

INPLASY

Effects of omega-3 fatty acid intake on biomarkers of biological ageing

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ADMINISTRATIVE INFORMATION**Support** - No support.**Review Stage at time of this submission** - Piloting of the study selection process.

Conflicts of interest - PCC acts as an ad hoc consultant/advisor to BASF, Bayer Consumer Care, Danone Nutricia Research, dsm-firmenich, Fresenius-Kabi, B. Braun Melsungen, Nestle, Baxter Healthcare, Abbott Nutrition, Haleon, Holland and Barrett, Royal Cosun, AAK and Natures Crops; has received speaking honoraria from dsm-firmenich, Fresenius-Kabi, Abbott Nutrition and Eology; and has recently received study products from dsm-firmenich. SC has no conflicts to declare. PCC acts as an ad hoc consultant/advisor to BASF, Bayer Consumer Care, Danone Nutricia Research, dsm-firmenich, Fresenius-Kabi, B. Braun Melsungen, Nestle, Baxter Healthcare, Abbott Nutrition, Haleon, Holland and Barrett, Royal Cosun, AAK and Natures Crops; has received speaking honoraria from dsm-firmenich, Fresenius-Kabi, Abbott Nutrition and Eology; and has recently received study products from dsm-firmenich. SC has no conflicts to declare.

INPLASY registration number: INPLASY2026100068

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 October 2026 and was last updated on 14 October 2026.

INTRODUCTION

Review question / Objective What is the effect of omega-3 fatty acid intake on biomarkers of biological ageing?

Rationale Omega-3 fatty acids (omega-3s) are a group of polyunsaturated fatty acids that are considered an essential nutrient. EPA and DHA are the most bioactive omega-3 fatty acids. They are important components in the structure of the cell membrane, act as precursors for anti-inflammatory and signalling molecules as well as being involved

with regulation of gene expression¹. Omega-3s can be sourced from the diet (by consuming oily fish (EPA and DHA) or nuts and seeds (alpha-linolenic acid)) or through supplementation. Biological ageing refers to the gradual decline in how well the body functions over time. This doesn't necessarily always match a person's chronological (actual) age. It can be measured using biomarkers such as telomere length and DNA methylation clocks. Faster biological ageing contributes to a person's overall quality of life. Identifying factors affecting biological ageing is

critical considering the continuing ageing population globally.

Omega-3s have been observed to maintain telomere length; longer telomeres are considered a marker of slower biological ageing and better overall health. This suggests that omega-3s may contribute to healthier ageing and potentially a longer health span. A recent study showed omega-3s slowed ageing related DNA methylation clocks.

It is important to consolidate the literature about omega-3s and biological ageing to know whether they represent a useful strategy to promote a longer health span. Therefore, this systematic review will bring together research from different study designs that has assessed the influence of omega-3 fatty acids on markers of biological ageing such as telomere length and DNA methylation clocks.

Condition being studied Biological ageing.

METHODS

Search strategy Literature search in three databases (Ovid Medline, EMBASE and CINAHL). The search terms used are (omega-3*, polyunsaturated fatty acid, eicosapentaenoic acid, docosahexaenoic acid, alpha-linolenic acid, fish oil, flaxseed, marine omega-3) AND (telomere, telomerase, DNA methylation clock, epigenetic clock, Horvathage, Phenoage, epigenesis), inflammation, and their synonyms.

Participant or population Human (male or female), aged ≥ 18 years, not diagnosed with age-related health conditions or pregnancy.

Intervention For cohort studies: high dietary intake of omega-3 fatty acids.

For RCTs: omega-3 fatty acids of any source or combined with exercise or other nutrients

For Mendelian randomization studies: possessing the gene variants linked with high intake or high blood levels of omega-3s.

Comparator For cohort studies: low dietary intake of omega-3 fatty acids.

For RCTs: placebo or control.

For Mendelian randomization studies: not possessing the gene variants linked with high intake or high blood levels of omega-3s.

Study designs to be included Clinical trials including RCTs, cohort studies, Mendelian randomization studies.

Eligibility criteria Inclusion criteria: Human (male or female), aged ≥ 18 years; Reported a biomarker of biological ageing; Publication available as a full-text article; Published in English;

Exclusion Criteria:

Animal studies; in vitro studies; reviews; conference abstracts; studies in pregnant women; studies in people with diagnosed age-related health conditions.

Information sources Ovid Medline, EMBASE and CINAHL.

Main outcome(s) Biomarkers of biological ageing including telomere length or shortening, telomerase activity, DNA methylation/epigenetic clocks, ageing clocks.

Additional outcome(s) None.

Data management Publications will be screened in Rayyan. Data including study characteristics and outcomes will be managed in Excel.

Quality assessment / Risk of bias analysis For RCTs: Cochrane RoB2

For cohort studies: Newcastle-Ottawa scale.

For Mendelian randomization studies: Tool yet to identified.

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 PUFA, n-3 PUFA, EPA, DHA, alpha-linolenic acid, telomere, telomerase, DNA methylation clocks.

Dissemination plans Scientific publication.

Contributions of each author

Author 1 - Shuzeda Chowdhury - Co-designed search strategy; Completed search; Paper selection; Data extraction and collation; Risk of bias analysis; Writing input into the manuscript; Supervision.

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Author 2 - Philip Calder - Conceptualized the research question; Co-designed search strategy; Paper selection; Data extraction and collation; Risk of bias analysis; Writing input into the manuscript; Supervision.
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