ALABAMA: ALlergy AntiBiotics And Microbial resistAnce

Penicillin allergy status and its effect on antimicrobial prescribing, patient outcomes, and antimicrobial resistance.

PARTICIPANT INFORMATION SHEET

You are being invited to take part in a research study. Before you decide if you would like to take part, it is important that you understand why we are doing this research and what it would involve for you.

Please take time to read the following information carefully and decide whether or not you wish to take part.

You may like to talk to others, friends or family members, about the study. Please ask if there is anything that is not clear or if you would like more information.

Why have I been invited to take part?

This study is all about trying to improve the care of patients with a record of penicillin allergy.

You have been invited to take part because your medical records state that you are allergic to penicillin antibiotics; you are over 18 years old, and; you have taken an antibiotic in the previous 12 months.

What is the purpose of the study?

Antibiotics are important medicines for fighting infections caused by bacteria. Their widespread use has caused a worrying rise in antibiotic resistant bacteria, which are bacteria that are harder to control or kill with antibiotics. Patients with infections caused by antibiotic resistant bacteria are often ill for longer and have an increased risk of serious harm, including death. We can slow the spread of resistant bacteria by using antibiotics more carefully. Penicillins are an important group of antibiotics that are recommended and the best treatment for many infections. Doctors will avoid prescribing penicillin for their patients who have a "penicillin allergy label" in their health records. These patients are usually prescribed different types of antibiotics for their infections. There is concern that these non-penicillin antibiotics may not work as well as penicillins, may cause more side-effects more often (including killing more of the body's "helpful" bacteria), and may be more expensive.

About 9 out of 10 people who have a record of penicillin-allergy are found to be not truly allergic to penicillin when thoroughly tested. This means they could safely take penicillins. The aim of ALABAMA is to find out if people with a penicillin-allergy record in their GP health records really do have an allergy by carrying out specialist testing, and to see if we can reduce the number of patients wrongly labelled as penicillin allergic. We will find out if this results in better use of antibiotics and fewer days of symptoms, when patients are prescribed antibiotics for infection.

We are asking GPs in West Yorkshire to help us with this research, and we hope to include 96 people in the initial feasibility study and 1994 people in the main study.

What will happen to me if I take part?

You have been contacted by us as your surgery is participating in the study and you have been reviewed as potentially eligible by a GP. If you are willing to take part, or wish to find out more information, the trial team will arrange either a face to face or telephone appointment for you to talk to a GP or a Research Nurse at a time that is convenient to you. You will receive you a reminder text message one week before your appointment and another text message 48 hours before your appointment. At this appointment, a GP or Research Nurse will check that you are eligible to take part in the study (including a review of your penicillin allergy history), and that you understand what being in the study involves. If you are eligible and would like to proceed you will be asked to give your consent to participate in the study. You will receive a copy of the consent form and another copy will be retained in your GP practice. We estimate that this first face to face or telephone appointment will take about 30 minutes.

Following this, a member of the trial team (a Research Nurse) will call you at a time that is convenient to you to ask you a series of questions reviewing your medical history, penicillin

allergy history and your personal understanding of your penicillin allergy and a quality of life questionnaire. This phone call will take about 40 minutes. You will then be randomly allocated to either usual care or the Penicillin Allergy Assessment Pathway (PAAP) study group.

If you are randomised to the usual care group, you will not be required to attend any further visits for the purpose of the trial. However, if your GP prescribes you antibiotics during the 12 months after randomisation you will be asked to complete a symptom diary for up to 28 days (up to 5 minutes per day). You will receive a text message on day 7, 14 and 21 to remind you about completing your daily diary. You will also receive daily email reminders if you decide to complete your symptom diary online. You can stop completing the diary before 28 days if you feel better and you have completed your antibiotic course. You will be contacted by the trial team to support you in the completion of this diary 2-4 days and 28-30 days after your GP appointment (each call will take up to 10 minutes).

If you are randomised to the PAAP study group, you will be asked to attend one clinic appointment at the immunology clinic at St James's University Hospital which will take half a day to complete. Prior to this appointment you will be sent an appointment letter and information booklet on penicillin allergy testing. You will also receive a text message one week and 48 hours before the appointment to remind you to attend. During the clinic appointment, you will go through the penicillin allergy testing which will happen in three stages. At the first stage, the doctor or nurse will ask you about your penicillin allergy history. Depending on your history you will either have a skin test or go straight to the 'oral challenge' test. The oral challenge involves taking a syrup solution containing penicillin. The skin test involves a tiny amount of penicillin being injected into your arm, just under the surface of the skin which takes about 5 minutes. After 15 minutes, your skin is examined to see if the test is positive. Sometimes a second skin test is needed which takes about 45 minutes. If there is no reaction, you will be moved on to the third stage, the oral challenge test. A doctor will ask you to take three doses of penicillin in an hour and you will be monitored closely throughout this time and also one hour after the last dose. If you have no reaction at this time, you will then be asked to take penicillin at home for 3 days to check there is no delayed reaction. A research nurse will tell you what to do if you experience any symptoms and she will call you a few days after to check for delayed reactions.

