ISRCTN15728847 https://doi.org/10.1186/ISRCTN15728847

PREVENTING PNEUMOcoccal disease through vaccination: PREVENTING PNEUMO 2

Submission date	Recruitment status	[X] Prospectively registered
13/02/2020	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
18/06/2021	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
17/02/2026	Respiratory	

Plain English summary of protocol

Background and study aims
In the UK, there are two vaccines currently used to provide protection against pneumococcus, a bacteria that causes pneumonia. PCV-13 (Prevenar 13) protects against 13 (of a total of more than 90) types of pneumococcus and is routinely given to children under 12 months old. PPV-23 (Pneumovax 23) protects against 23 types and is routinely given to adults over 65. Both are also used in children and adults with medical conditions that put them at higher risk of lung infections. However, better pneumonia vaccines are needed.

Research studies have shown that there is an increase in infection with some types of pneumococcus that should be covered by these vaccines. We do not know why this is occurring.

In this study, we are exploring how these two pneumonia vaccines affect the presence of two different types of pneumococcus (strains 3 and 6B) being present in the nose of older adults.

Who can participate?
Healthy adults aged 60 to 69 years old.

What does the study involve?
Participants will receive a vaccine of Prevenar 13, Pneumovax 23 or saline into the upper arm.

What are the possible benefits and risks of participating?
We will check for reasons that may put the participant at higher risk for taking part in the study. We also make sure that their participation will provide helpful information to us. If we find any reason that they may be at higher risk of infection, then we will not invite the participant to take part.

If they decide to take part, the participant would attend approximately 15 clinic visits over about 8 months and nose, throat, saliva, urine and blood samples will be collected to look at the immune response and for the bacteria. At one visit they would be given 1 of 3 different injections: 1 of 2 vaccines (PCV-13 or PPV-23) designed to protect against the pneumococcus

bacteria, or a saline injection. The injection received is assigned by a computer system in a ratio of 1:1:1 (1 out of every 3 participants will have PCV-13, 1 will have PPV-23 and 1 will have saline). Neither the participant or the research team can influence what injection is received.

Risks
As both PCV-13 and PPV-23 are licensed vaccines there are not any causes for concern anticipated. The research nurses and doctors will monitor symptoms you experience at each visit and will be available 24-hours a day by phone if needed.

Like all vaccines, the PCV-13 and PPV-23 vaccines can cause side effects, although not everybody gets them. If side effects are experienced, they usually happen in the first few days after vaccination, they are generally mild, and they do not last a long time. The most common side effects of these vaccines are (seen in more than 1 out of 10 people who are vaccinated):
1. Pain, swelling or redness at the site of injection
2. General side effects including headache, nausea (feeling sick), vomiting, decreased appetite, generally feeling unwell, diarrhoea, muscle or joint pain, rash, fever or chills.

As with any medication or vaccine, unexpected, severe allergic reactions may very rarely occur (less than 1 in a million chance). Participants are asked to stay in the clinic for at least 15 minutes after vaccination where the research nurses and doctors can monitor you and have medical equipment and training to manage an allergic reaction.

In rare cases, side effects can be serious or prolonged, although no serious concerns have been raised about these vaccines. It is important to let the research nurses or doctors know if you are worried about your symptoms.

Participants can take medicines after your vaccination to help reduce side effects. For example, paracetamol to treat a fever or pain. We ask you to let the research nurses or doctors know if any medication was taken.

We do not anticipate participants to have side effects from the saline injection. However, participants receiving the saline injection will be monitored in the same way as participants receiving PCV-13 or PPV-23.

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 as we screen participants carefully and monitor them closely. We have experience of using this model safely in more than 1,500 healthy participants with no serious side effects. We provide a safety pack as described above and participants have access to the research team by phone 24/7. We provide a leaflet for participants which explains the safety precautions and what to do if feeling unwell.

Blood sampling: The risks associated with blood sampling (venepuncture) 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 if we could inform your GP.

Nasal sampling: There are limited risks connected with 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 – this is very brief. Sometimes a small amount of blood can be seen on the sample probe, however, it is rare for it to cause a

nosebleed. The research nurses and doctors are trained to treat you in clinic if you had a nosebleed.

Throat swabs: There are limited risks associated with these samples. This sample may make you gag a little.

Saliva and urine sampling: There are no adverse effects of the saliva or urine sampling.

Benefits
The participants 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. Participants may learn more about their general health and wellbeing or receive some protection against pneumococcal disease if they receive either vaccination.

Where is the study run from?
Liverpool School of Tropical Medicine (UK)

When is the study starting and how long is it expected to run for?
July 2019 to December 2022

Who is funding the study?
Pfizer (USA)

Who is the main contact?
Ms Kelly Davies
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Contact information

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2019-004742-15

Integrated Research Application System (IRAS)
276247

ClinicalTrials.gov (NCT)
NCT04974294

Protocol serial number
19-104

Study information

Scientific Title
A phase IV double-blind randomised controlled trial (DBRCT) to investigate the effect of PCV-13 and PPV-23 on pneumococcal colonisation using the experimental human pneumococcal challenge (EHPC) model in healthy adults

Acronym
PREVENTING PNEUMO 2

Study objectives
For several years, scientists have been discussing which pneumococcal vaccine is best for older adults: PCV-13, which induces immunological memory but covers only 13 of more than 90 known pneumococcal serotypes, or PPV-23, with broader coverage but shorter duration of immunity and no induction of immunological memory. We postulate that PCV-13 but not PPV-23 will have a long-term impact on pneumococcal carriage in older adults.

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 21/06/2021, North West - Liverpool Central Research Ethics Committee (3rd Floor Barlow House HRA NRES Centre, Manchester, M1 3DZ, United Kingdom; +44 (0)207 104 8171; liverpoolcentral.rec@hra.nhs.uk), ref: 20/NW/0097

Study design
Three-arm single-centre double-blind randomized controlled trial (DBRCT)

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Pneumonia

Interventions
The PPV-23 vaccine is a 23-valent pneumococcal polysaccharide vaccine produced by Merck Sharp & Dohme Limited. It has marketing authorisation and is licensed for activate immunisation against pneumococcal disease in children and adults from the age of 2. In the UK, it is recommended for adults aged 65-79 years inclusive as part of the national immunisation programme.

The PCV-13 vaccine is a 13-valent, adsorbed pneumococcal polysaccharide conjugate vaccine produced by Pfizer Inc. It has marketing authorisation and is licensed for active immunisation for the prevention of invasive disease, pneumonia and acute otitis media caused by Streptococcus pneumoniae in infants, children and adolescents from 6 weeks to 17 years of age and for prevention of invasive disease and pneumonia in adults ≥18 years of age. In the UK, it is given as a part of the national immunisation schedule at 8 weeks, 14 weeks and 1 year.

The placebo control is commercially available sterile 0.9% sodium chloride (NaCl, saline) for injection

The intervention is given at one timepoint only through the study (vaccination visit) and the dosage for each arm is 0.5ml. The vaccine will be administered by intramuscular injection into the deltoid muscle of the upper arm (right or left).

Randomisation will be computer generated and occur in block sizes of 6. At the vaccination visit participants will be randomised to receive PCV-13 vaccine (0.5ml), PPV-23 vaccine (0.5ml) or 0.9% saline for injection (0.5ml placebo control) in a ratio of 1:1:1. The unblinded clinical study team member will record the allocation on an un-blinded case report form (CRF) and vaccine accountability form and allocate the participant the appropriate vaccine for administration.

Participants will be followed up 7 days after vaccination and then up until the end of the study (Day 218 +/- 3 days) regardless of which treatment arm they are allocated to.

Participants will face a pneumococcal challenge at 1 and 7 months after vaccination. The study team will use a dropper (pipette) to put a small amount of water containing a small number of pneumococcus into each nostril of participants. Participants will be ‘inoculated’ with a dose of the bacteria (80,000 colony forming units) in each nostril. They will lie down in the clinic for 15

min after the procedure and will have a blood sample taken. A brief clinical examination will be carried out. Participants may be asked to complete a daily symptoms questionnaire, this will be completed prior to inoculation and daily for 7 days following each inoculation. At the end of the pneumococcal challenge visit, participants will be given a safety pack including a course of antibiotics (to be taken if the participant is unwell), a thermometer, a safety information sheet, and a study contact card. Usually, participants have no symptoms afterward. There will be a doctor or nurse available by telephone 24 h a day, 7 days a week to answer questions. Participants will be asked to inform the study team of their temperature and symptoms daily for the next 5 days using text message or an App available on iPhones/Android phones. If participants are feeling unwell, they should contact the research team at the provided number.

Nasal wash samples are taken from participants and the presence of pneumococcus is determined by classical culture. These samples are taken on enrolment and then a further 11 times throughout the study at the following time points: day 7, day 23, day 30, day 35 day 42, day 50, day 191, day 198, day 203, day 210, day 218.

If a participant becomes carriage positive, saliva samples are requested from consenting friends and family members who they have had contact with.

Intervention Type
Biological/Vaccine

Phase
Phase IV

Drug/device/biological/vaccine name(s)
PCV-13 vaccine, PPV-23 vaccine

Primary outcome(s)
Rate of experimental pneumococcal colonization (SPN6B) determined by the presence of pneumococcus in nasal wash (NW) by classical culture at any time point following pneumococcal challenge (7-month challenge, Day 2 to Day 22) at 7, 23, 30, 35, 42, 50, 191, 203, 210 and 218 days following vaccination

Key secondary outcome(s))
1. Experimental pneumococcal colonization (SPN3) determined by the presence of pneumococcus in nasal wash (NW) by classical culture and throat, saliva, urine, and blood samples at any time point following pneumococcal challenge (1-month challenge, Day 2 to Day 22) at 7, 23, 30, 35, 42, 50, 191, 203, 210 and 218 days following vaccination
2. Experimental SPN3 in one or more ‘friends and family’ saliva samples at any time point following study participant inoculation requested at a single timepoint if the participant becomes carriage positive

Completion date
31/12/2022

Eligibility

Key inclusion criteria
Current inclusion criteria as of 14/04/2022:
1. Aged 18 to 50 years

2. Speak English fluently (to ensure a comprehensive understanding of the research project and proposed involvement)
3. Have the capacity to give informed consent
4. Have a urine pregnancy test and agree to use adequate contraception during the study (if able to bear children)

Previous inclusion criteria:
1. Aged 60 to 69 years
2. Speak English fluently (to ensure a comprehensive understanding of the research project and proposed involvement)
3. Have the capacity to give informed consent
4. Have a urine pregnancy test and agree to use adequate contraception during the study (if able to bear children)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
18 years

Upper age limit
50 years

Sex
All

Total final enrolment
549

Key exclusion criteria
1. Currently involved in another research study (unless observational or non-interventional)
2. Involved in a previous EHPC study in the last 3 years involving exposure to pneumococcus
3. Previously received a pneumococcal vaccination
4. Allergy to penicillin or amoxicillin
5. Have had a severe, life-threatening allergic reaction to a vaccine
6. Chronic ill-health, including but not limited to problems with the immune system, diabetes, asthma requiring regular medication, recurring ear infections, COPD, major heart/lung disease, cancer, and rheumatoid arthritis
7. Taking medication that may affect the immune system, including but not limited to steroids, nasal steroids, Roaccutane, and anti-rheumatoid drugs
7. Recent antibiotics, either within the last 28 days or long-term for a chronic infection
8. Pneumococcal illness requiring a stay in a hospital within the last 10 years
9. Any other condition that is deemed to possibly put personal safety or the study at risk as

decided by the clinical team
10. Employed in a direct caring role or close contact with individuals at higher risk of infection on a regular basis during the study, including but not limited to children under 5, and people with chronic ill-health or immunosuppression
11. Current smoker, or ex-smoker who has quit within the last 6 months, of regular cigarettes, cigars, e-cigarettes, vapes, and/or recreational drugs
12. Previous significant smoking history of >20 pack-years (20 cigarettes per day for 20 years or equivalent)
13. Pregnant, lactating or intending on becoming pregnant during the study
14. History or current drug or alcohol abuse as assessed by the clinical team
15. Overseas travel planned during the exposure stages of the study which is defined as the time of inoculation until the use of antibiotics
16. Natural pneumococcal carriage. It is anticipated that 10-15% of participants will have a natural pneumococcal carriage at the time of recruitment. Testing will be repeated a few weeks after the initial screening appointment to check if carrier status has changed.

Date of first enrolment
12/07/2021

Date of final enrolment
12/08/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Liverpool School of Tropical Medicine
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Sponsor information

Organisation
Liverpool School of Tropical Medicine

ROR
https://ror.org/03svjbs84

Funder(s)

Funder type
Industry

Funder Name
Pfizer

Alternative Name(s)
Pfizer Inc., Pfizer Consumer Healthcare, Davis, Charles Pfizer & Company, Warner-Lambert, King Pharmaceuticals, Wyeth Pharmaceuticals, Seagen, Pfizer Inc

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		13/02/2026	17/02/2026	Yes	No
Protocol article		07/07/2022	08/07/2022	Yes	No
HRA research summary			28/06/2023	No	No