

The clinical and cost-effectiveness of early, goal-directed, protocolised resuscitation for emerging septic shock

Submission date 18/11/2009	Recruitment status No longer recruiting	☒ Prospectively registered ☐ Protocol
Registration date 19/11/2009	Overall study status Completed	☒ Statistical analysis plan ☒ Results
Last Edited 20/04/2016	Condition category Infections and Infestations	☐ Individual participant data

Plain English summary of protocol

Background and study aims

Each year in the UK, about 31,000 people are admitted to critical care with severe sepsis, a syndrome where the body has an uncontrolled inflammatory response to infection which leads to damage to and subsequently failure of organs such as the lungs, heart and kidneys. Around one third of these patients die before discharge from hospital. Identifying these patients early and applying a strict protocol to control the amount of fluids, blood and drugs given may reduce the number of deaths and also the amount of time patients spend in hospital. However, we do not know whether this approach would be as successful if applied across all hospitals in the NHS. We aim to compare this protocol to the usual care delivered in NHS emergency departments and medical/surgical admissions units to establish the best approach to managing these patients.

Who can participate?

Patients aged 18 or over with the early signs of severe sepsis

What does the study involve?

Participants are randomly allocated either to be treated according to the new protocol or to receive the usual care. We assess the number of deaths within 90 days and the costs of each approach to determine whether the protocols offer good value for money to the NHS.

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 and Research Centre (ICNARC) (UK)

When is the study starting and how long is it expected to run for?

February 2011 to December 2013

Who is funding the study?

NIHR Health Technology Assessment Programme - HTA (UK)

Who is the main contact?
Prof Kathryn Rowan
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Contact information

Type(s)
Scientific

Contact name
Prof Kathryn Rowan

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Additional identifiers

Protocol serial number
HTA 07/37/47; ICNARC/01/01/09

Study information

Scientific Title
A multicentre, randomised controlled trial of the clinical and cost-effectiveness of early, goal-directed, protocolised resuscitation for emerging septic shock

Acronym
ProMISe

Study objectives
Current hypothesis as of 04/01/2013:
To evaluate a resuscitation protocol, with pre-determined haemodynamic goals, compared with usual resuscitation

Previous hypothesis until 04/01/2013:
To evaluate a resuscitation strategy with pre-determined haemodynamic endpoints compared to usual care for patients with severe sepsis or septic shock.

More details can be found at: <http://www.nets.nihr.ac.uk/projects/hta/073747>
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0014/51800/PRO-07-37-47.pdf

Ethics approval required

Old ethics approval format

Ethics approval(s)

Not provided at time of registration

Study design

Prospective multicentre randomised controlled trial

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Severe sepsis/septic shock

Interventions

Intervention arm: Early goal-directed protocolised resuscitation; targeting of specific haemodynamic goals including central venous pressure, mean arterial pressure and central venous oxygen saturation.

Control arm: Usual care

Patients admitted to Emergency Departments with severe sepsis or septic shock will undergo 6 hours of the intervention arm post-randomisation. For the control arm patients will be treated via usual care for these 6 hours. After this patients will be treated with standard care.

Patients will be followed up for a year post-admission to hospital. This will include assessments at 28 days, 90 days and 1 year. This trial is not classed as a CTIMP.

Intervention Type

Other

Phase

Not Applicable

Primary outcome(s)

1. Mortality at 90 days
2. Incremental cost-effectiveness at one year

Key secondary outcome(s)

Current secondary outcome measures as of 04/01/2013:

1. To compare:
 - 1.1. Mortality at one year
 - 1.2. Health-related quality of life at 90 days and one year
 - 1.3. Resource use and costs at 90 days and one year
 - 1.4. Requirement for, and duration of, critical care unit organ support
 - 1.5. Length of stay in the ED, critical care unit and acute hospital
2. To estimate:
 - 2.1. Lifetime incremental cost-effectiveness

Previous secondary outcome measures until 04/01/2013:

