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# Ketamine for the treatment of depression with anorexia nervosa

| Submission date | Recruitment status | [X] Prospectively registered |
|---|---|---|
| 17/06/2025 | Recruiting | [ ] Protocol |
| **Registration date** | **Overall study status** | [ ] Statistical analysis plan |
| 17/06/2025 | Ongoing | [ ] Results |
| **Last Edited** | **Condition category** | [ ] Individual participant data |
| 16/07/2025 | Mental and Behavioural Disorders | [X] Record updated in last year |

**Plain English summary of protocol**

Background and study aims

Anorexia nervosa is a serious eating disorder that can lead to dangerously low body weight and has one of the highest death rates of any mental health condition. Around one in three people with anorexia develop a long-lasting form of the illness, often alongside depression. Unfortunately, traditional antidepressants don't work well for people with both anorexia and depression. This study, called the EDEN project, is exploring whether a medication called ketamine—already used in the UK to treat depression—might help people with both conditions feel better and regain the motivation to recover.

Who can participate?

You may be able to take part if you:

-Are aged 18 or over

-Have had anorexia nervosa for at least 3 years

-Are currently experiencing depression that hasn't improved with treatment

-Weigh at least 40kg and have a BMI of 14 or higher

-Are willing and able to attend all study sessions in person and online

What does the study involve? (for participants)

The study includes 13 sessions over 6 months:

-1 screening session (in person) to check if you're eligible

-1 online session with questionnaires and computer tasks

-8 in-person sessions where you'll take either ketamine or a placebo (a dummy pill), chosen at random

-1 in-person follow-up session with more questionnaires, tasks, and a blood test

-2 online follow-up sessions with questionnaires and tasks

Each in-person dosing session lasts about 3 to 4 hours and takes place in the morning.

What are the possible benefits and risks of participating?

The main benefit is the potential for relief from depression, which may help improve motivation and hope for recovery from anorexia. However, as this is a research study, there is no guarantee

of benefit. There may also be side effects from ketamine, and some people may find the time commitment or procedures challenging. The study team will monitor your health closely throughout.

Where is the study run from?
King's College London (UK)

When is the study starting and how long is it expected to run for?
The study starts on 1st August 2025 and will be recruiting participants until 1st April 2027. Each person's involvement will last about 6 months.

Who is funding the study?
The study is funded by the Medical Research Council through its Developmental Pathway Funding Scheme (UK)

Who is the main contact?
eden@kcl.ac.uk

# Contact information

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Scientific, Principal investigator

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Public

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# Additional identifiers

### Integrated Research Application System (IRAS)
340838

### Central Portfolio Management System (CPMS)
67666

### Protocol serial number
MRC REF: MR/Y019504/1

# Study information

### Scientific Title
A randomised-controlled feasibility study of ketamine for the treatment of depression with anorexia nervosa

### Acronym
EDEN

### Study objectives
To assess the feasibility and acceptability of oral ketamine as a treatment for individuals with anorexia nervosa and severe depression which hasn't responded to one or more treatments.

### Ethics approval required
Ethics approval required

### Ethics approval(s)
approved 12/06/2025, London Riverside Research Ethics Committee (2 Redman Place, London, E20 1JQ, United Kingdom; +44 207 104 8150; riverside.rec@hra.nhs.uk), ref: 25/LO/0279

### Study design
Single centre double-blinded (participant researchers assessors and analyst) randomized placebo-controlled feasibility study

### Primary study design
Interventional

### Study type(s)
Other, Treatment, Safety, Efficacy

### Health condition(s) or problem(s) studied
Treatment of depressive symptoms in people with anorexia nervosa (duration of at least 3 years) and comorbid severe depression that has not responded to at least one treatment.

### Interventions
60 participants will be randomised (1:1) to receive four weeks of oral ketamine 60-180mg (2 x weekly) or placebo. Trial participation will consist of three phases: i) screening, ii) dosing sessions (comprising eight in-person dosing sessions), iii) follow-up phase (3 months and 6 months after baseline).

