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Exploring Co-infection with Live Attenuated Influenza Vaccine and PneumococcuS in healthy oldEr adults (ECLIPSE)

Submission date
23/09/2024

Recruitment status
No longer recruiting

Registration date
15/10/2024

Overall study status
Ongoing

Last Edited
25/02/2026

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
In this study, researchers aim to explore how the body will react to a combination of the flu virus and pneumococcal bacteria, focusing on respiratory infections and nasal immune responses. Pneumococcal bacteria are known to cause chest infections such as pneumonia, more often in young children and older adults. This study aims to investigate co-infection, which could help in developing new treatments and vaccines. An approved nasal vaccine for the flu called the Live Attenuated Influenza Virus (LAIV) will be used to mimic the way the immune system responds to the flu virus. Some participants will also have pneumococcal bacteria introduced into their nose. This co-infection model will have been well tested in younger adults, and the researchers will want to compare these results with a group of older adults. The primary goal of this study will be to understand if this will be safe and easy to study in this age group. Two groups, A and B, will be studied. Participants in the co-infection study (Group A) will be adults between the ages of 55 and 80 years old. They will receive the pneumococcal bacteria on Day 0, and LAIV either on Day –3 (before the pneumococcal bacteria) or Day 3 (after the pneumococcal bacteria). Participants in both groups will either get saltwater or the flu virus, and they will not know which. Group B will receive the LAIV only on Day 0. This group will be open to older (55-80 years old) and younger (18-49 years old) adults. They will not receive the pneumococcal bacteria. Throughout the study, samples will be taken from the nose, throat, saliva, and blood to observe how the immune system responds. Participants will be asked to complete a diary to track symptoms and will collect saliva and nasal samples at home.

Who can participate?
Healthy adults, between 55-80 years old OR 18-49 years old (Group B only).

What does the study involve?
There will be two study groups, A and B. Participants in the co-infection study (Group A) will receive pneumococcal bacteria intranasally (through the nose) on Day 0, and then an approved flu vaccine either on Day –3 (before the pneumococcal bacteria) or Day 3 (after the pneumococcal bacteria). Participants in both groups will either receive saltwater (saline) or the flu virus, and they will not know which one they received. This is called blinding. However, the

study staff will not be blinded and will know what each participant has had to ensure participant safety. Throughout the study, samples will be taken from the nose, throat, saliva, and blood to observe how the immune system responds, and a diary will be kept to track immune cells and markers. Participants will collect saliva and nasal samples at home.

What are the possible benefits and risks of participating?
Participants will be a valuable part of a research study that researchers hope will eventually lead to the development of new methods to prevent or treat respiratory infections. However, there will not be a direct benefit to the participant.

When challenging participants with the pneumococcal bacteria, there will be a small risk of infection to them or their close contacts. However, this pneumococcus bacterium has been given in previous studies to healthy adults and older adults with no serious side effects. Around 10% of adults will also carry pneumococcus at any one time without being aware of it. Every participant who tests positive for pneumococcus will take a course of antibiotics at the end of the study, or if they feel unwell, on the advice of a study doctor.

There will also be risks associated with performing study procedures such as fine needle aspirate sampling, throat swabs, and blood/nasal samples. The risks will be limited; however, there will be the potential for procedures to cause some mild discomfort, bruising, or mild pain.

Since several medical tests will be carried out throughout the study, it will be possible to detect previously unknown health issues (e.g., high blood pressure or abnormal blood results). If this does happen, any findings will be discussed with the participant and their GP if ongoing follow-up is required.

Where is the study run from?
Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital (UK)

When is the study starting and how long is it expected to run for?
May 2023 to January 2028

Who is funding the study?
Horizon Europe, UKRI

Who is the main contact?
Thejaswini Madupuri, info@ovg.ox.ac.uk

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
343692

ClinicalTrials.gov (NCT)
Nil known

UK Research and Innovation (UKRI) Grant Code
10077113

Central Portfolio Management System (CPMS)
62446

Study information

Scientific Title
Human co-Infection challenge study of S. pneumoniae (Spn) and Live Attenuated Influenza Vaccine (LAIV) in older healthy adults

Acronym
ECLIPSE

Study objectives

Primary Objective:
To determine if a co-infection human challenge model with LAIV and S. pneumoniae (Spn6B) is feasible and safe.

