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Using a ketogenic diet to help prevent muscle wasting in critically ill patients

Submission date
19/08/2025

Recruitment status
Not yet recruiting

Registration date
27/08/2025

Overall study status
Ongoing

Last Edited
15/04/2026

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
We aim to help patients regain their independence after serious illness by preventing muscle wasting that occurs after being sick. Each month over 50000 patients stay in hospital for more than a week, and spend time waiting for help at home or a place in a care home afterwards because of muscle weakness. Patients, carers and healthcare professionals know that muscle weakness causes major problems with daily activities (e.g. washing, dressing, walking). The more seriously ill patients are, the more muscle they lose and the weaker they become. Patients who are in intensive care lose a kilo of muscle mass every day, meaning that this treatment is needed urgently. One year later, half cannot return to work, and a third need help with daily activities. We have developed a safe, novel medical food to prevent muscle wasting and want to see if it can help patients in intensive care recover their independence, called a ketogenic diet.

Who can participate?
Patients who are critically ill on an adult intensive care unit

What does the study involve?
We will randomise 282 critically ill patients into a trial of ketogenic feeding against usual feeding, and see if this changes the number of times they can stand up from sitting in 30 seconds. This is an important movement as it allows patients to get out of a chair or go to the toilet and helps prevent falling over, meaning that they need less help with simple independent activities of daily living. We are working with a company that produces medical feeds already, and they will produce the ketogenic feed and deliver this to hospitals for the trial.

What are the possible benefits and risks of participating?
We cannot promise the study will help anyone specifically, but the feed that we are using in this trial may prevent muscle wasting in our patients, and help future patients who are in the ICU We are not expecting any important side effects to occur during this study. A ketogenic diet has been used safely in our previous study of critically ill patients, and in other groups, e.g. healthy people and those who have experienced accidents, fits, or heart disease. Minor gut symptoms may occur, e.g. diarrhoea (a lot of loose stools); we would like to collect additional safety information, from close monitoring during the study period to ensure the feed is safe. Ultrasound of the muscle does not carry risks. We would only be requiring a small additional

volume of blood from tests that would be routinely performed on you on the ICU. The main disadvantage will be the increased amount of questions asked.

Where is the study run from?
The study is run from Bart's Health NHS Trust (UK)

When is the study starting and how long is it expected to run for?
April 2026 to December 2028

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
Professor Zudin Puthucheary (z.puthucheary@qmul.ac.uk)

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Dr Zudin Puthucheary

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Additional identifiers

Integrated Research Application System (IRAS)
356548

Central Portfolio Management System (CPMS)
69253

National Institute for Health and Care Research (NIHR)
158620

Study information

Scientific Title

Prevention of acute muscle wasting in critically ill adults using enteral ketogenic feeding: the Alternative Substrates In the Critically Ill Subject II (ASICS –II) trial

Acronym
ASICS –II

Study objectives
Primary objective:
To assess and draw inference on the efficacy of a 10-day ketogenic enteral feeding regimen compared with standard enteral feeding in increasing the number of sit-to-stand repetitions performed in 30 seconds, 30 days after randomisation in critically ill patients

Secondary objectives:
1. To assess and draw inference on the difference between the 10-day ketogenic enteral feeding regimen and standard enteral feeding for the Core Outcome Set measures of functional recovery (mortality, SF-36, Barthel Index) 30 and 90 days after randomisation
2. To provide safety data on the use of a 10-day ketogenic enteral feeding regimen in critically ill patients compared with standard enteral feeding during the intervention period

Mechanistic objectives:
1. To collect routinely measured daily serum urea and creatinine data during the 10-day intervention period as biochemical markers of catabolism
2. To examine alterations in the causal pathway between trial arms (differential ketone and amino acid flux, urea cycle flux and tricarboxylic acid cycle intermediate generation) using serum metabolomics from samples on day 1 and 7 post-randomisation
3. To confirm the induction of ketosis at seven days post-randomisation

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 22/08/2025, Wales Research Ethics Committee 4 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 2922 940989; Wales.REC4@wales.nhs.uk), ref: 25/WA/0190

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acute muscle wasting in critically ill adults

Interventions
Randomisation:
Randomisation will use a 1:1 allocation ratio between arms and be stratified by site. Random permuted blocks of sizes 4 and 6 will be used within strata.

Patients will be randomised by a delegated member of the research team. The database is accessible via the NHS computers on site, with access only given to delegated members of the research team. Following randomisation, confirmation e-mail will be sent to the member of the research team randomising. This will be included in the patient's medical records and in the ISF.

Trial intervention:
Following consent, participants will be randomised to either receiving the ketogenic enteral feed or control enteral feed within 48 hours of critical care admission. Local protocols will be followed for all participants in both feeding arms with the only difference being the feed. Within the individual groups the feed will be tailored depending on the patient's clinical requirements, specifically the use of propofol which provides additional fat to the patient. Therefore, one feed will be used when patients receive propofol and one when patients stop receiving propofol. Feeding bags will be differentiated by colour to allow for a double-blind randomisation protocol. The control feed will be eucalorific to the intervention feed. Each patient will then have an individual feeding regimen calculated by the dietitian within 72 hours. If no dietetic review occurs, the feed rate will be increased over 24 hours until a dietetic review occurs or until the end of the intervention period. Trial enteral feeding will continue for the duration of the 10-day trial period unless oral intake is established. If patients are discharged to the ward before the end of the intervention period, enteral feeding will continue and follow local ward protocols or dietetic recommendations.

