ILLUMINATE THE SCIENCE

GOED CLINICAL STUDY DATABASE

EPA and DHA Supplementation and Dry Eye Disease / Dry Eye Syndrome

Date Prepared:

February 2025

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. The database catalogues more than 50,000 published papers on eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) omega-3s. Of these studies, ~5,000 are human clinical trials.

The published papers included within the CSD have been curated and organized in a comprehensive, searchable format. Details include data from 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:

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

Advanced Search:

The 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:

New research on EPA and DHA is ongoing. The database contains published research available through PubMed, and the GOED research team is constantly updating the database. At the time this report was compiled (out of all of the categorized research on EPA and DHA), the Abstract Search was evaluated to be 99.0% complete, and the Advanced Search was evaluated to be 94.7% complete.

To Aid in Understanding 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 Search and Advanced Search.

 Blue folder icon indicates more information available.

Dry Eye Disease / Dry Eye Syndrome and EPA and DHA Omega-3s

Background:

Dry eye disease is a multifactorial disease of the tears and ocular surface of the eye that results in symptoms of discomfort, visual disturbance and tear film instability, with potential damage to the ocular surface (National Eye Institute). These symptoms are accompanied by increased osmolarity of the tear film and inflammation of the ocular surface. Dry eye disease is a specific and well characterized health outcome. The utilization of the same assessments across studies allows for more efficient comparisons. Research findings generally support that EPA and DHA provides relief of symptoms, improves symptoms and supports proper tear function of dry eye disease.

Description of some common tests and measurements for dry eye disease symptom assessment:

- **Corneal fluorescein staining**: Detects areas of the cornea where the lining of cells may have been lost due to dryness or damage. Decrease in score highlights an improvement.
- **Ocular Surface Disease Index (OSDI)**: 12-item scale for the assessment of symptoms related to dry eye disease and their effect on vision. Decrease in score highlights an improvement.
- **Tear osmolarity**: Measures salt in the tears. Too much salt and higher osmolarity indicates issues with tear flow and tears evaporation. Decrease in score highlights an improvement.
- **Tear break up time (TBUT)**: The more time it takes for the tears to break up, the more stable the tear film. Increase in score highlights an improvement.
- **Schirmer test**: Assesses if the eyes produce enough tears to keep it moist. Increase in score highlights an improvement.

Purpose of the Report:

This report will answer the question, "What does the body of evidence around EPA and DHA supplementation and adult dry eye disease / dry eye syndrome (hereafter, dry eye disease) in human clinical trials show?

Key Findings:

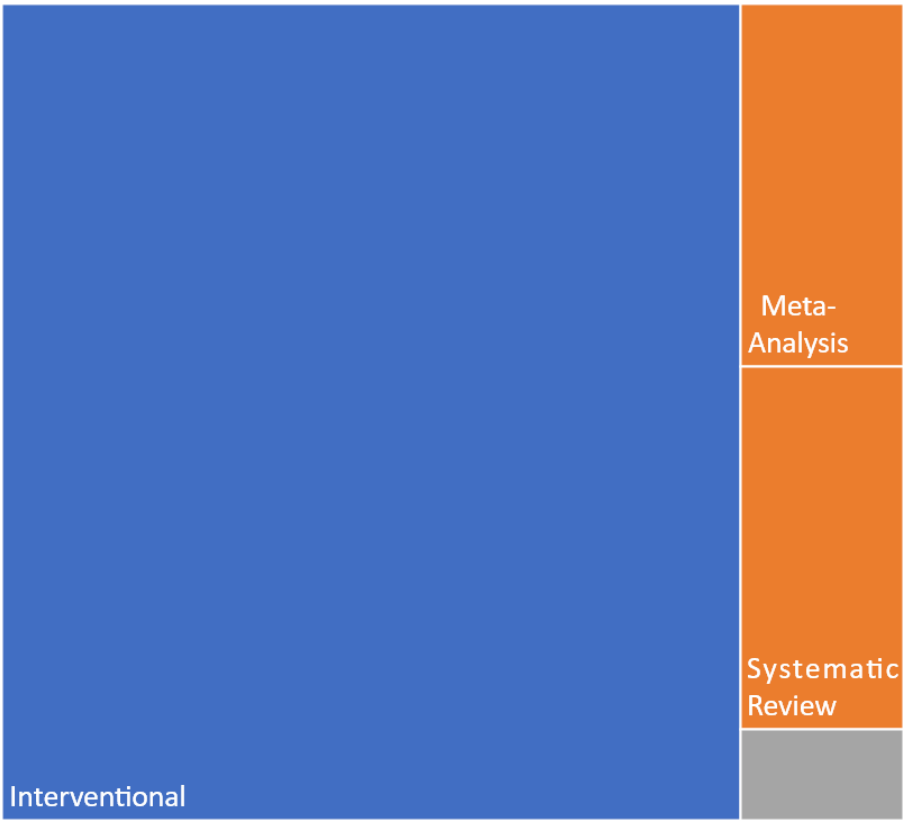
- Results for tear breakup time, tear osmolarity and the Schirmer test demonstrate that increased intake of EPA and DHA improve symptoms associated with dry eye disease, while results from corneal staining and conjunctival staining did not consistently demonstrate such benefit.

