

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

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<b>Registration date</b> 05/12/2025	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 06/03/2026	<b>Condition category</b> Other	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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?

March 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

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## Contact information

### Type(s)

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**Additional identifiers****Integrated Research Application System (IRAS)**

1012497

**Central Portfolio Management System (CPMS)**

61160

**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)**

approved 10/12/2025, East of England - Cambridge South Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, United Kingdom; +44 207 104 8084; cambridgesouth.rec@hra.nhs.uk), ref: 25/EE/0214

## 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

Current interventions as of 06/03/2026:

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 second randomisation 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

As some sites may not enrol patients to one of the interventions, the randomisation ratios may be adjusted from equal randomisation for some intervention combinations to achieve 1:1:1 randomisation overall. 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  $\leq$ 85g/L in children without acute brain injury or Hb  $\leq$ 100g/L in children with acute brain injury
2. Cardiac stratum: Hb  $\leq$ 100g/L in children aged  $>$ 28 days (non-neonate) or Hb  $\leq$ 120g/L in children aged  $\leq$ 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 second randomisation will be carried out. 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.

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Previous 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

Current key inclusion criteria as of 06/03/2026:

1. Gestational age at birth  $\geq 37$  weeks, or combined gestational age and post-birth age  $\geq 37$  weeks, and
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.

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  $\leq 85$  g/L in children without acute brain injury or Hb  $\leq 100$ g/L in children with acute brain injury

Cardiac stratum:

Hb  $\leq 100$  g/L in children aged  $>28$  days (non-neonate) or Hb  $\leq 120$ g/L in children aged  $\leq 28$  days (neonate)

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Previous key inclusion criteria:

Platform inclusion criteria:

1. Gestational age at birth  $\geq 37$  weeks, or combined gestational age and post-birth age  $\geq 37$  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.

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**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**

Current key exclusion criteria as of 06/03/2026:

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

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

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Previous key exclusion criteria:

Platform exclusion criteria:

1. Death perceived as imminent
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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**

30/03/2026

**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 Prescott 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

**ROR**  
<https://ror.org/03zydm450>

## **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