AGES-2

Experimental Human Pneumococcal Challenge in Older Adults

Phase B

PARTICIPANT INFORMATION SHEET

Thank you for your interest in our study. This leaflet explains the study and a member of the team will also discuss it in full if you are interested in participating. Please ask us if you have any questions. You may want to talk to other people about the study – please do so. Take your time to decide if you want to be involved.

What is this study?

This study is looking at a germ called a bacterium called *Streptococcus pneumoniae* ('pneumococcus', Spn). This germ can cause a variety of symptoms from cold-like illnesses to chest infections or sepsis. It is important to understand how this germ can cause infection in older adults.

In this study, we will carefully and safely expose ("challenge") volunteers to the germ in their nose to see how they respond. Participants are paid for their involvement.

Who are we?

We are researchers at the Liverpool School of Tropical Medicine (LSTM). We have been studying lung infections using healthy volunteers for over ten years to provide world-leading research into the pneumococcus germ using methods called an Experimental Human Pneumococcal Challenge (EHPC) model. More than 2000 participants have already been safely studied using our methods, including older adults.

What is the purpose of this study?

Pneumococcus is a major germ worldwide. It can cause a range of infections from a mild cold-like illness to pneumonia, meningitis or sepsis. It tends to affect older people worse than younger people, so it is important to understand how the body tries to fight it off in this age-group. Knowing exactly when someone's body first encountered the germ (i.e. at the time of 'challenge') gives scientists a lot of information. This will hopefully lead to scientists and doctors being able to design medications or vaccinations better for older people.

The strain of germ used is *Streptococcus pneumoniae* serotype 3 at a dose of 80,000 colony forming units per nostril.

Do I have to take part?

No. Taking part in this study is entirely voluntary. If you decide to participate, you can withdraw from the study at any time. This will not affect your healthcare.

Who can take part in the study?

We are looking for up to 15 volunteers aged 50-84 who are generally healthy. We will check for reasons that may put you at higher risk for taking part in the study. We also make sure that your participation will provide helpful information to us. If we find any reason that you (or the people you live with) may be at higher risk of infection, then we will not invite you to take part.

You are potentially eligible if:

- You are aged between 50-84 (inclusive)
- You are able to consent for yourself
- You speak English fluently

You are not eligible if any of the following apply to you:

- You are already enrolled for another clinical trial involving medications or vaccinations
- You are pregnant, breast-feeding or unable to practice adequate birth control measures during the study (females of childbearing potential)
- You suffer from chronic respiratory disease (such as asthma requiring an inhaler, COPD, or bronchiectasis)
- You have previously received certain types of pneumonia vaccine (PCV) – we will check this with you
- You have had a live vaccine within the last 28 days
- You have medical conditions that increase your risk of serious infection, such as cancer, diabetes, immunosuppression, heart disease, chronic kidney or liver disease, rheumatoid arthritis or suffer from recurrent ear infections
- You are a current smoker (including vaping or recreational drugs), have recently given up smoking (within the past 6 months) or were a heavy smoker in the past
- You have been admitted to hospital with pneumococcal infection within the last 10 years
- You are on any medication that might impact the study results, such as chemotherapy, steroids, Roaccutane, GTN or blood-thinners, or have taken antibiotics within the last 28 days
- You are allergic to penicillin or amoxicillin
- You have a direct caring role to people at high-risk of infection such as those under 5, those classified as extremely clinically vulnerable, or you are a healthcare worker
- You plan to travel overseas within four weeks after the first study intervention

What happens if I choose to take part?

If you choose to take part in the study, we will ask you to meet the research team in-person. At this visit, we will check if you are suitable, and you will be given the opportunity to ask questions. If you are happy to proceed, we will ask for your written signed consent. Following this, you will have a clinical examination and nasal and blood tests. The study involves a further 6 in-person visits (7 visits including the initial visit above). These are spaced out over approximately 4 weeks.

During the study, everyone will be exposed ('challenged') to the pneumococcus germ through drops in the nose.

Timeline of study visits and procedures

	Screening Visit	Challenge Visit	Day 2 Visit	Day 6 Visit	Day 9 Visit	Day 14 Visit	Day 28 Visit
Clinical Exam	X	X					
Bacterial challenge		X					
Nasal samples	X	X	X	X	X	X	X
Saliva samples	X		X	X	X	X	X
Blood samples	X	X	X	X	X	X	X
Cough samples			X	X	X	X*	X*
Shedding samples			X	X	X	X*	X*
Pregnancy test$	X	X					

*If positive at day 2, 6 or 9
$ If applicable

What happens at each visit?

Initial visit and Screening visit

These visits may happen separately or together. A member of the research team will discuss the study with you individually or in a group session. You will have the opportunity to ask questions and discuss the study directly with a researcher in private following the presentation. Some of this discussion may also happen over the phone prior to your first visit to the facility.

If you are happy to take part in the study, you will be asked to complete a questionnaire to demonstrate understanding of what the study involves before signing a consent form. We will ask you some questions to assess whether you are eligible to take part in the study. This will take about an hour.

We will ask routine questions about your medical health, your vaccination history and medications you are taking. We will take your blood pressure, heart rate and temperature, and we will carry out a brief examination. This is all done to make sure you are well enough for the study. Females of childbearing potential will have a urine pregnancy test. We will take blood tests, throat swabs, nasal wash, nasal cells and a COVID-19 test. We will also collect contact information for a close friend or relative who can act as a secondary contact if we can't get hold of you after challenge, to ensure your safety. Finally, we will add your national insurance number to a secure NHS website called The Over-Volunteering Prevention System (TOPS, www.tops.org.uk) that prevents you from being able to enrol in any other clinical trials whilst you are involved in this one.
So that we have the full details about your medical history to confirm your eligibility, we will ask for your consent to access your electronic GP record or request your GP to complete a questionnaire or provide your medical summary before the screening visit.

Challenge visit

We will check you are happy to continue and that you are feeling well prior to challenge. Another blood test will be taken. You will be asked to sit slightly reclined for 15 minutes and then the pneumococcus germ will be introduced to both nostrils by dripping in a small liquid sample with a dropper. You will be asked not to swallow so the fluid stays in the nose for as long as possible. The overall visit takes around 1 hour.

You will go home with a study pack including:

- A course of antibiotics to keep with you in case you are unwell
- A thermometer to check your temperature at home
- A safety information sheet
- The contact details for the study team doctors

At home you will keep a diary of any symptoms or medications (either online via a link we send you or on paper) for 7 days. You should inform the study team about any moderate/severe symptoms as soon as possible. Details on clinical symptom definitions will be given to you.

Follow-up visits

You will return to the clinic for further checks on your vital signs, to review any symptoms you might develop and for more nose, throat and blood tests at several timepoints after the challenge as shown in the table above. In total you will have at least 7 visits.

What samples do we collect from you?

We collect nose, throat, saliva, urine and blood samples to look at the germs and your immune response.

Nasal wash: We gently squirt a little salty water into your nose. After a few seconds the water runs out into a sample bowl. This will tell us about the germs in your nose and your immunity.

Throat swab: We take a small cotton swab and wipe the back of your throat in a circular motion. This is to test for germs in your throat.

Nasopharyngeal swab/Saliva: We use a small cotton swab and wipe the back of your throat and nose to test for COVID-19 and other respiratory germs. Saliva may be used as an alternative.

Nasal cells: We insert a very small and narrow plastic spoon (about the size of a toothpick) into the inner surface of the nose that is withdrawn in a sweeping motion to collect small cells. We will perform this twice on each nostril. This is to look at your immune response. We may also use a swab to collect these cells by rotating the swab in each nostril.

Blood samples: We take blood samples from a vein in your arm (using a needle). We will take up to 70mL (around 4 tablespoons) during a visit. This amount of blood is safe to have taken in one go, and your body will replace this blood quickly. Over the course of the four weeks of the study, the total amount will be approximately 240ml, which is just over half the amount taken from blood donors in one sitting. This is to look at your body's response to the bacteria.

Cough plates: We will ask you to hold an agar plate, without touching the agar, in front of your face and cough directly onto the plate twice.

Shedding samples: We ask you to rub your nose on the back of your hand repeatedly until your skin is moist. We then take a swab of the area to test for pneumococcal bacteria to determine if you are shedding the bacteria from your nose.

Urine: In females of childbearing potential, a urine pregnancy test will be performed at screening and challenge. The remainder of the sample will be discarded.

What are the risks from this study?

Challenge pneumococcal bacteria: Because the germ we expose you to is live, there is a very small risk of infection to you or your close contacts. You may get a sore throat, cold-like symptoms, headaches, earaches, a cough or a fever. However, the chance of severe infection is very low. We have used this type of the germ in over 500 participants without any serious adverse events, although this will be the first time it is used in this age-group. We will monitor you very closely through the e-diaries and ask about symptoms every time we see you to make sure you're OK.

We provide a safety pack as described above and you will have 24-hour access to the research team by phone. This includes clear safety precautions and what to do if you feel unwell. Everyone who tests positive for the pneumococcus germ will take a course of antibiotics at the end of the study, or if they feel unwell, before that. The germ is tested so we know the antibiotics should work against it. If the germ does get carried in your nose and remains there on the Day 28 visit, we will ask you to take your antibiotics for five days.

Blood sampling: The risks associated with blood sampling are minimal, but this may cause temporary pain, bruising and/or bleeding to your arm. The blood sampling will be performed by trained healthcare professionals. In the rare circumstance that we notice anything unusual or medically significant about your blood then we would let you know and ask your permission to inform your GP.

Nasal sampling: There are limited risks related to these samples. During a nasal wash, you may swallow a small amount of salty water, however, this is harmless. The nasal cell sample is slightly uncomfortable and may make your eyes water briefly. Sometimes a small amount of blood can be seen on the sample probe, however, it is rare for it to cause a nosebleed.

Incidental medical findings

Since we carry out several medical tests throughout the study, it is possible that we detect previously unknown health issues (*e.g.* high blood pressure or abnormal blood results). This will be discussed with yourself and with your permission, your GP informed for ongoing follow up.

What happens to my samples?

The samples taken in this study will be processed in the Liverpool School of Tropical Medicine or the Liverpool University Hospitals NHS Foundation Trust.

Samples will be taken to look at your immune response to the bacterium and whether you are carrying it in your nose after exposure. These experiments may involve the extraction of molecules, such as DNA, which make up the genes in your cells. These tests can be used to see if there are genetic factors that affect protection or susceptibility to these bacteria or viruses.

The blood samples we collect to assess your eligibility and safety will be processed in an NHS laboratory and results from these samples are connected to your NHS record. Your details and results from these samples are safeguarded under the NHS Trust's data protection policy and will only be accessed during the study by the researchers to assess your safety and eligibility.

We will also ask for your consent to retain leftover samples to be used for future ethically approved research in the UK and overseas. If you consent, samples are anonymised and will be transferred to a research tissue bank at the end of the study. You can decide whether or not you agree to genetic material being stored, however, your DNA is unique to you so it can never be completely anonymous. The stored samples will be analysed, as and when new technology becomes available, or when new scientific questions arise relating to protection and susceptibility of disease and carriage. If you agree, these samples would be stored indefinitely.

What if there is a problem?

The research team is available to contact 24/7 by phone. Please contact us as soon as possible if you are unwell or if you develop any symptoms including, but not exclusive to, sore throat, earache, headache, fever, cough, breathlessness, lack of taste or smell. We would also like to know about any new health or medication changes. Any medical care you need will be provided by the NHS.

The study is sponsored by the Liverpool School of Tropical Medicine and is insured in the unlikely event that you suffer any harm as a direct consequence of your participation in this study.

What if I change my mind or want to stop?

If you do start the study, you are free to stop at any time and without giving a reason. If you decide not to take part, or to withdraw from the study, this won't affect your future healthcare. If you have been exposed to the bacterium, we would still offer you care to ensure your safety even if you no longer wish to be part of the research.

If you decide to stop or lose capacity to consent to being in the study, we will only continue to use the samples that have already been taken and information that we have already collected from you – no further samples or data will be collected. You are free to request that your samples are destroyed at any time during or after the study. You will be paid for the visits completed up to that point.

The study team may stop your involvement in the study for the following safety reasons:

- If you develop a condition that is in the exclusion criteria
- If you start a new medication that is prohibited in the study
- If you become pregnant
- If you are unable to follow study instructions or the team are unable to contact you.

If you are withdrawn from the study, identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant

What if I wish to report a concern?

If you wish to report a concern about any aspect of the study, you can contact the research investigators on 07740410290. You can also alternatively contact the Chief Investigator Dr Ben Morton on ben.morton@lstmed.ac.uk or you may contact the sponsor, the Liverpool School of Tropical Medicine on lstmgov@lstmed.ac.uk. Reporting a concern will not affect the medical care you receive now or in the future.

Would my taking part in this study be kept confidential?

All information that is collected about you during the research will be coded with a study number and kept strictly confidential. Any information about you that leaves the clinic would have your name and address removed so that you could not be recognised, except for your signed consent form and letters sent to your own GP. To enrol into this study, we ask you to consent for us to contact your GP.

We will write to your GP to inform them when you enrol in the study, so they can update your medical records accordingly. Your GP will also be asked to share information about your medical history and give access to any other medical records as required to ensure there are no medical reasons that would prevent you from taking part. We would only notify your GP of the results of any medical tests with your permission.

Responsible members of the Liverpool School of Tropical Medicine or Liverpool University Hospitals NHS Foundation Trust involved in the research may also be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations. No one else will be told that you are involved in the study.

What are the benefits of taking part?

You will be a valuable part of a research study that we hope will eventually lead to the development of new methods to prevent or treat respiratory infections.

How much will I get paid?

All participants will be reimbursed for their time, travel and for inconvenience based on the following figures:

Initial appointment	£0
Screening appointment	£40
Challenge appointment	£40
Follow-up appointments x 5	£30
Diary completion	£35

If you are eligible for enrolment, all visits are completed and the required symptom e-diaries are completed, then you will be entitled to reimbursement of £265.

What will happen to my data?

United Kingdom data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The Liverpool School of Tropical Medicine, based in the United Kingdom is the 'data controller' and is responsible for looking after your information and using it properly. Your personal information will be kept confidential and handled in accordance with data protection laws in the UK. We will be using information from you and your medical records to undertake this study.

We will use minimum amount of personally identifiable information. Data will be collected and held by the Liverpool Vaccine Group. It will be accessible to staff at the Liverpool Vaccine Group, responsible staff from the Liverpool School of Tropical Medicine, regulatory authorities, independent auditors which may be appointed by Sponsor and funder in collaboration, who may monitor/audit the data collection process. The database servers are held by the sponsor. We will keep identifiable information about you such as contact details for a minimum of 5 years after the study has finished. The need to store this information for longer will be subject to ongoing review. De-identified research data will be stored indefinitely.

Data may be transferred outside of the UK where data protection laws may differ from the UK. Data that are transferred elsewhere will be pseudo anonymised (meaning any identifiable information will be replaced in a way that does not allow you to be directly identified).

A photocopy of your ID (driver's licence, passport or national ID card) and payment processing will be taken at the screening visit. We will securely retain copies until the end of the study. Your bank details will be stored for a minimum of 7 years in line with financial requirements. If you only complete online screening or telephone screening (before informed consent) your data will only be kept to the end of the trial.

At the completion of the study, unless you consent otherwise (e.g., if you request to be informed of other studies), your personal details will not be used to contact you other than in exceptional circumstances concerning your safety. If you consent to take part in another study carried out by the Liverpool Vaccine Group personal information and medical information including blood test results may be accessed to avoid unnecessary repetition.

UK data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available by contacting dataprotection@lstmed.ac.uk.

What will happen to the results of this study?

The results of this research study may be presented at scientific meetings or conferences and published in a scientific medical journal. This can take approximately 2 years after the study is completed. Your individual results would not be identifiable nor would you be identified in any report or publication. A copy of the main research publication will be shared with you and will also be published on our website.

Who has reviewed this study?

This study has been reviewed by the study sponsor, the Liverpool School of Tropical Medicine. This research has been looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given favourable opinion by the Research Ethics Committee of East of England – Cambridge South.

Who is organising and funding the study?

This study is sponsored by the Liverpool School of Tropical Medicine and funded by the Medical Research Council.

Further information and contact details

We hope this information sheet has given you enough information to make decision on whether to volunteer for this study. If you are interested in participating, you do not need to make a final decision straight away.

If you have further questions about the study that you would like to discuss with our team, please contact us at:

Email: Ages Study Agesresearch@lstmed.ac.uk

Tel: 07740410290

Thank you.