Participant information Leaflet

Research: working towards preventing pneumonia

SNEAS Trial:

***S**treptococcus pneumoniae* **N**asopharyngeal **E**xperimental carriage study of **A**ttenuated **S**trains

We will invite you to discuss the study with a research doctor or nurse who will answer any questions before you make your decision to take part or not. Please read this information leaflet and talk to other people about the study if you would like to. Take your time to decide if you want to be involved.

What is the purpose of the study?

Healthy adults and children often have bacteria *Streptococcus pneumoniae* in their nose. In most adults this is present at least once per year and more often in children. These bacteria may help to develop our natural immunity. However, there is also a risk in some vulnerable people that these bacteria can cause illness.

Mild infections with pneumococcus are very common, such as ear infections in children. Very young children and adults who are elderly or those who have other illnesses are more likely to become ill. These bacteria can infect the lung (causing pneumonia) or the brain (causing meningitis) or the blood (causing sepsis). These severe infections are very uncommon in healthy adults.

If we learn how our bodies respond to these bacteria, in future we may improve pneumonia vaccines. Our research team want to study what happens when small numbers of the bacteria are in the nose of healthy volunteers.

We have already studied this safely in more than 1000 volunteers using the strain (type) of these bacteria commonly found in healthy children and adults.

In this study we will modify the bacteria genetically to remove the part of the bacteria more likely to cause illness in at risk groups.

Stage I: we compare four groups of participants. This will allow us to compare the effect of the modified bacteria to the normal bacteria that we commonly carry in the nose. Some participants will be given a control (salt water).

Stage II: after a few months we will compare whether those who received the modified bacteria have acquired protection against the bacteria found in healthy adults.

It is important that participants plan to complete both Stage I and II for the data to contribute to this research.

Do I have to take part?

No. Taking part in this study is voluntary.

Who may take part?

We are looking for volunteers who are fit and healthy. If we find any reason you or your close contacts may be at higher risk of infection, then we will not invite you to take part.

You will not be eligible if you:

- Are younger than 18 or older than 50 years
- Taking antibiotics
- already vaccinated against pneumococcus (routine in UK if born since 2005 and higher risk groups)
- are allergic to penicillin or amoxicillin
- are pregnant or trying to conceive
- are at increased risk of infection due to a health condition or medication
- directly caring for someone who has lower immune levels (such as patients, young children and the elderly)
- have taken part in similar research before
- have overseas travel planned during the follow up visits.
- Are a regular smoker (includes e-cigarettes) or a significant history of daily smoking
- History of drug or alcohol abuse
- Are not available for the later follow up 'challenge' after approximately 6 months

It is important that you are available for Stage II the later follow up. There is flexibility over the time period between 5 and 12 months)- please discuss with the research team.

What happens if I choose to take part?

1. **Consent** –We ask you to sign a consent form when you are sure you want to take part.
2. **Health check and eligibility** – for safety. This includes a clinical assessment including a blood sample, listening to your heart /lungs and pregnancy test (females).
3. **Taking samples** – We take samples from the nose, throat and blood *(see below*).
4. **Being given drops of pneumococcus in the nose:** We put a few drops of either the modified bacteria (attenuated), or a control which may be saline, or the bacteria commonly found in adults (un-modified). You will be allocated to the group at random this is a fair way to ensure we have similar types of participants in each group.
   Booster: the dose is repeated after two weeks.
5. **Monitoring:** we will ask you to check in by contact us daily to make sure you are well for 3 days and any time if you have symptoms.
6. **Antibiotics:** after about six weeks we ask you to take an antibiotic that is known to treat these bacteria. You may be asked to take this again at the end of Stage II.
7. **Challenge:** after a further six months (approximately) we ask you to return and recheck you are healthy. Then we will put a few drops of the bacteria commonly found in healthy adults (not modified) in your nose to see if you have developed an immune response.
8. **Visits** – there are nine visits over the first six weeks then you return after approximately six months for the challenge when there are four more visits over two weeks.

