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An intensive care unit randomised trial - comparing two approaches to providing nutrition during critical illness

Submission date
13/11/2025

Recruitment status
Recruiting

Registration date
27/11/2025

Overall study status
Ongoing

Last Edited
27/11/2025

Condition category
Other

[_] 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
In the UK approximately 200,000 critically ill patients admitted to general adult ICUs each year. The standard method of enteral nutrition on ICU is continuous infusion liquid feed by a pump via a nasogastric tube. This may prevent the potential benefits of a night-time fast, and is disruptive to circadian function – which may lead to a disrupted sleep-wake cycle, known to cause delirium. Delirium occurs in over 80% of patients receiving mechanical ventilation. It is not known if the time of feeding in ICU patients will affect or re-synchronise the circadian rhythms. This is the key question which this study aims to examine.

Who can participate?
Adult patients who have an unplanned admission to intensive care, and require medical ventilation will be considered for the study.

What does the study involve?
Participants who are enrolled onto the study will be chosen at random to received either normal continuous feeding (over 24 hours), or to receive their feed during the day time only (8 am to 10 pm). Participants in the second group will not receive any less feed, but their prescribed feed amount will be given in full over a shorter period of time. All participants will continue to receive full care on the ICU, as they would do if they were not in the study. When the participant is considered to have re-gained mental capacity to discuss the study, they will be asked to provide their consent for their continued involvement. They will then be asked to complete two questionnaires after 90 days, for the researchers to understand how they are doing.

What are the possible benefits and risks of participating?
There is no evidence of harm or extra risk to patients with daytime only feeding. We cannot promise that participants will benefit directly by taking part, but we want to find out if daytime only feeding can help prevent delirium in patients admitted to the Intensive Care Unit (ICU).

Where is the study run from?
The study is being run from University Hospitals Plymouth NHS Trust, with a second site at University Hospitals Southampton NHS Trust (UK)

When is the study starting and how long is it expected to run for?
The study is expected to run from November 2025 until March 2027.

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

Who is the main contact?
The Peninsula Clinical Trial Unit team: daydream.penctu@plymouth.ac.uk

Contact information

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Public

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Additional identifiers

Central Portfolio Management System (CPMS)
61024

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NIHR207910

Integrated Research Application System (IRAS)
339029

Study information

Scientific Title
A feasibility randomised controlled trial of administering daytime-only enteral feeding compared to standard continuous enteral feeding, to reduce delirium in mechanically ventilated, critically ill adults, with qualitative and circadian mechanistic sub-studies

Study objectives
The primary study objective is to conduct a randomised feasibility study of DoF compared to continuous feeding in critically ill patients who have been admitted to ICU for up to 30 days post-randomisation (during ICU stay only).

To achieve this the feasibility objectives are:
1. To estimate rates of screening, recruitment and randomisation rates.
2. To ascertain retention and dropout rate (due to treatment and or trial demands).
3. To determine the fidelity of delivering DoF in adult critically ill patients.
4. Ascertain completeness of data collection throughout the trial including 90 days follow-up.
5. Acceptability of outcome measurements (measured by completion rates and qualitative study).
6. Identify intervention and trial barriers and develop methods to overcome these through a qualitative sub-study.

The secondary study objectives are as follows:
1. Assess for evidence of efficacy (early signs that daytime feeding might help patients) by measuring the number of
coma and delirium free days on ICU, any use of delirium related medication or physical restraints and whether a
Deprivation of Liberty (DoLS) is needed.
2. To monitor whether there are any additional safety issues when using daytime only feeding compared to 24 hour
feeding.
3. To collect data on the long term psychological and functional impact of daytime feeding.
4. To conduct a sub-study to inform more detailed mechanistic work of daytime only feeding in the critically ill.

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 07/11/2025, Wales REC 6 (Swansea) (No postal address supplied – remote committee, -, -, United Kingdom; +44 (0)2922940911, +44 (0)2922 940954, +44 (0)2922 941090; Wales.REC6@wales.nhs.uk), ref: 25/WA/0263

Study design
Randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Critical illness and delirium

Interventions
This trial has been designed as a feasibility study to inform a future definitive randomised controlled trail; exploring trial recruitment and retention, feasibility and acceptability of data collection procedures, and outcome measures, intervention fidelity and evidence of efficacy.

In standard care for this group of patients, concerns over malnutrition in critical illness, combined with the convenience of using a programmable feed pump, mean it is standard practice to deliver feed to critically ill patients continuously (over 24 hours). Whilst convenient, constant 24-hour feeding contrasts with usual human physiology and may be detrimental to health. Continuous feeding prevents the potential benefits of a normal night-time fast, and is disruptive to circadian function. This may lead to a disrupted sleep-wake cycle, which is known to cause delirium. Delirium is a state of severe confusion and can be a frightening experience. This state can fluctuate throughout the day. It occurs in up to 4 out of 5 patients who need support from a ventilator.

