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Examining the mechanisms that underlie the biological drive to eat

Submission date	Recruitment status	[X] Prospectively registered
11/06/2025	Recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
13/06/2025	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
12/06/2025	Nutritional, Metabolic, Endocrine	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
This study is looking at how losing weight at different speeds affects your body, metabolism, and overall health. Researchers want to understand whether losing weight quickly or slowly makes a difference in how your body responds.

Who can participate?
The study is open to healthy men and women aged 18 to 55 years who have a Body Mass Index (BMI) between 23 and 40 kg/m².

What does the study involve?
The study lasts between 9 to 11 months and has four phases:
Initial measurements (2 weeks): Researchers will collect information about your body and health before weight loss.
Weight loss phase: You'll be randomly placed into either a fast or slow weight loss group. You'll follow a free, total meal replacement diet until you lose 10% of your body weight. This could take 8–12 weeks (fast group) or 12–16 weeks (slow group).
Weight stability phase (4 weeks): You'll mix meal replacements with your own food to maintain your new weight.
Follow-up phase (6 months): You'll return to your normal diet and come back for a final check-up.
You'll need to attend 7 visits at the University of Leeds and 2 visits to Leeds General Infirmary for MRI scans. These visits include tests like body scans, blood and urine samples, and questionnaires about your lifestyle.

What are the possible benefits and risks of participating?
Benefits include:
-£100 voucher
-Free meal replacement products
-Personalised nutrition advice
-Detailed health information
Possible side effects may include temporary tiredness, mood changes, dizziness, irritability, or digestive issues. Not everyone will be suitable for the diet or procedures, so your medical history will be reviewed first.

Where is the study run from?
University of Leeds (UK)

When is the study starting and how long is it expected to run for?
June 2024 to May 2027

Who is funding the study?
UKRI Future Leaders Fellowship (UK)

Who is the main contact?
For general questions, you can email: embed.study@leeds.ac.uk
The lead researcher is Dr Mark Hopkins (M.Hopkins@leeds.ac.uk).

Study website
https://environment.leeds.ac.uk/faculty/dir-record/research-projects/1993/examining-the-biological-mechanisms-that-underlie-the-drive-to-eat-in-humans

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
350740

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
2024-NCT64

Study information

Scientific Title
Examining the Mechanisms that Underlie the Biological Drive to Eat in Humans: the EMBED Study

Acronym
EMBED

Study objectives
A greater loss of fat-free mass relative to fat mass during weight loss increases motivation to eat following weight loss and weight loss maintenance.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 21/05/2025, London - Harrow Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8154; harrow.rec@hra.nhs.uk), ref: 25/LO/0283

Study design
Open label 2-arm parallel design randomized weight loss trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
University/medical school/dental school

Study type(s)
Quality of life, Treatment, Efficacy

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Overweight and obesity

Interventions
Participants will be stratified by body mass index (23.0-24.9, 25.0-29.9, 30-40 kg/m²) and biological sex (Male/Female). Individuals in each of the 6 stratified groups will then be randomised using block randomisation and an allocation ratio of 1:1 for intervention arms. Randomisation will be undertaken by an investigator who has not had contact with participants before randomisation and is not involved in data collection.

Severe energy restriction (consuming 35% of total daily energy requirement) vs moderate energy restriction (consuming 50% of total daily energy requirement) until 10% weight loss is achieved.

The total duration of intervention and follow-up for all study arms is dependent on the rate at which participants achieve 10% weight loss. The researchers anticipate that the fast weight loss group will achieve 10% weight loss at approximately 8 weeks (with the maximum duration capped at 12 weeks), whereas the slow weight loss group will achieve 10% weight loss at approximately 12 weeks (maximum duration capped at 16 weeks). Therefore, the researchers anticipate the fast group will complete the follow-up in 9 months on average, while the slow group will complete the follow-up in 11 months on average.

Intervention Type
Other

Primary outcome measure
Body composition (body mass, fat mass, and fat-free mass) and the composition of weight loss (percentage fat and fat-free mass loss; fat to fat-free mass ratio) using dual x-ray absorptiometry at baseline, following weight loss, and weight maintenance.