Summary of Article Types

50 studies were found relating to "Eye Health."
41 of these were interventional studies.

Terms used in the Search included:
“dry eye OR (eye AND dry*)”

Figure 1: Types of Studies Found using "Dry Eye" as the Term(s) of Interest.



Note: Studies were categorized by study design, of which 82% (blue) were interventional studies, 8% (orange) were reviews, and 1% (grey) 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. The number of studies in the Abstract Search may not match the number of studies in the Advanced search. In the Abstract Search (used here) the database looks for studies tagged with the keyword(s) "Dry Eye." In some of these articles, "Dry Eye" might be mentioned, but may not have any data associated with it. If that's the case, those articles will not appear in the Advanced search.

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

Summary of Interventional Articles:

41 interventional studies were found relating to Dry Eye. According to the authors' conclusions in the Abstracts, most articles were positive.

Table 1: Example of the Article List for Abstracts.

YEAR	PMID	TITLE	TYPE	ABSTRACT CONCLUSION
2023	36626176	Association of Tear Osmolarity With Signs and Symptoms of Dry Eye Disease...	Interventional	neutral
2023	37026312	Omega-3 fatty acids supplements for dry eye - Are they effective or ineffective?	Interventional	positive
2019	29474306	Three year outcomes in a randomized single-blind controlled trial of intravitreal ranibizumab and oral ...	Interventional	positive

Table 2: Summary of Abstract Conclusions for Overall Article Impressions in the Abstract Search Results.

TOTAL INTERVENTIONAL STUDIES	POSITIVE	NEGATIVE	NEUTRAL
41	83%	0%	17%

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.

Related Keywords

Keywords are related terms found within the searched articles. They are divided into either terms 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: This list includes words most commonly found in articles related to the keyword of interest Dry Eye. This list is sorted from highest to lowest count. Words linked to Dry Eye two or fewer times are not displayed.

Not surprisingly, in an omega-3 specific search, the most commonly associated words were: fatty acids, omega-3; docosahexaenoic acids; eicosapentaenoic acid.

Term	Count
Fatty Acids, Omega-3	31
Docosahexaenoic Acids	6
Eicosapentaenoic Acid	5
Fatty Acids, Omega-6	5
Antioxidants	4
HLA-DR Antigens	3
Ophthalmic Solutions	3
Matrix Metalloproteinase 9	3
Fish Oils	3
Capsules	3

Table 4: Conditions most commonly found in articles for keyword of interest Dry Eye. This list is sorted from highest to lowest count. When Dry Eye was used as the search term, there were 34 studies were “Dry Eye Syndromes” were listed by the authors as a related keyword. Dry Eye was used in our search to catch other articles that may have used terms like “Dry Eye Disease” etc.

