharing	No formal data monitoring committee. Oversight by PI and sponsor. De-identified data will be shared upon reasonable request and in collaboration with the study investigators, beginning 12 months after publication of the main trial results.

2. Introduction

2.1 Background

There are several studies currently underway to explore the CM health effects of diets rich in potatoes on glucose metabolism, lipids, inflammation, and blood pressure/vascular function. However, to our knowledge, none investigate the potentially favourable impact of potatoes on the harmful triad of ***poor sleep - adverse glycaemic control - vascular dysfunction***.

Poor sleep quality is related to adverse glycaemic control: can increasing potassium intake help?

The deleterious impact of poor sleep on diet, obesity and CM health (1) has been consistently reported in observational and interventional studies (2). Potential mediating mechanisms include; impaired endothelial function (3), perturbed postprandial (4) and nocturnal glycaemic responses (5), raised blood pressure, and bi-directional associations between diet and poor sleep quality (6). Results from the PREDICT 1 cohort (n=1102) showed that participants with higher sleep efficiency (i.e. better sleep quality), measured objectively using wrist actigraphy, had lower postprandial blood glucose the next day following a standardised test meal than those with low sleep efficiency, and this relationship was replicated upon within-participant analysis, suggesting that better sleep quality could lead to improved glycaemic control in healthy individuals (4). This potential causal link between poor sleep quality and adverse glycaemic control may be mediated via poor diet quality in free-living conditions, as inadequate sleep increases cravings for less healthy foods (7) (and vice versa, poor dietary choices may impact on sleep quality (6)). However, there may also be a direct effect by increasing sympathetic outflow thereby suppressing insulin secretory responses to fluctuations in glucose (8).

High dietary glycaemic index (GI) is associated with greater subsequent risk of insomnia (9) whereas higher intakes of fruit, fibre and vegetables (9, 10, 11) are associated with better sleep quality. The effects of fruits and vegetables on sleep quality have been suggested to be related to their polyphenol, melatonin, and serotonin contents (6), but little attention has been paid to their potassium content as a putative sleep quality promoter. Preliminary data analysis using our PREDICT cohort show that there is a positive association between potassium intakes and sleep duration (P=0.02) and an inverse

association between fasting glucose and glycaemic variability with potassium intakes (P=0.03, P=0.04) respectively, adjusted for age, sex, BMI and energy intake. This requires further investigation as regards to the source of potassium and adjusting for background diet, as proposed in this application. Potassium may plausibly modify sleep quality (12), glycaemic control (via insulin secretion (13)) and cardiovascular function (14) by modifying autonomic function. For example, potassium supplementation in rats with chronic heart failure reduces sympathetic overactivity and restored baroreflex function (15) and reduces risk of CVD mortality (16) and reduces blood pressure in human studies (17, 18), the latter mediated in part by preservation of autonomic function (19), as well as reduction in renal sodium reabsorption and stimulation of endothelium-dependent vasodilation.

Endothelial function: can increasing potassium help?

Sufficient dietary potassium may improve sleep quality and glycaemic control, and consequently this may support better endothelial function. Poor sleep quality has been reported to be associated with lower FMD in a cohort of healthy adults (20) and restricting sleep by one-third causes endothelial dysfunction in healthy individuals (21). Likewise, oscillating blood glucose concentrations in healthy volunteers led to impaired endothelial function, likely to be mediated via vascular inflammation and oxidative stress (22). However, there is also evidence that potassium could directly act on the endothelium to increase nitric oxide production (and thus endothelial function) (14, 23), which could also potentially benefit autonomic function by enabling greater nitric oxide bioavailability in the brain as well as the blood vessels (24).

Potassium intakes and potato consumption in the UK and US

Low population dietary intake of potassium is a point of concern in both the UK (median intake 79% of the reference nutrient intake) and US. However, potatoes are the greatest contributors of dietary potassium for a single food (UK and US), contributing 14% of intakes in UK 19-64 y olds (consumers and non-consumers) (25) and 20% of intakes in US (for consumers) (26). Although regarded as a high glycaemic index food, potatoes that were boiled, roasted, or boiled then cooled, resulted in markedly lower nocturnal interstitial glucose concentrations compared to rice in individuals with type 2 diabetes despite there being no glycaemic differences in the acute postprandial period (27). Potatoes are rich in micronutrients, unlike commonly consumed starchy staples such as white rice and pasta. In addition to potassium, potatoes contribute 15% of vitamin B6 intake, 14% of vitamin C and 10% of folate in the UK (28), and therefore contain a range of components that may additively improve glucose metabolism, endothelial function and sleep quality beyond the immediate postprandial period.

2.2 Hypothesis and rationale

In the long term, a potato-rich diet could be an important strategy for reducing risk of CM diseases. This proposal aims to unravel an array of understudied CM health variables that may be beneficially affected by habitual consumption of nutrient-dense white potatoes.

We hypothesise that regular consumption of potatoes in place of other less nutrient-dense starchy foods increases sleep efficiency, reduces nocturnal glycaemic variability, and improves endothelial function in middle-aged to older adults.

To establish causality between potato consumption and these outcome measures, including mediating mechanisms, we plan to conduct a randomised, two-parallel arm-controlled trial in healthy adults between the ages of 40-80 years.

3.0 Study Objectives and Design

3.1 Study Objectives

To answer the following research questions:

Primary Objectives and endpoints (for detailed summaries of the outcomes, see section 3.3)

1) *Does regular consumption of white potatoes increase sleep quality, measurable as the ratio of total sleep time to time in bed: "sleep efficiency (SE)"?*

2) *Does regular consumption of white potatoes improve night-time glycaemic control compared with other, less nutrient dense starchy staples (white pasta, white rice etc.)?*

Secondary Objectives and endpoints

3) *Does regular consumption of white potatoes improve endothelial function?*

4) Does *regular consumption of white potatoes improve autonomic function?*

5) Does *regular consumption of white potatoes improve blood lipid profiles, and glucose control (fasting glucose, fasting insulin, glycated haemoglobin), when compared with other, less nutrient dense starchy staples?*

6) Does *regular consumption of white potatoes improve blood pressure?*

3.2 Intervention overview

Table 1. Summary of the Starchy Study's arms and Interventions, as written on ClinicalTrials.Gov

Arms	Assigned Interventions
Experimental: Habitual potato consumption At least 230g of white potatoes, including fresh and frozen, baked, boiled, and mashed potatoes, will be consumed in the evening meal, in replacement of non-nutrient-dense starchy staples, for 12 weeks.	Dietary Supplement: Habitual potato consumption Potatoes are to be consumed in the evening meal, every evening for 12-weeks.
Active Comparator: Habitual non-nutrient-dense staple consumption Isocaloric amounts of non-nutrient-dense starchy staples, such as white rice, white pasta, and white couscous, will be consumed in the evening meal for 12 weeks.	Dietary Supplement: Habitual non-nutrient-dense staple consumption White rice, white pasta or white couscous are to be consumed in the evening meal, every evening for 12-weeks.

Dietary Intervention

The intervention (potato group) will consume 230 g white potatoes as one of their 5-a-day fruits and vegetables, providing ~1000 mg potassium (enough to increase national median intakes up to

recommended intakes) in their evening meal (25% of energy intake from carbohydrates, or 12.5% of total energy intake, including fresh and frozen baked, boiled, mashed potato products), whereas the control group will consume isoenergetic amounts of non-nutrient dense starchy staples (white pasta, white rice, or couscous).

Participants will be given £5 per week, in renumeration for the purchasing of the starchy component.

Although participants cannot be blinded to what they're consuming, they will be blinded to whether they are in the control or the intervention group, to reduce risks of bias.

We have chosen not to adjust for % estimated energy requirements as potatoes are typically eaten as a standard portion size (e.g., standard baked potato is ~200g), and this simplifies the intervention for the participant.

Participants will be required to source the potatoes and make these meals themselves, however, they will be provided with rotating 4-weekly recipe cards, with instructions on how to prepare meals. Guidance on eating out will be provided to maintain study compliance, as successfully utilized in other studies (29). We believe this will sufficiently standardise nutrient intakes from the non-starchy staple dietary components both inter and intra arms. We plan to use the dietary recalls at weeks 2, 4 and 8 to reinforce dietary advice, and to make adaptations to rotating menus based on individual needs, if participants are struggling with adherence (30).

Recipes will be generated by modelling meals in Nutritics software and will aim to follow food based dietary guidelines for the UK (31) and the US (32).

Printed leaflets and dietetic/nutrition led coaching will be used to advise individuals on how to incorporate potatoes into their evening meal (to be eaten before 8pm) to ensure that the diet contains a mixed composition of potato categories, with consideration for habitual dietary intakes, as used in our previous dietary intervention studies (26,40). The study duration of 12 weeks has been selected as sufficient time to induce changes in fasting FMD (41), and glycaemic control (42). A parallel arm has been chosen to maintain compliance due to the duration of the intervention.

Dietary Advice (Week 2 dietary consultation).

Both arms will receive food-based dietary advice from an associate nutritionist, broadly consistent with UK dietary guidelines and USDA recommendations.

These recommendations will be inclusive of, but not limited to:

- Discourage snacking before bed and encourage food consumption before 8pm, to prevent unfavourable postprandial glycaemic responses as observed in clinical trials (33), and other metabolic dysfunction biomarkers (34), explained by chrono-nutrition (35). Although individuals tend to consume dinner later than at usual at the weekend (36), most of the UK and US population eat between 18:00-20:00 (37, 38), therefore we believe this is a feasible ask.
- Reduce excessive alcohol intake or excessive changes in exercise habits.
- To consume similar levels of salt, types of fat, and added sugars, to standardise across arms.
- Additionally, participants will receive personalised advice on front of package labelling, eating out and choosing convenience meals.

Compliance

Biochemical Assessment

Compliance will be monitored by 24 h urinary potassium excretion, which is shown to recover 75% of potassium intake (39). These samples will be analysed by flame photometry (40). No other appropriate biomarkers of compliance are specific enough to monitor differences in the control and potato interventions in this study design. Additionally, sodium excretion will be analysed to indicate dietary sodium intake. This is a relevant indicator in our study as sodium intake could confound the results of this study.

Urinary creatinine will be used as one marker to distinguish between complete and incomplete 24 h urine collections (41), specifically the Knuiman et al creatinine excretion method (urinary creatinine [mmol/d] x 113)/(21 x body weight [kg]) (42), which has been shown to be the most sensitive and specific (43). Samples with a creatinine index <0.7 will be discarded as incomplete.

Additionally, self-reported missing samples (more than a few drops, as assessed by word of mouth and urine collection forms) and samples with a total volume <400 mL will marked as incomplete, as outlined in the NHANES survey (44).

Midline urine samples will be analysed within a week of collection, to assess compliance.

Dietary Assessment

Dietary assessment evaluations will be built into the study design to evaluate and encourage compliance to treatments, including 4-d food records (WK 0, 6, 12), and 24h dietary recalls (WK 2, 4, 8) with the multipass method (45).

Additionally, self-reported compliance methods will be employed via an evening meal checklist in the data diaries provided to participants. This will determine the level of compliance (%) and may be used as stratum in analysis. ≥75% of overall days exposed to the starch, as well as 75% of the days exposed in the final four weeks, will be counted as compliant. Any rates below 75% in either of these time periods, will be counted as non-compliant for ITT.

3.3 Outcome variables

Primary Outcomes

Sleep efficiency: As aforementioned, increased dietary potassium may plausibly modify sleep quality, as previously seen in an interventional study by Drennan et al (46), through mediation of improvements to autonomic function (19) and improved vascular function by restoring baroreflex function (15) and improving endothelium-dependent vasodilation (47).

This is measured by using 7-d wrist actigraphy (MotionWatch8, CamNTech Ltd, Cambridge, UK) according to previously published procedures (7). Sleep quality (%) is measured as the amount of time spent asleep/ total amount of time spent in bed.

12-day mean nocturnal glucose*:* Potatoes may improve nocturnal glucose through several pathways, involving increased dietary quality (48), such as increased vitamin C (49), increased dietary potassium (50) and increased satiety, when compared to alternative starches (51).

Nocturnal measures were chosen to assess glycaemic regulation without the confounding influence of food intake. Whole sleep-time glycaemia parameters will be analysed is, and further sub analysis will

be done pre- and post-sleep, and mid-point to investigate potential differences according to sleep stages.

CGM (Abbott Freestyle Libre 3) will be used to measure glycaemic control for 12 consecutive days. The principal investigators have recently reported on the high precision of the Abbott CGM (52). Twelve days has been selected as the 1st and last day of the CGM period may give unreliable results, therefore day 1 and 14 will be excluded from the analysis.

Secondary outcomes

Other nocturnal glucose markers: We will further analyse 12-day nocturnal area under the curve, glycaemic variability (GV), time in range non-diabetic population (TIR_{ND}). GV reflecting glucose fluctuations, are more strongly associated with oxidative stress than prolonged elevated glucose and glucose nadir and peaks, including the number and size (% change from pre-meal baseline) due to the association of glucose nadirs with hunger, satiety, alertness and energy intake (at subsequent meals and over 24 h period) (53) and peaks with oxidative stress and impairment in glycaemic control. Increased TIR_{ND} is associated with improved cardiometabolic markers (lower HbA1c, HOMA-IR, and 10-y ASCVD risk) and with poorer glucose tolerance when TIR is low (higher 1- and 2-h OGTT glucose) (54).

Daytime glycaemic control: Additionally, we plan to look at the same markers across 12-day daytime and 24-hour period.

Endothelial function: Impaired nitric oxide (NO) production causes endothelial dysfunction and increases risk of CVD (55). Capacity to synthesize NO can be assessed by ultrasound imaging of brachial arterial diameter before and after hyperaemia to determine FMD, regarded as the most reliable *in vivo* index (56). Measurements (and blood samples) will be taken at the same approximate time of day to account for circadian fluctuations, and by the same operator to reduce measurement error. All videos will be analysed using a custom MATLAB program (VidArt V13.5, A.P. Hoeks, Department of Biomedical Engineering, Maastricht University Medical Center (MUMC)+, Maastricht, The Netherlands)

***Heart rate variability (HRV) and blood pressure (BP)*:** Improved HRV, a parameter of cardiac autonomic function, and BP are plausible health benefits of white potato consumption due to increased potassium intakes. Previous intervention studies have reported an improvement in clinic BP following potato consumption (18); however, the effects of potato intake on HRV have not been investigated to our knowledge. HRV is an indirect measure of autonomic nervous system function and predictive of risk of sudden cardiac death (57).

HRV will be measured using a small wireless heart rate/ECG monitor that continuously records interbeat intervals (eMotion Faros 180, Mega Electronics Ltd) to calculate 48-h, daytime and night-time parameters using Cardiscope Analytics software (HASIBA Medical GmbH) (58) Building on prior HRV analysis expertise (58, 59, 60), this will provide novel data on a hitherto unexplored risk factor for hypertension, T2D, chronic kidney disease and CVD events in relation to potato consumption, and will provide important mechanistic information underpinning the 3 primary outcomes. BP will be measured at home using optical blood pressure monitoring via a bracelet. 2-hour averages will be obtained continuously for 12-weeks.