Secondary outcome measures
1. Body composition (body mass, fat mass, fat-free mass) and the composition of weight loss (percentage fat and fat-free mass loss; fat to fat-free mass ratio) using a 4-compartmental body composition at baseline and following weight loss.
2. MRI derived organ and tissue mass (heart, liver, kidney, brain, skeletal muscle, and adipose tissue) at baseline and following weight loss.
3. Fasted and area under the curve (AUC-5 – 210 and iAUC-5 – 210) composite visual analogue subjective appetite scores at baseline, following weight loss, and weight loss maintenance.
3. Energy intake at an ad libitum laboratory test meal and self-reported total daily energy intake at baseline, following weight loss, and weight maintenance.
4. Fasted and area under the curve (AUC-5 – 180 and iAUC-5 – 180) concentrations in glucose, insulin, acyl ghrelin, liver-expressed antimicrobial peptide 2 (LEAP2), glucagon-like peptide-1 (GLP-1), peptide tyrosine tyrosine (PYY), and cholecystokinin (CCK) at baseline, following weight loss, and weight loss maintenance.
5. Total daily energy expenditure, resting metabolic rate, and adaptive thermogenesis as assessed using indirect calorimetry; and free-living physical activity energy expenditure as assessed using accelerometer at baseline, following weight loss, and weight loss maintenance.
6. Device measured sedentary behaviours (time spent sedentary, standing, sitting, lying down), steps per day, and minutes of physical activity per day (MVPA) at baseline, following weight loss, and weight loss maintenance.
7. State motivations to eat (reactive eating, restricted eating, negative emotional eating, positive emotional eating, homeostatic eating, eating for pleasure, and eating for health) as assessed using ecological momentary assessment at baseline, during weight loss, following weight loss, and weight loss maintenance.
8. Trait eating behaviours and motivations to eat (Motivations for Eating Profile, Three Factor Eating Questionnaire, Intuitive Eating Scale, Positive and Negative Emotional Eating Scale, Control of Eating Questionnaire, and Oxford Food and Activity Behaviours Questionnaire) at baseline, following weight loss, and weight loss maintenance.
9. Weekly estimates of free-living body weight measured using remote Bluetooth scales during weight loss.
10. Weekly estimates of total daily energy expenditure calculated from triaxial acceleration data

at baseline, during weight loss, and weight loss maintenance.
11. Weekly estimates of total daily energy intake calculated using the intake-balance approach at baseline, during weight loss, and weight loss maintenance.
12. Fasted leptin, glucagon, thyroid hormones, ghrelin, and myostatin concentrations at baseline, following weight loss and weight maintenance.
13. Upper limb strength as assessed using grip strength and lower limb strength as assessed using sit-to-stand test at baseline, following weight loss, and weight loss maintenance.
14. Blood pressure and resting heart rate at baseline, following weight loss, and weight loss maintenance.
15. Cardiovascular fitness (peak maximal aerobic capacity) at baseline.
16. Subjective (Pittsburgh Sleep Quality index) and device measured (accelerometery) sleep at baseline, following weight loss, and weight loss maintenance.
17. Chronotype as measured using the Ultra Short Munich Chronotype Questionnaire and Morning-Eveningness Questionnaire at baseline, following weight loss, or weight loss maintenance.
18. Eating rate, as measured during an oral processing characterisation procedure and ad libitum test meals, and cumulative energy intake assessed using a standardised laboratory test meal at baseline, following weight loss, and weight loss maintenance.
19. Expected satiety (visual analogue scale), food reward, and food preferences (explicit liking, implicit wanting and relative preference for high-fat, low-fat, sweet and savoury foods; Leeds Food Preference Questionnaire) at baseline, following weight loss and weight maintenance.
20. Variants in genes involved in regulation of appetite, eating behaviour, metabolism, and obesity at baseline (e.g. FTO, GHSR).

Overall study start date
01/06/2024

Completion date
31/05/2027

Eligibility

Key inclusion criteria
1. Males and female participants,
2. Age: 18-55 years,
3. BMI: 23 to 40 kg/m² (verified in the laboratory),
4. Healthy as determined from self-reported medical history or when no relevant medical condition exists,
5. Able to understand and be willing to sign the informed consent form, and to follow all the study procedures and requirements,
6. For female participants: continued use of contraceptive methods during the study or not planning to become pregnant for the duration of the study.

