ISRCTN70714783 https://doi.org/10.1186/ISRCTN70714783

The early use of antibiotics for at risk children with influenza

Submission date 11/12/2013	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 11/12/2013	**Overall study status** Completed	
Last Edited 19/04/2022	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Flu (influenza) and flu-like illness are among the most common reasons why parents and carers take children to see a doctor or nurse in winter. Flu is a viral infection that just causes a mild cough or cold in most children. However, when some children get flu, they develop bacterial infections, such as chest or ear infections, which can make them feel even more unwell. 'At risk' children with underlying medical conditions such as asthma and diabetes are particularly prone to becoming more unwell from bacterial infections if they get flu. The aim of this study is to find out whether giving an antibiotic called co-amoxiclav to 'at risk' children within 5 days of them becoming ill with flu or flu-like illness might:
1. Help stop them from developing bacterial infections and becoming more unwell
2. Help them get better more quickly
3. Affect how well antibiotics work against similar infections in future

Who can participate?
'At risk' children between 6 months and 12 years of age, who see a doctor or nurse within the first five days of developing flu or flu-like illness. 'At risk' children include children with medical conditions such as asthma, diabetes, cancer, cerebral palsy, Down's syndrome, heart problems, kidney problems and liver problems. 'At risk' children also include children under 2 years of age who were born prematurely.

What does the study involve?
A healthcare professional gains consent for each child to take part in the study from a parent or guardian. The healthcare professional then records some details about the child's flu-like illness. A nose swab and, if possible, a throat swab is taken from each child. Each child is randomly allocated to either receive an antibiotic (co-amoxiclav) or a placebo (dummy). Parents and guardians are asked to give children one dose of medication twice a day for five days and to fill in a study diary. Parents and guardians are asked if they would be willing for their child to have further optional throat swabs after 3, 6 and 12 months.

What are the possible benefits and risks of participating?
This study will help to work out whether giving antibiotics to 'at risk' children early on when they have flu or flu-like illness is worthwhile. It may also help the government plan how to use

antibiotics during future flu epidemics or pandemics (which is when lots of people get flu all at once). The study medication may help children get better more quickly and/or prevent them from becoming more unwell from a bacterial infection. However, this is not known for sure until the end of the study.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
Recruitment will take place over three winters (2015/6, 2016/7 and 2017/8). Each winter will be defined as October to March/April inclusive

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Dr Kay Wang
kay.wang@phc.ox.ac.uk

Study website
http://www.archiestudy.com

Contact information

Type(s)
Scientific

Contact name
Dr Sharon Tonner

Contact details
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Additional identifiers

EudraCT/CTIS number
2013-002822-21

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
15212

Study information

Scientific Title
The early use of Antibiotics for at Risk CHildren with InfluEnza in primary care (ARCHIE): a double-blind randomised placebo-controlled trial

Acronym
ARCHIE

Study objectives
In 'at risk' children with influenza, early use of antibiotics reduces the likelihood of subsequent re-consultation due to clinical deterioration during the same illness episode.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North West - Liverpool East, ref:13/NW/0621, First MREC approval date 10/10/2013, ref: 13/NW/0621

Study design
Double-blind randomised placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

Participant information sheet
Patient information can be found at: http://www.phctrials.ox.ac.uk/studies/archie

Health condition(s) or problem(s) studied
Influenza and influenza-like illness

Interventions
Co-amoxiclav 400/57 or matching placebo for 5 days.
Follow Up Length: 12 month(s).
Study Entry: Single Randomisation only.

Intervention Type

Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Co-amoxiclav

Primary outcome measure
Proportion of children re-consulting due to clinical deterioration within 28 days of study entry

Secondary outcome measures
1. Duration of fever from time of study entry
2. Duration of symptoms from time of study entry
3. Proportion of children prescribed medication (e.g. antibiotics, steroids) and/or requiring further investigations (e.g. chest X-ray) within 28 days of study entry
4. Proportion of children in whom adverse events are reported within 28 days of study entry
5. Proportion of children who are hospitalised or die within 28 days of study entry

