International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Effect of Omega-3 Fatty Acids on Adipose Tissue Inflammation: A Systematic Review of Clinical Trials

INPLASY202670123

doi: 10.37766/inplasy2026.7.0123

Received: 30 July 2026

Published: 30 July 2026

Albakri, A; Fisk, HL; Qattous, W; Saleh, E; Al-Obaidi, S; Haymoor, S; Calder, PC.

Corresponding author:
Philip Calder

pcc@soton.ac.uk

Author Affiliation:
University of Southampton

ADMINISTRATIVE INFORMATION

Support - No support.

Review Stage at time of this submission - Risk of bias assessment.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202670123

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 July 2026 and was last updated on 30 July 2026.

INTRODUCTION

Review question / Objective What is the effect of omega-3 fatty acids on adipose tissue inflammation in overweight and obesity?

Rationale Obesity is considered a chronic low-grade inflammation state that is characterized by diseased adipose tissue remodeling manifested mainly by increase macrophage infiltration, crown-like structure formation, increase in the expression of inflammatory-related genes, and fibrosis. Eicosapentaenoic (EPA) and docosahexaenoic acid (DHA) are widely studied omega-3 fatty acids known for their anti-inflammatory actions, characterized by reducing the concentrations of circulating pro-inflammatory cytokines and promoting an anti-inflammatory macrophages phenotype. Several clinical studies investigated the effect of omega-3 fatty acids on adipose tissue inflammation, but we lack a systematic review that specifically synthesized evidence from clinical trials that assess its effect on adipose tissue biopsies. Thus, the aim of this systematic review is to assess the current body of evidence that investigated the direct effect of omega-3 fatty acids on inflammatory markers in human adipose tissue.

Condition being studied Overweight, obesity (healthy or with impaired fasting glucose, impaired glucose tolerance, insulin resistance, metabolic syndrome, dyslipidemia, or type 2 diabetes).

METHODS

Search strategy Literature search in two databases, PubMed and Cochrane Central Register of Controlled Trials (CENTRAL). The search terms used were omega-3 PUFA, n-3 PUFA, EPA, DHA, polyunsaturated fatty acid, eicosapentaenoic acid, docosahexaenoic acid, adipose tissue, adipose tissue biopsy, inflammation, and their synonyms.

Participant or population Human (male or female) aged ≥ 18 years, who were overweight or obese (i.e. BMI ≥ 25 kg/m2).

Intervention Omega-3 fatty acids (total, EPA, DHA, EPA+DHA combined), fish oil, dietary fatty fish.

Comparator Placebo, control oil, habitual diet, low-calorie diet, standard nutrition counselling, or pre-intervention measurements in single-arm studies.

Study designs to be included Clinical trials including RCT (db-RCTs, sb-RCTS, open-label RCTs, RCTs with blinding not specified, crossover RCTs), and single-arm before-after intervention.

Eligibility criteria Inclusion criteria:
Reported a clinically relevant outcome; Publication available as a full-text article; Published in English; involved human (male or female) aged ≥ 18 years, involved participants who were overweight or obese (i.e. BMI ≥ 25 kg/m2), involved supplementation with omega-3 fatty acids in the form of fish oil or dietary fatty fish, or supplements of EPA, DHA, or EPA and DHA combined, utilized human adipose tissue (subcutaneous and/or visceral) biopsies, adipose tissue inflammatory outcomes reported.
Exclusion Criteria:
Animal studies, in vitro studies (including with primary human adipocytes), observational studies, reviews, and conference abstracts. Clinical trials were excluded if involved human participants aged > 18 years, participants were underweight or with normal BMI (i.e. BMI > 25 kg/m2) or were lactating or pregnant women, no AT biopsy was taken, no inflammatory markers were investigated in an AT biopsy, participants had HIV infection, AT other than subcutaneous or visceral was used (e.g. breast adipose tissue or epicardial fat), omega-3 fatty acid intervention that did not provide EPA and/or DHA was used (like flaxseed oil and walnut), or the intervention combined omega-3 fatty acids with other bioactives or drugs since an independent effect of EPA and DHA supplementation could not be identified.

Information sources PubMed and Cochrane Central Register of Controlled Trials (CENTRAL). In addition, the reference lists of the identified trials will be checked for additional relevant studies.

Main outcome(s) Inflammation-related measures including macrophage infiltration, crown-like structure (CLS) formation, fibrosis, relative expression of inflammatory related genes, expression of inflammation-related proteins including macrophage recruitment and infiltration-related markers (such as CCL2, CD68, and CD45), inflammation-related cytokines and adipokines (such as TNF-α, IL-6, IL-1β, adiponectin, leptin, and resistin), inflammasome activation or altered inflammation-related pathways using microarray or RNAseq.

Additional outcome(s) Adipocyte size
Adipocyte diameter
Adipose tissue area
Extracellular matrix remodeling (such as MMP9, MMP7).

Data management Data will be managed in Excel.

Quality assessment / Risk of bias analysis Cochrane RoB2.

Strategy of data synthesis We will complete a systematic review with narrative data synthesis. We will not conduct meta-analysis.

Subgroup analysis None.

Sensitivity analysis None.

Language restriction English.

Country(ies) involved United Kingdom; Jordan.

Keywords omega-3 PUFA, n-3 PUFA, EPA, DHA, polyunsaturated fatty acid, eicosapentaenoic acid, docosahexaenoic acid, adipose tissue, adipose tissue biopsy, inflammation, cytokine.

Dissemination plans Scientific publication.

Contributions of each author
Author 1 - Asma'a Albakri - Conceptualized the research question, Co-designed search strategy; Conducted literature search; Selected publications for inclusion; Extracted study/ participant characteristics and research; drafted manuscript.
Email: a.albakri@ju.edu.jo
Author 2 - Helena Fisk - Reviewing extracted data, helping interpreting the findings, revising the manuscript.
Email: h.fisk@soton.ac.uk
Author 3 - Wardeh Qattous - Extracted study characteristics and data.
Email: wqattous@gmail.com
Author 4 - Eman Saleh - Extracted study characteristics and data.
Email: e_saleh@ju.edu.jo
Author 5 - Sondos Al-Obaidi - Extracted study characteristics and data.
Email: sda9230132@ju.edu.jo
Author 6 - Shatha Haymoor - Extracted study characteristics and data.
Email: snd9230139@ju.edu.jo

Author 7 - Philip Calder - Conceptualized the research question; Co-designed search strategy; Writing input into the manuscript.
Email: pcc@soton.ac.uk