Section of Endocrinology and Investigative Medicine

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PROTOCOL

COVER PAGE

Official Title: Investigation of a New Diet for the Treatment of Obesity in the NHS

Brief Title: Investigation of a New Diet for the Treatment of Obesity in the NHS

Study Type: Interventional

NCT number: NCT05249439

Sponsor: Imperial College London, London, UK

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Study Protocol: Version 4, 12th June 2018

(IRAS ID: 189449; REC reference 16/LO1622)

Investigation of a new satiety inducing diet for the treatment of obesity in the NHS

Background

The obesity epidemic shows no sign of abating. In the UK in 1980, 6% of men and 8% of women were obese. Today, this has risen to 25% of all British adults with the cost of treating obesity and its co-morbidities estimated at £5.1 billion per year. The national obesity figures tell us that the standard low calorie 'eat less' advice is not working and there is, therefore, a need to improve the dietary advice given to obese patients if we are to stem the epidemic of obesity seen in the UK today.

The NHS advises a low calorie diet as the mainstay of obesity treatment. Most low calorie diets fail because when food intake falls, the body launches a powerful hormone counter-response that makes people hungry and which reduces the rate at which they burn energy (refs 1-3). This means that despite the NHS's advocacy of 'lifestyle' (i.e. dietary) measures as the cornerstone of obesity treatment, the advice being given will only work long term for a small minority of patients.

At the Imperial Weight Centre (IWC), Imperial College Healthcare NHS Trust (ICHNT), we currently manage obese patients in a specialist weight management programme known as Tier 3. Outcomes from patients following a standard NHS low calorie (LowCal) diet, who have recently completed our six month Tier 3 programme show that they fail to lose the requisite amount of weight to confer improvements in metabolic and cardiovascular health. In addition, we have data to show that patients following a low calorie diet have a reduced metabolic rate (the speed at which they burn energy).

Using the scientific literature we have developed a new fullness (satiety) inducing diet called Satiety Protocol (SatPro). The advice given in SatPro aims to increase fullness after eating and reduce feelings of hunger, therefore working with, rather than against the body's hunger-fullness system. In addition, unlike low calorie diets, SatPro does not ask patients to markedly reduce their caloric intake and we would therefore predict that SatPro will not lead to the same fall in metabolic rate seen with low calorie diets.

SatPro consists of five pieces of eating advice. Individually each piece of advice given in SatPro is followed by humans every day without reported adverse effects. SatPro does not require any special foods, supplements, medicines, equipment or facilities. Patients following SatPro will be eating foods that are commonly available to the general public (e.g. in the supermarket) all of which are subject to government regulation (e.g. freshness, constituent

ingredients etc.).

The **scientific background** for SatPro is laid out below:

SatPro versus LowCal:

1. **LowCal:** Reduce intake by 600kcal/day.

Evidence: Low calorie diets fail because they elicit hormonal changes that promote hunger and reduce metabolic rate (the rate at which the body burns energy) (ref 1-3).

SatPro: The scientific evidence (points 2-6 below) predicts that SatPro should not result in these hunger-inducing hormonal changes. Eat when you feel hungry. Stop when you feel full.

2. **LowCal:** Consume some protein (12% of intake/day).

Evidence: Protein promotes post-prandial fullness by stimulating a rise in circulating pro-satiety gut hormones, superior to that of any other macronutrient (ref 4).

SatPro: Eat protein (45g) at each meal (35% of intake/day).

3. **LowCal:** Eat plenty of starchy foods including bread, potatoes rice and pasta.

Evidence: Glycaemic index (GI) characterises the increment in blood glucose (BG) following carbohydrate consumption (ref 5). Starchy foods are high GI and require high levels of the pro-fat storage hormone insulin to normalise BG.

SatPro: Eat low GI carbohydrates (GI value <55) to keep insulin levels low, a physiological state that promotes fat breakdown (lipolysis) and inhibits fat storage (lipogenesis) (ref 6) and which results in increased post-prandial satiety.

4. **LowCal:** Occasional 'treats' permitted.

Evidence: High sugar foods stimulate a hedonic response that can cause cravings and uncontrolled eating (ref 7).

SatPro: Abstain completely from foods that trigger this hedonic response (an approach that is akin to the NHS advice on smoking cessation).

5. **LowCal:** Eat a low fat diet

Evidence: Dietary fat is satiating and certain fats have metabolic and cardiovascular health benefits (refs 8,9). In addition, 'low fat' diet foods frequently replace fat with sugar or other poor quality carbohydrates (ref 10) (see point 3 above).

