LEGAL REPRESENTATIVE SUMMARY INFORMATION SHEET

- for participants unable to give consent themselves.

AFLOAT Study

Antibiotics For uncomplicated Lower respiratory tract infection in Older AdulTs.

Introduction:

Your relative/friend/participant has been invited to participate in the AFLOAT clinical trial because he/she has been diagnosed with a chest infection, known medically as a lower respiratory tract infection (LRTI).

We feel that he/she is unable to decide for themselves whether to participate in this study.

To help decide if he/she should join the study, we would like to ask your opinion as to whether they would want to be involved. We would ask you to consider what you know of their wishes and feelings, and to consider their interests. Please let us know of any advance decisions they may have made about participating in research. These should take precedence.

If you decide that your relative/friend/participant would have no objection to taking part, we request that you read and sign the Legal Representative Declaration form. We will give you a copy to keep. We will keep you fully informed during the study so you can let us know if you have any concerns or think that your relative/friend/participant should be withdrawn from the study.

If you decide that your relative/friend/participant would not wish to take part, it will not affect the standard of the care they receive in any way.

If you are unsure about taking on the role of legal representative, you may seek independent advice. We will understand if you do not want to take on this responsibility.

What you need to know:

- The purpose of this trial is to find out whether patients who do not take antibiotics for a chest infection recover as quickly (are no worse off) as those who do take antibiotics.
- Why? Because most chest infections are caused by viruses, and antibiotics are not effective for these infections. Antibiotics may not speed up the healing process and can cause side effects, but this has not been tested in older adults.

- If you decide that your relative/friend/participant would have no objection to taking part, you are free to withdraw them at any time for any reason, and they will always receive the best possible care available.

Requirements to take part:

- Aged 80 or over with symptoms of a chest infection

OR

- Aged 65 or over with symptoms of a chest infection and one or more of:
  - meet the criteria for being considered frail (judged by a scoring system).
  - have had one or more unplanned hospital admissions in the last 12 months.
  - have one or more of: Diabetes, chronic cardiovascular disease, chronic lung disease, chronic kidney disease, chronic liver disease, chronic neuromuscular disease.

What you would be asked to do:

- You will be required to fill in a Legal Representative Declaration form to consent on behalf of your relative/friend/participant.
- Assist in completing a brief questionnaire today to provide information about your relative/friend/participant (like age, sex, ethnicity), and rate how they are feeling. This should take only a few minutes.

- Ascertain if your relative/friend/participant would be willing to have a finger prick blood test to measure inflammation in their body. This is optional.

- Your relative/friend/participant will be put into one of two groups at random (like tossing a coin).
  One group will be given antibiotic capsules to take for 5 days.
  The other group will be given dummy capsules that look identical to the antibiotic (known as a placebo) to take for 5 days.

- Your relative/friend/participant has equal chance of being put into either group and neither they, you nor their doctor will know which type of capsule they will be given.

- You will be asked to assist your relative/friend/participant to complete a daily diary for 28 days either on paper or using a phone or computer (your choice). This should not take up more than a few minutes of your time each day.
- A member of the central AFLOAT team may call and will send text prompts to help you and your relative/friend/participant with diary completion.

- If the AFLOAT team are informed that your relative/friend/participant has regained the ability to decide for themselves whether they would like to participate, they will be given the opportunity to review the Participant Information Sheet (attached). They are free to withdraw at any time for any reason, and they will always receive the best possible care available.

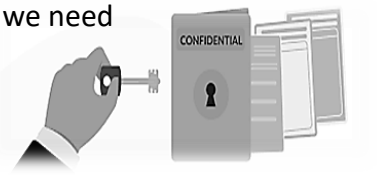
Safety:

- The antibiotic (doxycycline) used is the NHS-recommended treatment for a chest infection. The dummy capsule is completely harmless and contains no active medication
- If you feel that your relative/friend/participant's illness is getting worse or that they have symptoms that you are worried about, you are advised to contact your healthcare professional or 111. If you feel that it is an emergency, call 999 or go to the Accident and Emergency (A&E) department at your local hospital.

Confidentiality and Data Protection:

- We will need to use information from your relative/friend/participant's medical records, and their GP for this clinical trial. We will only use information that we need for the clinical trial. Their GP medical records may be accessed by the study team for a period of 3 months after the 28 day follow up period. Any data collected and any results produced will not identify your
  relative/friend/participant personally.