During the dosing phase, participants will be randomised, based on a computer-generated randomisation schedule, to either oral ketamine (KET-IR; Keticap® Immediate Release, manufactured by Neurocentrx Ltd.) or placebo, twice weekly for a total of four weeks. KET-IR is a novel formulation of immediate-release ketamine hydrochloride within a HPMC capsule. The medication is delivered as 60mg capsules, therefore participants in this trial will ingest one, two or three capsules (depending on their dosage) which will be delivered in a “double dummy” approach whereby participants will always ingest three capsules. The placebo will be visually identical.

On their first in-person dosing session, all participants will receive one capsule of IMP (equivalent to 60mg KET-IR) or placebo. Participants will self-administer the dose under supervision. Following adequate safety and tolerability, the dose will be increased to two capsules of IMP (equivalent to 120mg KET-IR) or placebo, at the second dosing session. If safety and tolerability is not met, the dose may remain at one capsule. The dose may be increased to a maximum of 180mg (3 capsules) following adequate safety and tolerability. A “double-dummy” approach will be taken whereby participants will always ingest three visually identical capsules. If allocated to the KET-IR arm, on the first dose, they will ingest one KET-IR capsule and two placebo capsules, and if the dose is increased, they will ingest two KET-IR capsules and one placebo, and so on. The placebo group will always ingest three placebo capsules.

## Intervention Type
Drug

## Phase
Phase II

## Drug/device/biological/vaccine name(s)
KET-IR a novel formulation of immediate-release ketamine hydrochloride within a HPMC capsule, and a visually-identical placebo capsule.

## Primary outcome(s)
Study feasibility:
1. Recruitment (expressed as total number recruited as percentage of the required sample size), at end of study
2. Lost to follow up rate, expressed as percentage who withdraw from data collection out of number randomised, by study arm, at end of study; and 28-days [primary], 3 months and 6 months, [secondary]
3. Assessment response rate (expressed as percentage of questionnaires fully completed, by study arm), at end of study; and 28-days [primary], 3 months and 6 months, [secondary]
4. Proportion who remained on the intervention (Ketamine or Placebo) (expressed as a percentage, by study arm), at end of study; and 28-days [primary], 3 months and 6 months, [secondary]
5. Adherence to treatment (expressed as a proportion of participants who take 60% of total prescribed dose; by study arm), at end of study; and 28-days [primary], 3 months and 6 months, [secondary]

## Key secondary outcome(s))
Study acceptability
1. Likert scales of acceptability (measured as a final value; expressed as a mean±standard

deviation, per study arm) at end of study
2. Perceived acceptability of interventional medicinal product and study design (from qualitative interviews, expressed as theme/subtheme, per study arm) at end of study

Exploratory preliminary assessment (descriptive only; no hypothesis testing will be carried out) of clinical measures:
3. Change in depression scores (MADRS change; measured as a change from baseline; expressed as a mean±standard deviation, per study arm) at 28 days [primary], 3 months and 6 months [secondary]
4. Change in eating disorder psychopathology (EDE-Q; measured as a change from baseline; expressed as a mean±standard deviation, per study arm) at 28 days [primary], 3 months and 6 months [secondary]
5. Change in quality of life (EQ-5D-5L; measured as a change from baseline; expressed as a mean±standard deviation, per study arm) at 28 days [primary], 3 months and 6 months [secondary]

Exploratory assessment (descriptive only; no hypothesis testing will be carried out) of safety and tolerability, at end of study
6. Incidence of adverse events (measured as a final value; expressed as a percentage who experienced in each arm, split by whether or not an SAE, relatedness to study drug and body system), at end of study
7. Incidence of side effects (measured as a final value per side effect category; expressed as a total sum, per study arm), at end of study