SatPro: Eat up to 90g/day of certain fats with health benefits (refs 8,9) e.g. olive oil and nuts. Do not eat 'diet', 'light' or 'low fat' processed foods (see also point 6 below).

This feasibility study will assess whether SatPro results in superior weight loss in obese patients compared with patients following standard low calorie advice (LowCal). We will also assess whether patients who lose weight on SatPro can do so without the reduction in metabolic rate that is seen in patients following LowCal. Lastly, we will investigate the mechanisms by which SatPro works. We have hypothesised that SatPro might work for the following reasons:

a. It causes levels of 'fullness' gut hormones to run high and 'hunger' gut hormones to run low.

b. It induces changes in the gut bacteria (gut microbiome) that promote a leanness and which lead to reduced appetite

It is not be associated with the fall in basal metabolic rate that is often seen in weight loss diets and which results in weight re-gain.

Inclusion Criteria:

- Aged ≥18 years
- Male or female
- Body mass index ≥35kg/m^2 with at least one obesity related co-morbidity
- Body mass index ≥40kg/m^2 with or without an obesity related co-morbidity
- Eligible for treatment under the NHS

Exclusion criteria:

- History of any medical, psychological or other condition, or use of any medications, which would either compromise the validity of the study or the safety of the participant
- English language fluency and/or comprehension insufficient to be able to participate in educational and group components of the programme
- Usual residence/place of work is sufficiently far from the study site or logistical/lifestyle factors mean that it is likely that the patient would be unable to attend for all sessions/components of the study
- Pregnancy or breast feeding
- Previous bariatric surgery
- Concurrent participation in another research study which would either compromise the validity of the study or the safety of the participant
- Previous participation in a study at any time point if the investigators judge that this would either compromise the validity of the study or the safety of the participant
- Unable to give informed consent

Protocol (Please also refer to Study Protocol, figure 1 and to table 1)

Study Overview

Feasibility study of SatPro conducted in obese patients seen for specialist weight management (Tier 3 Programme) in the Imperial Weight Centre, ICHNT.

Patients

Potential participants will be identified and recruited from obese patients referred to the Imperial Weight Centre, ICHNT for Tier 3 specialist weight management. All patients will be registered at ICHNT.

BACKGROUND:

Existing Imperial Weight Centre (IWC) Tier 3 Weight Management Programme:

NICE guidance states that obese people should be seen within a multidisciplinary specialist weight management service known as Tier 3 in which they receive specialist medical, dietetic and psychological input.

In the existing (currently running) NHS Tier 3 programme at the Imperial Weight Centre (IWC), Imperial College Healthcare NHS Trust (ICHNT) patients proceed through the Tier 3 pathway follow a step wise progression through the Tier 3 programme as detailed in points 1 to 4 below:

Current IWC Tier 3 Pathway

1. Patients attend for one to one consultations with each of the specialist obesity dietician, psychologist and physician.

2. Patients attend for ten fortnightly group weight management sessions (n= 8 - 10 patients) facilitated by the multidisciplinary IWC team lasting for a total of 20 weeks. During these sessions patients receive ongoing advice and support in helping them adhere to the standard NHS low calorie diet (LowCal).

3. After the final (tenth) group session, a member of the IWC multi-disciplinary team meets with the patient for a one to one exit appointment to discuss their Tier 3 weight and health outcomes and to agree on a plan for their future weight management.

4. Following on from this exit meeting, a minority of patients will be referred for bariatric (weight loss) surgery and the rest are discharged back to primary care or community based weight loss services.

How this SatPro Pilot Study will fit in:

Pre-registration:

1. Patients will be informed about the study by letter, telephone call, email or at the one to one consultation with a member of the Imperial Weight Centre multi-disciplinary team. A **patient information sheet** will be given to patients. Patients will be given at least 24 hours to decide whether they wish to take part in the study.

2. A member of the Imperial Weight Centre multi-disciplinary team will ask the patient if they wish to take part in the study. If the patient wishes to take part in the study they will subsequently be contacted by a study investigator to make arrangements for the screening visit.

Those **patients** referred for NHS Tier weight management **who do not wish to take part in the study will progress through the usual Tier 3 pathway** as described in points 1 to 4 above.

