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Empirical oral AntibioticS for possible urinary tract infection (UTI) in well-appearing Young febrile infants (EASY)

Submission date
29/11/2023

Recruitment status
Stopped

Registration date
26/01/2024

Overall study status
Stopped

Last Edited
22/10/2025

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Children between 1 and 3 months of age with a fever (raised body temperature) commonly undergo blood and urine tests to check for infection. They are admitted to the hospital for a minimum of 36 to 48 hours to wait for the results of their laboratory tests for infection and given intravenous antibiotics "just in case" while waiting for these results. Laboratory tests for infection involve watching to see if bacteria grow in the blood and urine samples for 36 to 48 hours. As well as these slow tests for infection, babies will usually also have some rapid tests done on a blood sample (that take a few hours) which are used to help assess how unwell a baby is. The most common infection requiring treatment with antibiotics, in babies aged 1 to 3 months is a urinary tract infection (UTI). These infections usually respond quickly to antibiotic treatment but can be difficult to diagnose. When doctors are unsure if there is a UTI, they often give intravenous antibiotics until the results of the laboratory tests for infection are available, which is typically 36 to 48 hours later. Research has shown that babies aged between 1 and 3 months who appear well and have reassuring results from rapid blood tests can be treated with oral antibiotics. Likewise, several international guidelines have been published that recommend oral antibiotics as first-line treatment for infants with a suspected UTI. The EASY study aims to determine if babies with a suspected UTI can be treated with oral antibiotics whilst they wait for their laboratory results. This approach has the potential to reduce the need for painful procedures such as injections, reduce hospital admissions with its associated stress for parents /guardians and reduce healthcare costs.

Who can participate?
Children aged 29 to 90 days old (infants from their 29th day of life to their 90th day of life inclusive) with suspected urinary tract infection (UTI) requiring treatment with antibiotics

What does the study involve?
Participants will be randomly allocated into two groups:
Oral antibiotics and continuation of oral treatment at least until urine culture results are known

(typically after 36 to 48 hours).
Continuation of parenteral antibiotics (standard care) at least until urine culture results are known (typically after 36 to 48 hours).

What are the possible benefits and risks of participating?
It is considered that the risk associated with the antibiotics proposed for use within the EASY study is no higher than the risk of standard care. The oral and parenteral antibiotics will be used within the terms of their marketing authorisation and local prescribing protocols.
If the participant is allocated to intravenous antibiotics they will receive the same antibiotic treatment infants receive when they present to the hospital with suspected urinary tract infection (standard care). The initial insertion of an intravenous line involves some discomfort but this is usually mild. Intravenous lines have a small risk of becoming infected themselves and very occasionally can cause irritation in the vein. If this happened the line would be removed. As it is currently standard practice to give antibiotics intravenously for febrile infants with a suspected urinary tract infection, these risks are no different whether the parent/guardian agrees that their child should participate in the study or not. Complications of peripheral venous access such as extravasation injury, tissued lines and line infections will be reported as adverse events (AEs).

In the EASY study, we are investigating the use of oral antibiotics before the urine culture results are known. This may lead to earlier hospital discharge and management at home. The decision to discharge home is not mandated by the allocation to the oral antibiotic treatment group. The local clinical team should determine when the participant should be discharged and have agreed that it is an appropriate management strategy.
Both oral and intravenous antibiotics may cause diarrhoea or rash. In general oral antibiotics are more likely to cause nausea and vomiting than antibiotics given by injection. There is a risk for children in the oral antibiotic group that their infection may not resolve as quickly compared with those who continue on intravenous antibiotics. This might require a change of antibiotics or a switch back to intravenous antibiotics. If discharged home, there is a small chance they may need to come back to the hospital and possibly be readmitted if doctors feel their infection is not settling or they are becoming more unwell.
Where the participant has been discharged from the hospital, follow-up assessments will be performed via telephone 24 hours after randomisation, 36-48 hours, day 7 and day 28, asking the parent/guardian to report if their child has an ongoing fever or other symptoms of concern. Symptom data will be monitored remotely during trial follow-up by the local clinical team. If there are any concerns parents/guardians will be advised to attend the emergency department so that a medical review can be undertaken. Parents/guardians will be provided with a dedicated telephone contact number, allowing direct access to the local clinical team between 8 am – 8 pm Monday to Friday. Parents/guardians will be provided with a telephone contact number for the paediatric emergency department at the local site, which can be used at all other times, should they have any questions or concerns. Parents/guardians will be advised to attend the emergency department at any time, should they have any questions or concerns.

