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STELLAR - STudying Early Life Live Attenuated influenza virus immune Responses

Submission date 27/08/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 30/08/2024	**Overall study status** Ongoing	
Last Edited 11/06/2025	**Condition category** Other	

Plain English summary of protocol

Background and study aims
This study will compare the protective response to infections (also called an immune response) in the nose to the protective response in the blood following vaccination with a safe and effective nasal influenza vaccine.
The nasal live-attenuated influenza virus vaccine is a licensed vaccine on the routine schedule yearly between ages 2 and 17 years old.

Who can participate?
Children aged between 2 and 5 years old can take part in this study. We are looking to include up to 40 children (vaccination is possible until the day before the child's 6th birthday).

What does the study involve?
Children will have two study visits over a 1-month period in autumn or winter. This will take place in the child's home or another convenient location.
Children will be immunised with live-attenuated influenza virus vaccine (LAIV) in their own home (or a convenient location) on the first visit. 'Live-attenuated' means the vaccine contains a live virus, which has been weakened so it does not cause infection in healthy people.
On each of the two visits we plan to obtain a small blood sample and a nasal swab. The blood sample volume with be equivalent to about two teaspoons at each visit and we will use a local anaesthetic cream to numb the skin for blood tests.
Children will also have nasal fluid (nasosorption) and saliva collected at both visits and additionally will be asking you to take samples at home on 8 days between the two visits. We will train parents in these simple procedures as their first study visit and guidance documents will be provided.
These home samples will be stored in your freezer until the end of the study, or earlier if convenient, in which they will be collected by the study team (or by a courier).

What are the possible benefits and risks of participating?
There are no direct benefits for the children participating in the study. However, the research may help improve future vaccines and treatments for children. The risks are very low, as the vaccine is safe and licensed, and the sample collection methods are gentle and performed by experienced professionals.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
August 2024 to January 2028

Who is funding the study?
UK Research and Innovation

Who is the main contact?
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Study website
https://www.ovg.ox.ac.uk/studies/stellar

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Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
340764

ClinicalTrials.gov number
Nil known

Secondary identifying numbers

CPMS 61221, Grant code 10077113, IRAS 340764

Study information

Scientific Title
In-depth analysis of the nasal mucosal and systemic immune response in children given a live-attenuated intra-nasal influenza vaccine

Acronym
STELLAR

Study objectives
In this study we propose to evaluate how the body's defence system (immune system) within the nose and blood responds to the nasal flu vaccine in children. This, we hope, will lead to us identifying blood indicators ("biomarkers") that could provide reliable information about the immune response within the nose. We may also discover "biomarkers" in the nose that tells us a protective immune response is occurring there. This could be groundbreaking for future research as we would better know what to look for and how to look for it. We hope that the discovery of these "biomarkers" will help us develop better nasal vaccines.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 12/08/2024, South Central - Hampshire B Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8088; hampshireb.rec@hra.nhs.uk), ref: 24/SC/0251

Study design
Interventional non-randomized

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
University/medical school/dental school

Study type(s)
Prevention

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
This study is to evaluate nasal mucosal and systemic immune response in children given a live-attenuated intra-nasal influenza vaccine

Interventions

Summary:
1. Routine live-attenuated influenza vaccine administration
2. Nasal cell collection
3. Blood sample (up to 10 ml)
4. Nasal fluid collection
5. Saliva sample collection

The study involves two visits to the participant's home by the OVG study team over a 1-month period. The participants are also asked to complete a daily symptom diary and perform nasal fluid and saliva collection (by the parent/legal guardian) at home 8 times between the two visits.

