ISRCTN79914298 https://doi.org/10.1186/ISRCTN79914298

Do young children need antibiotics when they have a mild or moderate chest infection when they go to a primary care clinician?

Submission date
18/08/2015

Recruitment status
No longer recruiting

Registration date
21/08/2015

Overall study status
Completed

Last Edited
13/07/2023

Condition category
Respiratory

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

Plain English summary of protocol

Current plain English summaryas of 26/03/2020:
Background and study aims
Chest infections are one of the commonest infections managed in children seen in GP surgeries. Most children who see the doctor with a chest infection currently get antibiotics. The trouble with prescribing antibiotics for most children is that we are using these medicines too much. This in turn is causing bacteria to become resistant, which is likely to lead in the future to serious infections for our children. The groups of children that are even more likely to get antibiotics at the moment are those who have one or more particular features - phlegm, fever, shortness of breath, or rattly noises heard in the chest when the doctor listens with the stethoscope. It is a real priority to show which groups of children that GPs prescribe for currently benefit from antibiotic treatment and which do not, so that antibiotics can be used appropriately and the effectiveness of antibiotics can be conserved for future generations.

Who can participate?
Children between 6 months and 12 years old with a chest infection.

What does the study involve?
We hope to recruit participants from local general practices across England and Wales. Participant recruitment will be done by a healthcare professional appropriately trained in the study procedures. They will gain consent for each child to take part in the study from a parent or guardian. The healthcare professional will then record some details about the child's illness. An optional throat swab and a simple measure of blood oxygen will be taken from each participant. Each child will be randomly allocated to an antibiotic (amoxicillin) or a matched placebo (dummy drug). Parents and guardians will be asked to give children one dose of medication three times a day for seven days and to fill in a study diary until the child recovers or 28 days, whichever comes soonest.

What are the possible benefits and risks of participating?
The benefit of participating is not yet certain. We do know that a study of chest infections in adults that was very similar to this study showed that adults only got better, on average, one day

quicker if they had antibiotics compared to no antibiotics. This is why we are doing this research. Many chest infections are not caused by bacteria but by viruses. Viruses are not killed by antibiotics. We do however know that taking antibiotics adds to what is called Antibiotic Resistance (AMR). This is when bacteria change how they respond to antibiotics and the result is the bacteria become less sensitive and less effective. This change stays within the body for as long as six months after taking even a short course of antibiotics. If we find children do not need antibiotics to recover from chest infections we will be helping everybody who needs these important medicines as we will be saving them for the times we need them in urgent use, as well as saving children from unnecessary antibiotic side effects.

Where is the study run from?
University of Southampton, University of Oxford, Cardiff University and University of Bristol (UK)

When is the study starting and how long is it expected to run for?
July 2016 to September 2021

Who is funding the study?
NIHR Health Technology Assessment Programme - HTA (UK), reference HTA 13/34/64

Who is the main contact?
Dr Kim Harman
Prof Paul Little

Previous plain English summary:
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Chest infections are one of the commonest infections managed in children seen in GP surgeries. Most children who see the doctor with a chest infection currently get antibiotics. The trouble with prescribing antibiotics for most children is that we are using these medicines too much. This in turn is causing bacteria to become resistant, which is likely to lead in the future to serious infections for our children. The groups of children that are even more likely to get antibiotics at the moment are those who have one or more particular features - phlegm, fever, shortness of breath, or rattly noises heard in the chest when the doctor listens with the stethoscope. It is a real priority to show which groups of children that GPs prescribe for currently benefit from antibiotic treatment and which do not, so that antibiotics can be used appropriately and the effectiveness of antibiotics can be conserved for future generations.