Where is the study run from?
The Trial Coordinating Centre is the Northern Ireland Clinical Trials Unit (NICTU) (UK). The Sponsor is the Belfast Health and Social Care Trust (BHSCT) (UK).

When is the study starting and how long is it expected to run for?
November 2023 to April 2025

Who is funding the study?
National Institute for Health and Care Research (NIHR) Health Technology Assessment (HTA) Programme (UK)

Who is the main contact?
Thomas Waterfield, t.waterfield@qub.ac.uk (UK)
Study Team, easystudy@nictu.hscni.net

Contact information

Type(s)
Scientific, Principal investigator

Contact name
Dr Thomas Waterfield

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Belfast
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BT9 7BL
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t.waterfield@qub.ac.uk

Type(s)
Public

Contact name
Dr Study Team

Contact details
-
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United Kingdom
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-
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1008782

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number

23012TW-CH, IRAS 1008782

Study information

Scientific Title
A multicentre, randomised controlled, open-label, non-inferiority trial, comparing parenteral antibiotics with oral antibiotics for the management of suspected UTI in low-risk infants

Acronym
EASY

Study objectives
Oral antibiotics are non-inferior to parenteral antibiotics for the treatment of suspected UTI in well-appearing febrile infants at low risk of meningitis and bacterial sepsis.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 22/12/2023, South Central - Hampshire A Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8120; hampshirea.rec@hra.nhs.uk), ref: 23/SC/0426

Study design
Multicentre randomized controlled open-label non-inferiority trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Urinary tract infection (UTI)

Interventions
This study investigates oral antibiotics and the continuation of oral treatment at least until urine culture results are known (typically after 36 to 48 hours).

Randomisation:
Participants will be randomised using an automated web-based or telephone system via randomly permuted blocks in a 1:1 ratio. There will be stratification by recruitment site, sex, age (29-60 days/61-90 days) and antibiotic use. Randomisation will be completed by an appropriately trained and delegated member of the research team. Each participant will be allocated their own unique Participant Study Number during the randomisation process, which will be used throughout the study for participant identification on all data collection forms and questionnaires.

Study arms:
Intervention: Oral antibiotics and continuation of oral treatment at least until urine culture

results are known (typically after 36 to 48 hours).
Comparator: Continuation of parenteral antibiotics (standard care) at least until urine culture results are known (typically after 36 to 48 hours).

The most commonly prescribed oral antibiotics are cephalexin, co-amoxiclav and trimethoprim as outlined within Table 4 of the protocol, and these will be considered as investigational medicinal products (IMP) in the EASY study. These will be used as per the manufacturer's authorisation and within their licensed range of indications, dosage, and form (according to the Summary of Product Characteristics (SPC).
The most commonly prescribed parenteral antibiotics are ceftriaxone, cefotaxime, gentamicin, amoxicillin, cefuroxime and co-amoxiclav as outlined within Table 5 of the protocol and these will be considered as investigational medicinal products (IMP) in the EASY study. These will be used as per the manufacturer's authorisation and within their licensed range of indications, dosage, and form (according to the Summary of Product Characteristics (SPC).

Intervention providers:
Clinicians, research nurses, and pharmacists will all be involved in providing the trial intervention to participants. All staff must comply with the protocol, standard operating procedures (SOPs), the principles of Good Clinical Practice (GCP), and regulatory requirements, and participate in appropriate trial training.

