

# Interventional Results Following EPA and/or DHA Supplementation: Arteriosclerosis

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Prepared for:

**GOED Members**

Prepared by:

**Kaitlin Roke, PhD**

[kaitlin@goedomega3.com](mailto:kaitlin@goedomega3.com)

# Understanding the Clinical Study Database Tool and This Report

## Using GOED's novel Clinical Study Database:

The GOED Clinical Study Database (CSD) is the first database of its kind, comprised of more than 40,000 published papers on eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) omega-3s.

The published papers in the CSD have been curated and organized in a comprehensive, searchable format and include details for human interventional studies such as demographics, dosage, study design, etc. The CSD is designed to bring together the evidence in an organized and succinct manner.

## About the Report:

This report includes details from two distinct sections of the Clinical Study Database, a high level Abstract Search and a detailed Advanced Search.

## Abstract Search:

Includes article lists, details on whether the studies are positive, negative or neutral (according to abstract outcomes), associated keywords, influential study authors and relevant journals.

## Advanced Search:

Includes data on every outcome from a given study, is fully searchable and can be filtered by variables including age, gender, study duration, interventional agent, and dosage of EPA and/or DHA.

## Database Status:

In addition to the published research, new research on EPA and DHA is ongoing. The database contains published research available through PubMed, and our team is constantly updating the database. At the time this report was compiled (out of all of the categorized research on EPA and DHA omega-3s), the Abstract Search was evaluated to be 95.6% complete, and the Advanced Search was evaluated to be 83.7% complete.

## To Aid in Your Understanding of the Report:

Terms, definitions and report methodology can be found in the Appendix of this report.

Additional resources include:

- A full user guide with more information and the CSD Methods publication.
- High resolution images.
- Full study lists from the Abstract and Advanced search.



Blue folder icon indicates more information can be found in the CSD Report folder.

# Health Outcome Background: Arteriosclerosis

## What is Arteriosclerosis?

Cardiovascular diseases (CVD) are the leading cause of death, taking 17.9 million lives globally each year (1). There are many types of CVD, as this is a general term for conditions affecting the heart or blood vessels (2). CVDs are associated with the build-up of fatty deposits inside the arteries (3). Healthy blood vessels and arteries are flexible and elastic; however, over time they become thick and stiff, causing the walls of the arteries to harden. Arteriosclerosis is defined as a change in blood vessels including a thickening and hardening of the walls of the arteries, and atherosclerosis is a subtype of arteriosclerosis, characterized by the narrowing of the artery because of plaque build-up. These disease conditions and physiological changes in the body cause downstream health complications and worsening of cardiovascular health (4).

Several lifestyle modifications such as changes to dietary intake and exercise habits have been suggested to slow down and reduce the build-up of artery plaque. Dietary intake, and specifically increased intake of EPA and DHA omega-3s, may modify this biological progress in a positive way.

## Purpose of the Report:

The current investigation was undertaken to showcase the capabilities of the clinical study database by evaluating the research available on arteriosclerosis. This report will answer the question, "What does the body of evidence around EPA and DHA supplementation and arteriosclerosis show?"

1. [https://www.who.int/health-topics/cardiovascular-diseases#tab=tab\\_1](https://www.who.int/health-topics/cardiovascular-diseases#tab=tab_1)

2. <https://www.nhs.uk/conditions/cardiovascular-disease/>

3. <https://www.nhlbi.nih.gov/health/atherosclerosis>

4. Vasan et al. (2021). Arteriosclerosis, Atherosclerosis, and Cardiovascular Health: Joint Relations to the Incidence of Cardiovascular Disease. *Hypertension*. 78(5), 1232–1240.

# Summary of Article Types: Arteriosclerosis

174 studies were found relating to "Arteriosclerosis."

138 of these were interventional studies.

**Figure 1:** Types of studies found using "Arteriosclerosis" as the term of interest.



**Note:** Studies were categorized by study design, of which 80% (blue) were clinical trials, 11% (grey) were literature reviews, and 9% (orange) were observational studies. This information is generated from PubMed then filtered through the GOED CSD criteria to ensure the studies are related to EPA and DHA omega-3s.



Find more information about Abstract Search Methods in the Help Guide in the CSD Report Folder.

# Summary of Interventional Articles: Arteriosclerosis

138 interventional studies were found relating to "Arteriosclerosis." According to the authors' conclusions in the Abstracts, most articles related to arteriosclerosis have a positive conclusion.