Secondary Objectives:
1. If co-infection with LAIV and Spn6B alters upper and lower respiratory tract infection symptoms
2. How primary LAIV vaccination alters the:
2.1. Risk of secondary Spn6B carriage
2.2. The density of secondary Spn6B carriage
2.3. Duration of secondary Spn6B carriage
3. How primary Spn6B challenge or carriage alters the: (a) Risk of secondary LAIV infection (ie. detection of LAIV)
3.1. Viral load of secondary LAIV infection (density over time)
4. If nasal colonisation with other respiratory viruses and bacteria is detectable
5. To evaluate changes in nasal cell phenotype and function over time

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 30/10/2024, East Midlands – Leicester South Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)2071048193; Leicestersouth.rec@hra.nhs.uk), ref: 24/EM/0200

Study design
Randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Human co-infection challenge study of S. pneumoniae (Spn) and live attenuated influenza vaccine

Interventions
Design
This will be a single-blind randomised controlled human co-infection study using a previously established pneumococcal and LAIV infection model. Eligible healthy, older adults will receive an intranasal challenge with LAIV/saline on Day -3 followed by a challenge with Spn6B on Day 0. Participants will receive a further intranasal challenge on Day 3 with the LAIV/saline option they did not receive on Day -3 (participants who received saline on Day 3 will receive a LAIV on Day 3, and those who received LAIV will receive saline). All study participants will be blinded to the order of challenge agents (LAIV first or saline first).

In parallel, a control group of younger and older adults will be vaccinated with intranasal LAIV only, for comparison. Data from the control group will allow the determination of the impact of immune responses to LAIV in the absence of pneumococcal co-infection.

Allowing for a 20% expected dropout, the study will enrol up to 60 participants into Group A to complete at least 40 participants. Recruitment may be stopped once the required datasets from 40 participants are available. A participant will be considered enrolled in the study at the point of Baseline Assessment. Recruitment will run over two seasons (autumn/winter 2024 and 2025).

Methodology
Study visits will occur at the study site. Timings vary between Groups A and B. The Online Screening Questionnaire includes a request to check the GP summary beforehand before inviting to the screening visit.

The participant will be invited to a screening visit. There is a different consent form for Groups A and B (reflecting different risks and things to be aware of). Group A also need to fill in an Informed Consent Quiz to show understanding of the study. Inclusion/exclusion criteria will be reviewed, including medical history. The participant will have a physical examination and a set of physical observations performed. The following investigations are performed: blood sampling, ECG, and pregnancy test (if applicable). The screening visit can be combined with a baseline visit if future appointments can be scheduled appropriately within the study timeline.

Samples:
The study will assess immune responses through samples including blood, nasal wash, nasal cells, throat swabs, nasosorption and saliva samples. They will be taken as per the Schedule of Events. The immune responses in the axillary lymph node tissue will be assessed in a subset of participants across Groups A and B (up to 10 volunteers).

Home Sampling:
When baseline research samples are taken (Day -7 Group A, Day -3 Group B), the participants will be trained in self-sampling. The home sampling will be conducted at the participant's place of residence. To ensure samples are collected within 15 minutes of the planned time, participants will be asked to fill in the details on redcap and label their samples. Samples will be stored at home in biohazard-appropriate packaging (supplied by the research team) in a freezer. Self-test will include a saliva sample, nasosorption and a symptom diary.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Controlled human infection model (CHIM) of live attenuated influenza vaccine (LAIV), Streptococcus pneumoniae (Spn)

Primary outcome(s)
The absence of SAEs/AESIs relating to inoculation throughout the study will be measured by clinical monitoring at D28 in Group A and D31 in Group B

Key secondary outcome(s))
1. The absence of SAEs/AESIs relating to inoculation throughout the study will be measured by clinical monitoring at D28 in Group A and D31 in Group B
2. Colonisation risk, density, and duration quantification of secondary Spn6B carriage will be measured by classical culture and molecular methods, including RT-qPCR, 3-5 days after the final

visit (Group A: D31-33, Group B: D34-36)
3. Secondary LAIV infection and viral load will be determined by RT-qPCR, 3-5 days after the final visit (Group A: D31-33, Group B: D34-36)
4. Detection of the most common respiratory viruses and other respiratory bacteria will be assessed by microfluidic qPCR, 3-5 days after the final visit (Group A: D31-33, Group B: D34-36)
5. Changes in cell populations, including antigen-specific T and B cells in the nasal mucosa, will be analyzed at different time points, 3-5 days after the final visit (Group A: D31-33, Group B: D34-36)

Completion date
31/01/2028

Eligibility

Key inclusion criteria
1. Participant is willing and able to give informed consent for participation in the study
2. Healthy adults, ages as specified depending on study group
3. In the Investigator's opinion, is able and willing to comply with all study requirements
4. Fluent spoken English – to ensure a comprehensive understanding of the research study
5. Willing to allow his or her General Practitioner and consultant, if appropriate, to be notified of participation in the study.
6. Agreement to provide their National Insurance/Passport number for the purposes of TOPS registration and for payment of reimbursement expenses.
7. Females of childbearing potential* with a negative urine pregnancy test at screening and willing to practice adequate contraceptive** measures as per UK Clinical Trial Facilitation Group during the study
8. Participant must live near to study site or in the surrounding area