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Who is the main contact?
Dr Kim Harman
Prof Paul Little

Contact information

Type(s)
Public

Contact name
Miss Natalie Thompson

Contact details
School of Primary Care, Population Sciences and Medical Education
University of Southampton
Aldermoor Health Centre
Aldermoor Close
Southampton
United Kingdom
SO16 5ST
+44 (0)2380 002380
artic-pc@soton.ac.uk

Type(s)
Scientific

Contact name
Prof Paul Little

Contact details

Primary Care & Population Science
Faculty of Medicine, University of Southampton
Aldermoor Health Centre
Aldermoor Close
Southampton
United Kingdom
SO16 5ST

Type(s)
Scientific

Contact name
Miss Natalie Thompson

Contact details
School of Primary Care, Population Sciences and Medical Education
University of Southampton
Aldermoor Health Centre
Aldermoor Close
Southampton
United Kingdom
SO16 5ST
+44 (0)2380 002380
N.Thompson@soton.ac.uk

Additional identifiers

EudraCT/CTIS number
2015-002455-97

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
13381; HTA 13/34/64

Study information

Scientific Title
Antibiotics for lower Respiratory Tract Infection in Children presenting in Primary Care (ARTIC PC)

Acronym
ARTIC PC

Study objectives
Acute respiratory infections are among the commonest conditions managed in primary care. The Department of Health recognises that antibiotic resistance is an increasingly serious public health problem in England, Europe and the world, with rising resistance rates for a range of

antibiotics and a clear relationship between primary care antibiotic prescribing (responsible for 80% of prescribing) and antibiotic resistance.

We are aware of no randomised placebo-controlled trials available to either support or dispute the common use of antibiotics in children with chest infections. Because of the lack of evidence in children it is difficult for GPs to go against the rising tide of antibiotic use to reduce prescribing antibiotics for children. Symptomatic predictors of prescribing include productive cough ('wet' cough/rattly chest/sputum), shortness of breath, audible wheeze and fever, which are present in between 30% and 65% of children presenting with chest infections. However, a study looking at the average effect of antibiotics would provide unconvincing evidence to persuade healthcare professionals not to prescribe, as all healthcare professionals tend to prescribe in the face of uncertainty, giving patents the 'benefit of the doubt', and continue prescribing to particular subgroups according to their own ad hoc criteria. Thus it is necessary to study the heterogeneity of these children with acute cough and explore whether clinical and pathophysiological determinants identify subgroups where antibiotic treatment is or is not effective.

Our aim is to provide evidence to inform the use of antibiotics for the management of chest infections in children. The objectives are:
1. To estimate the effectiveness of amoxicillin overall and in key clinical subgroups of children presenting with uncomplicated (non-pneumonic) lower respiratory tract infection in primary care
2. To estimate the cost-effectiveness of antibiotics overall and in key clinical subgroups of children presenting with uncomplicated lower respiratory tract infection in primary care.

Added 28/07/2016:
Our provisionally agreed list is children with:
1. Sputum seen and/or heard by parents ('rattly chest') or clinicians
2. History of fever
3. Physician rating of being unwell
4. Shortness of breath
5. Chest signs (non-focal coarse crepitations/rhonchi/wheeze)
The list of agreed primary and secondary subgroups will be finalised prior to agreeing the detailed analysis plan. The final list will take account of any new evidence and consensus among the study team, and the decision will be made blind to intervention group status.

3. To explore the estimates of effectiveness according to key pathophysiological subgroups (the presence of bacterial pathogens; raised C reactive protein measurement or white cell count; the presence of clinically undetected consolidation on X ray; oximetry; lung function)

On the assumption that the trial might demonstrate moderate benefit of antibiotic both overall and among subgroups, the potential benefits of the trial might include:
1. Reduced medicalisation and fewer unnecessary GP consultations in future episodes of LRTI
2. Reduced risk of anti-microbial resistance
3. Improved quality of care by providing evidence-based information to patients (parents) and reduced unwanted side effects in children

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/133464
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0008/164582/PRO-13-34-64.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
South West - Central Bristol Research Ethics Committee, 21/03/2016, ref: 15/SW/0300

Study design
Randomised controlled trial, with an observational study for participants ineligible for the trial (e.g. where pneumonia is suspected clinically) or where participants are unwilling to be randomised

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Lower Respiratory Tract Infection in children aged 6 months - 12 years

Interventions
Amoxicillin 50mg/kg/24 hours (in divided doses for 7 days) or placebo

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Amoxicillin

Primary outcome measure
Current primary outcome measure as of 26/07/2016:
Duration of moderately bad chest infection symptoms (from validated symptom diary; where the diary is not returned using a brief questionnaire completed either by post or by phone)