**Table 1:** Preview of the Article List for Abstracts.

YEAR	PMID	TITLE	TYPE	ABSTRACT CONCLUSION
2020	31543378	Administration of eicosapentaenoic acid...	Interventional	positive
2020	32014347	Fish oil reduces subclinical inflammation...	Interventional	positive
2020	32636128	Administration of EPA may alter lipoprotein particle...	Interventional	positive

**Table 2:** Summary of Abstract Conclusions for Abstract Search Results.

TOTAL INTERVENTIONAL STUDIES	POSITIVE	NEGATIVE	NEUTRAL
138	82%	2%	16%

**Note:** Abstract Conclusions are evaluated as positive, negative or neutral based on the overall article conclusions as written by the author in the Abstract. These conclusions may not be specifically related to the search term of interest, but reflect the overall outcomes of the results written in the Abstract.



Find the full Abstract Search List and additional details in the Help Guide in the CSD Report Folder.

# Related Keywords: Arteriosclerosis

Keywords are related terms found within the searched articles. They are divided into either biomarkers or conditions. This can inform other searches or illuminate connections linked to the term of interest. Keywords can be used for scope refinement or expansion.

**Table 3: Biomarkers** most commonly found in articles for term of interest "Arteriosclerosis." Sorted from highest to lowest count.

Not surprisingly, in an omega-3 specific search the most commonly associated biomarkers are "eicosapentaenoic acid" and "fatty acids, omega-3."

Term	Count
Eicosapentaenoic Acid	60
Fatty Acids, Omega-3	58
Triglycerides	30
Fish Oils	29
Biomarkers	28
Hydroxymethylglutaryl-CoA Reductase Inhibitors	26
Docosahexaenoic Acids	18
Cholesterol, LDL	16
Lipoproteins	15
Fatty Acids, Unsaturated	14

**Table 4: Conditions** most commonly found in articles for term of interest "Arteriosclerosis." Sorted from highest to lowest count.

In a search for "Arteriosclerosis," two of the most commonly associated condition terms were "coronary artery disease" and "atherosclerosis."

Term	Count
Coronary Artery Disease	52
Arteriosclerosis	34
Atherosclerosis	28
Hypertriglyceridemia	11
Disease Progression	9
Peripheral Arterial Disease	8
Diabetes Mellitus, Type 2	8
Thrombosis	8
Hypercholesterolemia	8
Inflammation	7
Hyperlipidemias	7

