

# Poly-unsaturated fats for improving nasal polyps and asthma

<b>Submission date</b> 14/04/2023	<b>Recruitment status</b> Stopped	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 05/09/2023	<b>Overall study status</b> Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 21/05/2025	<b>Condition category</b> Respiratory	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Some people with asthma are allergic to aspirin and similar painkillers, like ibuprofen which make their asthma worse. This type of asthma can be difficult to treat. Being allergic to aspirin causes high levels of inflammatory chemicals (called leukotrienes). Taking omega-3 fatty acid dietary supplements has been shown to change leukotrienes. This may reduce the inflammation in the lungs and improve asthma symptoms. The aim of this study is to test if dietary supplements improve asthma symptoms. This will be done using questionnaires, measuring breathing and chemicals in breath, sputum (spit), blood and urine to find out how the supplements may be working.

### Who can participate?

Patients aged 18 years and over who have troublesome aspirin-sensitive asthma

### What does the study involve?

At the beginning of the study, the researchers will ask patients to complete questionnaires about their asthma symptoms and general wellbeing, perform routine breathing tests and give blood and urine samples to measure inflammation. Some patients will be asked to produce a sputum sample after inhaling salty mist to measure standard and new tests of inflammation. People will be given either six omega-3 fatty acid capsules, or dummy capsules (placebo), every day for 6 months. The researchers will repeat these tests after 3 months and 6 months. They will measure the level of fats in patients' blood cells to work out if they have been taking the capsules.

### What are the possible benefits and risks of participating?

The results will show whether omega-3 fatty acids improve people's asthma symptoms or not and whether they change the inflammatory chemicals. The study will be undertaken by doctors and researchers with experience in asthma, aspirin sensitivity, omega-3 fatty acids and inflammatory chemicals. They will widely publicise their results in medical publications, media articles and social media. Hopefully, as a result of the study, asthma treatment guidelines will be changed.

The spirometry breathing tests may cause chest discomfort or tightness. If this happens it will wear off after a minute or two and participants will be able to take their reliever medication to help. Research staff will check with participants before the test commences if there are no clinical reasons the test is unsuitable for the participant.

For the nitric oxide test, participants will have to breathe out in a controlled manner into a tube. Sometimes this is a bit difficult to do. However, the test is not painful or uncomfortable.

It may be necessary for participants to travel to the hospital for visits in addition to their routine clinic visits. Visits are planned every 6 weeks (with leeway).

The blood tests may cause discomfort and bruising. The questionnaires will take between 15 and 30 minutes to complete. We will not be asking about any sensitive information.

Participants will be asked to take 6 capsules daily for 24 weeks. Capsules are to be swallowed rather than chewed. While omega-3 fatty acid supplements are usually well tolerated, if there are any side effects, a dose reduction (4 capsules daily) is permitted in the protocol. If the participant is unable to continue taking the capsules due to side effects they are requested to discuss this with their doctor. Adverse event information will be collected for safety reporting.

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

When is the study starting and how long is it expected to run for?  
April 2023 to December 2026

Who is funding the study?  
Efficacy and Mechanism Evaluation Programme (UK)

Who is the main contact?  
A.M.Wilson@uea.ac.uk (CI), Andrew Wilson (UK)

## Contact information

**Type(s)**  
Public

**Contact name**  
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**Type(s)**  
Scientific

**Contact name**

Dr Andrew Wilson

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**Type(s)**

Principal Investigator

**Contact name**

Dr Andrew Wilson

**Contact details**

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## Additional identifiers

**EudraCT/CTIS number**

2021-003641-38

**IRAS number**

1004006

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

173-12-20, IRAS 1004006, CPMS 56101

## Study information

**Scientific Title**

The efficacy and mechanisms of action of n-3 poly-unsaturated fatty acid supplementation in people with non-steroidal exacerbated airways disease and uncontrolled asthma

**Acronym**

PUFFIN

**Study objectives**

Primary objectives:

The main objective of the study is to see if participants treated with an omega-3 fatty acid

supplement will have greater improvement in asthma control after 24 weeks compared to participants treated with placebo as measured by an asthma control questionnaire (ACQ-6) test.

