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Evaluating the use of a lower blood pressure target to guide drug treatment in critically ill children with low blood pressure

Submission date
21/05/2021

Recruitment status
Recruiting

Registration date
24/05/2021

Overall study status
Ongoing

Last Edited
25/06/2025

Condition category
Circulatory System

[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
In critically ill children, hypotension (low blood pressure) is common, especially in patients with severe infections and is a key feature of shock. Untreated, hypotension compromises tissue perfusion (blood flow) and organ function, with an increased risk of multiple organ failure. Vasoactive agents (which also stimulate the heart) and fluids are mainstays of treatment. Central venous catheters (a tube inserted into a large vein) are often used to help with treatment. Around 80% of the 20,000 children admitted to UK PICUs each year receive fluid bolus therapy and around 30% receive vasoactive drugs at some point during their intensive care stay.
Though interventions to treat hypotension may be lifesaving, there are also harms. Excessive fluids are associated with prolonged Pediatric Intensive Care Unit (PICU) stay and increased illness and death. Most vasoactive drugs induce vasoconstriction (constriction of blood vessels), which may reduce blood flow and cause other effects. Central venous catheters are usually sited to give the patient vasoactive drugs; these catheters are associated with an increased risk of thrombosis (blood clots) and infection, particularly in very small children.
Current guidelines recommend maintaining mean arterial pressure (MAP – mean arterial or average blood pressure) for children with sepsis around the 50th centile for age. However, these guidelines are based on low-quality evidence and no guidance is given for an upper MAP limit. In adults with sepsis, the 5th centile value for mean blood pressure has been recommended. This strategy has been examined in a number of recent studies, all of which investigated a permissive blood pressure target in critically ill adults with a variety of pathology. None of these studies demonstrated any significant difference in the overall death rate between the lower and higher blood pressure target groups. However, a pooled analysis found an increased incidence of supraventricular tachycardia (abnormally fast heart rhythm) in the higher blood pressure target group and an increased death rate in those patients in the higher blood pressure target group enrolled after over 6 h of vasopressors (medicines that constrict blood vessels).
The aim of this study is to find out whether the benefits associated with a lower blood pressure target will outweigh the risks associated with lower MAP values and the medical interventions needed to raise blood pressure, improving outcomes and decreasing costs.

Who can participate?
Children under 16 years old admitted to one of the PICUs on invasive mechanical ventilation, who have started treatment with a vasoactive drug for hypotension in the last 6 hours and are expected to continue for at least 6 hours.

What does the study involve?
Patients will be randomly allocated between the intervention and control groups. The intervention group are treated with a permissive blood pressure target (MAP target of 5th centile for age). The permissive blood pressure target is to be followed at any point the patient needs vasoactive drugs during this critical care unit admission. The decision to discontinue vasoactive agents will be determined by the patients' ability to maintain the MAP target without vasoactive drugs. All other care will be at the discretion of the treating clinical team. The control group receive usual care. No specific blood pressure target will be set for usual care, with treating clinicians directed to follow their standard practice.

What are the possible benefits and risks of participating?
No promises will be made to participants. There are potential risks and benefits of being in both the intervention and control group but the overall effect is not known, which is why this study is needed. Very low blood pressure can be associated with organ damage or may even be life-threatening. However, interventions to treat hypotension may be lifesaving, there are also harms. Excessive fluids are now known to be associated with prolonged paediatric intensive care unit stay and increased death rate. Most vasoactive drugs commonly used in children cause vasoconstriction, which may reduce blood flow with secondary effects on organ function. Central venous lines are usually sited to administer vasoactive drugs; these are associated with an increased risk of thrombosis and infection, particularly in very small children in whom the central venous catheter may occupy most of the vessel lumen (the inside space). The results of this study will benefit critically ill children treated in PICU.

