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A platform trial to identify the best treatments for critically ill children admitted to paediatric intensive care

Submission date
13/09/2025

Recruitment status
Not yet recruiting

Registration date
05/12/2025

Overall study status
Ongoing

Last Edited
05/12/2025

Condition category
Other

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

Plain English summary of protocol

Background and study aims
There is an urgent need to improve treatment for critically ill children on paediatric intensive care units (PICUs). Randomised controlled trials provide the best evidence, but the way we do these trials is slow and expensive. It usually takes several years for enough children to be included in a study before we have enough information to tell which treatment is safer. A randomised adaptive platform is an alternative way of doing trials. It allows multiple treatments and research questions to be tested at the same time under one platform. An important feature is that the trial can 'adapt' as it goes along. For example, new treatments or research questions can be added when they become available. The results are also looked at during the trial, not just at the end. This means treatments that are working better in the trial can be given to more patients sooner, while those that are less safe or less effective can be stopped earlier. The primary objective is to evaluate multiple widely used treatments at the same time to improve clinical care for critically ill children on PICU, initially focusing on evaluating three treatment areas.

Who can participate?
Patients aged under 16 years who have face-to-face contact with PICU or transport team staff, are receiving at least one of respiratory, cardiovascular, or renal support, and are expected to remain on organ support the following day.

What does the study involve?
Patients who meet the platform-level eligibility will be assessed against specific treatment area eligibility criteria. Those eligible for one or more treatment areas will be enrolled into the trial. Patients will be followed up to 6 months after enrolment.

What are the possible benefits and risks of participating?
All treatments and strategies used in the PIVOTAL study are commonly used in PICU and reflect current practice in the UK so there is a little additional risk to participants. There is no guarantee that participating in this study will directly benefit the participants but may help to improve future care and outcomes for children in PICU requiring organ support. All participants,

regardless of which domain or treatment group they are in, will be monitored closely for any side-effects or serious adverse events by the site teams.

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

When is the study starting and how long is it expected to run for?
January 2026 to March 2030

Who is funding the study?
National Institute for Health and Care Research (NIHR) – Health Technology Assessment Programme (UK)

Who is the main contact?
Tasnin Shahid, PIVOTAL@icnarc.org

Contact information

Type(s)
Scientific, Principal investigator

Contact name
Prof Mark Peters

Contact details
30 Guildford Street
London
United Kingdom
WC1N 1EH
+44 (0)20 78138118
mark.peters@ucl.ac.uk

Type(s)
Public

Contact name
Ms Tasnin Shahid

Contact details
Napier House
24 High Holborn
London
United Kingdom
WC1V 6AZ
+44 (0)20 45136238
PIVOTAL@icnarc.org

Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Integrated Research Application System (IRAS)
1012497

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
23IF39

Study information

Scientific Title
Paediatric Intensive Care Adaptive Platform Trial (PIVOTAL)

Acronym
PIVOTAL

Study objectives
The principal research question aims to find out the effect of a range of intervention(s) to improve outcomes for critically ill children receiving organ support (for example to help their breathing, heart or kidneys) on a paediatric intensive care unit. This is defined by the outcome death or days alive and free from organ support to day 30 (this encompasses both survival and the number and duration of organs supported).

The primary health economic objective is to investigate the effect of the intervention(s) on incremental net-benefit at 180 days.

The secondary objectives are to investigate the effect of the intervention(s) on other important patient-, family- and healthcare-centred outcomes.

Ethics approval required
Ethics approval required

Ethics approval(s)
notYetSubmitted

Study design
Open randomized controlled parallel-group Bayesian adaptive platform trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions

PIVOTAL is a multi-centre, randomised, Bayesian adaptive platform trial which aims to evaluate multiple interventions simultaneously in paediatric intensive care. Patients who meet the platform eligibility criteria will be screened for each domain against the domain-specific eligibility criteria. Patients will be randomised if they are deemed eligible for one or more domains using the central web-based randomisation system Sealed Envelope. In circumstances where patients may later become eligible, pending a change to their condition or additional information becoming available, a delayed reveal may be used for individual domains.

