

Fever pilot trial

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| Submission date 31/07/2017 | Recruitment status No longer recruiting | <input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol |
| Registration date 14/08/2017 | Overall study status Completed | <input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results |
| Last Edited 20/09/2023 | Condition category Infections and Infestations | <input type="checkbox"/> Individual participant data |

Plain English summary of protocol

Background and study aims

A fever (high temperature) is a normal response by the body to infection. When a very sick child has a fever, the usual reaction from clinicians (doctors/nurses) is to cool down the child. This can be done using drugs, such as paracetamol, using a cooling mat or sponging the child with water. The temperature at which clinicians usually start these treatments is about 37.5°C. There is strong evidence, however, that fever may be an important bodily response and may actually help a child to recover from infection. In 2013, the National Institute for Health and Care Excellence (NICE) updated guidance for managing fever in children. It recommended that drugs should not be used only for the purpose of reducing a child's temperature. Most of the evidence for this recommendation came from research in non-critically ill children, therefore, it is unknown whether this recommendation should be applied to very sick children. The aim of this study is to compare giving treatments for fever at a higher temperature than usual, such as 39.5°C, with the usual temperature of around 37.5°C in children with infection admitted to an NHS paediatric intensive care unit (PICU). This is a small study to find out whether it is possible to perform a larger study to determine the effects of the current practice of strict control of fever with a more permissive approach. As large studies are expensive, it is important to be confident that this study can be done and that the different parts can work together. This study is the third part of an 18-month feasibility study. A feasibility study is research done before a full study to answer the question "can this trial be done?" It is used to estimate important factors such as willingness of parents/children to take part. The first part of this feasibility study (which has now completed) involved conducting interviews with parents/legal guardians to understand whether the proposed study is acceptable to them. Views were discussed on using deferred consent, as this study and the proposed bigger study will incorporate a deferred consent process. Deferred consent is an approach which has successfully been used in previous emergency/critical care studies and involves including a child in a study without prior consent from their parents /guardians and then seeking agreement later. The second part (which has almost completed) involved observing and collecting data on children with fever from infection in 22 PICUs to tell us how many children would need to take part in a full study and which are the best outcomes to use.

Who can participate?

Children aged under 16 with a confirmed or suspected infection causing a fever, admitted to PICU in four NHS hospitals

What does the study involve?

Participants are randomly allocated to either a permissive approach to fever management (starting drugs/cooling methods to control temperature once they reach a temperature of $>39.5^{\circ}\text{C}$), or a restrictive approach (starting drugs/cooling methods to control temperature at $\geq 37.5^{\circ}\text{C}$). Telephone interviews/questionnaires are conducted with parents/legal representatives of the recruited participants, and focus groups/questionnaires with staff in the research sites. This is to further understand the feasibility of the consent and study procedures for the potential larger study.

What are the possible benefits and risks of participating?

There is the possibility of a beneficial effect from the permissive treatment, therefore it is not considered as carrying any significant risk, but rather carrying a potential benefit. The patients not receiving permissive treatment receive usual care and are not prone to unknown risk either. Young children may have seizures during a fever, but reducing a fever does not reduce this risk. The seizures are likely to be caused by the infection that the fever is trying to help the body heal. Another possible risk is that a high temperature uses extra energy and can make the heart beat more quickly. Patients receiving permissive treatment are therefore closely monitored.

Where is the study run from?

1. Great Ormond Street Hospital (UK)
2. Alder Hey Children's NHS Foundation Trust (UK)
3. Evelina London Children's Hospital (UK)
4. Great North Children's Hospital (UK)

When is the study starting and how long is it expected to run for?

April 2017 to March 2018

Who is funding the study?

National Institute for Health Research (UK)

Who is the main contact?

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Contact information

Type(s)

Public

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Additional identifiers

Protocol serial number
34598

Study information

Scientific Title
A multi-centre randomised, parallel group pilot clinical trial investigating the feasibility of a definitive trial of a permissive temperature strategy in critically ill children with known or suspected infection

Study objectives
The aim of this study is to assess the feasibility of a trial comparing a permissive approach to fever (treat at ≥ 39.5 degC) with a standard restrictive approach (treat at > 37.5 degC).

Ethics approval required
Old ethics approval format

Ethics approval(s)
London – Hampstead Research Ethics Committee, 11/08/2017, ref: 17/LO/1139

Study design
Randomised; Interventional; Design type: Process of Care, Management of Care

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Specialty: Children, Primary sub-specialty: Allergy, Infection and Immunity ; UKCRC code/
Disease: Infection/ Other viral diseases

Interventions

Current interventions as of 04/05/2018:

The trial incorporates a pragmatic approach to temperature control in both the permissive group and restrictive group.

Permissive group: Treatments to reduce temperature are only permitted in response to a temperature at or above 39.5°C while mechanically ventilated.

Restrictive group: Treatments to reduce temperature are permitted in response to a temperature at or above 37.5°C while mechanically ventilated.

The treatment strategies for the restrictive and permissive group will commence from randomisation until PICU discharge or death.

Previous interventions:

The trial incorporates a pragmatic approach to temperature control in both the permissive group and restrictive group.

Permissive group: Treatments to reduce temperature are only permitted in response to a temperature at or above 39.5°C.