#### Secondary objectives:

To see if participants treated with an omega-3 fatty acid supplement:

1. Have better asthma control as measured by an asthma control questionnaire (ACQ-7) test
2. Have better asthma-related quality of life as measured by the asthma quality of life questionnaire (AQLQ)
3. Have better health-related quality of life measured by the euro-qol (5L-EQ-5D) questionnaire
4. Have more open airways as measured by different breathing tests
5. The omega-3 supplement is well tolerated with an acceptable level of side effects

#### Ethics approval required

Ethics approval required

#### Ethics approval(s)

Approved 30/08/2023, East of England - Essex Research Ethics Committee (2 Redman Place, London, EC20 1 JQ, United Kingdom; +44 (0)207 104 8106, (0)207 104 8263, (0)207 104 8177; Essex.REC@hra.nhs.uk), ref: 23/EE/0096

#### Study design

Double-blind randomized placebo-controlled parallel-group study

#### Primary study design

Interventional

#### Secondary study design

Randomised controlled trial

#### Study setting(s)

Home, University/medical school/dental school

#### Study type(s)

Treatment

#### 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

Non-steroidal exacerbated respiratory disease and uncontrolled asthma

#### Interventions

Randomisation will be performed centrally and generated by a secure web-based system on a 1:1 basis with stratification for recruiting site and inclusion into the sputum subgroup. Patients will be randomised to receive either of the following for 24 weeks:

ACTIVE ARM: 6 g of Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA) in a 1.3:1 ratio; respectively, as six Omega-3 ethyl ester 90 capsules, taken once daily, or in divided doses, with food.

or

CONTROL ARM: Matched capsules (six) containing palm olein IV 56 taken once daily, or in divided doses, with food.

The sputum sub-study is an optional smaller part of the trial requiring 52 participants (26 per group) which will involve participants undergoing induced sputum sampling at the baseline and 24-week visits to look at cells in the lungs. A spontaneous sputum sample may be considered an acceptable method of collecting sputum for all patients at a site if the site is unable to conduct induced sputum.

## **Intervention Type**

Drug

## **Phase**

Phase III

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

Eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), matched placebo capsules containing palm olein IV 56

## **Primary outcome measure**

Asthma control measured using the change in asthma control questionnaire (ACQ)-6 between baseline and 24 weeks post-randomisation

## **Secondary outcome measures**

1. Asthma control measured using the asthma control questionnaire (ACQ)-7 at baseline, 12 weeks and 24 weeks
2. General health-related and disease-specific quality of life measured using the Mini Asthma Quality of Life Questionnaire (mini-AQLQ), Health-related quality of life indicated by the EQ5D-5L questionnaire to estimate quality-adjusted life years; Sino-nasal disease-related quality of life measured using the Sino-Nasal Outcomes Test (SNOT)-22, at baseline, 12 weeks and 24 weeks
3. Lung and nasal function measured using peak nasal inspiratory flow (PNIF) (every 6 weeks, where possible), Peak expiratory flow (PEF) every 6 weeks and Forced expiratory volume (FEV)<sub>1</sub> and forced expiratory flow at 50% of vital capacity (FEF<sub>50</sub>) will be obtained from spirometry at baseline, 12 weeks and 24 weeks.
4. Type 2 airway inflammation measured using the fraction of exhaled nitric oxide (FeNO) at baseline, 12 weeks and 24 weeks; Induced or spontaneous sputum (subgroup) at baseline and 24 weeks; full blood count for assessment of the concentration of eosinophils at baseline, 12 weeks and 24 weeks.
5. Cyclooxygenase pathway: urine analysis for LTE<sub>4</sub> and PGD<sub>2</sub> measured using radioimmunoassay and corrected for urinary creatinine at baseline and 24 weeks.
6. Adherence measured using the red blood cell fatty acid concentration at baseline, 12 weeks and 24 weeks and; Food frequency questionnaire (FFQ) at baseline and 24 weeks.
7. Specialised pro-resolving mediators (SPM): Induced or spontaneous sputum (subgroup) at baseline and 24 weeks.
8. Asthma attacks and safety: Asthma attacks will be defined as those resulting in death, hospitalisation, A&E attendance, out-of-hours medical contact, or a course or boost in oral corticosteroids (prednisolone) of at least 3 days for asthma. Adverse events will be recorded at each study visit following randomisation. Full blood count, renal and liver function tests, and coagulation for those receiving warfarin will be measured in local laboratories at baseline, 12 weeks and 24 weeks.