You will receive the results of the PAAP test via letter (at least 3 days after your appointment). In addition, if you have tested negative for penicillin allergy you will receive a leaflet explaining the result. Your GP surgery will be informed of the test result and will update your health records as needed.

If you are prescribed an antibiotic by your GP during the 12 months after being entered into the study, you will be asked to complete a daily symptom diary. We ask you to complete your diary for up to 28 days when you start taking your antibiotic (up to 5 minutes per day). You will receive two text messages to remind you about completing your daily diary at day 7, 14 and 21. You will also receive daily email reminders if you decide to complete your symptom diary online. You can stop completing the diary before 28 days if you feel better and you have completed your antibiotic course. You will be contacted by the trial team to support you in the completion of this diary 2-4 days and 28-30 days after your GP appointment (each call will take up to 10 minutes).

Some of the participants will be invited to take part in a telephone interview after receiving their results to ask about their experiences of taking part in the study. This will take about 30-45 minutes (only participants that have consented to take part in the interviews will be contacted).

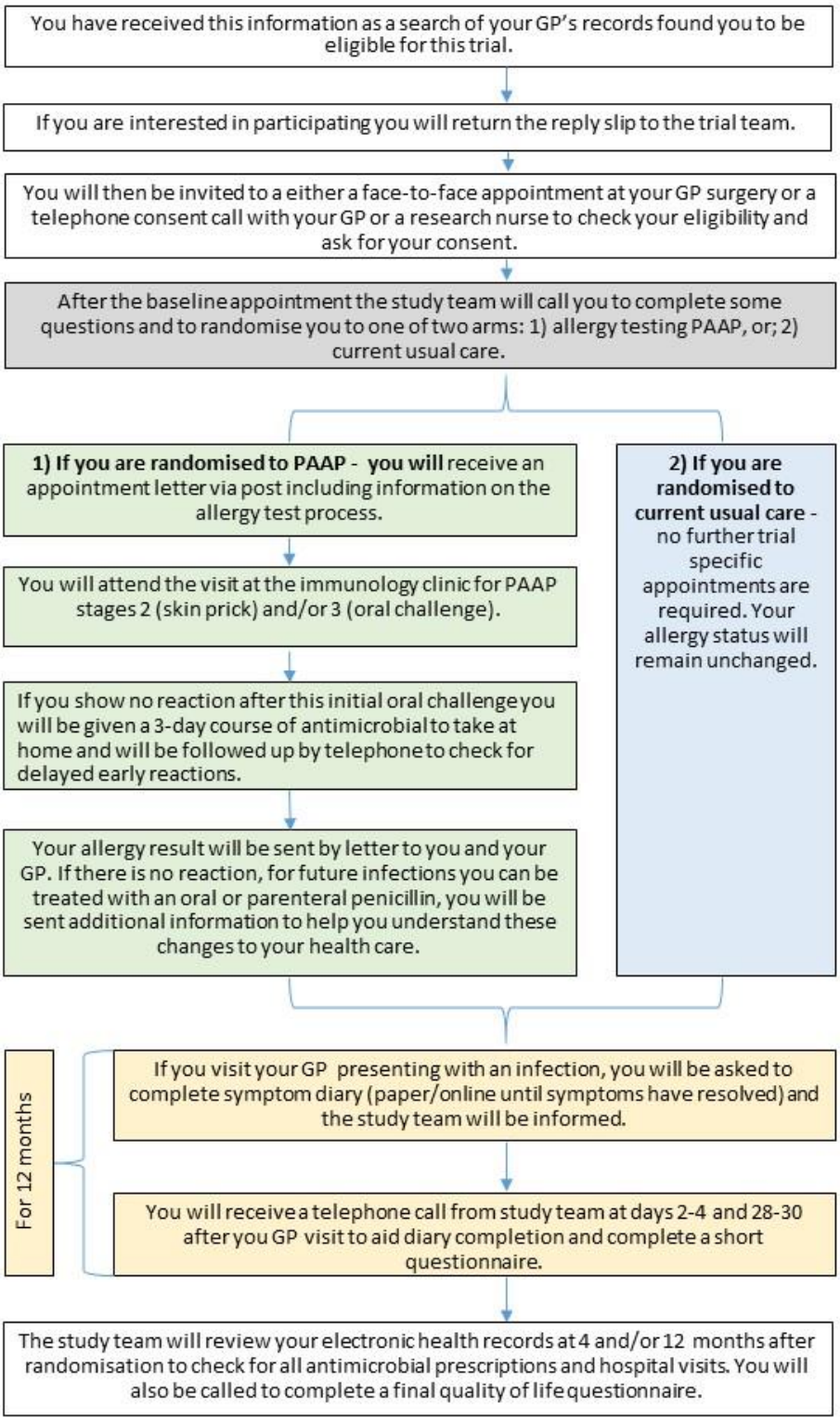
If you are randomised to the PAAP study group and do not wish to proceed with the testing, you will still be followed up as per the PAAP arm and your data will be analysed the same way.

Regardless of which group you have been randomised to, if you have been recruited during the feasibility phase you will be called on a monthly basis for 4 months by the study team to complete a safety questionnaire, to see if you are feeling ok, If you have received any antibiotic prescription and if you have suffered any delayed reaction after your allergy test at the clinic (if in PAAP arm). These phone calls will take up to 30 minutes.

During the study and at the end of this follow up period the study team will review your health records for any information on infections, antibiotic prescriptions and hospital admissions during the previous 12 months. After 12 months a member of the study team will call you to ask you to complete a final quality of life questionnaire. A review of your health records will be repeated annually until the end of the study.

Once the study has finished we would like to continue to collect data on any infections, antibiotic prescriptions and hospital admissions you may have for an additional 10 years. To do this we will need to access your medical records and collect routine health data using NHS Digital. We will not require any further contact with you and we will ask for your consent to do this follow up.

Study Participation Flowchart



Do I have to take part?

No. You are free to decide whether or not to take part. If you decide to take part, you are still free to withdraw at any time, without giving a reason. A decision not to take part or to withdraw will not affect the standard of care you receive from your healthcare team.

What are the possible benefits of taking part?

If your penicillin allergy status is changed, first-line penicillin treatment for many infections can resume. That means you can access a wider range of antibiotics including the recommended antibiotic for the condition you are suffering from when you need them. We also hope the outcomes of this study will improve access to penicillin-allergy testing; improve patient outcomes related to infection e.g. fewer days of symptoms; reduce antibiotic prescriptions and reduce resistant bacteria; and benefit the NHS by saving GP time and improving value for money.

What we will expect from you?

By taking part in the trial we would expect you to:

- ✓ Attend a face to face or a telephone call appointment to confirm eligibility and give consent.
- ✓ Answer a short phone call from the research team to answer a baseline questionnaire and be given the result of the random selection which will decide which trial group you are in.
- ✓ If you are randomised to the PAAP allergy testing, you are required to attend a hospital clinic for skin testing and/or oral challenge.
- ✓ 4 – 6 and 28 – 30 days after completing the PAAP testing answer short phone calls from the research team to check for any delayed reactions and complete a short questionnaire.
- ✓ The first 96 study participants will receive four short phone calls from the research team, monthly, during the first four months of their participation, to check for again for any possible delayed reaction to the test.
- ✓ For the following 12 months after your baseline appointment each time you attend your GP surgery with an infection that requires antibiotics you will complete a diary about your symptoms for 28 days. You can stop completing the diary when you feel better.
- ✓ You will also be required to answer 2 phone calls by the research team, 2-4 and 28-30 days after visiting your GP with an infection requiring antibiotic treatment and one phone call after 12 months of your participation, each phone call will require you to answer a short questionnaire.

Will my taking part in the study be kept confidential?

Yes. You will be given a study participant identification number. Any information you provide will be recorded against that number, not your name. Therefore all information is anonymous, as is any data we collect from your medical records.
The University of Leeds is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will

act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The University of Leeds will keep identifiable information about you for 10 years after the study has ended.
Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. To safeguard your rights, we will use the minimum personally-identifiable information possible.
You can find out more about how we use your information by contacting Data Protection Officer at the University of Leeds using the dpo@leeds.ac.uk email address. Your GP will use your name, NHS number and contact details (address, telephone number, email) to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from University of Leeds, University of Oxford and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Your GP will pass these details to the University of Leeds and University of Oxford along with the information collected from you and your medical records. The only people who will have access to information that identifies you will be people who need to contact you to ask you the follow up questionnaires, collect information from your medical records or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name or contact details.
Your GP will keep identifiable information about you from this study for 15 years after the study has finished.
Your information could be used for research in any aspect of health or care, and could be combined with information about you from other sources held by researchers, the NHS or government.
Where this information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of health and care research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you, such as insurance.
Where there is a risk that you can be identified your data will only be used in research that has been independently reviewed by an ethics committee.

