

A clinical trial of the safety of the live, attenuated influenza vaccine nasal spray in children aged 12 - 23 months

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| Submission date 28/06/2025 | Recruitment status Recruiting | <input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol |
| Registration date 27/08/2025 | Overall study status Ongoing | <input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results |
| Last Edited 07/10/2025 | 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

Influenza (known as flu) causes substantial illness every winter, especially among older people, those with weakened immune systems, and young children. The NHS currently offers a nasal flu vaccine to children over 2 years, which also helps protect others by reducing transmission. Although children under 2 years are at the highest risk from flu, they haven't yet been offered the vaccine as sufficient safety data was not available for this age.

Who can participate?

12- to 23-month-old children

What does the study involve?

Participants are randomly allocated to receive the nasal flu vaccine or a placebo nasal spray at their first visit. The parents will not know which one the child receives. Over the next 4 weeks, the researchers will record/monitor the number of children in each group who return to their GP with a wheezing diagnosis. At the second visit, each child will receive whichever nasal spray they did not get at the first visit. Rates of wheezing will be compared after the second visit. Every child will receive both the vaccine and a placebo. If the rate of wheezing after the vaccine is the same (or lower) than after the placebo, the UK's vaccination advisory committee may decide to offer the nasal flu vaccine to all children from 12 months of age next winter.

This trial will be conducted with a company called uMed, a clinical research technology platform, who partners with UK Healthcare Providers to access NHS Electronic Health Record data and invite patients to participate in research. The uMed system was used in the HARMONIE study of nirsevimab (preventing RSV in infants) performed in general practice and hospitals in autumn 2022. uMed will be involved in aspects including digital screening and invitations, remote eConsent and electronic monitoring, ensuring it runs efficiently.

What are the possible benefits and risks of participating?

Allergic reactions from mild to severe may occur in response to any constituent of a medicine. Anaphylaxis or other allergic reactions are known to occur in between 1/1000 and 1/100 recipients of live-attenuated influenza vaccine (LAIV).

More than 1 in 10 people may experience a runny nose, reduced appetite or weakness, and up to 1 in 10 people may experience fever, muscle aches or headaches following vaccination with LAIV. The investigation of whether chest (lower respiratory tract) side effects occur or not is the primary reason for this trial.

Remote surveys reduce clinic visits; clear guidance will be provided for parents to seek usual NHS care, preserving normal healthcare-seeking behaviour if they are worried about their child (this is being measured in the trial in relation to specific chest (lower respiratory tract) reasons for doctor visits.

Where is the study run from?

University Hospital Southampton NHS Foundation Trust (UK)

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

June 2025 to January 2026

Who is funding the study?

National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?

1. Prof. Saul Faust, s.faust@soton.ac.uk

2. Dr Alasdair Munro, a.munro@soton.ac.uk

Contact information

Type(s)

Scientific

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

1012411

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

RHM CHI 1293, NIHR204677

Study information

Scientific Title

A Phase II randomised, single-blinded, placebo-controlled, cross-over trial of a single dose of live attenuated influenza vaccine in 12-23-month-old children (FluSNIFF-toddler)

Acronym

FluSNIFF-toddler

Study objectives

Primary objective:

To determine the safety of the live, attenuated influenza vaccine (Fluenz) in children aged 12 to 23 months, as determined by rates of medically attended wheezing compared to placebo.

Secondary objective:

To determine the safety of the live, attenuated influenza vaccine (Fluenz) in children aged 12 to 23 months, as determined by all-cause healthcare attendance compared to placebo.

Ethics approval required

Ethics approval required

Ethics approval(s)

Approved 20/08/2025, London - Hampstead Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)2071048171, +44 (0)207 104 8284; hampstead.rec@hra.nhs.uk), ref: 25/LO/0534

Study design

Single-blind randomized placebo-controlled cross over trial

Primary study design

Interventional

Secondary study design

Randomised cross over trial

Study setting(s)

Hospital

Study type(s)

Safety

Participant information sheet

Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied

Influenza

Interventions

Randomisation is via an online tool. Each group will receive both 0.2 ml of Fluenz (Live, attenuated influenza vaccine) via nasal spray and 0.2 ml of inert placebo via nasal spray, each as a single administration.

Participants are randomly allocated to receive the nasal flu vaccine or a placebo nasal spray at their first visit. The parents will not know which one the child receives. Over the next 4 weeks, the researchers will record/monitor the number of children in each group who return to their GP with a wheezing diagnosis. At the second visit, each child will receive whichever nasal spray they did not get at the first visit. Rates of wheezing will then again be compared after the second visit. Every child will receive both the vaccine and a placebo.

Follow-up activities include an electronic diary at days 7 and 14 post administration after visits one and two, and a final digital questionnaire given 4 weeks after visit two.