3. **Screening visit and informed consent:** The patient will have the opportunity to ask questions and to discuss the study with the investigator. If the patient wishes to proceed, informed consent will be taken at this visit (this will be done at least 24 hours after receipt of the patient information sheet). This will be done by the patient reading the study consent form. They will be asked to initial each point on the form to indicate that they have read, understood and been given the opportunity to ask questions. Once all points on the consent form have been initialled by the patient, the patient will sign the consent form. The consent form will then be co-signed by the investigator conducting the consultation.

All participants will be screened to assess whether they meet inclusion criteria and this process will comprise a medical history, routine physical examination and fasting blood tests.

Patients will be required to fast overnight (12 hours) prior to blood tests. Patients can drink plain water while fasting.

Fasting blood tests will be taken for full blood count, iron studies, folate, vitamin B12, renal function, liver function tests, bone profile, vitamin D, thyroid function, glucose, insulin, C-peptide, HbA1c, lipids.

All women of child bearing age will be asked to undergo testing for pregnancy by measurement of the urine concentration of beta human chorionic gonadotrophin (beta-hCG). The test will be deemed negative for pregnancy if beta-hCG cannot be detected.The test will be deemed positive for pregnancy if beta-hCG is detectable at any level.

Study Protocol:

All patients recruited into this study will receive standard structured Tier 3 care described in points 1 to 4 above.

In addition to standard care all participants will be required to participate in the following visits/measurements/assessments (which are in excess of what they would normally experience in the standard Tier 3 experience) **(Please also refer to Study Protocol, figure 1 and to table 1):**

1. An initial study visit (Study Visit A) lasting for a total of 4.5 hours.

At Study Visit A the following baseline assessments will be recorded:

Body weight, height, body mass index, body composition (using bio-impedance weighing scales), blood pressure (three seated readings) and hip, waist and neck circumference (measured with a tape measure).

Blood tests for fasting gut hormones

Resting energy expenditure will be measured by indirect calorimetry.

The patient will be asked to provide a mid-stream urine sample. From this, two 10ml urine samples will be aliquoted. One 10ml sample to be analysed for urinary by-products of metabolism. The second 10ml urine sample will be analysed for urinary urea (a waste product of protein metabolism) which is necessary to measure in order to accurately calculate resting energy expenditure as measured by indirect calorimetry.

During Study Visit A, patients will be asked to complete the following questionnaires:

- Dutch Eating Behaviour Questionnaire (30 minutes)
- SF-36 health and well-being questionnaire (30 minutes)
- Life experiences questionnaire (45 minutes)
- Three factor hunger questionnaire (30 minutes)

At Study Visit A, patients will be given a 7-day food diary and a 7-day food expenditure diary to complete at home.

At Study Visit A, patients will be given a a stool specimen pot and will be asked to collect a stool specimen at home within 24 hours of the first group weight management session. Patients will return the stool sample to the research team at the first group weight management session.

2. Patients will be randomised to the SatPro group or to the Control group using a randomisation table generated by an independent researcher in our department.

3. At the fourteen fortnightly group weight management sessions (a total of 26 weeks), the Control group following the standard NHS Low Calorie diet (LowCal) will be supported to follow this diet. LowCal is based on reducing caloric intake and following a low fat diet.

At the fourteen fortnightly group weight management sessions (a total of 20 weeks), the group following SatPro will be supported to follow the eating principles of SatPro.

<u>Summary of SatPro dietary advice:</u>

1. Eat when you feel hungry. Stop when you feel full.

2. Eat protein (~45g) at each meal.

3. Eat low glycaemic index (GI) carbohydrates, e.g. fruits, vegetables, wholegrains and pulses.

4. Abstain completely from foods that trigger a hedonic (excessive reward) response e.g. high sugar foods.

5. Eat healthy fats.

<u>Example SatPro daily menu:</u>

Breakfast: Scrambled eggs (2 eggs cooked with whole milk and butter), grilled kippers

Lunch: Chicken legs baked with lemon and oregano. Steamed broccoli, cooked red lentils

Plain yoghurt with roasted nuts

Dinner (evening meal): Frozen cod fillet with mixed herbs baked with olive oil. Green beans, stir-fried bean sprouts Strawberries

3. At each fortnightly group weight management session the following will be measured in both groups (LowCal and SatPro):

Anthropometrics: body weight, body composition (measured by bio-impedance scales), blood pressure (three seated mesaurements)

4. During the course of the study, both the Control group and SatPro group will be asked to complete the following:

i. A 7-day food diary to be completed by the patient at home on three separate occasions during the study period (baseline [to be returned at group weight management session 1], after session five of the fourteen group weight management sessions [to be returned at group weight management session 6] and during the follow-up period, 48 weeks after starting the group weight management sessions, [to be returned at week 50 follow-up visit]).

ii. A 7-day food expenditure diary (listing all food expenditure for 7 days) to be completed by the patient at home on two separate occasions during the study (baseline [to be returned at group weight management session 1], and after session six of the ten group weight management [to be returned at group weight management session 6]).

iii. An end of study questionnaire (at Study Visit C) which will take 30 minutes to complete.

