

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

<b>Submission date</b> 28/06/2025	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 27/08/2025	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 07/10/2025	<b>Condition category</b> 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

## Clinical Trials Information System (CTIS)

Nil known

## Integrated Research Application System (IRAS)

1012411

## ClinicalTrials.gov (NCT)

Nil known

## Protocol serial number

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

## Study type(s)

Safety

## 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

## Phase

Phase II

## Drug/device/biological/vaccine name(s)

Fluenz [Influenza Vaccine (Live attenuated, nasal)]

## Primary outcome(s)

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.

## Key secondary outcome(s)

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

## 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

**Healthy volunteers allowed**

No

**Age group**

Child

**Lower age limit**

12 months

**Upper age limit**

2 years

**Sex**

All

**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  $\leq 14$  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**

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United Kingdom

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## **Sponsor information**

**Organisation**

University Hospital Southampton NHS Foundation Trust

**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

**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?
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Protocol file</a>	version 2.0	14/08/2025	07/10/2025	No	No