  At the end of the trial, we will save some of the data in case we need to check it, or for future research.



Need more information?

More detailed information about the AFLOAT Study and contact details for the AFLOAT Study team may be found in the AFLOAT Participant Information Sheet – attached.

PARTICIPANT INFORMATION SHEET

AFLOAT STUDY

Antibiotics for uncomplicated Lower respiratory tract infection in Older AdulTs.

You have been invited to participate in the AFLOAT clinical trial.

Contents

1. What is the purpose of the study?

The question we are looking at is whether patients with a chest infection who are not given antibiotics recover at the same rate (are no worse off) as those given antibiotics.

Acute cough and chest infections which affects the airways are the most common reasons for prescribing antibiotics in GP practices. Antibiotics are a type of medicine that work by killing the bacteria that is making you poorly, like in pneumonia (a more serious lung infection affecting the small air sacs). However, most chest infections are caused by viruses, so antibiotics are not effective. Antibiotics are therefore unlikely to speed up the healing process and can cause side effects.

The more antibiotics are used to treat conditions when they may not be necessary, the more likely they are to become ineffective for treating more serious conditions. Over the years, with overuse of antibiotics, there has been an increase in 'superbugs', which are bacteria that have changed in form (mutated) and have adapted to become better able to fight the effect of our antibiotics. This leads to more severe illnesses that are very hard to treat.

The public healthcare guideline developer, NICE, agrees and generally advises *against* the use of antibiotics for most patients with an uncomplicated chest infection.

2. Why are we doing the study?

Despite the general advice against the use of antibiotics for uncomplicated lower respiratory tract infection (LRTI), currently in the UK, most adults aged over 65 are treated with antibiotics. Why is this? The reason is because there is a dilemma around the best treatment of older adults with other / additional chronic medical conditions or frailty that puts them at risk of complications. In this patient group, NICE recommends that doctors *consider* treating people with antibiotics because this age group is more vulnerable to a prolonged illness and possibly the development of pneumonia. This puts doctors in a bit of a predicament trying to prescribe the best treatment to their older patients.

The problem is that the over-use of antibiotics has serious implications as they cause antibiotic-resistant organisms to be generated which then become much more difficult to treat. Antibiotic resistance is increasing and is a big public health threat, leading to serious infections becoming untreatable. The World Health Organisation (WHO) states that antimicrobial resistance is one of the top global health concerns and,

in 2019, estimated that this was directly responsible for 1.27 million global deaths. Antibiotics can also cause serious side effects and may have other harmful effects on the body.

The other issue is cost to the NHS, and it is estimated that LRTI costs the UK NHS over £190 million each year.

Therefore, we are conducting this study to determine if patients who do not take antibiotics for a LRTI are no worse off in terms of the time it takes them to recover from their illness than those prescribed the antibiotics. This will help clinicians and patients to make decisions about best use of antibiotics in the future.

3. *Can I take part?*

We are inviting people aged 65 or over who are presenting in primary care and have been diagnosed with a non-complicated respiratory tract infection (LRTI) and have at least one of the following:

- Are age 80 or over
- Meet the criteria for being considered frail judged by a scoring system
- Have had one or more unplanned hospital admissions in the past year
- Or have one or more of the following conditions: Diabetes (type 1 or 2), chronic cardiovascular disease, chronic lung disease, chronic kidney disease, chronic liver disease, chronic neuromuscular disease.

4. *Do I have to take part?*

No, taking part in the study is entirely voluntary and if you do not want to take part this will not affect your treatment in any way, now or in the future. Your legal rights will not be affected by whether you decide to take part or not.

If you do decide to take part, you will be given this information sheet to keep and asked to sign a consent form.

If you do not wish to take part in this study, you will have no further involvement in the study and will be treated as normal by the NHS service you have contacted. It is important to understand that if you are feeling unwell, you should not hesitate to contact your GP with any health concerns (as you normally would).

5. *If I start the study, can I stop if I want to?*

Yes. If you choose to take part in the study, you are free to stop at any point without giving a reason, and without affecting the care that you receive, but we will keep information about you that we already have. We will need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see of change the data we hold about you.

We would like to continue to collect information about your health from your medical records, if you do not want this to happen, tell us and we will stop. You will also have the option to take part in future research using your data saved from this study. Should you wish to withdraw, please contact the study team using the details below.

6. *What does taking part involve?*

A healthcare professional will review your medical history and examine you as usual. During the consultation, the clinician will complete a screening assessment and if you are eligible, you will be invited to take part in the study. You will also be asked to:

- sign a consent form.
- confirm your contact details

- provide demographic information (for example, age, sex, ethnicity)
- complete a simple healthcare questionnaire to give an indication of how you are feeling
- consider having a finger-prick blood test for C-reactive protein (CRP) taken. This is a blood test that detects inflammation in the body that may be useful in predicting pneumonia. The CRP test will only be analysed when the trial has been completed and is for research purposes and will not be used to guide your treatment. This test is not compulsory for participation in this study.

You will then be given a medication pack that will contain a total of 6 capsules. Two capsules are to be taken by mouth as a single dose on the first day, and then one capsule should be taken each day for the following four days.

If the medication is being delivered to your relative/ friend/ participant's home address it should arrive on the same or next day, using tracked delivery.

It is very unlikely that it will be delayed. However, if they have not received the study medication within 30 hours of agreeing to take part in the study, they may not be able to take part in the clinical trial. Please call the participants General Practice to inform them that the study medication has not arrived. We would be grateful if you could let the trial team know if this is the case.

If during this time your relative/ friend/ participant feel like their illness is deteriorating, we recommend that you contact their general practice or 111 to discuss how best to manage their illness, or if you feel it is an emergency, call 999 or go to the Accident and Emergency (A&E) department at their local hospital.

You will be asked to complete a brief questionnaire every day for the duration of your illness, up to a maximum of 4 weeks or until you have recovered (whichever comes first). Each day we will ask you to rank the severity of your symptoms, tell us about any medications you have taken, and about any possible side effects.

Over a 28-day period, on a weekly basis, we will ask you to record how you are feeling generally, using a health-related quality of life scale, and to record any additional prescription or over-the-counter medications that you have taken over each week.

7. What data will be collected?

We will collect information such as demographics, (inc. age, sex, ethnicity, post code), medical history and drug history, which will remain confidential throughout.

8. Design of the study.

The study will be carefully explained to you by your healthcare professional. At any stage, feel free to ask any questions you might have.

The medication pack you receive will have capsules that either contain an antibiotic called doxycycline or an identical placebo dummy capsule that contains no active medication. Whether you receive the antibiotic, or placebo will be decided at random (like tossing a coin), and you will have an equal chance of receiving either type of capsule.

Doxycycline is the common treatment for LRTI and is recommended by the National Institute for Health and Care Excellence (NICE) in the UK. Most people don't experience side effects; however, common side effects include feeling sick or being sick. This type of antibiotic can also cause immune reactions, such as a worsening of an inflammatory disease called systemic lupus erythematous (SLE) and inflammation affecting the lining around the heart (pericarditis). Uncommon side effects (may affect up to 1 in 100 people) include heartburn and vaginal infection.

This trial is blinded, which means that neither you nor your healthcare professional will know which treatment group you have been randomly put into.

9. What will happen to the results?

We will use the data from all trial participants to see if there is a difference in recovery between those who took antibiotic compared with those who took placebo. We will also look at any differences in side effects, complications, and costs between the two groups. We will publish our findings in scientific papers and present at scientific conferences. The confidentiality of all participants will be maintained, and you will not be personally identified in any reports or publications resulting from the study. If you would like to see a plain English summary of the results, please let us know by emailing the study team at afloat@soton.ac.uk.

10. What will happen to the pin-prick blood sample?

The finger-prick blood test for CRP is voluntary. If you consent, the CRP finger-prick test is collected as a capillary Dried Blood Spot sample which will be sent to a laboratory in Birmingham. We will use the results to see if there is a difference in response to antibiotics in those that have a high CRP value compared to those that have a low value. The blood sample will not be used for any other tests and your data will be kept confidential.

11. What are the possible benefits of taking part in the study?

There are no specific benefits for individuals taking part in the study. The main impact of this research study will be to provide a solid evidence base for antibiotic treatment of LRTI in older adults at risk of complications in primary care. Both the clinical and economic implications of this will help educate and potentially modify the decisions of prescribing clinicians.

12. What are the possible risks?

There are no major risks to taking part in the study. The study will be in accordance with the UK Policy Framework for Health and Social Care Research and Good Clinical Practice (GCP) and does not pose any unusual or challenging ethical issues.