Modes of delivery and type of location where the intervention occurs:
Oral and parenteral antibiotics will be given as per locally determined scheduled prescription. Recruitment for the trial will take place in at least 18 paediatric emergency departments (EDs) and assessment units from across the UK, from within the Paediatric Research in the UK and Ireland (PERUKI) research network and the General and Adolescent Paediatric Research in the United Kingdom & Ireland (GAPRUKI) research network. When a febrile infant (under three months of age) attends hospital they should undergo blood and urine testing and may receive broad-spectrum parenteral antibiotics in the EDs or assessment unit pending laboratory results. This initial hospital assessment will be unaffected by the EASY study. Administration of initial parenteral antibiotics, if required based on national clinical guidelines and local policy, should not be delayed pending consent discussions. Following randomisation and where the participant is an inpatient, administration of parenteral antibiotics and oral antibiotics will occur at the hospital site and will be overseen by the clinical team. Post-discharge from the hospital, administration of the oral antibiotic will be undertaken by parents/guardians.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Amoxicillin [Amoxicillin] , Cefotaxime [Cefotaxime] , Ceftriaxone [Ceftriaxone] , Cefuroxime [Cefuroxime] , Co-amoxiclav [Amoxicillin, Clavulanic acid] , Gentamicin [Gentamicin] , Cefalexin [Cefalexin] , Co-amoxiclav [Amoxicillin, Clavulanic acid] , Trimethoprim [Trimethoprim]

Primary outcome(s)
Current primary outcome measure as of 30/04/2024:

Treatment failure (i.e. additional parenteral antibiotics) within seven days of randomisation.

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Previous primary outcome measure:

Additional parenteral antibiotics measured using data obtained from medical notes within seven days of randomisation

Key secondary outcome(s))

Current secondary outcome measures as of 30/04/2024:

The following secondary outcome measures are assessed up to 28 days after randomisation unless otherwise stated:
1. Treatment failure (i.e. additional parenteral antibiotics) assessed at day 28
2. Escalation in care defined as, escalation in the level of care (i.e. admission from home, admission to intensive care or a high dependency unit) OR change in antibiotic therapy OR death due to poor response. Assessed at 7 and 28 days.
3. Time to defervescence
4. Time to normal feeding (as reported by parent/guardian)
5. Time to normal activity (as reported by parent/guardian)
6. Length of stay
7. Antibiotic-associated adverse events (including diarrhoea and allergic reaction)
8. Antibiotic adherence (full course taken or no more than two missed doses)
9. Paediatric quality of life (measured using PedsQL acute infant version) within 24 hours of randomisation, day 7 and day 28
10. Family impact (measured using PedsQL Family Impact Module acute version) at day 7
11. Health service use and costs

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Previous secondary outcome measures:

The following secondary outcome measures are assessed up to 28 days after randomisation unless otherwise stated:
1. Treatment failure defined as, escalation in the level of care i.e. admission from home, admission to intensive care or a high dependency unit OR change in antibiotic therapy due to poor response OR Death measured using data obtained from medical notes at 7 and 28 days
2. Treatment failure in those children with a confirmed UTI measured using data obtained from medical notes within 28 days of randomisation
3. Time to defervescence measured using data obtained from medical notes
4. Time to normal feeding (as reported by parent/guardian)
5. Time to normal activity (as reported by parent/guardian)
6. Length of hospital stay measured using data obtained from medical notes
7. Antibiotic-associated adverse events (including diarrhoea and allergic reaction) measured using data obtained from medical notes and as reported by parent/guardian
8. Antibiotic adherence (full course taken or no more than two missed doses) measured using data obtained from medical notes and as reported by parent/guardian
9. Paediatric quality of life measured using the Pediatric Quality of Life Inventory (PedsQL acute infant version) within 24 hours of randomisation, day 7 and day 28
10. Family impact measured using the PedsQL (Family Impact Module acute version) at 7 days
11. Health service use and costs measured using a Health Resource Use and Activities Questionnaire as reported by the parent/guardian and data obtained from medical notes

Completion date
12/04/2025

Reason abandoned (if study stopped)
Lack of funding/sponsorship

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 18/12/2024:
1. 29 to 90 days of age (Infants from their 29th day of life to their 90th day of life inclusive. Day of birth is day 1 of life)
2. Suspected urinary tract infection (UTI) requiring treatment with antibiotics
3. History of fever as defined as temperature ≥38°C measured by any method OR likely fever in last 24 hours including subjective fever reported by the caregiver
4. Abnormal urinalysis defined as: (1) abnormal urinary dipstick test (leucocyte esterase ≥1+, or nitrite ≥Trace) OR (2) abnormal urine microscopy (≥5 white cells per high-power field in centrifuged urine or ≥10 white cells per mm3 in un-centrifuged urine or bacteriuria with any bacteria per high power field)

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Previous participant inclusion criteria as of 30/04/2024 to 18/12/2024:
1. 29 to 90 days of age (Infants from their 29th day of life to their 90th day of life inclusive. Day of birth is day 1 of life)
2. Suspected urinary tract infection (UTI) requiring treatment with antibiotics
3. History of fever as defined as temperature ≥38°C measured by any method OR likely fever in last 24 hours including subjective fever reported by the caregiver
4. Abnormal urinalysis defined as: (1) abnormal urinary dipstick test (leucocyte esterase ≥1+, or nitrite ≥Trace) OR (2) abnormal urine microscopy (≥5 white cells per high-power field in centrifuged urine or ≥10 white cells per mm3 in un-centrifuged urine or bacteriuria with any bacteria per high power field)
5. Well on global clinical assessment using the paediatric assessment triangle* assessed by a consultant grade doctor.

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Previous participant inclusion criteria:
1. 29 to 90 days of age (infants from their 29th day of life to their 90th day of life inclusive)
2. Suspected urinary tract infection (UTI) requiring treatment with antibiotics
3. History of fever as defined as temperature ≥38°C measured by any method OR likely fever in last 24 hours including subjective fever reported by the caregiver
4. Abnormal urinalysis defined as: (1) abnormal urinary dipstick test (leucocyte esterase ≥1+, or nitrite ≥Trace) OR (2) abnormal urine microscopy (≥5 white cells per high-power field in centrifuged urine or ≥10 white cells per mm3 in un-centrifuged urine or bacteriuria with any bacteria per high power field)
5. Well on global clinical assessment using the paediatric assessment triangle*[28]
6. C-Reactive Protein <20mg/l and Absolute Neutrophil Count >500 and <5200/mm3

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
29 days

Upper age limit
90 days

Sex
All

Total final enrolment
27

Key exclusion criteria
Current participant exclusion criteria as of 18/12/2024:
1. Born at <30 weeks gestation
2. Discharged from hospital more than 7 days after birth
3. History of re-admission to hospital that required treatment with parenteral antibiotics
4. Known or suspected structural renal abnormality
5. Evidence of sepsis and/or meningitis (appear unwell, shock, hypotension, altered mental state, bulging fontanelle, lumbar puncture suggestive of bacterial meningitis)
6. Received vaccination within 48 hours of attendance

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Previous participant exclusion criteria as of 30/04/2024 to 18/12/2024:
1. Born at <30 weeks gestation
2. Discharged from hospital more than 7 days after birth
3. Required re-admission to hospital after birth for more than 24 hours
4. Known or suspected structural renal abnormality
5. Evidence of sepsis and/or meningitis (appear unwell, shock, hypotension, altered mental state, bulging fontanelle, lumbar puncture suggestive of bacterial meningitis)
6. Received vaccination within 48 hours of attendance
7. Sodium < 128mmol/l on lab or blood gas sample
8. Potassium > 6.5 mmol/l on lab sample
9. Plasma creatinine > 50 micromol/l
10. Inability to tolerate oral medication
11. Urine sample was not sent for culture
12. Received additional antibiotics (with the exception of the parenteral antibiotic administered within 24 hours of hospital attendance)
13. Declined consent for participation

