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Poly-unsaturated fats for improving nasal polyps and asthma

Submission date 14/04/2023	**Recruitment status** Stopped	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 05/09/2023	**Overall study status** Stopped	
Last Edited 21/05/2025	**Condition category** Respiratory	

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

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-003641-38

Integrated Research Application System (IRAS)
1004006

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
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

Study type(s)
Treatment

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

Key secondary outcome(s))
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)1 and forced expiratory flow at 50% of vital capacity (FEF50) 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 LTE4 and PGD2 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.

Completion date
31/12/2026

Reason abandoned (if study stopped)
Lack of funding/sponsorship

Eligibility

Key inclusion criteria
1. Aged ≥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 (≥300 x 10e6/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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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
United Kingdom

England

Study participating centre
Norfolk and Norwich University Hospital
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Study participating centre
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Sponsor information

Organisation
Norfolk and Norwich University Hospitals NHS Foundation Trust

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, Efficacy and Mechanism Evaluation (EME), EME

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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