Should I Take Vitamins For My Eyes

Pamela Theriot, OD, FAAO
Public Awareness Committee, TFOS Lifestyle Workshop

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Pam Theriot - Financial Disclosures

Speaker Bureau:
RVL Pharmaceuticals
Viatris Pharmaceuticals
Johnson & Johnson Vision
Sun Pharma
Lumenis Be
Tarsus Pharmaceuticals
Dompe

Brand Ambassador:
Eyes are the Story
UNClog Mask

KOL/Consultant:
Novartis
Merakris Therapeutics
Scope Eyecare
NuLids
Tear Film and Ocular Surface Society, Public Awareness Committee Member
Twenty/Twenty Beauty
NovaBay
Mallinckrodt Pharmaceuticals
Bruder Heathcare Company
Alcon

*All relevant financial relationships have been mitigated. The content of this COPE-accredited CE activity was planned and prepared independently by Pamela Theriot, OD, FAAO without input from members of an ineligible company.

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Pam Theriot, OD, FAAO

Lusk Eye Specialists
- Clinical Director of Dry Eye Relief Center

TFOS Lifestyle Workshop
- Public Awareness committee Member

Optometric Management
- Dry Eye Columnist

Author
- Alleviate Dry Eye

Website / Blog / Courses
- www.pamtheriot.com

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Outline

Why Are Vitamins Important for my Eyes?
Let's Dive in:
- Ocular Surface Disease
  - TFOS
  - LCD Supplement
  - Omega Fatty Acid Supplement
- Digital Eye Strain
- Age Related Macular Degeneration
- Diabetic Eye Disease
- Cataracts

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Ocular Surface Disease

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Dry Eye Disease

- Dry eye disease (DED) is a multifactorial disorder characterized by a loss of tear film homeostasis that leads to a self-perpetuating cycle of tear film instability, tear hyperosmolarity, and inflammatory events, resulting in ocular surface inflammation and injury[1-4]
- The presence of inflammation in participants with DED is associated with increased symptomology, including ocular surface irritation, worsening tear dysfunction, and disrupted function of ocular components, including the meibomian glands[5]
- Artificial tears remain the mainstay of DED treatment, but do not address the underlying pathophysiology[2,6]
- Nutritional supplementation could meet the patient need for a treatment beyond artificial tears[7,8,9]

DED, dry eye disease;
1. Huang R, et al. Int J Ophthalmol. 2022;4 2(0):3253-3272; 2. Sheppard J, et al. Ann Med. 2023;55(1):241-252; 3. Bron AJ, et al. Ocul Surf. 2017;15(3):438-510; 4. Craig JP, et al. Ocul Surf. 2017;15(3):276-283; 5. Rao SK, et al. Int J Ophthalmol. 2022;2 15(5):820-827; 6. Jones L, et al. Ocul Surf. 2017;15(3):575-628; 7. Pelligrini M, et al. Nutrients. 2020;12 952; 8. Castro-Castaneda CR, et al. Nutrients. 2022;14:5014; 5019. Mcz OE, et al. Pharmaceuticals (Basel). 2020; 13(10): 295.

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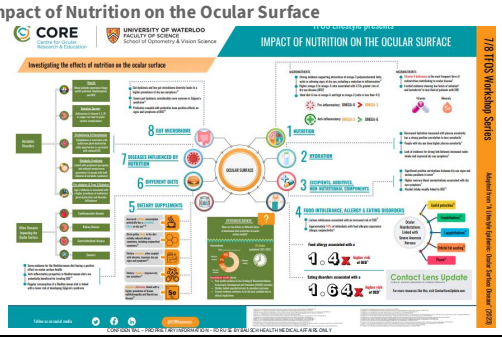
7: Impact of Nutrition on the Ocular Surface



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Micronutrients

tfos

- **Strong evidence**[1]
  - Vitamin A[2,3]
  - Vitamin B_{12}
  - Vitamin C
  - Vitamin D
- **Limited evidence**
  - Selenium[4]
  - Lactoferrin[5]

1. Fogagnolo P, et al. Nutrients. 2021;13.
2. Marriott BP, et al. Present Knowledge in Nutrition: Basic Nutrition and Metabolism; 2020.
3. Tei M, et al. Invest Ophthalmol Vis Sci. 2000;41:82-8.
4. Higuchi A, et al. Sci Rep. 2016;6:36903.
5. Sonobe H, et al. Ocul Surf. 2019;17:160-6.

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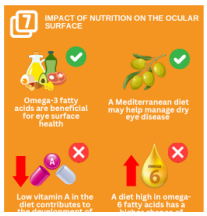
surface diseases include vitamin A, B_{12}, C and D. Deficiency of vitamin A is the most frequent form of malnutrition that contributes to ocular disease;

Of the minerals, the levels of selenium in tears have been found to be decreased in a dry eye model.

And, one study reported a relationship between low levels of tear lactoferrin and the development of dry eye disease.

TFOS Lifestyle Workshop Report

- Nutrition and the Ocular Surface Conclusions:
- Good Nutrition is pivotal to good health
- Nutrition impacts ocular surface function
- Consider the available Evidence prior to providing recommendations
-



https://contactlensupdate.com/2023/11/03/patient-handout-tfos-lifestyle-recommendations/

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Hyper Hydration Drink

Provides **2-3 TIMES** the impact of water alone

Delivers hydration to your bloodstream and cells more efficiently

Helps to decrease inflammation and improve ocular health.

Blend of vitamins, minerals and anti-inflammatories

Anti-Inflammatory Ingredients to Reduce Inflammation

- Green Tea extract, Turmeric, Taurine, Omega-3 (DHA from algae)

Vitamins have been shown to enhance eye health

- A, B3, B6, B12, C

Electrolytes to improve absorption

- Calcium Lactate. Potassium Chloride, Malic Acid, Sodium Chloride, Citric Acid Anhydrous

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Lutein/Zeaxanthin, Curcumin, Vit D3 Formula (LCD)*[1,2]

Test Ingredient	Composition*,[2]	Description/Rationale For Inclusion
Lutein and Zeaxanthin isomers	40 mg of micronized marigold concentrate[2] providing **20 mg lutein and 4 mg zeaxanthin**	• Lutein and zeaxanthin are carotenoids that are uniquely concentrated as pigments in the human macula and widely recommended as dietary supplements for preventing vision loss from age-related macular degeneration.[3] • Following ingestion as a supplement, lutein has demonstrated antioxidant and anti-inflammatory effects, protecting the retina against photo-oxidative damage and inflammatory cytokine production caused by exposure to blue light.[4]
Curcuminoids	238 mg micronized 95% curcumin extract providing **200 mg curcuminoids**	• Curcumin is a polyphenol extracted from turmeric that has established anti-inflammatory properties; evidence demonstrates its effect on oxidative stress and cytokine pathways implicated in the pathogenesis of ophthalmic conditions such as glaucoma, dry eye disease, and age-related macular degeneration.[5,6] • In vitro, curcumin can reduce proinflammatory cytokines in corneal epithelial cells and act as a neuroprotector of retina precursor cells.[5,6]
Vitamin D3	15 mcg of **Vitamin D3 providing 600 IU**	• Vitamin D3 is a prohormone, with antioxidant, immunomodulatory, and anti-inflammatory properties, which can affect the functions of corneal epithelial cells, including barrier provision and response to inflammation and infection.[7] • In patients with DED, low levels of vitamin D3 are associated with increased DED severity, poor tear film stability, and reduced tear volume; supplementation has been shown to improve the efficacy of artificial tears and reduce disease severity, in both vitamin D3-deficient and non-deficient patients.[5,7,8]

* Production of the LCD supplement incorporated novel formulation techniques, including micronization of the active herbal ingredients by jet milling to reduce particle size, and a combination of functional oils to support improved absorption in the small intestine. †Approximately 336 mg of excipients, including functional oils to aid absorption in the small intestine. ‡Optimized marigold extract as a source of lutein and zeaxanthin at a 5:1 ratio as occur in fruits and vegetables. (Nur et al. Pharmaceuticals (Basel) (2020) 13(10):291)

1. Radkar P, et al. Ophthalmol Ther. 2021;10:581–590; 2. Gioia N, et al. Front Ophthalmol. 2024;4:1362113; 3. Bernstein PS, et al. Prog Retin Eye Res (2016) 50:34-66; 4. Cristaldi M, et al. Appl Sci (2022) 12(3):1268 5. Castro-Castaneda CR, et al. Nutrients (2022) 14(23):5014; 6. Davis BM, et al. Sci Rep (2018) 8(1):13066; 7. Gorimanipalli B, et al. Indian J Ophthalmol (2023) 71(4):1127-1134; 8. Hwang JS, et al. Cornea (2019) 38(3):304-10; 9. Nagarjan M, et al. Clin Exp Optom (2023) 106(3):257-62.