5. At the final (fourteenth) group weight loss session, patients will be given a stool specimen pot and will be asked to collect a stool sample at home within 24 hours of Study Visit B. Patients will return the stool sample to the research team at Study Visit B

6. After the patient has completed the last specialist group weight management session (session 14) they will be asked to attend for Study Visit B which will last for a total of 3.5 hours.

At Study Visit B the following assessments will be recorded:

Body weight, body mass index, body composition (using bio-impedance weighing scales), blood pressure (three seated readings) and hip, waist and neck circumference (measured with a tape measure).

Patients will be required to fast overnight (12 hours) prior to blood tests. Patients can drink plain water while fasting.

Fasting blood tests will be taken for full blood count, iron studies, folate, vitamin B12, renal function, liver function tests, bone profile, vitamin D, thyroid function, glucose, insulin, C-peptide, HbA1c, lipids, gut hormones.

Resting energy expenditure will be measured by indirect calorimetry.

The patient will be asked to provide a mid-stream urine sample. From this, two 10ml urine samples will be aliquoted. One 10ml sample will be analysed for urinary by-products of metabolism. The second 10ml urine sample will be analysed for urinary urea (a waste product of protein metabolism) which is necessary to measure in order to accurately calculate resting energy expenditure as measured by indirect calorimetry.

At Study Visit B patients will be asked to complete:

- Dutch Eating Behaviour Questionnaire (30 minutes)
- SF-36 health and well-being questionnaire (30 minutes)
- Three factor hunger questionnaire (30 minutes)

7. After Study Visit B, patients will be asked to patients will be asked to attend for five months for twice monthly checks of anthropometrics (body weight, percentage body fat) and blood pressure (three seated readings). At the last monthly follow up visit, patients will be given a stool specimen pot and will be asked to collect a stool sample at home within 24 hours of Study Visit C. Patients will return the stool sample and the urine sample to the research team at Study Visit C.

8. One year after starting the study (week 52), patients will be asked to attend for the End of Study Visit, Study Visit C.

At Study Visit C the following assessments will be recorded:

Body weight, body mass index, body composition (using bio-impedance weighing scales), blood pressure (three seated measurements) and hip, waist and neck circumference (measured with a tape measure).

Patients will be required to fast overnight (12 hours) prior to blood tests. Patients can drink plain water while fasting.

Fasting blood tests will be taken for full blood count, iron studies, folate, vitamin B12, renal function, liver function tests, bone profile, vitamin D, thyroid function, glucose, insulin, C-peptide, HbA1c, lipids, gut hormones.

Resting energy expenditure will be measured by indirect calorimetry.

The patient will be asked to provide a mid-stream urine sample. From this, two 10ml urine samples will be aliquoted. One 10ml sample will be analysed for urinary by-products of metabolism. The second 10ml urine sample will be analysed for urinary urea (a waste product of protein metabolism) which is necessary to measure in order to accurately calculate resting energy expenditure as measured by indirect calorimetry.

At Study Visit C patients will be asked to complete:

- Dutch Eating Behaviour Questionnaire (30 minutes)
- SF-36 health and well-being questionnaire (30 minutes)
- Three factor hunger questionnaire (30 minutes)
- End of Study Questionnaire