### Completion date
01/05/2028

# Eligibility

### Key inclusion criteria
1. Signed informed consent form
2. SE-AN as defined by i) a primary diagnosis of AN as specified in the International Classification of Diseases (ICD)-11 and ii) at least 3 years history of AN (since diagnosis), based on medical records, clinical assessment, BMI, MINI at screening
3. Severe depression with a failed treatment attempt, as defined by i) severe depression as specified in the ICD-11 and ii) non-response or failure to achieve remission after one or more treatments recommended by NICE for severe depression.
4. Aged 18 years old or above at screening
5. Capacity to consent
6. Screening Body Mass Index (BMI) ≥14kg/m²
7. Weight above 40kg
8. At low risk for suicidality as assessed by the research team
9. Medically stable as determined by screening: clinical interview, clinical laboratory values, vital signs, ECG and medical history.
10. Agreement to follow the contraception requirements of the study.
11. Registered with a General Practitioner (GP) in the UK, and agreement for the team to maintain contact with the GP and/or specialist ED team for the duration of the study.

### Participant type(s)
Patient, Service user

## Healthy volunteers allowed
No

## Age group
Adult

## Lower age limit
18 years

## Upper age limit
100 years

## Sex
All

## Key exclusion criteria
1. Cardiovascular conditions, including stroke, myocardial infarction or clinically significant arrythmia within 1 year of screening, uncontrolled hypertension, bradycardia, abnormalities on ECG (e.g., elongated QT interval corrected by Fridericia), based on an assessment of medical history and ECG and vital signs at screening.
2. Clinically significant abnormalities in laboratory tests at screening, including full blood count, total bilirubin, creatinine, glomerular filtration rate (GFR), alanine aminotransferase (ALT) and aspartate aminotransferase (AST).
3. Any other clinically significant physical illness or contraindication (e.g. but not limited to, renal, hepatic, pulmonary, cardiovascular, gastrointestinal) that the investigator deems may interrupt the participation in the study or pose a health risk for the participant if they were to take part in the study.
4. Relevant neurological comorbidity, in particular dementia; lifetime seizures; epilepsy; increased intracranial pressure.
5. Recent heart or head surgery.
6. Significant weight loss (≥2kg) in the month before screening.
7. Weight loss of over 1kg per week between screening and baseline.
8. (For females of childbearing potential) Unwillingness to follow the contraceptive requirements of the study, and to take pregnancy tests throughout the study.
9. (For females) Current breastfeeding.
10. Recent illicit drug use as determined by urine drug screening at the screening visit.
11. Hypersensitivity to the study drug (KET-IR or placebo) or any of its excipients
12. Dosage in any investigational drug or device study within three months of screening or any other study that may constitute a contraindication for taking ketamine.
13. Blood or needle phobia.
14. No email access.
15. Previous or current alcohol or substance use disorder as assessed by medical history, the MINI, ASSIST and urine toxicology at screening.
16. Previous or current psychotic disorder or bipolar disorder, as assessed by a review of medical history and the MINI.
17. Previous or current schizoid, schizotypal, paranoid, histrionic, antisocial or narcissistic personality disorder, as based on medical history, the Standardised Assessment of Personality (SAPAS), the Personality Assessment Questionnaire for DSM-11 (PSQ-11) and clinical judgment
18. Current panic disorder or panic attacks/episodes within the past year, as determined by the MINI and clinical judgment
19. Significant suicide risk at screening, as assessed by suicidal behaviours during the previous

year as assessed through clinical interview and medical records; suicidal ideation or significant suicidal risk expressed in the C-SSRS or during clinical interview.
20. Self-reported exposure to ketamine therapeutically or recreationally within the past six months.
21. Use of contraindicated medications as listed in the protocol.

### Date of first enrolment
01/08/2025

### Date of final enrolment
01/10/2027

## Locations

### Countries of recruitment
United Kingdom

England

### Study participating centre
**King's College London**
Institute of Psychiatry, Psychology & Neuroscience
16 De Crespigny Park
London
United Kingdom
SE5 8AB

## Sponsor information

### Organisation
King's College London

### ROR
https://ror.org/0220mzb33

### Organisation
South London and Maudsley NHS Foundation Trust

### ROR
https://ror.org/015803449

# Funder(s)

### Funder type
Research council

### 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
The data-sharing plans for the current study are unknown and will be made available at a later date

### IPD sharing plan summary
Data sharing statement to be made available at a later date