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NIHR | National Institute for Health and Care Research

PICU Platform Trial

Study to develop a platform trial for critically ill children

icnarc | intensive care national audit & research centre

Great Ormond Street Hospital for Children NHS Foundation Trust

UNIVERSITY OF LIVERPOOL

This project was funded by the National Institute for Health Research Health Technology Assessment Programme (NIHR 155476). The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the HTA Programme, NIHR, NHS or the Department of Health.

RESEARCH REFERENCE NUMBERS

PROTOCOL VERSION NUMBER AND DATE 1.0, 10.03.23

REC NUMBER

SPONSOR

Intensive Care National Audit & Research Centre

FUNDER NAME AND REFERENCE

National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (NIHR 155476)

CHIEF INVESTIGATOR

Paul Mouncey (ICNARC), Mark Peters (GOSH) and qualitative lead Kerry Woolfall (UoL)

SPONSOR REPRESENTATIVE

Peter Hyde, ICNARC

Signature Page

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to appropriate research governance frameworks and any subsequent amendments of regulations, GCP guidelines, the Sponsor's SOPs and other regulatory requirements as amended.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Date:

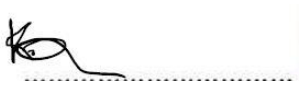
17/10/2016

Name: Peter Hyde

Position: Chief Operating Officer, ICNARC

Qualitative study lead

Signature:



Date:

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Table of Contents

Abbreviations

PICU paediatric intensive care unit
NHS National Health Service
RCT randomised controlled trial
REC Research Ethics Committee
SMG study management group

General information

This document describes qualitative work packages in the PICU Platform Trial study and provides information about procedures for the study. Participant recruitment will be undertaken in compliance with this document.

1 STUDY SUMMARY

1.1 Protocol summary

Title:	Study to develop a platform trial for critically ill children
Short title:	PICU Platform trial development study
REC number:	
Sponsor name and reference:	ICNARC 16032023
Funder name and reference:	NIHR 155476
Study design:	Qualitative focus group style workshops and interviews
Study objectives:	To conduct preparatory work necessary for the establishment of a large, ambitious, Bayesian, randomised, multifactorial, adaptive, platform trial for paediatric intensive care. To address this overarching aim, a qualitative study will explore the views of parents, carers, young people and PICU staff on how the trial should be developed.
Study centres:	N/A
Population:	UK parents with experience their child's admission to of intensive care, NIHR Young Person Advisory Group members and Paediatric Intensive Care Unit staff
Planned sample size:	56
Duration:	11 months
Follow up duration:	N/A
Planned study period:	March 2023 to February 2024

2 BACKGROUND INFORMATION

2.1 Introduction and rationale

What is the problem being addressed?

In recent years, the number of randomised controlled trials (RCTs) aiming to answer important research questions and find the best treatments for children in PICUs has increased substantially. The current way of conducting these RCTs is that selected patients are allocated to receive one of two alternative treatments and the different questions (or RCTs) are tested one after another. Once each RCT recruits a fixed number of participants, it stops and the next one starts. This is inefficient, costly to the NHS and means that it takes a long time to answer important research questions and identify the best treatments for critically ill children. A randomised adaptive platform trial is an alternative to the current way of conducting RCTs. A platform trial is designed specifically to allow multiple research questions and treatments to be tested at the same time. An 'adaptive' platform trials also allow for changes (or 'adaptations') to the design of the trial as it is being conducted. This means that new treatments or research questions can be added to the trial as they are identified. The data from patients are also looked at more often rather than just at the end of the trial. This helps inform the treatments that stay in the study. Over time this means that patient in the trial will be offered the treatments that look like they work best, and less safe or not as effective treatments are stopped. This means that more questions can be answered, more efficiently and in less time. Platform trials were used with huge success to identify the best treatments during the COVID-19 pandemic. We want to use the experience from these trials in COVID-19 to develop an adaptive platform trial in PICU. To do this, first we need to do some research to inform the how an adaptive platform trial would work in PICU so that we can appropriately design the study and its procedures. The aim of this research is to conduct some targeted work involving key stakeholders to design a randomised adaptive platform trial in paediatric intensive care units (PICUs).