In a search for Dry Eye, all other conditions found are listed on the table.

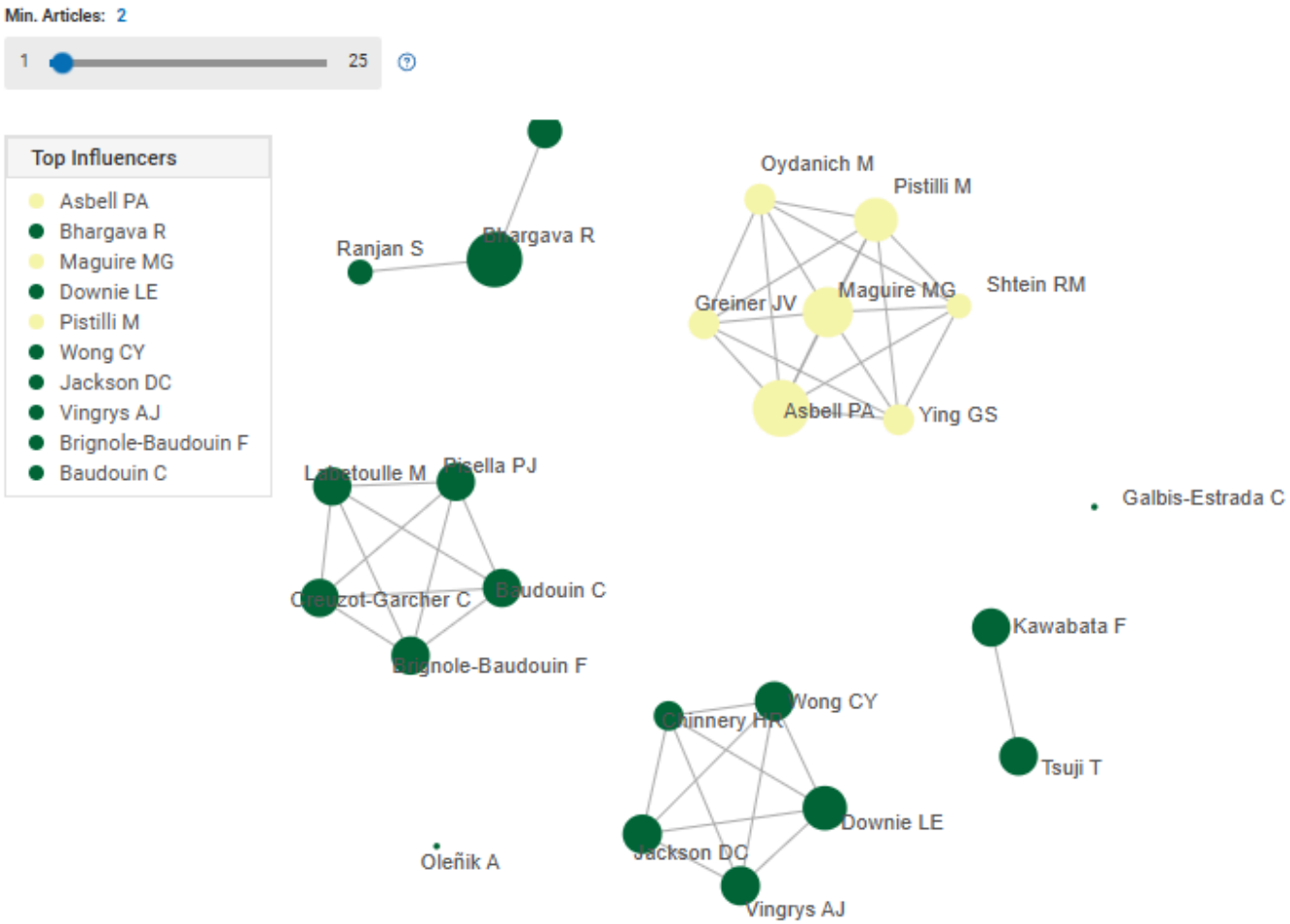
Term	Count
Dry Eye Syndromes	34
Eyelid Diseases	3
Keratoconjunctivitis Sicca	2
Sjogren's Syndrome	1
Inflammation	1
Cataract	1
Postoperative Complications	1
Myopia	1
Diabetes Mellitus, Type 2	1
Rosacea	1
Syndrome	1
Body Weight	1
Asthenopia	1

Find more information about Keywords in the Help Guide.