Previous primary outcome measure:
Duration of moderately bad symptoms (from validated symptom diary)

Secondary outcome measures
Current secondary outcome measures as of 26/07/2016:
1. Symptom severity (days 2-4) (measured as with the 1y outcome); duration of symptoms until

little or no problem (measured as with the primary outcome); re-consultation with non-resolving, new or worsening symptoms (from structured review of medical records); complications (from structured review of medical records)
2. Health-related quality of life will be measured by proxy methods in which the EuroQoL (EQ5D 5Y) will be completed by patients or carers (on days 1, 3, 7, 14, 21, 28)
3. Follow-up (at 1 month): measure lung function (if aged 6+; using PEFR meter)

Previous secondary outcome measures from 23/03/2016 to 26/07/2016:
1. Symptom severity (days 2-4); the development of new or worsening symptoms; complications
2. Health-related quality of life will be measured by proxy methods in which the Pediatric Quality of Life Inventory (PedsQL) and EuroQoL (EQ5D) will be completed by patients or carers (on days 1, 3, 7, 14, 21, 28)
3. Follow-up (at 1 month): measure lung function (if aged 6+)

Original secondary outcome measures:
1. Symptom severity (days 2-4); the development of new or worsening symptoms; complications
2. Health-related quality of life will be measured by proxy methods in which The Health Utilities Index (HUI-Mark III) and EuroQoL (EQ5D) will be completed by patients or carers (on days 1, 3, 7, 14, 21, 28)
3. Follow-up (at 1 month): measure lung function (if aged 6+)

Overall study start date
01/07/2016

Completion date
17/04/2020

Eligibility

Key inclusion criteria
Children between 6 months and 12 years old presenting with an acute lower respiratory infection (LRTI), defined as an acute cough as the predominant symptom, judged by the GP to be infective in origin, lasting <21 days, and with other symptoms or signs localising to the lower tract (shortness of breath, sputum, pain)

Added 26/07/2016:
Individuals who are allergic to penicillin, who cannot be randomised (e.g. with known immune deficiency, or where a complication such as pneumonia is suspected on clinical grounds), or are unwilling to be randomised, are still eligible for the observational study where the same outcomes will be measured.

Participant type(s)
Patient

Age group
Child

Lower age limit
6 Months

Upper age limit

12 Years

Sex
Both

Target number of participants
503 in the RCT

Total final enrolment
438

Key exclusion criteria
1. The cough is judged by the clinician to have a non-infectious aetiology (e.g., hayfever or non-infective exacerbation of asthma) or almost certain viral aetiology (croup, where antibiotics are not commonly prescribed)
2. Immune-compromised
3. Antibiotic use in previous 30 days
4. For the trial, suspected pneumonia based on clinical examination or being very severely ill as judged by the GP is an exclusion (but such children can still enter the observational study which will allow for an assessment of trial participants' external validity)
5. Only one child from each household will be recruited

Date of first enrolment
01/08/2016

Date of final enrolment
17/04/2020

Locations

Countries of recruitment
England

United Kingdom

Wales

Study participating centre
University of Southampton
Southampton
United Kingdom
SO16 5ST

Study participating centre

University of Oxford
Oxford
United Kingdom
OX2 6GG

Study participating centre
Cardiff University
Cardiff
United Kingdom
CF14 4XN

Study participating centre
University of Bristol
Bristol
United Kingdom
BS8 2PS

Sponsor information

Organisation
University of Southampton (UK)

Sponsor details
Research and Innovation Services Building 28
Highfield Campus
Southampton
England
United Kingdom
SO17 1BJ

Sponsor type
University/education

ROR
https://ror.org/01ryk1543

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
30/06/2022

Individual participant data (IPD) sharing plan
For anyone asking where the request is reasonable we will release the data; in the unlikely case where we feel the request is not reasonable we will ask the NIHR to arbitrate.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version v10.0	03/06/2019	26/03/2020	No	No
Results article		22/09/2021	27/09/2021	Yes	No
HRA research summary			28/06/2023	No	No
Results article		01/06/2023	13/07/2023	Yes	No