Doxycycline is licenced for use for LRTI and has been extensively used. We do not know whether antibiotics are helpful in the treatment of LRTI and there are no known risks associated with taking the placebo.

There are no risks associated with the optional finger-prick blood test.

If you feel that your illness is getting worse or have symptoms that you are worried about, you should contact your healthcare professional or 111 for further advice. If you feel it is an emergency, call 999 or go to the Accident and Emergency (A&E) department at your local hospital.

13. Will my taking part be kept confidential?

Yes. If you decide to take part in the AFLOAT trial, data collected, and any results produced will not identify you personally. Your medical records will only be available to the research doctors, individuals from the Sponsor organisation, Southampton Clinical Trials Unit, and regulatory authorities. It is possible that your records will be selected for examination by people involved in the trial for quality assurance purposed (auditors / monitors). All trial personnel have a duty to maintain confidentiality.

Access to all data will be strictly controlled, and all current Data Protection Regulations will be followed. We will only use information that we need for the clinical trial. Their GP medical records may be accessed by the study team for a period of 3 months after the 28 day follow up period.

When you join the study, you will be assigned a study number which will be used instead of your name and will be linked to all your study data. This is called 'pseudonymised data' and you cannot be directly identified from this.

Your pseudonymised data will be held on computer servers located in the EU and USA but access to this data will be strictly controlled by Southampton Clinical Trials Unit and in compliance with all applicable current data protection regulations.

The University of Southampton is the sponsor for this study based in the United Kingdom. The sponsor will keep identifiable information about you for up to 25 years after the study is finished, when this will be destroyed. This is in accordance with regulatory requirements.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways for the research to be reliable and accurate. To safeguard your rights, we will use the minimum personally identifiable information possible.
If you withdraw from the study, any data already collected will be kept, unless you explicitly tell us that you do not want data already collected to be used.

Please use the link below to learn more about how we will use and protect your data
https://www.southampton.ac.uk/assets/sharepoint/intranet/ls/Public/Research%20and%20Integrity%20Privacy%20Notice/Privacy%20Notice%20for%20Research%20Participants.pdf]

14. What if something goes wrong?

This study has been approved by an independent NHS Research Ethics Committee. Furthermore, the study has Professional Indemnity and Clinical Trials Insurance from the University of Southampton.

We will provide compensation for any injury caused by taking part in this study. We will pay compensation where the injury probably resulted from: - A drug being tested or administered as part of the trial protocol; - Any test or procedure you received as part of the trial. Any payment would be without legal commitment. (Please ask if you wish more information on this). We would not be bound by these guidelines to pay compensation where the injury resulted from a drug or procedure outside the trial protocol or where the protocol wasn't followed.

If you have complaints about the way your illness was managed, this study will not affect your normal rights to pursue a complaint within the NHS in the normal way.

If you have complaints about the study, you can contact the researchers (see below) or use the normal arrangements in the health service. Your GP will remain responsible for your overall care whilst taking part in the trial.

If the study participant is unhappy or has a complaint about any aspect of this study, please contact the University of Southampton Head Research Ethics and Governance (023 8059 5058, rgoinfo@soton.ac.uk)

15. Who is organising and funding this research?

This trial is funded by the National Institute for Health and Care Research (NIHR), which is funded by the Department of Health and Social Care. The study is co-ordinated by the University of Southampton and the Southampton Clinical Trials Unit. The University of Southampton is the Sponsor for this research. This means that they have overall responsibility for making sure that the research programme is conducted in accordance with the relevant regulations.

16. Contact for further information

If you have further questions about your illness or clinical studies, please discuss them with your doctor.

If during the study you have any questions regarding your participation or would like further study-specific information, please contact:

Central AFLOAT study team:
Email:Afloat@soton.ac.uk or Telephone: 02380 599156

Or

Co-Lead Investigators for the study and Medical Experts:

Dr Mark Lown
Professor Nick Francis

Primary Care Research Centre,
Faculty of Medicine,
University of Southampton.

Please note that these contact details are specific to this study. If you have an urgent medical problem, please contact your own doctor in the normal way.

If you find the wording difficult to understand or would like us to explain things to you once more, please feel free to ask your doctor or nurse.

Thank you for taking the time to read this information sheet. If you wish to take part, you will be given a copy of this information sheet and a signed consent form to keep.