Influencers

The information about Influencers showcases the authors with the greatest impact on 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 Who have Published at Least Two Articles Related to Term of Interest Dry Eye.



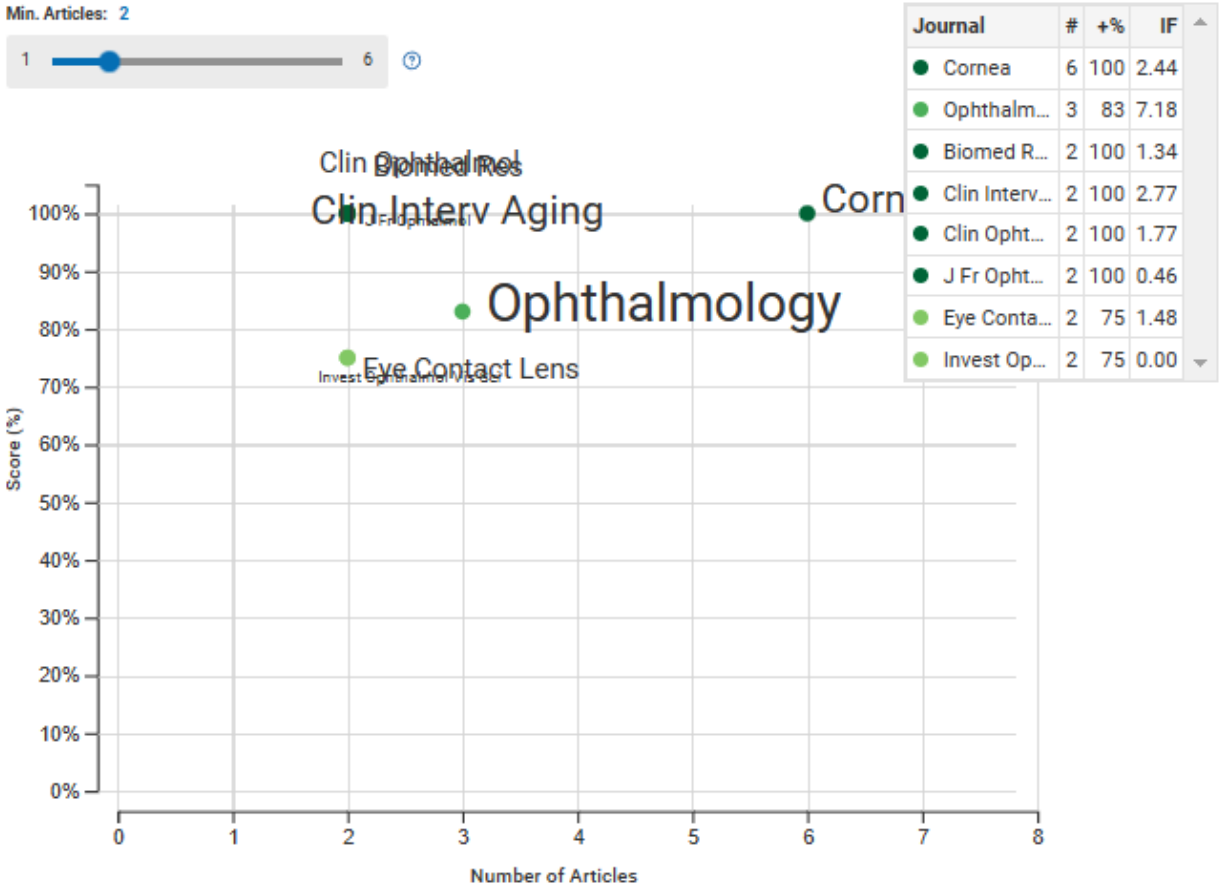
Find more information about Influencers in the Help Guide.
A high resolution image is available.