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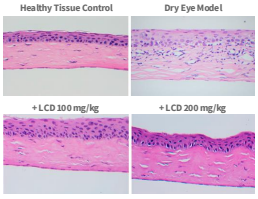
LCD improved DED symptoms, tear homeostasis and inflammation in an *in vivo* model

- In a rat model of DED induced by benzalkonium chloride, LCD improved corneal morphology, tear quantity and quality, and ocular surface health, as demonstrated by:
  - Improved tear production and tear film stability
  - Reduced oxidative stress and inflammatory markers
  - Increased production of tear proteins

Corneal histopathology changes



Nur OE, et al. Pharmaceuticals (Basel). 2020;13(10):295.

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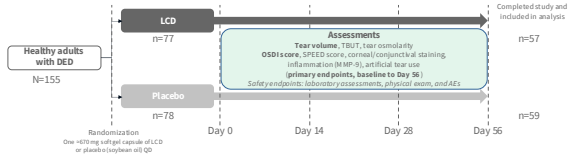
Two clinical trials have evaluated the safety and efficacy of LCD in adult participants with DED

- Data in subjects from India (n=30 LCD; n=29 placebo) demonstrated that LCD significantly improved tear production, stability, and quality, and reduced inflammation and ocular surface damage in patients with mild-to-moderate DED[1]
- A prospective, randomized, double-blind, placebo-controlled study of the efficacy and safety of LCD in Dry Eye Disease (DED) was conducted at four centers in the USA[2]



AE, adverse event; MMP-9, matrix metallopr oteinase-9; OSDI, Ocular Surface Disease Index; SPEED, Standard Patient Evaluation of Eye Dryness; TBUT, Tear Film Break-Up Time; QD, Once Daily.
1. Radkar P, et al. Ophthalmol Ther. 2021;1 0:581–599; 2. Gioia N, et al. Front Ophthalmol. 2024;4:1362113.

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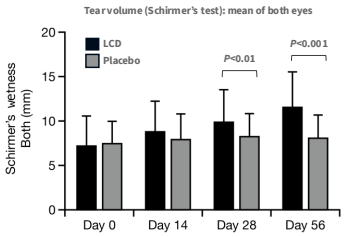
Primary Efficacy Outcome: Tear Volume

- The overall mean tear volume of both eyes was significantly better for the LCD group versus placebo at Day 28 and Day 56
  - The LCD group also demonstrated significantly better results in left and right eyes at Day 28 ($P<0.05$ for each eye) and Day 56 ($P<0.001$ for each eye), and additionally for the left eye at Day 14 ($P<0.05$)



Length of wetting Schirmer's test strips without anesthesia
Gioia N, et al. Front Ophthalmol. 2024;4:1362113.

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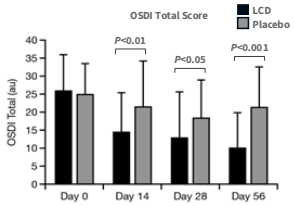
Primary Efficacy Outcome: OSDI Total Score

- Improvement from baseline in total OSDI score was significantly better (lower scores) for subjects in the LCD group versus the placebo group by Day 14, which was maintained to Days 28 and 56



au, arbitrary units;
Gioia N, et al. Front Ophthalmol. 2024;4:1362113.

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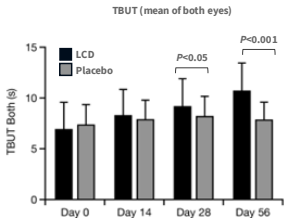
Secondary Efficacy Outcome: TBUT

- The LCD group had significant improvement in mean TBUT values, versus the placebo group, in the left eye, right eye, and the mean of both eyes at Day 56 ($P<0.001$ for each)
  - At Day 28 values for the left eye and the mean of both eyes were also significantly improved vs the placebo group ($P<0.05$)



Gioia N, et al. Front Ophthalmol. 2024;4:1362113.

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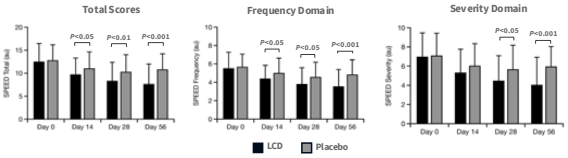
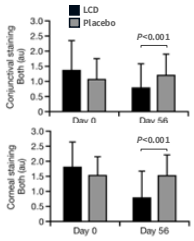
Secondary Efficacy Outcome: SPEED Scores

- For subjects in the LCD group, improvement in total SPEED score was significantly better versus the placebo group by Day 14, and this improvement was maintained to Days 28 and 56
- Scores for the frequency domain mirrored the pattern for total scores and scores for the severity domain in the LCD group also decreased from baseline to Day 14 versus placebo; this improvement in severity became significant at Day 28 and was maintained at Day 56



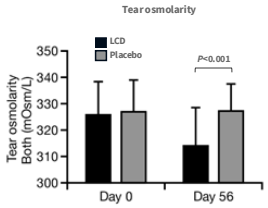
Secondary Efficacy Outcome: Corneal and Conjunctival Staining

- Mean corneal and conjunctival staining scores significantly decreased for the LCD group from baseline to Day 56 versus placebo for the overall mean of both eyes
  - Staining scores specifically for the right and left eyes also significantly decreased in the LCD group, versus placebo, at Day 56 (*P*<0.01 for each eye)



Secondary Efficacy Outcome: Tear Osmolarity

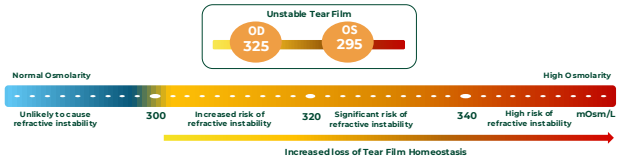
- Tear osmolarity was significantly improved for the LCD group, versus the placebo group, at Day 56 for the overall mean of both eyes
  - Osmolarity values specifically for the right and left eyes also significantly decreased in the LCD group, versus placebo, at Day 56 (*P*<0.001 for each eye)



Tear osmolarity assessed using TearLab Osmolarity System *in vitro* osmometer. mOsm/L, milliosmole per liter.
Gioia N, et al. Front Ophthalmol. 2024;4:1362113.

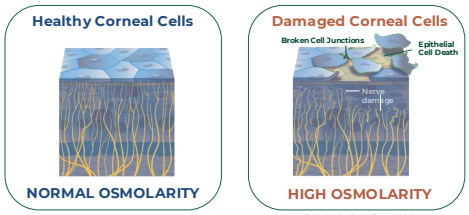
Knowing the Osmolarity Score Helps Guide Effective Treatment and Optimize Vision

- Test result will show within 10 seconds
- Elevated readings of >300 mOsm/L indicates abnormal osmolarity[1]
- Inter-eye differences of >8 mOsm/L in dry eye disease is a hallmark of tear film instability[2]



1. Lemp MA, Bron AJ, Baudouin C, et al. Tear osmolarity in the diagnosis and management of dry eye disease. *Am J Ophthalmol*. 2011 May;151(5):792-798.
2. Craig JP, Nelson JD, Azar DT, et al. TFOS DEWS II Report Executive Summary. *Ocul Surf*. 2017;15(4):802-812.