END OF STUDY

Figure 1 –SatPro Study Protocol

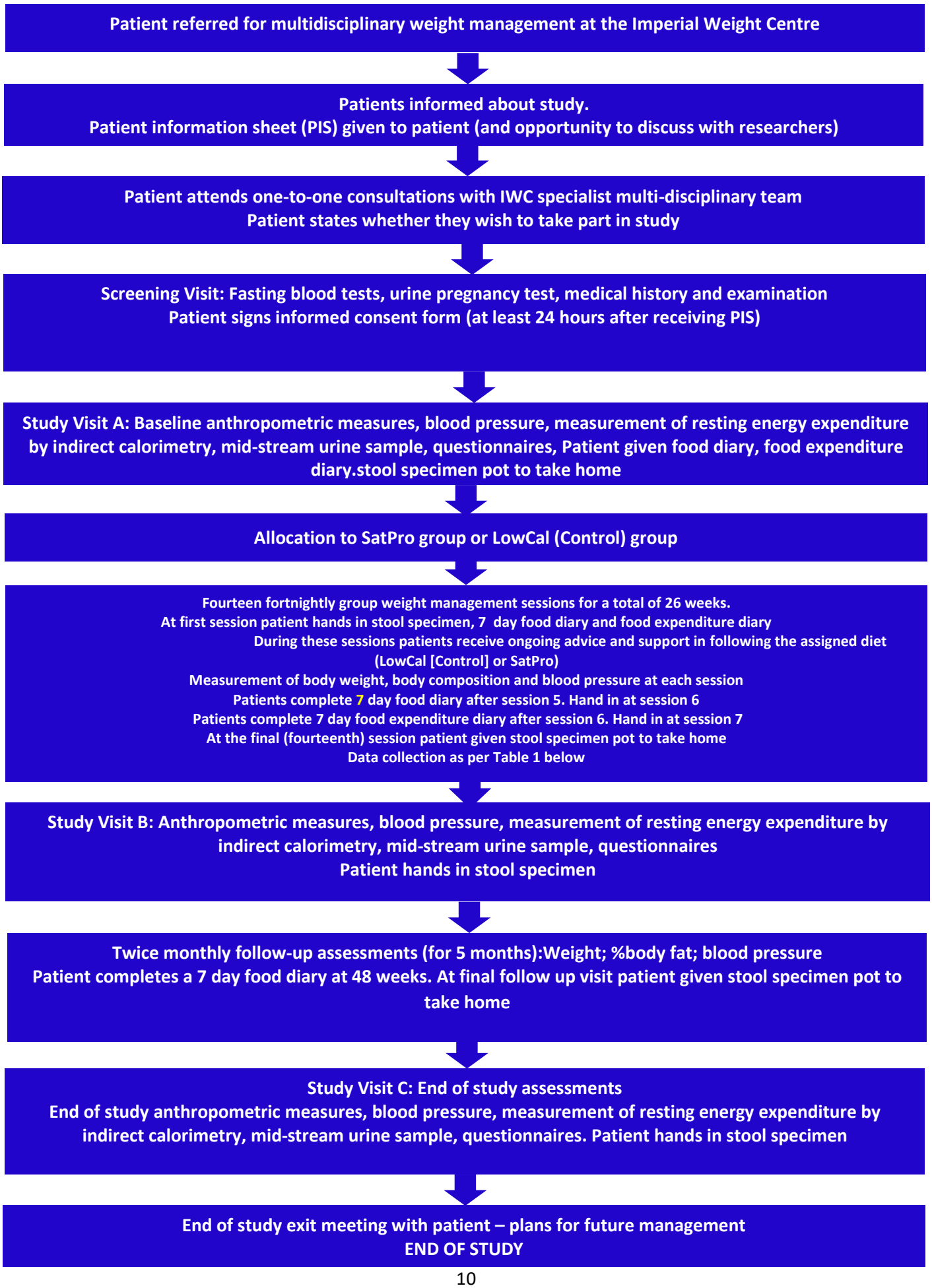

Table 1 : Details of Study Protocol

STUDY JOURNEY	One to one consultation with member of IWC MDT	One to one appointment/telephone/email/letter	Screening	Study visit A	Fortnightly group weight management sessions														Study visit B	Bi-monthly follow-up sessions										Study visit C	Exit appointment
					1	2	3	4	5	6	7	8	9	10	11	12	13	14		1	2	3	4	5	6	7	8	9	10		
1:1 consultation with IWC MDT	X																													X
Patient informed about study	X	X																												
Patient Information sheet	X	X																												
Patient asked if they would like to take part		X																												
Fasting blood tests			X																X										X	
Fasting gut hormones (blood test)				X															X										X	
Pregnancy test (urinary beta-hCG)			X																											
History and examination			X																											
Consent			X																											
Measurement of body weight	X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Measurement of height	X																													
Anthropometric assessments body composition (bio-impedance)				X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Waist, hip and neck circumference				X															X										X	
Measurement of blood pressure	X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Measurement of resting energy expenditure by indirect calorimetry				X															X										X	
Mid-stream urine sample				X															X										X	
Patient given stool specimen pot				X														X										X		
Patient hands stool sample					X														X										X	
Fortnightly group weight management session (14 in total)					X	X	X	X	X	X	X	X	X	X	X	X	X	X													
Life experiences questionnaire				X																										
SF-36 Questionnaire				X															X										X	
Dutch Eating Behaviour Questionnaire				X															X										X	
3 factor eating behaviour questionnaire				X															X										X	
Patient given 7 day food diary				X					X																		X			
Patient hands in 7 day food diary					X					X																		X		
Patient given 7 day food expenditure diary				X						X																				
Patient hands in7 day food expenditure diary					X						X																			
End of study questionnaire																													X	