What kind of samples do you take?

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 more about the bacteria in your nose and your immune response.

Throat swab: we wipe the back of your mouth with a sterile swab (like a cotton bud) to find out if there are any viruses or bacteria.

Blood samples: We take blood samples from a vein in your arm (using a needle). We will take up to 50 mL (about the same as 10 teaspoons)

You may choose to allow the researchers to study the DNA from your blood sample. If you choose not to donate your DNA you may still take part in the study.

Sub-groups – additional options:

Nasal scrapes: Some participants may be asked to provide nasal cells using a rhinoprobe (small tooth pick) to collect cells from the inside of the nostril (small scratch). An additional payment will be made for these participants.

Nasosorption: to collect cells from your nose we place a small piece of paper inside your nostril for one or two minutes.

Saliva: we ask you to spit into a small tube.

Shedding: we may use gentle methods to find out if bacteria move from the nose to the hand (for example a swab or coughing).

Monitoring bacteria: we want to learn more about how bacteria move from the nose when you cough or rub your nose. We may gently wipe your hand with a cotton bud (swab) or we may ask you to cough or breathe over a laboratory sample plate, so the laboratory can look for the bacteria.

Home samples: You may be invited to take part in home sampling. You do not have to take part, it is optional and explained in a separate information sheet; you can participate in this study without completing home sampling.

Home sampling involves taking a saliva and nasosorption sample at set time points. The samples are taken before bacteria are put in your nose then at 15 minutes, 1, 2, 4, 8, 24, 36 and 48 hours after the inoculation. The samples must be taken within 15 minutes of the proposed time. You will be given a sampling bag with cool packs to keep the samples cool, a thermometer to record the temperature of the samples and a sampling timetable explaining exactly when the samples are due to be taken. You will be asked to photograph the sample once taken and send the photo to the research team to demonstrate compliance with the schedule.

What will happen to my samples?

We will process your samples in laboratories at the Liverpool School of Tropical Medicine (LSTM) and at the Royal Liverpool University Hospital. We will measure the levels of bacteria and viruses in your nose, and we will look in detail at how your immune system responds to the pneumococcus bacteria. To make full use of your samples, we ask that you "gift" your samples to LSTM. We will store them so that we may use them in the future or send to collaborators involved in pneumonia research globally (universities, NHS organisations or companies involved in health and care research in this country or abroad). We would not send your personal details (see below).

What are the benefits of taking part?

There are no direct benefits to you other than a health check. You will be a part of what we believe is a valuable research study that may help us to improve medical care for others.

Stage I: **Nine visits over six weeks (additional samples may be collected for sub-groups at some visits as described above**

Visit (V) 1: ***Screening*** *check, consent, and samples*

Health Check: we make sure you are fit to take part in the study by asking relevant questions about your health, check your blood pressure, temperature and listen to your heart and lungs. Check your height and weight. For women, we check that you are not pregnant using a urine test. We collect samples including a throat swab, nasal wash and blood test.

We book your next appointments - we will try to be flexible

⇩ *between 1 to 7 days later*

V2: given pneumococcus ***bacteria*** *up the nose*

Bacteria: We use a dropper to put a small number of bacteria or a control into each nostril. Usually, volunteers have no symptoms afterwards.

Safety: a doctor or nurse are available by telephone 24 hours a day. We will give you a course of antibiotics in case you are unwell. Each day for the next 3-4 days we will ask you to contact the research team by phone or text to ensure that all is well and to check your temperature reading (a thermometer is provided).