2.2 Aims and objectives

The aim of the study is to conduct preparatory work necessary for the establishment of a large, ambitious, Bayesian, randomised, multifactorial, adaptive, platform trial for paediatric intensive care. To address this overarching aim, a mixed methods approach will be employed encompassing patient, service user and parent engagement, paediatric intensive care stakeholder engagement and statistical modelling and methodological work. This protocol outlines two qualitative work packages that will involve workshop style focus groups and interviews with parents, young people, Patient and Public Involvement partners and PICU medical, nursing and research staff.

3 STUDY DESIGN AND CONDUCT

3.1 Setting

Parents and young people in the UK with knowledge of, or involvement in, paediatric clinical trials

3.2 Work package 1 Exploring parent and young people's perspectives on the platform trial design.

There is a lack qualitative insight into parent, child and young persons' perspectives on acceptable and optimal PICU platform trial design. We have carefully designed a qualitative work package involving focus group style workshops and interviews to review and explore the views of a diverse group of parents and young people who do and do not have experience of PICU or clinical trials. This research will address the following objectives:

- To review and agree trial design, including initial domains and consent process
- To identify important, relevant, patient-centred primary and secondary outcomes for the PICU platform trial
- To review plans for patient and community information needed for a PICU platform trial and initiate a codesign of materials
- To establish optimal approaches for ongoing parent, patient and carer involvement in the PICU platform trial

Eligibility criteria

Inclusion criteria

- Young people who are members of an NIHR Young Persons advisory Group (YPAG)
- Parents who are patient and public involvement members of a clinical trial (e.g. who are on a trial steering group or trial management group)
- Parents with experience of PICU and/or have been involved in a PICU study in the last three years

Exclusion criteria

- Unable to speak English

Recruitment and sampling

YPAG members

We will send a direct email to YPAG coordinators (e.g. Liverpool and Birmingham) and ask them to forward an invitational email or letter (whichever is preferred) and participant information sheet to their members. The invite and YPAG PIS will explain the aims of this study, what a platform trial is and invite them to take part in a workshop style focus group. The focus will be face to face (preferred) or online if the particular YPAG no longer meets face to face. We will ask YPAG members to register interest in taking part in the workshop style focus group with the aim of involving 8-10 young people in one of two groups. This letter will also state that we are particularly interested in involving young people with experience of hospital or PICU admission, but this is not essential.

Following parental consent (see below) A suitable date for the face to face or online focus group will be arranged to coincide with one of the regular YPAG meetings or as a separate meeting if their timetable does not have a long enough slot available. The invite will explain that the option of taking part in one of up to ten (online via Zoom or Microsoft Teams or by telephone) individual interviews will also be provided if YPAG members are unable to attend the focus group, or would prefer a one to one online interview format.

Parents

We will invite parents to participate in one of two online workshop style focus groups using our existing networks and databases of parents involved in previous engagement activities, or those involved in previous and ongoing NIHR funded studies (e.g. FEVER, First-ABC, Oxy-PICU, PRESSURE, PICnIC, TOAST, TOSCIN) who provided consent for contact for future related studies. For existing databases, we will send a personalised email (specific to the study their child was involved in and which team they had previous contact with) and Parent Participation Information Sheet (Parent PIS) to our contacts and ask them to register interest in taking part in an online focus group. We will recruit 6-8 parents in each group.

To ensure the inclusion of disadvantaged and ethnic minority groups and those less familiar with clinical trial design (but with PICU experience) we will also advertise the focus groups through the Paediatric Critical Care Society and use targeted advertisements on social media.

Arranging focus group workshops and interviews

The UoL researcher will contact those who register interest in participation. Focus groups or interviews will be arranged at a time (and preferred format) suitable for the participant or scheduled YPAG meeting. Parents and young people will be asked to read the Participant information sheet and draft platform trial PIS before the scheduled focus group or interview.