At the first visit, study staff will:
1. Provide an explanation of the study to parents/legal guardians.
2. Obtain written informed consent from the parents/legal guardians of the participant (consent may take place at an earlier visit if parent/legal guardians need more time to consider the study).
3. Perform a thorough check to ensure the child is eligible for the study.
4. We will then record relevant data about the participant, including date of birth and gender, for subsequent data analysis. We will also measure and record the participant's axillary (armpit) temperature.
5. We will then perform nasal cell sampling, salivary sampling, Nasosorption sampling, and blood sampling, ideally in this order. Collecting a maximum of 10 ml of venous blood (local anaesthetic cream will have been applied prior to collecting blood).
6. We will then administer the influenza vaccine via the nose as per the product instructions.
7. Following this, we will observe the participant for 15 minutes after vaccination for any significant acute reactions, with adrenaline readily available in case of anaphylactic reaction. Any adverse events that occurred during the observation period in relation to either the vaccination or study procedures will be recorded.
8. On this visit, we will also instruct the parents/legal guardians as to the use of the 'nasosorption' and salivary sampling techniques, labelling and storage. We will also instruct the parents/legal guardians on how to complete the 'Symptom and home sample collection' e-diary and the backup paper diary, should they need that. This is primarily to observe any other acquired upper respiratory tract infection and note the timing of this. However, it will also record the expected short-term side effects of the LAIV itself. They will also be requested to record the collection dates and times for the home samples on this electronic diary.
9. We will provide topical anaesthetic cream and instructions for use at the next visit.
10. We will schedule the next visit for as close to Day 28 post-vaccination as possible for the parents/legal guardians, with a window of between days 28 and 35 from vaccination.
11. We will complete the "Redbook" (parent-held child record) if available.

After this visit, study staff will:
1. Notify the participant's General Practitioner of the child's participation in the study and that the child's routine influenza immunisation has been administered by the study doctor or nurse.
2. Notify the Child Health Information Services, or equivalent NHS database that the participant's routine vaccine has been administered.

Between the two visits, phone, text or email messages will be sent out on days 1, 2, 3, 4, 6, 9, 14 and 21 to remind parents that home samples are due to be taken. We recognise that it is ambitious to expect participants to tolerate both sample types on all of these time points but the sample size has taken this into account, from previous similar studies using these study procedures.
At the second visit – this will be from day 28 to day 35 post-vaccination (as close to Day 28 as

possible), the study staff will:
1. Check that the consent remains valid, and the parents/legal guardians are willing to proceed with the follow-up sampling.
2. Check that the eligibility criteria are still valid. Review medical history and record any new illnesses or concomitant medications.
3. Ensure that local anaesthetic cream has been applied (allowing sufficient time between application and venepuncture, in accordance with our protocols).
4. Collect the nasosorption and salivary samples, if not previously collected, and the backup paper diary, if used.
5. Perform nasal cell sampling, nasosorption sampling, salivary sampling and blood sampling. Collect a maximum of 10 ml of venous blood, in accordance with our official procedures.
6. The new and collected samples will be transported to the laboratory as per local SOP guidelines. Samples taken during the study visits (Day 0 and Day 28) by the study team will be carefully labelled with the participant details, the time and date of the samples, and transported from the participant's home to our laboratories following local SOPs by the research team.
7. The nasosorption and saliva samples collected at home and stored in the home freezer will preferably be collected by the study team at the end of the last visit. However, they may also be collected by a courier prior to the last visit for logistical reasons, if required.

Intervention Type
Biological/Vaccine

Pharmaceutical study type(s)
Not Applicable

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Live-attenuated influenza vaccine (LAIV)

Primary outcome measure
Viral load of LAIV from the nose and in saliva will be assessed by RT-qPCR using nasosorption and saliva sampling on days 0, 1, 2, 3, 4, 6, 9, 14, 21 and 28 of the study.