Other outcome measures:
6. Health-related quality of life measured using the EQ-5D-Y and EQ-5D-Y proxy on days 1, 4, 7, 14 and 28
7. Healthcare resource utilisation and parental/informal care costs within 28 days of study entry
8. Minimum inhibitory concentrations (MICs) of alpha-haemolytic streptococci (including Streptococcus pneumoniae), Haemophilus influenzae and Staphylococcus aureus in relation to a representative range of antibiotics 3 months, 6 months and 12 months after study entry
9. Proportion of ampicillin-resistant alpha-haemolytic streptococci (including Streptococcus pneumoniae), Haemophilus influenzae and Staphylococcus aureus 12 months after study entry
10. Prevalence of alpha-haemolytic streptococci (including Streptococcus pneumoniae), Haemophilus influenzae and Staphylococcus aureus at 12 months after study entry

Overall study start date
02/12/2013

Completion date
01/05/2019

Eligibility

Key inclusion criteria
Current inclusion criteria as of 09/08/2017:
1. Male and female, aged 6 months to 12 years inclusive
2. In 'at risk' category, including:
2.1. Aged under 2 years and born prematurely
2.2. Respiratory/renal conditions
2.3. Cardiac conditions/cancer/cerebral palsy
2.4. Hepatic/haematological conditions
2.5. Immunodeficiency
2.6. Endocrine/metabolic conditions
3. Presenting with influenza-like illness (i.e., cough and fever) during influenza season
4. Presenting within 5 days of symptom onset

5. Permanently registered at a general practice in UK
6. Parent/guardian able to complete study diary and questionnaires

Previous inclusion criteria:
1. Male and female, aged 6 months to 12 years inclusive
2. In 'at risk' category, including:
2.1. Aged under 2 years and born prematurely
2.2. Respiratory/renal conditions
2.3. Cardiac conditions/cancer/cerebral palsy
2.4. Hepatic/haematological conditions
2.5. Immunodeficiency
2.6. Endocrine/metabolic conditions
3. Presenting with influenza-like illness (i.e., cough and fever) during influenza season
4. Presenting within 5 days of symptom onset
5. Permanently registered at a general practice in England
6. Parent/guardian able to complete study diary and questionnaires

Participant type(s)
Patient

Age group
Child

Lower age limit
6 Months

Upper age limit
12 Years

Sex
Both

Target number of participants
Planned Sample Size: 650; UK Sample Size: 650; Description: randomised 1:1

Total final enrolment
271

Key exclusion criteria
Current exclusion criteria as of 09/08/2017:
1. Known contraindication to co-amoxiclav
2. Child given antibiotics for treatment of an acute infection within the last 72 hours
3. Child requires immediate antibiotics (clinician’s judgement)
4. Child requires immediate hospital admission for treatment of an influenza-related complication (clinician’s judgement)
5. Child has been observed on hospital ward or ambulatory care unit for longer than 24 hours
6. Presence of any reason to prevent healthcare professional from obtaining nasal swab
7. Child with known cystic fibrosis
8. Child previously entered into the ARCHIE study
9. Child has been involved in another medicinal trial within the last 90 days

Previous exclusion criteria:
1. Known contraindication to co-amoxiclav
2. Child given antibiotics within the last 72 hours
3. Child requires immediate antibiotics or hospital admission (clinicians judgement)
4. Presence of any reason to prevent healthcare professional from obtaining high nasal swab
5. Child with known cystic fibrosis
6. Child previously entered into the ARCHIE study
7. Child has been involved in another medicinal trial within the last 90 days

Date of first enrolment
01/10/2014

Date of final enrolment
20/04/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Nuffield Department of Primary Care Health Sciences
Oxford
United Kingdom
OX2 6GG

Study participating centre
80 active sites (most of them GP practices) - please see study website (www.archiestudy.com) for complete list of recruiting centres
United Kingdom
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Sponsor information

Organisation
University of Oxford (UK)

Sponsor details
Joint Research Office
Block 60
Churchill Hospital

Oxford
England
United Kingdom
OX3 7LE

Sponsor type
University/education

ROR
https://ror.org/052gg0110

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
United Kingdom

Results and Publications

Publication and dissemination plan
1. The protocol will be published in 2017/18
2. The results will be published in a peer-reviewed journal and disseminated to the public and patient groups via the study website (http://www.archiestudy.com) in 2019/20

Intention to publish date
30/09/2020

Individual participant data (IPD) sharing plan
The trial protocol, statistical analysis plan and de-identified participant-level data collected for the trial are available on request. Research data requests should be submitted to the

corresponding author Kay Wang (kay.wang@phc.ox.ac.uk) for consideration by the research team.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	16/05/2018		Yes	No
Results article		18/03/2021	22/03/2021	Yes	No
Other publications	Economic analysis	15/04/2022	19/04/2022	Yes	No
HRA research summary			28/06/2023	No	No