Journals

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.
- The larger the size of the font the greater the impact factor.
- Score (%) represents the percentage of Abstract Conclusions reported as positive.

Figure 3: Journals Publishing at Least Two Interventional Articles Related to Dry Eye.

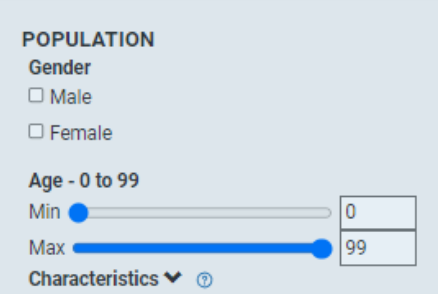


Notes: The list of the abbreviated journal names are listed on the right hand side, as some overlap occurs on the diagram below. Journal - abbreviated journal name; # - number of articles published in that journal; +% - the percentage of positive article conclusions; and IF - impact factor of the journal.

Find more information about Journals in the Help Guide.
A high resolution image is available.

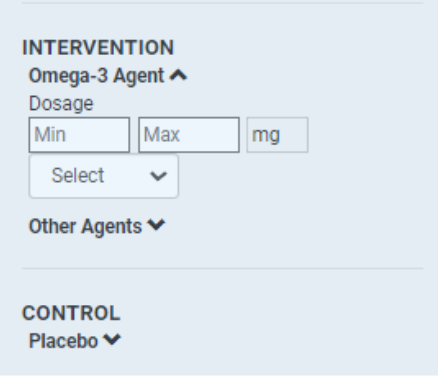
Customized Study Filters

In the Advanced Search, the CSD uses additional filters to further define the search data. Specified filters for this particular report for the search term(s) of interest for Dry Eye include:



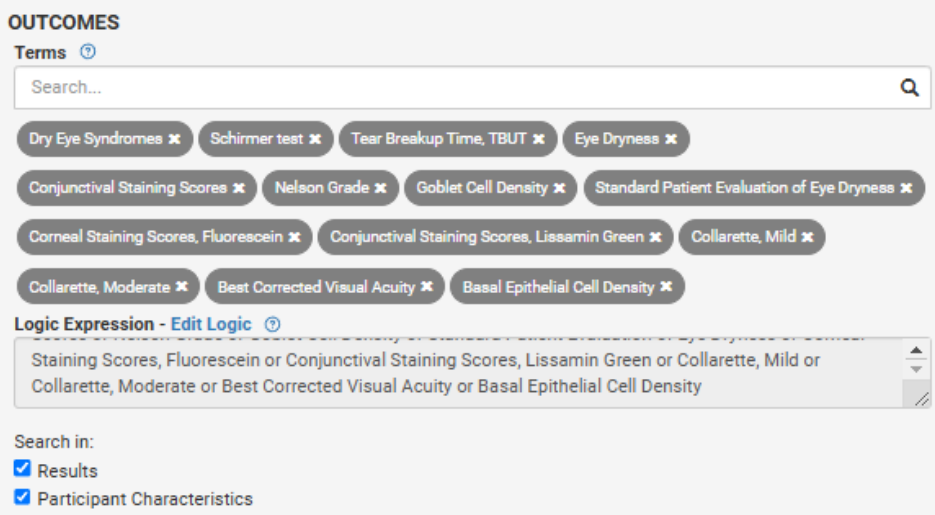
Population:

All genders, ages and participant characteristics were included in this search.