Diet quality will be measured using dietary indices associated with health including PDI (61) (uPDI, hPDI), aMED (62), aHEI (62) and HFD (63, 64) to demonstrate the impact of potatoes on overall diet quality and for inclusion as a covariate in analysis.

Body composition: *Weight* will be measured (weekly) using home weighing scales. Percentage body fat will be assessed (baseline & endline) using bio-electrical impedance, and waist circumference will be measured with a tape measure at clinic visits.

Blood biomarkers: Plasma lipids (total, HDL-, and LDL-cholesterol and TAG, and calculated TC:HDL-C ratio) will serve as clinically relevant biomarkers of metabolic dysregulation alongside fasting plasma glucose, insulin and HbA1c. Urine and serum potassium will be used to assess compliance as well as a potential stratifier in the analysis of outcomes.

Urinary calystegine biomarker: Calystgeines will be analysed as an exploratory biomarker of potato consumption (a polyhydroxylated nortropane alkaloid) (65) by Triple Quadrupole mass spectrometry (MS/MS). This will accompany existing self-reported compliance records and increase the reliability of this outcome. To our knowledge, this will be the first time this biomarker has been used in a clinical trial setting.

3.4 Study Design & Flowchart

Overall study flow diagram is described in Figure 4, and a more detailed event and outcome matrix is summarised in Table 1.

3.5 Population description.

Participants will be aged 40-80 years old. As cardiometabolic health declines with age, this age group is typical of an at-risk population for cardiometabolic health disorders. This declination of health also offers more room to observe intervention improvements when compared to a younger population.

The ethnicity will be reflective of the of the central London location of KCL. Previously, large dietary intervention trials conducted by the principal investigators, such as: MARINA, RISCK, DRFRUITNVEG and CRESSIDA, have recruited 66-85 % white, 9-10 % South Asian, 5-10 % Black African/Caribbean, and 2-4 % other ethnic groups (30, 39, 66).

Participants will have less favourable self-reported sleep quality scores (<85%) (67), as assessed at screening. This sleep efficiency score has been chosen to allow more scope to detect intervention-lead improvements.

Participants will also consume <4 fruits and vegetables/day, as assessed at screening, which is representative of the typical UK/US diet (25).

3.6 Recruitment methods

Volunteers will be recruited from the public using Kings College emails (circular) and using social media adverts (Twitter, Facebook and Instagram). These methods successfully recruited 164 participants in the CRESSIDA trial (30).

Previous trial participants from the Department of Nutritional Science, who have consented to be contacted, will be emailed.

Lastly, other institutions/universities, with publicly available contact addresses, may be emailed and asked to advertise our study via email and/or poster advertisement.

Drop-outs will be monitored in cohort 1 to assess recruitment targets. We have estimated that recruitment should roughly span one year from the study start.

3.7 Sample screening

Participants will be screened remotely with the use of questionnaires, to match them against the inclusion/exclusion criteria. At baseline clinic, participants BMI will be calculated via calibrated equipment to ensure they're within range. They will also have a finger prick test to measure their fasting glucose, to screen participants for hyperglycaemia (>7mmol). If participants have hyperglycaemia, they will be excluded from the study and be referred to their GP for further tests.

Email exchange: Upon showing interest in the advertisement, participants will be sent a Participant Information Sheet (PIS) along with an online screening questionnaire (using Qualtrics software) which matches participants against the inclusion/exclusion criteria).

Introductory call: All eligible participants will receive a telephone/video call with a member of the study team, both to introduce themselves and the study. This call will serve as an opportunity for participants to ask questions, and to have their understanding of the study checked prior to giving consent. This call also allows the study team to build rapport with participants. After this call, a consent form (Qualtrics software), will be emailed out.

Once consent is remotely obtained, participants will be invited to a virtual 1:1 run-in induction.

An overview of the flow from advertisement to identifying an eligible population, is summarised in Figure 5.

3.8 Inclusion and exclusion criteria

- **Inclusion criteria**
- Healthy adults
- Aged 40-80 years old
- Intake of ≤4 portions of fruits and vegetables (excluding potatoes) per day
- Low sleep quality- <85% sleep efficiency score on the PSQI
-
- **Exclusion criteria**
- Shift workers and those with multiple jobs or carers who are required to wake through the night
- Unwilling to refrain from dietary supplements
- Unwilling to follow protocol and/or give informed consent
- Diagnosed with Cardiovascular Disease (CVD), Type 2 Diabetes, Celiac disease, Insomnia, Sleep apnoea
- Presence of gastrointestinal disorder
- Users of drugs that are likely to alter gastrointestinal motility or nutrient absorption
- History of substance abuse or alcoholism
- Currently pregnant, planning pregnancy, breastfeeding or having had a baby 12-month prior
- Weight change of >3kg in preceding 2-months
- BMI <18.5kg/m2 or > 35kg/m2,
- Current smokers, or individuals who quit smoking in the last 6-months
- Frequently consume wholemeal products (1-2 times per day, in the short screening FFQ)
- Never consumed refined starchy staple, such as white pasta or rice (rarely or never, in the short screening FFQ)
- High potato consumption (4-6 times per week, in the short screening FFQ)
- High risk of obstructive sleep apnoea (answer yes to >3 questions, in STOP-Bang questionnaire)

- Vegan
- Sleep-related medications, or medications that may interfere with sleep
- Fasting glucose >7mmol/l (finger prick test at baseline clinic)

Table 2. Event and Outcome matrix

			Time point												
Event	**Responsible party for taking measurement**	**Relevant outcome**	**Remote screening**	**Intro call**	**Run-in induction**	**Run-in**	**Baseline Clinic**	**Wk 2**	**WK 4**	**WK 6**	**WK 8**	**Wk 10**	**Endline Clinic (Wk 12)**	**Every day**	**Every week**
Screening/prior to study															
Eligibility questionnaire incl Pittsburgh index and STOP-Bang questionnaire.	Researcher	Eligibility	✓												
Consent	Researcher	GCP		✓											
Posting equipment to participants	Researcher	Nocturnal glycaemia and sleep efficiency			✓							✓			
Virtual Run-in induction	Researcher	To discuss study equipment			✓										
Finger prick blood test	Researcher	Indication of hyperglycaemia *(eligibility criteria)*					✓								
Outcome related indicators															
CGM	Participant	Primary outcome				✓						✓			
Motion Watch	Participant	Primary outcome				✓						✓			
Fasted bloods	Researcher	Clinically relevant biomarkers of metabolic dysregulation *Plasma lipids* *Plasma glucose* *HbA1C* *Insulin*					✓						✓		
		Adherence *Serum potassium*					✓						✓		
FMD	Researcher	Indicator of cardiometabolic health *% change in arterial flow-mediated dilation*					✓						✓		

Body composition (Tanita scales)	Researcher	Secondary outcome					✓						✓		
HRV (48-hours and acute response to stress)	Researcher	Secondary outcome					✓						✓		
Weight	Participant	Secondary outcome													✓
Blood pressure	*(Automated via bracelet)*	Secondary outcome												✓	
4-day food diary + appetite visual analogue scale	Participant Baseline and Endline: *24-hr before clinics* Midline*: taken at home and sample posted*	Dietary data for quality indices/covariates *PDI (uPDI,hPDI)* *aMED* *aHEI* *HFD*					✓			✓			✓		
Compliance indicators															
Telephone 24-hour food recall, multipass method	Researcher	Measures adherence						✓	✓		✓				
24-hour Urine collection	Participant	Adherence *Urinary Potassium, Sodium and Creatinine*					✓			✓			✓		
Photographs of evening meals														✓	
Self-reported adherence: Evening meal checklist														✓	

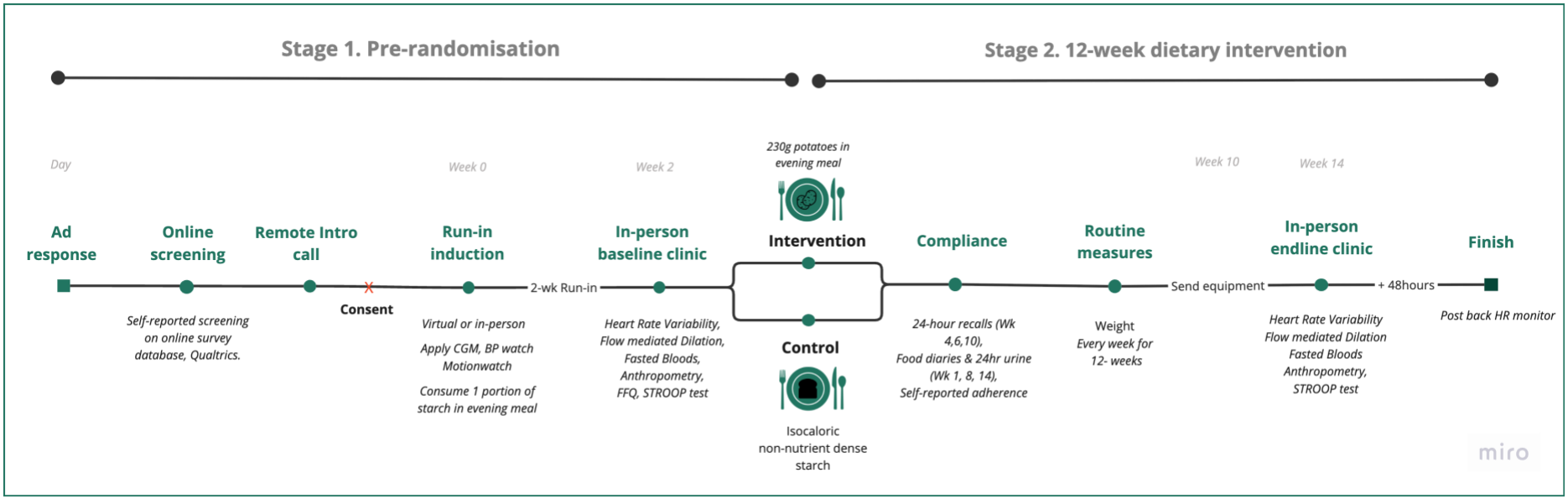


Figure 4. Flow diagram of RCT process.

4.0 Sample Size, Statistics, Selection and Withdrawal of Participants

4.1 Sample size

This study aims to recruit a total of 80 men and women, 1:1 intervention to control, to have 68 people (~15% dropout) complete the study. 34 people in each arm will provide 80% power to detect a difference of 0.468 mmol/L nocturnal glucose concentrations (SD 0.61), based on our CGM data from PREDICT 1 (unpublished data). Additionally, only 24 people are needed to provide 80% power to detect a difference of 4.2% sleep efficiency units, with SDs based on our previous sleep extension intervention (SLuMBER study) (7). These parameters are based on a significance level of 0.025, for two outcomes (calculated with *G*Power* software)

4.2 Study statistical plan

Mean differences between groups will be assessed at endpoint, adjusting for baseline values and other potential other covariates (maximum 3, as per the rule of 1 covariate per 10 participants).

For the outcomes with 3 timepoints (urinary Na, K, Na:K and calystegines), this will be assessed using a using Linear mixed models (mixed command) with change being the dependent factor, participant ID as random effect, treatment and season as fixed effects, and baseline outcome as a covariate. Variables with 2 timepoints (all other outcomes) will be assessed with an ANCOVA regression model (regress command), with baseline as a covariate. BMI, sex and age may also be covariates depending on the balancing of the arms. Sex differences will also be explored in some outcomes with known sexual dimorphisms, with the use of a sex interaction term.

A 2 -sided P value <0.05 will be considered as showing statistical significance.

Normality will be assessed visually with histogram and Q-Q plot of residuals, and heteroscedasticity with a fitted-residual plot, to satisfy the model assumptions.

We will primarily analyse outcomes on an intention-to-treat basis, analysing participants as randomised. Per-protocol analyses—restricted to participants meeting prespecified adherence criteria—will be performed to assess robustness.

All statistics will be run on Stata/MP 18.0.

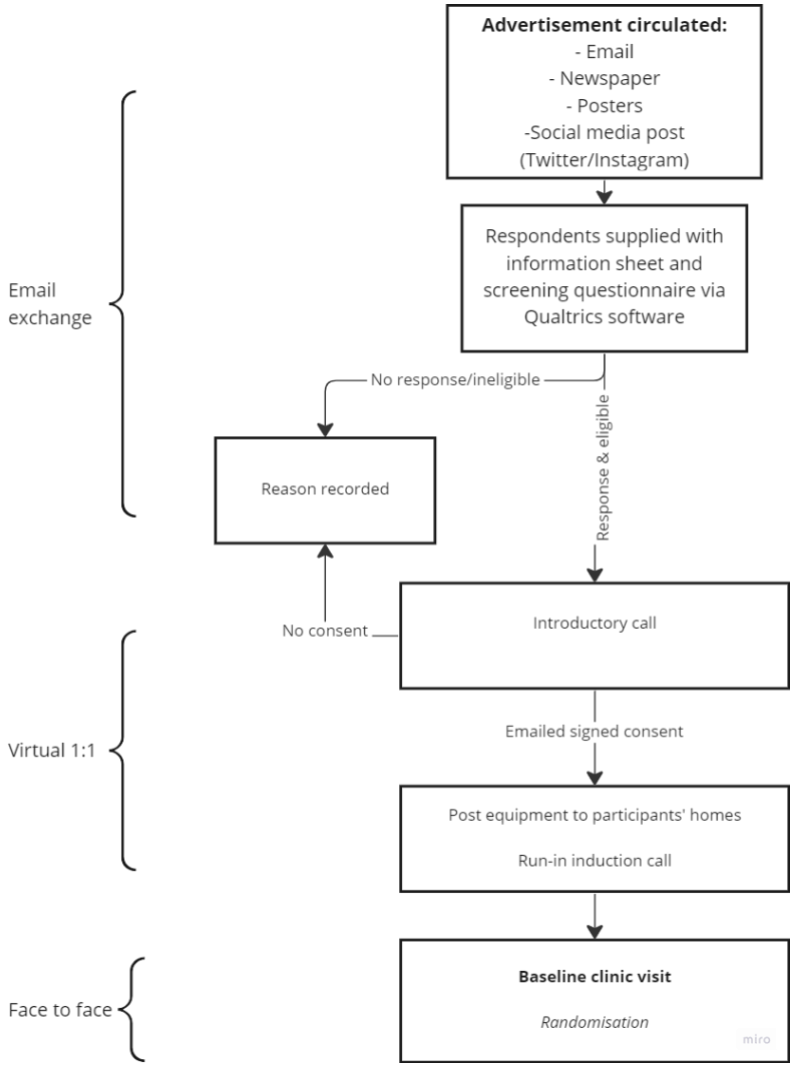


Figure 5. Flow chart of the recruitment procedures

4.6 Criteria for Premature Withdrawal

This is an 'Intention to treat study', participants will only be withdrawn for the reasons outlined below:

1. Participant voluntarily withdraws from the study.
2. Participant death.
3. Participant acquires any of the listed exclusion criteria.

