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

Vision Expo Has Gone Green!

We have eliminated all paper session evaluation forms. Please be sure to complete your electronic session evaluations online when you login to request your CE Letter for each course you attended! Your feedback is important to us as our Education Planning Committee considers content and speakers for future meetings to provide you with the best education possible.

vision expo

Should I Take Vitamins For My Eyes

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

Pam Theriot - Financial Disclosures

KOL/Consultant:

Scope Eyecare
NuLids
Tear Film and Ocular Surface Society, Public Awareness Committee Member
Twenty/Twenty Beauty
NovaBay
Mallinckrodt Pharmaceuticals
Bruder Healthcare Company
Alcon
Hoot Health
CSI Dry Eye
NeuroTears

Speaker Bureau:

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

Brand Ambassador:

Eyes are the Story
UNClog Mask

*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.

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

TEDx Grandview Heights
- A Plan for Clear Vision in the Digital Age

4

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

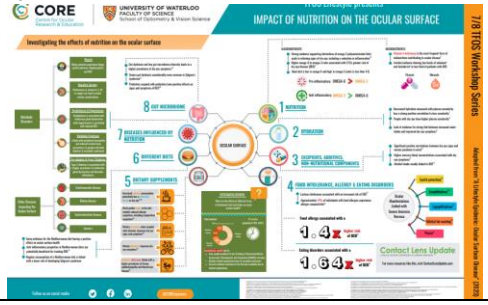
Ocular Surface Disease

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 P, et al. Int Ophthalmol. 2020;40(8):1923-1937. 2. Bergandi J, et al. Ann Med. 2020;52(5):249-259. 3. Brown A, 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. 2021;14(5):800-807. 6. Jones L, et al. Ocul Surf. 2017;15(3):575-628. 7. Pellegrini M, et al. Nutrients. 2020;12(9):2622. 8. Castro-Castaneda CR, et al. Nutrients. 2022;14(9):1850. 9. Muz OE, et al. Pharmaceuticals (Basel). 2021;14(1):8. 2021

7: Impact of Nutrition on the Ocular Surface



Micronutrients

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

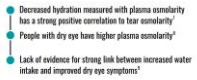
1. Fogagnolo P, et al. Nutrients. 2021;13.
2. Marriott BP, et al. Present Knowledgein Nutrition: Basic Nutrition and Metabolism; 2020.
3. Tei M, et al. Invest Ophthalmol Vis Sci. 2000;41:82-8.
4. Higuchi A, et al. Sci Rep. 2016;6:36903.
5. Sonobe H, et al. Ocul Surf. 2019;17:60-6.

TFOS Lifestyle Workshop Report

Nutrition and the Ocular Surface Conclusions:

- Decreased Hydration Measured with plasma osmolarity has a strong positive correlation to tear osmolarity
- Dry Eye sufferers have higher plasma osmolarity

- No strong evidence to link increased water intake and improvement in dry eye symptoms



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

TFOS Lifestyle Workshop Report

Nutrition and the Ocular Surface Conclusions:

- Ideal ratio of Omega-6 to Omega-3 is: 4:1

- Omega-3 Fatty Acids are shown to relieve signs of DED, including reducing inflammation

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

11

TFOS Lifestyle Workshop Report

Nutrition and the Ocular Surface Conclusions:

- Good Nutrition is pivotal to good health – consider mediterranean diet
- Nutrition impacts ocular surface function – consider Omega 3 fatty acids
- Consider the available Evidence prior to providing recommendations

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

12

TFOS Lifestyle Workshop Report

Nutrition and the Dietary Supplements:

- Increased Caffeine Intake has a protective effect on Dry Eye Disease
- Birch-pollen honey in the diet notably reduced allergic symptoms
- Dietary Curcumin (Tumeric), when coupled with vitamins, improves dry eye symptoms
- Dietary Vitamin A improves Dry Eye symptoms: eggs, sweet potato, carrot, and cantaloupe
- Selenium Deficiency linked to higher prevalence of Graves ophthalmopathy and Thyroid eye disease

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

13

Hyper Hydration Drink

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

Delivers hydration to your blood stream 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