Currently available domains:

Fluid Domain:
Patients receiving invasive mechanical ventilation in PICU will be eligible for the domain and must be randomised within 12 hours of meeting the platform and domain inclusion criteria. If the patient is deemed eligible, they will be randomised on a 1:1 basis to receive either of the following:
1. Conservative fluid management, this is comprised of two components: (i) conservative fluid administration and (ii) active fluid removal
2. Usual fluid management
The intervention will continue until the end of study day 7 or the child is no longer on organ support or PICU discharge, whichever comes first.

Sedation Domain:
Patients receiving invasive mechanical ventilation and receiving or about to receive a continuous IV sedative will be eligible for the domain and must be randomised within 12 hours of meeting the platform and domain inclusion criteria. If the patient is deemed eligible, they will be randomised to receive one of the following:
1. Continuous IV infusion of dexmedetomidine
2. Continuous IV infusion of clonidine
3. Continuous IV infusion of midazolam
Patients will initially be randomised 1:1:2 to dexmedetomidine, clonidine and midazolam in the non-cardiac stratum and 1:1:3 in the cardiac stratum for those sites offering all interventions. Patients will be randomised 1:1 to dexmedetomidine and clonidine in those sites opting out of midazolam. The intervention will continue until clinical decision to discontinue or 30 days after randomisation, whichever comes first.

Blood Transfusion Thresholds Domain:
Patients with a Hb less than or equal to the relevant threshold outlined below will be eligible for the domain:
1. Non-cardiac stratum: Hb <85g/L in children without acute brain injury or Hb <100g/L in children with acute brain injury
2. Cardiac stratum: Hb <100g/L in children aged >28 days (non-neonate) or Hb <120g/L in children aged ≤28 days (neonate)
Where a patient meets all eligibility criteria at the time of randomisation, their allocation will be revealed immediately. In circumstances where patients may later become eligible, pending a change to their condition or additional information becoming available, a delayed reveal will be used. If the patient is deemed eligible, they will be randomised on a 1:1 basis to receive either of the following:
1. Restrictive transfusion strategy
2. Liberal transfusion strategy
The intervention will continue until day 30 or PICU discharge, whichever comes first.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Dexmedetomidine, clonidine, midazolam

Primary outcome(s)
1. Clinical outcome: Ordinal outcome of death or days alive and free from organ support to day 30. Organ support will be defined as receipt of respiratory, cardiovascular, or renal support within PICU according to the Paediatric Critical Care Minimum Dataset. This will be measured from medical records and linkage to death registrations and PICANet.
2. Health economic outcome: Incremental net benefit at 180 days will be assessed using data from linkage to national hospital episode statistics, death registrations and PICANet.

Key secondary outcome(s))
1. Duration of PICU and hospital stay measured from medical records and linkage to PICANet at the relevant timepoints
2. 90- and 180-day mortality post-randomisation measured from medical records and linkage to death registrations and PICANet
3. Serious adverse events/reactions during the PICU stay (censored at 30 days post-randomisation) collected from medical records
4. Health-related quality of life at 180 days measured using age-appropriate PedsQL questionnaire

Completion date
31/03/2030

Eligibility

Key inclusion criteria
Platform inclusion criteria:
1. Gestational age at birth ≥37 weeks, or combined gestational age and post-birth age ≥37 weeks, and <16 years at the time of randomisation
2. Face-to-face contact with PICU or transport team staff
3. Receiving at least one of respiratory, cardiovascular or renal support
4. Expected to remain on organ support the following day

Patients who meet the platform eligibility criteria will then be screened for each domain against the domain-specific eligibility criteria. Patients will be randomised if they are deemed eligible for one or more domains. In circumstances where patients may later become eligible, pending a change to their condition/additional information available, a delayed reveal may be used for individual domains.

Fluid domain:
1. Receiving invasive mechanical ventilation

Sedation domain:
1. Receiving invasive mechanical ventilation
2. Receiving, or about to receive, a continuous intravenous (IV) sedative

Blood transfusion thresholds domain:

Non-cardiac stratum:
Hb <85 g/L in children without acute brain injury or Hb <100g/L in children with acute brain injury

Cardiac stratum:
Hb <100 g/L in children aged >28 days (non-neonate) or Hb <120g/L in children aged ≤28 days (neonate)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
0 years

Upper age limit
16 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Platform exclusion criteria:
1. Death perceived as imminent
2. Previously recruited to a domain in PIVOTAL either in the last 30 days or during the same hospital admission

Patients who meet the platform eligibility criteria will then be screened for each domain against the domain-specific eligibility criteria. Patients will be randomised if they are deemed eligible for one or more domains. In circumstances where patients may later become eligible, pending a change to their condition/additional information available, a delayed reveal may be used for individual domains.