We hypothesise that the intervention of daytime only feeding is a strategy to synchronise circadian rhythms and so reduce the incidence of delirium in mechanically ventilated patients in ICU.

No previous studies of daytime only feeding or intermittent fasting in critically ill patients have used delirium as the outcome measure. While it is plausible that daytime only feeding will realign circadian rhythms in humans, it has not been demonstrated.

If a simple, cost-free intervention of daytime only feeding reduces the incidence of delirium, this could reduce mortality and morbidity and increase the quality of life. It would reduce the burden on nursing staff, length of hospital stay and subsequent use of the health service. It requires no extra resources or roll out time.

For this trial, the proposed sample size of 40 participants has been determined based on 80% power and 5% significance. Based on previous years ICNARC data of the UHP ICU population, a 20% enrolment rate across 2 sites should be achieved within 12 months of enrolment. The first patient is planned to be recruited in November 2025, with the 12 month period allocated to recruit 40 patients across two sites.

Chronologically, the trial will be carried out as follows:
The recruiting principal investigator/delegate will establish patient eligibility prior to enrolment, and also whether or not the participant has the capacity to provide prior consent. The patient will then be enrolled within 24 hours of their admission to the ICU.

The recognised model of Research Without Prior Consent (RWPC) will be applied at this point. Consent will be obtained from patients once they have stabilised and are deemed to have capacity. In the interim, a personal or nominated consultee will be approached to provide their opinion as to whether or not the patient would object to taking part. All stages of the consent process will be fully documented.

Participants will be randomised into one of two groups:
For group 1 – the intervention group - feeding is provided via a naso/orogastric tube continuously over 14 hours (08:00-22:00) and then paused between the hours of 22:00 and 08:00 (i.e. a 10 hour overnight fast).
For group 2 - the control group – feeding is provided via a naso/orogastric tube continuously over 24 hours as per standard of care.

Patients in both groups will be prescribed their standard nutritional goals. The use of catch-up feeding after a pause in feeding is advised for both the intervention and control groups to ensure their optimum nutrients are provided. Catch up feeding is permitted up to 2 hours before the end of the feeding period.

Blood glucose levels will be monitored overnight, and the use of insulin will be reviewed.

Ongoing data will be collected over the course of the study regarding when the patient is coma-free, when they shows any signs of delirium, and any medication prescribed for it.

Daily data collection is stopped when:
- the enrolled patients are receiving >50% of their diet by eating, or
- are changed to parenteral nutrition or
- are changed to end of life care or
- are discharged from the ICU.

The circadian sub-study aims to explore whether we can obtain more information on circadian rhythms and responses to stress on the body. In order to do this, the following things will be collected:

For patients at both sites:
On the 3rd, 4th and 5th day we will record body temperature every 3 hours.
On the 3rd, 4th and 5th day, we will collect a small amount of blood (for cortisol analysis) - four times over each day.

For patients at the Plymouth site only:
A small amount of extra blood (for mRNA analysis) will also be collected on the 3rd and 4th days.
Ambient light and background sound around the patients bed will also be measured – to help us understand their effect on circadian rhythms.
All extra blood samples will be taken from existing line inserted as part of standard ICU care - so there will be no extra pain or discomfort as a result of these extra samples.
Any blood samples collected as part of the study will be transferred, stored, and analysed at approved Laboratories in line with the Human Tissue Act (2004).

Approximately 90 days after enrolment on the study, a member of the research team will contact them by phone to go through two very short questionnaires - to see how they are and if they are suffering with any longer-term effects of being in ICU (quality of life and post-traumatic stress). These will take approximately 10 minutes each to complete.
Alternatively, the questionnaires can be sent by post or electronically - to complete them on a phone or laptop.

Finally the qualitative sub-study is aimed at the ICU staff who deliver the intervention of daytime only feeding. They will be invited to semi-structured interviews, focus groups, or online surveys to help us understand the experience of delivering the intervention. This data will also help to inform delivery of a future randomised controlled trial.
Staff members will be asked to provide a signed informed consent form in order to participate in this sub-study. In-person interviews and focus groups will take place at Derriford Hospital in Plymouth.

A Patient Advisory Group and clinical staff have advised on all aspects of data collection to ensure any participant burden is minimal.