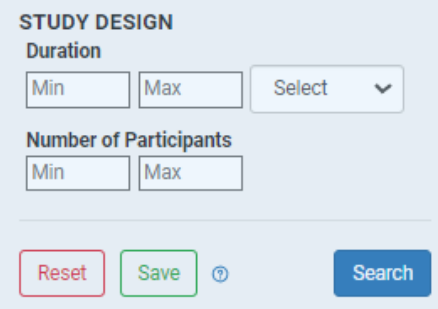
Intervention:

All omega-3 agents, dosages, other agents and placebos were included in this search.



Outcomes:

One search including both "Results and Participant Characteristics" was conducted. Terms of interest are included on the left.



Study Design:

All study durations and studies with any number of participants were included in this search.

Summary of Results

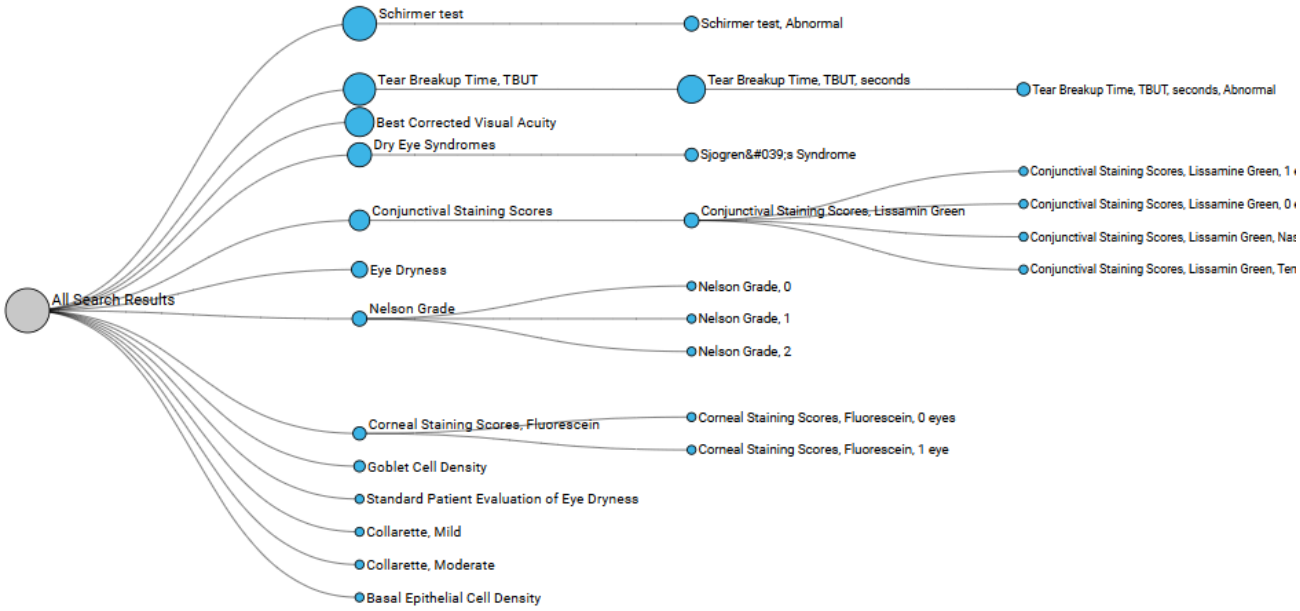
The CSD displays the results by generating a lineage plot (as shown below). For purposes of this report, and for the remainder of the report, the general term Dry Eye will encompass all terms.

In total, there were 45 interventional studies. All 45 studies reported on various associated scores and assessments in the Results.

In the Abstract Search, there were 41 studies found. This means that four additional studies were part of the Advanced Search results. This could be because outcomes related to those four studies were measured, but the primary objective was not about Dry Eye (therefore, not captured in the Abstract Search).

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.

Figure 4: Lineage plot for the terms of interest "Dry Eye" measured in the Results of the studies in the CSD. The size of the dot represents the number of studies.