Secondary outcome measures
1. Measurement of antibody levels against the Influenza virus strains contained in LAIV by ELISA or comparable technical approaches on days 0, 1, 2, 3, 4, 6, 9, 14, 21 and 28 of the study
2. Detection of pneumococcus, most common respiratory viruses and other respiratory bacteria will be assessed by microfluidic qPCR on days 0, 1, 2, 3, 4, 6, 9, 14, 21 and 28 of the study
3. Measurement of antibody levels against the Influenza virus strains contained in LAIV by ELISA or comparable technical approaches by blood test at day 0 and day 28 post-vaccination

Overall study start date
01/08/2024

Completion date
31/01/2028

Eligibility

Key inclusion criteria
1. Children aged between 2 and 5 years old eligible for yearly LAIV vaccination in the UK, in good health
2. Parents/legal guardian(s) have capacity to give informed consent
3. Parents/legal guardian(s) are willing and able to comply with all study procedures
4. Parents/legal guardian(s) who are over 18 years of age and are able and willing to provide written informed consent for their child's participation in the study

Participant type(s)
Healthy volunteer

Age group
Child

Lower age limit
2 Years

Upper age limit
5 Years

Sex
Both

Target number of participants
Planned Sample Size: 40; UK Sample Size: 40

Key exclusion criteria
Children may not participate in the study if any of the following apply:
1. Are enrolled in another clinical trial unless observational or follow-up phase (or at the discretion of the lead clinician)
2. Are taking daily medications that may affect the immune system
3. Are currently taking a steroid therapy (inhaled, nasal, oral or intravenous), or have been on these medications in the previous 6 months
4. Are confirmed or suspected to have any disease or syndrome associated with altered immunity or immunodeficiency
5. Have household contacts with a severe immunodeficiency (for example, someone who has had a recent bone marrow transplant)
6. Have already had an influenza vaccine in the current influenza season
7. Have a history of hypersensitivity to any of the following constituents – Sucrose, Dipotassium phosphate, Potassium dihydrogen phosphate, gelatin (porcine, Type A), arginine hydrochloride, monosodium glutamate monohydrate, gentamicin
8. Have a history of an allergic reaction to a nasal spray flu vaccine in the past
9. Are on or have a condition that needs salicylate therapy
10. Have unrepaired craniofacial malformations
11. Have a history of Guillain-Barré syndrome or Leigh syndrome
12. The nasal spray vaccine contains small traces of gelatine derived from pigs (porcine gelatine). If the use of porcine gelatine in medical products is unacceptable, they will excluded.
13. The influenza strains for the nasal spray vaccine are cultured in chicken eggs. This does not increase the risk of anaphylaxis in children with egg allergy, but if the use of chicken eggs is unacceptable, they will be excluded.
14. Are a child of a study site staff member

15. Any other issue, in the opinion of the study staff, may:
15.1. Put the children or their contact at risk because of participation in the study, or
15.2. Adversely affect the interpretation of the study results

Temporary Exclusion Criteria
Children are temporarily excluded from participating if they:
1. Are currently experiencing an exacerbation of asthma or wheeze symptoms when due the LAIV, including the increased use of relieving inhalers in the preceding 72 hours
2. Have received any other vaccine within 14 days prior to the study vaccine
3. Have scheduled elective surgery, planned admission or other procedures requiring general anaesthesia within the study period
4. Have a febrile illness (axillary temperature ≥38.0°C) within the previous 72 hours of the scheduled vaccination

Date of first enrolment
13/09/2024

Date of final enrolment
28/02/2026

Locations

Countries of recruitment
England

United Kingdom

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Sponsor type
University/education

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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

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Conference presentation
3. Publication on website
4. Other publication
5. Submission to regulatory authorities

Participants will not be identifiable from shared or published data. De-identified participant data will be made available upon requests directed to the chief investigator. Proposals will be reviewed and approved by the sponsor, chief investigator, and collaborators on the basis of scientific merit. After approval of a proposal, data can be shared through a secure online platform after signing a data access agreement.

Intention to publish date
31/01/2029

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be 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 1.1	05/08/2024	09/09/2024	No	Yes
Participant information sheet	version 2.1	14/01/2025	11/02/2025	No	Yes