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?
August 2020 to November 2026

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

Who is the main contact?
Dr David Inwald
di260@cam.ac.uk

Study website
https://www.icnarc.org/Our-Research/Studies/Current-Studies/Pressure

Contact information

Type(s)
Scientific

Contact name
Dr David Inwald

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https://orcid.org/0000-0001-9518-7821

Contact details
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
289545

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 48813, IRAS 289545, HTA - NIHR128895

Study information

Scientific Title
PRESSURE: PRotocolised Evaluation of permiSSive blood pressure targets versus Usual caRE. Evaluating the clinical and cost-effectiveness of using a permissive blood pressure target to guide titration of vasoactive drugs in critically ill children with hypotension

Acronym
PRESSURE

Study objectives
A permissive blood pressure target (mean arterial pressure (MAP) target of 5th centile for age) to guide treatment (as compared with usual care) is clinically and cost-effective in mechanically ventilated, critically ill children with hypotension, on vasoactive drugs.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 10/05/2021, East of England - Cambridge South Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)02071048065; cambridgesouth.rec@hra.nhs.uk), REC ref: 1/EE/0084

Study design
Randomized; Interventional; Design type: Treatment, Management of Care

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
https://www.icnarc.org/Our-Research/Studies/Current-Studies/Pressure

Health condition(s) or problem(s) studied
Critically ill children with hypotension

Interventions
Eligible patients will be randomised on a 1:1 basis to either permissive blood pressure targets or usual care using a central web-based randomisation service (sealed envelope). Randomisation will be stratified by site and age.

Intervention group:
Participants allocated to the intervention group will be treated using an allocated lower blood pressure target whilst receiving vasoactive drugs. The target allocated will depend on the participant's age. The decision to discontinue vasoactive drugs will depend on the patient's ability to maintain the target. All other usual care will be provided at the discretion of the treating clinical team, according to local practice.

Usual care:
Participants allocated to this group will receive usual care, according to local practice.

A follow-up questionnaire will be provided to those who have agreed to it 12 months post randomisation.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)

Vasoactives

Primary outcome measure

Clinical effectiveness:
Composite of mortality and duration of ventilator support, defined by the Paediatric Critical Care Minimum Dataset (PCCMDS), from randomisation to day 30

Cost-effectiveness:
Incremental net monetary benefit (INB), evaluated at the NICE recommended threshold of £20,000 per quality-adjusted life-year (QALY), at 90 days

Secondary outcome measures

Current secondary outcome measures as of 25/06/2025:

1. Mortality collected via sites on case report form (CRF) at PICU discharge, 30 days, 90 days and 12 months
2. Duration of survival collected via sites on CRF and NHS digital if necessary to 12 months
3. Time to liberation from invasive ventilation, collected via sites on CRF, from PICU admission to PICU discharge
4. Functional status measured by the Pediatric Overall Performance Category (POPC) and Pediatric Cerebral Performance Category (PCPC) scales between PICU admission and PICU discharge
5. Receipt and duration of renal replacement therapy collected via sites on CRF and PICANet at 30 days
6. Length of PICU and hospital stay collected via sites on CRF from PICU admission to PICU discharge
7. Health-related quality of life (HrQoL), measured by the child self-or parent-proxy reported PedsQL-4.0 with age-appropriate versions covering the wide range included in the trial (1 month-16 years) and the Child Health Utility 9D Index (CHU-9D), at 1 year
8. Incremental costs measured using CRF data, PICANet and NHS Digital at 30 days

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Overall study start date

01/08/2020

Completion date
30/11/2026

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 11/08/2023:

1. Age >37 weeks corrected gestational age and <16 years
2. Enrolled within 6 hours of first meeting all the following criteria:
2.1. Accepted for or admitted to a participating PICU
2.2. Face-to-face contact with PICU staff or transport team
2.3. On invasive mechanical ventilation
2.4. Receiving a continuous infusion of vasoactive drug for hypotension
2.5. Vasoactive drug expected to continue for at least 6 hours or more

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Previous participant inclusion criteria:

1. Age >37 weeks corrected gestational age and <16 years
2. Accepted for or admitted to PICU
3. Receiving a continuous infusion of a vasoactive drug for hypotension commenced within the previous 6 hours
4. Vasoactive drug expected to continue for at least 6 hours or more
5. On invasive mechanical ventilation