1. Duration of survival
2. Mortality at 28 days
3. Mortality at discharge from critical care and discharge from hospital
4. Mortality at one year
5. Sequential Organ Failure Assessment (SOFA) score at 6 hours and 72 hours (adjusted for baseline)
6. Requirement for, and duration of, monitoring and support of specific organ systems (CCMDS)
7. Duration of ED, critical care unit and hospital stay
8. Health-related quality of life (EQ-5D) at 90 days and one year
9. Resource use and costs at 90 days and one year
10. Lifetime incremental cost-effectiveness

Completion date

31/12/2013

Eligibility

Key inclusion criteria

1. Greater than or equal to 18 years of age, either sex
2. Known or presumed infection
3. Two or more systemic inflammatory response syndrome (SIRS) criteria:
 - 3.1. Core temperature less than or equal to 36°C or greater than or equal to 38°C
 - 3.2. Heart rate greater than or equal to 90 beats/min
 - 3.3. Respiratory rate greater than or equal to 20 breaths/min (or hyperventilation indicated by partial pressure of carbon dioxide in arterial blood [PaCO₂] 4.3 kPa or mechanical ventilation for an acute process)
 - 3.4. White blood cell count less than or equal to 4×10^9 l or greater than or equal to 12×10^9 l (or the presence of greater than 10% immature neutrophils "bands")
4. Refractory hypotension or hypoperfusion:
 - 4.1. Hypotension is confirmed by the presence of systolic blood pressure less than 90 mmHg despite an intravenous (IV) fluid challenge of at least 20 ml/kg within 30 minutes of Emergency Department (ED) arrival (including IV fluids administered by pre-hospital/Emergency Medical Services [EMS] personnel)
 - 4.2. Hypoperfusion is confirmed by a blood lactate concentration greater than or equal to 4 mmol/L)
5. First dose of IV antimicrobial therapy commenced prior to randomisation

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 04/01/2013:

1. Age less than 18 years
2. Known pregnancy
3. Primary diagnosis of:
 - 3.1. an acute cerebral vascular event
 - 3.2. acute coronary syndrome
 - 3.3. acute pulmonary oedema
 - 3.4. status asthmaticus
 - 3.5. major cardiac arrhythmia (as part of primary diagnosis)
 - 3.6. seizure
 - 3.7. drug overdose
 - 3.8. injury from burn or trauma
4. Haemodynamic instability due to active gastrointestinal haemorrhage
5. Requirement for immediate surgery
6. Known history of AIDS
7. Do-Not-Attempt-Resuscitation (DNAR) status
8. Advanced directives restricting implementation of the resuscitation protocol
9. Contraindication to central venous catheterization
10. Contraindication to blood transfusion
11. Attending clinician deems aggressive resuscitation unsuitable
12. Transferred from another in-hospital setting
13. Not able to commence resuscitation protocol within one hour of randomisation or complete six hours of protocol treatment from commencement

Previous exclusion criteria until 04/01/2013:

1. Aged less than 18 years
2. Known pregnancy
3. Primary diagnosis of acute cerebral vascular event, acute coronary syndrome, acute pulmonary oedema, status asthmaticus, major cardiac arrhythmia (as part of primary diagnosis), seizure, drug overdose, injury from burn or trauma
4. Haemodynamic instability due to active gastrointestinal (GI) haemorrhage
5. Immunosuppressive agents including chemotherapy for uncured cancer, immunosuppression for organ transplantation or from systematic disease
6. Requirement for immediate surgery
7. Do not resuscitate status
8. Advanced directives restricting implementation of the protocol
9. Contraindications to central venous catheterisation
10. Contradiction to blood transfusion (i.e. Jehovah's Witness)
11. Attending physician deems aggressive care unsuitable
12. Participation in another interventional study
13. Transferred from another in-hospital setting
14. Not able to start within 1 hour of randomisation or finish within 6 hours

Date of first enrolment

15/02/2011

Date of final enrolment

31/12/2013

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

Intensive Care National Audit and Research Centre (ICNARC)

London

United Kingdom

WC1V 6AZ

Sponsor information

Organisation

Intensive Care National Audit and 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	02/04/2015		Yes	No
Results article	results	01/11/2015		Yes	No
Statistical Analysis Plan	statistical analysis plan	01/12/2013		No	No