Tear Osmolarity Matters

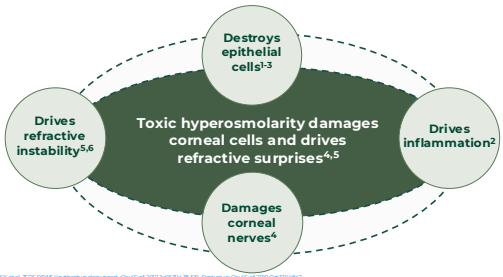


Illustrations by Virginia Ferrante-Iqbal

- Increase in tear osmolarity is a central mechanism in the pathogenesis of ocular surface damage[1]
- When hyperosmolarity occurs, salt content can be elevated to toxic levels—when left undiagnosed can adversely impact corneal health[1]

1. Bron AJ, de Paiva CS, Chauhan SK, et al. TFOS DEWS II pathophysiology report. *Ocul Surf* 2017;15(3):438-510. Erratum in *Ocul Surf* 2019 Oct;17(4):842.

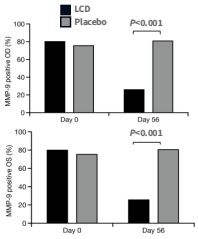
Impact of High Osmolarity



1. Bron AJ, de Paiva CS, Chauhan SK, et al. TFOS DEWS II pathophysiology report. *Ocul Surf* 2017;15(3):438-510. Erratum in *Ocul Surf* 2019 Oct;17(4):842.
2. Huet E, Vallée B, Delbé J, et al. EMMPRIN modulates epithelial barrier function through a MMP-mediated occludin cleavage: implications in dry eye disease [published correction appears in *Am J Pathol* 2011 Nov;179(5):2674]. *Am J Pathol* 2011;179(2):1278-1286.
3. Kam W, Sullivan DA, Sullivan BD, Venkiteshwar M. Does hyperosmolarity induce an irreversible process leading to human corneal epithelial cell death? *Invest Ophthalmol Vis Sci*. 2018; Sept;57(12):6181.
4. Mrugacz M, Moneta K, Martuni CP, Rosenblatt MI. Hyperosmolar tears induce functional and structural alterations of corneal nerves: electrophysiological and anatomical evidence toward neurotoxicity. *Invest Ophthalmol Vis Sci*. 2018;59(9):B52-B60.
5. Kuen R, Lawless M, Sutton G, Hodge C. Prevalence of tear film hyperosmolarity in 150 patients presenting for refractive surgery assessment. *J Cataract Refract Surg*. 2022;48(4):387-392.
6. Kontopoulos AT, Matossian C, Reidy CJ, et al. Effect of tear osmolality on repeatability of keratometry for cataract surgery planning. *J Cataract Refract Surg*. 2018;44(8):972-7.

Secondary Efficacy Outcome: Inflammatory Biomarker, MMP-9

- There was a significant difference in the presence of MMP-9 between the LCD and placebo groups, from baseline to Day 56 in both eyes
  - Incidence of positive tests in the LCD group was −67.4% (right eye) and −61.4% (left eye), but did not decrease for the placebo group (+6.7% and +8.7% for right and left eyes, respectively)



Presence of MMP-9 measured using the InflammaDry MMP-9 test kit.
OD, right eye; OS, left eye.
Gioia N, et al. Front Ophthalmol. 2024;4:1362113.

Safety

- There were no clinically meaningful differences detected in blood safety values or resting vital signs between the LCD and placebo groups
- Two AEs were reported during the study: increased nasal bleeding in one subject in the LCD group and increased blurred vision in one subject in the placebo group.
  - The subject who experienced nasal bleeding (3 instances prior to discontinuation) reported a history of nasal bleeding triggered by vitamin D3 supplementation*
  - The single incidence of blurred vision was reported by one placebo group subject; this was considered mild in severity and not related to the study intervention.
- No drug treatments were used to intervene with either AE reported in this study and no serious AEs occurred.

AEs	LCD (n=57) n (%)	Placebo (n=59) n (%)	Overall (n=116) n (%)
Subjects reporting at least one AE	1 (1.75)	1 (1.69)	2 (1.72)
Total number of AEs reported	3 (5.26)	1 (1.69)	4
Total number of SAEs reported	0	0	0
Subjects reporting serious AEs	0	0	0
Subjects reporting drug-related AEs	0	0	0
Subjects reporting AEs leading to early discontinuation	1 (1.75)	0	1 (0.86)
Number of deaths	0	0	0

Gioia N, et al., Front Ophthalmol. 2024;4:1362113.

LCD significantly improved the signs and symptoms of DED and was well-tolerated[1,2]

- Once-daily LCD supplementation in adult subjects with DED significantly:
  - improved the production, stability and quality of tears
  - reduced ocular surface damage and inflammation
  - improved subjects' DED symptoms
- Both studies met their primary endpoints, with significant changes reported in some measures by 2 weeks

These studies highlight the potential of LCD nutritional support to improve patient experience of DED symptoms and address the underlying loss of tear film homeostasis and ocular inflammation

1. Radkar P, et al. Ophthalmol Ther. 2021;1 0581-599; 2. Gioia N, et al. Front Ophthalmol. 2024;4 1362113.

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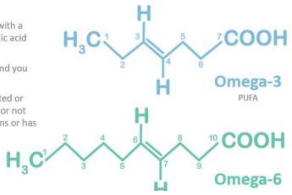
Fatty Acids – building blocks of cell membranes

- Fatty acids are a long chain of carbon atoms, with a methyl group (CH_3) at one end and a carboxylic acid group (COOH) at the other.
- Combine 1 glycerol (3 OH) with 3 fatty acids and you have a triglyceride form FA.
- A fatty acid can be unsaturated, polyunsaturated or monounsaturated. Whether a fat is saturated or not depends on whether it if full of hydrogen atoms or has double bonds instead.



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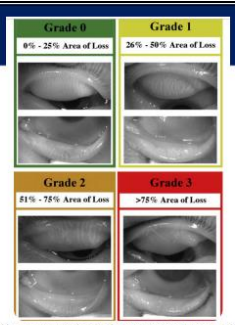
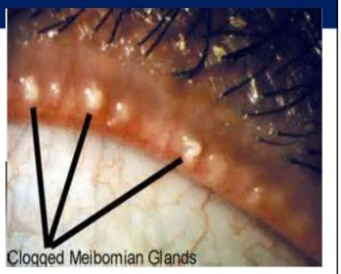
Meibum = Visual Representation of Diet





https://www.ajo.com/article/S0002-9394(18)30675-5/fulltext

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Typical American Diet Today: Severe Omega Imbalance

- A healthy diet approaches a 1:1 ratio of omega-3's to omega-6's
- The average American Diet is 1:25, as high as 1:50
- This occurred when healthy unsaturated fats were replaced with trans fatty acids and diets full of processed foods (high in omega-6)

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Nutrition 101: Omega-3 & 6 Initials

Omega-3
Anti-Inflammatory

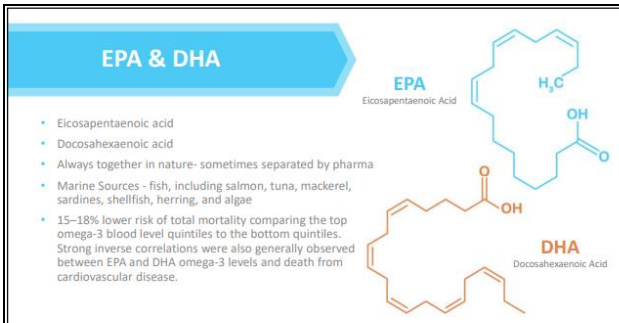
- **Alphalinolenic Acid** (ALA)
  - Plants, Nuts
- **Eicosapentaenoic** (EPA)
  - Fish
- **Docosahexaenoic** (DHA)
  - Fish

Omega-6
Inflammatory

- **Linolenic Acid** (LA)
  - Vegetable Oils, Saturated Fats, Fast Foods
- **Gamma-Linolenic Acid** (GLA)
  - Evening Primrose Oil, Borage Oil, Black Currant Oil
- **Arachidonic Acid** (ARA)
  - Vegetable Oils, Saturated Fats, Fast Foods

EPA & DHA

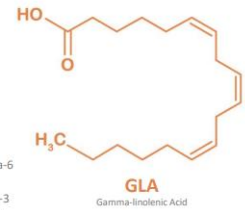
- Eicosapentaenoic acid
- Docosahexaenoic acid
- Always together in nature- sometimes separated by pharma
- Marine Sources - fish, including salmon, tuna, mackerel, sardines, shellfish, herring, and algae
- 15–18% lower risk of total mortality comparing the top omega-3 blood level quintiles to the bottom quintiles. Strong inverse correlations were also generally observed between EPA and DHA omega-3 levels and death from cardiovascular disease.



