ISRCTN17386141 https://doi.org/10.1186/ISRCTN17386141

Clinical and cost-effectiveness of early nutritional support in critically ill patients via the parenteral versus the enteral route

Submission date	Recruitment status	[X] Prospectively registered
25/03/2009	No longer recruiting	[ ] Protocol
Registration date	Overall study status	[ ] Statistical analysis plan
09/04/2009	Completed	[X] Results
Last Edited	Condition category	[ ] Individual participant data
24/06/2020	Nutritional, Metabolic, Endocrine	

Plain English summary of protocol
Background and study aims
Current research does not provide clear guidance as to whether intravenous nutritional support (where nutrients are infused into the blood stream) is better than gastric tube feeding (where nutrients are infused into the stomach) for critically ill patients. Previous research studies indicate that intravenous nutritional support has the advantage of being more likely to deliver the intended nutrition, but may be more dangerous. The danger, or complications, can result from problems with the devices used to access the vein (e.g. lung puncture and infection from the tube, or cannula, used), and from metabolic effects due to the fact that the nutrients bypass the normal route of absorption. The aim of this study is to compare intravenous nutritional support with gastric tube feeding in adult critically ill patients.

Who can participate?
Critically ill patients aged 18 or over in critical care units

What does the study involve?
Patients are randomly allocated to intravenous nutritional support or gastric tube feeding, thus allowing us to compare their outcomes in terms of survival and also quality of survival. For those receiving intravenous nutritional support, after 5 days they are weaned onto gastric tube feeding. Those receiving gastric tube feeding but who are not achieving adequate nutrition by day 5 are provided with intravenous nutritional support for as long as is necessary.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Intensive Care National Audit & Research Centre (UK)

When is the study starting and how long is it expected to run for?
June 2011 to December 2013

Who is funding the study?
NIHR Health Technology Assessment Programme - HTA (UK)

Who is the main contact?
Prof Kathy Rowan

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Protocol serial number
HTA 07/52/03; 09/0082

Study information

Scientific Title
A phase III, open, multicentre, randomised controlled trial comparing the clinical and cost-effectiveness of early nutritional support in critically ill patients via the parenteral versus the enteral route

Acronym
CALORIES

Study objectives
Current study hypothesis as of 08/01/2013:
Is parenteral nutrition (PN) the optimal route of early nutritional support for adult critically ill patients, in terms of clinical and cost-effectiveness, when compared with enteral nutrition (EN)?

Previous study hypothesis until 08/01/2013:
Is parenteral nutrition (PN) the optimal route of early nutritional support for adult critically ill patients, in terms of clinical and cost-effectiveness, when compared with enteral tube feeding (ETF)?

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/075203
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0006/51882/PRO-07-52-03.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Phase III open randomised parallel-group multicentre trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Enteral/parenteral feeding

Interventions
Current interventions as of 08/01/2013:
Early PN versus early EN within 36 hours of the date/time of original admission to a critical care unit.

The protocol for PN (intervention):
1. Initial central venous catheter (including peripherally inserted central venous catheter) insertion and positioning should be in accordance with NHS guidelines with a dedicated lumen
2. Standard feed should be obtained from the units usual stock/supplier, used within the licence indication and fall within the following ranges: energy 1365-2540 total kcal bag-1 and nitrogen 7.2-16.0 total kcal bag-1
3. Units should aim to feed patients to a target of 25 kcal kg day-1 within 48-72 hours, using actual body weight
4. Enteral trickle feeding is not permitted for the five days (120 hours)

Local practice and polices should be followed for PN and should include provision for:
1. Ensuring that the patient receives a nutritionally complete feed
2. Inclusion of additional micronutrients if clinically indicated, and as prescribed by the clinician /and or dietician in accordance with National Institute of Clinical Excellence (NICE) guidelines. Additions must be made under appropriate pharmaceutically controlled environmental conditions before administration
3. Adjustment of total volume according to fluid balance requirements
4. Monitoring for specific nutritional-related complications
5. Regular review of patients for their ongoing nutritional support needs
6. Energy requirements for those in extreme BMI categories (e.g. <18.5 and >30kg/m2)