4. Participant's well-being, in the opinion of the investigators, would be compromised by study continuation.

If participants wish to withdraw, details on their reasoning will be formally documented. If withdrawal occurs after screening but prior to baseline visits, data will not be used on this participant, however if they withdraw during the study, the data will only be receded upon request, as stipulated in the information sheet (appendix 1). Data will be unable to be receded when published, and this will be clearly outlined in the PIS, but all data will be fully anonymised as per GDPR protocol.

5. Study procedures

5.1 Informed Consent Procedures

Upon showing interest in the study, participants will be given a Participant Information Sheet (PIS) (appendix 1) by email or post, to explain in detail what the study involves, their role within the trial, highlight the anticipated benefits and hazards of the study. This is then further accompanied by an introductory call, for eligible participants, to discuss the PIS and run through the consent form (template is in appendix 2). After this call, the consent form will be emailed to the participants to digitally sign online (Qualtrics form).

Adequate time between reading the PIS and consenting will be given, to ensure there is time allocated for follow up questions on behalf of the participant.

The PIS will be updated and recirculated in the event of any new information or protocol deviations, to confirm participants wish to continue taking part.

Clear indication of withdrawal rights will be made known at each point of contact.

The lead investigator and trial coordinator, Anya Klarner, has received inhouse training on Good clinical practice, as well has covered informed consent practises through the Human Tissues Act training. She will be registered on the site delegation log.

Due to the remote nature of the initiation of the trial, informed consent will be provided remotely, to reduce participant burden.

5.2 Risks/burdens

Venepuncture

Foreseeable discomfort may be experienced with the venepuncture such as:

- Stress regarding the process
- Insertion of the needle
- Minor bleeding on the area where the needle was inserted. This will be covered with a bandage to minimise the bleeding and reduce skin exposure.
- Minor bruising and/or irritation on the skin. This is normal and will typically last 2-3 days.

- A sore arm. This is normal and will typically last 1-2 days.
- During and/or after the blood sample, a participant may feel dizzy and/or faint. Should fainting occur, the participant will receive all the medial care required until they are fit to leave the Metabolic Research Unit.

To minimise these risks, a trained phlebotomist will conduct the venepuncture procedure.

Equipment

For some volunteers, the requirement of self-applying equipment might cause some stress regarding technical capabilities. To reduce this all volunteers will be well trained through supplied multimedia resources, a 1:1 induction with a study team member and will have continued access to the study team in case of any queries.

CGMs may cause slight discomfort in their application, as a very small needle will puncture the skin to sit just below the skin which will measure interstitial fluid glucose levels. As the sensor protrudes a few cm above the skin, there is a small risk that the sensors can get caught on everyday objects and rip out. To reduce this risk, sensor patches will be provided to cover the whole sensor and keep it fixed to the arm. There may be minor bleeding from the insertion of this needle, in which case participants are instructed to apply some pressure. If the bleeding does not stop after a few minutes of applying pressure, the sensor will be removed and reported to the study team. There is also the possibility of skin irritation to adhesives. If this is the case, the CGM should be removed, and the research team should be instructed for further action.

Participant burden

The initial screening and run-in session (as outlined in section 3.4, study flow), will be held remotely, via online documents and video/telephone calls. This we believe will reduce participant burden in needing to attend in-person clinics, thereby increasing study retention, and may further increase the comfort of the individuals.

The volunteer will attend 4 events: An introductory call, a virtual run-in, and a baseline and endline clinic. Additionally, they will be required to apply and wear study equipment and take urinary samples. To negate this burden, participants will be paid upon completion of the study for their time. Even if participants do not complete the study, pro rata payments will be made.

Dietary intervention

Potatoes contain a natural group of toxins called glycoalkaloids, which are harmful to health in vast consumption, and can cause gastrointestinal symptoms, such as nausea, vomiting and diarrhoea (68). Guidelines at the grower level restrict the amount of these toxins available for consumption, to a maximum value of 200mg/kg of fresh weight potatoes (69). Despite this, these toxins can become concentrated within the sprouting nodules (lenticels), of aging potatoes. To reduce risks of glycoalkaloid consumption, participants will be instructed on how to store their potatoes to increase

their shelf life, as well as reducing light exposure, and will be provided with a picture of a germinating potato of what not to consume. Additionally, cooking and preparation methods can significantly reduce the glycoalkaloid concentrations (70), which will be utilised in the recipe instructions.

With a change in diet, especially one with increasing fibre, it is possible volunteers may experience some changes in gastrointestinal motility and discomfort, such as bloating, diarrhoea or constipation. Any adverse effects should be immediately reported to the study team who will assist and provide guidance as to how to best continue.

Incidental findings

The detection of adverse or incidental findings such as undiagnosed dyslipidaemia, pre-diabetes or diabetes may arise following the fasted blood samples obtained during the baseline and endline visits. Should the blood samples result in out-of-range values, the volunteer will be informed by phone (or by email) and will be referred to their general practitioner (GP).

Weekly blood pressure outputs from each participant will be monitored throughout the study. If blood pressure readings result out of range, the volunteer will be supplied with a letter to take to their GP for further investigation.

Additionally, the use of the doppler ultrasound may highlight abnormalities in arterial health. Should this be the case, the same processes above are to be followed.

Any out-of-range results will only be shared with the participant. The participant will be supplied with a letter addressed to their GP and with a copy of their results. This will be recorded in the case report form and the volunteer will be excluded from participating in the study.

5.3 Screening Procedures

Online screening via Microsoft form. Location at the discretion of the volunteer. 30-60 minutes.

Participants will complete an online questionnaire screening session where they will be screened against the eligibility criteria (template for this is in appendix 3). The food survey will be specifically designed to ascertain if participants habitually consume <4 fruits and vegetables/day, habitually consume wholegrains, and if they do not consume red meat.

We estimate this not to exceed 30-40 minutes.

Data will then be reviewed by the study team, who will contact eligible participants to progress. Those who do meet the criteria will also be informed and thanked for their interest.

5.4 Randomisation Procedures

Participants will be randomised to either the intervention or control arm, with an allocation ratio of 1:1. A minimisation procedure will be used that considers gender, age, ethnicity, BMI) in the randomization, by using the Shiny App software, which can be accessed at:

https://fsella.shinyapps.io/VM_app/?_ga=2.186170153.125318758.1628174827-961835063.1626383516 (71).

Screening data will be entered into minimisation software, by the research lead (See randomisation SOP). This database will balance the treatment arms for the following variables:

1. *Gender*. 2 groups: Male; Female
2. *Age*. 2 groups: 40-59; 60-80 y
3. *BMI*. 2 groups: Healthy weight 18.5-24.9; Overweight-Obese ≥ 25

Randomisation codes will be generated by the software and recorded on the relevant documentation in the Case Report Form and enrolment log. The randomization protocol follows the same protocol as used previously by our group for a parallel, two-arm, randomized controlled trial (30) for which a study statistician was employed. It has not been deemed necessary to employ a study statistician on the current trial due to the similarity of the study design, but the protocol will be discussed with a statistician from the King's Joint Clinical Trials Unit.

Participants will be blinded to whether they are receiving the intervention or the control, but it is not possible to blind them to the food itself. Also, as the study team is limited by resources, observer blinding is also impossible; however, the researcher undertaking statistical analysis will be blinded prior to analysis using a second set of study ID codes. FMD analysis will be conducted through semi-automated software analyses, which will reduce bias.

5.4 Schedule of Treatment for each visit

Details of screening methods are summarized in Section 5.3

NB: All times allocated are estimates. Although the study team endeavours to keep within the limits of these suggestions, there may be deviations due to unprecedented circumstances or varying participant needs.

1st contact: Email exchange, online.

Upon responding to advertisements, volunteers will be emailed a participant information sheet, and an electronic questionnaire (via Qualtrics software). All forms will be reviewed by a study team member and will be assessed against inclusion/exclusion criteria. Participants will be informed the outcome at the earliest opportunity. If eligible, participants will then be invited to attend an introductory call.

2nd contact: Introductory call. Location, online, to be held at the discretion of the volunteer. 15-30 minutes.

All eligible participants will receive a telephone/video call (depending on the participant's preference) with a member of the study team, both to introduce themselves and the study. The information sheet will be discussed, and the consent form will be introduced. This call will serve as a chance for participants to ask questions and have their understanding of the study checked before giving

consent. This call also allows the study team to build rapport with participants. After this call, a consent form (online form), will be emailed out, and upon return, they will be invited to a virtual 1:1 run-in induction.

Once consent is obtained, participants will be posted a '**study pack'** consisting of:

1. Participant information guide
2. Study diary for writing data (sleep, BP, weight, evening meal compliance checklist)
3. Recipes
4. Equipment
    a. CGM (primary outcome)
    b. Motion Watch (primary outcome)
    c. Aktiia blood pressure bracelet (secondary outcome)
    d. 24-hour urine collection kits (X3) (adherence)
    e. Kitchen Scales (to weigh 24hr urine at midline)
    f. Bathroom scales (only if participant does not own any, secondary outcome)
5. Equipment leaflets, including SOPs with photos for guidance.
6. 4-day food diary incl VAS for appetite (X3)
7. Packaging to post equipment/diaries

3rd contact: Virtual (or in-person) run-in. Location at the discretion of the volunteer. 60 minutes.

Before this session, volunteers will be given leaflets and videos on the equipment they will apply and/or measure to give them a good understanding.

This follow-up session will be an overview and a chance for participants to ask outstanding questions. This will ensure that the study lead is happy that participants have suitable understanding of the process and are happy to continue with the process.

A summary of the training needs that will be addressed are written below:

<u>Self-taken measurements include:</u>

1. Body weight with home scales (Weekly, from wks.0 - 12)

<u>Need to apply the following equipment alone:</u>

1. Motion watch (7days)
2. Aktiia bracelet (7 days)
3. CGM (12 days)

Participants will be made aware that they are able to contact the study team at any time when they need. The contact details (study email and phone number) will be provided in the participant information guides they receive along with their equipment, as well as on email invitations.

4th contact: Clinic visit 1 (Wk 0), MRU at KCL. ~130 minutes.

The study team will have correspondence with participants to arrange a suitable date for their baseline clinic visit.

Participants will attend the MRU, 4th Floor, Franklin Wilkins Building, Kings College London and have the following procedures:

1. Urine samples collected (~0 mins)
2. Finger prick blood test (~10 minutes)
3. Blood pressure (~10 mins)
4. Fasted bloods (~20 mins)
5. Heart rate variability monitor fitted (ECG), to keep on for 48-hours (~10 mins)
6. Ultrasound imaging (~30 mins)
7. STROOP test (~15 mins)
8. Body composition and waist circumference (~10 mins)*
9. Questionnaires (ZOE FFQ) (~15 mins)
10. Dietary consultation (20 mins)***

**Optional break for a snack post measurements.*

***Participants will then be instructed to start the dietary protocol after 48 hours after the baseline clinic, when participants' baseline HRV has been recorded.*

*******Participants will be required to attend a brief consultation with the associate nutritionist on the dietary intervention they have been assigned to. This will cover cooking methods, appropriate food items, and menu card run throughs. It will also provide an opportunity to problem-solve around identified conflicting commitments such as holidays or celebrations, where the participants may not be able to follow the intervention. Standardised advice on eating out will be given to all participants. General healthy eating advice will also be delivered, roughly in line with UK and US dietary guidelines.

5th contact: Dietary assessments for compliance

1. Video/telephone call. 24-hour food recall, multipass method. ~30-60 mins. (Wks 2, 4, 8)

Participants will have 2 phone calls in weeks 4 and 8, to carry out a 24-hour food recall, a well-regarded measure of dietary intake (45). This will be conducted by an associate nutritionist, with experience of conducting these methods.

Participants will be contacted by the study lead or supervised delegate, to arrange a suitable time for these calls.

As the study is long-term (12 weeks) and free-living, we have built in these compliance checks to allow us to make suggestions to tailor the programme to the needs of the participants if necessary.

7th contact: Clinic visit 2 (Wk 11-12), MRU, KCL. 110 minutes

Participants will attend the MRU, 4th floor, Franklin Wilkins Building, Kings College London for their final engagement. And have the following procedures:

1. Urine samples collected (~0 mins)
2. Blood pressure (~10 mins)
3. Body composition and waist circumference (~10 mins)
4. Fasted bloods (~20 mins)
5. Ultrasound imaging (~30 mins)
6. Heart rate variability monitor fitted (ECG), to keep on for 48-hours (~10 mins)
7. STROOP test (~20 mins)
8. *Optional break for a snack ultrasound.*

Additional measurements made outside of the study visits:

- **4-day diet diaries:** participants will be asked to complete 4-day diet diaries during week 1, week 6 and week 12 of the diet intervention. The 4-day diet diaries are to be completed on non-consecutive days to reflect the intakes of 3 weekdays and 1 weekend day. It will also ask participants to record their satiety from their dinner, on day 1, using 100mm visual analogues scales, at 1-, 2- and 3-hours post meal.
- **Blood pressure** will be taken at home using an automated BP bracelet. Participants will need to put the bracelet on during the study run, and wear it throughout the study. As the bracelet is no waterproof, it will need to be taken off and reapplied after bathing/water activities. It will also need to charged every 25 days and initialized with an accompanying blood pressure cuff to calibrate it.
- **Weight** will be taken by the participant at home, using home weighing scales. Advice will be given on how to standardize these measurements to account for inter and intra variability. This measurement will be taken in the morning before food or drink on even hard flooring at monthly intervals (Table 2). Weighing scales will be provided to participants if they are not in possession of any.

5.6 Equipment overview

At home, at baseline and endline, participants will be wearing an Abbott's Freestyle Libre 3 for 14 days (A), a MotionWatch 8 for 7-days (B), a waterproof eMotion-Faros 180 for 3 days (C), and an Aktiia blood pressure bracelet for 14-weeks (D). Training will be given on how to apply A, B & C. D will be applied at the study visit.

Participants will take their own weight weekly throughout the study (with bathroom scales, which can be provided if they do not own any).

Participants will receive leaflets and/or videos on how to apply and use this equipment, entailing any contraindications or warnings of the study equipment (i.e. original models of Aktiia not being waterproof). In addition to this, all equipment will be discussed during the run-in 1:1 induction call,

where any questions can be asked, and the study team can check participants are comfortable and happy to proceed. Participants will also receive a copy of the manuals of each item via email, should they need to refer to it.

All study equipment will be returned to the study team upon finishing their participation.

5.7 Methods of engagement

Engagement strategy

As our methods are over a longer study period, we will implement the following methods to reduce study drop out and improve adherence:

- Introductory call to build rapport
- Video/telephone call through run-in induction
- Compliance measures: 24-hour food recalls and food diaries
- Email reminders of milestone events: Intervention start, clinic days, midline urine samples, when equipment has been sent.

5.8 Follow up Procedures

Not relevant for this study.

