



Nuffield Department of Primary Care Health Sciences

Clinical Trials Unit
Radcliffe Observatory Quarter
Woodstock Road
Oxford, OX2 6GG

Lead Investigator: Dr Kay Wang
Study co-ordinator: Tricia Carver
E-mail: archie@phc.ox.ac.uk
Telephone: (01865) 617 842



www.archiestudy.com

The early use of **A**ntibiotics in at **R**isk **C**hildren
with **I**nflu**E**nza

Information leaflet for parents and guardians

We would like to invite you and your child to take part in the ARCHIE study.

This information leaflet explains why we are doing this research study and what it will involve for you and your child if you decide to take part. Please read it carefully before making your decision. Please ask if you have any questions.

Why have my child and I been invited to take part?

We would like to invite you and your child to take part in the ARCHIE study because your child is unwell with a flu-like illness which started within the last 5 days.

Your doctor or nurse thinks that your child has more than just a simple cough or cold, but does not have any obvious signs at the moment of a bacterial infection which needs to be treated with antibiotics. Bacterial infections can cause chest, ear, throat or sinus infections, which can make children feel more unwell. Children who get flu (also called influenza) are more prone to developing bacterial infections than children who get other types of viral infections.

‘At risk’ children with a long-term medical condition or disability are particularly prone to developing bacterial infections if they get flu or a flu-like illness. ‘At risk’ children include children with lung problems (e.g. asthma), type 1 or type 2 diabetes, cerebral palsy, Down’s syndrome, cancer, kidney problems, heart problems and problems with the immune system. Even though the ‘flu jab’ (flu vaccination) helps protect these children against some types (strains) of flu, other types of flu and viruses similar to flu can still cause flu or flu-like illness.

Why are we doing the ARCHIE study?

We would like to find out whether giving an antibiotic called co-amoxiclav to 'at risk' children (aged 6 months to 12 years) early on when they have 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.

When children first start feeling unwell, it can be difficult for doctors and nurses to tell whether they are in the early stages of a bacterial infection which might need to be treated with antibiotics. Doctors and nurses often see children who have more than just a simple cough or cold, but do not have obvious signs of a bacterial infection. Sometimes they give these children antibiotics 'just in case'. However, some of these children might have got better just as quickly without them. Giving antibiotics to children who do not need them may change the types of bacteria we find in their nose and throat and affect how well similar antibiotics work against infections in the future.

What is co-amoxiclav?

Co-amoxiclav (also known as 'Augmentin') is an antibiotic which contains a type of penicillin antibiotic. Co-amoxiclav is effective against more types of bacterial infection than ordinary penicillin antibiotics and is already licensed and commonly used to treat many types of infections in children. These include chest, ear, throat and sinus infections.

At the moment, co-amoxiclav is not licensed to prevent children, who see their doctor or nurse early on in a flu-like illness, from coming down with bacterial infections.

The ARCHIE study will help us find out whether co-amoxiclav can be used to help ‘at risk’ children in this way.

What will happen if we decide to take part?

If you and your child decide to take part, you will need to fill in and sign a consent form. If your child wants to, they may also fill in a form to say they are willing to take part.

Your doctor or nurse will then:

- Ask you some questions about your child’s flu-like illness.
- Take a nose swab and a throat swab from your child.
- Give you some study medication for your child.
- Give you a study diary to fill in.

Your child’s swabs

- If possible, your doctor or nurse will take two swabs from your child: one from the nose and another from the back of the throat.
- Your child’s swabs will be sent to the laboratories of the Alder Hey Children’s Hospital in Liverpool. The nose swab will be tested to see if your child has any respiratory viruses. The throat swab will be tested to see if your child has any respiratory bacteria.
- If you think that it won’t be possible for your doctor or nurse to take a throat swab from your child, you and your child can still take part in the rest of the study. However, you and your child will not be able to take part if it won’t be possible to take a nose swab from your child.
- Your child’s nose swab may tickle a bit and the throat swab may make him or her ‘gag’ momentarily. However, this is normal and will not hurt your child. You will be able to

comfort and support your child while the doctor or nurse is taking his or her swabs.

Your child's study medication

- Your child's study medication will either be the antibiotic (co-amoxiclav) or a 'placebo' and will be given to you in liquid form. A placebo is an inactive preparation which is otherwise identical to the medication being studied. In this study, the placebo liquid will look and taste the same as the antibiotic liquid, but will **not** contain the antibiotic itself.
- We will ask you to give your child his or her study medication twice a day for five days. Please ask your doctor or nurse to advise you if your child does not usually swallow medication.
- The type of study medication your child is given will be decided by chance, like a coin toss, and not by your doctor or nurse. Neither you nor your doctor or nurse will know whether your child has been given the antibiotic or the placebo liquid.
- The research team will also not know which type of study medication your child has been given until after the end of the study. They will only be told this sooner if any issues arise before the end of the study, which could affect the safety of children taking part.
- This is a normal part of research studies like ours. By giving some children the placebo liquid and others the antibiotic, we will be able to find out whether the antibiotics themselves really work.

What side-effects might my child get from the study medication?

- Most children will not have any side-effects from the antibiotic. However, up to 1 in 10 might get minor side-effects such as a slight stomach upset (feeling sick, vomiting or diarrhoea) or thrush (a type of fungal infection). Other less

common side-effects include skin rashes, dizziness and headaches.

