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Association Of Circulating Omega-3 Fatty Acids and Cardiometabolic Outcomes: A Systematic Review of Publications from UK Biobank

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - WTF has no conflicts to declare. PCCPC has received consulting/advising honoraria from Abbott, BASF, Bayer Consumer Care, Baxter Healthcare, Bunge, Danone Nutricia, dsm-firmenich, Fresenius Kabi, H&H Group, Haleon Consumer Healthcare, Nestle and Royal Cosun and speaking honoraria from Abbott, dsm-firmenich and Fresenius Kabi.

INPLASY registration number: INPLASY202610041

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 January 2026 and was last updated on 12 January 2026.

INTRODUCTION

Review question / Objective Are higher blood plasma or serum omega-3 fatty acids (total omega-3, DHA, non-DHA omega-3) associated with lower risk or severity of cardiometabolic outcomes in UK BioBank?

Rationale The relationship between omega-3 fatty acid status (e.g. blood levels) and cardiometabolic outcomes in a healthy population at study inception remains unclear. The UK BioBank is a large-scale study that recruited approximately 500,000 participants aged between 40 and 69 years between 2006 and 2010. Plasma omega-3 fatty acids were measured by nuclear magnetic resonance spectroscopy and total omega-3 fatty acids, one individual omega-3 fatty acid (docosahexaenoic acid (DHA), the major omega-3 fatty acid in plasma) and non-DHA omegsa-3 fatty acids were reported. UK BioBank participants were followed as a prospective cohort study, with health outcomes collected from linked medical records. Therefore UK BioBank allows the association between plasma omega-3 fatty acids and cardiometabolic outcomes to be investigated. A number of studies looking at this association have been published. The aim of this systematic review is to collate the findings from these publications in order to add new knowledge to the existing literature base on omega-3 fatty acids and cardiometabolic disease risk and severity.

Condition being studied Cardiometabolic disease to include incidence of coronary heart disease, cardiovascular disease, major adverse cardiovascular event, stroke, heart failure, atrial fibrillation, or hypertension; mortality from coronary

heart disease, cardiovascular disease or stroke; incidence of type-2 diabetes, non-alcoholic fatty liver disease, or metabolic dysfunction-associated steatotic liver disease; mortality from liver disease.

METHODS

Search strategy Literature searching in MEDLINE, EMBASE and CINAHL. Searches using keywords and their alternative terms, such as ("omega 3", “omega-3”, “polyunsaturated fatty acid”, "eicosapentaenoic acid", "docosahexaenoic acid ", “EPA”, “DHA”) and (“UK Biobank", "UK BioBank").

Participant or population UK Biobank participants.

Intervention Omega-3 fatty acids (total, EPA, DHA, non-DHA) in blood plasma.

Comparator High omega-3 vs low omega-3 levels (e.g. across tertiles, quartiles or quintiles) or omega-3 levels as a continuum.

Study designs to be included Cross-sectional or longitudinal follow-up.

Eligibility criteria
Reported a clinically relevant outcome;
Reported omega-3 fatty acid concentrations in plasma;
Publication available as a full-text article;
Published in English.

Information sources MEDLINE, EMBASE and CINAHL.

Main outcome(s) Incidence of coronary heart disease, cardiovascular disease, major adverse cardiovascular event, stroke, heart failure, atrial fibrillation, or hypertension; mortality from coronary heart disease, cardiovascular disease or stroke; incidence of type-2 diabetes, non-alcoholic fatty liver disease, or metabolic dysfunction-associated steatotic liver disease.

Additional outcome(s) Mortality from liver disease.

Quality assessment / Risk of bias analysis Newcastle-Ottawa Quality Assessment Scale for Case-Control Studies; Newcastle-Ottawa Quality Assessment Scale for Cohort Studies.

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.

Keywords Omega-3 fatty acids; Docosahexaenoic acid; UK Biobank; Cohort study; Incidence; Mortality; Cardiovascular disease; Heart disease; Stroke; Type-2 diabetes; NAFLD; MASLD.

Dissemination plans Journal publication.

Contributions of each author
Author 1 - Warda Tul Firdous - Co-designed search strategy; Conducted literature search; Selected publications for inclusion; Extracted study/ participant characteristics and research findings; Drafted the manuscript.
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Author 2 - Philip Calder - Conceptualised the research question; Co-designed search strategy; Co-selected publications for inclusion; Writing input into the manuscript.
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