**Overall study start date**

12/04/2023

**Completion date**

31/12/2026

**Reason abandoned (if study stopped)**

Lack of funding/sponsorship

## Eligibility

**Key inclusion criteria**

1. Aged  $\geq 18$  years. N-ERD does not occur at birth and it rarely occurs in children
2. Diagnosis of N-ERD according to one of:
  - 2.1. Positive aspirin challenge plus history of nasal polyposis or asthma
  - 2.2. More than one typical reaction to NSAIDs or aspirin plus history of nasal polyposis or asthma
  - 2.3. A single typical reaction to NSAIDs or aspirin and a history of nasal polyposis plus moderate to severe asthma\*
  - 2.4. History of nasal polyposis plus asthma plus blood eosinophilia ( $\geq 300 \times 10^6/l$ ) or raised FENO ( $>25$  ppb) within last 12 months plus urinary leukotriene E4/creatinine  $>800$  pg/mg
3. ACQ of more than 1.5 as this indicates poor control. This is required to ensure there is a clinical need or a requirement to alter medication
4. Stable disease, as evidenced by a lack of change in asthma therapy within the last 6 weeks

\*Defined as asthma requiring at least low dose inhaled corticosteroid plus long acting bronchodilator or resulting in at least two asthma attacks per year

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

98

**Key exclusion criteria**

1. Tolerant to aspirin or NSAID with no respiratory or nasal reaction on exposure
2. Significant cardiac disease, respiratory disease or other cause for breathlessness which, according to the principal investigator, contributes to the patient's symptoms of breathlessness or other respiratory symptoms to a greater degree than the patient's asthma
3. Severe or uncontrolled co-morbid disease (other than nasal polyps) which is likely to affect the outcome of the study
4. Having had an upper or lower respiratory tract infection requiring antibiotics within four

weeks of randomisation

5. Receiving biologic agents

6. Receiving n-3 fatty acid oral supplements or more than two dietary portions of oily fish per week

7. Current smoker or more than 15 pack-year smoking history

8. Consumption of more than 21 units of alcohol per week as alcohol-induced respiratory symptoms are more common in N-ERD.

9. Pregnant or breastfeeding women and those less than 4 weeks postpartum

10. Women of child bearing potential (WOCBP) not using a highly effective form of contraceptive. Pregnancy tests will be required at trial start and at 12 weeks. Highly effective forms of contraception defined as: Methods of birth control which result in a low failure rate (i.e. less than 1% per year) when used consistently and correctly such, as implants, injectables, combined oral contraceptives, some intrauterine devices (IUDs), sexual abstinence or vasectomized partner. This will apply to all women under 55 years of age unless they are postmenopausal or sterile. Postmenopausal is defined as at least 12 months of spontaneous amenorrhea or 24 weeks of spontaneous amenorrhoea with serum FSH >40 mIU/ml. Surgically sterile is defined as females who have had a hysterectomy, bilateral salpingectomy or bilateral oophorectomy at least 6 weeks prior to enrolment.

11. Participation in the active phase of another CTIMP or within 4 weeks (or the half life of the drug if longer) of last study drug administration. Participation in observatory trials can occur if agreed between the PI of each trial and where this does not impact the patient or the outcomes of either trial

12. Patients unable to give written informed consent

#### **Date of first enrolment**

02/10/2023

#### **Date of final enrolment**

31/01/2026

## **Locations**

#### **Countries of recruitment**

England

United Kingdom

#### **Study participating centre**

**Norfolk and Norwich University Hospital**

Colney Lane

Colney

Norwich

United Kingdom

NR4 7UY

#### **Study participating centre**

**Addenbrookes Hospital**

Hills Road  
Cambridge  
United Kingdom  
CB2 0QQ

**Study participating centre****Southampton General Hospital**

Tremona Road  
Southampton  
United Kingdom  
SO16 6YD

**Study participating centre****Aberdeen Royal Infirmary**

Foresterhill Road  
Aberdeen  
United Kingdom  
AB25 2ZN

**Study participating centre****Northern General Hospital**

Northern General Hospital NHS Trust  
C Floor, Huntsmnan Building  
Herries Road  
Sheffield  
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S5 7AU

**Study participating centre****Heartlands Hospital**

Bordesley Green East  
Bordesley Green  
Birmingham  
United Kingdom  
B9 5ST

## **Sponsor information**

### **Organisation**



Norfolk and Norwich University Hospitals NHS Foundation Trust

**Sponsor details**

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**Sponsor type**

Hospital/treatment centre

**Website**

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

**ROR**

<https://ror.org/01wspv808>

**Funder(s)****Funder type**

Government

**Funder Name**

Efficacy and Mechanism Evaluation Programme

**Alternative Name(s)**

NIHR Efficacy and Mechanism Evaluation Programme, EME

**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. Internal report
3. Conference presentation
4. Publication on website
5. Submission to regulatory authorities

Participants will be asked to consent to sharing their anonymous data and samples at the end of the trial, for other research.

Access to the anonymous dataset will be made available after publication of the main trial, through reasonable requests made to the Chief Investigator and Sponsor.

**Intention to publish date**

31/12/2027

**Individual participant data (IPD) sharing plan**

The data-sharing plans for the current study are unknown and will be made available at a later date

**IPD sharing plan summary**

Data sharing statement to be made available at a later date