Participant information sheet: Healthy Smokers (Group 1)

Research: Experimental Human Pneumococcal Challenge in Chronic Obstructive Pulmonary Disease (COPD) and Cigarette Smoking

Would you like to take part in our research? This information leaflet tells you how you could take part. A member of our team will also discuss it with you: please ask us 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 some bacteria called pneumococcus. We think that small numbers of bacteria present in the nose ("nasal colonisation") may protect people against disease. Small numbers of these bacteria are often found in the nose of healthy adults (at least once per year) and more often in children. Usually, the carrier does not know the bacteria are there but, in some people, it can cause illness. Mild infections with pneumococcus are very common, such as ear infections in children. Pneumococcus can also infect the lung (causing pneumonia); more severe infections of the brain (causing meningitis) or the blood (causing sepsis) are very uncommon in healthy adults: about 50 cases in Liverpool per year. Very young children and adults who are elderly or those who have other illnesses are more likely to become ill.

For the purpose of this study we will put small number of the bacteria in the nose of volunteers similar to the amount commonly carried by healthy adults. This will allow us to learn about the protective mechanism that occur in the nasal lining and use this later in the development of new vaccine against pneumonia.

More than 1000 participants have already been studied safely using this method of putting bacteria in the nose.

Samples taken during the study can help us to understand more about the immune responses and inflammatory process and help to develop better vaccines for the future.

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 participants that smoke cigarettes daily and are fit and healthy. We check for reasons which may put you at higher risk from the study. We also make sure that your participation will provide helpful information to us. If we find any reason you may be at higher risk of infection, then we will not invite you to take part.

You will be eligible if:

- Adults aged 18 - 50 years
- Current regular cigarette smoker - smoking an average ≥5 cigarettes per day for the preceding 3 months
- Fluent spoken English - to ensure a comprehensive understanding of the research project and their proposed involvement
- Access to telephone (safety and timely communication)
- Capacity to give informed consent

You will not be eligible if:

- In a caring role or with intimate physical contact with at-risk individuals (children under 5yrs, immunosuppressed adults) during the period of pneumococcal colonisation
- History of or current regular drug or alcohol abuse (frequently drinking alcohol: men and women should not regularly drink > 3-4 units/day and >2-3 units/day respectively)
- Taking daily medications that may affect the immune system e.g. systemic steroids, systemic corticosteroids, antibiotics, or disease-modifying anti-rheumatoid drugs.
- Any acute illness (new symptoms within preceding 14 days which are unexplained by the known past medical history)
- Taken any antibiotics in the preceding 28 days
- History of culture-proven pneumococcal disease
- Involved in another clinical trial unless observational or in follow-up (non-interventional) phase.
- Have been involved in a clinical trial involving EHPC and bacterial inoculation in the past three years
- Have disease associated with altered immunity, including diabetes, alcohol abuse, malignancy, rheumatological conditions
- Taking medication that affects blood clotting (except aspirin and clopidogrel) e.g. warfarin or other oral or injectable anticoagulants
- At the clinician's discretion any unstable or poorly controlled co-morbidity
- Have any **uncontrolled** medical/ surgical conditions such as but not restricted to: hypertension, mental health conditions, epilepsy, narcolepsy, chronic conditions requiring pain medication such as osteoarthritis, skin conditions, allergies, hay fever, and any other condition at the discretion of the PI.
- Allergy to penicillin/amoxicillin AND clarithromycin
- Concern of the study doctor about the participant's health
- ≥20 pack year smoking history

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 suitable, you will be asked to sign the consent form. A copy of this information sheet and your signed consent form will be given to you to keep.

The study will involve 9 clinic visits over a minimum of 6 weeks. (A subgroup may attend further a further visit).

What samples do you take?

We collect nasal and blood samples to look at the immune response and bacteria in the nose.

Nasosorption: We put a small piece of blotting paper inside your nostril and hold it there for up to 3 minutes. This takes some concentrated secretions from inside your nose.

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 immunity.

Nasal swab: We take a cotton swab (similar to a cotton bud) and insert it into your nose. We pass this into your nose until we can sample the nasopharynx. This will take some cells from the nasopharynx so that we can look at bacteria and viruses.

Throat swab: We take a small cotton swab (as above) and wipe the back of your throat in a circular motion. This is used to detect bacteria and virus in your throat.

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) during this visit.

Nasal cells: We insert a very small plastic spoon (similar to a tooth pick) 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.

Urine sample: We take a small amount of urine to test for nicotine levels. Female participants will have a urine pregnancy test during the pre-screen and/or screen visit.

What will happen at each visit?

Screening Period	
Consent Visit	A member of the research team will discuss the study involvement with you, this may be done as a group presentation. You will have the opportunity to ask questions and discuss the study directly with the researcher in private following the presentation. If you are happy 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.
Pre-Screen Visit	This appointment will take approximately 30-45 minutes. During the appointment we will ask some routine questions about your medical health and we will listen to your heart and lungs. This is done to make sure you are fit and well. A small (3ml) blood sample will be taken to check that you are well (less than one teaspoon). A urine sample will be taken to check for pregnancy (females only). All participants will have a urine test to check nicotine levels. We will assess your breathing, the results may require you to have a breathing test, this is called a spirometry. This involves taking a deep breath and exhaling rapidly and forcefully into a machine. This technique is repeated ≥3 times to achieve an accurate result.
Screen Visit	This appointment will take approximately 30 minutes. We will take blood, throat swabs, nasal wash, nasal cells, nasosorption and a urine sample.

	Female patients will have a urine pregnancy test performed if ≥2 weeks since the pre-screen visit.
Inoculation	
Inoculation Visit (Putting the bacteria into your nose)	We collect nasosorption. We use a dropper to put a small amount of water containing a small number of bacteria into each nostril. Usually volunteers have no symptoms afterwards. There will be a doctor or nurse available by telephone 24hours 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 • Thermometer to check your temperature at home • Safety information sheet • Study contact card We will ask that you inform us of your temperature and symptoms daily for the next 3-4 days using an App available on android phones and complete a symptoms log daily for 7 days.
Monitoring Period	
Clinic appointments on day 2, 7, 9, 14, 22* and 29 post inoculation	At each visit, a number of samples will be taken which may include throat swab (s), nasosorption, nasal wash, nasal cells and blood tests
End of the study	Participants that are colonised with the bacteria at any time point will be asked to take the antibiotics from the safety pack to clear the bacteria Amoxicillin 500mg three times per day for 5 days OR Clarithromycin 500mg twice daily for 5 days *.
Saccharin test	Optional extra visit see below for details.

* Colonisation positive participants only

What does Home Sampling involve?

You may be invited to take part in home sampling. You do not have to take part in this, it is optional, you can participate in this study without completing Home Sampling.

Home sampling involves taking a saliva and nasosorption sample at 8 time points following the inoculation. The samples are taken 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 does the Saccharin test involve?

You may be invited to take part in the saccharin test, this will be an additional visit at 7-28 days following Day 29. You do not have to take part in this, it is optional, you can participate in this study without attending this visit. During this visit a small saccharin tablet (like a sweetener) will be inserted into one of your nostrils. We will time how long it takes for you to taste the saccharin. This will help us to measure how well the cells in your nose (called cilia) can clear debris.

What are the risks of being in the study?

The risks that you should consider *before* participation in this study are the risks associated with venepuncture, nasal sampling and inoculation with live bacteria.

Blood sampling: The risks associated with blood sampling (venepuncture) and cannulation are minimal, but this may cause temporary pain, bruising and/or bleeding to your arm. The blood sampling and cannula insertion will be performed by trained medical professionals.

Nasal sampling: There is limited risks associated with these samples. During a nasal wash, you may swallow a small amount of salty water however this is harmless. The throat swab may make you gag a little. The nasal swab can be a little uncomfortable (this passes very quickly) and may cause a small amount of bleeding but this is uncommon. The nasosorption can tickle your nose a little. The nasal cell sample is slightly uncomfortable and may make your eyes water, this is very momentary. Sometimes a small amount of blood can be evident on the sample probe, it is highly unusual for it to cause an actual nose bleed.

Inoculation with Pneumococcal Bacteria: Because the bacteria are alive, there is a very small risk of infection to you or your close contacts. We do not expect anyone to develop an infection, but this is why we choose participants carefully and monitor them closely. We have experience of using this model safely in more than 1000 healthy volunteers 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 if there is a problem?

You can contact the research team 24 hours-a-day by phone. They will answer any questions, and an emergency service will be available day and night. Any medical care you need will be provided by the NHS.

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 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 and is covered by Clinical Trial Insurance.

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.

Will my details be kept confidential?

Yes. For safety, we collect information about your medical history and contact details before you take part. The clinical research team use this information to check you are healthy, and to contact you when needed.

We will also collect information which allows us to understand more about the samples, for example, you age or sex. However, those outside of the clinical team are never given information that can identify you. Your samples are given a unique number, and your name is not used.

We will ask your permission to inform your GP that you are taking part in the trial as this may be relevant to your medical care outside 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.

All data will be collected and stored at the Royal Liverpool University Hospital and the Liverpool School of Tropical Medicine. It will be stored for a minimum period of 10 years. Your medical notes and research data are may be looked at by those who monitor the research.

What will happen to my samples?

The samples taken during this study will be processed and stored in the LSTM. These samples will be gifted for future use in ethically approved research.

At the end of the study, remaining samples will be transferred to a research tissue bank held at the LSTM. All samples will be anonymised at the point of sampling. The stored samples will be analysed as and when new technology becomes available, 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 however all identifiable information will be removed.

DNA will be extracted from your samples and stored to determine if there are genetic factors that relate to protection or susceptibility to pneumonia.

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 a new methods to prevent respiratory infections through vaccination. You will not gain any direct benefit in this study.

How much will I get paid?

The money you are paid is compensation for inconvenience, loss of income, and possible risks of taking part. The first payment will be made at the end of part one. If you are eligible and choose to take part in the second study you will receive a second payment at the end of part two. Our payments are below.

Procedure	Duration	Payment
Initial visit (study information, eligibility questions, informed consent)	60 mins	£0

Pre-screen appointment Clinical exam, vital signs, medical history + safety bloods	30 mins	£ 30
Pre-screen appointment Clinical exam, vital signs, medical history, safety bloods + Spirometry	45 mins	£ 35
Screening appointment (samples)	30 mins	£ 30
Inoculation with pneumococcus. Also includes participant making daily contact for the first 3-4 days using App; contact payment may be withheld if the participant does not make daily contact	45 mins	£ 40 Includes the daily contact at £5/day
Clinic visit samples on day 2, 7 and 29	30 mins	£ 20
Clinic visit for samples only on day 9	20 mins	£ 15
Clinic visit for samples on day 14 and day 22[1]	15 mins	£ 10
Optional home samples [2]	8 timepoints over 48 hours	£48
Saccharin test [2]	30 mins	£10
Total Remuneration £185-£200 (Plus Optional Home samples £48)		

[1] For colonisation positive participants only [2] A subgroup of participants

Contact details

General questions: please contact the research team on 07740 410 290 or 0151 702 9424 during normal working hours. Web site: http://www.lstmed.ac.uk/research/topics/pneumonia

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 and the Royal Liverpool and Broadgreen University Hospitals. It is funded by the Medical Research Council. The research has been reviewed for scientific content by an external panel. The National Research Ethics Service Committee Liverpool East has reviewed the study and given approval for it to take place.*

Liverpool School of Tropical Medicine (LSTM) 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. LSTM will keep identifiable information about you 10 years after the study has finished.

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. 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.

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

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 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. 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 10 years after the study has finished.

LSTM will collect information about you for this research study from you and/or your GP records. Your GP will not provide any identifying information about you to LSTM. We will use this information to confirm your eligibility

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

Experimental Human Pneumoccocal Challenge Model

EHPC in COPD and Cigarette Smoking Consent Form Healthy Smokers (Group 1)

Participant Study number

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 **2.1** for the above study. I have been able to consider the information and to ask questions. I confirm that the study procedures and information have been explained to me. I have had the opportunity to ask questions and I am satisfied with the answers and explanations provided.	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 the section of my medical notes relevant to my taking part in this research and data collected may be seen by the regulatory authorities or NHS Hospital. I give permission for these people to access my medical records.	Initial
I agree to my GP to be informed of my participation, and to provide 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 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 will gift these samples so that they may be used for future ethically approved research in the UK and overseas.	Initial
I understand that these samples will be transferred to a research tissue bank for future use in ethically approved research at the end of this study.	Initia
I give permission for the DNA to be extracted from these samples and gifted for use in future studies and may be sent to research collaborators national/international.	Initial
I confirm that I am not planning to conceive, and I will use effective contraception if required during the study.	Initial
I agree to take part in this study.	Initial

I DO NOT agree to take part in Home Samples	Initial	I agree to take part in Home Samples	Initial
I DO NOT agree to take part in saccharin testing	Initial	I agree to take part in saccharin testing	Initial

…….	…….	_ _/_ _ _/_ _ _ _
Name of patient (print)	Signature	Date
…….	…….	_ _/_ _ _/ _ _ _ _
Name of person taking consent	Signature	Date

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