Fluid domain:
1. Admitted with a condition that requires a specific fluid management regimen (e.g. diabetic ketoacidosis, tumour lysis syndrome, diabetes insipidus)

2. Participating in another research study that determines fluid management
3. Receiving renal replacement therapy (RRT) or Extracorporeal Membrane Oxygenation (ECMO)
4. Over 12 hours since meeting the platform and domain inclusion criteria

Sedation domain:
1. Known hyper-sensitivity or contraindication to one of the sedative agents
2. Known pregnancy
3. Over 12 hours since meeting the platform and domain inclusion criteria

Blood transfusion thresholds domain:
1. Haemoglobinopathies (e.g. sickle cell disease, thalassemia) where red blood cell transfusions may be used to prevent haemolytic or aggregation crises
2. Unrepaired cyanotic congenital heart disease and/or functionally single ventricle circulation and/or palliated parallel circulation
3. Known advance decision refusing blood/blood component transfusions (e.g. Jehovah's Witnesses)
4. Receiving Extracorporeal Membrane Oxygenation (ECMO)
5. Receipt of RBC transfusion for a reason other than bleeding or extracorporeal support (on ECMO or for priming renal replacement circuit) since meeting the platform inclusion criteria

Date of first enrolment
01/01/2026

Date of final enrolment
01/09/2029

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Study participating centre
Addenbrooke's Hospital
Hills Road
Cambridge
England
CB2 0QQ

Study participating centre

Alder Hey Children’s Hospital
E Prescot Rd
Liverpool
England
L14 5AB

Study participating centre
Birmingham Children's Hospital
Steelhouse Lane
Birmingham
England
B4 6NH

Study participating centre
Bristol Royal Hospital for Children
Upper Maudlin Street
Bristol
England
BS2 8BJ

Study participating centre
Evelina London Children's Hospital
St Thomas' Hospital
Westminster Bridge Road
London
England
SE1 7EH

Study participating centre
Freeman Road Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
England
NE7 7DN

Study participating centre
Great North Children's Hospital
Victoria Wing
Royal Victoria Infirmary
Newcastle upon Tyne

England
NE1 4LP

Study participating centre
Great Ormond Street Hospital for Children
Great Ormond Street
London
England
WC1N 3JH

Study participating centre
John Radcliffe Hospital
Headley Way
Headington
Oxford
England
OX3 9DU

Study participating centre
Leeds Children's Hospital
Clarendon Wing
Leeds
England
LS1 3EX

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
England
LE1 5WW

Study participating centre
Nottingham Children's Hospital
Queen's Medical Centre
Derby Road
Lenton
Nottingham
England
NG7 2UH

Study participating centre
Royal Brompton Hospital
Sydney Street
London
England
SW3 6NP

Study participating centre
Royal London Hospital
Whitechapel Road
London
England
E1 1FR

Study participating centre
Royal Manchester Children's Hospital
Oxford Road
Manchester
England
M13 9WL

Study participating centre
Royal Stoke University Hospital
Newcastle Road
Stoke-on-trent
England
ST4 6QG

Study participating centre
Sheffield Children's Hospital
Western Bank
Sheffield
England
S10 2TH

Study participating centre
Southampton Children’s Hospital
Tremona Road
Southampton

England
SO16 6YD

Study participating centre
St George's Hospital
Blackshaw Road
Tooting
London
England
SW17 0QT

Study participating centre
St Mary's Hospital
Praed Street
London
England
W2 1NY

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

Study participating centre
Royal Hospital for Sick Children (Glasgow)
1345 Govan Road
Glasgow
Scotland
G51 4TF

Study participating centre
Noahs Ark Childrens Hospital for Wales
Cardiff & Vale University Health Bd
Heath Park
Cardiff
Wales
CF14 4XW

Study participating centre
The Royal Belfast Hospital for Sick Children
274 Grosvenor Road
Belfast
Northern Ireland
BT12 6BA

Sponsor information

Organisation
Great Ormond Street Hospital for Children NHS Foundation Trust

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

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	Participant information sheet	11/11/2025	11/11/2025	No	Yes