Key Findings of Interventional Studies

There were 45 studies analyzed.
Within these 45 studies, the outcomes and terms described may have been included as a single outcome, or multiple terms may have been part of the results of one article. The populations studied, statistics analyzed, outcomes measured and study length were further evaluated.

Descriptive statistics and results are presented for various outcomes of interest.

Dosage:

- The range of doses from 40 of the studies spanned from >130mg EPA+DHA per day to 3,000mg EPA+DHA per day. The average dose across those 40 studies was ~1250mg/day EPA+DHA. Three studies provided dosages over 3,000mg/day EPA+DHA. There were two studies that didn‘t specify the amounts of EPA or DHA provided.

Treatments

- Only 18 studies evaluated the effects of EPA and DHA supplementation only (without other dietary additives, and/or without any eye-specific treatments). Multi-nutrient interventions are common in studies about eye health.
- Other studies evaluated the effects of EPA and DHA *plus:*
  - A multi-nutrient supplement (11); various eye treatments (8) (example: artificial tears, eyelid wipes, eyelid cleaning, moisturizing gel); antioxidants (2); lutein (4); other fatty acids (2).

Study Duration:

- The range of study durations across 42 of the studies spanned four weeks to 104 weeks (two years). The average intervention length was 25 weeks. There were two studies three years in length, and one study six years in length, and those studies were not included in the average or the range.

Populations Studied:

- Out of 45 studies:
  - 40% of studies (n=18) included people with dry eye disease.
  - 16% of studies (n=7) included people considered to be healthy.
  - 28% of studies (n=13) included patients with varying medical and health conditions.
  - 9% of studies (n=4) included people with diagnosed age-related macular degeneration.
  - 7% of studies (n=3) included people with type two diabetes.

Descriptive Findings: Supplementation with Only EPA + DHA Omega-3s

Results Evaluated:

- Across the 45 studies, there were 18 studies that supplemented oral EPA and DHA without other nutrients or adjunctive treatments.

Overall Study Conclusions and Statistics:

Results below represent the EPA+DHA group compared to the placebo group, or the EPA+DHA group compared from baseline to final timepoint.

- Tear Breakup Time
  - 83% of outcomes (10/12 studies) had a statistically significant positive change; (2/12) of the outcomes were not significant (no change); no studies showed a detriment.
- Schirmer Test
  - 73% of outcomes (8/11 studies) had a statistically significant positive change; (3/11) of the outcomes were not significant (no change); no studies showed a detriment.
- Eye Staining Scores - Including Corneal and Conjunctival Staining
  - 29% of outcomes (2/7 studies) had a statistically significant positive change; (5/7) of the outcomes were not significant (no change); no studies showed a detriment.
  - *For these tests, fewer studies showed a benefit with EPA and DHA only. Data to date suggests that eye staining outcomes aren't impacted consistently after EPA/DHA intake.*
- Tear Osmolarity
  - 100% of outcomes (3/3 studies) had a statistically significant positive change.

- Other Results
  - 2/2 studies measuring goblet cell density had a statistically significant positive change
  - 1/1 study measuring Sjorgren's syndrome were not significant (no change)
  - 1/1 study measuring tear film instability was not significant (no change)
  - 1/1 study measuring Goblet Cell density had a statistically significant positive change
  - 1/1 study measuring basal epithelial cell density was not significant (no change)
  - 3/3 studies measuring Nelson Grade scoring had a statistically significant positive change
  - 1/3 studies measuring Best Corrected Visual Acuity had a statistically significant positive change, and 2/3 were not significant (no change)

Descriptive Findings Continued: Supplementation with EPA + DHA Omega-3s and Other Interventions

Results below represent interventions with EPA+DHA and other nutrients, or other eye-related treatments (mixed interventions, not only EPA+DHA)

Results Evaluated:

- Across the 45 studies, there were six main results or metrics used:
  - Tear Breakup Time (n=24; 22%)
  - Schirmer Test (n=22; 20%)
  - Best Corrected Visual Acuity (n=15; 14%)
  - Corneal Staining Scores (n=13; 12%)
  - Eye Pain (n=8; 7%)
  - Conjunctival Staining Scores (n=7; 6%)
- Other results or metrics include:
  - Dry eye disease (n=5); tear osmolarity (n=4); goblet cell density (n=3); nelson grade staining (n=3); basal epithelial cell density (n=1); chemosis (n=1); Sjorgren's syndrome (n=1); Standard Patient Evaluation of Eye Dryness (n=1).

