ISRCTN36628439 https://doi.org/10.1186/ISRCTN36628439

Pancreas lipotoxicity in type 2 diabetes: Edinburgh Diabetes Remission Study (EDRS)

Submission date
13/01/2026

Recruitment status
Recruiting

Registration date
19/01/2026

Overall study status
Ongoing

Last Edited
16/01/2026

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
This study looks at how excess fat in the pancreas may cause type 2 diabetes and whether losing weight can reverse this process. Previous research shows that weight loss can lead to diabetes remission, but the reasons why are not fully understood. We aim to find out how the liver makes fat (de novo lipogenesis) and how fat moves in the blood, and how these affect the pancreas and insulin production. The study will compare four groups of participants (non-diabetic, pre-diabetic, short-duration type 2 diabetes, and long-duration type 2 diabetes) to understand the sequence of changes that lead to diabetes remission.

Who can participate?
Adults aged 45–79 years with a BMI between 30 and 45 kg/m². We will include four groups:
1. People without diabetes
2. People with pre-diabetes
3. People with type 2 diabetes for less than 6 years
4. People with type 2 diabetes for more than 10 years
Participants must be able to give informed consent, communicate in English, and be willing to follow the study diet and attend follow-up visits. Women must be post-menopausal.

What does the study involve?
All participants will follow a low-calorie diet (around 800 kcal per day) for 8–12 weeks, then receive support to maintain weight loss for up to 12 months. We will carry out blood tests, MRI scans of the pancreas and liver, and other assessments to understand changes in fat and metabolism. Some participants will also have a small fat biopsy.

What are the possible benefits and risks of participating?
Benefits may include weight loss and better blood sugar control, and in some cases remission of type 2 diabetes. Risks include hunger, changes in blood pressure or blood sugar when stopping medication, and discomfort during tests. Safety will be monitored throughout the study.

Where is the study run from?
Clinical Research Facility, Royal Infirmary of Edinburgh, Scotland (UK)

When is the study starting and how long is it expected to run for?
The study will start in January 2026 and is expected to run until December 2028.

Who is funding the study?
The study is funded by the Medical Research Council and sponsored by ACCORD (Academic and Clinical Central Office for Research and Development) (UK)

Who is the main contact?
Study Team, edrs@ed.ac.uk

Contact information

Type(s)
Public

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Scientific, Principal investigator

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Additional identifiers

Study information

Scientific Title
Mechanisms mediating reversible lipotoxicity of the pancreas in obesity-induced type 2 diabetes: Edinburgh Diabetes Remission Study (EDRS)

Acronym
EDRS

Study objectives
To investigate how excess fat accumulation in the pancreas contributes to the pathophysiology of type 2 diabetes and how structured weight loss can reverse this process. The study will compare metabolic responses across four groups: non-diabetic, pre-diabetic, short-duration T2D (<6 years), and long-duration T2D (>10 years). Specifically, the study aims to:
1. Quantify hepatic de novo lipogenesis (DNL) and lipoprotein metabolism before and after weight loss.
2. Assess changes in intrapancreatic fat, beta-cell function, and pancreas morphology.
3. Determine whether changes in DNL and intra-organ fat are associated with diabetes remission.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 03/07/2025, North West – Greater Manchester West Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; -; gmwest.rec@hra.nhs.uk), ref: 23/NW/0368

Primary study design
Interventional

Allocation
Non-randomized controlled trial

Masking
Open (masking not used)

Control
Uncontrolled

Assignment
Parallel

Purpose
Treatment

Study type(s)

Health condition(s) or problem(s) studied
Type 2 diabetes

Interventions
All participants will follow a Total Diet Replacement (TDR) program providing ~800 kcal/day using commercially available soups and shakes for 8–12 weeks, followed by a 2-week food reintroduction phase and structured weight maintenance support for up to 6–12 months, supervised by a research dietitian. The intervention includes dietary counseling, monitoring, and metabolic assessments (blood tests, MRI scans, mixed meal tests, and adipose tissue biopsies in a subgroup).

Intervention Type
Behavioural

Primary outcome(s)
1. Body weight and T2D remission measured using using calibrated scales in kilograms at 6 months and 12 months

2. Hepatic de novo lipogenesis (DNL) measured using stable isotope tracer methodology at baseline, 6 months, 12 months

Key secondary outcome(s))
1. Intrapancreatic and hepatic fat measured using MRI at baseline, 6 months, 12 months

2. Change in beta-cell function measured using C-peptide modeling during a standard mixed meal test at baseline, 6 months, 12 months

3. Circulating lipoproteins and lipids measured using ultracentrifugation and mass spectrometry techniques at baseline, 6 months, 12 months

4. Pancreas morphology and inflammation measured using MRI at baseline, 6 months, 12 months

5. Adipose tissue biology measured using MRI to assess fat saturation, and fat biopsies to evaluate molecular changes in adipose tissue biology at baseline and 6 months post-intervention

6. Circulating markers measured using standard kits (adipokines, inflammatory markers, exosomes) at baseline and 6 months and 12 months post-intervention

7. Blood pressure and lipid profile measured using automated sphygmomanometer (resting systolic/diastolic blood pressure). Blood samples taken for total cholesterol, LDLC, HDLC, triglycerides (standard clinical assays) at baseline, 6 months, and 12 months

Completion date
31/12/2028

Eligibility

Key inclusion criteria
1. Obese (BMI: 30-45 kg/m²) who have had T2D for less than 6 years or longer than 10 years, and are on treatment with diet alone or diet plus oral medication
2. Obese (BMI: 30-45 kg/m²) who are at the pre-diabetes stage, defined as fasting blood glucose 5.6-6.9 mmol/L
3. Obese (BMI: 30-45 kg/m²) who are non-diabetic (control group)
4. Age between 45 and 79 years inclusive

5. Men and women, however, post-menopausal women only (to exclude sex hormone effects on lipid metabolism)
6. Good communication in English (able to give informed consent and follow dietary advice)
7. Willing and able to adhere to the study protocol, including dietary intervention and scheduled follow-up visits

Healthy volunteers allowed
Yes

Age group
Mixed

Lower age limit
45 years

Upper age limit
79 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Insulin therapy
2. HbA1c >12% (108 mmol/mol)
3. Weight loss >5 kg in the last 6 months
4. Recent MI (within 6 months)
5. Known cancer in the last 5 years
6. First-degree relatives of people with T2D (control group)
7. History of gestational diabetes
8. MRI contraindications (metal implants, claustrophobia)
9. Alcohol >14 units/week
10. Advanced kidney or liver disease
11. Use of steroids or antipsychotics
12. Participation in another clinical trial
13. Life expectancy <1 year
14. Allergy to local anaesthetic (for biopsy subgroup)
15. Any disorder that may jeopardise safety or compliance

Date of first enrolment
12/01/2026

Date of final enrolment
01/06/2028

Locations

Countries of recruitment

United Kingdom

Scotland

Study participating centre
Clinical Research Facility, Royal Infirmary of Edinburgh
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Sponsor information

Organisation
Accord (United Kingdom)

ROR
https://ror.org/01x6s1m65

Organisation
NHS Lothian

ROR
https://ror.org/03q82t418

Funder(s)

Funder type

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research 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