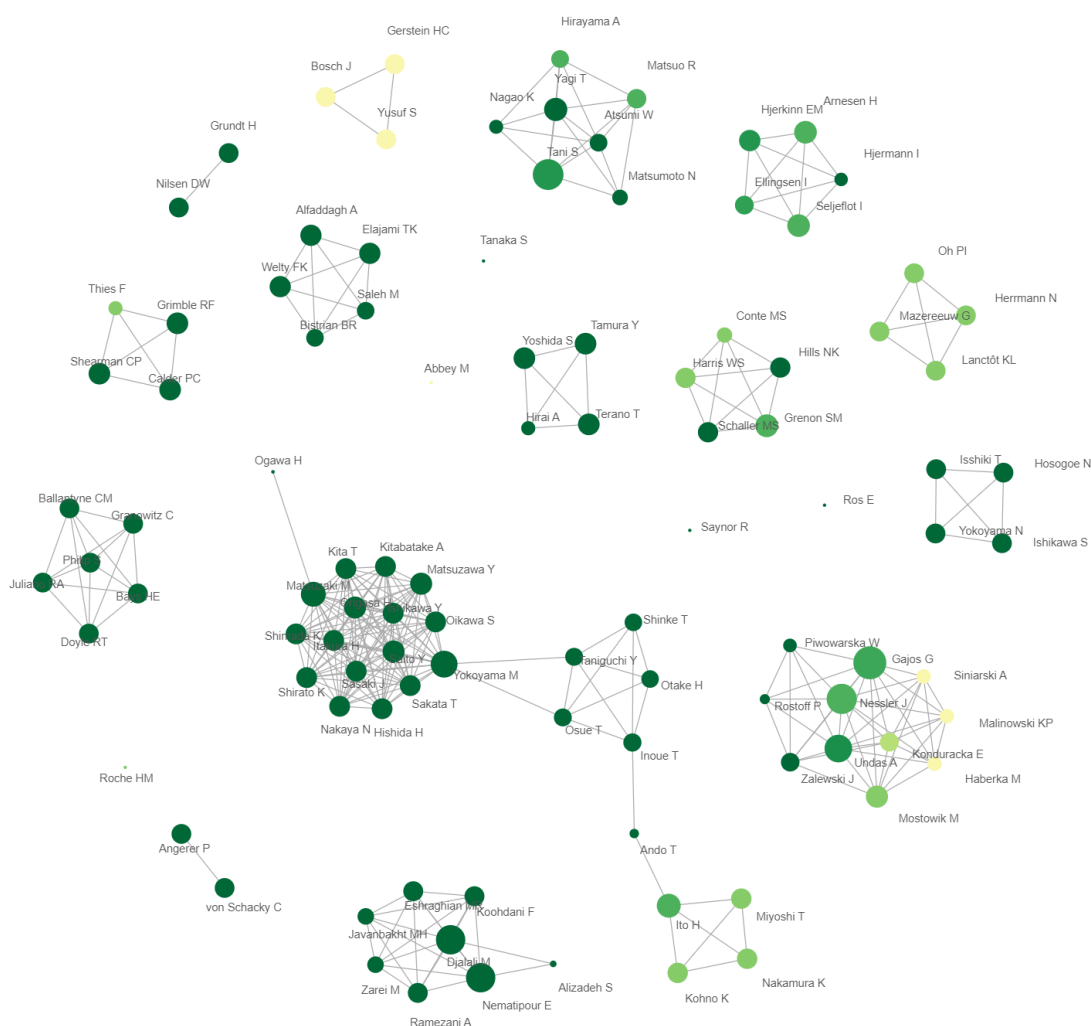


Find more information about Keywords in the Help Guide in the CSD Report Folder.

# Influencers: Arteriosclerosis

The information about Influencers showcases the authors with the greatest impact to and the most published research related to the term of interest. The size and color of the dots are relevant to the interpretation. The larger the dot, the greater the influence. The clusters show groups of people who have published studies together. The color of the dots represents the Abstract Conclusions: Green represents positive, yellow represents neutral, and red represents negative. The darker the green, the greater the number of studies with positive abstract conclusions.

**Figure 2:** Authors influencing the field related to term of interest "Arteriosclerosis" (this example Includes authors publishing at least two articles related to this topic of interest).