5.9 Laboratory Assessments

Fasting blood samples

The blood samples will be analysed at certified laboratory, Affinity Biomarker Laboratories, Suite 602, Cumberland House, 80 Scrubs Ln, London NW10 6RF. Tracy Neal will be the recipient of the samples (tracy@affinitybiomarkerlabs.com). This laboratory has been used before, so all necessary contracts between the laboratory and KCL have been established. Quotations for the analytes have been received and will be confirmed upon receiving favourable opinion from the board of ethics.

The analytes and the respective diagnostic tests are summarised below.

Analyte		Analysis method [1]
Full lipid profile	Cholesterol	Clinical Chemistry Analyser: SIEMENS ADIVA 1800. Chemistry cholesterol method. *(Cholesterol (CHOL-2) reagent catalogue number 10376501)*
	HDL	Clinical Chemistry Analyser: SIEMENS ADIVA 1800. Chemistry Direct HDL method. *(Direct HDL (HDL) reagent catalogue number 07511947)*
	LDL	Clinical Chemistry Analyser: SIEMENS ADIVA 1800. Chemistry Direct LDL method. *(Direct LDL reagent catalogue number 09796248)*
	TAG	Clinical Chemistry Analyser: SIEMENS ADIVA 1800. Chemistry Triglyceride method. *(Triglyceride (TRIG-2) reagent catalogue number 10335892)*
Serum potassium		Clinical Chemistry Analyser: SIEMENS ADIVA 1800. Indirect ion selective electrode (ISE). *(ISE reagent catalogue number 06135445 (Potassium))*
Plasma glucose		Clinical Chemistry Analyser: SIEMENS ADIVA 1800. Chemistry Glucose oxidase method. *(Glucose (GLUO) reagent catalogue number 10492319)*
HbA1C		Clinical Chemistry Analyser: SIEMENS ADIVA 1800. Chemistry A1c_E assay.

	(Glycated haemoglobin HBA1 (A1c-E) reagent catalogue number 10720857)
Insulin	Siemens Adiva Centaur assay (two site-sandwich assay). *(Insulin reagent catalogue number 2230141)*

(1) Methods obtained from Affinity Biomarker labs.

Urine samples

The following biomarkers in urine will be analysed in the urine.

Analyte	Analysis method
Urinary potassium	Flame photometry
Urinary sodium	Flame photometry
Urinary creatinine	Jaffe reaction via Ilab clinical chemistry analyser

All samples will be analysed by either the study lead or a delegated trained research student under their supervision, in the Department of Nutritional Science's main laboratory, 4th Floor, Franklin Wilkins Building, Stamford Street, London, SE1 9NH.

FMD

Doppler ultrasound videos will be analysed using automated software (unnamed thus far) with our collaborators in Maastricht university, Netherlands. No laboratories will be required for their analysis.

Ideal parameters for %FMD are between 5-8%, but this can vary on the population. As there is considerable overlap between healthy and non-healthy populations (72), there are no out of range values considered in the analysis.

5.91 Radiology Assessments

This study is proposing to use Doppler ultrasound imaging to measure brachial arterial dilation, in response to 'shear stress,' as described by the Flow-Mediated Dilation method.

There is some evidence to suggest that increased potassium consumption can improve endothelium-dependent vasodilation (73). This thought to be explained by the role of potassium in nitric oxide secretion, which induces vasodilation, and therefore improves the relative % increase in brachial arterial dilation, although specific mechanisms are not yet well understood.

As potatoes are rich in potassium (those in the intervention group will have 1000mg extra of potassium per day), we hypothesize that the potato intervention arm will have higher % FMD, when compared to our control.

FMD assessments will be conducted at baseline clinic visit (Wk 0) and the endline clinic visit (Wk 12), in the MRU, 4th Floor, Franklin Wilkins Building, Kings College London, by a trained researcher.

As there is no ionizing radiation exposure associated with ultrasound imaging, and it is non-invasive, this procedure is deemed low risk.

5.92 End of Study Definition

The end of the study will be when the final study report is produced. This is anticipated to be January 2026.

6. Sample handling and laboratories

6.1 Sample Collection, Labelling and Logging

Sample collection

Bloods

Blood samples (9.5mL) on each study visit, totalling ~20mL for the whole study) will be obtained (with participants' consent) by trained phlebotomists. Participants will be asked to sit or lie down and asked to hyperextend their arm. Venepuncture sites will primarily be the median cubital (or the largest vein in the antecubital fossa), and cephalic veins in the forearm. A tourniquet will be placed 3-4 inches above the selected puncture site and the participant's arm cleansed using an alcohol prep wipe. Blood will be drawn into labelled vacutainers, mixed, and promptly delivered to the laboratory for processing.

Blood collection tubes

Vacutainers that are required for this study are summarised in the table below.

Blood component	Vacutainer (1)	Analyte	Sample required for analyses (ul)	Total blood required (ul) (2)	Number of vacutainers needed and	Storage processing

					overall blood drawn	
Serum	SST *(gold top) 3.5mL*	Insulin, full lipid profile (Total cholesterol, HDL-C, LDL-C, TAG), serum potassium	300	~2400	1 vacutainer (3.5mL)	Samples will be left to clot for 30 minutes at room temperature. They will then be centrifuged at 1000 X g, aliquoted into sample Eppendorf and stored at ≤ 20 °C
		Spare for insulin, full lipid profile and serum potassium.	300			
		Spare for exploratory analyses	300			
		Spare for exploratory analyses	300			
		Total	*1200*			
Plasma	Fluoride Oxalate *(grey top) 4mL*	Plasma glucose	300	~2250ul	1 vacutainer (4mL)	Samples will be centrifuged within 30 minutes of collection at 1000 x g for 15 minutes. Aliquoted samples will be stored at ≤ 20 °C
		Spare for plasma glucose	300			
		Spare for exploratory analyses	300			
		Total	*900*			
Whole blood	EDTA *(purple top) 2mL*	HbA1C	200	400ul	1 vacutainer (2mL)	Whole blood will be aliquoted into eppendorf and stored at ≤ 20 °C
		Spare for HbA1C	200			
		Total	*400*			
		Total			**9.5mL**	

1) *BD Vacutainers specifications obtained at: https://www.bd.com/en-us/products-and-solutions/products?tabindex=1&publishedAt=all-dates.*
2) *Based on obtaining 400uL of plasma/serum for every 1mL of blood. Total amount of sample multiplied by a factor of 2.5.*

(total samples are 1440)

Urine

24-hour urine samples will be self-collected by the participant. Participants will be provided with full 24hour urine collection kits and training on storage and methods.

Full samples will be brought into clinic at baseline and endline and will be processed by the study lead, or delegated research student.

For the midline measure, to reduce participant visits, they will be asked to record the full weight of the 24-hour urine sample using scales that are provided by the study team. They will then be responsible for mixing the sample and carefully decanting their sample with use of a funnel, into a 20mL subsample tube. These samples will be sent to KCL via usual courier services (royal mail or UPS) for the same day delivery. These will be packaged in line with dangerous substances regulations, as a category B parcel, and will be packaged to comply with packaging instruction 650. Once these parcels have been received by the study team, they will be processed in the laboratory by the study team.

Participants must fill out urinary collection forms (appendix 5), to accompany the samples at each time point.

Sample Labelling:

All participants will be assigned a unique study ID code. Participant documentation and specimens will be labelled with the unique study ID code which is a pseudonymised code used on all study documents and samples. There will be no identifiable information recorded on participant documents or samples. The study ID code will take the following format:

STY/PARTICIPANT_ID/
STUDY_TIME_POINT/PARTIICPANT_ID/ANALYTE

STY – STARCHy trial

STUDY TIME POINT – Baseline or Endline

ANALYTE – e.g., GLUC (glucose), INS (insulin)

Sample Logging and sample chain

Fasting bloods

The fasting blood samples collected at baseline and at the end point will be sent altogether to Affinity Laboratories in one batch on dry ice following storage at -80°C in a secure freezer in the Department

of Nutritional Sciences laboratory, following processing specifications. A sample accountability log and a box map of the samples will be inserted into the cryogenic storage boxes and emailed to the recipient (Tracy Neal).

All samples will have the appropriate accompanying documents and will be appropriately packaged and sent to Tracy Neal at Affinity Biomarker Laboratories.

Urine

The study team will be responsible to ensure that all containers with urine are labelled prior to processing. The study team will also be responsible for the labelling of subsequent samples and aliquots upon processing. 20mL subsample falcons will be spun down with the centrifuge at X 1300g, 4 °C for 15 minutes to render the sample acellular. 1mL of the sample, from the top half of the 20mL falcon, will be pipetted into 4 Aliquots (4mL total), which will be labelled and frozen at -80 ° C for storage.

These samples will be analysed in batches fortnightly in the Urine lab in the MRU, via flame photometry.

6.2 Sample Receipt/Chain of Custody/Accountability

The fasting blood samples will be collected from participants in accordance with the participant consent form and participant information sheet. The custodian (Dr Wendy Hall) will use the fasted blood samples for the STARCHy study, only.

The fasting blood samples will be appropriately sent using a medical courier to Tracy Neal (Affinity Biomarker Laboratories) who will process, store, and dispose of the fasting blood samples in accordance with all applicable legal and regulatory requirements, including the Human Tissue Act 2004 and any amendments thereto.

Additionally, midline urine samples will be sent to the laboratory at KCL in line with transporter regulations.
The recipient shall only use the fasted blood samples and urine in accordance with the consent provided by the participants and shall always treat these samples with the upmost of care alongside safe laboratory practices.

The fasting blood samples and urine will not be transferred to any party not identified in this protocol and are not to be processed and/or transferred other than in accordance with the participants' consent. After ethics approval for the study has expired, the fasting blood samples will be disposed of in accordance with the Human Tissue Act 2004.

6.4 Sample Storage Procedures (if applicable)

Urine and blood sample aliquots will be racked in 10x10 cryogenic storage boxes. Each aliquot will be labelled with the participant study ID code and the time point of collection. The storage boxes will be labelled according to the analyte measured. The sample storage will be mapped on an excel spreadsheet and a printed copy of this box map will be inserted into completed boxes. The storage boxes will be stored in -80°C freezers at FWB at KCL. The 'spare' aliquots will be used if there are any losses during analysis. Long-term storage of spare aliquots will be in FWB, 4th floor laboratory, in freezers approved by the Human Tissues Authority, which are supplied with a back-up power source and card ice/dry ice.

The sample custodian is Anya Klarner, under the supervision of Dr Wendy Hall and Dr Sarah Berry and Dr Wendy Hall, who will be responsible for the safe keeping, analysis, and disposal of the samples.

6.5 Data Recording/Reporting

All researchers involved in the study will undertake HTA training prior to commencing work on the study.

The recruitment (eligibility) questionnaire will be used to record non-anonymised data such as names, addresses, email, and telephone number details, which will be on the same document used to record medical history, lifestyle, and body measurements. If volunteers are not eligible or not interested in participating and do not proceed to the screening visit, these questionnaires will be shredded and disposed of.

Eligible volunteers will be assigned a participant code at the screening visit. At the screening visit all further records, databases and reports will refer to each participant by their code, not by their name. Recruitment questionnaires containing identifiable information will be kept securely in a locked cupboard in a locked office (Room 4.43, 4th floor, Franklin–Wilkins Building, King's College London, 150 Stamford Street, SE1 9NH) during the study. Personal data held within computers will be password protected and stored on encrypted memory sticks or restricted server access when not in use. Access to such data will be granted only to appropriate members of the research team. On completion of the study, the research project's paper records will be archived in a filing cabinet in Dr Hall's locked office.

Data will be entered onto an Excel spreadsheet database.

Medical results will not be disclosed to any other party than the participant, and their GP by providing the participant with a letter addressed to their GP (with the participant's permission). The research records will be held securely at King's College London, according to the Data Protection Act 2018 and General Data Protection Regulation (EU) 2016/679, and in accordance with the College Guidelines

7. Assessment of Safety

7.1 Adverse events

Expected advents: the following adverse events may occur during the study and will not require formal reporting to the authorities.

Study Procedure	Anticipated Risks	Risk Mitigation
Venepuncture	Discomfort, slight bruising, fainting	Trained phlebotomists will perform all blood draws. Strict aseptic technique.
CGM application/venepuncture	Skin Irritation from adhesives	Participants will be asked if they have sensitive skin and are usually allergic to plasters. In this case, we will find allergenic alternatives or may need to exclude them from the study.
FMD/	Bruising from cuff inflation, especially from FMD arterial occlusion	For these processes we are required to reach certain pressure from the cuff, so although it will not be able to be mitigated, participants will be forewarned of this effect to reduce stress surrounding the presence of bruising.
Health screening	Possibility of detecting undiagnosed dyslipidaemia, pre/diabetes	Participant's GP will be informed of results and early treatment can be initiated.
Ultra-sound scanning	Possibility of detecting cardiac abnormalities (atherosclerosis)	A referral for further investigation will be made if any abnormalities are detected.
Fasting blood testing	Possibility of fainting	Participants more prone to fainting (as known through screening as well as those with low blood pressure as defined in the venepuncture protocol, will have their bloods taken lying down to reduce risk of unconsciousness). The phlebotomist will also be trained to deal with an unconscious participant and will never be alone in the MRU unit.

7.2 Serious Adverse Events

The Principal Investigators (Dr Wendy Hall and Dr Sarah Berry) will oversee the safety of the study, including careful assessment and appropriate reporting of adverse/serious adverse events (AEs, SAEs) (appendix 6), following the 'Adverse Events Form Guidance' and Adverse event flow diagram

(appendix 7), provided by KCL's Research Governance Office. Reports of SAEs will be submitted within 15 days of the principal investigator becoming aware of the event, using 'Serious Adverse Events Reporting Form'.

8. Ethics & Regulatory Approvals

The study will be conducted following the principles of the Declaration of Helsinki (2013), the principles of GCP and in accordance with all applicable regulatory requirements including but not limited to the UK policy framework for health and social care research and the Mental Capacity Act 2005.

This protocol and related documents will be submitted for review to Kings College London Health Faculties Research and Ethics subcommittee, Waterloo Campus, 57 Waterloo Road, London, SE1 9WA.
Any subsequent protocol amendments will be resubmitted for approval before implementation. The Principal Investigator will submit a final report at conclusion of the trial to the funder and the REC.

9. Data Handling

9.1 Confidentiality

Volunteers will be randomised and assigned a participant code. Following screening and acceptance onto the study, all further sample labels, records, databases, and reports will refer to each participant by their code, not by their name. All samples, records, databases, and reports will be kept in a safe place and only the Principal Investigators and research students will have access to them. Medical results will not be disclosed to any other party than the participant, and their GP by providing the participant with a letter addressed to their GP (with the participant's permission). The research records will be held securely at King's College London, according to the Data Protection Act 2018 and General Data Protection Regulation (EU) 2016/679, and in accordance with the College Guidelines. The Principal Investigators and other members of the research team will have access to the anonymised data.

