

# A paediatric intensive care study comparing the use of non-absorbable antibiotics and standard infection control to prevent secondary infection in critically ill children

<b>Submission date</b> 14/10/2020	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 30/10/2020	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 01/03/2024	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Each year, around 20,000 children are admitted to paediatric intensive care units (PICUs) in the UK. Critically ill children are at a higher risk of hospital-acquired infections. Many of these infections are caused by 'bad' bacteria in the digestive tract, such as those in the mouth and stomach. Normally there are higher levels of 'good' bacteria in the digestive tract. When someone is very poorly, the number of 'bad' bacteria may rise and spread to other organs. This can then cause severe illnesses, such as pneumonia and sepsis, and lead to long-term health problems, increased hospital costs and even death.

All PICUs have several methods to reduce the risk of hospital-acquired infections, such as providing antibacterial gel on units. One possible method is to treat patients with antibiotics that stop the growth of bacteria in the digestive tract. This treatment is called selective decontamination of the digestive tract (SDD). It has been shown in adults to reduce the number of hospital-acquired infections and improve survival. However, it is unclear if it works in children.

As large clinical trials are expensive, it is important to be confident that a trial can be done and that the different components of the trial can all work together. Before embarking on a full trial, we will conduct an 18-month feasibility study including a pilot trial. A feasibility study is a piece of research done before the main trial to answer the question "Can this trial be done?" and is used to estimate important factors such as willingness of patients to take part. A pilot trial is a miniature version of the full trial and is done to check that the different components, such as recruiting patients, delivering treatment and follow-up, all run smoothly.

Our aim is to compare giving SDD with not giving SDD (usual care) in children admitted to an NHS PICU. We also need to be sure that if SDD is used, it does not lead to a rise in resistance to antibiotics either in the patient or in the whole community

### Who can participate?

A child can participate in the study if they are admitted to one of the 6 PICUs taking part in the trial and are expected to be on a breathing machine for at least 48 hours. We plan to include up to 324 patients and estimate 90 will receive SDD.

This study will also involve conducting interviews with parents of participating children to understand whether the study was acceptable to them, review how they were approached and the information provided, and what outcome measures are most important to them.

### What does the study involve?

Six PICUs will be randomly assigned to either deliver, or not, SDD to eligible patients. All PICUs will start off not delivering SDD. Then halfway through, 3 of the PICUs will switch to delivering SDD. This type of study is known as a cluster randomised controlled trial. It ensures that the two groups of units, and the patients in those units, are as similar as possible, except for the delivery and receipt of SDD. It therefore allows us to see whether SDD is any more or less beneficial than the usual care given in the NHS. We will also monitor levels of antibiotic resistant bacteria in all participating PICUs by taking swabs from patients.

SDD is a mixture of antibiotic and antifungal in paste and liquid forms given in the following ways:

- A pea-sized amount of paste in your child's mouth
- 0.5 - 2 teaspoons of liquid through their feeding tube

This is done four times a day until the child no longer needs help from the ventilator.

### What are the possible benefits and risks of participating?

SDD a treatment that can be used to reduce the number of bacteria within the gut which prevents any "bad" bacteria moving to other organs and causing serious infections. There are very few risks to a child from taking part. SDD has been in use for more than 30 years and is routine practice in many hospitals. The paste can taste a little bitter but will stop being used once the child is no longer ventilated.

### 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?

April 2020 to October 2022

### Who is funding the study?

National Institute for Health Research (NIHR) (UK) Health Technology Assessment (HTA) Programme (project number: 16/152/01)

### Who is the main contact?

Dr Nazima Pathan, np409@medschl.cam.ac.uk

### Study website

<https://www.icnarc.org/Our-Research/Studies/Picnic/About>

## Contact information

### Type(s)

Scientific

**Contact name**

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**Contact details**

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**Additional identifiers****EudraCT/CTIS number**

Nil known

**IRAS number**

239324

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

CPMS 44969, IRAS 239324

**Study information****Scientific Title**

A pilot cluster randomised clinical trial of the use of selective gut decontamination in critically ill children: Paediatric Intensive Care and Infection Control (PICnIC)