Intervention Type

Biological/Vaccine

Pharmaceutical study type(s)

Not Applicable

Phase

Phase II

Drug/device/biological/vaccine name(s)

Fluenz [Influenza Vaccine (Live attenuated, nasal)]

Primary outcome measure

Medically attended wheeze, measured via GP SNOMed codes for "viral induced wheeze", "asthma", "wheeze", or a prescription for "salbutamol" or "ipratropium bromide" collected from the GP record in the 4 weeks post receipt of vaccine or placebo. Any medically attended wheeze events reported via the electronic diary will also be included.

Secondary outcome measures

All cause medical attendances, measured by GP electronic records and electronic diaries in the 4 weeks post vaccine or placebo

Overall study start date

25/06/2025

Completion date

31/01/2026

Eligibility

Key inclusion criteria

1. Aged between 12 months up until 1 day before their second birthday
2. Parent/legal guardian is willing and able to give written informed consent for participation in the trial
3. In good health as determined by a trial clinician. Participants may have well-controlled or mild-moderate comorbidity, specifically including a personal history of eczema, bronchiolitis or viral-induced wheeze
4. In the Investigator's opinion, is able and willing to comply with all trial requirements
5. Willing to allow their General Practitioner and consultant, if appropriate, to be notified of participation in the trial
6. Willing to allow investigators to discuss the volunteer's medical history with their General Practitioner and access all medical records when relevant to study procedures

Participant type(s)

Healthy volunteer

Age group

Child

Lower age limit

12 Months

Upper age limit

2 Years

Sex

Both

Target number of participants

3000

Key exclusion criteria

1. Previous receipt of an IM seasonal influenza vaccine
2. Receipt of any investigational vaccine other than the study intervention within 30 days before and after each study vaccination
3. Living in close contact with someone with a severely weakened immune system
4. Administration of immunoglobulins and/or any blood products within the 3 months preceding the planned administration of the vaccines
5. Children eligible for annual influenza immunisation according to the national NHS programme, including those with any confirmed or suspected immunosuppressive or immunodeficient state; asplenia; recurrent severe infections and use of immunosuppressant medication within the past 6 months, except topical steroids or short-term oral steroids (course lasting ≤ 14 days).
6. History of allergic disease or reactions likely to be exacerbated by any component of study

vaccines (e.g. hypersensitivity to gentamicin, gelatin, or other ingredients of Fluenz). Allergy to egg is only a contraindication if the participant has previously had anaphylaxis to egg.

7. Any history of anaphylaxis

8. Current diagnosis of or treatment for cancer

9. Any other significant disease, disorder or finding which may significantly increase the risk to the volunteer because of participation in the study, affect the ability of the volunteer to participate in the study or impair interpretation of the study data

10. Severe and/or uncontrolled cardiovascular disease, respiratory disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder and neurological illness, defined broadly as currently requiring frequent hospital/specialist input or recently resulting in hospital admission, or as determined by the investigator (mild/moderate well controlled comorbidities are allowed)

11. History of active or previous auto-immune neurological disorders (e.g. Guillain-Barre syndrome, transverse myelitis).

12. Scheduled elective surgery during the trial

13. Participants who have participated in another research trial involving an investigational product in the past 12 weeks.

14. Parent or guardian has an insufficient level of English language to undertake all study requirements in the opinion of the Investigators, except where translation has been able to be provided and is available. If at Visit 1 Screening & Vaccination, the volunteer has any of the following, they will not be enrolled that day.

15. Acute respiratory illness with or without wheeze (moderate or severe illness with or without fever)

16. Fever (oral temperature greater than 37.8°C)

17. Active wheezing at the time of dosing/randomisation (including use of bronchodilators within the past 72 hours).

They may be considered for enrolment later in the trial if they recover in sufficient time

Date of first enrolment

31/08/2025

Date of final enrolment

30/11/2025

Locations

Countries of recruitment

United Kingdom

Study participating centre

-

United Kingdom

-

Sponsor information

Organisation

University Hospital Southampton NHS Foundation Trust

Sponsor details

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Sponsor type

University/education

Website

<http://www.uhs.nhs.uk/home.aspx>

ROR

<https://ror.org/0485axj58>

Funder(s)**Funder type**

Government

Funder Name

National Institute for Health and Care Research

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Peer-reviewed scientific journals
Conference presentation
Publication on website

Data will be presented to the UK Joint Committee on Vaccination and Immunisation as soon as analyses are available to inform their decision-making for the 2026 influenza season.

The results of the trial will be published in peer-reviewed journals, and publicly accessible results published via the NIHR, University and NHS site/Trust news and social media channels.

The results will be made available on the website of the National Immunisation Schedule Evaluation Consortium.

A newsletter outlining the results of the study will be sent to parents of the participants via their site investigator.

Following the completion of the study, all study data will be made available on reasonable request to the chief investigator and lead co-investigator.

Intention to publish date
01/12/2028

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request to the chief/lead investigators, Prof. Saul Faust (s.faust@soton.ac.uk) and Dr Alasdair Munro (a.munro@soton.ac.uk).

IPD sharing plan summary
Available on request

Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|-------------------------------|-------------|--------------|------------|----------------|-----------------|
| Protocol file | version 2.0 | 14/08/2025 | 07/10/2025 | No | No |