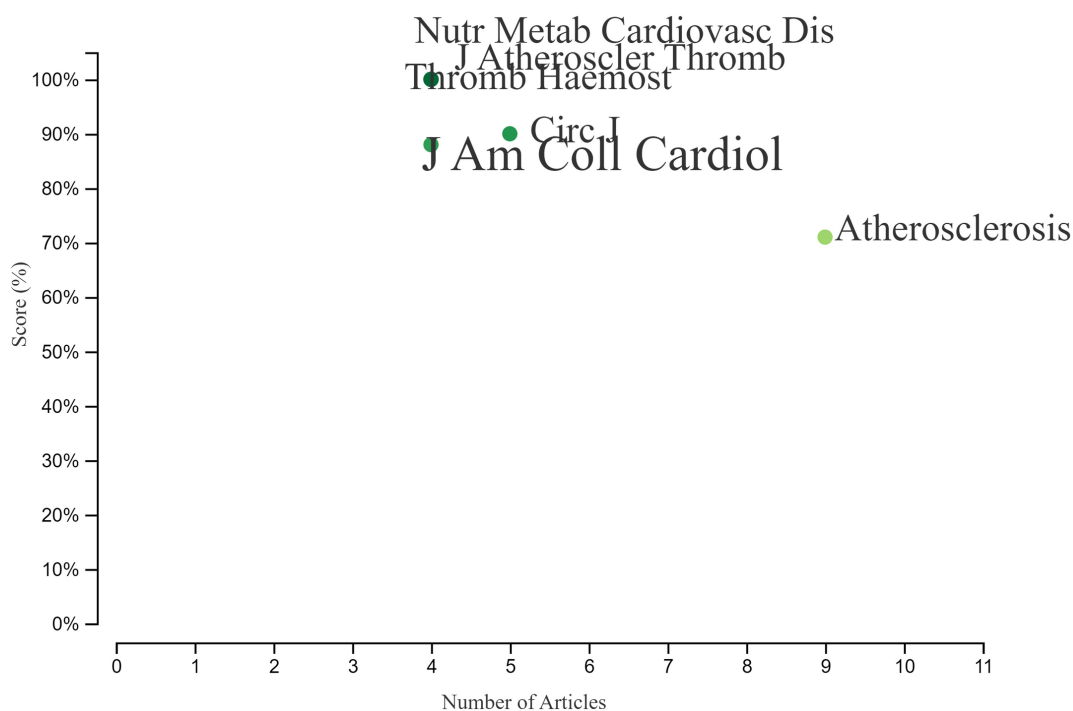


Find more information about Influencers in the Help Guide in the CSD Report Folder.  
Find a high resolution Lineage image in the CSD Report Folder.

# Journals: Arteriosclerosis

The database and the figure below showcases the scientific journals that have published articles related to the term of interest. The size and color of the dots are relevant to the interpretation. The larger the dot, the greater the number of publications. The color of the dots represents the Abstract Conclusions: green represents positive, yellow represents neutral, and red represents negative. Score (%) represents the percentage of Abstract Conclusions reported as positive.

**Figure 3:** Journals publishing articles related to term of interest "Arteriosclerosis" (this example includes journals publishing at least three articles related to this topic of interest).



Find more information about Journals in the Help Guide in the CSD Report Folder.  
Find a high resolution image in the CSD Report Folder.



# Customized Study Filters: Arteriosclerosis

In the Advanced Search, the CSD can use additional filters to further define the search data. Specified filters for this particular report for the search term of interest "Arteriosclerosis" include:

<p><b>POPULATION</b></p> <p>Gender</p> <p><input type="checkbox"/> Male</p> <p><input type="checkbox"/> Female</p> <p>Age - 0 to 99</p> <p>Min <input type="range" value="0"/> 0</p> <p>Max <input type="range" value="99"/> 99</p> <p>Characteristics <input type="checkbox"/> <a href="#">?</a></p>	<p><b>Population:</b></p> <p>All genders, ages, and participant characteristics were included in this search.</p>
<p><b>INTERVENTION</b></p> <p>Omega-3 Agent <input type="checkbox"/></p> <p>Dosage</p> <p>Min <input type="text"/> Max <input type="text"/> mg</p> <p>Select <input type="button" value="v"/></p> <p>Other Agents <input type="checkbox"/></p> <hr/> <p><b>CONTROL</b></p> <p>Placebo <input type="checkbox"/></p>	<p><b>Intervention:</b></p> <p>All omega-3 agents, dosages, other agents and placebos were included in this search.</p>
<p><b>OUTCOMES</b></p> <p>Terms <input type="button" value="i"/></p> <p>Search... <input type="text"/></p> <p>Arteriosclerosis <input type="button" value="x"/></p> <p>Logic Expression - <a href="#">Edit Logic</a> <input type="button" value="i"/></p> <p>Arteriosclerosis <input type="text"/></p> <p>Search in:</p> <p><input checked="" type="checkbox"/> Results</p> <p><input type="checkbox"/> Participant Characteristics</p>	<p><b>Outcomes:</b></p> <p>"Arteriosclerosis" was the search term of interest for this report. There was no additional logic expression (and/or/not) applied. "Arteriosclerosis" was searched for in the Results (and not the Participant Characteristics) of the indexed studies.</p>
<p><b>STUDY DESIGN</b></p> <p>Duration</p> <p>Min <input type="text"/> Max <input type="text"/> Select <input type="button" value="v"/></p> <p>Number of Participants</p> <p>Min <input type="text"/> Max <input type="text"/></p> <p><input type="button" value="Reset"/> <input type="button" value="Save"/> <input type="button" value="Search"/></p>	<p><b>Study Design:</b></p> <p>All study durations and studies with any participant number were included in this search.</p>

# Summary of Results: Arteriosclerosis

The CSD displays the results of the search conducted by generating a lineage plot which includes terms of interest relating to "Arteriosclerosis" (as shown below).

**There were 21 interventional studies that measured "Arteriosclerosis" as a Result.**

As the diagram moves to the right, associated terms linked to the main term are displayed. These terms are typically connected through a lineage, and may represent more specific iterations of the main term. Arteriosclerosis represents an umbrella term for a variety of conditions, so in this case we expect to see both conditions and biomarkers as part of the lineage.