*William S. Harris, Nathan L. Tintle, Fumiaki Imamura, et al. (2021) Blood n-3 fatty acid levels and total and cause-specific mortality from 17 prospective studies, NATURE COMMUNICATIONS | (2021) 12:2329

GLA

- Gamma-linolenic acid
- Plant sources: evening primrose oil (EPO), borage oil, and black currant seed oil.
- Most omega-6 fatty acids in the diet come from vegetable oils in the form of linoleic acid (LA). The body converts linoleic acid to GLA and then to arachidonic acid (AA).
- A healthy diet contains a balance of omega-3 and omega-6 fatty acids.
- Omega-3 fatty acids help reduce inflammation while omega-6 fatty acids promote inflammation.
- Many physicians blame this high rate of omega-6 to omega-3 fatty acids for the large number of inflammatory diseases in the American population.



GLA
Gamma-linolenic Acid

	Effect of Oral Re-esterified Omega-3 Nutritional Supplementation on Dry Eyes	Long-term Supplementation with n-6 and n-3 PUFAs Improves Moderate-to-Severe Keratoconjunctivitis Sicca: A Randomized Double-Blind Clinical Trial
Tear Osmolarity	Stat Sig P = 0.004 ave - 19	Not Studied
MMP-9	Stat Sig P value = 0.024 -68%	Not Studied
Corneal Staining	NOT Stat Sig P value = 0.712. -7 oxford	NOT Stat Sig Central Fluorescein Staining P = 0.1, Lissamine Corneal Staining P = 0.9
TBUT	Stat Sig P = 0.002 +3.5	NOT Stat Sig P = 0.8
OSDI	Stat Sig P = 0.002. -17	Stat Sig P = 0.05. -19
Omega Index	Stat Sig P = <0.001. +3%	Not Studied
Schirmers	NOT Stat Sig P = 0.78 +1.7mm	NOT Stat Sig P = 0.3
Corneal Topography	Not Studied	Surface Regularity: NOT Stat Sig P = 0.1 Surface Asymetry: Stat Sig P = 0.005***
HLA-DR & CD11C Intensity Conjunctival Impression Cytology	Not Studied	Stat Sig P = 0.001, 24 weeks***

Nutritional anterior seg support ….

Take homes:

- EPA and DHA (marine based) as source of Omega 3's - not ALA
- 2240 mg a day in the 3:1 EPA :DHA rTG biochemical form is clinically proven to meet both signs and symptoms of dry eye
- 2240 mg a day is 37 cans of tuna a week- tough to get there with diet alone
- Supplements should mimic nature whenever possible- look for rTG form Omega 3 supplements as opposed to ethyl ester form
- Avoid high levels of Vitamin E d alpha tocopherol preservative (bleeding risk) or enteric coatings
- Consider more than just dry eye uses- recurrent styes, blepharitis, episcleritis, etc

Ancillary VITAL Study

- Ancillary Study, Placebo Controlled, VITAL Clinical Trial (Lovaza)
- **23,523 participants** – approx. 52% men and 48% women
- 2011-2017
- **Daily supplementation** with vitamin D3, 2000 IU, and marine ω-3 fatty acids, 1g, **for a median of 5.3 years**
- Published JAMA Ophthalmology, June 9, 2022

CONCLUSIONS AND RELEVANCE In this randomized clinical trial, long-term supplementation with 1 g per day of marine ω-3 fatty acids for a median (range) of 5.3 (3.8-6.1) years did not reduce the incidence of diagnosed DED or a combined end point of diagnosed DED or incident severe DED symptoms. These results do not support recommending marine ω-3 fatty acid supplementation to reduce the incidence of DED.

Omega 3 Blood Index level never reached the accepted therapeutic level of 8% with this 1 gr ethyl ester form supplement (Lovaza) even after 5 years of study

No ophthalmology examination was performed- only review of records

Re-confirms previous studies which clearly demonstrate that the form and dose of the omega 3 supplement matters when it comes to omega 3's for ocular health – **1 gr of an ethyl ester form** does not reduce the incidence of dry eye disease

Digital Eye Strain

Terminology

Digital environment - any technology requiring viewing of a digital display for a cognitive task

Digital eye strain (the preferred terminology) –
the **development** or **exacerbation** of **recurrent** **ocular symptoms** and/or **signs,** related **specifically** to digital device screen viewing

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Diagnosis

Based on symptomology – frequency / severity

No criteria to link to digital device use + 1 symptom required
⇒ high prevalence ☹

Typical symptoms include burning, eye pain, headache, eye redness, photophobia, tearing, repeated/frequent blinking, heavy eyelids, itching, blurred vision at distance and near, double vision, eyestrain, and foreign body sensation

No gold standard; Rasch analysed:

- Computer Vision Syndrome Questionnaire (CVS-Q) 16 symptoms; frequency and severity (each on a 0-2 scale), multiplied together and summed for a total score out of 36, with a cut off of ≥6 (sensitivity 75.0% and specificity 70.2%)
- Computer-Vision Symptom Scale (CVSS17) - 17 items exploring 15 different symptoms, but with two to four response categories.

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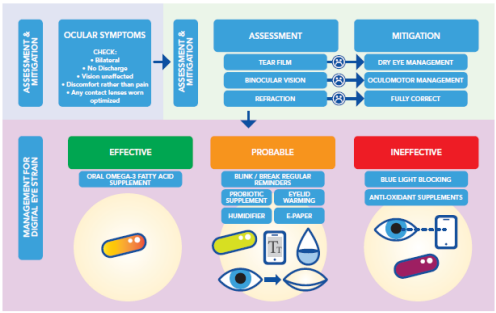
Digital Eye Strain Management



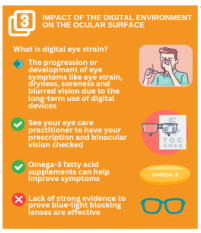
39

Recommendations from TFOS

Omega Fatty Acid Supplementation:
Modulate systemic inflammatory pathways
Reduce tear pro-inflammatory cytokine levels

Probiotics:
Limited evidence of effectiveness

Anti-Oxidants:
Increase contrast sensitivity in the macula
No evidence of reduction in Digital Eye Strain



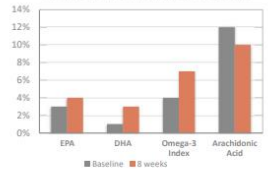
Acquah, Alex Muntz, Karim Mohamed-Noriega, Sotiris Plainis, Michael Read, Rony R. Sayegh, Sumeer Singh, Tor P. Utheim, Jennifer P. Craig, TFOS Lifestyle: Impact of the digital environment on the ocular surface, The Ocular Surface, Volume 28, 2023, Pages 213-252,

40

Creating Healthy Meibum: Presented to the Cornea Society

Objective: To study the penetration of rTG omega-3 into the meibomian glands after oral administration (1680mg EPA/560mg DHA/ 1000IU Vitamin D3)

Positive results for patients in 4 - 8 weeks



82% of patients showed EPA and DHA present in the meibum at 8 weeks (compared to 0% at baseline)

- **70% became completely asymptomatic**
- **100% noted decrease in primary complaint**
- **Improvement in TBUT** was statistically significant
- All patients with corneal staining at baseline significantly improved
- Patients with **hyperosmolarity (>308 mOsm/L) at baseline improved 25%**

S. Gregory Smith MD, Attending Surgeon Wills Eye Institute Presented at 2011 Cornea Society/EBAA Fall Educational Symposium

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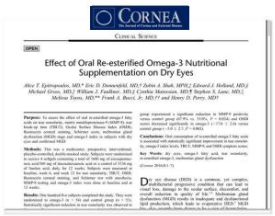
Study Design & Subject Selection


CORNEA
Clinical Science
OPEN
Effect of Oral Re-esterified Omega-3 Nutritional Supplementation on Dry Eyes

Study Design

- Multicenter
- Prospective
- Interventional
- Randomized
- Double-Masked
- Placebo Controlled

Subjects

- 105 completed study
- 54 in treatment group (received 2 grams re-esterified Omega-3)
- 51 in placebo group
- Average Age: 56.8 Years
- Gender: 71.4% female

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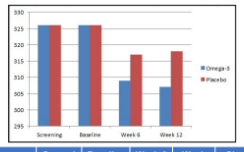
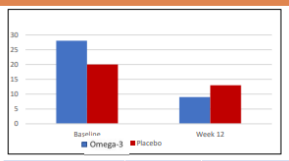
Tear Osmolarity & MMP-9 Change from Baseline



Tear Osmolarity (N=105)	Screening	Baseline (Week 0)	Week 6	Week 12	Change from Baseline
Omega-3	326	326	309	307	-19
Placebo	326	326	317	318	-8
p-value*			0.042	0.004	0.004



MMP-9 biomarker (N=105)	Baseline	Week 12
Omega-3	28	9*
Placebo	20	13
p-value*		0.024

* 68% reduction in MMP-9 Positivity

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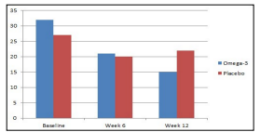
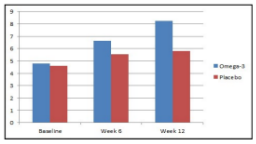
OSDI & TBUT Change from Baseline by Visit



OSDI (N=105)	Baseline	Week 6	Week 12	Change from Baseline
Omega-3	32	21	15	-17
Placebo	27	20	22	-5
p-value*		0.285	0.002	0.002



TBUT(n=105)	Baseline	Week 6	Week 12	Change from Baseline
Omega-3	4.78	6.64	8.25	3.47
Placebo	4.61	5.55	5.81	1.20
p-value*		0.126	0.002	0.002

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Meta Analysis – *Cornea* 2019

Purpose: To assess whether omega-3 fatty acid (FA) supplementation is more efficacious than placebo in amelioration of signs and symptoms of dry eye disease.

Conclusion: This meta-analysis provides evidence that omega-3 FA supplementation significantly improves dry eye symptoms and signs in patients with dry eye disease. Therefore, our findings indicate that omega-3 FA supplementation may be an effective treatment for dry eye disease.

Efficacy of Omega-3 Fatty Acid Supplementation for Treatment of Dry Eye Disease: A Meta-Analysis of Randomized Clinical Trials

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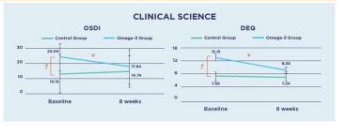
Corneal Staining, DEQ and OSDI



In conclusion, the results from this study demonstrated that oral ingestion of re-esterified omega-3 supplement for 8 weeks significantly improved the signs and symptoms of non-specific typical dry eye after uncomplicated cataract surgery. The beneficial effects of rTG omega-3 might be related to decreased inflammation of the ocular surface rather than increased secretion of tears. Dietary supplementation of re-esterified omega-3 could be added to postoperative management after cataract surgery to improve postsurgical dry eye syndrome.

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Age Related Macular Degeneration

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Omega-3s and Maintaining Macular Health (2008)

Be careful with ALA in supplements!!! (like flaxseed oil)

ARCHIVES

Dietary Omega-3 Fatty Acid and Fish Intake in the Primary Prevention of Age-Related Macular Degeneration

10-Jun-2008 - **A high intake of omega-3 fatty acids and fish may reduce the risk of age-related macular degeneration (AMD) by up to 38 per cent, suggests a new meta-analysis.**

Pooling the data from nine studies, researchers from the University of Melbourne in Australia report that the benefits were most pronounced against late (more advanced) AMD, while eating fish twice a week was associated with a reduced risk of both early and late AMD.

Combining the results showed that a high dietary intake of omega-3 EPA was associated with a 23 per cent reduction in the risk of early AMD, whereas DHA was associated with a 30 per cent reduction. **A high intake of alpha-linolenic acid (ALA) however was associated with a 49 percent increase in risk.**

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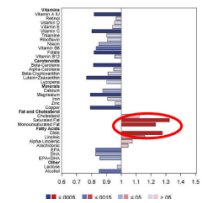
Nutrients and OVERALL AMD Progression



Hazard Ratio of Each Nutrient in RED
Protective Associations in BLUE
Smaller p values are darker

This graph is the most clinically useful as we don't know in advance whether a patient will progress toward GA or NVM

Figure 1. Butterfly plots showing proportional hazards regression modeling of progression to late age-related macular degeneration (AMD) outcomes in the combined Age-Related Eye Disease Study (AREDS) and AREDS2 cohort (At) late AMD, (B) geographic atrophy, and (C) neovascular AMD. For each nutrient, the hazard ratio of dietary intake quintile 5 (with quintile 1 as reference) is shown on the x-axis, with protective associations in blue and harmful associations in red; smaller P values are denoted by darker colors. DHA = docosahexaenoic acid; EPA = eicosapentaenoic acid; IU = international unit.

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Nutritional retinal support ….

Take homes:

- Omega 3s are not just for dry eye! Dietary and rTG form Omega 3 fatty acid supplement formulas are part of the basic nutritional support of the retina
- Omega 3s for retinal support should be considered for AMD, Diabetics, and for those with risk factors for retinal decline.
- AREDS 2 is STANDARD OF CARE for intermediate to advanced AMD --- large drusen, GA, and NV - it is not standard of care for anything else!
- Advise to reduce saturated fat and Omega 6 consumption in addition to other typical modifiable risk factors we mention

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Macular Degeneration – the disease stage matters!

Table 1
Clinical classification of AMD based on phenotype characteristics

Classification	Characteristics
No abnormal findings	No aging changes: • Absence of drusen • No pigmentary abnormalities
	Normal aging changes: • Drupelets only (small drusen ≤63 μm) • No pigmentary abnormalities
Early AMD	• Medium-sized drusen >63 μm and ≤125 μm • No pigmentary abnormalities
Intermediate AMD	• Large drusen >125 μm and/or pigmentary abnormalities
Late AMD	• Neovascular AMD and/or any geographic atrophy

Abbreviation: AMD, age-related macular degeneration.

*as recommendations for AREDS 2
AREDS study background: National Eye Institute (2018) 'Age-related Eye Disease Study' https://www.nei.nih.gov/research/clinical-trials/age-related-eye-disease-studies-areds-areds2/areds-areds2-frequently-asked-questions

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Omega 3 and Macular Health

ω-3 Long-chain polyunsaturated fatty acid intake and 12-y incidence of neovascular age-related macular degeneration and

Results: Participants who reported the highest ω−3 LCPUFA intake (median: 0.11% of total energy intake) were 30% less likely than their peers to develop CGA and NV AMD. The respective odds ratios were 0.65 (95% CI: 0.45, 0.92; $P \leq 0.02$) and 0.68 (95% CI: 0.49, 0.94; $P \leq 0.02$).

Conclusions: The 12-y incidence of CGA and NV AMD in participants at moderate-to-high risk of these outcomes was lowest for those reporting the highest consumption of ω−3 LCPUFAs.

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Omega 3 for Prevention-2011

ONLINE FIRST

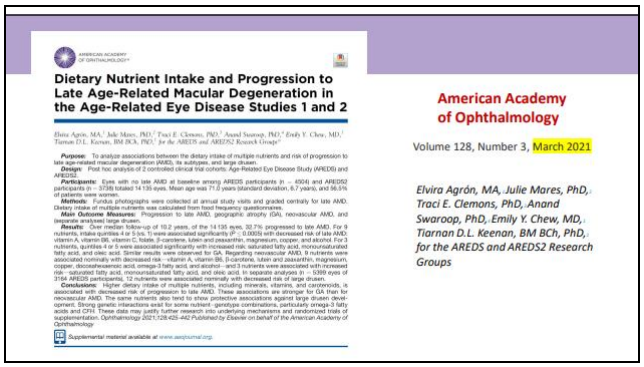
Dietary ω-3 Fatty Acid and Fish Intake and Incident Age-Related Macular Degeneration in Women

William G. Christen, ScD; Debra A. Schaumberg, ScD; Robert J. Glynn, ScD; Julie E. Buring, ScD

Arch Ophthalmol.
Published online March 14, 2011.
doi:10.1001/archophthalmol.2011.34