Overall Study Conclusions and Statistics:

Results below represent the EPA+DHA group compared to the placebo group, or the EPA+DHA group compared from baseline to final timepoint.

- Tear Breakup Time
  - 70% of outcomes (17/24 studies) had a statistically significant positive change; the rest of the outcomes were not significant (no change); no studies showed a detriment.
- Schirmer Test
  - 59% of outcomes (13/22 studies) had a statistically significant positive change; the rest of the outcomes were not significant (no change); no studies showed a detriment.
- Best Corrected Visual Acuity
  - 20% of outcomes (3/15 studies) had a statistically significant positive change; the rest of the outcomes were not significant (no change); no studies showed a detriment.
- Corneal Staining Scores
  - 46% of outcomes (6/13 studies) had a statistically significant positive change; the rest of the outcomes were not significant (no change); no studies showed a detriment.
- Eye Pain
  - 75% of outcomes (6/8 studies) had a statistically significant positive change; the rest of the outcomes were not significant (no change); no studies showed a detriment.
- Conjunctival Staining Scores
  - 57% of outcomes (4/7) had a statistically positive significant change; the rest of the outcomes were not significant (no change); no studies showed a detriment.

Suggested Next Steps

The CSD saves time in gathering the scientific literature compared to traditional search engines. The CSD can aid in identifying gaps, and can therefore help to set the stage for future projects or future research questions. Often after a topical review of the CSD is completed, action could be warranted.

Based on GOED's review of the data, some overall research recommendations include:

Dosage:

- The studies in this report provided a higher dosage compared to other areas of health research, so dosage recommendations for improvement of dry eye disease should be commensurate with the positive research results. Therefore, a higher (>1,000mg EPA+DHA / day) dose may be needed to have noticeable differences in dry eye disease symptoms.

Outcomes of Interest:

- Interpreting the research results for dry eye disease is simplified by the use of the same assessments across multiple studies. This provides an advantage where the main use of tests can be used to repeat efficacy. For example, EPA and DHA have a positive impact on TBUT and eye pain across many studies; therefore, someone increasing their intake of EPA+DHA may see a benefit for those outcomes (compared to other dry eye disease symptoms).

Comparison Groups:

- Many studies didn't have a placebo group, and focused on changes between participants in the baseline and final assessments. Randomized controlled trials are the gold standard, and thus more trials with this study design would be helpful to evaluate the effects of EPA and DHA on symptoms of dry eye.

Future Research:

- To clearly assess the impacts of EPA+DHA and other eye-related treatments, a future study needs to include more intervention groups. For example, with four intervention groups: Placebo, EPA+DHA, eye-related treatment (like artificial tears), EPA+DHA plus eye-related treatment. This would allow for the evaluation of the impact of EPA+DHA alone, and then the potential for combined or additive effects of EPA+DHA and an eye-related treatment.
- Another suggestion is related to environmental factors. For example, screen time. Does screen time contribute to eye dryness? If it does, does the dosage needed to alleviate symptoms correlate with the duration of screen time?

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/or 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.

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 allows users to refine the search to fit the 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, typically but not always generating a longer study list. The Advanced Search captures the term of interest only if there is an associated data point in either the Participant Characteristics or the Results.

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Find more information in the Help Guide.

Questions or Suggestions? Contact us.

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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 use science-based information to promote consumption of and enable access to quality EPA & DHA from all sources for a positive impact on public health.

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