The protocol for EN (control):
1. Initial nasogastric/nasojejunal tube insertion and positioning in accordance with National Patient Safety Agency (NPSA) guidelines
2. Standard feed should be obtained from the units usual stock/supplier, used within the licence indication and fall within the following ranges: energy 1365-2540 total kcal day-1 and nitrogen 7.2-16.0 total kcal day-1

3. Units should aim to feed patients to a target of 25 kcal kg day-1 within 48-72 hours, using actual body weight

Local practice and polices should be followed for EN and should include provision for:
1. Ensuring that the patient receives a nutritionally complete feed
2. Adjustment of total volume according to fluid balance requirements
3. Monitoring for specific nutritional-related complications
4. Regular review of patients for their ongoing nutritional support needs
5. Energy requirements for those in extreme BMI categories (e.g. <18.5 and >30kg/m2)

Both protocols will be followed for five days (120 hours), unless the patient transitions to exclusive oral feeding or is discharged from the critical care unit before this time. Patients may start oral feeding if clinically indicated during the five days.

Previous interventions until 08/01/2013:
Planned interventions:
Early PN versus early ETF within 24 hours but no later than 36 hours after admission.

CALORIES PN protocol will cover:
1. Initial central line (jugular/subclavian) insertion/positioning according to NHS Guidelines with dedicated lumen
2. Standard feed (provided free-of-charge from major manufacturers) with lipid calories (30-60%), nitrogen (0.14 - 0.20 g/kg) and non-nitrogen energy requirement estimated using a suitably adjusted Schofield equation plus standard addition of vitamins, trace elements and electrolyte concentrations according to clinical requirements
3. Intravenous glutamine at 20 g/day (note: standard enteral feed preparations based on casein protein typically contain approximately 10% glutamine and 10% glutamate and further supplementation of ETF with glutamine has not been shown to be beneficial)
4. Total volume adjusted according to fluid balance requirements
5. Starter regimens at 25 - 50% (for day one) and 35 - 65% (for day two) of intended final prescription may be used for those considered at risk of refeeding syndrome
6. Likely maximum delivery in five days
7. Frequency of measurement for specific nutritional-related complications e.g., biochemistry tests

CALORIES ETF protocol will cover:
1. Initial nasogastric tube insertion/positioning according to NPSA Guidelines
2. Isocaloric (1 kcal/ml) standard feed with/without fibre (more concentrated will be permitted if required for fluid balance)
3. Commencement rate and target rates to achieve goal (cal/kg) for objective weight (or estimated weight where objective weight not available)
4. Time period over which goal is to be achieved
5. Nutritional intake of 25 kcal/kg/day
6. Likely maximum delivery in five days
7. Frequency of measurement of aspirates
8. Patient positioning
9. Frequency of measurement for specific nutritional-related complications e.g., diarrhoea

CALORIES will not dictate the use of one ETF protocol and one PN protocol but will review all ETF and PN protocols in use by participating units and ensure that those used by participating units fall within common boundaries. There will be no restriction to products from a single manufacturer. Both, however, will be limited to an agreed range of products fulfilling the criteria. Criteria for will be based on recommendations from the Guidelines of the Canadian Society for Clinical Nutrition for artificial nutritional support in critical care. Both protocols will be based on current standard protocols in use in critical care units in the NHS informed by clinical consensus and literature review.

Proposed duration of intervention:
The PN and ETF protocols will be followed for five days unless the patient transitions to oral feeding beforehand. Patients will be reviewed regularly to enable re-instigation of oral feeding, when appropriate. Crossovers will only be those patients going from ETF to PN or PN to ETF within five days.

