INPLASY PROTOCOL

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Support: **None.**

Review Stage at time of this submission: **Formal screening of search results against eligibility criteria.**

An umbrella review of systematic reviews and meta-analyses of omega-3 fatty acids supplementation: effects on lean mass and muscle function

Nunes, EA[1]; D'Souza, AC[2]; Steen, J[3]; and Phillips, SM[4].

Rationale: **Data have emerged suggesting that supplementation with n-3 fatty acids may benefit skeletal muscle. Work in younger and older adults has demonstrated that supplementing the diet with n-3 fatty acids for 8wk potentiated rates of mixed muscle protein synthesis in response to a hyperinsulinemic-hyperaminoacidemic clamp and increased bone and fat-free (lean) mass in free-living older men and women. There is also evidence that n-3 fatty acid supplementation enhances strength gains during resistance exercise training, an effect that appears more pronounced in women. With this review, we aim to arrive at a consensus, using an umbrella review of systematic reviews, on whether n-3 fatty acid supplementation affects skeletal muscle mass (or proxies such as lean mass and fat-free mass).**
Condition being studied: **n-3 lipid supplementation and effects on skeletal muscle and muscle function.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 June 2023 and was last updated on 15 July 2023 (registration number INPLASY202360012).

INTRODUCTION

Review question / Objective: **Study Design**
A. Only systematic reviews and meta-analyses are considered.
B. No narrative reviews or scoping reviews are considered.
Participants
Does the study involve adults aged ≥18 years?

Groups that may be covered:
A. Healthy older adults
B. Older adults within clinical populations
C. Clinical populations
Intervention
1. Does the study evaluate omega-3 fatty acids interventions?
2. Does the study evaluate the mechanisms of omega-3 fatty acids?

3. Are these interventions aimed at the prevention or treatment of sarcopenia?
4. Are the interventions aimed at treating people losing muscle mass due to disease?
6. Does the study report effects on sarcopenia-related outcomes?
7. Does the study report effects on ICU-related outcomes?
Omega-3 fatty acids supplementation includes:
1. Studies in which the effect of omega-3 fatty acids supplementation (as food or other form) is compared with no supplementation
2. Studies in which omega-3 fatty acids supplementation is added to an exercise program and compared with a control group of exercise without supplementation
Relevant outcomes include:
A. Lean (muscle) mass
B. Muscle strength
C. Muscle endurance
D. Flexibility
E. Mobility
F. Physical function
G. Disability
H. Function and participation

Rationale: Data have emerged suggesting that supplementation with n-3 fatty acids may benefit skeletal muscle. Work in younger and older adults has demonstrated that supplementing the diet with n-3 fatty acids for 8wk potentiated rates of mixed muscle protein synthesis in response to a hyperinsulinemic-hyperaminoacidemic clamp and increased bone and fat-free (lean) mass in free-living older men and women. There is also evidence that n-3 fatty acid supplementation enhances strength gains during resistance exercise training, an effect that appears more pronounced in women. With this review, we aim to arrive at a consensus, using an umbrella review of systematic reviews, on whether n-3 fatty acid supplementation affects skeletal muscle mass (or proxies such as lean mass and fat-free mass).

Condition being studied: n-3 lipid supplementation and effects on skeletal muscle and muscle function.

METHODS

Search strategy: OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present – Jan 25th -2023. – 1599 results
1. omega 3 fatty acids.mp. or exp Fatty Acids, Omega-3/ 31883
2. eicosapentaenoic acid.mp. or exp Eicosapentaenoic Acid/ 12564
3. docosahexaenoic acid.mp. or exp Docosahexaenoic Acids/ 17300
4. EPA.mp. 22400
5. DHA.mp. 17282
6. omega-3.mp. 26033
7. systematic review.mp. or exp "Systematic Review"/ 288148
8. meta-analysis.mp. or exp Meta-Analysis/ 265849
9. n-3 fatty acids.mp. or exp Fatty Acids, Omega-3/ 30340
10. fish-oil.mp. or exp Fish Oils/ 34648
11. 1 or 2 or 3 or 4 or 5 or 6 or 9 or 10 66796
12. 7 or 8 416669
13. exp Body Composition/ or lean mass.mp. or exp Sarcopenia/ or exp Muscle, Skeletal/ 362283
14. exp Body Composition/ or fat free mass.mp. 66631
15. 13 or 14 365524
16. 11 and 15 1599
Embase 1974 to 2023 January 24 - Jan 25th -2023. – 323 results
15 13 and 14 323
14 10 or 11 669780
13 9 and 12 16886
12 exp Body Composition/ or lean mass.mp. or exp Sarcopenia/ or exp Muscle, Skeletal/ or fat free mass.mp. 524543
11 systematic review.mp. or exp "systematic review"/ 501183
10 meta-analysis.mp. or exp meta analysis/ 394943
9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 675741
8 n-3 fatty acids.mp. 5440
7 fish-oil.mp. or exp fish oil/ 21422
6 omega-3.mp. 45407
5 DHA.mp. 22896
4 EPA.mp. 25979
3 docosahexaenoic acid.mp. or docosahexaenoic acid/ 28421

