ISRCTN12873692 https://doi.org/10.1186/ISRCTN12873692

The Runny Ear STudy (REST)

Submission date
12/04/2018

Recruitment status
No longer recruiting

Registration date
24/04/2018

Overall study status
Completed

Last Edited
08/06/2023

Condition category
Ear, Nose and Throat

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Middle ear infections (medical term: acute otitis media or AOM) are common painful infections in children. Germs multiply in the confined middle ear resulting in a build-up of pressure that stretches the ear drum. In around 1 in 7 children, the ear drum bursts, releasing a liquid (medical term: discharge or otorrhoea) that can be seen coming out of the ear. It is commonly believed that the pain of AOM improves when the ear drum bursts, but research shows that the pain is similar with or without the ear drum bursting. At the moment nearly all UK children with AOM and discharge (AOMd) seen by their GP/nurse are treated with antibiotics by mouth. These can cause side effects like rashes, diarrhoea and vomiting and more rarely, severe allergic reactions. They can also make the germs in a child's body resistant to antibiotics. It may be possible to use alternative treatments for ear discharge. One possibility is to use antibiotic eardrops. Research has shown these are better than antibiotics by mouth for children with runny ears and grommets, probably because the antibiotics are given directly to the place they are most needed. Another potential treatment is a 'delayed' antibiotic prescription (where parents are advised to wait to see if the child's infection improves without antibiotics). Studies in other infections suggest this can be just as effective and safe, but with fewer side effects. Since AOMd is painful and distressing for children and their families it is important to show that any new treatments work at least as well as the current standard treatment (immediate antibiotics by mouth). The aim of this study is to test whether giving an antibiotic ear drop or a delayed antibiotic by mouth is as good as immediately giving antibiotics by mouth for children (without grommets) who have developed AOMd.

Who can participate?
Children aged 1 to 16 with AOMd

What does the study involve?
Participants are randomly allocated to one of three treatments: immediate antibiotic ear drops, delayed oral antibiotics or immediate oral antibiotics (usual care), all for 7 days. AOMd symptoms (pain, fever, being unwell, sleep disturbance, discharge, and episodes of distress) are assessed at the start of the study and after 14 days.

What are the possible benefits and risks of participating?
The NHS has paid for and approved this study because evidence suggests the treatment might work. Participants will be helping research to improve the future treatment for children with ear

discharge. Risks include possible allergic reactions to the antibiotic drops or antibiotics taken by mouth, but the medicines are routinely prescribed in the UK and are considered safe to use for children. The advice to gently press on the outer ear flap to help the ear drops flow into the ear hole may cause discomfort to some children. If this happens, it is not necessary to continue using the “pumping” method but to simple keep the child’s head tilted to one side for a few extra minutes, to make sure the drops have reached the ear drum. The collections of the stool samples may prove to be a sensitive issue, and therefore the stool sample collection is optional.

Where is the study run from?
175 GP practices (to be determined) (UK)

When is the study starting and how long is it expected to run for?
January 2018 to June 2020 (updated 06/02/2020, previously: October 2020)

Who is funding the study?
NIHR Health Technology Assessment Programme (UK)

Who is the main contact?
Kathryn Curtis
Kathryn.curtis@bristol.ac.uk

Contact information

Type(s)
Public

Contact name
Mrs Kathryn Curtis

Contact details
Centre for Academic Primary Care
Population Health Sciences
Bristol Medical School
University of Bristol
Canynge Hall, 39 Whatley Road
Bristol
United Kingdom
BS8 2PS
+44 (0)117 3313906
Kathryn.curtis@bristol.ac.uk

Type(s)
Scientific

Contact name
Prof Alastair Hay

ORCID ID
https://orcid.org/0000-0003-3012-375X

Contact details

Centre For Academic Primary Care
Population Health Sciences
Bristol Medical School
University of Bristol
Canynge Hall, 39 Whatley Road
Bristol
United Kingdom
BS8 2PS

Additional identifiers

Clinical Trials Information System (CTIS)
2017-003635-10

Protocol serial number
2814; HTA 16/85/01

Study information

Scientific Title
Immediate oral, immediate topical or delayed oral antibiotics for acute otitis media with discharge: the Runny Ear STudy (REST)

Acronym
REST

Study objectives
To determine whether either ciprofloxacin 0.3% drops, or delayed oral amoxicillin (clarithromycin if penicillin allergic or other suitable oral antibiotic as chosen by the GP), is non-inferior to current usual care (immediate oral antibiotics) for overall illness duration in children with Acute Otitis Media (AOMd) presenting to primary care.

More details can be found at: https://www.journalslibrary.nihr.ac.uk/programmes/hta/168501/#/

Ethics approval required
Old ethics approval format

Ethics approval(s)
South central Oxford B- Research Ethics Committee, 10/04/2018, REC ref: 18/SC/0181, IRAS ID: 229293

Study design
Multi-centre pragmatic three-arm individually randomised non-inferiority open trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acute otitis media with discharge (AOMd)

Interventions
Children will be randomised, stratified by age (<2 years and ≥2 years, since children <2 years' experience longer illness duration). Two randomisation lists will be generated as per the stratification. Blocks of 12 will be used for allocation (4 in each arm), since most practices will recruit one or two patients only. The sequence will be supplied to the TRANSFoRm platform to be allocated to each successive participant recruited.

1. Immediate topical ciprofloxacin (0.3%) solution, four drops three times daily for 7 days with written advice regarding how to administer drops
2. Delayed 'dose-by-age' amoxicillin suspension three times daily (clarithromycin twice daily if penicillin allergic or other suitable oral antibiotic as chosen by the GP) for 7 days, with structured delaying advice
3. Immediate 'dose-by-age' amoxicillin (clarithromycin) for 7 days (usual care)

Follow up will be 3 months.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Ciprofloxacin, amoxicillin, clarithromycin

Primary outcome(s)
Time to resolution of all of the following:
1. Pain
2. Fever
3. Being unwell
4. Sleep disturbance
5. Otorrhoea
6. Episodes of distress/crying being rated 'no' or 'very slight' problem (without need for analgesia)

Recorded by parents/carers using a validated Symptom and Recovery Questionnaire (SRQ) with Research Nurse telephone support at baseline to 14 days after randomisation

Key secondary outcome(s))
Secondary outcomes will include (as recorded in the first 14 days of participant entry to the trial on the symptom
recovery questionnaire):
1. Time until symptoms (pain, fever, being unwell, sleep disturbance, otorrhoea, episodes of distress/crying, appetite
and interference with normal activities) are no longer rated 'moderately bad or worse' (score of ≥3 on validated
scale) measured using the symptom recover questionnaire
2. Adverse events diarrhoea, rash, vomiting and severe complications measured on the symptom recovery questionnaire at day 7 and 14

3. Parent carer satisfaction with treatment is measured on the symptom recovery questionnaire at day 14
4. Treatment adherence and analgesic use to symptom resolution is measured using the symptom recovery questionnaire up to day 14
5. Details of NHS resource use is measured using the symptom recovery questionnaire at day 7 and 14
6. Burden of resistance is measured using stool sample at day 7 and 3 months

Completion date
30/06/2020

Eligibility

Key inclusion criteria
1. Children aged ≥12 months to <16 years
2. Presenting with recent onset (≤7 days) unilateral AOM with recent onset (≤7 days) otorrhoea currently visible (or seen by parent/carer ≤24 hours)
3. Child attending with parent/carer who is legally able to give consent in person or parent able to give verbal consent via telephone call
4. Parent/carer willing and able to administer ear drops
5. Parent/carer willing, able and available to complete the daily SRQ and received regular telephone calls from the study team

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
12 months

Upper age limit
16 years

Sex
All

Total final enrolment
22

Key exclusion criteria
Current exclusion criteria as of 04/12/2018:
1. Symptoms/signs suggestive of bilateral AOM/AOMd
2. Child has symptoms/signs suggestive of serious illness and/or complications e.g. mastoiditis and/or requires immediate hospitalisation
3. Child requires immediate oral antibiotics (e.g. for another infection or AOMd considered

severe);
4. As per NICE guidelines13, child at high risk of serious complications:
4.1. Significant immunosuppression
4.2. Heart, lung, renal, liver or neuromuscular disease (defined as requiring ongoing inpatient or outpatient care from specialist teams) co morbidities
4.3. Trisomy 21 (Down's Syndrome), Cystic Fibrosis or craniofacial malformation such as cleft palate (these children are known to be at higher risk of AOM)
5. Grommet (ventilation tube) in situ in the otorrhoea ear
6. Currently on oral (for a respiratory tract infection) or topical (in the affected ear) antibiotics
7. Allergy to ciprofloxacin
8. Allergy to penicillin/anaphylaxis to another beta lactam agent and allergy to clarithromycin
9. Child has already participated in this trial

Previous exclusion criteria 7 to 9:
7. Known allergy or sensitivity to ciprofloxacin
8. Child has taken part in any research involving medicines within the last 90 days
9. Child has already participated in this trial

Date of first enrolment
12/12/2018

Date of final enrolment
31/03/2020

Locations

Countries of recruitment
United Kingdom

Study participating centre
175 GP practices (to be determined)
United Kingdom
-

Sponsor information

Organisation
The University Of Bristol

ROR
https://ror.org/0524sp257

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 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	protocol	01/11/2021	25/11/2021	Yes	No
Protocol article		03/06/2020	06/01/2021	Yes	No
Basic results		22/07/2021	01/09/2021	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet			08/06/2023	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes