Experimental Human Pneumoccocal Challenge Model (EHPC)

Participant Information Leaflet (PIL)

Challenge 3 Study:

This information leaflet tells you how you could take part in our research. Please ask a member of the team if you have 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 the purpose of the study?

We are studying a bacteria called pneumococcus which are often found in the noses of healthy adults and children without causing any symptoms or disease. However, in some people, such as older age, chronically ill adults or very young children, it is more likely to cause illness. Mild infections with pneumococcus are very common, such as ear infections in children. Less frequently, the bacteria can infect the lung (causing pneumonia), the brain (causing meningitis) or the blood (causing sepsis). These more serious illnesses are very uncommon in healthy adults. It is thought that small numbers of this bacteria in the nose ("nasal colonisation") may actually protect against pneumococcal disease such as pneumonia.

The 'Experimental Human Pneumococcal challenge' (EHPC) model is a way of putting drops of bacteria into the nose. We have studied this model of putting bacteria in the nose safely in over 1500 volunteers over the past decade with no serious side effects. We will now use a different strain of the bacteria that is commonly found in the community, called SPN3, in this model.

The aim of this study is to determine how much pneumococcus is needed to achieve nasal colonisation and how long the bacteria live in the nose for before it is cleared by natural immunity. By doing this, we will then be able to test how well future vaccines may work to prevent pneumococcal colonisation and ultimately pneumococcal infections such as pneumonia.

Do I have to take part?

No. Taking part in this study is voluntary.

Why have I been asked to take part?

We are looking for up to 117 participants aged 18-50 years old and that are fit and healthy. If we find any reason that you or your close contacts may be at higher risk of infection, then we will not ask you to take part.

The main reasons that you would not be able to take part:

- Current daily smoking (includes e-cigarettes) or significant history of smoking
- Currently involved in another study or involvement in EHPC studies in past year (3 years if involving SPN3)
- Received a pneumococcal vaccine (routine in UK if born since 2005)
- Allergy to Penicillin/ Amoxicillin
- Increased risk of infection due to chronic condition or medication
- Long term use of antibiotics
- Pregnancy or trying to conceive
- History of drug or alcohol abuse
- Directly caring for someone who has lower immune levels (patients, children under 5, the elderly) without personal protective equipment
- Overseas travel planned in follow up period

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What happens if I choose to take part?

If you choose to take part in this study and the research team agrees that you are eligible, you will be asked to sign the consent form.
The study will involve 8-9 clinic visits over approximately 4-5 weeks.

What samples do you take and what are the risks?

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 bacteria in your nose and your immune response.
Risk: may swallow some salty water, temporary discomfort.

Throat swab(s): We take a small cotton swab and wipe the back of your throat in a circular motion. This is used to detect bacteria and viruses in your throat.
Risk: might make you gag a little.

Nasosorption: To collect cells from your nose we place a small piece of paper into your nostril for two minutes.
Risk: Little if any discomfort

Nasal cells: We insert a very small plastic spoon (like a tooth pick) to collect cells from inside the nose. We will perform this twice on each nostril.
Risk: Temporary discomfort, eyes watering, spots of blood from the scrape.

Blood samples: We take a blood sample from a vein in your arm (using a needle). We will take up to 80mL (about the same as 8 tablespoons) during a visit. This amount of blood is safe to give, and your body will replace this blood quickly.
Risk: some people may feel faint or experience bruising.

Shedding: We use gentle methods to find out if bacteria move from the nose to the hand. For example a swab of your hand after rubbing your nose or coughing onto a plate that is used to grow bacteria.

Exhaled Detection Facemask: You wear a facemask with a special filter for 15 minutes
Risk: Can feel claustrophobic

Saliva: We will ask you to spit into a tube to provide approx 1ml.

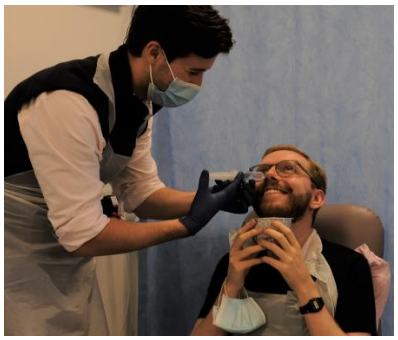


Fig 1. Nasal Wash

The risks that you should consider *before* participation in this study are the risks associated with having blood taken, nasal sampling as listed above and inoculation with live bacteria.

Inoculation with pneumococcal bacteria: Because the bacteria are alive, there is a very small risk of infection to you or your close contacts. There is a low risk of middle ear infection and very low risk of sinusitis, pneumonia, meningitis or sepsis. The study is designed to ensure any risk is minimal and we do not expect anyone to develop an infection; we choose participants carefully and monitor them closely. We have experience of using this model safely in more than 1500 healthy participants with no serious side effects. We provide a safety pack as described above and access to the research team by phone 24/7. We give you a separate leaflet which explains the

safety precautions and what to do if you feel unwell.

What will happen at each visit?

This study involves 6-9 visits to the research clinic. Each appointment takes between 10 minutes up to a maximum of 60 minutes.

Consent

A member of the research team will discuss the study involvement with you, this may be done as a group presentation. You will then have the opportunity to ask questions and discuss the study with the researcher in private. If you choose to take part in the study, you will be asked to complete a questionnaire to demonstrate that you understand the study involvement before signing a consent form. We will inform your GP that you are taking part in the study.

Screening

This will take approximately 30 minutes. We will ask routine questions about your medical health and we will listen to your heart and lungs to make sure you are fit and well. At this visit, a number of samples will be taken which may include throat swabs (including a COVID-19 test), nasal wash, bloods, nasal scrapes, nasosorption and shedding samples.

Inoculation Visit

We use a dropper (pipette) to put a few drops of water containing a small number of pneumococcal bacteria into each nostril (inoculation). You will lie down in the clinic for 15 minutes after the procedure. Usually participants have no symptoms afterwards. There will be a doctor or nurse available by telephone 24 hours a day, 7 days a week to answer questions. We will give you a safety pack to keep with you throughout the study, this includes:

- 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
- A study contact card
- A symptom log

We will ask that you inform us of your temperature and symptoms daily for the next 3-5 days.

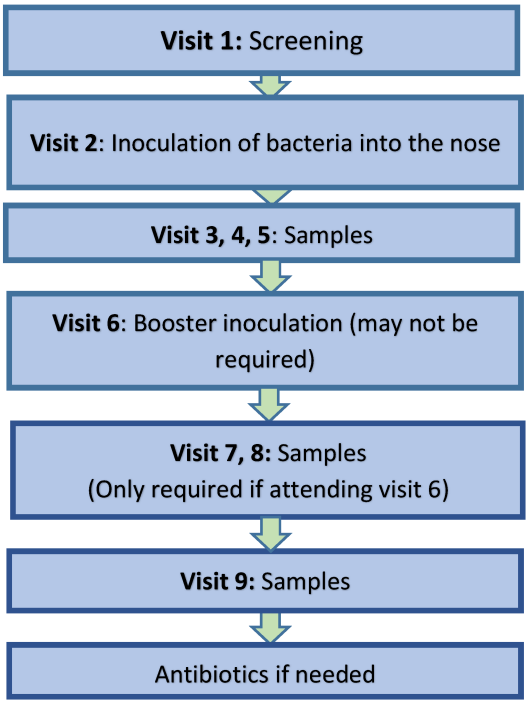
Clinic appointment visits

At each visit, a number of samples will be taken which may include throat swab(s), nasal wash, bloods, nasosorption, shedding, saliva and nasal cell samples.

End of the study

Participants that are carriers of pneumococcal bacteria at any time point, who do not go on to have negative samples, will be asked to take the antibiotics (amoxicillin 500mg 3 times per day for 5 days) from the safety pack to clear/ reduce the amount of the pneumococcus in the nose.

Appointment Flow Chart



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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 respiratory infections through vaccination. You will not gain any direct benefit other than a health check.

What if there is a problem?

You can contact the research team 24 hours a day by phone to answer any questions. Any medical care you need will be provided by the NHS.

What about the risk of COVID-19?

The bacteria in this study does not increase your risk of developing COVID-19 infection. To reduce the risk of COVID-19 when attending for your clinic visits the latest UK Health Security Agency guidance for 'infection prevention and control for COVID-19' will be strictly followed and you will be advised of any specific measures to be taken closer to your appointment. A swab to check for COVID-19 infection may be performed at your appointments. If you were to develop symptoms that are suggestive of COVID-19 infection (fever, cough, shortness of breath, loss of sense of smell or taste) you will be advised to follow the latest UKHSA guidance with regards to self-isolation and if required seek urgent medical attention via normal routes of healthcare.

What if I wish to complain?

If you wish to complain about any aspect of the study, you can contact the study doctor or nurse. You can also contact the sponsor by email on lstmgov@lstmed.ac.uk or telephone on 0151 702 9396. Complaining will not affect the medical care you receive now or in the future.

The study is sponsored by the Liverpool School of Tropical Medicine (LSTM) and is covered by Clinical Trial Insurance.

How much will I get paid?

The money you are paid is compensation for inconvenience, loss of income, and possible discomfort. Payments are as seen in the table below.

You will be paid between £170 and £285 for taking part in this study depending on how many visits are required and how many samples are taken on each visit

*these visits may not be required

Visit	Payment
Screen/Re-screen	£40
Inoculation	£40
Day 2	£20-£35
Day 7	£20-£35
Day 13	£20-£30
Booster inoculation Day 14*	£40*
Day 16*	£20-£25*
Day 21*	£20-£25*
Day 28	£25-£30
Minimum total:	**£170**
Maximum Total	**£285**

What if I change my mind, or want to stop?

If you do start the study, you are free to stop at any time without giving a reason. If you decide not to take part, or to withdraw from the study, this will have no effect on your future health care.

If you decide to stop, or if you lose capacity to consent during the study, we will continue to use the samples that have already been taken and information that we have already collected unless you ask us not to. You will be paid for the visits completed up to that point.

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

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Will my details be kept confidential?

Yes. For safety, we collect contact details and information about your medical history before you take part.

We will ask your permission to inform your GP that you are taking part in the study as this may be relevant to your medical care outside of the study. We do not expect to find anything which would affect your health care. If we do, we will let you and your GP know about it.

We will also collect information that allows us to understand more about the samples, for example, your age or sex. This will be stored on a password protected database and/or in a locked cupboard. This data may be used by LSTM researchers who need to contact you or record relevant information about the study.

Your medical notes and research data may be viewed by regulatory teams who assess the quality of the research. This is to ensure that it is conducted in accordance with Good Clinical Practice guidelines.

All data will be collected and stored at the LSTM for a minimum period of 25 years. This includes data such as your name and contact details. We use this to check if participants have already taken part in our research. We will also send newsletters and inform you about future studies.

You can find out more about how we use your information by contacting dataprotection@lstmed.ac.uk.

What will happen to my samples?

The samples taken during this study will be processed and stored in the LSTM. All samples will be anonymised at the point of sampling, the people analysing the samples and data will not have access to your personal information. The samples that you give will be gifted for future use in respiratory/infection research and stored in a research tissue bank after the study has closed. 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 respiratory disease. Samples may be sent to national and international collaborating laboratories for their expertise. All identifiable information will be removed.

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Contact details

General questions: please contact the research team on

07740 410 290

during normal working hours.

Web site: https://www.lstmed.ac.uk/arc-volunteer-database

Emergency contact details at any time day or night: Mobile: 07912 053 981

The Chief Investigator for this study is **Dr Andrea Collins**. You may contact her at the Liverpool School of Tropical Medicine, Liverpool Life Sciences Accelerator Building, 1 Daulby Street, Liverpool, L7 8XZ, UK. Telephone: 0151 702 9439.

This research is sponsored by the Liverpool School of Tropical Medicine. It is funded by Merck. The research has been reviewed for scientific content by an external panel. The National Research Ethics Service Committee Liverpool Central has reviewed the study and given approval for it to take place.

Data protection: *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.*

Data access: *The only people in LSTM who will have access to information that identifies you will be people who need to contact you to regarding your participation in the research or audit the data collection process. LSTM will use your name, NHS number and contact details 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 LSTM and regulatory organisations may look at your medical and research records to check the accuracy of the research study. LSTM (research site) will pass these details to LSTM (sponsor) along with the information collected from you and your medical records. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.*

LSTM (research site) will keep identifiable information about you from this study for a minimum of 5 years after the study has finished.

Information for research: *The information will only be used for the purpose of research and cannot be used to contact you or to affect your health care. It will not be used to make decisions about future services available to you, such as insurance.*

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Consent Form

Participant Study number

Challenge 3 Study:

Please initial the box if you agree with each statement. Then, print and sign and date below.

I have read and understand the information sheet version ____**dated__/___/____** for the above study. I have been able to consider the information and ask questions. I confirm that the study procedures and information have been explained to me.	Initial
I understand that this study is voluntary and that I am free to withdraw without giving any reason without my medical care or legal rights being affected.	Initial
I understand that research notes relevant to taking part in this research and data collected may be seen by the regulatory authorities. I give permission for these people to access my records.	Initial
I agree that anonymous data and samples can be transferred outside of the UK for the purpose of the research.	Initial
I agree to my GP being informed of my participation and providing information or for the researcher to access my electronic GP summary record relevant to the study.	Initial
I understand that the samples collected will be anonymised and used and stored for the research described above, and that samples may be sent to national and international collaborating laboratories as part of the study.	Initial
I gift my samples to be used for future research in the UK and overseas. I understand that my samples are anonymised and will be transferred to a research tissue bank at the end of the study. I agree that my samples may be used in future research to investigate factors affecting infection and immunity. ……	Initial
I give permission for the study team to store my contact details in order to invite me to participate in future research	Initial
Biologically female participants of child-bearing potential: I confirm that I am not planning to conceive, and I will use effective contraception if required during the study.	Initial N/A ☐
I agree to take part in this study.	Initial

……	……	_ _/_ _ _/_ _ _ _
Name of participant (print)	Signature	Date
……	……	_ _/_ _ _/ _ _ _ _
Name of person receiving consent	Signature	Date

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Copies: 1 for participant, original for site file and one scanned or filed in research case notes