**Figure 4:** Lineage plot for the term of interest "Arteriosclerosis" measured in the Results of the studies in the CSD. The size of the dot represents the number of studies.



Find a high resolution Lineage image in the CSD Report Folder.

# Key Takeaways: Arteriosclerosis

In a typical report we could analyze any number of variables, depending on the query, to determine key takeaways. In this report, we dug deeper into the results by Outcomes and by Dosage. Key Takeaways are presented on this page and details about the results are presented in the following pages.

**Analysis by Outcome:** Based on the information reviewed for this report and the data available from the CSD, we made several interesting observations. In the studies we reviewed, the biomarker "atherogenic index of plasma" was used to assess change in arteriosclerosis over time. According to our data review and analysis, there were significant changes to the biomarker atherogenic index of plasma after EPA+DHA omega-3 supplementation. Biomarkers can provide value in disease or condition assessment in order to track improvement or worsening of health. On the other hand, there were no changes in the health conditions measured (described below). Further analysis focused on these health conditions may reveal important information about whether we can expect consumption of EPA and/or DHA omega-3s to impact these health conditions in a measurable or meaningful way.

The figures on the following pages include data across three studies and those associated data points. Six of seven datapoints show a negative change in the atherogenic index of plasma (proxy for arteriosclerosis) over time or between groups. Change % and Difference in "Arteriosclerosis" (as measured by the atherogenic index of plasma) are also available in chart format.

**Analysis by Dosage:** The dosages of EPA+DHA omega-3s supplemented across the 21 interventional trials were reviewed and the studies were divided into three groups (<500mg/day EPA+DHA, 501-1,000mg/day EPA+DHA, >1,000mg/day EPA+DHA, no dosage recorded) for further analysis. After compiling the data, we noticed that the most promising results were in the studies where the intervention groups consumed greater than 1,000 mg/day of EPA+DHA omega-3s. Therefore, the results of this data suggest that further investigation into studies with dosages over 1,000 mg/day EPA+DHA omega-3s may be valuable to further define potential health benefits.



Find full Advanced Search detailed results document in the CSD Report Folder.

# Results by Outcome: Arteriosclerosis

**Results by Outcome:** For this report analysis, we examined the results by the outcomes measured in the studies. There were five outcomes measured across the 21 studies related to "Arteriosclerosis."

- Atherogenic Index of Plasma, a biomarker of arteriosclerosis
- Coronary artery disease
- Multi-vessel disease
- Peripheral artery disease
- Arteriosclerosis obliterans

**Notes:** Data related to subject characteristics or data collected only at baseline were excluded. Omega-3 treatment groups and their placebo comparison groups are shown in more detail below. Other comparison groups (like other interventional groups without omega-3) were excluded.

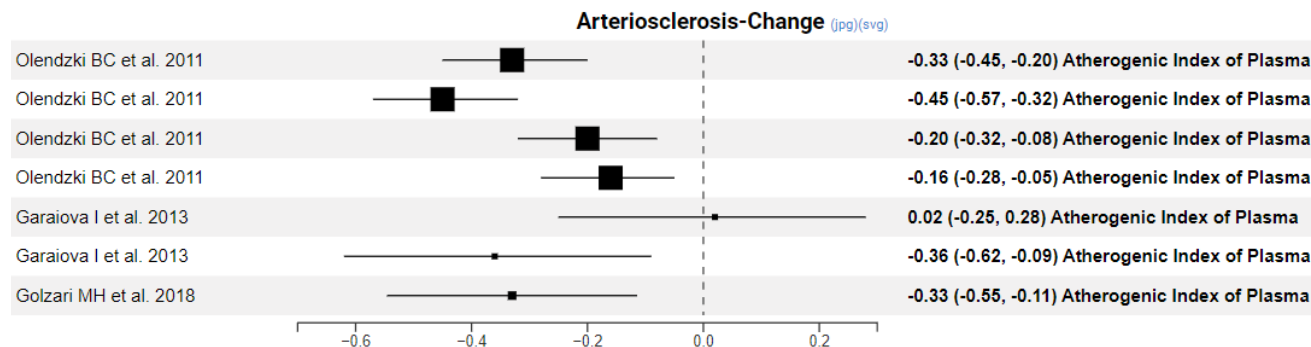
- 1) Atherogenic Index of Plasma, a biomarker of arteriosclerosis (12 studies)
  - Significant difference between omega-3 groups and placebo groups at the final timepoints. Final timepoints included study durations of: 3, 8, 10, 12, and 16 weeks, and 39 (9 months) and 78 (1.5 years) weeks (12 results).
  - No significant differences between the omega-3 groups and the placebo groups when assessing change over time (7 results).
- 2) Coronary artery disease (2 studies)
  - No significant differences between omega-3 groups and placebo groups when assessing final timepoints.
- 3) Multi-vessel disease (2 studies)
  - No significant differences between omega-3 groups and placebo groups when assessing final timepoints.
- 4) Peripheral artery disease (1 study)
  - No significant difference between omega-3 group and placebo group when assessing final timepoints.
- 5) Arteriosclerosis obliterans (1 study)
  - No significant difference between omega-3 group and placebo group when assessing final timepoints.