COMMENT

In this large prospective cohort study of female health professionals, regular consumption of DHA and EPA and fish was associated with a 35% to 45% lower risk of visually significant AMD during 10 years of follow-up. This inverse association was independent of other AMD risk

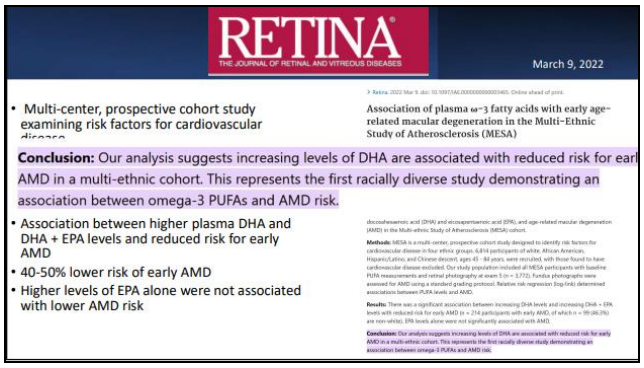


Dietary Nutrient Intake and Progression to Late Age-Related Macular Degeneration in the Age-Related Eye Disease Studies 1 and 2

American Academy of Ophthalmology

Volume 128, Number 3, March 2021

Elvira Agrón, MA, Julie Mares, PhD, Traci E. Clemons, PhD, Anand Swaroop, PhD, Emily Y. Chew, MD, Tiarnan D.L. Keenan, BM BCh, PhD, for the AREDS and AREDS2 Research Groups



RETINA
THE JOURNAL OF RETINAL AND VITREOUS DISEASES

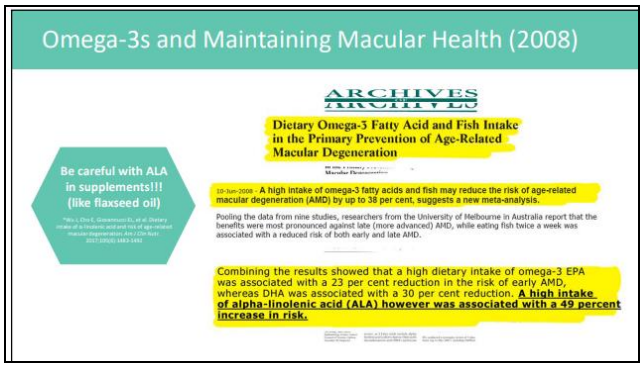
March 9, 2022

- Multi-center, prospective cohort study examining risk factors for cardiovascular disease

Association of plasma ω−3 fatty acids with early age-related macular degeneration in the Multi-Ethnic Study of Atherosclerosis (MESA)

Conclusion: Our analysis suggests increasing levels of DHA are associated with reduced risk for earl AMD in a multi-ethnic cohort. This represents the first racially diverse study demonstrating an association between omega-3 PUFAs and AMD risk.

- Association between higher plasma DHA and DHA + EPA levels and reduced risk for early AMD
- 40-50% lower risk of early AMD
- Higher levels of EPA alone were not associated with lower AMD risk



Omega-3s and Maintaining Macular Health (2008)

ARCHIVES OF OPHTHALMOLOGY

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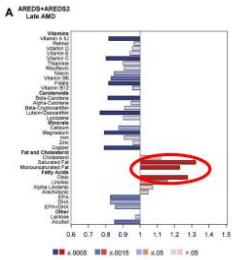
Be careful with ALA in supplements!!! (like flaxseed oil)

10-June-2008 – A high intake of omega-3 fatty acids and fish may reduce the risk of age-related macular degeneration (AMD) by up to 38 per cent, suggests a new meta-analysis.

Pooling the data from nine studies, researchers from the University of Melbourne in Australia report that the benefits were most pronounced against late (more advanced) AMD, while eating fish twice a week was associated with a reduced risk of both early and late AMD.

Combining the results showed that a high dietary intake of omega-3 EPA was associated with a 23 per cent reduction in the risk of early AMD, whereas DHA was associated with a 30 per cent reduction. **A high intake of alpha-linolenic acid (ALA) however was associated with a 49 percent increase in risk.**

Nutrients and OVERALL AMD Progression



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Classification of AMD

Classification	Characteristics
Epidemiological classification	
Early AMD	• Large (≥125 µm) drusen or retinal pseudodrusen, or pigmentary abnormalities
Late AMD	• Neovascular AMD or geographic atrophy
Basic Clinical Classification	
No aging changes	• Absence of drusen • No pigmentary abnormalities
Normal aging changes	• Drupelets only (small drusen ≤63 µm) • No pigmentary abnormalities
Early AMD	• Medium size drusen >63 µm and ≤125 µm • No pigmentary abnormalities
Intermediate AMD	• Large drusen >125 µm and/or Pigmentary abnormalities
Late AMD	• Neovascular AMD and/or any geographic atrophy
Age-Related Eye Disease Study (AREDS) simplified severity scale points	
0 1 2 3 4	• No large drusen (>125 µm) or pigment changes in either eye • Large drusen or pigment changes in one eye only • Large drusen and pigment changes in one eye only; or large drusen or pigment changes in both eyes; or neovascular AMD or geographic atrophy in one eye • Large drusen and pigment changes in one eye; and large drusen or pigment changes in the fellow eye • Large drusen and pigment changes in both eyes

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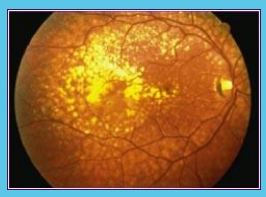
AMD Oxidation Hypothesis

- Breakdown of antioxidant systems in the central retina
  - ➢Aerobic metabolism
  - ➢Light exposure
  - ➢Free radicals
  - ➢Complement factor H
- Antioxidant deficiency may predispose to disease
- Importance of antioxidant (nutrient) supplementation



khandhadia S, Lotery A. Oxidation and Age-Related Macular Degeneration: Insights From Molecular Biology. Exp Rev Mol Med 2010;12:e34.

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Protective Antioxidant Systems in the Macula

Primary Defenses

Antioxidant Enzymes
- Superoxide dismutase (SOD)*
- Catalase*
- Glutathione peroxidase (GSH peroxidase)

* Many are zinc-containing molecules or require zinc for optimal functioning

Secondary Defenses

Antioxidant Vitamins	Macular Carotenoids	Other molecules
• Vitamin C • Vitamin E	Lutein & Zeaxanthin Quench singlet oxygen Blue light filter	Metallothionein • Zinc-binding molecule • Scavenger of free hydroxyl radicals

1. Winkler BS, Boulton ME, Gottsch JD, Sternberg P. Oxidative damage and age-related macular degeneration. *Mol Vis.* 1999;5:32-42.
2. Cai J, Kasey C, Nelson MW, Sternberg P, Jones DP. Oxidative damage and protection of the RPE. *Prog Retin Eye Res.* 2000;19(2):205-221

60

Guidelines for AREDS Supplementation in AMD

Recommendation	Diagnoses Eligible	Follow-up Recommendations	
		Intervals	Testing
Observation with no medical or surgical therapies	• Early AMD (AREDS category 2) • Advanced AMD with bilateral subfoveal geographic atrophy or disciform scars	• Return exam at 6—24 months if asymptomatic or prompt exam for new symptoms suggestive of CNV • Return exam at 6—24 months if asymptomatic or prompt exam for new symptoms suggestive of CNV	• No fundus photos or fluorescein angiography unless symptomatic • No fundus photos or fluorescein angiography unless symptomatic
Antioxidant vitamin and mineral supplements as recommended in the AREDS reports	• Intermediate AMD (AREDS category 3) • Advanced AMD in one eye (AREDS category 4)	• Return exam at 6—24 months if asymptomatic or prompt exam for new symptoms suggestive of CNV	• Monitoring of monocular near vision (reading/Amsler grid) • Fundus photography as appropriate • Fluorescein angiography if there is evidence of edema or other signs and symptoms of CNV

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1. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; 2019. Available at http://www.aao.org/ppp. Accessed July 10, 2020.

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AREDS2

Study Objectives

- Effects of adding high doses of macular xanthophylls and/or OM-3 FAs to AREDS on AMD progression and cataract
  - Effects of these supplements on moderate vision loss*
- Impact of eliminating beta-carotene and/or reducing zinc in the original AREDS formulation on AMD development and progression

*Doubling of the visual angle or the loss of 15 or more letters on the ETDRS chart

Age-Related Eye Disease Study 2 Research Group. JAMA. 2013;309(19):2005-2015.