14

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

Test Ingredient	Composition[1,2]	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 prevention of vision loss from age-related macular degeneration.[3] • Follow-up 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 hepatic fibrogenesis of ophthalmic conditions such as glaucoma, dry eye disease, and age-related macular degeneration.[5,6] • In vitro, curcumin can reduce pro-inflammatory cytokines in corneal epithelial cells and act as a neuroprotector of retinal precursor cells.[5,6]
Vitamin D3	15 mg of **Vitamin D3 providing 600 IU**	• Vitamin D3 is a prohormone, with antioxidant, immunomodulatory, and anti-inflammatory properties, which can affect helper T cells of corneal epithelial cells, including barrier provision and response to inflammation and infection.[7] • In patients with DED, low levels of vitamin D 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.[8,9]

*Production of the LCD supplement incorporated novel formulation technique, 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 386 mg of active ingredients, including functional oils to aid absorption in the small intestine. ‡Optimized marigold extract as a source of lutein and zeaxanthin as 5:1 ratio of occurring fats and vegetables. (Mustafa I. Pharmaceutics (Basel) (2020) 13 (2):20.)

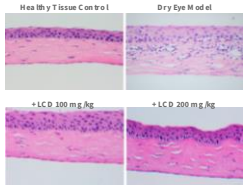
1. Rathke P, et al. Ophthalmol Ther. 2023;12(5):2581-2592. 2. Gilson N, et al. Front Ophthalmol. 2024;4:1361232. 3. Bernstein PS, et al. Prog Retin Eye Res (2016) 50:34-66. 4. Cristaldi M, et al. Appl Sci (2021) 11(3):1266. 5. Calton-Carbrey D, et al. Nutrients (2022) 14(23):5048. 6. Dario BM, et al. Sci Rep (2018) 8(1):3846. 7. Gombash R, et al. Invest Ophthalmol (2013) 7(4):1227-1234. 8. Hwang JS, et al. Cornea (2018) 38(3):304-309. 9. Najarian M, et al. Clin Exp Optom (2023) 106(3):267-62.

15

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

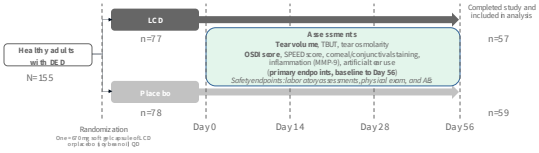
Corneal histopathology changes



Huo DE, et al. Pharmaceuticals (Basel). 2021;14(3):215.

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]

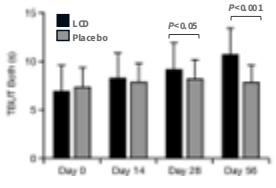


AE, adverse event; MMP-9, matrix metalloproteinase-9; OSDI, Ocular Surface Disease Index; SPEED, Standard Patient Evaluation of Eye Dryness; TBUT, Tear Film Break-Up Time; QD, Once Daily.
1. Reddy P, et al. Ophthalmol Ther. 2021;10:501–519; 2. Gisch N, et al. Front Ophthalmol. 2024;4:1362122.

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 ($P<0.05$)

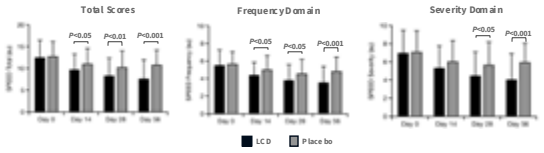
TBUT (mean of both eyes)



Gisch N, et al. Front Ophthalmol. 2024;4:1362122.

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

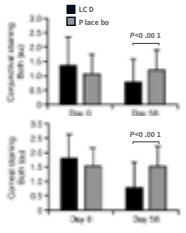


Gidaki, et al. Front Ophthalmol. 2024;3:1362121.

19

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)

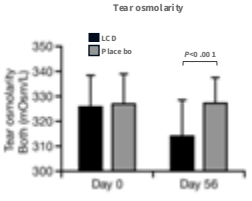


Gidaki, et al, Front Ophthalmol. 2024;3:1362121.

20

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)

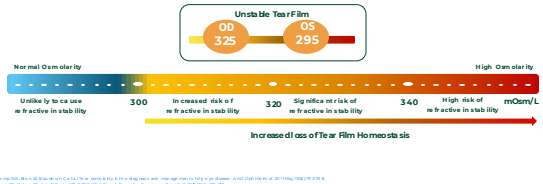


Tear osmolarity assessed using TearLab Osmolarity System in situ osmometer. mOsm/L, millimole per liter.
Gidaki, et al. Front Ophthalmol. 2024;3:1362121.

