PRotocolised Evaluation of permiSSive blood pressure targets versus Usual caRE (PRESSURE)

Randomisation training

(SOP 004 Patient randomisation)
Eligibility

Inclusion Criteria

• Age >37 weeks corrected gestational age and <16 years

• Accepted for or admitted to PICU

• Receiving a continuous infusion of vasoactive drug for hypotension commenced within previous 6 hours

• Vasoactive drug expected to continue for at least 6 hours or more

• On invasive mechanical ventilation
Exclusion Criteria

- Admitted post cardiac surgery
- Known cardiomyopathy
- Neonates with suspected or proven duct dependent circulation
- Brain injury
- Pulmonary hypertension
- Malignant hypertension
- Death perceived as imminent
- Previously recruited to PRESSURE
Intervention

Permissive Blood Pressure Target - intervention arm

- Target range based on age (5th centile MAP threshold to 5th centile MAP threshold + 5 mmHg)

<table>
<thead>
<tr>
<th>Age range (completed months/years)</th>
<th>Target range</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 6 months</td>
<td>40 - 43</td>
</tr>
<tr>
<td>6 months – less than 1 year</td>
<td>40 - 45</td>
</tr>
<tr>
<td>1 - 3 years</td>
<td>45 - 50</td>
</tr>
<tr>
<td>4 - 9 years</td>
<td>50 - 55</td>
</tr>
<tr>
<td>≥10 years</td>
<td>55 - 60</td>
</tr>
</tbody>
</table>

Usual care - control arm

- As per local practices
Access to the randomisation service

• Eligible patients can be randomised using Sealed Envelope
  o Accessible by either telephone or web
  o Available 24 hours a day/seven days a week.

• Only staff members that have received trial training, as recorded on the Training Log, are able to randomise patients into the trial.

• A hard copy of the Randomisation Form must be completed for each patient at the point of randomisation.

• Immediately after each randomisation, an auto-generated email will be sent to nominated members of the site research team and ICNARC CTU confirming the details.
Timing

• Once a patient is confirmed eligible using the Randomisation Form, randomisation should occur as soon as possible (but no longer than 6 hours from first fulfilling the eligibility criteria).

• Randomisation will occur prior to the start of any trial treatment.

• Randomisation will occur prior to written informed consent.
# Randomisation Form

## Eligibility check

### Inclusion – all must be yes

- Age >37 weeks corrected gestational and <16 years
- Accepted for or admitted to PICU
- Receiving a continuous infusion of vasoactive drug for hypotension commenced within previous 6 hours*
- Vasoactive drug expected to continue for 6 hours or more
- On invasive mechanical ventilation

*Please Note: If the patient is not on vasoactive drugs, please consider them for Oxy-PICU

### Exclusion – all must be no

- Admitted post cardiac surgery
- Known cardiomyopathy
- Neonates with suspected or proven duct dependent circulation
- Brain injury
- Pulmonary hypertension
- Malignant hypertension
- Death perceived as imminent
- Previously recruited to PRESSURE

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**Patient Initials / Hospital Number:**

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Randomisation form

How to randomise

If all inclusion criteria are "Yes" and all exclusion criteria are "No" dial: 020 3384 6368

Study number: 2996 Investigator number: xxx

or log on to: https://www.sealedenvelope.com/access

<table>
<thead>
<tr>
<th>Telephone/web randomisation</th>
<th>Telephone/web randomisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does the patient meet all inclusion criteria?</td>
<td>Yes</td>
</tr>
<tr>
<td>Age: (In completed years or months)</td>
<td>Y</td>
</tr>
<tr>
<td>If less than 1yr put '0' in years (YY), then complete months (MM)</td>
<td>M</td>
</tr>
<tr>
<td>When did patient commence continuous infusion of vasoactive drug for hypotension?</td>
<td>Today</td>
</tr>
<tr>
<td>What is the patient's Mean Arterial Pressure at randomisation?</td>
<td>mmHg</td>
</tr>
</tbody>
</table>

Details required by randomisation service

Unique 3 digit Investigator number will be provided for each site
Randomisation form

Details from randomisation service

Randomisation: Permissive Blood Pressure Target P

Usual care C

If randomised to "Permissive Blood Pressure Target", please tick off the correct limit on the right hand table

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</table>

Date/time of randomisation: DD MMM YY HH:MM (24-hour clock)

Randomised by: 
(print name)

Eligibility confirmed by 
(if different to above): 
(print name)

Signature:

Once complete, ensure form is stored in ISF

Confirmation of randomisation

Sign off by trained staff member
Telephone randomisations
Telephone randomisations

To access the telephone randomisation service - trained staff members should call the randomisation line on

020 3384 6368

and enter the Study Number (2996) and the 3 digit Investigator Number of your site
Retrieval Teams

- Each retrieval team has a specific Randomisation Form which contains the Investigator Numbers for the sites they may be going to.

- Please ensure when you randomise an eligible participant, you input the Investigator Number for the hospital you are taking the patient to.

- Please note that not all hospitals have green light approval, therefore please ensure to only randomise patients to hospitals that are open for PRESSURE recruitment and the patient has been accepted there.
Telephone randomisations

• The caller is taken through the randomisation process by a pre-recorded voice which asks questions regarding:
  
  o Patient’s eligibility
  o Age
  o Commencement of vasoactive drugs
  o MAP at randomisation

• The instructions given on the telephone should be followed, with all answers given using the digits on your telephone keypad.

• The caller is asked at various points to confirm the details which have been provided.
Telephone randomisations

- The caller will then be told the:
  - Treatment group that the patient has been randomised to
    - Permissive Blood Pressure Target (and the appropriate range for their age) or Usual care
  - Date/time of randomisation
  - Patient’s Trial ID.

- These details must be recorded on the Randomisation Form (and in the patient’s medical notes).

- The Randomisation Form must be signed off by the person conducting the randomisation and retained in the ISF at the receiving site.

- Retrieval Teams, please ensure to hand over the completed Randomisation Form with the patient at the receiving hospital.
Web randomisations
Web randomisations

• To access the web randomization system, a trained member should log onto the randomisation service website at:

https://www.sealedenvelope.com/access

• The user will be prompted to enter data regarding:
  
  o Patient’s eligibility
  o Age
  o Commencement of vasoactive drugs
  o MAP at randomisation
Web randomisations

Randomisation

Eligibility Criteria

Does the patient meet all inclusion criteria? *

- Yes
- No

[reset]

Does the patient meet any exclusion criteria? *

- Yes
- No

[reset]
# Web randomisations

## Patient details

<table>
<thead>
<tr>
<th>Field</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial ID</td>
<td>Automatically generated</td>
</tr>
<tr>
<td>Age - years (in completed years)</td>
<td>If the patient is completed months only, this option will open up follow ‘0’ being entered in year</td>
</tr>
<tr>
<td>Number (up to 2 digits)</td>
<td></td>
</tr>
<tr>
<td>When did the patient commence continuous infusion of vasoactive drug for hypotension?</td>
<td></td>
</tr>
<tr>
<td>1 today</td>
<td></td>
</tr>
<tr>
<td>2 yesterday</td>
<td></td>
</tr>
<tr>
<td>What time did the patient commenced continuous infusion of vasoactive drug for hypotension?</td>
<td>hh:mm</td>
</tr>
<tr>
<td>What is the patient’s Mean Arterial Pressure at randomisation?</td>
<td>mmHg. Number (up to 3 digits)</td>
</tr>
</tbody>
</table>
Web randomisations

Select the site the patient is being randomised to using the drop down menu.
Web randomisations

Review and sign

This form has not yet been saved. Please complete the declaration below to save the form.

Investigator's declaration

By entering my password below I declare that the information presented in this form accurately reflects the medical records, including the results of tests and evaluations performed on the dates specified.

Name
Raul Szekely (ID 12960 - Investigator)

Date
24 Aug 2021 13:56 (UTC)

Password *

Confirm

After selecting ‘Randomise’ the user will be instructed to save the form by completing the Investigator’s declaration.

The user must then scroll down to the Investigator’s declaration section, enter their password and select ‘Confirm’.
Web randomisations

• Once submitted, the user will be presented with the:
  o **Treatment group** that the patient has been randomised to
  o **Date/time of randomisation**
  o **Patient’s Trial ID**.

• These details must be recorded on the Randomisation Form (and in the patient’s medical notes).

Randomisation

The subject was successfully randomised.

Randomised to **Permissive Blood Pressure Target with a lower limit of 55 and upper limit of 60** on 24 Aug 2021 14:57 (BST)
Randomisation problems/errors

- **General problems with randomisation?**
  - Contact your local site research team in the first instance.
- **Patient is randomised incorrectly?**
  - Notify the ICNARC CTU on **020 7269 9277** during office hours;
  - Continue with the randomised treatment (unless deemed clinically inappropriate), and consent and data collection procedures must be carried out as per protocol.
- **Same patient is accidentally randomised more than once?**
  - Use the first patient Trial ID and treatment group, and notify the ICNARC CTU. Do not re-use the second patient Trial ID.
- **Unsure if a randomisation has been carried out?**
  - Double check randomisation notification emails or the web randomisation system;
  - Alternatively, contact your local site research team or the ICNARC CTU.
ICNARC CTU PRESSURE Team

Email: pressure@icnarc.org

Tel: 020 4514 6248 (Alanna Brown)
    020 7831 6878 (Raul Szekely)

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