Data Collection: Patients will be screened against the trial inclusion/exclusion criteria. The medical records of participants will be reviewed during the intervention period of 10 days and for up to 30 days. Within 48 hours of critical care admission, informed consent, medical history, and medical record review will take place. On days 1 7 and 10, muscle ultrasound, bioimpedance analysis, and blood sampling will be conducted. Upon ICU discharge, patients will have a 30STS assessment. The 30-day follow-up will include the 30 Second Sit to Stand, Barthel Index, and PICUPS/PICUPS community tests. The 90- day follow-up will include the SF-36 test. A retrospective Barthel Index, Short Form-36 questionnaire (SF-36) will be collected during the trial.

Intervention Type
Other

Primary outcome(s)
The number of sit-to-stand repetitions performed in 30 seconds 30 days after randomisation.

Key secondary outcome(s))
1. All-cause mortality within 30 days of randomisation
2. All-cause mortality within 90 days of randomisation
3. Barthel Index at 30 days after randomisation
4. Short Form 36 quality of life questionnaire at 90 days after randomisation
5. PICUPS or PICUPS community questionnaire Index at 30 days after randomisation

Safety outcome measures:
1. New (post initiation of intervention) metabolic acidosis (Base Excess of >4 mEq/l) not in keeping with the clinical condition, in the opinion of the treating clinician within 10 days of randomisation.
2. Hypoglycaemia episodes not in keeping with the clinical condition (normoglycaemia defined as 4.0-10.0 mmol/l), assessed from routine blood monitoring within 10 days from randomisation.
3. Hyperglycaemia episodes not in keeping with the clinical condition (normoglycaemia defined

as 4.0-10.0 mmol/l) assessed from routine blood monitoring within 10 days from randomisation.
4. Days when an episode of diarrhoea (defined as a Bristol School Score ≥5) is recorded on nursing observation charts during the first 10 days from randomisation.
5. Days where an episode of vomiting is recorded on nursing observation charts during the first 10 days from randomisation.
6. Nausea defined as when an anti-emetic is given for patient-reported nausea assessed daily during the first 10 days from randomisation.

Mechanistic outcome measures:
1. Daily serum urea and creatinine concentrations, for the first 10 days after randomisation.
2. Plasma metabolomic profiling at day one and day seven after randomisation.
3. Ketone body generation at day one and day seven after randomisation.

Completion date
31/12/2028

Eligibility

Key inclusion criteria
Adults (≥18 years) admitted to Critical Care who are:
EITHER:
• Hospitalised with acute respiratory failure (PaO2/FiO2 ratio of ≤39.9 KPa)
AND
• Expected to require advanced respiratory support (High-Flow Nasal Oxygen, non-invasive or invasive ventilation for >48 hours)
AND
• C-reactive Protein ≥75 mg/l indicating systemic inflammation
AND
• Nasogastric feeding planned for >48 hours
OR
• In multi-organ failure (Sequential Organ Failure Assessment Score [SOFA] Score ≥2 in two or more domains)
AND
• Nasogastric feeding planned for >48 hours

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex

All

Total final enrolment
0

Key exclusion criteria
1. Pre-existing inability to perform a sit-to-stand test (e.g., significant cognitive impairments that would impact their ability to engage in physical activity testing, Clinical Frailty score of > = 6, amputations, acute or chronic disability expected to preclude the sit-to-stand test at 30 days. amongst others)
2. New (pre-randomisation) inability to perform a sit-to-stand test. e.g., Primary neuromyopathy, acute intracerebral pathology, new or existing weight bearing restrictions or new neurological impairment amongst others)
3. Deemed unlikely to survive to 30 days OR presence of a treatment limitation
4. Contraindications to nasogastric feeding
5. Clinical need for specialist feeds
6. Patients with known inborn errors of metabolism

Date of first enrolment
01/06/2026

Date of final enrolment
01/06/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Barts Health NHS Trust
Royal London Hospital
Newham Hospital
Whipps Cross Hospital
Whitechapel Road
London
England
E1 1BB

Study participating centre
Guys and St Thomas' NHS Foundation Trust
249 Westminster Bridge Road
London
England
SE1 7EH

Study participating centre
St George's Healthcare Nhst
Blackshaw Road
London
England
SW17 0QT

Study participating centre
University Hospitals of North Midlands NHS Trust
Newcastle Road
Stoke-on-trent
England
ST4 6QG

Study participating centre
University Hospital Southampton NHS Foundation Trust
Southampton General Hospital
Tremona Road
Southampton
England
SO16 6YD

Study participating centre
Barking, Havering and Redbridge University Hospitals NHS Trust
Queens Hospital
Rom Valley Way
Romford
England
RM7 0AG

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Cambridge Biomedical Campus
Hills Road
Cambridge
England
CB2 0QQ

Study participating centre
Cardiff & Vale University Lhb
Woodland House
Maes-y-coed Road
Cardiff
Wales
CF14 4HH

Study participating centre
Kings College Hospital
Mapother House
De Crespigny Park
Denmark Hill
London
England
SE5 8AB

Sponsor information

Organisation
Barts Health NHS Trust

ROR
https://ror.org/00b31g692

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

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
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	03/06/2025	26/08/2025	No	Yes
Protocol file	version 2.0	24/07/2025	16/01/2026	No	No