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
Yes

Age group
Mixed

Lower age limit
18 years

Upper age limit
80 years

Sex
All

Total final enrolment
65

Key exclusion criteria

The participant may not enter the study if ANY of the following apply:
1. Severe and/or uncontrolled cardiovascular disease, respiratory disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder, or neurological illness, as judged by the Investigator (note, mild/moderate well-controlled comorbidities are allowed). Including but not limited to:
1.1. Asplenia or dysfunction of the spleen
1.2. Chronic respiratory disease (e.g. asthma [requiring medication (including salbutamol inhaler) within last 12 months], COPD, bronchiectasis and sleep apnoea)
1.3. Chronic heart disease (e.g. angina, ischaemic heart disease, chronic heart failure) – controlled and stable hypertension may be included
1.4. Severe chronic kidney disease (e.g. nephrotic syndrome, kidney transplant, requires dialysis)
1.5. Chronic liver disease (e.g. cirrhosis, biliary atresia, hepatitis)
1.6. Chronic neurological disease that limits mobility, bulbar or respiratory function (including stroke, Parkinson's disease, dementia and multiple sclerosis)
1.7. Diabetes mellitus (including diet-controlled)
2. Receipt of immunosuppressive therapy such as anti-cancer chemotherapy or radiation therapy within the preceding 12 months or long-term systemic corticosteroid, Roaccutane, or disease modifying anti-rheumatoid drugs therapy (for more than 7 consecutive days within the 3 months prior to enrolment)
3. Individuals with cochlear ear implants
4. Individuals with major cerebrospinal fluid leaks (e.g. following traumatic, major skull surgery, or requiring CSF shunts)
5. Subjects with known or suspected immune deficiency (e.g. known IgA deficiency, immotile cilia syndrome, or Kartagener's syndrome)
6. History of frequent nose bleeds
7. Bleeding disorders
8. No major pneumococcal illness requiring hospitalisation in the last 10 years
9. Maternal (Group B)
10. Female participants who are pregnant
11. Female participants who are lactating
12. Female participants who intend to become pregnant during the study
13. Female participants unable to take contraception measures during the study (from consent to final study visit)
14. Close contact with individuals at increased risk of pneumococcal disease (eg. children under 5 years, immunocompromised individuals
15. Healthcare workers
16. On medication that may affect the immune system in any way eg. steroids
17. Taking long term antibiotics, nasal/inhaled steroids, oral antiplatelets or warfarin therapy
18. Allergy to penicillin, amoxicillin, gentamicin, gelatin, lidocaine or any ingredient of the influenza vaccine
19. Current regular smoker/vaper (smokes daily) or previous regular smoker/vaper than has stopped smoking/vaping less than 12 months ago (up to 10 pack-years smoking history allowed)
20. History of drug or alcohol abuse (frequently drinking over the recommended alcohol intake limit: men and women should not regularly drink more than 14 units per week)
21. Any clinically significant finding on screening investigation bloods
22. Not able to make specific inoculation/vaccination visit dates required for the study, or overseas travel booked for 21 days following baseline testing
23. Received any influenza vaccine in the same winter season as they are recruited
24. Pneumococcal vaccination (which we can confirm is not the PCV vaccine) in the last 1 year (older adults who have had pneumococcal vaccination but not influenza may be considered for Group B – LAIV only)
25. Participants who have received the Pneumococcal Conjugate Vaccine specifically within the

last 3 years (this would not be given routinely in the UK schedule)
26. Previous involvement in a clinical trial with Pneumococcal inoculation in the last 3 years
27. Scheduled elective surgery or other procedures requiring general anaesthesia during the study
28. Participants who have participated in another research trial involving an investigational product in the past 12 weeks
29. Any other issue which, in the opinion of the study staff, may:
29.1. Put the participant or their contacts at risk because of participation in the study
29.2. Adversely affect the interpretation of the study results, or
29.3. Impair the participant's ability to participate in the study

Date of first enrolment
08/11/2024

Date of final enrolment
20/02/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
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Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
UK Research and Innovation

Alternative Name(s)
UKRI

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.1	02/10/2024	20/11/2024	No	No
Protocol file	version 2.1	09/04/2025	06/06/2025	No	No
Protocol file	version 3.0	03/06/2025	14/08/2025	No	No
Protocol file	version 4.0	14/11/2025	17/12/2025	No	No
Protocol file	version 4.1	29/12/2025	06/01/2026	No	No
Protocol file	version 4.2	20/01/2026	26/01/2026	No	No
Study website		11/11/2025	11/11/2025	No	Yes