We will also share identifiable data (name, date of birth and NHS number) in a secure manner (including encryption during data transfer) with NHS Digital. As soon as the required information has been gathered your contact details will be destroyed. NHS digital provide us with some additional health data from databases including Hospital Episode Statistics data and Mortality data for up to 10 years after the study has finished. The data will be returned to us in an encrypted format and we will use a study ID before access is granted to the researcher. The data supplied by NHS Digital will be linked using the participant ID assigned to you at the time of enrolment into the ALABAMA study.

The study identifiers will be kept separately in a password protected file and only the study team will have access to these. We will use the data we collect from NHS Digital only for this study and not for any other purposes.

You are free to withdraw your consent for data linkage with NHS Digital at any time and it will not affect your ongoing care.

What are the possible disadvantages or side effects of taking part?

If you take part in this study there is a small risk from skin testing and oral challenge testing and a risk from any antibiotics that are prescribed as part of your usual clinical care during the time of the study. Skin testing is generally safe and severe reactions following testing are rare. For example, five patients (0.5%) had severe reactions in one eight year study including 998 skin tests. Severe reactions to an oral challenge test in patients with negative skin-tests are uncommon but do occur. Among 580 orally challenged patients with a history of non-serious skin reactions to penicillin, 14 had reactions, 11 of which were early and 3 delayed. A reaction was more likely if the allergy report was within 15 years. We will use a series of increasing drug doses during the oral challenge, and it will take place in a specialist unit with facilities to deal with any potential severe allergic reactions. You will be called 4– 6 days after the PAAP appointment by a study research nurse to check how you are feeling and if you have had any delayed adverse reactions.

Penicillin allergy testing is routinely carried out in the NHS but it carries a very small risk of anaphylaxis and death. This risk will be minimised by excluding any patient with a prior history suggestive of anaphylaxis or a previous serious reaction.

Will the GP be informed of participation?

Your GP is aware that you have been invited to take part in this study. If you decide to participate in this study your first visit will be at your own GP surgery. Any changes to your medical records will be made by your GP and your GP is aware we will need to access your medical records for prescribing and hospital attendance information.

Will I be reimbursed for taking part?

We will cover the cost of your travel to immunology clinic at St James's University Hospital.

Who is organising and funding the research?

The researchers are from the University of Leeds and the University of Oxford. The programme lead and the Chief Investigator is Dr Jonathan Sandoe, Associate Clinical Professor of Medical Microbiology, University of Leeds, joint lead co-applicant Prof Sue Pavitt, Professor in Translational and Applied Health Research, University of Leeds, and Co-Investigator Professor Christopher Butler, Professor of Primary Care, University of Oxford. The funding for this research comes from the National Institute for Health Research (NIHR). Your GP surgery is being paid for including you in this study.

What happens if I don't want to carry on with the study?

You can withdraw from the study at any time without giving a reason. Withdrawing from the study will not affect your future medical care.
If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

If you wish to withdraw from the study or you want to find out more about how we use your information, please contact the trial team using the contact details on the back page.

What happens once the trial has stopped?

Once you have finished the trial you will be looked after as usual by your GP. Any changes to your penicillin allergy status will remain in your health records beyond the end of the trial.

What if new information becomes available?

Sometimes we get new information about the intervention being studied. If this happens, the research team will contact you and ask if you wish to continue in the study. If you decide to continue we may ask you to sign an updated consent form. It may be that the new information means that we think it's best to withdraw you from the study, or stop the study altogether, in which case we will let you know and explain the reasons.

What if there is a problem?

If you have any queries about this study, then please contact the study team who will do their best to answer your questions. You can either call them on 01865 289336 or email: **alabama@phc.ox.ac.uk.**

If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should firstly contact the study co-ordinator on the details above or you may contact the University of Leeds, Faculty of Medicine and Health Research Office, on 0113 343 4897 (email: **governance-ethics@leeds.ac.uk**).

The University of Leeds has arrangements in place to provide compensation for non-negligent harm arising from participation in the study for which the University of Leeds is the Research Sponsor. NHS indemnity operates in respect of the clinical treatment with which you are provided.

What will happen to my test results and samples?

Your GP will receive your PAAP allergy results via letter or electronically and if your status has changed your GP will be asked to update your medical records with your new allergy status. You will also be sent the PAAP test results via letter or electronically as you prefer.

What will happen to the results of the research study?

We will publish the results in scientific journals and present them at scientific meetings. The results will also be available to all GP practices that participate in the study and also be published on the ALABAMA study website page (at **https://www.phc.ox.ac.uk/phctrials/trial-portfolio/ALABAMA-study**). Your details will remain strictly confidential, with no personal information being included in any results or publications.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee, who protect your safety, rights, wellbeing and dignity. This study has been reviewed and given a favourable opinion by London Bridge NRES Committee.

Thank you for taking the time to read this information sheet

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