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AREDS2

- Randomized, double-masked, placebo-controlled, 2X2 factorial trial
- Enrollment period: Oct 2006 – Sep 2008
- Subjects: 4203 participants, mean age 73 yrs., in 82 clinical sites
  - Caucasian (4058; 96%), female (2088; 57%)
- Follow up: Annual visits, phone contact 3 moths post randomization and every 6 months thereafter
  - Comprehensive eye exam, BCVA, fundus photography at annual visit
  - Median follow up period: 4.9 years
- Efficacy outcome measures:
  - CGA or CNV in fundus photographs or treatment for AAMD
  - Loss of ≥ 3 lines from baseline/treatment for CNV
- Safety Outcomes: Serious AEs, mortality

Age-Related Eye Disease Study 2 Research Group. JAMA. 2013;309(19):2005-2015.

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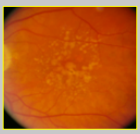
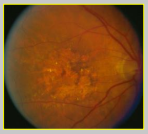
AMD Categories in AREDS2

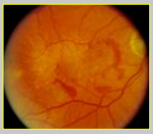
- Bilateral Large Drusen (65 %)
- Large Drusen in One Eye and Late AMD in Other (35 %)



Large Drusen



GA



NV AMD

1. The Age-Related Eye Disease Study 2 (AREDS2) Research Group. JAMA 2013;309(19):2005-15 ePu
2. b

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AREDS2

Randomization

Primary Randomization Agents

Placebo	Lutein/Zeaxanthin	DHA/EPA	Lutein/Zeaxanthin + DHA/EPA
	10 mg/2 mg	350 mg/650 mg	10 mg/2 mg; 350 mg/ 650 mg

Secondary Randomization Agents

Formulation #	Vitamin C	Vitamin E	Beta -carotene	Zinc oxide	Cupric oxide
1	500 mg	400 IU	15 mg	80 mg	2 mg
2	500 mg	400 IU	0 mg	80 mg	2 mg
3	500 mg	400 IU	0 mg	25 mg	2 mg
4	500 mg	400 IU	15 mg	25 mg	2 mg

AREDS2 protocol; version 5.2, 23September 2009, accessed at : https://web.emmes.com/study/areds2/resources/areds2_protocol.pdf Feb 2011

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AREDS2: Assumptions for the Statistical Plan

- In the original study, AREDS supplementation was associated with a 25% reduction to advanced AMD compared to placebo for categories 3 and 4 combined
- AREDS2 was powered to assess a *similar further reduction* in the primary treatment arms compared to control i.e., AREDS supplements
- 5-year progression rates were assumed based on the original AREDS as follows:
  - An estimated combined 5-year weighted progression rate of ~ 36%
  - An estimated 5-year weighted progression rates in primary treatment groups of ~ 28%
- In summary, L/Z and/ OM-3 had to provide *an additional 25% reduction* in the risk of progression, to that provided by AREDS supplementation for AREDS2 to meet its primary endpoint

AREDS2 Repot 1 Ophthalmology 2012;119:2282-9; AREDS2 Research Group JAMA 2013;309(19):2005-2015

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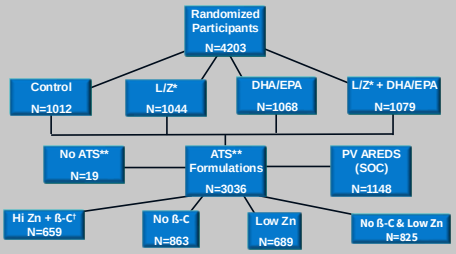
Age-Related Eye Disease Study 2



*Lutein/Zeaxanthin
**AREDS type supplements
†AREDS formula
SOC: Standard of care

AREDS2 Report 1 Ophthalmology 2012;119:2282-2289

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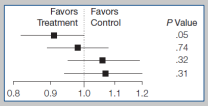
Main Effects of L/Z, OM-3, Low Zinc, and BC on AMD Progression

	Treatment		Control		
Treatment Main Effect	Eyes	Advanced AMD Events	Eyes	Advanced AMD Events	Hazard Ratio (95% CI)
Lutein + zeaxanthin	3451	940	3440	1000	0.91 (0.82-1.00)
DHA + EPA	3491	979	3400	961	0.98 (0.89-1.08)
Low-dose zinc	2468	726	2501	704	1.06 (0.95-1.19)
Beta carotene	2221	647	2212	622	1.07 (0.94-1.20)

Control: There is no true placebo group; all participants but 19 were also either randomized secondarily to one of 4 variations of the AREDS formula or received standard of care, i.e., PV AREDS outside of secondary randomization

With regard to progression to advanced AMD
- Taking L/Z was shown to be better than not taking L/Z
- OM-3 intake conferred no added benefit
- Differences with low dose zinc and BC were not significant



AREDS2 Research Group. JAMA 2013;309(19):2005-2015.

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Safety Outcome: Lung Cancer and Beta-carotene

Beta-carotene	No Beta-carotene	P value
N = 1348 23 cases (2.0%)	N=1341 11 cases (0.9%)	0.04

- Increased risk for lung cancer with beta-carotene
- Most cases were former smokers (N =31; 91%) who had quit >I year prior to randomization
- No similar increased risk reported with L+Z

AREDS2 Research Group. *JAMA* 2013;309(19):2005-2015.

AREDS2: Summary of Key Findings

- In the primary analysis, adding L+Z and/OM-3 to AREDS-like supplements did not further reduce risk of progression to advanced AMD as defined by the primary endpoint
- However, in the secondary analyses, beneficial effects were observed in patients who received L+Z:
  - Overall, L+Z supplementation reduced the risk of progression by ~ 10% versus no supplementation with L+Z
  - There was a 26% reduction in risk for progression in those given L+Z who had the lowest dietary intake of L and Z
    - These analyses included all groups receiving L+Z, including +/- omega-3, and all AREDS variants
  - Supplementation with an AREDS supplement containing L+Z without BC (vs. BC without L+Z) reduced risk of progression by 18%

AREDS2 Research Group. *JAMA* 2013;309(19):2005-2015.

AREDS2: Summary of Key Findings

- While the study did not test for equivalency between high and low dose Zn and between no beta carotene and beta carotene
  - An increased risk of lung cancer in former smokers* was associated with beta-carotene
  - No differences were observed in risk reduction or adverse events for low (25 mg) zinc vs. high (80 mg) zinc
    - There is not sufficient evidence to change the high zinc recommendation that was confirmed in the original AREDS
- Based on the data from AREDS2, the NEI recommends an adjusted AREDS formula for AREDS categories 3 and 4

* Quit smoking > 1 year before randomization

AREDS2 Research Group. *JAMA* 2013;309(19):2005-2015.

AREDS2: Recommendation

NEI Recommended AREDS2 formulation

- Vitamin C (500 mg)
- Vitamin E (400 IU)
- ~~Beta Carotene (15 mg)~~
- Lutein (10 mg)/Zeaxanthin (2 mg)
- Zinc (80 mg zinc oxide)
- Copper (2 mg cupric oxide)
- ~~Omega 3 fatty acids (DHA/EPA)~~

AREDS2 Follow-on Study

Age-Related Eye Disease Study 2

- Final follow-up for subset of AREDS2 participants: 10-years
- N=3,887 (6,360 eyes)
- **Patients randomized to receive lutein/zeaxanthin and/or omega-3 fatty acids or placebo**
  Secondary randomization for 0 or 15 mg beta-carotene and 25 vs 80 mg zinc
- Follow-up with AREDS2 participants by phone every 6 months for 5 years to collect safety data

Objectives

Assess the long-term effects of adding lutein-zeaxanthin and omega-3 fatty acids to AREDS supplements on:

- AMD progression
- Incidence of adverse side effects

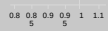
AMD, age-related macular degeneration; AREDS2, Age-related Eye Disease Study 2; LCPUFA, long-chain polyunsaturated fatty acid.