Participants' personal details (name, address, etc) will be kept securely in the Research Team's office (Nutritional Sciences Division, Franklin–Wilkins Building). Personal data stored in filing cabinets, cupboards and/or rooms will be kept in a locked room when not in use. Personal data held within computers, will be password protected and stored on restricted server access when not in use. Access to such data will be granted only to appropriate members of the Research team. Extra care will be taken to ensure the security of research material containing personal data, which is participant to the provisions of the UK GDPR, under the Data Protection Act, 2018.

Data will include questionnaires (paper and electronic), laboratory analysis results (electronic), vascular and ultrasound images (electronic) and case report forms (paper and electronic).

Data will be collected and labelled as outlined in section 5.0.

The principal investigators will be custodians of the data.

Participant details will not be transferred outside of the EU.

The patients will be anonymised with regards to any future publications relating to this study.

9.2 Case Report Form

Digital Case report forms (CRFs) will be completed by the PhD student, or trained delegate student. They will be completed after every study visit. The following will be included in CRFs:

1. Inclusion/exclusion criteria
2. Randomisation form
3. Date of informed consent
4. Date of birth
5. Current medications
6. Notes of participant's general wellbeing on study days
7. Participant eligibility prior to study days: i.e., adherence to diet intervention and fasting protocol
8. Visit dates
9. Visit number
10. Participant randomisation number
11. Blood glucose (from finger prick test)
12. Blood pressure measurements
13. Weight
14. Waist circumference
15. Body composition (%body fat).
16. Notes and checklists for:
    - 24-hour urine
    - HRV
    - FMD
    - Aktiia BP watch
17. Urine collection form
18. Copy of data from home data diaries:
    - Home weight measures
    - Evening meal adherence checklist
    - Sleep and wake times
19. STROOP test time, and results.
20. Any study interventional delays and reasons if able to state
21. AEs
22. Page for toxicities
23. Withdrawal from study
24. Study completion
25. Follow up of outcomes
26. Death
27. SAE form
28. Comments form

9.3 Record Retention and Archiving

Anonymised data from the study will be stored for at least 10 years as outlined above in the confidentiality section of the data handling section.

9.4 Compliance

The Chief Investigators will ensure that the trial is conducted in compliance with the principles of the Declaration of Helsinki (1996), and in accordance with all applicable regulatory requirements including but not limited to the Research Governance Framework, Trust and Research Office policies and procedures and any subsequent amendments.

9.5 Clinical Governance Issues

The investigator will permit study-related monitoring, audits, and inspections by the Ethics Committee, the sponsor, government regulatory bodies, and University compliance and quality assurance groups of all study related documents (e.g., source documents, regulatory documents, data collection instruments, study data etc.). Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable University compliance and quality assurance offices.

9.6 Non-Compliance

Compliance will be monitored from several sources as outlined below:

1. 24 hr diet recalls
2. Urine sample analysis (potassium levels, as indicated by intake) (baseline, midline and endline)
3. Daily photographs of evening meals

A 24-hour dietary recall is a dietary assessment method that involves asking individuals to recall all the food and beverages they consumed in the past 24 hours. This method can be used to assess compliance with a dietary intervention by comparing the reported food intake to the prescribed dietary intake. During the 24hour dietary recall, the trained nutritionist will used a standardised protocol to assess compliance from answers. Upon finding compliance issues, this will be noted, and the nutritionist will make informed suggestions to increase access to the diet. These persons will be noted and will receive email follow ups to see if the suggestions aided adherence in the following weeks, between recalls.

The researchers will maintain a log of the non-compliances to ascertain if there are any trends developing which need to be escalated. The researcher will assess the non-compliances and action a timeframe in which they need to be dealt with.

11. Finance and Publication Policy

Source of funding

Alliance for Potato Research and Education (APRE)
PO Box 803312
Chicago, IL 60680
Email: research@apre.org

Amount of funding
$185,166 USD

Kings College London will receive and manage the funding in accordance with specification outline in the Agreement between KCL and APRE (APRE_KCL_Agreement_Revised).

The data for the study will be published in manuscript form in peer review journals and in abstract and poster format at conference proceedings/ presentations according to the research agreement between the Alliance for Potato Research and Education and Kings College London (APRE_KCL_Agreement_Revised). In brief, Kings College London will be free to publish the results of the research after providing the Alliance of Potato Research and Education with a 30-day period in which to review each publication for potentially patentable information.

Following ethical approval, the study will be registered at clinicaltrials.gov.

12. References

1. Lao XQ, Liu X, Deng H-B, Chan T-C, Ho KF, Wang F, et al. Sleep Quality, Sleep Duration, and the Risk of Coronary Heart Disease: A Prospective Cohort Study With 60,586 Adults. Journal of Clinical Sleep Medicine. 2018;14(01):109-17.
2. Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. Eur Heart J. 2011;32(12):1484-92.
3. Hill LK, Wu JQ, Hinderliter AL, Blumenthal JA, Sherwood A. Actigraphy-Derived Sleep Efficiency Is Associated With Endothelial Function in Men and Women With Untreated Hypertension. Am J Hypertens. 2021;34(2):207-11.
4. Tsereteli N, Vallat R, Fernandez-Tajes J, Delahanty LM, Ordovas JM, Drew DA, et al. Impact of insufficient sleep on dysregulated blood glucose control under standardised meal conditions. Diabetologia. 2022;65(2):356-65.
5. Hur MH, Lee M-K, Seong K, Hong JH. Deterioration of Sleep Quality According to Glycemic Status. Diabetes & Metabolism Journal. 2020;44(5):679-86.
6. Zuraikat FM, Wood RA, Barragan R, St-Onge MP. Sleep and Diet: Mounting Evidence of a Cyclical Relationship. Annu Rev Nutr. 2021;41:309-32.
7. Al Khatib HK, Hall WL, Creedon A, Ooi E, Masri T, McGowan L, et al. Sleep extension is a feasible lifestyle intervention in free-living adults who are habitually short sleepers: a potential strategy for decreasing intake of free sugars? A randomized controlled pilot study. Am J Clin Nutr. 2018;107(1):43-53.
8. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol. 1994;49(2):M85-94.

9. Gangwisch JE, Hale L, St-Onge MP, Choi L, LeBlanc ES, Malaspina D, et al. High glycemic index and glycemic load diets as risk factors for insomnia: analyses from the Women's Health Initiative. Am J Clin Nutr. 2020;111(2):429-39.
10. Cao Y, Taylor AW, Wittert G, Adams R, Shi Z. Dietary patterns and sleep parameters in a cohort of community dwelling Australian men. Asia Pac J Clin Nutr. 2017;26(6):1158-69.
11. Velazquez-Kronen R, Millen AE, Ochs-Balcom HM, Mnatsakanova A, Gu JK, Andrew M, et al. Sleep Quality and Dietary Patterns in an Occupational Cohort of Police Officers. Behav Sleep Med. 2022;20(5):543-55.
12. M D Drennan, D F Kripke, H A Klemfuss, Moore JD. Potassium affects actigraph-identified sleep. Sleep. 1991;14(4):357-60.
13. Rowe JW, Tobin JD, Rosa RM, Andres R. Effect of experimental potassium deficiency on glucose and insulin metabolism. Metabolism. 1980;29(6):498-502.
14. Gijsbers L, Dower JI, Schalkwijk CG, Kusters YH, Bakker SJ, Hollman PC, et al. Effects of sodium and potassium supplementation on endothelial function: a fully controlled dietary intervention study. Br J Nutr. 2015;114(9):1419-26.
15. Schwarz KG, Pereyra KV, Toledo C, Andrade DC, Diaz HS, Diaz-Jara E, et al. Effects of enriched-potassium diet on cardiorespiratory outcomes in experimental non-ischemic chronic heart failure. Biol Res. 2021;54(1):43.
16. Chang HY, Hu YW, Yue CS, Wen YW, Yeh WT, Hsu LS, et al. Effect of potassium-enriched salt on cardiovascular mortality and medical expenses of elderly men. Am J Clin Nutr. 2006;83(6):1289-96.
17. Filippini T, Naska A, Kasdagli MI, Torres D, Lopes C, Carvalho C, et al. Potassium Intake and Blood Pressure: A Dose-Response Meta-Analysis of Randomized Controlled Trials. J Am Heart Assoc. 2020;9(12):e015719.
18. Stone MS, Martin BR, Weaver CM. Short-Term RCT of Increased Dietary Potassium from Potato or Potassium Gluconate: Effect on Blood Pressure, Microcirculation, and Potassium and Sodium Retention in Pre-Hypertensive-to-Hypertensive Adults. Nutrients. 2021;13(5):1610.
19. Lin Z, Wong LYF, Cheung BMY. Diuretic-induced hypokalaemia: an updated review. Postgrad Med J. 2022;98(1160):477-82.
20. Behl M, Bliwise D, Veledar E, Cunningham L, Vazquez J, Brigham K, et al. Vascular endothelial function and self-reported sleep. Am J Med Sci. 2014;347(6):425-8.
21. Calvin AD, Covassin N, Kremers WK, Adachi T, Macedo P, Albuquerque FN, et al. Experimental sleep restriction causes endothelial dysfunction in healthy humans. J Am Heart Assoc. 2014;3(6):e001143.
22. Ceriello A, Esposito K, Piconi L, Ihnat MA, Thorpe JE, Testa R, et al. Oscillating glucose is more deleterious to endothelial function and oxidative stress than mean glucose in normal and type 2 diabetic patients. Diabetes. 2008;57(5):1349-54.
23. Oberleithner H, Callies C, Kusche-Vihrog K, Schillers H, Shahin V, Riethmüller C, et al. Potassium softens vascular endothelium and increases nitric oxide release. Proceedings of the National Academy of Sciences. 2009;106(8):2829-34.
24. Gamboa A, Okamoto LE, Diedrich A, Choi L, Robertson D, Farley G, et al. Sympathetic activation and nitric oxide function in early hypertension. Am J Physiol Heart Circ Physiol. 2012;302(7):H1438-43.
25. Public Health England and Food Standards Agency. National Diet and Nutrition Survey. Rolling programme Years 9 to 11. (2016/2017 to 2018/2019). London, England; 2020.

26. Storey ML, Anderson PA. Contributions of white vegetables to nutrient intake: NHANES 2009-2010. Adv Nutr. 2013;4(3):335S-44S.
27. Devlin BL, Parr EB, Radford BE, Hawley JA. Lower nocturnal blood glucose response to a potato-based mixed evening meal compared to rice in individuals with type 2 diabetes. Clin Nutr. 2021;40(4):2200-9.
28. Gibson S, Kurilich AC. The nutritional value of potatoes and potato products in the <scp>UK</scp> diet. Nutrition Bulletin. 2013;38(4):389-99.
29. Gardner CD, Landry MJ, Perelman D, Petlura C, Durand LR, Aronica L, et al. Effect of a ketogenic diet versus Mediterranean diet on glycated hemoglobin in individuals with prediabetes and type 2 diabetes mellitus: The interventional Keto-Med randomized crossover trial. Am J Clin Nutr. 2022;116(3):640-52.
30. Reidlinger DP, Darzi J, Hall WL, Seed PT, Chowienczyk PJ, Sanders TA. How effective are current dietary guidelines for cardiovascular disease prevention in healthy middle-aged and older men and women? A randomized controlled trial. The American Journal of Clinical Nutrition. 2015;101(5):922-30.
31. National Health Service. The Eatwell Guide 2022 [Available from: https://www.nhs.uk/live-well/eat-well/food-guidelines-and-food-labels/the-eatwell-guide/.
32. Dietary Guideline for Americans, 2020-2025: Make every bite count witht the dietary guidelines. Washington, US: USDA; 2020.
33. Nakamura K, Tajiri E, Hatamoto Y, Ando T, Shimoda S, Yoshimura E. Eating Dinner Early Improves 24-h Blood Glucose Levels and Boosts Lipid Metabolism after Breakfast the Next Day: A Randomized Cross-Over Trial. Nutrients. 2021;13(7):2424.
34. Moon S, Kang J, Kim SH, Chung HS, Kim YJ, Yu JM, et al. Beneficial Effects of Time-Restricted Eating on Metabolic Diseases: A Systemic Review and Meta-Analysis. Nutrients. 2020;12(5):1267.
35. Henry CJ, Kaur B, Quek RYC. Chrononutrition in the management of diabetes. Nutrition & Diabetes. 2020;10(1).
36. Castro-Acosta ML, Sanders TAB, Reidlinger DP, Darzi J, Hall WL. Adherence to UK dietary guidelines is associated with higher dietary intake of total and specific polyphenols compared with a traditional UK diet: further analysis of data from the Cardiovascular risk REduction Study: Supported by an Integrated Dietary Ap. British Journal of Nutrition. 2019;121(4):402-15.
37. Coulthard JD, Pot GK. The timing of the evening meal: how is this associated with weight status in UK children? British Journal of Nutrition. 2016;115(9):1616-22.
38. Kant AK GB. Within-person comparison of eating behaviors, time of eating, and dietary intake on days with and without breakfast: NHANES 2005–2010. American Journal of Clinical Nutrition,. 2015;102:661-70.
39. Berry SE, Mulla UZ, Chowienczyk PJ, Sanders TAB. Increased potassium intake from fruit and vegetables or supplements does not lower blood pressure or improve vascular function in UK men and women with early hypertension: a randomised controlled trial. British Journal of Nutrition. 2010;104(12):1839-47.
40. E.S Dipietro MMB, P.E Stroud, B.J Smarr B.J Burgess, W.E Turner, J.W. Neese. Comparison of an inductively coupled plasma-atomic emission spectrometry method for the determination of calcium, magnesium, sodium, potassium, copper and zinc with atomic absorption spectroscopy and flame photometry methods. The Science of the Total Environment. 1988;74:249-62.