⇩ *Daily contact to confirm you are well (app, phone /text etc). Then after 2 days later…*

V3: Monitoring

Monitoring: Nasal wash

⇩ *Continue with a daily contact. Then 4 days later:*

V4: Monitoring

Monitoring: Nasal wash

⇩ *Then 8 days later*

V5: ***Booster***

Booster of bacteria *in the nose, safety check and blood sample*

⇩ *then after 2 days*

V6: Monitoring

Monitoring: Nasal Wash

⇩ after 6 days

V7: Monitoring

Monitoring: Nasal Wash and Bloods

⇩ after 6 days

V8: Monitoring

Monitoring: Nasal Wash

⇩ after 7 days

V9: Monitoring

⇩ Monitoring: Nasal wash– if positive carriage then participants will be invited to an additional nasal wash before Stage 2 and a further course of antibiotics

Antibiotics: take a 3-day course of antibiotics

Stage II 'challenge'

We think that having small number of bacteria in your nose might protect you against illness from these bacteria possibly for a long time. But we cannot be certain. To test this, after about six months all participants will have the pneumococcus bacteria (the type commonly found in healthy adults) put into their nose to see if the is an immunising effect from bacteria given in Stage I.

Stage II Visits - Four visits over two weeks (additional samples may be collected for sub-groups at some visits as described above

Visit 1:

Screening check, consent, and taking samples

We make sure you are still fit to take part in the study, by repeating the questions, pregnancy test (women) and examination done at Stage I.

We take a throat swab, the nasal wash and a blood test.

⇩ *between 1-7 days later*

Visit 2:

Being given drops of bacteria up the nose

Bacteria: we put a small number of the bacteria into each nostril.

Safety Check in: each day for the next 3-4 days we will ask you to contact the research team by phone or text to ensure that all is well and to check your temperature reading (a thermometer is provided in the study)

⇩ *Daily contact (app, phone call or text SMS). Then 2 days later…*

Visit 3: Monitoring

Monitoring: Nasal wash

⇩ *Continue with daily contact. Then 4 days later…*

Visit 4: Monitoring

Monitoring: Nasal wash and blood sample

⇩ *Then after 8 days…*

Visit 5: Monitoring

Monitoring: Nasal wash and blood sample

⇩

End of the study

At the end of Stage II if our laboratory confirm that the study bacteria was found on nasal washes we will ask you to take the antibiotic (amoxicillin for 3 days).

Additional samples:

At any visit you may be asked to monitor if bacteria move from the nose to the hand for example a swab or coughing onto a microbe plate . Some participants may be asked to have nasal cell samples at some of the above visits this time will be reimbursed (see below). At the end of stage 1 some participants may be asked to attend an additional nasal wash or take another course of antibiotics.

What are the risks of being in the study?

Live bacteria: there is a very small risk of infection to you or your close contacts. A safety leaflet explains what to do if you feel unwell or have symptoms, we provide a thermometer. We check participants are at a low risk of infection then monitor them closely. We provide antibiotics to treat symptoms without delay if required. At the end of Stage I we ask all participants to take the antibiotics. At the end of Stage II, we ask those who had this bacteria in nasal wash to take antibiotics.

Pregnancy: we advise participants not to become pregnant during the study and to advise the research team if they do.

Nasal wash: the only side effect is a little discomfort and some experience a runny nose.

Nasal cells: a little discomfort, spot of blood from scratch or may trigger a response to briefly make your eyes water.

Nasosorption: little if any discomfort.

Blood: Some people can feel light-headed. Sometimes, may have a bruise.

What if there is a problem?

If you have any concerns, you or your health provider can contact the research team 24 hours-a-day by phone. We advise you to follow your usual route of health care to avoid any delay in treatment as symptoms may be unrelated to the study. If you wish to complain about any aspect of the study, you can contact the study team or LSTM Research and Development Team.

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

Even if you do start in 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 will have no effect on your future health care. If you decide to stop, we will continue to use the samples and information that we have already collected unless you tell us not to. You will be paid for the visits completed up to that point.

How much will I get paid?

Participants are compensated for their time, travel, inconvenience and discomfort. Participants will receive an early payment of £70 at the end of Stage I and the balance for visits attended at the end of Stage II.

Visit	Payment
Screen	£25*
Day 0 1st Bacteria and Safety	£25
Day 2	£10*
Day 6	£10*
Day 14 Booster and safety	£30
Day 16	£10*
Day 22	£10
Day 27	£15*
Day 36	£10
Sub-group: nasal wash	£10
Challenge (Stage II)	
Re-Screen	£25*
Inoculation	£25
Day 2	£10*
Day 6	£10*
Day 14	£15*
Minimum Stage 1&2 – all participants	**£230**
Additional Sub-group payments (selected participants)	
Home Samples £6 per sample up to £48 after inoculation and £48 after booster if collected within the 15 minute time frame	£48 £48
Nasal Scrapes £45 (*at these times)	£45
Nasal wash between stage 1 & 2	£10
Maximum total payment for those selected to have additional samples:	**£381**

In the event that participants are rescreened they will be reimbursed for an addition visit.

Will my details be kept confidential?

Yes. For safety, we collect information about your medical history to check you are healthy and contact details before you take part. You have the right to request to view your data.

We will also collect information 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 accessed by LSTM researchers who need to contact you or record relevant information about the study. Also, by the regulatory teams who oversee the quality of the study. We do not share information that can identify you with people who analyse the research or who we may share samples with; as your samples and data are given a unique number.

We will ask your permission to inform your GP that you are taking part in the trial. We do not expect to find anything which would affect your health care but if we do, we will let you and your GP know.

Data will be stored at Liverpool School of Tropical Medicine for a minimum period of 10 years. These data include your name, and contact details and are used to check if participants have already taken part in our research and to let you know about future research studies or send newsletters. The information will only be used for the purpose of health care research. It will not be used to make decisions about future services available to you, such as insurance.

If you have questions on the use of your data, contact:dataprotection@lstmed.ac.uk.

Should you wish to make a complaint regarding the use of your data please contact the Information Commissioners Office at https://ico.org.uk/

If at any time you no longer want to be contacted by this team, please email 2volresearch@lstmed.ac.uk or select unsubscribe.

Contact Research Team:

Emergency contact details any time day or night: Mobile: 07919 480 736

Contact during normal working hours**:** 0151 702 9486 or 077 404 10290

Chief Investigator is Dr Andrea Collins, Liverpool School of Tropical Medicine.
Funder: Medical Research Council **Approved by**: National Research Ethics Service
Sponsor: Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA, UK who act as the data controller for this study who are responsible for looking after your information and using it properly.

Consent form SNEAS Study

Study number

Research: working towards a nasal vaccine for pneumonia:

***S**treptococcus pneumoniae* **N**asopharyngeal **E**xperimental carriage study of **A**ttenuated **S**trains

If you agree with each sentence please **INITIAL** the box. Then, print and sign your name below and add today's date

I have read and understand the information sheet version 4.0 for the above study. I have been able to consider the information then answer the questionnaire and had an opportunity to ask questions.	Initial
I gift my blood and other samples to LSTM. I consent to their long-term storage, and to their future use in medical research in the UK and overseas	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 give permission for relevant sections of my medical notes and data collected during the study to be seen by those conducting or monitoring this research.	Initial
At this stage I plan to be available to attend study visits including Stage II after about 6 months	Initial
I agree to my GP being informed of my participation in the study.	Initial
I understand that I should not become pregnant during this study for safety reasons.	Initial

Optional: I agree to take additional home samples if requested — Initial to decline / Initial to agree

Optional: I **agree** to my gifted samples undergoing genetic analysis in the UK or overseas.

Initial to decline / Initial to agree

Initial

I agree to take part in this study.

……	……..	……
Name of patient	Signature	Date
……	……..	……
Name of person taking consent	Signature	Date

1 copy for patient: 1 for the case report form and 1 to be filed in the hospital notes