21

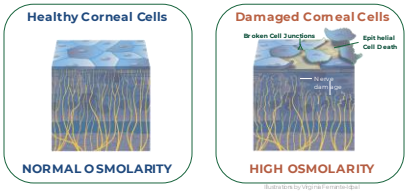
Knowing the Osmolarity Score Helps Guide Effective Treatment and Optimize Vision

- 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. Report of the National Eye Institute/Industry Workshop on Clinical Trials in Dry Eyes. CLAO J. 1995;21(4):221-232.
2. Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II Definition and Classification Report. Ocul Surf. 2017;15(3):276-283.

Tear Osmolarity Matters

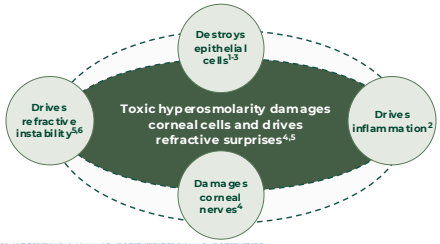


Illustrations by Vignale Fernandez-Iqbal

- 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]

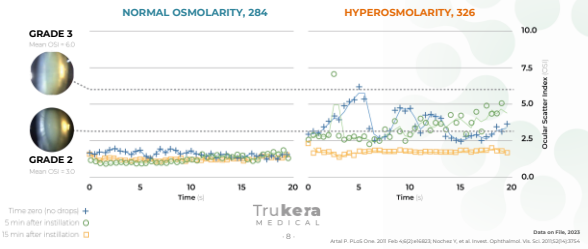
1. Bron AJ, de Paiva CS, Chauhan SK, et al. TFOS DEWS II Pathophysiology report. Ocul Surf. 2017;15(3):438-510.

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.

Hyperosmolarity Creates Light Scatter Equivalent to a Grade 2-3 Cataract



Ariel P. PLoS One. 2011 Feb 4;6(2):e16823. Nochez Y, et al. Invest. Ophthalmol. Vis. Sci. 2013;52(14):3754

Hyperosmolarity Can't be Seen in Slit Lamp

NORMAL

40 Patients | < 310 mOsm/L | 12.4 +/- 2.2 sec TBUT | 100% Stain = 0–1

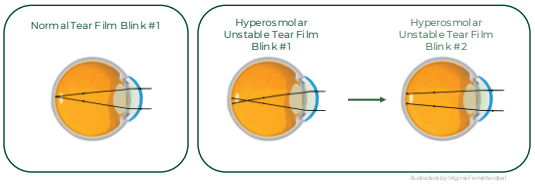
HYPEROSMOLAR

41 Patients | > 310 mOsm/L | 9.0 +/- 1.8 sec TBUT | 90.2% Stain = 0–1

Kunnen A, et al. Cornea. 2023 Apr. 2023;11:5

Higher Osmolarity Leads to Unstable Tear Film

Tear film instability has the potential to affect vision



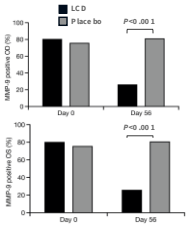
Light scattering effect of a hyperosmolar tear film can result in fluctuating vision and biometry measurements[1-3]

1. Bron C, Argüeso P, Irkec M, et al. Clinical relevance of the preocular tear film in health and disease. Ocul Surf. 2017;15(3):438-510.
2. Goto T, Klyce SD, Zheng X, et al. Tear film stability analysis system: introducing Drop Pattern Analysis for advanced research and routine clinical evaluation of the ocular surface. Cornea. 2004;23(1):65-70.
3. Goto T, Zheng X, Klyce SD, et al. A new method for tear film stability analysis using videokeratography. Am J Ophthalmol. 2003;135(5):607-612.

27

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)

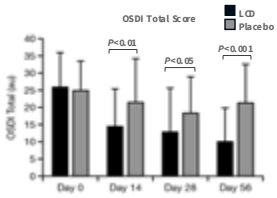


Presence of MMP-9 measured using the InflammaDry MMP-9 test kit.
OD, right eye; OS, left eye.
Gidfar S, et al. Front Ophthalmol. 2024;4:1362122.

28

Primary Efficacy Outcome: OSDI Total Score (Symptom)

- 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

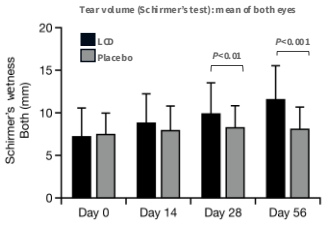


au, arbitrary units;
Gidfar S, et al. Front Ophthalmol. 2024;4:1362122.