**Acronym**

PICnIC

**Study objectives**

PICnIC is a feasibility study designed to determine whether it is possible to conduct a cluster randomised trial (cRCT) of Selective Decontamination of the Digestive tract (SDD) in critically ill children who are likely to be ventilated for >48 hours, and to explore and test the acceptability of key components of the study to healthcare professionals and families of patients.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Approved 23/09/2020, West Midlands – Black Country Research and Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 104 8010; blackcountry.rec@hra.nhs.uk), ref: 20/WM/0061

**Study design**

Interventional cluster randomized case controlled study

**Primary study design**

Interventional

**Secondary study design**

Cluster randomised trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

Not available in web format, please use the contact details to request a patient information sheet

**Health condition(s) or problem(s) studied**

Digestive tract infection in critically ill children

**Interventions**

The PICnIC study is a pilot, parallel group cluster randomised clinical trial (cRCT) that includes an integrated mixed methods study. We will discuss the cRCT and mixed-methods separately. The whole study has designed as a miniature version of a potential definitive cRCT and will test feasibility and the study procedures.

**cRCT**

Participating sites will undergo an 8-week baseline period of usual care, during which sites will be randomised to either continuing usual care (control) or delivering SDD (intervention) in the second 8-week period. There will be a 2-week transition period between the delivery of usual care and starting the intervention. The trial is unblinded, SDD will become usual practice for participating PICUs randomised to deliver the intervention.

There will be three 1-week observational ecological assessments over the course of the study: pre-trial; during the transition period; post-trial.

Eligible patients will be:

1. AgeD >37 weeks (corrected gestational age) and <16 years
2. Receiving mechanical ventilation expected to last at least 48 h (and expected to remain so until the day after tomorrow)

All patients admitted to the study PICU during the ecological surveillance weeks will be included, regardless of their ventilation status.

The intervention will be started in all eligible patients as it will form part of the standard infection control strategy in the participating PICU. In addition to usual care, the follow SDD regimen will be adopted:

1. A 6-hourly topical, application of a pea-sized (0.5 g) amount of paste to the mouth
2. A 6-hourly administration of liquid given via the existing feeding tube into the stomach via the nose. The amount of liquid given will vary based on the child's age between half a teaspoon – 2 teaspoons (2.5 – 10 ml)

Treatment will be given 30 minutes before feeds, where feeding is not continuous. This dosing regimen is based on that in use in a UK PICU for a period of over 10 years. The intervention will start in all eligible patients within 6 h of the child fulfilling the inclusion criteria. It will continue until the patient is extubated or for 30 days, whichever is sooner.

Readmitted patients will continue to receive the intervention, as it will form part of the standard care bundle but would not be counted as a separate enrolment.

Per standard practice, routine surveillance swabs will be taken from all patients on admission. Additional surveillance swabs will then be taken twice-weekly until discharge (or on the day of discharge for admission durations less than 7 days). Samples taken will be:

1. Respiratory
2. Urine
3. Stool or rectal
4. Wound (where present)

Data collection will be restricted to data required to address the objectives. Where possible, data will be obtained from standard data collection via PICAnet to maximise efficiency. A number of additional data points will be collected to inform possible outcomes for a definitive trial (duration of invasive mechanical ventilation, days alive and free of mechanical ventilation censored at 30 days, infectious episodes during PICU admission, total antibiotic usage in PICU, duration of PICU stay and hospital stay, mortality at PICU discharge and 30 days post-randomisation).

Adverse events will be monitored and reported up to 30 days post-randomisation.

#### Mixed Methods study

##### Health Care Professionals

All health care professionals currently working in a UK PICU will be invited to take part in an online survey. Additionally, focus groups will be held with healthcare professionals from two of the participating PICUs, with opportunities for telephone interviews for those unable to attend the group.

These will explore health care professionals' views on:

- acceptability of the trial design including selection of, and adherence to, the SDD intervention;
- acceptability of recruitment and deferred consent procedures in the trial; and
- acceptability of the overall trial procedures.

##### Parents/Guardians

The parents/guardians of each recruited child will be asked to complete a short, anonymous questionnaire which will seek their experiences of:

- recruitment and emergency consent;
- content and format of the PIS;
- decision-making in the PICU setting; and
- acceptability of the overall trial procedures.

Parents/guardians will also be invited to take part in a more detailed telephone interview. Interviews will be completed until data saturation (anticipated to be 15-25 based on previous studies).

## **Intervention Type**

Drug

## **Phase**

Not Applicable

## **Drug/device/biological/vaccine name(s)**

Colistin, tobramycin, nystatin

## **Primary outcome measure**

Feasibility outcomes:

1. Adherence to the SDD intervention assessed by the proportion of eligible children allocated to the intervention that receive SDD using case report forms
2. Estimation of recruitment rate measured using ...
3. Questionnaires and interviews will be used to explore parents/legal representatives' views on: the acceptability of conducting a definitive trial; the content and understanding of the information materials; acceptability of the recruitment and consenting procedures; and the selection of important, relevant, patient-centred, primary and secondary outcomes for a definitive trial.
4. Two focus groups and up to 10 interviews with practitioners involved in the pilot cRCT, as well as an online survey of all UK PICU staff will be used to assess: the acceptability of the implementation of the SDD intervention; interest in participation in a definitive trial in the wider PICU community; the acceptability of the recruitment and consenting procedures for the definitive trial; and the acceptability of collecting data for assessing the selected clinical and ecological outcomes

## **Secondary outcome measures**

There are no secondary outcome measures

## **Overall study start date**

01/04/2020

## **Completion date**

31/10/2022

# **Eligibility**

## **Key inclusion criteria**

Pilot cRCT:

1. Aged >37 weeks (corrected gestational age) and <16 years
2. Receiving mechanical ventilation expected to last at least 48 h (and expected to remain so until the day after tomorrow)

Mixed methods study:

3. Online survey/telephone interviews: All health care professionals working in a PICU within the

UK

4. Focus Groups: All healthcare professionals working in the two PICUs selected for focus groups

5. Survey/telephone interviews: Parents/legal representatives of all recruited patients

**Participant type(s)**

Patient, Health professional

**Age group**

Mixed

**Lower age limit**

37 Weeks

**Upper age limit**

16 Years

**Sex**

Both

**Target number of participants**

Planned Sample Size: 324; UK Sample Size: 324

**Total final enrolment**

361

**Key exclusion criteria**

1. Known allergy, sensitivity or interaction to polymyxin E, tobramycin, or nystatin
2. Known to be pregnant
3. Death perceived as imminent

**Date of first enrolment**

20/09/2021

**Date of final enrolment**

13/02/2022

**Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Addenbrookes Hosital**

Hills Road

Cambridge

United Kingdom

CB2 0QQ

**Study participating centre**  
**Birmingham Children's Hospital**  
Steelhouse Lane  
Birmingham  
United Kingdom  
B4 6NH

**Study participating centre**  
**John Radcliffe Hospital**  
Headley Way  
Oxford  
United Kingdom  
OX3 9DU

**Study participating centre**  
**Southampton General Hospital**  
Tremona Road  
Southampton  
United Kingdom  
SO16 6YD

**Study participating centre**  
**Bristol Royal Hospital for Children**  
Upper Maudlin Street  
Bristol  
United Kingdom  
BS2 8BJ

**Study participating centre**  
**St. Georges Hospital**  
Blackshaw Road  
London  
United Kingdom  
SW17 0QT

**Sponsor information**



**Organisation**

Cambridge University Hospitals NHS Foundation Trust

**Sponsor details**

Addenbrookes Hospital  
Hills Road  
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CB2 0QQ  
+44 (0)1233 245151  
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: 16/152/01

**Funder Name**

National Institute for Health Research (NIHR) (UK)

**Alternative Name(s)**

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

# Results and Publications

## Publication and dissemination plan

The Protocol will be uploaded to website <https://www.icnarc.org/Our-Research/Studies/Picnic/About>

The Final Report will be submitted to the NIHR HTA Programme for publication in Health Technology Assessment. The findings from PICnIC will also be published in appropriate peer reviewed scientific journals and relevant professional journals.

## Intention to publish date

30/04/2023

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>		11/03/2022	14/03/2022	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Results article</a>		07/12/2023	11/12/2023	Yes	No
<a href="#">Results article</a>		01/02/2024	01/03/2024	Yes	No