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
Both

Target number of participants
64

Key exclusion criteria
1. BMI ≥ 22.9 kg/m² or < 40.0 kg/m²,
2. Stage 2 hypertension or above (≥160/100 mmHg),
3. Alcohol or drug dependency,
4. Medication or supplement use known to affect appetite, body weight/composition, or metabolism within the past month and/or during the study,
5. Present contraindications for dual energy x-ray absorptiometry (DXA) scans or unwilling to undertake DXA scans,
6. Pregnant or breastfeeding in the previous 3 months, or planning to become pregnant,
7. History of anaphylaxis to food,
8. Food allergy, intolerance, restriction or avoidance of any of the study foods
9. Participants with vegan or gluten-free dietary needs.
10. Smokers (including nicotine containing vapes) and those who have recently ceased smoking (<6 months),
11. Volunteers having lost significant amount of weight in the previous 3 months (±3kg)
12. Participants who do night or late shift work (ending later than 11pm) on a permanent basis,
13. Persons who do not have access to mobile phone and the internet (this is necessary for data collection during the study).
14. Self-reported or clinically diagnosed eating disorders, including binge eating (or a history of),
15. Diagnosed anaemia,
16. Hepatic or renal impairments (contraindications for following a very low energy/total meal replacement diet),
17. Diagnosed diabetes mellitus,
18. Hyperthyroidism or hypothyroidism,
19. Abnormal gastro-intestinal function or structure such as malformation, angiodysplasia, active peptic ulcer,
20. Active inflammatory bowel disease, celiac disease, chronic pancreatitis or other disorder potentially causing malabsorption,
21. History of gastro-intestinal surgery with permanent effect (i.e. surgical treatment of obesity),
22. Medical history of CVD (e.g. current angina; myocardial infarction or stroke within the past 6 months; heart failure; symptomatic peripheral vascular disease),
23. Significant liver disease, e.g. cirrhosis (fatty liver disease allowed),
24. Pre-existing injuries or medical conditions that could be aggravated by physical activity or exercise,
25. Malignancy which is currently active or in remission for less than five years after last treatment (local basal and squamous cell skin cancer allowed),
26. Psychiatric illness (e.g. clinical depression, bipolar disorders).
27. Individuals who perform structured exercise bouts for 30 minutes or more four or more days per week or have significantly changed their physical activity patterns in the past three months.
28. High-risk occupation for drowsy driving (e.g. commercial truck driver or airline pilot),
29. Diagnosis of a sleep disorder other than obstructive sleep apnoea (e.g. periodic limb

movement disorder),
30. Predominantly central sleep apnoea or requiring oxygen or bi-level positive airway pressure or advanced positive airway pressure modalities during periods of sleep,
31. Co-existing hypoventilation (e.g. documented hypercarbia).

Date of first enrolment
13/06/2025

Date of final enrolment
30/06/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Leeds
School of Food Science and Nutrition
Leeds
United Kingdom
LS2 9JT

Study participating centre
Leeds General Infirmary
Great George Street
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United Kingdom
LS1 3EX

Sponsor information

Organisation
University of Leeds

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Sponsor type
University/education

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ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Government

Funder Name
UK Research and Innovation

Alternative Name(s)
UKRI

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. The study design, protocol and methods will be published as a protocol paper in a relevant peer-review scientific journal.
2. After completion of the study, regardless of whether the findings are positive, negative or inconclusive, study findings will be submitted for publication in an international peer-reviewed scientific journal.
3. Study outcomes will also be submitted for dissemination at scientific conferences as either poster or oral abstracts.
4. Study outcomes may also be reported in non-scientific lay publications and relevant media (including social media).

Intention to publish date

Individual participant data (IPD) sharing plan
Participants who have consented for their de-identified research data to be shared for future ethically approved research and teaching may be available upon request from the Principal Investigator Dr Mark Hopkins (M.Hopkins@leeds.ac.uk). The research team will adhere to the University of Leeds data protection policies (https://dataprotection.leeds.ac.uk/), and will ensure appropriate data sharing or material contracts be in place prior to any transfer of data or material (including blood and urine samples).

IPD sharing plan summary
Available on request