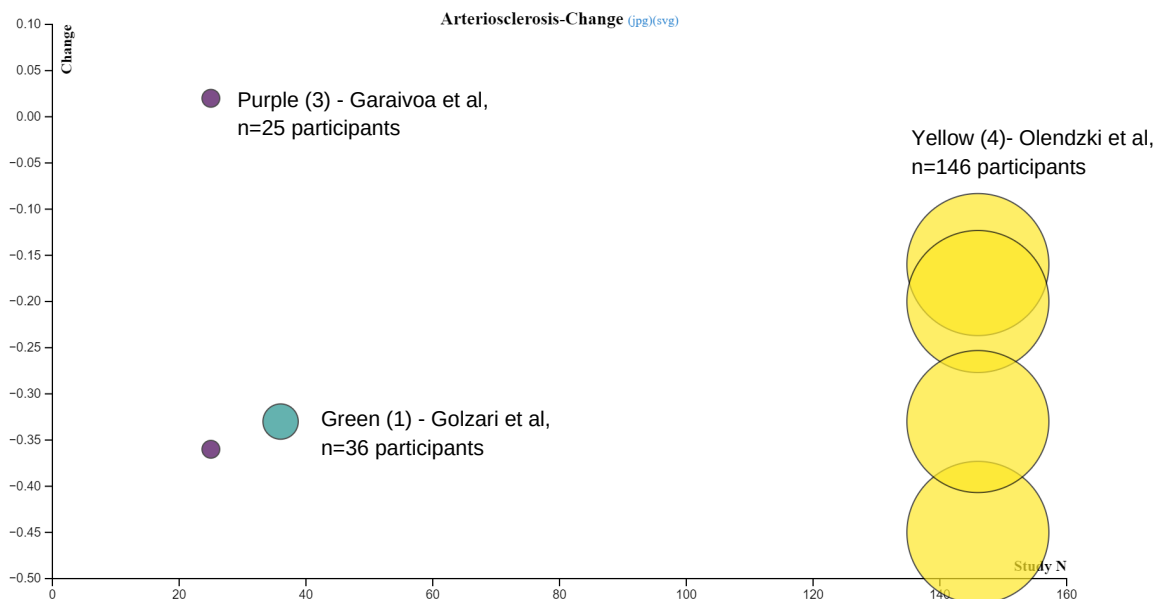
Find full Advanced Search detailed results document in the CSD Report Folder.

# Results by Outcome (Continued): Arteriosclerosis

**Figure 5:** Forest Plot displaying "change in arteriosclerosis" across studies, as measured by the "atherogenic index of plasma." This figure represents data from three of the 21 studies included in this report.



**Figure 6:** Bubble Plot displaying "change in arteriosclerosis" across studies, as measured by the "atherogenic index of plasma." Number of Participants (Study N) is displayed on the x-axis. The larger the dot, the greater the number of participants. This figure represents data from three of the 21 studies included in this report. Based on this figure, it appears that across three studies, there was a negative "change in arteriosclerosis" over time or between groups.



 Find high resolution images for both Charts and more information about Charts in the Help Guide in the CSD Report Folder.

# Results by Dosage:

## Arteriosclerosis

**Results by Dosage:** For this report analysis, we divided the dosages provided in the studies into three main groups. There were 16 studies where the dosage of EPA and DHA was clearly recorded. The dosages of EPA + DHA ranged from 275 - 6,000mg EPA + DHA per day.