Intervention Type
Other

Primary outcome(s)
1. Rates of screening, recruitment, and randomisation measured using Number of patients screened, recruited and randomised (overall and by centre) at End of Trial

2. Rates of retention and loss to follow-up measured using Number of patients remaining in the trial for up to 90 days follow-up (or until death) (overall and by centre) at End of Trial

3. Fidelity of the intervention measured using Delivery of at least 65% of prescribed feed during set feeding hours (08:00-22:00 for intervention, 07:00-07:00 for control) for at least 80% of days in ICU. at End of Trial

4. Acceptability and completeness of data collection measured using Completeness of data collection addressing primary and secondary outcomes of a future definitive trial at End of Trial

5. Intervention and trial barriers and methods to overcome these measured using Qualitative focus groups/interviews at End of Trial

Key secondary outcome(s))
1. Delirium and coma free days on ICU measured using Richmond Agitation Scale (RASS) (to demonstrate coma), Part of Delirium Assessment at a minimum of 12-hourly and recorded for each 07.00 - 07.00 24-hour time period

2. Delirium and coma free days on ICU measured using Confusion Assessment Method for ICU (CAM-ICU) (primary delirium assessment), Part of Delirium Assessment at a minimum of every 12 hours if RASS is ≥- 3. (which means not in a coma), summary recorded for 24 hours 07.00 - 07.00 time period

3. Delirium and coma free days on ICU measured using Intensive Care Psychological Assessment Tool (IPAT) (additional delirium assessment), Part of Delirium Assessment at if CAM-ICU is negative, maximum 24 hourly

4. Delirium and coma free days on ICU measured using Data from the prescription chart to assess if delirium related drugs have been administered to the participant (additional delirium assessment) at Daily

5. Delirium and coma free days on ICU measured using Use of physical restraints and Deprivation of Liberty Safeguards authorisation (DoLS) (additional delirium evidence) at Daily

6. Incidence of feed intolerance measured using Worsening gastrointestinal function with raised gastric residual volumes (GRV), or a failure to reach nutritional targets and gastrointestinal symptoms in response to feeding attempts at Captured as adverse event of special interest

7. Incidence of feed intolerance measured using Prokinetic drugs administered as per feeding guide based on ESPEN guide at Daily

8. Incidence of hypoglycaemic events measured using Glucose <4.0 mmol/L at Captured as adverse event of special interest

9. Long-term psychological and functional impact measured using EQ-5D-5L (Proxy Version 1 may be used) at 90 days post-recruitment via email, post, or phone call from ICU research nurse

10. Long-term psychological and functional impact measured using PTSS-14 at 90 days post-recruitment via email, post, or phone call from ICU research nurse

11. Safety measured using AEs and SAEs at Daily (as required)

12. Mortality measured using Date of death at Up to 90-days follow-up

Completion date
01/03/2027

Eligibility

Key inclusion criteria
1. Adults (aged 18 years and above)
2. Unplanned admission to ICU within 48 hours of admission
3. Mechanically ventilated, with a clinical view it will be for >48 hours
4. Plan to start enteral feeding (providing nutrition via a tube into the gastrointestinal tract) or enteral feeding has commenced during the daytime only so far
5. Likely to require enteral feeding 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. Planned admissions unless unexpectedly ventilated during the first 24 hours of admission
2. Continuous enteral feeding already commenced overnight (22:00-08:00)
3. Known intolerance to enteral feeding or currently unable to absorb enteral feed
4. Post-emergency bowel surgery
5. Type 1 diabetes or pre-existing insulin therapy (with risk of significant dysglycaemia on fasting for 10 hours)
6. Hyponatraemia; serum Na <115 mmol/L
7. Nil-by-mouth
8. Clinician considers daytime-only feeding unsuitable for the patient
9. Pregnancyand breastfeeding
10. Post-pyloric feeding via jejunostomy tube
11. Receiving parenteral nutrition
12. Dementia, psychosis, bipolar disorder and pre-existing use of antipsychotic drugs (haloperidol, olanzapine, quetiapine) or alcohol use, daily and to excess
13. Prone position ventilation

Date of first enrolment
03/11/2025

Date of final enrolment
30/11/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospitals Plymouth NHS Trust
Derriford Hospital
Derriford Road
Derriford
Plymouth
England
PL6 8DH

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

Sponsor information

Organisation
University Hospitals Plymouth NHS Trust

ROR
https://ror.org/05x3jck08

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

The datasets generated during and/or analysed during the current study will be available upon request from the study sponsor - University Hospitals Plymouth NHS Trust, The Research Office, Level 2 MSCP, Bircham Park Offices, 1 Roscoff Rise, Derriford Plymouth, PL6 5FP.
Data will be shared with (or access to the data will be provided to) requestors whose proposed use of the data has been approved by the Sponsor, under an appropriate data sharing agreement.
All participant data within the database will be fully pseudonymised.
The Sponsor (UHPT) will be responsible for archiving the study data in a secure location for at least 5 years after the end of the trial.
Study participants will be asked to provide consent for future sharing of anonymised data – this is an optional clause on the consent forms.
There are no extra ethical or legal restrictions regarding the sharing of this anonymous dataset.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.1	13/10/2025	25/11/2025	No	No