Statistical analysis

Outcomes will be compared between the SatPro group and patients who have followed a low calorie diet (LowCal).

Primary outcome: Change in body weight

Secondary outcomes:

Change in body composition

Change in waist to hip ratio

Change in neck circumference

Change in blood pressure

Change in glycaemic control

Change in energy expenditure

Satiety, hunger and dietary restraint

Acceptability to patients

Diet sustainability/adherence

Changes in gut and urine microbiome and metabolome

Changes in hunger and fullness gut hormones

Quantitative data will be analysed using the appropriate statistical software (GraphPad Prism and SPS) in conjunction with guidance from the Imperial College Statistical Advisory Service. Comparisons between the LowCal and SatPro groups will be performed in an intention to treat manner and sub-stratified where possible.

Qualitative data, for example free text responses in questionnaires, will be subject to thematic analysis based in Grounded Theory. Food diaries will be analysed using the appropriate software and food expenditure diaries will be analysed using the DEFRA template.

Safety and protection of patients

Clinical care

All patients, will receive multidisciplinary weight management and will progress through the standard Tier 3 pathway that is currently in operation at ICHNT.

Dietary intervention

SatPro advocates eating foods that are readily available to the general public e.g. from supermarkets and which have been subjected to governmental regulation regarding freshness, constituent ingredients etc. Adverse events (see below) related to the dietary protocol are not anticipated.

Blood sampling

Blood will be taken only by an NHS phlebotomist or by a medical practitioner or registered nurse trained in the procedure.

Withdrawal from the study

Patients will be free to withdraw at any point during the study. In addition the investigators will withdraw a patient from the study if they have identified clinical grounds for doing so.

Contact information

Patients will be given contact information for the trial investigators which they can use at any point during the study if there has been a change in their clinical condition that they wish to report. This contact cannot be used by patients to supplement routine clinical care as this could potentially bias the outcome of the study.

Investigators

The Chief Investigator is Professor Tricia Tan, Investigative Medicine, Imperial College London and Imperial Weight Centre, ICHNT. Co-investigators and collaborators are Dr Saira Hameed, NIHR Clinical Lecturer, Investigative Medicine, Imperial College London and Imperial Weight Centre, ICHNT; Professor Sir Stephen Bloom, Head of Department of Investigative Medicine, Imperial College London; Dr Harvinder Chahal, Consultant Endocrinologist and Lead Bariatric Physician, Imperial Weight Centre, ICHNT, Honorary Clinical Senior Lecturer, Investigative Medicine, Imperial College London; Mr Ahmed Ahmed, Consultant Upper GI and Bariatric Surgeon and Clinical Lead for Bariatric Surgery, Imperial Weight Centre, ICHNT, Professor Gary Frost, Chair in Nutrition and Dietetics, Imperial College London; Miss Rhian Houghton Specialist Obesity Management Dietician, Imperial Weight Centre, ICHNT; Dr Meila Roy, Clinical Bariatric Psychologist, Imperial Weight Centre, ICHNT; Dr Victoria Salem, NIHR Clinical Lecturer, Investigative Medicine, Imperial College London and Imperial Weight Centre, ICHNT; Dr George Tharakan, Clinical Research Fellow, Investigative Medicine, Imperial College London; Dr Alexander Miras, Clinical Senior Lecturer, Imperial College London; Dr Samantha Scholtz, Consultant Psychiatrist, Imperial Weight Centre, ICHNT; Ms Haya Alessemii, Doctoral Research Student, Investigative Medicine, Imperial College London

Adverse Events

Definitions

Adverse Event (AE): any untoward medical occurrence in a patient or clinical study subject

Serious Adverse Event (SAE): any untoward and unexpected medical occurrence or effect that:

- Results in death
- Is life threatening – refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe

- Requires hospitalisation, or prolongation of existing inpatients' hospitalisation
- Results in persistent or significant disability or incapacity
- Is a congenital anomaly or birth defect

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

Reporting Procedures

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

Non serious AEs

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

Serious AEs

An SAE form should be completed and faxed to the Chief Investigator within 24 hours.