- 0-500 mg/day EPA+DHA (3 studies)
- 501-1,000 mg/day EPA+DHA (4 studies)
- 1,001+ mg/day EPA+DHA (9 studies)
- No clear EPA and DHA dosage listed (5 studies)

**Notes:** Data related to subject characteristics or data collected only at baseline were excluded. Omega-3 treatment groups and their placebo comparison groups are shown in more detail below, other comparison groups (like other interventional groups without omega-3) were excluded.

- 0-500mg/day EPA+DHA - actual range: 250-530mg/day EPA+DHA (3 studies)
  - 2 studies reported no change in the atherogenic index of plasma.
  - 1 study reported a significant difference in the atherogenic index of plasma.
- 501-1,000 mg/day EPA+DHA - actual range: 832-900mg/day EPA+DHA (4 studies)
  - 4 studies reported no changes across four distinct outcomes, one measured in each study - peripheral artery disease, coronary artery disease, multi-vessel disease, or atherogenic index of plasma.
- 1,000+ mg/day EPA+DHA - actual range: 1,800-6,000mg/day EPA+DHA (9 studies)
  - 5 studies reported a significant difference in the atherogenic index of plasma.
  - 1 study reported a significant difference in the atherogenic index of plasma after 16 weeks of supplementation, but no difference after 8 weeks of supplementation.
  - 1 study reported a significant difference in arteriosclerosis obliterans, and in the hazard ratio of coronary artery disease.
  - 1 study reported no change in coronary artery disease.
  - 1 study reported no change in multi-vessel disease.
- No clear EPA+DHA dosage listed (5 studies)
  - 3 studies provided omega-3 fats but didn't specify the dosage of EPA and DHA.
  - 2 studies provided food which contained EPA and DHA omega-3s as part of a dietary intervention, but amounts of EPA and DHA weren't specified.



Find the full Advanced Search study list, and the Detailed Results Analysis in the CSD Report Folder.

# Results by Dosage (Continued): Arteriosclerosis

**Table 5:** Sample Article List for Articles Related to the Term of Interest "Arteriosclerosis" sorted by Dosage.

Year	PMID	Title	Dosage ▼	Duration	Number of Subjects	Abstract Conclusion ⓘ
1989	2568519	Randomised trial of fish oil for prevention of restenosis after coronary angioplasty.	6000 mg (EPA + DHA)	6 Months	204	Neutral
2011	22007257	Treatment of rheumatoid arthritis with marine and botanical oils: influence on serum lipids.	3500 mg (EPA + DHA)	18 Months	146	Positive
2017	29017158	Beneficial Effects of n-3 Fatty Acids on Cardiometabolic and Inflammatory Markers in Type 2 Diabetes Mellitus: A Clinical Trial.	2700 mg (EPA + DHA)	10 Weeks	170	Positive
2012	22186099	Relationship between coronary artery disease and non-HDL-C, and effect of highly purified EPA on the risk of coronary artery disease in hypercholesterolemic patients treated with statins: sub-analysis of the Japan EPA Lipid Intervention Study (JELIS).	1800 mg (EPA + DHA)	5 Years	81683	Positive
2015	25444760	Effects of eicosapentaenoic acid on peri-procedural (type IVa) myocardial infarction following elective coronary stenting.	1800 mg (EPA + DHA)	27 Days	165	Positive



Find the full Advanced Search study list, and the Detailed Results Analysis in the CSD Report Folder.

# Suggested Next Steps:

## Arteriosclerosis

In this report, we included a detailed analysis on Outcomes and Dosage. Additional analysis and filtering can be done by sorting the study list according to:

- **Year of Publication**
  - The studies in this list range from years 1989 - 2020.
- **Duration of Study**
  - The studies ranged in duration from 27 days - 6 years.
    - Removing studies > 4 years (n=2), the average length of a study was 12 weeks (~3 months).
- **Number of Subjects**
  - The number of participants in each study ranged from 12-81,683.
    - Removing studies >27,621 (n=2), the average number of people per study was 138.
- **Abstract Conclusion** (overall, not specific to term of interest).
  - 19/21 studies (90%) had a positive abstract conclusion
  - 2/21 studies (10%) had a neutral abstract conclusion

Studies can also be sorted by:

- PubMed reference number (PMID)
- Title of Article

The CSD helps to save time gathering the scientific literature and ideally can help to set the stage for the next set of project or research questions. Often after this process is completed, further action is needed. In this case, suggested next steps might include:

- Researching a specific term of interest related to arteriosclerosis for further investigation. A smaller, more focused review of a specific area may provide more detailed insights.
- Using the information gathered from these articles to propose a mechanism of action linking EPA and DHA to reduction in build-up of artery plaque.
- Preparing a systematic review or meta-analysis.
- Is there a population that hasn't been studied yet?
- Determining if gender-specific or age-specific analyses are warranted. Is there enough evidence to evaluate an effect for a certain age group?
- If there are gaps in the research, are further clinical studies needed?