Participant type(s)
Patient

Age group
Child

Lower age limit
37 Weeks

Upper age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 1900; UK Sample Size: 1900

Key exclusion criteria
Current exclusion criteria as of 25/06/2025:

1. Admitted post cardiac surgery
2. Known cardiomyopathy
3. Neonates with suspected or proven duct dependent circulation
4. Acute brain injury
5. Currently being treated for pulmonary hypertension
6. Admitted with malignant hypertension
7. Death perceived as imminent
8. Previously recruited to PRESSURE either in the last 30 days or during the same hospital admission

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Date of first enrolment
01/11/2021

Date of final enrolment
30/11/2025

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
St Mary's Hospital
Imperial College Healthcare NHS Trust
The Bays
South Wharf Road
London
United Kingdom
W2 1BL

Study participating centre
Leicester Royal Infirmary
University Hospitals of Leicester NHS Trust
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
King's College Hospital
King's College Hospital NHS Foundation Trust
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
John Radcliffe Hospital
Oxford University Hospitals NHS Foundation Trust
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Bristol Royal Infirmary
University Hospitals Bristol and Weston NHS Foundation Trust
Trust Headquarters
Marlborough Street

Bristol
United Kingdom
BS1 3NU

Study participating centre
Gartnavel Royal Hospital
NHS Greater Glasgow and Clyde
J B Russell House
1055 Great Western Road
Glasgow
United Kingdom
G12 0XH

Study participating centre
St. James's University Hospital
Leeds Teaching Hospitals NHS Trust
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Alder Hey Hospital
Alder Hey Children's NHS Foundation Trust
Eaton Road
West Derby
Liverpool
United Kingdom
L12 2AP

Study participating centre
Manchester Royal Infirmary
Manchester University NHS Foundation Trust
Cobbett House
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre

Addenbrooke's Hospital
Cambridge University Hospitals NHS Foundation Trust
Cambridge Biomedical Campus
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
The Royal London Hospital
Barts Health NHS Trust
80 Newark S
London
United Kingdom
E1 2ES

Study participating centre
Royal Stoke University Hospital
University Hospitals of North Midlands Nhs Trust
Newcastle Road
Stoke-On-Trent
United Kingdom
ST4 6QG

Study participating centre
Sheffield Children's Hospital
Sheffield Children's NHS Foundation Trust
Western Bank
Sheffield
United Kingdom
S10 2TH

Study participating centre
Queens Medical Centre
Nottingham University Hospitals NHS Trust
Trust Headquarters
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Freeman Hospital
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Great Ormond Street Hospital for Children
Great Ormond Street Hospital for Children NHS Foundation Trust
Great Ormond Street
London
United Kingdom
WC1N 3JH

Study participating centre
University Hospital of Wales
Cardiff & Vale University LHB
Woodland House
Maes-Y-Coed Road
Cardiff
United Kingdom
CF14 4HH

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

Study participating centre
Birmingham Children's Hospital
Birmingham Women's and Children's NHS Foundation Trust
Steelhouse Lane
Birmingham
United Kingdom
B4 6NH

Study participating centre
Royal Hospital for Children and Young People
50 Little France Crescent
Edinburgh
Lothian
United Kingdom
EH16 4TJ

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

Sponsor details
Addenbrookes Hospital
Hills Road
Cambridge
England
United Kingdom
CB2 0QQ
+44 (0)1223 217418
research@addenbrookes.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.cuh.org.uk/

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR128895

Results and Publications

Publication and dissemination plan

1. The protocol will be uploaded to https://www.icnarc.org/Our-Research/Studies/Current-Studies
2. The Final Report will be submitted to the NIHR HTA Programme for publication in Health Technology Assessment
3. The findings from PRESSURE will also be published in appropriate peer-reviewed scientific journals and relevant professional journals

Intention to publish date

31/05/2027

Individual participant data (IPD) sharing plan

An anonymised dataset will be prepared for sharing by request from Dr David Inwald (di260@cam.ac.uk) and requests will be approved by the Trial Management Group (TMG).

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		17/04/2024	15/05/2024	Yes	No