29

Primary Efficacy Outcome: Tear Volume (Sign)

- 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 ($P<0.05$)



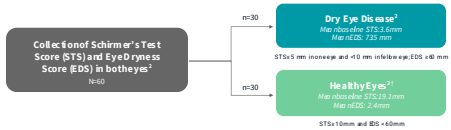
Length of wetting Schirmer's test strips without anaesthesia
Gidfar S, et al. Front Ophthalmol. 2024;4:1362122.

30

Understanding the correlation of tear film with inflammatory biomarkers on the ocular surface[1]

Study Design and Purpose[2]

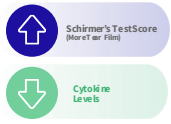
- Mah et al* assessed the differential expression of inflammatory cytokines in tears of subjects with dry eye disease versus those with healthy eyes
- Nine of the most common inflammatory cytokines related to dry eye disease were collected and evaluated in the tear composition from subjects with dry eye disease compared to those with healthy eyes
- Most study participants were white female swith a mean age of 57 to 59 years



*Presented at World Cornea Congress VIII. Study was funded by Oyster Point Pharma.
†Subjects matched by age (±5 years) and gender.
1. Tsubota K, et al. Int J Mol Sci. 2020;21(23):9272. 2. Mah F, et al. Oral presentation at: World Cornea Congress VIII; September 2022; Chicago, IL.

Significant correlation of tear film (STS) with cytokine levels[1]

A higher baseline STS was correlated with lower pro- and anti-inflammatory cytokine levels[1]



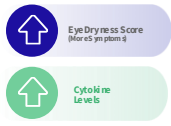
Cytokine	Pearson's Correlation Coefficient Baseline STS	*P* value
Pro-inflammatory		
IFN-γ	-0.5 6	*P*<0. 001
IL-12p 70	-0.5 1	*P*<0. 001
IL-17a	-0.5 6	*P*<0. 001
IL-1β	-0.5 5	*P*<0. 001
IL-2	-0.6 1	*P*<0. 001
TNF-α	-0.4 4	*P*=0. 014
Anti-inflammatory		
IL-4	-0.6 2	*P*<0. 001

IL-6 (pro-inflammatory cytokine) and IL-10 (anti-inflammatory cytokine) removed due to low n.

STS, Schirmer's Test Score.
1. Mah F, et al. Oral presentation at: World Cornea Congress VIII; September 2022; Chicago, IL.

Significant correlation of symptoms (EDS) with cytokine levels[1]

A higher baseline EDS was correlated with higher pro- and anti-inflammatory cytokine levels[1]



Cytokine	Pearson's Correlation Coefficient Baseline EDS	*P* value
Pro-inflammatory		
IFN-γ	0.6 4	*P*<0. 001
IL-12p 70	0.5 5	*P*<0. 001
IL-17a	0.6 6	*P*<0. 001
IL-1β	0.4 4	*P*<0. 001
IL-2	0.6 7	*P*<0. 001
TNF-α	0.4 3	*P*=0. 017
Anti-inflammatory		
IL-4	0.6 2	*P*<0. 001

IL-6 (pro-inflammatory cytokine) and IL-10 (anti-inflammatory cytokine) removed due to low n.

EDS, Eye Dryness Score.
1. Mah F, et al. Oral presentation at: World Cornea Congress VIII; September 2022; Chicago, IL.

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

Gidaik, et al, Front Ophthalmol 2024;3:1362113.

34

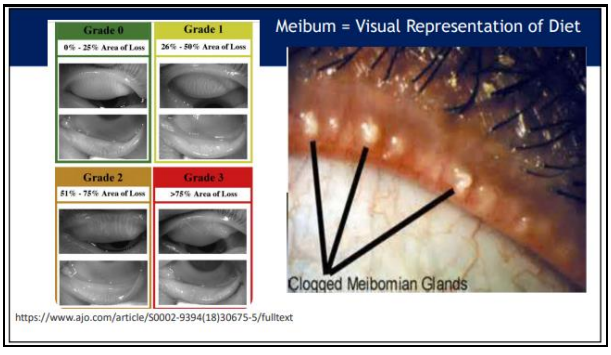
LCD significantly improved the signs and symptoms of DED and was well-tolerated[1,2]

- 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. Rather P, et al. Ophthalmol Ther. 2023;10:501–519; 2. Gidaik, et al. Front Ophthalmol 2024;3:1362113.

