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GendAge weight loss study: sex hormones as regulators of the age- and sex-dependent benefits of caloric restriction

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02/04/2026

Recruitment status
Recruiting

Registration date
10/04/2026

Overall study status
Ongoing

Last Edited
07/04/2026

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Almost two-thirds of people in the UK are living with excess weight, which raises the risk of serious health conditions including type 2 diabetes, heart disease, and some cancers. Cutting calories is one of the most effective ways to lose weight and body fat, but surprisingly little is known about how age and sex affect the way people respond to dieting.
Previous research suggests that younger women lose less weight and less body fat than younger men when following the same diet. Interestingly, this difference seems to disappear in older adults. The research team think the hormone oestrogen - which declines around the time of the menopause - may be the reason for this. This study aims to gain an understanding of why this happens to help develop better, more personalised dietary advice for weight loss that works for everyone, regardless of age or sex.

Who can participate?
Adults aged 18 to 65 years who are overweight or obese (BMI 27–45 kg/m²) and in good general health can take part. The study recruits both men and women across two age groups: younger adults aged 40 years or under, and older adults aged 55–65 years. Older women must be postmenopausal (defined as having had no menstrual period for at least 12 months). The older women's group includes two sub-groups: those who are not taking hormone replacement therapy (HRT), and those who have been taking oestrogen-based HRT continuously for at least 24 months.

What does the study involve?
For the first 7 days of the study, participants will be asked to record a food diary to assess their normal food intake. From day 8 of the study, they will be provided with all the food and drink that participants should consume as part of the study. Participants will be asked to only eat the food and drink the drinks that are provided. The study will last 53 days in total for each participant. Participants will be asked to attend the Rowett Institute on four occasions for test day measurements and on a further 17 occasions to collect food and have body weight measured.

Dietetic staff will prepare all the meals to be consumed during the study. The study meals will be designed to meet the participants individual energy requirements.
• Phase 1: 3-day Maintenance Diet (fixed macronutrient composition of 15% protein, 30% fat and 55% CHO), provided at 1.3 x RMR (130%) to keep body weight stable.
• Phase 2: 6-week Calorie Restricted Weight Loss Diet (30% protein, 35% fat and 35% CHO), provided at 80% RMR. After 2 weeks and 4 weeks on the diet there will be a 100-calorie reduction in the energy per day of the meals provided.
For the food to be as fresh as possible the study meals are to be collected on Mondays, Wednesdays & Fridays. Body weight will be measured on these mornings to follow their progress and provide them with a cooked breakfast. The menus are common dishes i.e., Cheese & Crumpets, Pasta Bolognaise, Chicken Curry, Sandwiches and Puddings. Only decaffeinated drinks (tea, coffee etc) are to be consumed during the study. Participants will be provided with a selection of these. No alcohol will be provided or allowed during the study.