Any participants who express an interest in taking part but are not selected for an interview (due to sufficient interest) will be contacted via telephone or email to thank them for their interest in the study.

Informed consent

Parents of YPAG members: When the YPAG member registers interest in participation the researcher will check eligibility ask for parental contact details (email or telephone number) and contact parents to share the young person Participant Information Sheet so they can see what their child is being asked to participate in. The researcher will then provide and opportunity for questions and seek parental consent for their child's participation. This will involve the researcher phoning the parent and seeking verbal, audio recorded parental consent for their child to take part in the study and the researcher will complete a consent form (YPAG Parental consent form). The researcher will sign the consent form and send a copy to parents via email or post (whichever the parent prefers) after the telephone call.

Face to face focus groups: The RA will seek written informed consent for the study using the Participant Consent (for Parents and PICU staff) or Assent Form (for YPAG). The participant and the researcher will read and sign the consent form before the focus group commences.

Telephone or online interviews*:* The researcher will begin by explaining the aims of the study, providing an opportunity for questions and verbally obtaining informed consent for the study. This will involve the researcher reading each aspect of the consent or assent form to participants, including consent/assent for audio recording and to receive a copy of the findings when the study is complete. The RA will tick each box on the consent form when the participant provides verbal consent/assent. Informed consent discussions will be audio recorded for auditing purposes. After the interview is complete the researcher will sign the consent form and send a copy to participants. If a focus group takes place online we will use break out rooms to seek consent from each participant individually before the session begins.

Interview and workshop style focus group conduct

Consent for audio recording of the focus group or interview will be checked verbally before they commence. All focus groups and interviews will be conducted by the researcher using the relevant topic guide. Topic guides will be developed to explore study aims and objectives with age-appropriate presentations (focus groups) or descriptions (interviews) from the researchers which will cover:

- an overview of platform trials and how these differ from standalone RCTs;
- acceptability of a proposed PICU Platform trial including, initial trial domains, outcome measures, and consenting process; and
- potential content of information sheets and any proposed leaflets, posters, videos/animations.

For the future PICU platform trial, we will seek views on areas where patient and carer involvement are needed, such as involvement in the future domain prioritisation process. Respondent validation will be used so that unanticipated topics identified in the early analysis of focus groups and interviews will be added to topic guides and researcher presentations/descriptions as the study progresses.

Given the topic of the research, we do not envisage the interviews or focus groups will cause participants upset or distress. However, any distress during the interviews or focus groups will be managed with care and compassion. Participants will be free to decline to answer any questions that they do not wish to answer or to stop the interview or leave the focus group at any point. Any such families will be supported in obtaining appropriate help.

3.3 Work package 2

This Work Package will engage with the wider PICU community to explore their perspectives on the platform trial design, including governance and collaborations necessary to support the delivery. We will maximise input from the key PICU community and how PICU platform trial workshops where we will present the proposed design and governance structure of the PICU platform trial. Objectives will be to:

- Explore composition of the governance structure to oversee the PICU platform trial.

- Explore views on initial domains, interventions and clinical leads for the PICU platform trial and process for prioritisation of new domains.
- Explore views of the primary outcome, patient group and test case scenarios to inform the statistical modelling.
- Discuss options for the practical implementation of the PICU platform trial, including patient consent, randomisation and data collection/management.

Eligibility

- Research active PICU clinicians including medical, nursing and research nurse staff

Recruitment and sampling

To ensure input from a wide variety of stakeholders involved in paediatric intensive care research, we will host two online focus group style workshops involving 6-10 participants in each.

We will invite participants using a social media and direct email to existing research networks, including all members of the PCCS-SG and via contacts at research teams at sites from ongoing (and recently completed) PICU trials (FEVER, First-ABC, Oxy-PICU, PRESSURE, PICnIC).

We will ask people to register interest in taking part in the workshop style focus group with the aim of involving 6-10 participants in one of two groups. Selection will aim for variance in role (e.g. mix of medical, nursing) and geographical location (across the UK).