- Unexpected serious allergic reactions can very rarely occur with symptoms such as lip swelling, throat tightness and difficulty breathing. If this happens, please seek medical advice immediately, or go to hospital or call for an ambulance if your child is very unwell.

What if my child gets the placebo?

- If your child gets the placebo, this does not mean that he or she will definitely get worse or develop a bacterial infection.
- If your doctor or nurse had felt that your child needed antibiotics straightaway, he or she would not have invited you to take part in the ARCHIE study.
- Whatever type of medication your child gets, a doctor or nurse or someone from the research team will give you a call one week and two weeks after your child enters the study to ask you how your child is. However, please seek advice from your doctor or nurse or take your child to hospital sooner if you think he or she is becoming more unwell.

Your study diary

We will ask you to fill in a diary about your child's flu-like illness and any complications which arise from this. In your diary, we will ask you to record:

- your child's symptoms (*e.g.* cough, shortness of breath, disturbed sleep).
- your child's temperature (we will provide you with an armpit thermometer).
- when you give your child study medication and any other medication.
- any side-effects your child has from the study medication.

- any time you take off from work, and any time that your child takes off from school or nursery.
- any visits or telephone calls with a doctor or nurse.
- your child's overall wellbeing after 4 days, 1 week, 2 weeks and 4 weeks. We can send you reminders by text or e-mail.

Your child may also fill in some questionnaires about him or herself – we will let you and your child decide this together.

We will phone you after one week and two weeks

Your doctor or nurse or a member of the research team will ask you if you have had to seek medical advice or go to hospital because of your child's flu-like illness or complications of this. They will also check with you if your child has had any side-effects from his or her study medication.

We will review your child's medical notes

We will collect some information from your child's medical notes about your child's health, medications, vaccinations and visits or telephone calls with a doctor, nurse or other healthcare professional.

We will ask you for permission to take extra swabs from your child

We will ask you if we can take three more throat swabs from your child once he or she is feeling better: one swab after 3 months, another after 6 months and a final swab after 12 months.

These swabs will help us find out what types of infections your child might be carrying in his or her throat and how effective antibiotics might be at treating these infections in the future. Your child may still take part in the rest of our study even if you

decide not to let us take these extra swabs. Please let your doctor or nurse know what you decide.

Thank you for reading about our study. If you are still interested in taking part, please read on for further information....

Do I have to allow my child to take part?

No. It is entirely up to you, and you can change your mind at any time without giving a reason. If you decide not to take part, or agree but later change your mind, you and your child will still receive the same standard of medical care.

What are the possible benefits and disadvantages of taking part?

This study will help us 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).

Giving your child his or her study medication and completing your study diary will take some of your time, around 5 to 10 minutes a day. However, all the information we ask you for is important, so please try and complete as much as you can, even if you cannot complete everything.

The study medication may help your child get better more quickly and/or prevent your child from becoming more unwell from a bacterial infection. However, we will not know this for sure until the end of the study.

What will happen to the information about my child?

The research team have a duty of confidentiality to your child as a research participant. All data will be kept securely according to the Data Protection Act 1998. Responsible people from the Universities of Oxford, Liverpool, Bristol or Southampton, the NHS Trust or the Medicines and Healthcare Products Regulatory Agency (MHRA) may be given access to data for monitoring and/or audit of the study to ensure we are complying with regulations. Your child's GP will be informed that your child is taking part in the study and they will be given a copy of the signed consent form for their records.

Non-cellular material from your child's swabs will be stored securely and confidentially in the specialist laboratories and continue to be stored there after our study has finished for use in further research. This will help the laboratories study better ways of finding infections and working out how likely they are to get better with antibiotics in the future.

What will happen if I don't want my child to carry on with the study?

If you decide you no longer wish your child to take part in our study, please let your doctor or nurse know. Alternatively, you can phone, write to or e-mail the study co-ordinator. You and your child can withdraw from the study at any time without giving a reason.

What will happen to the results of the study?

The results will be published in a scientific journal and on our website www.archiestudy.com for you to read.

Who is organising and funding the research?

This research study is part of a series of research studies known as the ARCHIE programme (The early use of Antibiotics for at Risk CHildren with Influenza in primary care). The ARCHIE programme is funded by the National Institute for Health Research. The University of Oxford is the Research Sponsor.

What will happen if there is a problem or something goes wrong?

The University of Oxford has arrangements in place in case of harm arising from participation in a study for which it is the Research Sponsor. NHS indemnity operates in respect of the clinical treatment which is provided. If you wish to complain about any aspect of the way in which you have been approached or treated during this study, you should contact the study co-ordinator or the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 572224. You may also contact the head of the CTRG office by e-mail, ctrg@admin.ox.ac.uk.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee, to protect patients' safety, rights, wellbeing and dignity. This study has been reviewed and approved by the NRES Committee North West - Liverpool East.

Thank you for reading this leaflet.

Please ask us if you have any questions.

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Nuffield Department of Primary Care Health Sciences

Clinical Trials Unit

Radcliffe Observatory Quarter

Woodstock Road

Oxford, OX2 6GG

Tel: 01865 617 842

Email: archie@phc.ox.ac.uk

Dr Kay Wang, Lead Investigator

Tricia Carver, Trial Manager

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