Intervention Type
Other

Phase
Phase III

Primary outcome(s)
Current primary outcome measures as of 08/01/2013:
1. To estimate the effect of early (defined as within 36 hours of the date/time of original critical care unit admission) nutritional support via the parenteral route (PN) compared with the enteral route (EN) on mortality at 30 days
2. To estimate the incremental cost-effectiveness of early PN compared with EN at one year

Previous primary outcome measures until 08/01/2013:
30-day all cause mortality and cost-effectiveness at one year.

Key secondary outcome(s))
Current secondary outcome measures as of 08/10/2013:
To compare PN with EN for:
1. Duration of specific and overall organ support in the critical care unit
2. Infectious and non-infectious complications in the critical care unit
3. Duration of critical care unit and acute hospital length of stay
4. Mortality at discharge from the critical care unit and from hospital
5. Mortality at 90 days and at one year
6. Nutritional and health-related quality of life at 90 days and at one year
7. Resource use and costs at 90 days and at one year
8. Estimated lifetime incremental cost-effectiveness

Previous secondary outcome measures until 08/10/2013:
1. Duration of specific and overall organ support
2. Infectious and non-infectious complications in the critical care unit
3. Duration of critical care unit and acute hospital length of stay
4. Mortality at discharge from the critical care unit and hospital
5. Mortality between 90 days and one year
6. Nutritional and health-related quality of life at 90 days and at one year
7. Resource use and costs at 90 days and one year

Completion date
31/12/2013

Eligibility

Key inclusion criteria
Current inclusion criteria as of 08/01/2013:
Patients who either on, or soon after admission (but within a timeframe to consent/obtain agreement, randomise and start nutritional support within 36 hours of the date/time of original admission to a critical care unit) are:
1. Adult (defined as age 18 years or over)
2. An unplanned admission (including planned admissions becoming unplanned e.g. unexpected post-operative complications)
3. Expected to receive nutritional support for two or more days in the unit
4. Not planned to be discharged within three days (defined by clinical judgment) from the unit

Previous inclusion criteria until 08/01/2013:
1. Male and female adults (defined as age 18 years or over)
2. Unplanned admission (defined as per the Critical Care Minimum Data Set [CCMDS]
3. Original critical care unit admission (defined as not transferred in from another critical care unit/bed)
4. Not planned to discharge within three days (defined by clinical judgment)
5. Not expected to receive oral feeding within two days

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 08/01/2013:
1. Patients who have been in a critical care unit for more than 36 hours (i.e. from the date/time of original admission to a critical care unit)
2. Patients previously randomised into CALORIES
3. Patients with pre-existing contraindications to PN or EN
4. Patients who have received PN or EN within the last seven days
5. Patients admitted with a percutaneous endoscopic gastrostomy, percutaneous endoscopic jejunostomy, needle/surgical jejunostomy or nasojejunal tube in situ
6. Patients admitted to the critical care unit for treatment of thermal injury (burns)
7. Patients admitted to the critical care unit for palliative care
8. Patients whose expected stay in the UK is less than six months
9. Women who are pregnant

Previous exclusion criteria until 08/01/2013:
1. Pre-existing contraindication to ETF or PN
2. Pregnant women
3. People whose expected stay in the UK is less than six months
4. Patients admitted to the unit for treatment of thermal injury (burns)
5. Patients admitted to the unit for palliative care
6. Patients with percutaneous endoscopic gastrostomy (PEG), percutaneous endoscopic jejunostomy (PEJ) or needle/surgical jejunostomy (JEJ)

Date of first enrolment
17/06/2011

Date of final enrolment
31/12/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Intensive Care National Audit & Research Centre
London
United Kingdom
WC1V 6AZ

Sponsor information

Organisation
Intensive Care National Audit & Research Centre (ICNARC) (UK)

ROR
https://ror.org/057b2ek35

Funder(s)

Funder type
Government

Funder Name
NIHR Health Technology Assessment Programme - HTA (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	30/10/2014		Yes	No
Results article	results	01/04/2016		Yes	No
Results article	results	01/08/2019	24/06/2020	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes