

A pneumococcal human challenge study in adults aged 50-84 years

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Registration date 12/04/2024	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 10/03/2025	Condition category Infections and Infestations	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

The germ 'pneumococcus' (*Streptococcus pneumoniae*, a bacteria) is a major cause of pneumonia, meningitis and sepsis around the world leading to over a million deaths per year. The biggest impact is on young children and older adults, especially in low-income countries. However, most of the information that we have about how the body responds to this infection comes from younger adults. These younger adults are less likely to develop severe infection and how they respond to bugs is different to how older adults respond. This study looks at how pneumococcus lives in the noses of older adults and causes infection. The aim is to better understand how this bug affects older people, which will hopefully help us design medication and vaccinations better for this age group.

Over the past decade, the research group has developed innovative methods to study pneumococcus infection in healthy volunteers. People are carefully screened for safety and then infected ("challenged") with small amounts of bacteria in their nose, which allows us to understand why some people who are exposed to the bacteria develop infection whilst others don't. This kind of study (a "human challenge" study) can improve understanding of how bugs cause disease and is a cost-efficient way of designing and testing drugs and vaccinations. To date, over 2000 participants have been challenged with pneumococcus, including older people, demonstrating that these studies can be done safely without harm to participants. In this study, older adults will be given pneumococcus in their noses so that tests can be run to see how the bug affects them and sticks to their noses. Samples will be taken throughout the study to understand how the immune system responds to it.

Who can participate?

Healthy older adults and seniors aged 50-84 (inclusive) years old

What does the study involve?

All participants are screened to check they are eligible for the study and are not at high risk of infection. Following this, they will have a clinical examination and nasal and blood tests. All participants are exposed ('challenged') to the pneumococcus germ through drops in the nose.

The study involves a further 6 in-person visits (7 visits including the initial visit above). These are spaced out over approximately 4 weeks. At these visits, participants are checked for any symptoms and will have certain nasal and blood samples taken.

What are the possible benefits and risks of participating?

Participants will be a valuable part of a research study that is hoped will eventually lead to the development of new methods to prevent or treat respiratory infections.

Safety will be paramount in this study. Participants will have access to a study doctor 24/7 and be given backup antibiotics to take if needed. The team will work closely with participants so that they understand the study requirements and will address their questions and concerns.

Challenge pneumococcal bacteria: Because the germ participants are exposed to is live, there is a very small risk of infection to them or their close contacts. However, the germ has been used in previous studies in older adults with no serious side effects. They may however get cold-like symptoms, headaches, earaches, a cough or a fever.

A safety pack is provided and they will have 24-hour access to the research team by phone. This includes clear safety precautions and what to do if they feel unwell. Everyone who tests positive for the pneumococcus germ will take a course of antibiotics at the end of the study, or if they feel unwell, before that.

Blood sampling: The risks associated with blood sampling are minimal, but this may cause temporary pain, bruising and/or bleeding to the arm. The blood sampling will be performed by trained healthcare professionals. In the rare circumstance that anything unusual or medically significant is noticed about your blood then the team will inform them and ask their permission to inform your GP.

Nasal sampling: There are limited risks related to 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 briefly. Sometimes a small amount of blood can be seen on the sample probe, however, it is rare for it to cause a nosebleed.

Incidental medical findings

Since several medical tests are carried out throughout the study, previously unknown health issues (e.g. high blood pressure or abnormal blood results) may be detected. This will be discussed with the participant and with their permission, their GP informed for ongoing follow-up.

Where is the study run from?

The study is run by the Liverpool Vaccine Group at the Liverpool School of Tropical Medicine in Liverpool, UK. We have been studying lung infections using healthy volunteers for over ten years to provide world-leading research into the pneumococcus germ using methods called an Experimental Human Pneumococcal Challenge (EHPC) model. More than 2000 participants have already been safely studied using our methods, including older adults.

When is the study starting and how long is it expected to run for?

October 2023 to October 2025

Who is funding the study?

The Medical Research Council (MRC), UK

Who is the main contact?

Dr Oliver Hamilton, Oliver.hamilton@lstmed.ac.uk

Contact information

Type(s)

Scientific, Principal Investigator

Contact name

Dr Ben Morton

ORCID ID

<https://orcid.org/0000-0002-6164-2854>

Contact details

Liverpool School of Tropical Medicine, Pembroke Place
Liverpool
United Kingdom
L3 5QA
+44 (0)7740410290
ben.morton@lstmed.ac.uk

Type(s)

Public

Contact name

Dr David Oliver Hamilton

ORCID ID

<http://orcid.org/0000-0001-9475-5030>

Contact details

Liverpool School of Tropical Medicine, Pembroke Place
Liverpool
United Kingdom
L3 5QA
+44 (0)7740410290
oliver.hamilton@lstmed.ac.uk

Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

340045

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

24-004, IRAS 340045, CPMS 61054

Study information

Scientific Title

Experimental human pneumococcal challenge in older adults

Acronym

Ages-2

Study objectives

The primary aim of this exploratory study is the detection of pneumococcus within nasal cells using confocal microscopy and comparing this against data from younger adults

Ethics approval required

Ethics approval required

Ethics approval(s)

Approved 29/02/2024, East of England - Cambridge South Research Ethics Committee (Equinox House City Link, Nottingham, NG2 4LA, United Kingdom; +44 (0)207 104 8084; cambridgesouth.rec@hra.nhs.uk), ref: 24/EE/0038

Study design

Single-centre open-label controlled human-challenge study

Primary study design

Interventional

Secondary study design

Non randomised study

Study setting(s)

Internet/virtual, Telephone, University/medical school/dental school

Study type(s)

Other

Participant information sheet

See study outputs table

Health condition(s) or problem(s) studied

Pneumococcal carriage

Interventions

Current interventions as of 10/03/2025:

This is a single-centre, open-label controlled human infection study in older healthy participants using a previously established and safe model of pneumococcal challenge across two phases.

Participants will be older adults and seniors aged 50-84 years old. All participants will be inoculated with live pneumococcus and followed up for evidence of pneumococcal carriage and immune responses through mucosal and systemic sampling.

In Phase A, healthy participants will undergo a challenge with *Streptococcus pneumoniae* serotype 6B (Spn6B) BHN418 strain at a dose of 80,000 colony-forming units (CFU)/naris. This will be administered intra-nasally using a P200 micropipette to give 0.1ml of pneumococcus-containing fluid instilled into each nostril in our human challenge facility. This will occur once during the study in all participants, who will not be randomised or blinded to the intervention. All participants will be followed up for 28 days at Day 2, 6, 9, 14 and 28.

Phase B will be identical to Phase A, except the inoculum will be *Streptococcus pneumoniae* serotype 3 (Spn3) LIV014-S3 strain at the same dose of 80,000CFU/naris

Previous interventions:

This is a single-centre, open-label controlled human infection study in older healthy participants using a previously established and safe model of pneumococcal challenge. Participants will be older adults and seniors aged 50-84 years old. All participants will be inoculated with live pneumococcus (serotype 6B) and followed up for evidence of pneumococcal carriage and immune responses through mucosal and systemic sampling.

Healthy participants will undergo a challenge with *Streptococcus pneumoniae* serotype 6B (Spn6B) BHN418 strain at a dose of 80,000 colony-forming units (CFU)/naris. This will be administered intra-nasally using a P200 micropipette to give 0.1ml of pneumococcus-containing fluid instilled into each nostril in our human challenge facility. This will occur once during the study in all participants, who will not be randomised or blinded to the intervention. All participants will be followed up for 28 days at Day 2, 6, 9, 14 and 28.

Intervention Type

Biological/Vaccine

Pharmaceutical study type(s)

Live pathogen

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Streptococcus pneumoniae serotype 6B (Spn6B) BHN418 strain, *Streptococcus pneumoniae* serotype 3 (Spn3) LIV014-S3 strain

Primary outcome measure

The detection of pneumococcus within nasal epithelial cells, obtained through minimally-invasive superficial nasal scrape biopsies, measured using confocal microscopy and association with nasal colonisation outcome (measured by classical microbiology and multiplex PCR) following pneumococcal inoculation within 28 days from pneumococcal challenge.

Secondary outcome measures

Current secondary outcome measures as of 10/03/2025:

The following secondary outcome measures are assessed at Day 2, 6, 9, 14 and 28 post pneumococcal challenge:

1. Rates of colonization by pneumococcus and its density and duration by detection of pneumococcus serotype 6B (Phase A) or serotype 3 (Phase B) from one or more nasal wash samples by microbiological culture or multiplex qPCR in the 28 days following the initial pneumococcal challenge
2. Changes in the population of immune/inflammatory cells, specifically innate immune cell dynamics, activation and functionality in the nasal mucosa, in response to challenge and/or colonisation, measured using immunophenotyping on nasal epithelial cell samples
3. Quantification of a systemic and mucosal humoral immune response to nasopharyngeal (NP) carriage by measuring pneumococcal serotype-specific antibodies on nasal and blood samples using ELISAs
4. Quantification of a systemic and mucosal cellular immune response to NP carriage by measuring pneumococcal-specific T-cell recall responses using immunophenotyping
5. Demonstration of functional activity of participant anti-pneumococcal antibodies measured using assays including opsonophagocytic killing assays

Previous secondary outcome measures:

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4. Quantification of a systemic and mucosal cellular immune response to NP carriage by measuring pneumococcal-specific T-cell recall responses using immunophenotyping
5. Demonstration of functional activity of participant anti-pneumococcal antibodies measured using assays including opsonophagocytic killing assays

Overall study start date

16/10/2023

Completion date

30/10/2025

Eligibility

Key inclusion criteria

1. Healthy adults aged 50-84 (inclusive, at the time of consent and inoculation) years old
2. World Health Organisation performance status 0 (able to carry out all normal activity without restriction) or 1 (restricted in strenuous activity but ambulatory and able to carry out light work)
3. Access to telephone and e-mail
4. Fluent spoken English – to ensure a comprehensive understanding of the research project
5. Capacity to provide written informed consent in English

Participant type(s)

Healthy volunteer

Age group

Mixed

Lower age limit

50 Years

Upper age limit

84 Years

Sex

Both

Target number of participants

30 (15 in both Phases)

Key exclusion criteria

Current exclusion criteria as of 10/03/2025:

Individuals may not participate in the study if they are/have:

Research participant:

1. Currently involved in another study unless observational or non-interventional, excluding the EHPC bronchoscopy study (at the discretion of the study team) and exceptions may be applied at the discretion of the CI/PI to ensure no harm comes to the participants (e.g. excessive blood or nasal sampling)
2. Participated in a previous Spn6B/Spn3 EHPC study within 3 years

Nasal carriage:

Participants who have natural pneumococcal identified at screening

Vaccination:

1. Had any vaccination within 28 days of enrolment (defined as the time of inoculation) other than against influenza or COVID-19 which is permissible up to 14 days before inoculation
2. Had a pneumococcal conjugate vaccine*

Allergy:

Allergy to beta-lactam antibiotics (including penicillin and amoxicillin)

Medical history leading to increased risk of severe infection, illness including but not limited to:

1. Asplenia or dysfunction of the spleen
2. Chronic respiratory disease (e.g. asthma [requiring medication (including salbutamol inhaler) within last 12 months], COPD, bronchiectasis)
3. Chronic heart disease (e.g. angina, ischaemic heart disease, chronic heart failure) - controlled and stable hypertension may be included
4. Chronic kidney disease (e.g. kidney transplant, regular dialysis, CKD3-5)
5. Chronic liver disease (e.g. cirrhosis, hepatitis)
6. Chronic neurological disease that limits mobility, bulbar or respiratory function (including stroke, Parkinson's disease, dementia and multiple sclerosis)
7. Diabetes mellitus (including diet controlled)
8. Cancer within the past 5 years (except for basal cell carcinoma of the skin, melanoma in situ and cervical carcinoma in situ)
9. Receipt of immunosuppressive therapy such as anti-cancer immunotherapy, chemotherapy or

radiation therapy within the preceding 5 years or long-term systemic corticosteroid, Roaccutane, or disease-modifying anti-rheumatoid drugs therapy (for more than 7 consecutive days within the 3 months before enrolment)

10. Individuals with cochlear ear implants

11. Individuals with major cerebrospinal fluid leaks (e.g. following traumatic, major skull surgery, or requiring CSF shunts)

12. Subjects with known or suspected immune deficiency (e.g. HIV, known IgA deficiency, immotile cilia syndrome, or Kartagener's syndrome)

13. History of frequent nose bleeds within the last two years

14. Bleeding disorders

15. Significant mental health disorders

16. Other uncontrolled comorbidities, as determined by the clinical investigator, which would be expected to increase the risk of pneumococcal disease

17. Any major pneumococcal illness or pneumonia requiring hospitalisation in the last 10 years

18. Meeting STOP criteria

Medication

1. Any medication that may affect the immune system in the last 3 months (e.g. systemic steroids [IM/IV], steroid nasal spray, Roaccutane, disease-modifying anti-rheumatoid drugs)

2. Long-term antibiotic use or any antibiotics (other than topical) in the past 28 days

3. Recipient of monoclonal antibodies in the last six months for any indication

4. Recipient of blood transfusion products within the last year

5. Any medication that may affect the coagulation system in the last 3 months (excluding low-dose aspirin)

6. Use of any medication or other product (prescription or over-the-counter) for symptoms of rhinitis or nasal congestion within the last 1 month

Maternity:

1. Pregnancy

2. Lactation

3. Intend to become pregnant during the study

4. Female participants of child-bearing potential** unable to take effective contraception measures***

Direct caring role or share living accommodation with individuals at a higher risk of infection

1. Children ≤ 5 years of age

2. Adults with immunosuppression

3. Adults at high risk of invasive pneumococcal disease at the discretion of the investigator

4. Adults classified as clinically extremely vulnerable by the National Health Service

5. Health-care worker (unless willing to wear a surgical face mask at all times with patients)

Smoking

1. Current or ex-smoker (regular cigarettes ≥ 5 per week] /cigars/e-cigarette/vaping/smoking of recreational drugs) in the last 6 months

2. Previous significant smoking history (more than 5 cigarettes per day for 20 years or the equivalent [i.e. >5 pack years])

Current alcohol and recreational drug use

1. Regularly drinks ≥ 14 units/week (male or female)

2. Regularly uses recreational drugs

Overseas travel planned within the study period (28 days after the primary challenge)

Any other issue which, in the opinion of the study staff, may:

1. Put the participant or their contacts at risk because of participation in the study
2. Adversely affect the interpretation of the study results, or
3. Impair the participant's ability to participate in the study

*However previous pneumococcal polysaccharide vaccination (PPV) will not be an exclusion criterion as this vaccine does not confer protection against mucosal carriage and will therefore not impact on our primary outcome measure. We will endeavour to document the vaccination status of all participants to explore the potential for confounding within the study.

**A woman is considered of childbearing potential, i.e. fertile, following menarche and until becoming post-menopausal unless permanently sterile. Permanent sterilisation methods include hysterectomy, bilateral salpingectomy and bilateral oophorectomy. A post-menopausal state is defined as no menses for 12 months without an alternative medical cause. A high follicle-stimulating hormone (FSH) level in the post-menopausal range may be used to confirm a post-menopausal state in women not using hormonal contraception or hormonal replacement therapy. However, in the absence of 12 months of amenorrhoea, a single FSH measurement is insufficient.

*** Acceptable effective forms of contraception for female volunteers include:

1. Established use of oral, injected or implanted hormonal methods of contraception
2. Placement of an intrauterine device (IUD) or intrauterine system (IUS)
3. Total abdominal hysterectomy
4. Bilateral tubal occlusion
5. Barrier methods of contraception (condom or occlusive cap with spermicide)
6. Male sterilisation, if the vasectomised partner is the sole partner for the subject
7. Sexual abstinence is defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments (for this trial from inoculation until D28). The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the subject.

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8. Cancer within the past 5 years (except for basal cell carcinoma of the skin, melanoma in situ and cervical carcinoma in situ)
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Date of first enrolment

01/04/2024

Date of final enrolment

01/10/2025

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

Liverpool School of Tropical Medicine

Pembroke Place

Liverpool

United Kingdom

L3 5QA

Sponsor information

Organisation

Liverpool School of Tropical Medicine

Sponsor details

Pembroke Place

Liverpool

England

United Kingdom

L3 5QA

+44 (0)151 705 3100

lstmgov@lstmed.ac.uk

Sponsor type

University/education

Website

<https://www.lstmed.ac.uk/>

ROR

<https://ror.org/03svjbs84>

Funder(s)

Funder type

Research council

Funder Name

Medical Research Council

Alternative Name(s)

Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Publication and dissemination plan

The findings from this study will be disseminated amongst the scientific community. We intend to publish our findings in peer reviewed scientific journals and present data at appropriate local, national and international conferences. In addition, we will produce a lay report of our findings, which will be made available to all participants.

Intention to publish date

30/10/2026

Individual participant data (IPD) sharing plan

Data sharing statement to be made available at a later date

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?
Participant information sheet	version 2.0	06/03/2024	02/04/2024	No	Yes