41. John KA, Cogswell ME, Campbell NR, Nowson CA, Legetic B, Hennis AJM, et al. Accuracy and Usefulness of Select Methods for Assessing Complete Collection of 24-Hour Urine: A Systematic Review. The Journal of Clinical Hypertension. 2016;18(5):456-67.
42. Knuiman JT, Hautvast JG, van der Heijden L, Geboers J, Joossens JV, Tornqvist H, et al. A multi-centre study on within-person variability in the urinary excretion of sodium, potassium, calcium, magnesium and creatinine in 8 European centres. Hum Nutr Clin Nutr. 1986;40(5):343-8.
43. Murakami K, Sasaki S, Takahashi Y, Uenishi K, Watanabe T, Kohri T, et al. Sensitivity and specificity of published strategies using urinary creatinine to identify incomplete 24-h urine collection. Nutrition. 2008;24(1):16-22.
44. Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey (NHANES): 24-hour Urine Study Procedures Manual. 2017.
45. Holmes B, Dick K, Nelson M. A comparison of four dietary assessment methods in materially deprived households in England. Public Health Nutrition. 2008;11(5):444-56.
46. Drennan MD, Kripke DF, Klemfuss HA, Moore JD. Potassium affects actigraph-identified sleep. Sleep. 1991;14(4):357-60.
47. Blanch N, Clifton PM, Petersen KS, Keogh JB. Effect of sodium and potassium supplementation on vascular and endothelial function: a randomized controlled trial. Am J Clin Nutr. 2015;101(5):939-46.
48. Bakhshi B, Sultana N, Lin H, Fei D, Vallejo V, Gatanti A, et al. Associations of diet composition and quality with continuous glucose monitor-derived glycemic metrics in a community-based cohort. The American Journal of Clinical Nutrition. 2025.
49. Ashor AW, Werner AD, Lara J, Willis ND, Mathers JC, Siervo M. Effects of vitamin C supplementation on glycaemic control: a systematic review and meta-analysis of randomised controlled trials. Eur J Clin Nutr. 2017;71(12):1371-80.
50. D'Elia L, Masulli M, Cappuccio FP, Zarrella AF, Strazzullo P, Galletti F. Dietary Potassium Intake and Risk of Diabetes: A Systematic Review and Meta-Analysis of Prospective Studies. Nutrients. 2022;14(22).
51. Akilen R, Deljoomanesh N, Hunschede S, Smith CE, Arshad MU, Kubant R, et al. The effects of potatoes and other carbohydrate side dishes consumed with meat on food intake, glycemia and satiety response in children. Nutrition & Diabetes. 2016;6(2):e195-e.
52. Merino J, Linenberg I, Bermingham KM, Ganesh S, Bakker E, Delahanty LM, et al. Validity of continuous glucose monitoring for categorizing glycemic responses to diet: implications for use in personalized nutrition. Am J Clin Nutr. 2022;115(6):1569-76.
53. Wyatt P, Berry SE, Finlayson G, O'Driscoll R, Hadjigeorgiou G, Drew DA, et al. Postprandial glycaemic dips predict appetite and energy intake in healthy individuals. Nature Metabolism. 2021;3(4):523-9.
54. Berry S, Bermingham K, Smith H, Gonzalez J, Duncan E, Valdes A, et al. Glycaemic variability, assessed with continuous glucose monitors, is associated with diet, lifestyle and health in people without diabetes. 2023.
55. Yeboah J, Crouse JR, Hsu F-C, Burke GL, Herrington DM. Brachial Flow-Mediated Dilation Predicts Incident Cardiovascular Events in Older Adults. Circulation. 2007;115(18):2390-7.
56. Corretti MC, Anderson TJ, Benjamin EJ, Celermajer D, Charbonneau F, Creager MA, et al. Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery: a report of the International Brachial Artery Reactivity Task Force. J Am Coll Cardiol. 2002;39(2):257-65.

57. Electrophysiology TFotESoCtNASoP. Heart Rate Variability: Standards of Measurement, Physiological Interpretation, and Clinical Use. Circulation. 1996;93(5):1043-65.
58. Pinto AM, Bordoli C, Buckner LP, Kim C, Kaplan PC, Del Arenal IM, et al. Intermittent energy restriction is comparable to continuous energy restriction for cardiometabolic health in adults with central obesity: A randomized controlled trial; the Met-IER study. Clinical Nutrition. 2020;39(6):1753-63.
59. Pinto AM, Maclaughlin HL, Hall WL. Heart Rate Variability and Long Chain n-3 Polyunsaturated Fatty Acids in Chronic Kidney Disease Patients on Haemodialysis: A Cross-Sectional Pilot Study. Nutrients. 2021;13(7):2453.
60. Pinto AM, Sanders TAB, Kendall AC, Nicolaou A, Gray R, Al-Khatib H, et al. A comparison of heart rate variability, n-3 PUFA status and lipid mediator profile in age- and BMI-matched middle-aged vegans and omnivores. British Journal of Nutrition. 2017;117(5):669-85.
61. Satija A, Bhupathiraju SN, Spiegelman D, Chiuve SE, Manson JE, Willett W, et al. Healthful and Unhealthful Plant-Based Diets and the Risk of Coronary Heart Disease in U.S. Adults. J Am Coll Cardiol. 2017;70(4):411-22.
62. Fung TT, Meyer HE, Willett WC, Feskanich D. Association between Diet Quality Scores and Risk of Hip Fracture in Postmenopausal Women and Men Aged 50 Years and Older. Journal of the Academy of Nutrition and Dietetics. 2018;118(12):2269-79.e4.
63. Asnicar F, Berry SE, Valdes AM, Nguyen LH, Piccinno G, Drew DA, et al. Microbiome connections with host metabolism and habitual diet from 1,098 deeply phenotyped individuals. Nature Medicine. 2021;27(2):321-32.
64. Vadiveloo M, Parekh N, Mattei J. Greater healthful food variety as measured by the US Healthy Food Diversity index is associated with lower odds of metabolic syndrome and its components in US adults. J Nutr. 2015;145(3):564-71.
65. Beckmann M, Lloyd AJ, Wilson T, Torres DPM, Goios ACL, Willis ND, et al. Calystegines are Potential Urine Biomarkers for Dietary Exposure to Potato Products. Molecular Nutrition & Food Research. 2020;64(20):2000515.
66. Sanders LM, Dicklin MR, Palacios OM, Maki CE, Wilcox ML, Maki KC. Effects of potato resistant starch intake on insulin sensitivity, related metabolic markers and appetite ratings in men and women at risk for type 2 diabetes: a pilot cross-over randomised controlled trial. Journal of Human Nutrition and Dietetics. 2021;34(1):94-105.
67. Buysse DJ, Reynolds CF, 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28(2):193-213.
68. EFSA. Outcome of a public consultation on the draft risk assessment of glycoalkaloids in feed and food, in particular in potatoes and potato-derived products. EFSA Supporting Publications. 2020;17(8).
69. Friedman M. Potato Glycoalkaloids and Metabolites: Roles in the Plant and in the Diet. Journal of Agricultural and Food Chemistry. 2006;54(23):8655-81.
70. Nie X, Zhang G, Lv S, Guo H. Steroidal glycoalkaloids in potato foods as affected by cooking methods. International Journal of Food Properties. 2018;21(1):1875-87.
71. Sella F, Raz G, Cohen Kadosh R. When randomisation is not good enough: Matching groups in intervention studies. Psychonomic Bulletin & Review. 2021;28(6):2085-93.
72. Bots ML, Westerink J, Rabelink TJ, de Koning EJ. Assessment of flow-mediated vasodilatation (FMD) of the brachial artery: effects of technical aspects of the FMD measurement on the FMD response. Eur Heart J. 2005;26(4):363-8.

73. Blanch N, Clifton PM, Keogh JB. A systematic review of vascular and endothelial function: effects of fruit, vegetable and potassium intake. Nutr Metab Cardiovasc Dis. 2015;25(3):253-66.

11. Appendices

Appendix 1. Participant Information Sheet

Participant Information Sheet

Title of project
STARchy staples: a randomised clinical trial on **C**ardiometabolic **H**ealth.
Short title: The STARCHy study.

Invitation
You are being invited to take part in a research project at Kings College London. Before you decided it is important for you to understand why the research is being done and what participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part. Thank you for reading this.

What is the purpose of this study?
This study aims to investigate the health effects of consuming starchy staples in an evening meal, including effects on sleep quality, nocturnal blood sugars, arterial health, fasting blood profiles, blood pressure and other related parameters. As this study is focused on habitual consumption, the duration needs to reflect a long period, which is why this study is set to last for 12-weeks. There will be a two-week run-in period prior to starting to ensure you are comfortable with the study process and one-week after baseline to standardise both groups, so in total the trial will span 14-weeks.

The data collected from the trial will help us to understand the nutritional benefits of the intervention foods, and in the longer-term help shape dietary advice for the prevention of chronic diseases.

Why have I been asked to take part?

You have been asked to take part as you are an adult in the London area, who has interests in being involved in clinical trials. To be eligible for the study, you must be between 40-80 years of age. There are other eligibility criteria which will be assessed via a questionnaire in the screening call. In total, we aim to recruit a total of 80 participants in the study.

Do I have to take part?

No. It is up to you to decide whether to take part and your decision to not take part will not impact you in any way. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form prior to enrolling.

You can withdraw at any time without giving a reason, although for this we do appreciate you notifying us.

What will happen to me if I take part?

This study will involve you consuming self-prepared evening meals containing starchy foods. All participants will be split into 2 groups, both consuming different starchy foods in their evening meal. Is it not possible to blind you to which diet you will be consuming, as you will be preparing it, however, to improve the quality of the data, you will be concealed to whether what you're consuming is the intervention (what we're investigating), or the control (what we're comparing against). ***NB: If you choose to enrol, you will not get to decide which group you are allocated to as this process is randomised.*** The recipes for these meals will be provided on recipe cards and will be very simple and easy to follow.

In terms of your study involvement, you will be asked to attend an initial introductory call to meet the study team, a 60-minute virtual induction to run through the study equipment, a 20 minute online dietary consultation, and 2 clinic visits at week 1, and then at again at week 12 (both lasting an estimate of 120 minutes).

During the clinic visits, we will take a finger prick blood sample, fit a small painless and safe heart rate monitor with 2-leads: one connecting to a pad on your upper chest (collar bone) and lower chest (rib cage), to leave on for 48 hours (10 mins). We will then take fasting bloods (10 mins), an ultrasound image of your arm (30 mins), your weight, height, waist circumference and body fat % (10 minutes). Lastly you will be asked to complete a brief computer game (15 minute) and food frequency question (15 mins).

For the clinic visits, you will be reimbursed for travel expenses of up to £10.

Before your clinic visits at week 1 and week 12, and at week 6 at home, we will ask you to provide a 24-hour urine sample for us to use for analysis of study related biomarkers. All equipment will be provided, and training will be given. Courier services will be provided where necessary.

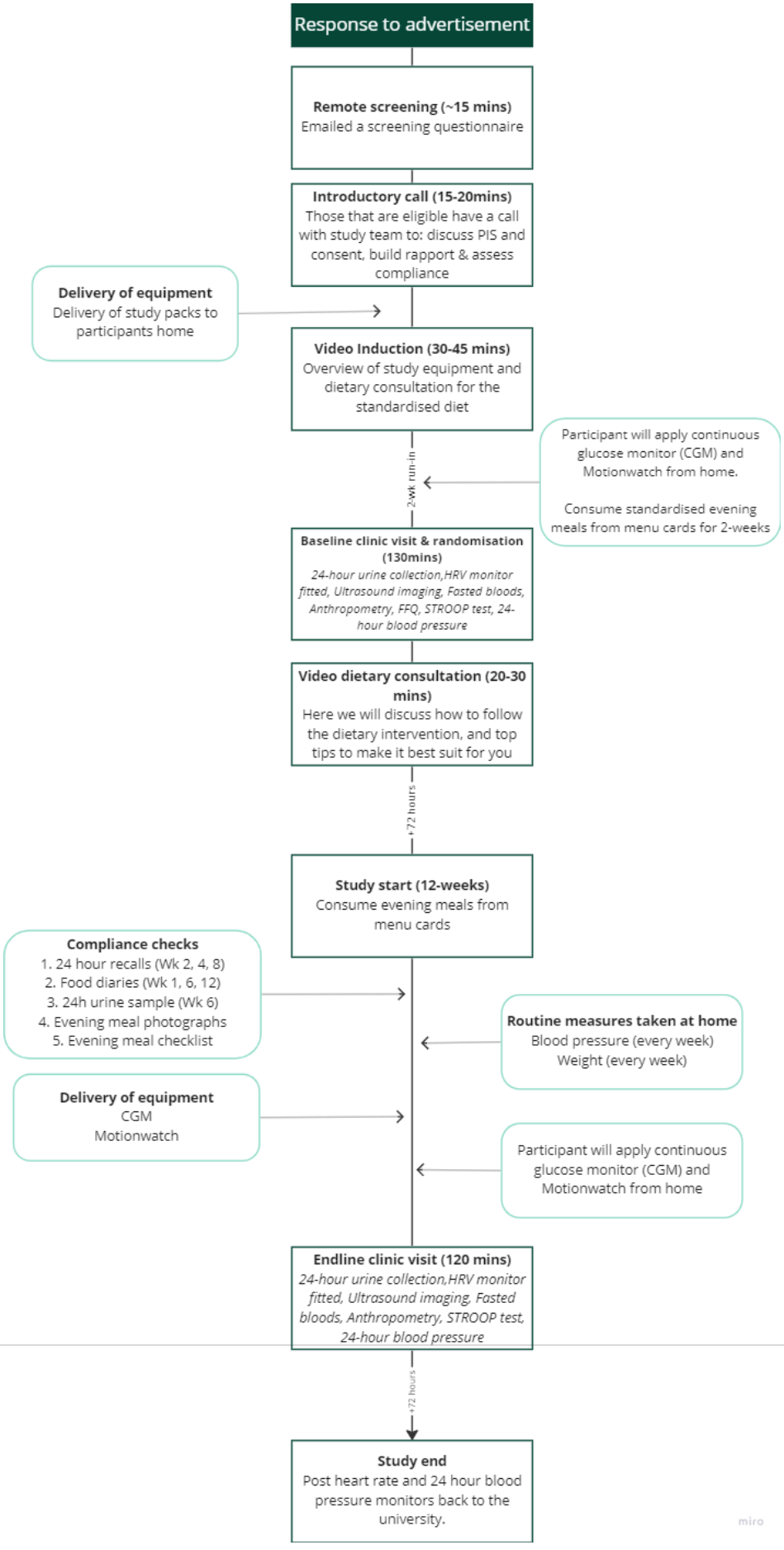
The urine and blood samples will be handled in line with the Human Tissues Act regulations. We will dispose of any unused material in accordance with these regulations. 10mL of blood and approximately 10mL of urine will be taken at week 1 and week 12, with a further 10mL of urine at week 6, which will be taken by you at home.

There will also be 3 telephone calls (~60 minutes) at weeks 2, 4 and 8 for a dietary assessment, to ensure that you're coping well with the study and so to be able to provide personalised advice to tailor the programme to suit your needs. Further, a food diary will be provided, and you'll be asked to fill in everything you eat prospectively for 4 days at weeks 1, 6 and 12.

To reduce clinic visits, we will provide you with some study equipment to take readings yourself at home. These include blood pressure monitors, continuous glucose monitors and urine collection kits that you will need to use at the beginning of the study and again at the end. We will provide full

training on this equipment through leaflets, videos, and tutorial instruction in the induction video call. The study team will also be on hand to answer any arising issues so you will have plenty of support.

We appreciate this is a lot of information so below is a schematic for you to visualise the process.


Response to advertisement
Remote screening (~15 mins)
Emailed a screening questionnaire
Introductory call (15-20mins)
Those that are eligible have a call with study team to: discuss PIS and consent, build rapport & assess compliance
Delivery of equipment
Delivery of study packs to participants home
Video Induction (30-45 mins)
Overview of study equipment and dietary consultation for the standardised diet
2-wk run-in
Participant will apply continuous glucose monitor (CGM) and Motionwatch from home.
Consume standardised evening meals from menu cards for 2-weeks
Baseline clinic visit & randomisation (130mins)
24-hour urine collection,HRV monitor fitted, Ultrasound imaging, Fasted bloods, Anthropometry, FFQ, STROOP test, 24-hour blood pressure
Video dietary consultation (20-30 mins)
Here we will discuss how to follow the dietary intervention, and top tips to make it best suit for you
+72 hours
Study start (12-weeks)
Consume evening meals from menu cards
Compliance checks
1. 24 hour recalls (Wk 2, 4, 8)
2. Food diaries (Wk 1, 6, 12)
3. 24h urine sample (Wk 6)
4. Evening meal photographs
5. Evening meal checklist
Routine measures taken at home
Blood pressure (every week)
Weight (every week)
Delivery of equipment
CGM
Motionwatch
Participant will apply continuous glucose monitor (CGM) and Motionwatch from home
Endline clinic visit (120 mins)
24-hour urine collection,HRV monitor fitted, Ultrasound imaging, Fasted bloods, Anthropometry, STROOP test, 24-hour blood pressure
+72 hours
Study end
Post heart rate and 24 hour blood pressure monitors back to the university.
miro

What do I have to do?

To enrol in the study, you will firstly need to sign the consent form.
During the study you will need to adhere to the evening meal plans as instructed on the menu cards for a total of 14-weeks. You will be required to consume these meals ideally before 8:00pm.

You will need to be willing to attend all **eight events** with the study's associate nutritionist, including three virtual video calls, three telephone calls and two clinic visits at King College London, Waterloo campus, Franklin-Wilkins Building. Further you will be asked to provide 2 fasting blood samples, three 24-hour urine samples, two ultrasound images of your arm and three 4-day food diaries.

You will further be asked to apply some equipment at home that will be provided to you (continuous glucose monitor, Motionwatch and blood pressure machines), and to take some equipment readings (weight, blood pressure) at regular intervals from home throughout the study, after training. You will be asked to write your measurements down into a data diary which will be broken up into 3 month stages.

You will also be asked to record your sleep time for one week whilst wearing the sleep monitoring Motionwatch at week 1 and again at week 12. Lastly, we will ask you to take a picture of your evening meal in addition to a written record of what you ate for the 12-weeks. You will be provided with a small booklet to keep these recordings together and we will collect it at the end of the trial.

What study equipment be used?

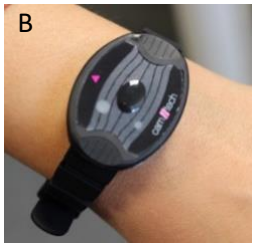
You will be using a range of different equipment, both at home and within the clinic. So here is just a brief summary:

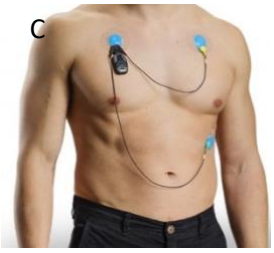
At home, at baseline and endline, you will be wearing a continuous glucose monitor for 14 days (A), an activity tracking watch (MotionWatch) for 7-days (B), a heart rate variability monitor for 3 days (C), and a 24-hour blood pressure machine for 24 hours (D). Training will be given on how to apply A & B. C & D will be applied for you at the study visit. You will also receive a copy of the manuals of each via email.

Intermittently throughout the study you will be using a blood pressure machine, that will be provided, and you will weigh yourself using bathroom scales. If you do not own your own bathroom scales, we will provide these for you.

Additionally, in clinic, a study team member will use an ultrasound to scan to get a video image of your brachial artery, running through your upper arm.

None of the study equipment is harmful.





All study equipment will be returned to the study team upon finishing your participation.

When will I have to do it?

Once you reply confirming you have read this information sheet and would like to proceed, we will email you an online screening questionnaire. If you are eligible, we will arrange an introductory call with the study team. This study is aiming to recruit participants from the earliest June 2023 to the latest August 2024.

What are the possible disadvantages and risks of taking part?

Some participants may feel discomfort in having their bloods taken. This procedure will be carried out by a trained and experienced researcher, with assistance from an onsite paramedic.

Some participants may experience a change in bowel habit following changes to their diet, such as bloating, diarrhoea or constipation. Any adverse reactions arising from the diet must be reported directly to the trial team who will provide guidance on how best to continue.

The pressure initiated from the blood pressure monitor cuff may induce some bruising, although this is not dangerous, it may be tender for a few days. The 24-hour blood pressure measures, requires a monitor to be worn for 24 hours. The cuff will inflate at regular intervals, throughout the day and the night, which may cause some disruption of sleep. The degree of cuff inflation will adjust based on your blood pressure so this should be less obvious during the night.

During the ultrasound imaging, you will wear a tight blood pressure cuff for 5 minutes on your lower right arm. This may induce some discomfort, such as numbness and ‘pins and needles’, but this is completely normal and will not affect long-term blood flow.

Travelling with the 24-hour urine sample may cause some inconvenience for participants. Suitable equipment for transporting these samples will be provided to ensure safe passage.

Study visits could be up to 2 hours, which we are aware may cause some inconvenience. For around 1 half hours of this, you will need to be in the fasted state as measurements can be inaccurate when foods are eaten. The study lead will ensure to be as quick and thorough as possible in the time available. Toast or a cereal bar will be provided as a snack to consume after the clinical measurements have been made. You’re also welcome to bring in other snacks for after the measurements, which can be consumed in the onsite dining facility.

ECG pads will need to worn on the chest during the ultrasound imaging process. This may cause some distress for those who do not wish to show their skin, or to remove their top. To mitigate against this, we suggest that you wear light and baggy clothing, or strappy garments, so the pads can be accessed without needing to remove your top. There is also the option for you to apply these yourself with instruction from the study team member.

Additionally, ECG pads on the collar bone and on the rib cage will need to be applied for the heart rate variability monitor (see diagram C above). Any chest hair local to where the pads will need to be attached will need to be shaved.

The blood sampling may reveal some undiagnosed conditions, such as dyslipidaemia, pre-diabetes or diabetes, due to the parameters we are testing. Additionally, your blood pressure readings may indicate signs of hypertension. Should your samples come back with out-of-range values, you will be informed at the earliest by phone (or by email) and will be referred to your general practitioner (GP).

What are the possible benefits of taking part?

You will receive dietary advice from an AfN registered Associate Nutritionist on healthy eating and lifestyle practice and will have access to nutritionist approved meal recipes and cooking techniques to maximise available nutrients, which you're able to keep post study.

You will also have training on state-of-the-art health technology that will be provided for free, for use during the study.

We also hope that you will feel satisfaction in your ability to help shape dietary advice on chronic disease prevention, by providing your data. You are also welcome to receive a copy of the final report upon request.

Lastly, we offer £100 renumeration for your commitment to this study.

What if something goes wrong?

If you have any concerns with the day to day running of the trial, or need further assistance, your questions will be welcomed by the study teams lead, Anya Klarner, who can be contacted at starchy@kcl.ac.uk. If you wish to report an adverse event, as defined as an undesired effect of the intervention, please forward the event along with a through description to the above address or call the study team on XXXXXXXX. If you experience any other symptoms, please use your usual means of care, such as your doctors surgery or emergency care, as you see fit.

Alternatively, if you wish to raise a complaint, you can do this by contacting the co-ordinating supervisor, Dr Wendy Hall, at wendy.hall@kcl.ac.uk.

Kings College London holds insurance policies which apply to this study. If you experience harm or injury from taking part in this study, you may be eligible to claim compensation.

What samples will I have to provide and what will happen to them?

This study will require 2 blood tests, one at the baseline study visit, and one at the last study visit in week 12. At each visit we will take 10mL of blood (3 small tubes). These samples will be processed and frozen in Kings college London's labs in accordance with the Human Tissues Act. These blood

samples will be analysed by a certified laboratory, Affinity Biomarker Laboratories (Suite 602, Cumberland House, 80 Scrubs Ln, London NW10 6RF).

2 serum samples (with no human cells) will be stored for future investigative analysis for additional nutrients, but this will not contain any identifiable information.

The study also requires you collect 24-hour urine, at baseline and endline study visits, which will be processed by the study team in clinic, and then again at home in the middle of the study, which you will process and post a sub-sample. In each 24-hour collection, we will take a small sub-sample of 20mL, and then freeze 4mL of this. The rest will be safely discarded. The analysis of these samples will be in-house at Kings laboratories.

Will my taking part in this project be kept confidential?

Yes, all the information that we collect about you during the research will be kept strictly confidential. Any traceable information will be stored in a secure premises with restricted access for the study lead and their direct supervisor. Any identifiable data will be destroyed within 3-years of the study end date, which is estimated to be 01/02/2029, unless you wish to stay on the mailing list for further studies. You **will not** be identifiable in any ensuing reports or publications. Upon enrolling, you will be given a unique code to label your samples and ultrasound images, so you are untraceable. All data procedures are compliant with GDPR regulations.

Should you require further information on this, please do get in touch.

What will happen to the results of the research project?

These results will be used to write up a scientific article, with the aim to publish in a nutrition related scientific journal. This is estimated to be submitted in Feb 2026. Please note, you **will not** be identifiable in any report or publication. An email will be circulated to all study participants to inform them of any publications should you be interested in reading it.

Who is organising the research?

This trial is being organised by a PhD candidate, Anya Klarner, on behalf of the Department of Nutritional Sciences, Kings College London, in fulfilment of a doctoral degree. This study is supervised by Associate Professors within the department, Dr Wendy Hall, who can be contacted via email at wendy.hall@kcl.ac.uk and Dr Sarah E Berry, on sarah.e.berry@kcl.ac.uk.

This research is being funded by an Industry-associated not-for-profit organisation. Further details on the organisation will be provided upon completion of the study, so to reduce bias in the results. Any queries on this please don't hesitate to get in touch.

Can I change my mind about taking part?

Yes, you can withdraw from the study at any time. You just need to tell the researcher (Anya), that you don't want to be in the study anymore.

Should you decide to proceed with the study, you can keep a copy of this information sheet for reference throughout the study. You will also be given a copy of a consent form that you will need to sign after the introductory call to progress in the study.

Thank you for your attention!

Appendix 2. Informed consent declaration form

CONSENT FORM FOR PARTICIPANTS IN RESEARCH PROJECTS

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research

Title of project: STARchy staples: A randomised controlled trial on Cardiometabolic Health		
Ethical review reference number: HR/DP-22/23-35587	**Version number: 1, 17/03/23**	
		Tick or initial
1. I confirm that, to my knowledge, I meet the following criteria: I am 40-80 years old. I do not have a history of heart disease, stroke, high blood pressure, diabetes, chronic gastrointestinal disorder. I do not have a history of excess alcohol intake or substance abuse.		
2. I confirm that I have read and understood the participant information sheet, dated 10/03/23 Version 1, for the above project. I have had the opportunity to consider the information and asked questions which have been answered to my satisfaction.		
3. I consent voluntarily to be a participant in this project and understand that I can refuse to take part and can withdraw from the project at any time, without having to give a reason, up until January 2025.		
4. I consent to the processing of my personal information for the purposes explained to me in the Information Sheet. I understand that such information will be handled under the terms of UK data protection law, including the UK General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018.		
5. I understand that my information may be subject to review by responsible individuals from the College for monitoring and audit purposes.		
6. I understand that confidentiality and anonymity will be maintained, and it will not be possible to identify me in any research outputs		
7. I agree that the researcher/ research team may use my data for future research and understand that any such use of identifiable data would be reviewed and approved by a research ethics committee. (In such cases, as with this project, data would not be identifiable in any report).		

8. I understand that I must not take part if I fall under the exclusion criteria as detailed in the information sheet and explained to me by the researcher.	
9. I have informed the researcher of any other research in which I am currently involved or have been involved in during the past 12 months	
10. I understand that the information I have submitted will be published as a report	
11. I consent to the collection (20mL) and storage of my blood	
12. I consent to the collection (24-hour samples) of my urine, and the storage of 8mL for analysis on this project.	
13. I consent to participate in the use of an ultrasound scan on my arm, and the recording of pseudonymised ultrasound video (15 minutes).	
14. I agree to be re-contacted in the future by King's College London researchers regarding this project.	
Optional	
15. I agree that my GP may be contacted if any unexpected results are found in relation to my health.	
16. I wish to receive a copy of the final report.	
17. I agree that the researcher may retain my contact details so that I may be contacted in the future by King's College London researchers who would like to invite me to participate in future studies of a similar nature.	

_____	_____	_____
Name of Participant	**Date**	**Signature**
_____	_____	_____
Name of Researcher	**Date**	**Signature**

Appendix 3. Eligibility questionnaire, word template

Screening Questionnaire

Demographics

1. What gender were you assigned at birth? MALE ☐ FEMALE ☐

2. What is your age? ☐ *Years*

3. How tall are you?

☐ metres ☐ cm OR ☐ feet ☐ inches

4a. What is your weight?

☐ kilograms OR ☐ stones ☐ pounds

4b. Have you had weight loss >3kg in the last 2 months?

Yes ☐ No ☐

5. What is your ethnic group?

White		Asian or Asian British	
British	☐	Indian	☐
Irish	☐	Pakistani	☐
Other White background	☐	Bangladeshi	☐
Mixed		Other Asian background	☐
White and Black Caribbean	☐	Black or Black British	
White and Black African	☐	Caribbean	☐
White and Asian	☐	African	☐
Other Mixed background	☐	Other Black background	☐
		Chinese	☐
		Any other Group	☐

Health

5. Over the last 12 months, would you say that on the whole, your health has been:

(Please ✓ the one box which applies to you)

Excellent	☐
Very good	☐
Good	☐

6. Do you now, or have you ever had:

Diabetes:	Yes	☐	No	☐
High blood pressure:	Yes	☐	No	☐
Coeliac Disease	Yes	☐	No	☐
Insomnia	Yes	☐	No	☐
Sleep Apnoea	Yes	☐	No	☐
Kidney disease	Yes	☐	No	☐
Hyperkalaemia	Yes	☐	No	☐
Gastrointestinal disorders	Yes	☐	No	☐
Substance abuse or alcoholism	Yes	☐	No	☐
Cardiovascular disease	Yes	☐	No	☐
Clinical mental health disorder	Yes	☐	No	☐

7. Has a doctor ever told you that you have had a heart attack?

	Yes	☐	No	☐

8. Are you taking any routine medications?

Yes ☐ No ☐

If yes, please provide details ☐

9. Are you taking any routine supplements?

Yes ☐ No ☐

If yes, please provide details ☐

Would you be willing to stop these supplements throughout the study period?

Yes ☐ No ☐

Lifestyle

10. Do you work?

Yes ☐ No ☐

If yes, please provide your occupation ☐

11. Do you hold any care responsibilities that require you to be awake through the night?

Yes ☐ No ☐

12. Are you pregnant, planning pregnancy, breastfeeding or had a baby in the last 12-months?

Yes ☐ No ☐

13. Do you own a smart phone?

Yes ☐ No ☐

If yes, please provide the brand name and the model ☐

14. Do you have any dietary preferences?

Yes ☐ No ☐

Vegetarian ☐
Vegan ☐
Pescetarian ☐
Flexitarian ☐
Other ☐ ☐

Food and Drinks

The following questions ask about some foods & drinks you might have during a 'typical' week, over the past month or so. Do not be concerned if some things you eat or drink are not mentioned.

8. Please tick how often you eat at least ONE portion of the following foods & drinks: (a portion includes: a handful of grapes, an orange, a serving of carrots, a side salad, a slice of bread, a glass of pop).

(Please only put one tick, but answer EVERY line)

	Rarely or never	Less than 1 a Week	Once a Week	2-3 times a Week	4-6 times a Week	1-2 times a Day	3-4 times a Day	5+ a Day
Fruit (tinned / fresh)	☐	☐	☐	☐	☐	☐	☐	☐
Fruit juice (not cordial or squash)	☐	☐	☐	☐	☐	☐	☐	☐
Salad (not garnish added to sandwiches)	☐	☐	☐	☐	☐	☐	☐	☐
Vegetables (tinned / frozen / fresh, but not potatoes)	☐	☐	☐	☐	☐	☐	☐	☐
Chips / fried potatoes	☐	☐	☐	☐	☐	☐	☐	☐
Other potatoes (boiled, baked, mashed)	☐	☐	☐	☐	☐	☐	☐	☐
Wholemeal bread, rice, pasta	☐	☐	☐	☐	☐	☐	☐	☐
White bread, rice and pasta	☐	☐	☐	☐	☐	☐	☐	☐
Red meat (pork, lamb, beef)	☐	☐	☐	☐	☐	☐	☐	☐
Fish	☐	☐	☐	☐	☐	☐	☐	☐
Chicken	☐	☐	☐	☐	☐	☐	☐	☐

9. On average, how many portions of FRUIT do you eat a day?

(examples include a handful of grapes, an orange, a glass of fruit juice, a handful of dried fruits).

_____

10. On average, how many portions of VEGETABLES do you eat a day? (examples include: 3 heaped tablespoons of carrots, a side salad, 2 spears of broccoli). _____

11. What milk do you usually use or drink, such as in hot & cold drinks or on cereal? (including tea, coffee, hot milk, milk shakes, or on cereal)

Whole / full-fat milk	☐	Semi-skimmed milk	☐
Skimmed milk	☐	Rarely/never use milk	☐
Other (please write its name)			

12. On average, how much alcohol do you drink over a complete seven day week?

(One unit is a standard glass of wine, half a pint of beer or lager, a single measure of spirits, a measure of sherry)

I rarely/never drink alcohol	☐	Less than 14 units	☐
Between 14 & 21 units	☐	More than 21 units	☐

13. Last week (or a week before that if you have been poorly or on holiday), how much exercise did you do, if any?

(a) I didn't do any exercise ☐

(b) I did some LIGHT exercise ☐

This was fairly easy and I didn't get out of breath (Eg. Gentle walking, playing bowls or snooker, light DIY/housework).

I did this _____ times during the week.

Each time I did this lasted about _____ minutes

AND / OR

(c) I did some MODERATE exercise ☐

This made my breathing a little harder or made me sweat. (Eg fast walking, swimming, golf, heavy housework).

I did this _____ times during the week.

Each time I did this lasted about _____ minutes

AND / OR

(d) I did some VIGOROUS exercise ☐

This made my breathing hard & made me sweat. (Eg running, squash, hard swimming, aerobics).

I did this _____ times during the week.

Each time I did this lasted about _____ minutes

14. Regarding smoking, are you?

A current smoker ☐

An ex-smoker	☐	When did you give up?	☐ *Months*
I have never smoked more than 100 cigarettes	☐		

STOP-Bang questionnaire for Sleep Apnoea *(Chung et al., 2008)*

Height _____ inches/cm Weight _____ lb/kg

Age _____ Male/Female BMI _____

Collar size of shirt: S, M, L, XL, or _____ inches/cm

Neck circumference* _____ cm

***S* noring**

Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?

Yes | No

***T* ired**

Do you often feel tired, fatigued, or sleepy during daytime?

Yes | No

***O* bserved**

Has anyone observed you stop breathing during your sleep?

Yes | No

Blood *p* ressure

Do you have or are you being treated for high blood pressure?

Yes | No

* Neck circumference is measured by staff

Thank You

Appendix 4. **Participant Information Sheet on Urinary collection**

Background

Urinary samples are a good indicator for mineral intake, as most minerals are not stored in the body but excreted out. This is why we ask for urine to be collected for the whole 24-hours, so we have a complete view of the whole day. This method is used routinely for national dietary surveys (25).

Overview

- The 24-hour period starts with the first early morning urine. Please discard this urine and record it as the "Start time".
- All urine passed after this will be collected, starting from the second morning urine passed of the 24-hour collection day, and ending with the first urine passed the following morning.
- The collection day will always be the day before your clinic visit and one time point midline.

Collection

1. Upon passing your first urine of the day, please record the time point as the start of your study.
2. To collect your first urine of the study, use the plastic jug provided and try to collect the whole urine stream.
3. Open the lid on the 5L container and place the funnel in the neck.
4. Carefully decant the urine into the larger container.
5. If you are not at home when you need to collect your urine, please follow the same instructions as above, but instead you can decant your urine into the 2L container, to make carrying the sample around less arduous.
6. Please keep your urine in a dark cool environment (explained in FAQs).

Important information:

- **Transporting urine:** When transporting any urine, please use the plastic bags and ensure that lids are tightly sealed so to avoid spillages.
- If you are menstruating on the day of urinary collection, please seek advice from the study lead to find an appropriate collection day, contact details are at the end of this document.
- Please ensure you fill out the **urine collection form** as it guides you, this information is essential for accurate processing.

FAQs

- *What happens if I forget a sample?* This isn't a natural process, so it's normal to forget your need to urinate in the sample jug. But please try to be mindful during this period. Top tip is to take the sample on a weekend day when you're pottering around the house and keep your sample jug in the bathroom as a reminder!
- *What happens if I spill some of my sample?* Please record the event and try to estimate, where possible, how much you think was lost.
- *What happens if I leave my sample somewhere warm?* Cooling the sample slows the growth of bacteria and stops it from interfering with the analysis.

Please note, you will have a call with a study team member to run through this process, and we'll be able to answer any questions you may have.

Appendix 5. 24-hour urine collection form

Urine Collection Form

Participant ID	
Urinary sample number *(1/2/3)*	
Start Date *(Please only record the date from when you collect your first sample, which will be your second urination of the day)*	
End Date	
Start time of 24hour urine collection: *(Time after first urine of the day)*	
Finish time of 24hour urine collection *(First urine of the following day)*	
Did you miss any collections? *(If yes, please state how many collections you missed, and if possible, try to estimate the amount lost)*	
Did you have any spillages? *(If yes, please try to estimate the amount lost, e.g., 3-4 drops or 10mL from measuring jug)*	

Did you use any medications used during this time? *(Please list all)*	
Please only fill out the following for your midline measure.	
What is the weight of your empty 5L bottle? *(Please record this before you fill up the bottle)*	
What is the weight of your total 24-hour sample? *(Please give us the weigh to the nearest gram)*	
What is the weight of your sub-sample tube without any urine in it? *(Please record this before you fill it up, ensure the lid is on for this measure and the for the end measure)*	
What is the weight of your sub-sample with urine in it? *(Please ensure the lid is on for this measure)*	
The below box is for staff to fill in only.	

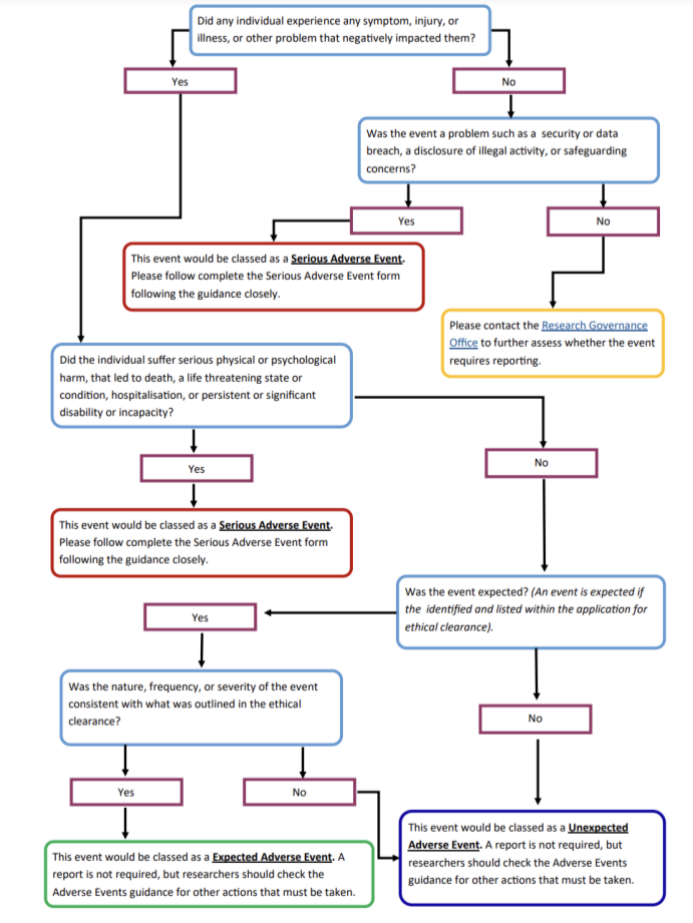
Is your 24-hour sample greater than 400mL?	
Research staff name and signature:	

Appendix 6. Information with regards to Safety Reporting in Non-CTIMP Research

	Who	When	How	To Whom
SAE	Chief Investigator	Within 15 days of CI becoming aware of the event	SAE Report form for Non-CTIMPs, available from NRES website.	Main REC with a copy to the sponsor
Urgent Safety Measures	Chief Investigator	Immediately Within 3 days	By phone Notice in writing setting out reasons for the urgent safety measures and the plan for future action.	Main REC Main REC with a copy sent to the sponsor. The MREC will acknowledge this within 30 days of receipt.
Progress Reports	Chief Investigator	Annually (starting 12 months after the date of favourable opinion)	Annual Progress Report Form (non-CTIMPs) available from the NRES website	Main REC with a copy to the sponsor
Declaration of the conclusion or early termination of the study	Chief Investigator	Within 90 days (conclusion) Within 15 days (early termination) *The end of study should be defined in the protocol*	End of Study Declaration form available from the NRES website	Main REC with a copy to the sponsor
Summary of final Report	Chief Investigator	Within one year of conclusion of the Research	No Standard Format However, the following Information should be included:- Where the study has met its objectives, the main findings and arrangements for publication or dissemination	Main REC with a copy to be sent to the sponsor

			including feedback to participants	

Appendix 7. Flow diagram, provided by Kings College London Research Governance Office, outlining Adverse Events definitions and procedures



Appendix 8. Pittsburgh sleep quality index questionnaire

Name:_____ Date: _____

Pittsburgh Sleep Quality Index (PSQI)

Instructions: The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. **Please answer all questions.**

1. During the past month, what time have you usually gone to bed at night? _____
2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night? _____
3. During the past month, what time have you usually gotten up in the morning? _____
4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.) _____

5. During the past month, how often have you had trouble sleeping because you…	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a. Cannot get to sleep within 30 minutes				
b. Wake up in the middle of the night or early morning				
c. Have to get up to use the bathroom				
d. Cannot breathe comfortably				
e. Cough or snore loudly				
f. Feel too cold				
g. Feel too hot				
h. Have bad dreams				
i. Have pain				
j. Other reason(s), please describe:				
6. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?				
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?				
	No problem at all	Only a very slight problem	Somewhat of a problem	A very big problem
8. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?				
	Very good	Fairly good	Fairly bad	Very bad
9. During the past month, how would you rate your sleep quality overall?				

Appendix 9. Advertisement Poster

Appendix 10. Advertisement Instagram post/Tweet

"Do you want to help with cardiometabolic research by consuming carbs?

@Kings College London is running a new 12-week dietary study and needs healthy volunteers! This study is free-living so you can take part from the comfort of your own home, with just 2 visits to Kings College London, near Waterloo station. If you're interested, please contact the study team at starchy@kcl.ac.uk. #clinicaltrial #diet #nutritionalscience #starch"

Appendix 11. Advertisement Email

Dear [NAME]

I am writing to you to invite you to take part in a study in affiliation with the Kings College London titled:

"STARchy staples: a randomised controlled trial on Cardiometabolic Health".

Can you help us understand how different starchy staples impact our cardiometabolic health? We are looking for healthy volunteers (40-80y) to take part in a research project. The aim of this study is to investigate if habitually consuming starchy staples in the evening meal, can improve one's sleep quality, nocturnal blood sugars, arterial health, fasting blood profiles, blood pressure and other related parameters.

Your participation will involve completing an online screening questionnaire, attending an introductory call, an induction and dietary consultation via videocall, and two clinic visits, as well as consuming starchy staples such as potatoes, pasta, rice, couscous, or bread alongside your evening meal for a total of 14-weeks, including a two-week study run-in to trial your suitability for this study. This study will be used to inform dietary advice on starchy staples in the prevention of chronic disease.

We will offer you £100 renumeration and up to £10 travel reimbursement for each visit to Kings College London, Waterloo.

Attached to this email is an information sheet where you can find all the details on the study on what will happen, why it is being conducted and your role in the research. Before you decide whether to take part, please take time to read the enclosed information sheet and take your time to decide.

If you have any questions or would like further clarification and information about the study then please get in contact by emailing at starchy@kcl.ac.uk or calling on +44XXXXXX, and we will be happy to discuss with you.

If you are interested in taking part, please reply to this email expressing your interest and we can arrange a date that suits you for our introductory call.

Please note that participation is voluntary, so if you decide you would no longer like to participate, then you are free to drop out at any stage.

Best wishes,

Anya Klarner, ANutr | PhD student
Department of Nutritional Sciences | School of Life Course Sciences | Faculty of Life Sciences & Medicine

King's College London | Franklin Wilkins Building | 150 Stamford Street | SE1 9NH

Appendix 12. Gatekeeper Email

Dear (University/Institution),

RE: Advertisement of The STARCHy study (Ref XXXX)

We are contacting you to request the opportunity to advertise our research study to members of your organisation. We have included a brief description of our study below for your consideration. We have also attached a more detailed proposal with explanation of rationale and what the study entails. The study has full ethical approval from the King's College London Research Ethics Committee (HR/DP-22/23-35587).

We would be very grateful if you would consider advertising our study in your organisations' Newsletter/Bulletin. Alternatively, we are keen to advertise via poster/leaflets placed in institutions and will deliver some to your organisation if this is permitted.

Below is a brief description of our study:

"STARchy staples: a randomised controlled trial on Cardiometabolic Health- The STARCHy study"**.**

Can you help us understand how different starchy staples impact our cardiometabolic health? We are looking for healthy volunteers (40-80y) to take part in a research project. The aim of this study is to investigate if habitually consuming different starchy staples in the evening meal, can improve glycaemic, blood and endothelial profiles, thereby reducing one's risk for chronic diseases. You will be reimbursed with £100 upon completing the study."

If you require any further documentation from us for advertisement/regulatory purposes, please do not hesitate to contact us.

We look forward to hearing from you.

Best wishes,

Anya Klarner