All SAEs should be reported to the Hampstead REC where in the opinion of the Chief Investigator, the event was:

- 'related', i.e. resulted from the research protocol and
- 'unexpected', i.e. an event that would not be an expected occurrence of the protocol

Reports of related and unexpected SAEs should be submitted within 15 days of the Chief Investigator becoming aware of the event, using the NRES SAE form for non-IMP studies. The Chief Investigator must also notify the Sponsor of all SAEs.

Contact details for reporting SAEs

Fax: 020 8383 8320, attention of: Professor Tricia Tan

Please send SAE forms to: Section of Investigative Medicine, Division of Diabetes, Endocrinology and Metabolism, Imperial College London

Tel: 020 8383 3242 (Mon to Fr 09.00-17.00h)

Possible Adverse Events

Patients will be encouraged to report any unusual or unpleasant sensations or new symptoms to the investigator immediately. Any significant adverse effects will lead to withdrawal of the individual and any serious adverse effects will terminate the whole study.

Throughout the study there will be at least one physician available in case of a possible adverse event. Although we do not anticipate any serious adverse effects, patients will be provided with contact details and clear instructions that, if they feel unwell, they should contact us.

It will be made clear to patients that they will be free to withdraw from the study at any time without providing any reason. Patients will be given an adverse event form to fill in and this will be reviewed at each attendance. Any possible adverse event will then be reviewed with the senior clinicians. Any significant adverse effects would lead to withdrawal of the individual and any serious adverse effects would terminate the whole trial. Any serious adverse event suspected to be related to the study would be reported to the ethics committee and the sponsor (Imperial College London).

Regulatory Issues:

Ethics approval

Ethical approvals will be sought by the Chief Investigator from Hampstead REC/HRA. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

Consent

Consent to enter the study must be sought from each participant only after a full explanation has been given, an information leaflet offered and time allowed for consideration. The patient will have at least 24 hours after receipt of the patient information sheet to decide whether to take part. Signed participant consent should be obtained. The right of the participant to refuse to participate without giving reasons must be respected. After the participant has entered the study, the clinician remains free to give alternative treatment to that specified in the protocol at any stage if he/she feels it is in the participant's best interest, but the reasons for doing so should be recorded. In these cases the patients remain within the study for the purposes of follow up and data analysis. All patients are free to withdraw at any time from the protocol treatment without giving reasons and without prejudicing further treatment.

Loss of capacity to consent during the study

If a participant, who has given informed consent, loses capacity to consent during the study, the participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant. Consent for these arrangements in the event of loss of capacity will be explicitly sought in the informed consent form.

Confidentiality

The Chief Investigator will preserve the confidentiality of patients taking part in the study. The confidentiality of NHS records pertaining to study patients will be maintained as set out in the NHS Confidentiality Policy 2014 (http://www.england.nhs.uk/wp-content/uploads/2013/06/conf-policy-1.pdf).

Patient identifiable data will only be accessible to members of the direct care team. Researchers named in this application who are not members of the direct care team will only have accessed to anonymised data. A single computer file with all personal data will be kept on a password protected Imperial College Healthcare NHS Trust (ICHNT) computer. Only data which has been anonymised will be analysed within Imperial College London.

Indemnity

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study.

Funding

Dr Hameed is the recipient of BRC Funding Support for NIHR Academic Trainees. The IWC weight management programme (Tier 3) service will be funded as per previous NHS funding arrangements.

Audits

The study may be subject to inspection and audit by Imperial College London under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the NHS Research Governance Framework for Health and Social Care (2nd edition).

Study Management

The day-to day management of the study will be co-ordinated through Professor Tan and Dr Hameed with assistance from those named ICHNT medically qualified personnel as well as allied health professionals working within the Imperial Weight Centre, ICHNT. A data monitoring committee comprising the trial investigators as well as an external assessor will meet on a quarterly basis. The results of the study will be shared with the participants. The study will be published in peer review scientific journals.

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