2 eicosapentaenoic acid.mp. or exp icosapentaenoic acid/ 22522
1 exp fatty acid/ or exp omega-3 fatty acid/ 646053
Web of Science Core Collection – Jan 25th -2023 – 90 results
Entitlements:
- WOS.IC: 1993 to 2023
- WOS.CCR: 1985 to 2023
- WOS.SCI: 1976 to 2023
- WOS.AHCI: 1976 to 2023
- WOS.BHCI: 2005 to 2023
- WOS.BSCI: 2005 to 2023
- WOS.ESCI: 2018 to 2023
- WOS.ISTP: 1990 to 2023
- WOS.SSCI: 1976 to 2023
- WOS.ISSHP: 1990 to 2023
Searches:
1: ALL=(omega 3 fatty acids) Results: 34857
2: ALL=(eicosapentaenoic acid) Results: 19749
3: ALL=(docosahexaenoic acid) Results: 26730
4: ALL=(EPA) Results: 107079
5: ALL=(DHA) Results: 26197
6: ALL=(omega-3) Results: 32598
7: ALL=(systematic review) Results: 425703
8: ALL=(meta-analysis) Results: 294150
9: ALL=(n-3 fatty acids) Results: 26253
10: ALL=(fish-oil) Results: 26210
11: #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #9 OR #10 Results: 188045
12: #8 OR #7 Results: 569087
13: (((ALL=(lean mass)) OR ALL=(muscle mass)) OR ALL=(fat free)) OR ALL=(muscle) Results: 1074923
14: #11 AND #12 AND #13 Results: 90
SPORTDiscus – Filter: Academic Journals - 40 results
TX (omega-3 fatty acids or omega 3 or omega-3 or fish oil or n-3 or pufa or epa or dha or eicosapentaenoic or docosahexaenoic) AND TX (fat-free mass or lean mass or muscle mass or muscle or strength) AND TX (review or meta-analysis or systematic review).

Participant or population: Adults >18 years.

Intervention: N-3 fatty acid supplementation.

Comparator: Placebo (nothing) or an oil that is not n-3.

Study designs to be included: Systematic reviews.

Eligibility criteria: Adults >18yr taking n-3 fatty acids.

Information sources: Embase, PubMed, and the Web of Science core collection.

Main outcome(s): muscle mass, lean mass, fat-free mass, strength.

Additional outcome(s): function, sarcopenia-related outcomes.

Data management: All data are stored in secure databases using coded Excel files. References are de-duplicated using EndNote.

Quality assessment / Risk of bias analysis: Consensus Analysis strategy for Umbrella Review
1. All reviews will be scored using the AMSTAR (A Measurement Tool to Assess Systematic Reviews) tool (Shea et al. BMC Med Res Methodol.2007;7:10). This 11-item tool assesses the degree to which review methods avoided bias. The methodological quality is rated as high (score 8–11), moderate (score 4–7) or low (score 0–3).
2. To organize the evidence, authors will systematically synthesize the extracted data of each review. This results in standardized effectiveness statements (i.e., sufficient evidence, some evidence, insufficient evidence, insufficient evidence to determine) about the treatment effect of the interventions in the individual systematic reviews.
3. The quality of the evidence (QoE) supporting each bottom-line statement will be rated by using a method based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for primary evidence (1 - very low; 2 - low; 3 - moderate; 4 - high). This method considers study design (meta-analysis: yes or no) and AMSTAR rating of the included systematic reviews.

Strategy of data synthesis: Synthesis of reviews in terms of conclusions, quality of evidence, and standard effectiveness

statements per our previous work (An umbrella review of systematic reviews of β-hydroxy-β-methyl butyrate supplementation in ageing and clinical practice: https://onlinelibrary.wiley.com/doi/10.1002/jcsm.13030).

Subgroup analysis: Supplementation with and without resistance training
Younger (18-50) vs. Older (>50)
Males vs. Females.

Sensitivity analysis: None planned.

Language restriction: English.

Country(ies) involved: Canada.

Keywords: N-3 fatty acid, Omega-3 fatty acid, Sarcopenia, Muscle.

Dissemination plans: Publication in a scientific journal.

Contributions of each author:
Author 1 - Everson Nunes - Conceived ideas for review, conducted searches, screened articles, conducted analysis, and drafted the paper.
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Conflicts of interest: EAN reports receiving non-financial support from different companies (Laboratory Tiaraju (Santo Andre-RS, Brazil), Phytomare (Governador Celso Ramos-SC, Brazil) and Herbarium Laboratório Botânico Ltda (Colombo, PR, Brazil)) in the form of fish oil supplements to conduct clinical trials in clinical situations and pre-clinical research not directly related to the current review.