What measurements and tests will be done?
All measurement visits take place at the Rowett Institute in Aberdeen after an overnight fast (no food or drink from 10pm the night before). Breakfast is provided at the end of each visit.
*Body weight and height are measured at the screening visit and at each food collection visit throughout the study (three times a week). Participants will be asked to change into a dressing gown for these measurements.
*Resting Metabolic Rate (RMR) is a measure of how much energy the body burns at complete rest — just to keep basic functions like breathing and circulation going. Participants lie on a bed for about 30 minutes with their head under a clear plastic hood while their breathing is analysed. This is called ventilated hood indirect calorimetry. It is completely painless and non-invasive.
*Body composition — Dual Energy X-ray Absorptiometry (DXA) scan is a very low-dose X-ray (less than a tenth of a standard chest X-ray) that measures how much of their body is fat, muscle, and bone, and where the fat is distributed around the body. They lie still on a flat bed for about 15 minutes while a scanner passes over them.
*Body composition — BodPod measures body fat and lean mass by air displacement. Participants sit inside a small, egg-shaped chamber for about 5 minutes wearing a swimming costume. It is quick, comfortable, and involves no radiation.
*Blood samples (venepuncture) are collected from a vein in their arm on three occasions during the study (Days 8, 32, and 53), with 12ml taken each time — about one large tablespoon. The blood is tested for fats in the blood (plasma non-esterified fatty acids, or NEFAs), metabolic hormones (leptin, adiponectin, and cortisol), and sex hormones (oestrogens, progesterone, and androgens). These are measured using standard laboratory techniques including ELISA and liquid chromatography-mass spectrometry (LC-MS).
*Fingerprick blood test is a small drop of blood collected from the fingertip using a lancet at the same test day visits. It is used to measure blood glucose (blood sugar) and ketone levels using a disposable testing strip. Ketones are a sign that their body is breaking down fat for energy.
*Continuous Glucose Monitoring (CGM) — FreeStyle Libre sensor is a small, water-resistant sensor applied to the back of the upper arm. A thin, flexible sterile fibre sits just under the skin and records blood sugar levels continuously throughout the study (Days 1–53). The sensor is held in place with an adhesive pad and is worn for up to 14 days at a time, then replaced. Data is downloaded using a smartphone app.
*Physical activity — ActiGraph accelerometer is a watch-like device worn on the wrist throughout the study (Days 1–52) to record daily movement and activity levels automatically.
*Fat biopsy (fine needle aspiration) is a small sample of fat tissue (about 0.4g — roughly the size of a small pea) taken from just under the skin of the abdomen, near the belly button. A local anaesthetic injection is given first to numb the area, and the sample is collected using a needle and syringe by trained research staff. There may be minor bruising or a small mark afterwards. This is done on Days 8 and 53 only.

*Total Body Water (TBW) — deuterium dilution involves drinking a glass of water containing a small, safe dose of deuterium (a naturally occurring, non-radioactive form of hydrogen). Urine samples collected before and 4–5 hours after the drink are analysed to calculate the total amount of water in the body, which is used to work out the body composition. This is done on Day 53 only.
*Energy expenditure — Doubly Labelled Water (DLW) is a similar technique to TBW but used to measure how many calories the body burns over the 6-week diet period. Participants drink a small dose of water containing two safe, stable isotopes (deuterium and oxygen-18) on Days 11, 25, and 39. Urine samples are then collected every other day to track how the isotopes leave the body, which allows the research team to calculate their total daily energy expenditure over time. This is one of the most accurate methods available for measuring energy use in free-living people. Urine samples are collected throughout the study to support the DLW and TBW measurements described above. Sample collection cups and instructions are provided.
*Weighed food intake records are completed throughout the study using a diet booklet and food scales provided at the screening visit, so the team can track exactly how much of each meal they consumed.

What are the possible benefits and risks of participating?
Most participants can expect to lose weight and body fat during the study, which may improve blood sugar control and other aspects of metabolic health. They will also receive detailed, gold-standard measurements of their body composition, resting metabolic rate, and hormone levels — information that is not routinely available outside of a research setting — along with a personalised summary of their results.

The main risks are minor. Blood tests may cause brief discomfort or bruising at the needle site. The small fat sample taken from the abdomen is collected by trained staff using a fine needle and may cause temporary discomfort or tenderness. The calorie-restricted diet is individually tailored and supervised throughout, but they may notice some hunger or tiredness, particularly in the early weeks. All procedures are carried out by trained research staff following strict safety guidelines.

Where is the study run from?
The study is run from the Human Studies Intervention Unit (HISU) at the Rowett Institute, University of Aberdeen, Aberdeen, Scotland, UK.

When is the study starting and how long is it expected to run for?
July 2025 to March 2028.

Who is funding the study?
The Medical Research Council (MRC), UK.

Who is the main contact?
Professor Alexandra Johnstone, alex.johnstone@abdn.ac.uk

Contact information

Type(s)
Principal investigator, Scientific, Public

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT07065643

Integrated Research Application System (IRAS)
354348

Protocol number
2-034-25

Study information

Scientific Title
Gender- and age-dependent effects of caloric restriction on body composition, glucose homeostasis, energy balance and adipose metabolism in overweight and obese adults: a controlled dietary intervention study comparing younger and older men and women, with an embedded sub-study examining the role of oestrogen hormone replacement therapy (HRT) in postmenopausal women (GendAge Study)

Acronym
GendAge

Study objectives
Objective 1: To determine how age and sex influence the effects of CR on body composition, glucose homeostasis, energy balance, and adipose metabolism in humans. This is achieved by a controlled dietary intervention study in younger and older men and women, to study the effect of CR on body mass and composition and adipose tissue markers.
Objective 2: To establish the role of oestrogen in modulating the CR response in post-menopausal women. This is achieved by a controlled dietary intervention study which includes a cohort of menopausal women who are not taking HRT and a group who are, participating in a controlled dietary CR study.

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 25/06/2025, South Central - Berkshire B Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +442071048276; berkshireb.rec@hra.nhs.uk), ref: 25/SC/0193

Primary study design
Interventional

Allocation
Non-randomized controlled trial

Masking
Open (masking not used)

Control
Active

Assignment
Factorial

Purpose
Basic science

Study type(s)

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

Interventions
Run-in period of 10 days (7 day ad libitum food diary at home and 3 days maintenance diet provided to energy balance). Followed by a weight loss diet for 6 weeks (42days), as a nonrandomised allocation. The study lasts 53 days in total for each participant comprising twenty-two study visits to the Human Intervention Studies Unit (HISU); a screening visit during which potential volunteers will be asked to fill in a health questionnaire at the screening visit to assess their suitability for the study. This is followed by four test day visits (representing pre- and post- dietary phases) and seventeen occasions to collect food and have body weight measured.

All food provided to free-living participants is prepared at the HISU by dietetic staff. The study meals are adjusted (scaled) to individual energy requirements based on measured basal energy requirements (RMR – Resting Metabolic Rate).
• Phase 1: 3-day maintenance diet (MT, fixed macronutrient composition of 15% protein, 30% fat and 55% CHO), fed to energy requirements (1.3 X RMR)
• Phase 2: 6-week calorie restricted weight loss diet (CR, fixed macronutrient composition as 30% protein, 35% fat and 35% CHO) fed to energy requirements (0.8 X RMR), with stepwise reduction of 100kcal/d at week 3 and 5 (Days 15 and 29)

Intervention Type
Other

Primary outcome(s)

1. Change in body fat mass (kg) measured using four-compartment (4C) model at baseline (day 8) to end of intervention (day 53)

Key secondary outcome(s))

1. Change in total energy expenditure (kcal/day) measured using doubly labelled water (DLW) stable isotope method with urine sample collection at baseline (day 8) and end of intervention (day 53)

2. Change in resting metabolic rate (kcal/day) measured using ventilated hood indirect calorimetry at baseline (day 8) and end of intervention (day 53)

3. Change in body mass expressed as weight in kilograms (kg) measured using digital scale at baseline (day 1 and day 8) and end of intervention (day 53); additionally measured three times weekly throughout the intervention

4. Change in bone mineral content (g) measured using dual-energy X-ray absorptiometry (DXA) at baseline (day 8) and end of intervention (day 53)

5. Change in total body water in litres (l) measured using deuterium dilution with urine sample collection at baseline (day 11) and end of intervention (day 53)

6. Change in total body density expressed in litres (l) measured using air displacement plethysmography (BodPod) at baseline (day 8) and end of intervention (day 53)

7. Change in fasted serum non-esterified fatty acid (NEFA) concentration measured using KONE analyser at baseline (day 8), midpoint of calorie-restricted diet (day 32), and end of intervention (day 53)

8. Change in fasted blood caloric restriction-related hormone concentrations (leptin, adiponectin, cortisol) measured using ELISA at baseline (day 8), midpoint of calorie-restricted diet (day 32), and end of intervention (day 53)

9. Change in fasted blood sex hormone concentrations (oestrogens, progesterone, androgens) measured using high-sensitivity liquid chromatography-mass spectrometry (LC-MS) at From day 8 (start of the maintenance diet) to end of the intervention (day 53); also measured at midpoint of calorie restricted diet (day 32)