Restrictive group: Treatments to reduce temperature are permitted in response to a temperature at or above 37.5°C.

The treatment strategies for the restrictive and permissive group will commence from randomisation until PICU discharge or death.

Intervention Type

Other

Primary outcome(s)

Number of eligible patients recruited per site, per month is measured using the proportion of eligible children recorded in trial screening logs that were recruited to the Fever Pilot Trial at baseline

Key secondary outcome(s)

1. Proportion of parents/legal representatives refusing deferred consent is measured as the proportion of recruited children whose parents subsequently declined to give consent or who withdrew their child from the Fever Pilot Trial having initially given consent through study complete (an average of 24 hours)
2. The acceptability of the information and documentation and of the consenting procedures is measured using the survey responses from parents who gave and declined to give consent; and qualitative evaluation of telephone interview transcripts from interviews with parents who gave and declined to give consent at study complete (an average of 24 hours)
3. Adherence to the selected temperature thresholds for antipyretic intervention in both the higher temperature threshold (intervention) and standard care groups is measured as the proportion of time spent below the allocated threshold; and the proportion of children that received antipyretic intervention on days when their maximum temperature did not reach the allocated threshold; and the proportion of children that did not receive antipyretic intervention on days when their maximum temperature exceeded the allocated threshold at six hourly observations of temperature and antipyretic use over the first seven days as well as daily maximum peak temperature until 28 days.
4. Separation between the randomised groups in peak temperature measurement over the first 48 hours following randomisation is assessed as the difference in the mean of the maximum

temperature recorded during the first 48 hours following randomisation between the higher temperature threshold and standard care groups, presented with a 95% confidence interval at baseline

5. Length of ventilation and Length of PICU stay is measured as the proportion of randomised patients with outcome available in each group, mean (standard deviation) in each group, median and quartiles in each group at study completion (an average 2 days)

6. PICU mortality is measured as the proportion of randomised patients with outcome available in each group

number (percentage) in each group through study completion (an average 2 days)

7. Days of organ specific support is measured as proportion of randomised patients with outcome available in each group

through study completion (an average 2 days)

Completion date

13/04/2018

Eligibility

Key inclusion criteria

Current inclusion criteria as of 04/05/2018:

1. Unplanned PICU admission
2. Age \geq 28 days and $<$ 16 years
3. Referral requiring PICU admission to a participating unit
4. Fever \geq 37.5°C in the first 48 hours following contact with the paediatric retrieval service/PICU
5. New requirement for mechanical ventilation
6. Treating clinician presumes the cause of the fever is an infective process

Previous inclusion criteria:

1. Unplanned PICU admission
2. Age \geq 28 days and $<$ 16 years
3. Referral requiring PICU admission to a participating unit
4. Fever \geq 37.5°C in the first 48 hours following contact with the paediatric retrieval service/PICU
5. Receiving or requiring mechanical ventilation
6. Treating clinician presumes the cause of the fever is an infective process

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Key exclusion criteria

Current exclusion criteria as of 04/05/2018:

1. Acute encephalopathy, including convulsive status epilepticus
2. Post-cardiopulmonary bypass or known/suspected cardiomyopathy/myocarditis
3. Rhabdomyolysis
4. Malignant hyperthermia, neuroleptic malignant syndrome or drug-induced hyperthermia
5. Receiving palliative care or death perceived as imminent
6. Previously recruited to the Fever Pilot Trial

Previous exclusion criteria:

1. Acute encephalopathy, including convulsive status epilepticus
2. Post-cardiopulmonary bypass or known/suspected cardiomyopathy/myocarditis
3. Severe rhabdomyolysis
4. Sickle cell disease
5. Malignant hyperthermia, neuroleptic malignant syndrome or drug-induced hyperthermia
6. Receiving palliative care or death perceived as imminent

Date of first enrolment

01/10/2017

Date of final enrolment

31/01/2018

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

Great Ormond Street Hospital

Great Ormond Street Hospital for Children NHS Foundation Trust

Great Ormond Street

London

United Kingdom

WC1N 3JH

Study participating centre

Alder Hey Children's NHS Foundation Trust

Eaton Road

Liverpool

United Kingdom

L12 2AP

Study participating centre

Evelina London Children's Hospital

St Thomas' Hospital
Westminster Bridge Road
London
United Kingdom
SE1 7EH

Study participating centre**Great North Children's Hospital**

Victoria Wing
Royal Victoria Infirmary
Newcastle upon Tyne
United Kingdom
NE1 4LP

Sponsor information

Organisation

Intensive Care National Audit And Research Centre (ICNARC)

ROR

<https://ror.org/057b2ek35>

Funder(s)

Funder type

Government

Funder Name

National Institute for Health Research

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

Results and Publications

Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date.

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? |
|--------------------------------------|--|--------------|------------|----------------|-----------------|
| Results article | results | 01/02/2019 | 25/02/2019 | Yes | No |
| Results article | Permissive versus restrictive temperature thresholds | 07/03/2019 | 20/09/2023 | Yes | No |
| Results article | acceptability findings | 10/03/2021 | 20/09/2023 | Yes | No |
| Protocol article | | 15/06/2022 | 12/08/2022 | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |
| Study website | Study website | 11/11/2025 | 11/11/2025 | No | Yes |