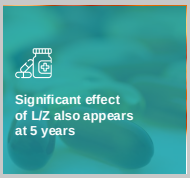
Chew EY, et al. The Results of the 10 Year Follow-on Study of the Age-Related Eye Disease Study 2 (AREDS2). Invest Ophthalmol. Vis. Sci. 2021;62(8):1215

At 10 years, Participants Taking AREDS 2 Supplements with L/Z Had ~10% Reduced Progression to Late AMD

Factorial design by the 4 treatment arms

Treatment	No. Eyes (No. Events)	Hazard Ratio (95% CI)	P Value
Lutein/Zeaxanthin	1592 (739)	0.88 (0.79-0.99)	0.04
DHA/EPA	1618 (788)	0.97 (0.87-1.09)	0.65
Lutein/Zeaxanthin +DHA/EPA	1591(739)	0.92 (0.82-1.03)	0.13
Control	1691(439)		

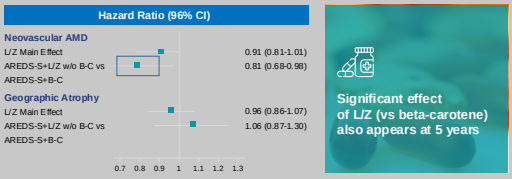




AMD, age-related macular degeneration; AREDS2, Age-related Eye Disease Study 2; CI, confidence interval; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; L/Z, lutein/zeaxanthin.

Chew EY, et al. The Results of the 10 Year Followon Study of the Age-Related Eye Disease Study 2 (AREDS2). Invest. Ophthalmol. Vis. Sci. 2021;62(8):1215

Participants Taking AREDS 2 Supplements with L/Z (vs Beta-carotene) Had ~20% Reduced Progression to NV AMD (10 Years)



AMD, age-related macular degeneration; AREDS 2, Age-related Eye Disease Study 2 B-C, beta-carotene; CI, confidence interval; L/Z, lutein/zeaxanthin; NV, neovascular; OCT, optical coherence tomography.

Chew EY, et al. The Results of the 10 Year Follow-on Study of the Age-Related Eye Disease Study 2 (AREDS2). Invest. Ophthalmol. Vis. Sci. 2021;62(8):1215

Effects of AREDS 2 Supplements at 10 Years: Risk of Lung Cancer

- **Lutein vs no lutein**
  - OR: 1.15 (95% CI: 0.82-1.71; *P* = 0.46)
  - Subgroup for lutein vs beta-carotene:
    - OR: 1.00 (95% CI: 0.54-1.83; *P* = 0.99)
- **Beta-carotene vs no beta-carotene**
  - OR: 1.8 (95% CI: 1.11-3.31; *P* = 0.03)

As previously shown in the AREDS2 study, beta-carotene at 10 years significantly increased the risk of lung cancer—nearly doubling the rate

AREDS2, Age-related Eye Disease Study 2; CI, confidence interval; OR, odds ratio.

NEI Recommends an AREDS 2 Nutrient Formula for Patients with Moderate to Advanced AMD

The NEI recommends

that these patients take a vitamin formulation that contains the exact amount of all 6 nutrients based on the AREDS2 clinical study

Nutrients	Amount per day
Beta- carotene	0
Vitamin C	500 mg
Vitamin E	400 IU
Zinc	80 mg
Copper	2mg
Lutein	10 mg
Zeaxanthin	2 mg
Omega-3 fatty acids	0

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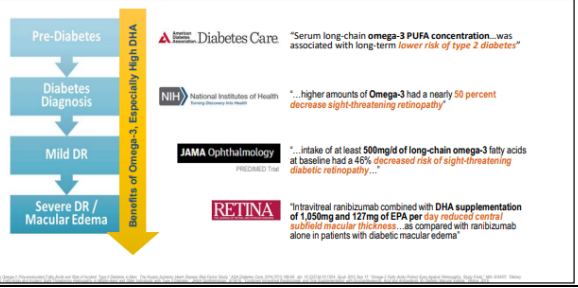
AMD, age-related macular degeneration; AREDS2, Age-related Eye Disease Study 2; NEI, National Eye Institute

Diabetic Eye Disease

Mounting Evidence that Omega-3s can Delay the Onset and Slow the Progression of Diabetic Retinopathy



Omega 3 Fatty Acids

N = 43
Type I diabetics
1,800 Omega 3 Fatty Acid supplement
Length of time = 180 Days

Oral omega-3 fatty acid supplements, in various formulations, have been extensively investigated as a potential therapy for dry eye disease. These agents are generally considered to modulate systemic inflammatory pathways, and have been shown to reduce tear pro-inflammatory cytokine levels in patients with dry eye disease [568] and promote corneal nerve regeneration in individuals with diabetes

O3FA supplements impart corneal neuroregenerative effects in type 1 diabetes, indicating a role in modulating peripheral nerve health.

A.C. Britten-Jones, J.T. Kamel, L.I. Roberts, S. Braat, J.P. Craig, R.J. Macisaac, *et al.* Investigating the neuroprotective effect of oral omega-3 fatty acid supplementation in type 1 diabetes (nPROOFS1): a randomized placebo-controlled trial Diabetes, 70 (2021), pp. 1794-1806

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Vitamins recommended to support Diabetic Retinopathy (DR)

DR from both type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) have similar retinal findings and responses to nutritional therapies.

Conventional therapies to reduce disease risk and severity. Optimal combinations are identified for protecting the retina and choroid:

Vitamins B1, B2, B6, B12

Vitamin C, D, E

Lutein

Zeaxanthin

Alpha-lipoic acid

N-acetylcysteine

Shi C, Wang P, Airen S, Brown C, Liu Z, Townsend JH, Wang J, Jiang H. Nutritional and medical food therapies for diabetic retinopathy. Eye Vis (Lond). 2020 Jun 18;7:33. doi: 10.1186/s40662-020-00199-y. PMID: 32582807; PMCID: PMC7310218.

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Cataracts

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Cataracts and Vitamins

Dietary supplements containing beta-carotene (vitamin A), vitamin C or vitamin E can neither prevent age-related cataracts nor slow the progression of the condition.

The researchers analyzed 9 studies

N = 120,000 people

Ages = 35 - 85.

Vitamins Studied: Vitamin C, E and/or beta-carotene

Study Length = up to twelve years.

Results = Oral vitamin supplements are not effective against cataract formation

Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. Cataracts: Research summaries – Can vitamin supplements help maintain your vision? [Updated 2022 Nov 22]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK390313/

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Cataracts are caused by Oxidative Stress

Oxidative stress and the subsequent oxidative damage to lens proteins is a known causative factor in the initiation and progression of cataract formation, the leading cause of blindness in the world today.

Antioxidants have been trialed as therapeutic options to delay cataract formation

Yet a formulation does not exist.

Lens is an avascular tissue

Lens receives it nutrients and antioxidants from the aqueous and vitreous

Hypothesis:

Lens cannot rely on passive diffusion alone to deliver nutrients to the distinctly different metabolic regions

Instead, it could utilizes an internal microcirculation system to actively deliver antioxidants

Key to product development:

Selecting antioxidants that can utilize this system will lead to developing novel nutritional therapies which would delay the onset and progression of cataracts.

Braakhuis AJ, Donaldson CI, Lim JC, Donaldson PJ. Nutritional Strategies to Prevent Lens Cataract: Current Status and FutureStrategies. Nutrients. 2019 May 27;11(5):1186. doi: 10.3390/nu11051186. PMID: 31137834; PMCID: PMC6566364.

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N-acetylcysteine Drops to Reduce Cataracts?

Equilibrium between the production of reactive oxygen species and their scavenging is disrupted,
Free radical generation overwhelms the endogenous antioxidant stores
Leads to oxidative stress-related eye disorders and aging.

Results of studies investigating the efficacy of antioxidant supplementation have been mixed or inconclusive

Future research is needed to highlight the potential of antioxidant molecules and to develop new preventive nutritional strategies.

Rodella U, Honisch C, Gatto C, Ruzza P, D'Amato Tóthová J. Antioxidant Nutraceutical Strategies in the Prevention of Oxidative Stress Related Eye Diseases. Nutrients. 2023 May 12;15(10):2283. doi: 10.3390/nu15102283. PMID: 37242167; PMCID: PMC10221444.

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On behalf of Vision Expo, we sincerely thank you for being with us this year.

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