Arranging focus group workshops

The UoL researcher will contact those who register interest in participation. Focus groups or interviews will be arranged at a time suitable for the participants and will take place on Zoom or Microsoft Teams. Potential participants will be sent a Participant Information Sheet, which they will be asked to read before the scheduled focus group.

Any participants who express an interest in taking part but are not selected (due to sufficient interest) will be contacted via telephone or email to thank them for their interest in the study.

Focus groups: The RA will seek written informed consent for the study using the Participant Consent Form. The participant will sign the consent form and return it to the research team via email before the focus group commences. There will also be an option to complete the consent process in a break out room before the focus group begins following the same protocol for online interview consent outlined above.

Workshop style focus group conduct

Consent for audio recording of the focus group or interview will be checked verbally before they commence. All focus groups and interviews will be conducted by the researcher using the relevant topic guide. Early findings from WP1 will be fed into focus group discussions in this work package. Areas of discussion will include, the composition of oversight committees, and confirming how intervention will be prioritised for the platform. Vital to this will be ensuring there is a clear pathway for the identification of new study domains and new investigators/clinical leads, but also to establish the relationship between other interventional studies (i.e. co-enrolment), which are not part of the platform. Respondent validation will be used so that unanticipated topics identified in the early analysis of focus groups and interviews will be added to topic guides and researcher presentations/descriptions as the study progresses.

3.4 Data analysis for WP1 and WP2

Recordings from the meetings and interviews will be transcribed, checked and anonymised as the study progresses. QSR NVivo software will be used to assist in the organisation and indexing of qualitative data. Whilst thematic analysis[1] will be informed by the constant comparison approach[2] of grounded theory, the focus will be modified to fit with the criterion of catalytic validity, whereby findings should be relevant to future research and practice (i.e. the design of the proposed PICU platform trial).

4. Dissemination and outputs

Outputs from Work package 1 will include: 1. Recommendations for trial design, including initial trial domains. 2. Confirmation of the important, patient-centred, outcomes 3. Establish roles and responsibilities for ongoing parent, patient and carer involvement in the PICU platform trial, including formation of a Patient and Parent Advisory Group. 4. Agreed informed consent process and related patient-facing materials.

Outputs from Work package 2 will include: 1. Agreed governance structure to oversee the PICU platform trial. 2. Agreed initial domains, interventions and clinical leads for the PICU platform trial and process for prioritisation of new domains. 3. Confirmation of the primary outcome, patient group and test case scenarios to inform the statistical modelling (see Work package 3). 4. Agreed plan for practical implementation of the PICU platform trial, including patient consent, randomisation and data collection/management.

5. Plan of investigation and timetable:

Work Package 1 – Qualitative research with parents and young people

Months 1-3 Workshops with YPAGs and parents

Months 4-8 Qualitative analysis

Work Package 2 – PICU community engagement

Months 1-3 Workshops with members of PICU community

Months 4-8 Qualitative analysis

6. Project management

Paul Mouncey is the chief investigator and Mark Peters is the clinical co-Chief Investigator for the overall study, which includes statistical modelling workplaces that are not part of this protocol. Kerry Woolfall will lead on the qualitative research outlined in this protocol alongside Julies Menzies who is leading on Patient and Public Involvement. A study management group will be set up to oversee the study.

7. Ethical approval

This protocol, patient information resources (e.g. PISs), consent forms and other study-related documents will be reviewed and approved by the NIHR HTA Programme and an NHS Research Ethics Committee (REC) with respect to scientific content and compliance with applicable research regulations involving human subjects. Any modification to the protocol and/or study-related documents which may impact on the conduct of the study, potential benefit to patients or patient safety will require a formal amendment. Such amendments will be submitted for approval by the NHS REC.