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Previous participant exclusion criteria:
1. Born at <30 weeks gestation
2. Discharged from hospital more than 7 days after birth
3. Required re-admission to hospital after birth for more than 24 hours
4. Known or suspected structural renal abnormality
5. Evidence of sepsis and/or meningitis (appear unwell, shock, hypotension, altered mental state, bulging fontanelle, lumbar puncture suggestive of bacterial meningitis)
6. Received vaccination within 48 hours of attendance
7. Sodium < 128mmol/l on lab or blood gas sample
8. Potassium > 6.5 mmol/l on lab or blood gas sample
9. Plasma creatinine > 50 micromol/l
10. Inability to tolerate oral medication
11. Urine sample was not sent for culture
12. Received additional antibiotics (with the exception of the parenteral antibiotic administered during initial emergency care)
13. Declined consent for participation

Date of first enrolment
01/05/2024

Date of final enrolment
12/03/2025

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Alder Hey Childrens Hospital
Eaton Road
West Derby
Liverpool
United Kingdom
L12 2AP

Study participating centre
Birmingham Childrens Hospital
Steelhouse Lane
Birmingham

United Kingdom
B4 6NH

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

Study participating centre
Oxford Children's Hospital
John Radcliffe Hospital
Headington
Oxford
United Kingdom
OX3 0AG

Study participating centre
James Cook Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Musgrove Park Hospital (taunton)
Musgrove Park Hospital
Taunton
United Kingdom
TA1 5DA

Study participating centre
Queens Medical Centre, Nottingham University Hospital
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Peterborough City Hospital
Edith Cavell Campus
Bretton Gate
Bretton
Peterborough
United Kingdom
PE3 9GZ

Study participating centre
Poole Hospital
Longfleet Road
Poole
United Kingdom
BH15 2JB

Study participating centre
The Royal Belfast Hospital for Sick Children
274 Grosvenor Road
Belfast
United Kingdom
BT12 6BA

Study participating centre
Royal Berkshire Hospital
London Road
Reading
United Kingdom
RG1 5AN

Study participating centre
Royal Cornwall Hospital (treliske)
Treliske
Truro

United Kingdom
TR1 3LJ

Study participating centre
Sheffield Childrens Hospital
Western Bank
Sheffield
United Kingdom
S10 2TH

Study participating centre
Sunderland Royal Hospital
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre
University Hospital of Wales
Heath Park
Cardiff
United Kingdom
CF14 4XW

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

Study participating centre
Countess of Chester Hospital
Countess of Chester Health Park
Liverpool Road
Chester
United Kingdom
CH2 1UL

Study participating centre
St Mary's Hospital
Imperial College London, St. Mary's Campus, Medical School, Room 231, Norfolk Place
London
United Kingdom
W2 1PG

Study participating centre
Salisbury District Hospital Laboratory
Salisbury District Hospital
Odstock Road
Salisbury
United Kingdom
SP2 8BJ

Study participating centre
Addenbrookes
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Ninewells Hospital
Ninewells Avenue
Dundee
United Kingdom
DD1 9SY

Sponsor information

Organisation
Belfast Health and Social Care Trust

ROR
https://ror.org/02tdmfk69

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
The datasets generated and/or analysed during the current study will be available upon request following the publication of the primary and secondary outcomes. Formal requests for data should be made in writing to Dr Tom Waterfield (Chief Investigator) via the Northern Ireland Clinical Trials Unit (the trial co-ordinating centre) at EASYSTUDY@nictu.hscni.net Requests will be reviewed on a case by case basis in collaboration with the Sponsor.

The study will comply with the good practice principles for sharing individual participant data from publicly funded clinical trials and data sharing will be undertaken in accordance with the required regulatory requirements. Following the publication of the primary and secondary outcomes, any requests for data will need to be made in writing to the Chief investigator via the CTU, who will liaise with the Sponsor and obtain approval for the release of the data. The participant information sheet informs parents/guardians that the data may be used in other research studies but if it is used in this way all personal identifiers will be removed and it will not be possible to identify any individual. Parent/guardian consent will also be obtained.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other files			01/10/2025	No	No
Participant information sheet	version 1.0	13/10/2023	07/02/2024	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Preprint results		17/10/2025	22/10/2025	No	No

Protocol file	version 1.0	11/10/2023	24/01/2024	No	No
Protocol file	version 2.0	20/03/2024	14/05/2024	No	No
Protocol file	version 3.0	25/09/2024	18/12/2024	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes