THE COLLEGE OF MEDICINE
Malawi-Liverpool-Wellcome Trust
Clinical Research Programme
www.mlw.medcol.mw

Participant information leaflet

Feasibility study of Experimental Human Pneumococcal Carriage in Malawi

Introduction

We invite healthy adults to participate in a research project to determine if it is possible to transfer established and safe procedures from Liverpool, UK to Blantyre, Malawi to experimentally put the bacteria *Streptococcus pneumoniae* (called "pneumococci") into their nose.

Healthy adults and children commonly have pneumococci living in their nose without any symptoms. In most adults this is present at least once per year but more often in children. The presence of these bacteria, called "carriage", may help to develop our natural immunity against infection. However, there is also a risk in some vulnerable people that these bacteria can cause illness.

Mild infections can progress from carriage in vulnerable children and adults. Certain infections with pneumococci are very common, for example ear infections in children. More serious infections may develop in very young children or in elderly adults or those who are weak with other illnesses. These include infections of the lung (pneumonia) or the brain (meningitis) or the blood (sepsis). These severe infections are very uncommon in healthy adults.

We have studied what happens when pneumococci are experimentally put into the nose of healthy volunteers in Liverpool, United Kingdom for ten years. We have completed this safely, causing carriage in half of the participants but no infections, in over 1,000 participants. We use the experiment to test if new vaccines prevent pneumococci remaining in the nose. Our aim is to safely transfer this successful research to Malawi so that we may develop more effective vaccines for people who need them most.

This leaflet will explain what the study involves, and what will happen if you agree to take part in the study. If you decide to participate in the study, there is a three in four chance of pneumococci being put into your nose. A research doctor or nurse will discuss the study with you and answer any questions you may have 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.

Who is undertaking this study?

The study is run by the Malawi-Liverpool-Wellcome Trust Clinical Research Programme (MLW), part of the College of Medicine at the University of Malawi. The Wellcome Trust, United Kingdom funds this research.

What is the purpose of this study?

The purpose of this study is to test the research techniques and procedures used in Liverpool, UK to make sure they work and are safe in Blantyre, Malawi. In this study we will compare three groups of healthy participants, putting different numbers (doses) of pneumococcus bacteria into their noses to cause carriage. This will allow us to make sure that the dose of bacteria used to cause carriage in healthy volunteers in Liverpool has the same effect on healthy volunteers in Malawi. Some volunteers will be given a control (no bacteria, salt water used instead) to make sure any changes that we see happen because of the bacterial dose and not for other reasons.

Who may take part?

We are looking for adult volunteers who are fit and healthy. You are eligible if you:

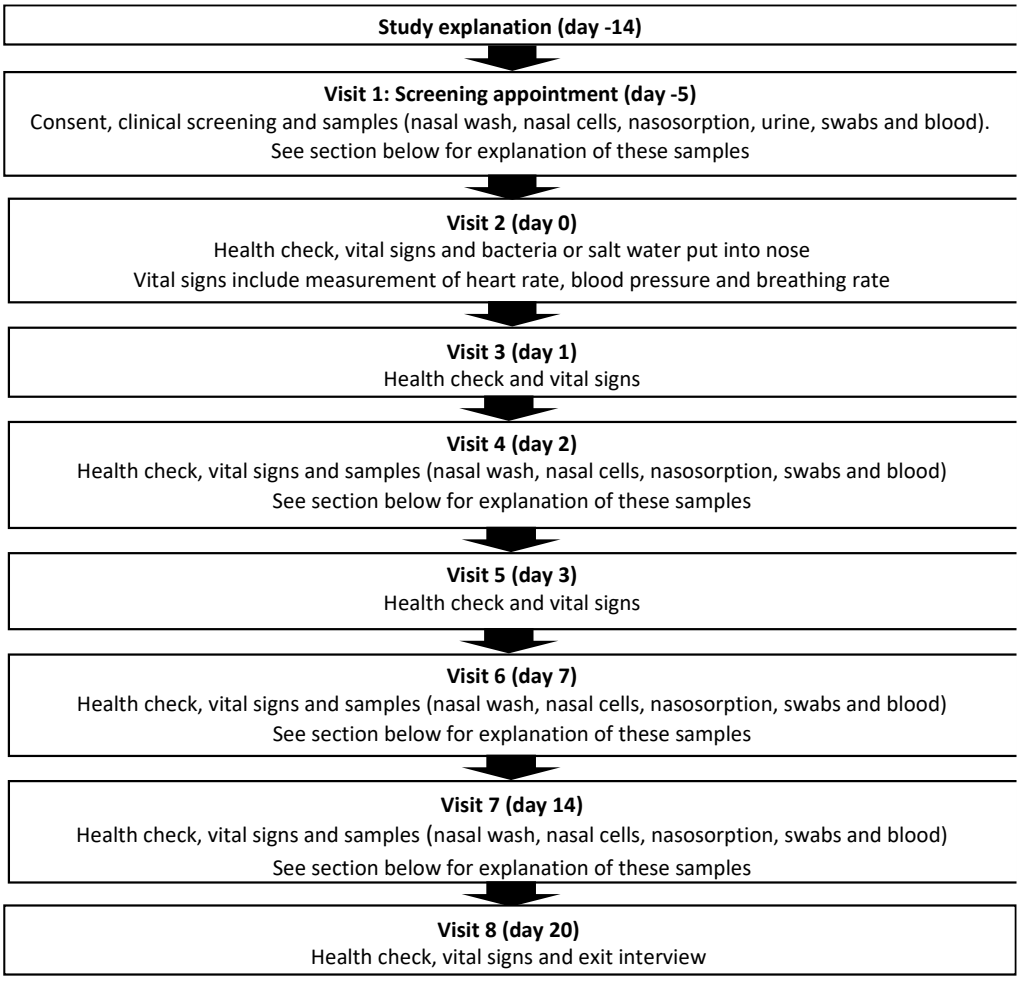
- Are between 18 and 40 years old, fit and healthy.
- Speak and read Chichewa or English fluently (this is for safety so that you can follow safety instructions in the unlikely event that you become unwell).

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:

- Cannot read Chichewa or English (this is for safety so that you can read materials that describe when and how to contact us in the event of a problem)
- Are already vaccinated against pneumococci
- Are allergic to penicillin or amoxicillin
- Are pregnant or trying to conceive
- Are elderly (aged more than 65)
- Are at increased risk of infection due to a health condition or medication that increases your risk of developing infection (you will be offered a HIV-infection test as part of this study)
- Are unable to attend the planned follow up visits
- Are or have recently been a regular smoker
- Have a history of drug or alcohol abuse
- Have close physical contact (e.g. sleeping in the same room or nursing) with people at higher risk of severe infection (e.g. children under 5 years age, the elderly, or people with chronic ill health)

What is going to happen?

Visits – there are seven visits to the research clinic over the two-week period. The diagram below explains what will happen and when if you decide to take part:



Visit 1

a) **Consent** –We ask you to sign a consent form when you are sure you want to take part and we are sure that you understand all the procedures.
b) **Health check and eligibility** – for safety. This includes a clinical assessment including a blood sample, listening to your heart /lungs, a HIV-infection test, and a pregnancy test (females).
c) **Taking samples** – We take samples from the nose, throat and blood *(see below*).

Visit 2

Put drops of pneumococcus bacteria in your nose: We will put a few drops of carefully measured pneumococci or a salt water drop into your nose. You will be allocated to pneumococci or salt water at random as this is a fair way to ensure we have similar types of participants in each group. You will not know if you have been given the bacteria or the salt water. We do not expect that the groups will feel any differences.

Visits 3-8

a) **Monitoring:** We will ask you to stay over-night at the Grace Bandawe Centre in Blantyre for the first three nights after the bacteria/salt water is given. This is to ensure that you are safe and so that we can provide medical care quickly (at Mwai Wathu Pvt Hospital) in the unlikely event that it is required. You will be provided with their own room and food paid by us. After that, we will continue to monitor you at home for 7 days. This will be by visit to the research clinic on days 7 and 14 and by mobile phone on other days. We will check your vital signs (temperature, respiratory rate, pulse rate and oxygen levels) at each visit to make sure you are well. The final check will be made at 14 days after the bacteria/salt water is given.
b) **Taking samples –** we will take samples on days 2, 7 and 14 to determine if you have achieved carriage of pneumococci in your nose and if the body has responded to the pneumococci.
c) **Antibiotics:** We may ask you to take the antibiotics provided if you are carrying pneumococci. This will occur on visit 7 or by telephone call within three days of visit 7. You will be required to return the antibiotics if these are not required during the study period.

What kind of samples will you take?

- **Nasal wash:** we gently wash 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 sweep the back of your mouth with a sterile swab (like a cotton bud) to find out if there are any bacteria.
- **Blood samples:** We take blood samples from a vein in your arm (using a needle). We will take up to 100 ml (about the same as 20 teaspoons) over the course of the seven visits.
- **Nasal scrapes:** You will be asked to provide nasal cells using a rhinoprobe (small tooth pick) to collect cells from the inside of the nostril (small scratch).
- **Nasosorption:** to collect cells from your nose we place a small piece of paper inside your nostril for one or two minutes and then remove it when soaked.
- **Saliva:** we ask you to spit into a small tube or use a swab for you to soak with saliva.

The benefits of participating in the study are:

You will receive a medical check-up including a HIV-infection test. We will refer you onto specialist care if we identify any problems. You will be a part of what we believe is a valuable research study that may help us to improve medical care for others in the future.

The inconvenience or risks of participating in the study are:

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 will provide you with a thermometer (you can keep this) and antibiotics. We will thoroughly check that you are at a low risk of infection before joining the study then will monitor you closely to ensure that there are no problems. We will provide antibiotics

(amoxicillin 500mg three times daily 5 days) to treat symptoms without delay if required. If you decide to participate, a safety information leaflet will be provided to explain what to do in the unlikely event that you become unwell.

Pregnancy: we advise you not to become pregnant during the study and to inform us if they do. We ask you to tell us this information as pregnancy can affect the immune system, putting you at increased risk of infection.

Nasal wash: the only side effect is a little discomfort. Some people experience a runny nose.

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

Nasosorption: minimal discomfort.

Blood: Some people can feel light-headed and sometimes they may develop a bruise. Trained individuals experienced in taking blood and in performing the procedures listed above will take your samples to minimise any pain or inconvenience.

Overnight accommodation: You will be requested to spend three nights at the Grace Bandawe Centre following on from study visit two. We will pay any costs associated with this. Overnight stays away from home may be an inconvenience.

How confidential is the information I give you?

Only the team concerned with your care will have access to your personal information. For safety, we will collect information from you and your health passport to check you are healthy. We will also collect your contact details and information to understand more about your samples, for example, your age or sex.

The information, separated from your personal details, will be used by MLW researchers and by the regulatory teams who oversee the quality of the study. We will store the information you give us on a secure computer drive in Blantyre. Any written information will be kept in a locked filing cabinet. We will keep the information for a maximum of 5 years.

What will be done with the samples you collect?

We will study the samples in the laboratory at MLW and will send samples to some other laboratories outside Malawi if our laboratory cannot do the test needed. You are welcome to visit the laboratory to understand how they will be managed for the best use. Your samples are given a unique number and not linked to your name. We will store your samples for a maximum of three years. After this time the samples will be destroyed.

How will the research findings be shared?

Results of this project, with no personal details, will be presented at research conferences in Malawi and other countries and published in academic journals. The results will also be shared with the Ministry of Health, Research Ethics Committees in Malawi and the Malawi Liverpool Wellcome Trust. We will also share findings with you and the wider public.

Do I have to take part?

No, taking part in the study is entirely your decision. If you decide to take part, you will be given this sheet to keep and we will ask you to sign a consent form. If you decide not to take part, there will be no change to the way in which you are treated at the hospital. You do not have to give a reason. You are free to change your mind and decide not to be involved at any time. 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 I be compensated for taking part?

You will be compensated for your out of pocket expenses, travel, time spent and burden. You will be paid after each study visit. The payment schedule is based on 8400 MK per visit and will therefore expect to be 67200 MK if the study is completed. You will be provided with overnight accommodation at the Grace

Bandawe Centre for three nights from visit 2 (day 0) to visit 5 (day 3). We will pay for the costs of this accommodation and food in addition to the reimbursements highlighted above.

What if there is a problem?

If you have any concerns, you or your friends and family can contact us 24 hours-a-day by phone. In the event of emergency you will be admitted to the Mwaiwathu Private Hospital with a pre-arranged payment schedule. You will not pay any medical costs for this admission. If you decide to participate in the study you will be provided with a safety leaflet with clear explanation of what to do if there is a problem. Telephone contact numbers are provided below. If you wish to complain about any aspect of the study, you can contact us or the National Health Science Research Committee (NHSRC)

Who can I contact for more information?

If you want any more information you can speak directly to us or contact by telephone or email (see below). If you want to complain about anything to do with the study, you can do so through the MLW complaints procedure or by contacting the Secretariat of the **National Health Science Research Committee (NHSRC)** in Lilongwe.

The relevant contact details are provided below:

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