10. Change in Body Mass Index (BMI) expressed as kg/m^2 measured using mathematical formula based on body weight and height at baseline (day 1) and end of intervention (day 53); additionally measured three times weekly throughout the intervention

11. Change in adipose tissue adipocyte size measured using fine needle aspiration of abdominal subcutaneous fat biopsy with histomorphometry at baseline (day 8) and end of intervention (day 53)

12. Change in adipose tissue hormone-sensitive lipase (HSL) phosphorylation measured using fine needle aspiration of abdominal subcutaneous fat biopsy with immunoblotting at baseline (day 8) and end of intervention (day 53)

13. Change in glycaemic control assessed by interstitial glucose concentration measured using continuous glucose monitoring (CGM; FreeStyle Libre) at throughout the intervention (days 1–53)

14. Change in fasting capillary blood glucose concentration (mmol/L) measured using finger-prick blood sampling at baseline (day 8) and end of intervention (day 53); also measured at midpoint of calorie restricted diet (day 32)

15. Change in fasting capillary blood ketone concentration (mmol/L) measured using finger-prick blood sampling at baseline (day 8) and end of intervention (day 53); also measured at midpoint of calorie restricted diet (day 32)

16. Change in fasting concentration of Glucose Ketone Index (GKI) measured using capillary blood glucose and ketone values at baseline (day 8) and end of intervention (day 53); also measured at midpoint of calorie restricted diet (day 32)

17. Change in moderate-to-vigorous physical activity (MVPA; minutes/day) measured using accelerometry (ActiGraph wearable device) at throughout the intervention (days 1–53)

18. Change in food intake measured using weighted intake record at during the ad libitum period (days 1–7) and throughout the study diet period (days 8–52)

Completion date
31/03/2028

Eligibility

Key inclusion criteria
Adults (aged over 18years) who are healthy but overweight/obese (BMI 27-45kg/m2):
1. 15 women (age 40 or less years)
2. 15 men (age 40 or less years)
3. 15 women (age 55-65 years) in menopause*; not taking Hormone Replacement Therapy (HRT)
4. 15 men (age 55-65 years)
5. 15 women (age 55-65 years) in menopause; taking HRT**

*menopause definition is no menstrual period for 12 months
**HRT inclusion criteria - women will have continuously taken oestrogen HRT for 24 months

Healthy volunteers allowed
Yes

Age group
Mixed

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Total final enrolment

0

Key exclusion criteria
Medication exclusion criteria, current use:
1. Weight loss medication (e.g. GLP agonists), β-blockers, antihistamines, antipsychotics, benzodiazepines, barbiturates, melatonin, Ritalin, modafinil, soporifics, hypnotics, antiepileptic drugs, diabetes medication (e.g. metformin or insulin).

Self-reported medical exclusion criteria:
1. Females who are planning to be pregnant, are pregnant or are breastfeeding
2. Coeliac disease or gluten intolerance or food allergy
3. Diagnosed T1 or T2 diabetes
4. Suffering from a psychiatric disorder or any type of substance abuse

Other exclusion criteria:
1. Vegetarian or vegan diet
2. Following a weight loss programme (that may be affecting lifestyle, physical activity & diet) or undergone gastric band/reduction surgery; including GLP agonist (e.g. Semaglutide injection, Ozempic®)
3. Currently participating in another research study
4. Unsuitable veins for blood sampling
5. Unable to fluently speak, read and understand English
6. Unable to comply to an alcohol-free diet for 6 weeks
7. Unable to give fully informed consent

Date of first enrolment
09/07/2025

Date of final enrolment
04/02/2028

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
Human Intervention Studies Unit
Rowett Institute, School Of Medicine, Medical Sciences and Nutrition, University of Aberdeen, Foresterhill
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Sponsor information

Organisation
University of Aberdeen

ROR
https://ror.org/016476m91

Funder(s)

Funder type

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available