8. Patient and Public Involvement

Engagement and communication with the patients, service users and wider PICU stakeholders will be central to this research and shape the design of the PICU platform trial. We have, therefore, developed PPIE and PICU stakeholder work packages to be completed in the early stages of the award that will inform later work packages focussed around developing the Bayesian statistical. modelling and health economic methods required to appropriately design and conduct a PICU platform trial. Building on work already conducted in preparation for developing a PICU platform trial, we will set-up and convene an a patient and public involvement advisory group (PPAG) to develop and agree arrangements for patient, service user and carer involvement in the PICU platform trial and who will continue to advise on all aspects of the set-up, conduct, delivery and oversight with the aim of changing the paradigm of doing research 'to' patients/service users into doing research 'with' and 'by' the patients/service users. Once convened, the PPAG will work closely with the other oversight committees and PICU stakeholders (including PICU clinical and research staff) to help agree the trial population (including inclusion/exclusion criteria), domains/interventions to be tested as well as co-produce the study procedures, including patient consent, randomisation and data collection/management (Work package 2). Further to the PPIE and PICU stakeholder work packages, during the final months of the Acceleration Award and in preparation for the PICU platform trial, we will undertake a wider public and community engagement and insights programme where we will begin to review the patient and community information needed and initiate a co-design of materials for the PICU platform trial.

9. Participant confidentiality and data protection

Names and full addresses (postal and email) will be collected from participants whom wish to take part in an interview. These details will be used to contact them to arrange interviews and send copies of the consent form and study findings (if participants request a copy). We will also seek consent to contact parents/legal representatives in the future about related studies. The contact details collected will not be used for any other purpose. All personal data will be. held at the University of Liverpool. No personal data will be transferred electronically between sites. All files bearing participant identifiers (e.g. contact details) will be destroyed at the end of the study and only participants' consent forms will be retained.

Audio recordings of interviews and focus groups will be uploaded by the RA securely to a professional transcription company website (UK Transcription) in accordance with the Data Protection Act 2018. Interview audio recordings will be anonymised by the researcher as soon as the transcript is received from the professional transcription company. Any names or potentially identifying information will be removed. Audio recordings will be deleted when the researcher has checked transcripts against the audio recordings for accuracy. Audio recordings of consent for interviews will be held for auditing purposes.

All data will be securely stored in a locket cabinet or in an encrypted electronic file. The digital audio recordings are likely to contain details that could identify participants. Audio recordings of interviews and focus groups will be anonymised during transcription. All original files will be labelled with a unique identity number, encrypted and held on password protected University of Liverpool desktop computers. As soon as the digital recordings have been transcribed, the digital files will be archived securely at the University of Liverpool. Publication of direct quotations from participants is necessary to report the results of qualitative research, but no identifying information will appear in transcripts and therefore none will appear in quotations.

Participation will be entirely voluntary and parents/guardians will be able to withdraw at any time without giving a reason by contacting the RA or Woolfall. This will be described in the PIS.

The datasets for each work-stream will remain stored at their host institutions as outlined above and the members of the research team based there will provide summary data and analysis for publications as required. There will be no final data transfer combining the data into one raw dataset.

10. Sponsorship

Sponsor Name: Intensive Care National Audit & Research Centre
Address: Napier House, 24 High Holborn, London WC1V 6AZ
Contact: Peter Hyde
Email: Peter.Hyde@icnarc.org

11. Funding

The study is supported by grant funding from the NIHR Health Technology Assessment (HTA) Programme.

12. Publication policy

Participants from Work Packages 1 and 2 will be asked for consent to retain contact details and to receive a summary of the findings and a summary of the planned PICU platform trial. The findings of this Acceleration Award grant and outline for the PICU platform trial will also be presented at future PCCS-SG and PICS meetings which will be attended by all key stakeholders. With input from the YPAG and PPIE partners, we will agree a wider dissemination strategy for the findings and the planned PICU platform trial.

13. References

1. Braun V, Clarke V, Hayfield N, et al. Thematic Analysis. In: Liamputtong P (ed) *Handbook of Research Methods in Health Social Sciences*. Singapore: Springer Singapore, 2019, pp.843-860.
2. Glaser B. The Constant Comparative Method of Qualitative Analysis. *Social Problems* 1965; 12: 436-445.