**Note:** With a database license, each article from the Advanced Search (n=21) can be evaluated in further detail to review individual study datapoints and measurements related to arteriosclerosis or all measurements captured in each study.



# Terms and Definitions

## What is the Abstract Search?

For the Abstract Search, the GOED CSD asks PubMed (academic search engine) to generate the list of studies. PubMed is consistently monitoring and updating the articles published. Next, the GOED CSD scans thousands of articles, allowing for a curated list to be generated. Each article abstract that appears on the list has been assessed based on three questions:

- Is the study actually about EPA and DHA?
- What is the type of study?
- Was the abstract conclusion as indicated by the author reported to be positive, negative, or neutral?

**Abstract Conclusions** - Based on the overall outcomes stated by the authors in the abstract, GOED's research team categorized the Abstract Conclusions to be positive, negative or neutral. Two researchers reviewed each article, and if there was a conflict, a third researcher evaluated the article in greater detail.

- **Positive** - Abstract included at least one statistically significant positive outcome, and zero negative outcome(s);
- **Negative** - Abstract included at least one statistically significant negative outcome;
- **Neutral** - Abstract included no statistically significant outcome(s).

**Influencers** - Influencers represent authors related to the topic. These authors may have contributed one or more scientific papers to this topic area, and/or may have also contributed comments in the media or in other scientific sources about the topic.

**Journals** - Journals refers to the list of academic journals that have published articles containing the term of interest. Knowing what journals publish regularly on a given topic - and which are more likely to publish positive versus negative studies - can help inform choices for publishing similar work or suggest journals to peruse for additional research.



Find more information in the Help Guide in the CSD Report Folder.

# Terms and Definitions

## What is the Advanced Search?

This portion of the database includes data extracted from published literature. The data from each article was extracted by one independent research assistant and reviewed for accuracy by a second. The data collected and input was in accordance with the Cochrane guidelines for systematic reviews and meta-analyses. Using this information, the advanced search scans the available data to look for the term(s) of interest. This term of interest may be found and measured in the Results and/or the Participant Characteristics sections of the scientific articles.

**Customized Filters** - Filters allow you to refine the search to fit your desired project goals, including specifying for age and gender of the participants, length of study, number of people in the study, and various intervention components.

**Explanation of MeSH** - This database and PubMed draw from a scientific dictionary called "MeSH - Medical Subject Headings." This dictionary plays an important role in linking topics together and providing relevant results after a search. In addition to the MeSH dictionary, the CSD also uses a supplemental database that includes terms that are not part of the MeSH dictionary.

**Differences between the Abstract and Advanced Search Study Lists** - The number of interventional studies will differ between the Abstract and Advanced Search. The Abstract Search captures the term of interest and other related terms, generating a longer study list. The Advanced Search only captures the term of interest if there is an associated data point in either the Participant Characteristics or the Results, generating a shorter study list.

**Charts** - In order to compare results between studies, the GOED CSD looks for the same terms across studies and then matches statistics to highlight what results can be compared. Not all studies will use the same term or the same statistics for their analysis. These charts only reflect studies that have measured the term of interest using comparable statistics. These statistics include: odds ratio, hazard ratio, change and % change.



Find more information in the Help Guide in the CSD Report Folder.

## **Questions or Suggestions? Contact us.**

**Kaitlin Roke, PhD**

Director of Science Communications and Outreach  
[csd@goedomega3.com](mailto:csd@goedomega3.com)

## **About GOED**

GOED represents the worldwide EPA and DHA omega-3 industry, and our membership is built on a quality standard unparalleled in the market. Our mission is to increase consumption of EPA and DHA omega-3s and ensure that our members produce quality products that consumers can trust.

GOED is a recognized expert in the omega-3 industry. We gather and share information on a variety of EPA and DHA-related topics.