35



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

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)

Nutrition 101: Omega-3 & 6 Initials

Omega-3
Anti-Inflammatory

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

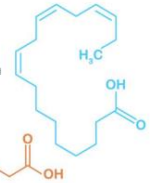
Omega-6
Inflammatory

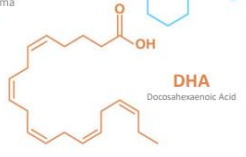
- **Linolenic Acid** (LA)
  - Vegetable Oils, Saturated Fats, Fast Foods
- **Gamma-Linolenic Acid** (GLA)
  - Evening Primrose Oil, Borage Oil, Black Currant Oil
- **Arachidonic Acid** (ARA)
  - Vegetable Oils, Saturated Fats, Fast Foods

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.

EPA
Eicosapentaenoic Acid



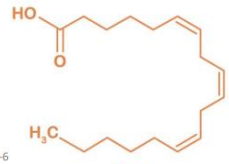


DHA
Docosahexaenoic Acid

*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
Tear Osmolarity	Stat Sig P = 0.004 ave - 19
MMP-9	Stat Sig P value = 0.024 -68%
Corneal Staining	NOT Stat Sig P value = 0.712. -7 oxford
TBUT	Stat Sig P = 0.002 +3.5
OSDI	Stat Sig P = 0.002. -17
Omega Index	Stat Sig P = <0.001. +3%
Schirmers	NOT Stat Sig P = 0.78 +1.7mm

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

46

Diagnosis

Based on symptomology – frequency / severity

No criteria to link to digital device use + 1 symptom required

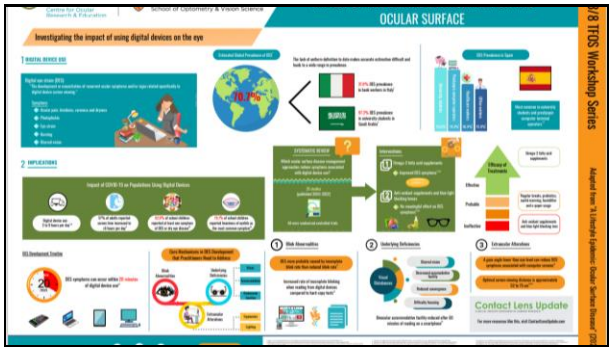
⇒ high prevalence ⊗

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

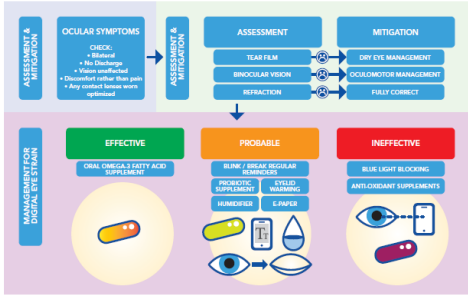
No gold standard; Rasch analysed:

- 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.

47



Digital Eye Strain Management



49

Recommendations from TFOS

Omega Fatty Acid Supplementation:

Modulate systemic inflammatory pathways

Reduce tear pro-inflammatory cytokine levels

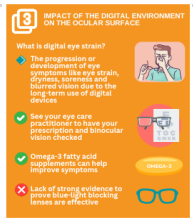
Probiotics:

Limited evidence of effectiveness

Anti-Oxidants:

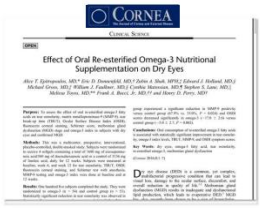
Increase contrast sensitivity in the macula

No evidence of reduction in Digital Eye Strain



Acquah,Alex Muntz, Karim Mohamed-Noriega, Sotiris Plainis, Michael Read ,Ron yR. Sayegh, Sumeer Singh, Tor P.Utheim, Jennifer P.C raig, TFOS Lifestyle: Impact of the digit alenvironment on the ocular surface, TheOcular Surface Volume 28, 2023,Pages 213-252,

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

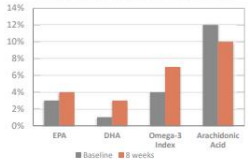
Subjects

- 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

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

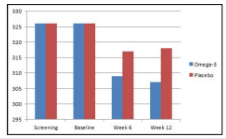


82% of patients showed EPA and DHA present in the meibum at 8 weeks (compared to 0% at baseline)

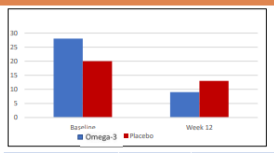
- **70% became completely asymptomatic**
- **100% noted decrease in primary complaint**
- **Improvement in TBUT** was statistically significant
- All patients with corneal staining at baseline significantly improved
- Patients with **hyperosmolarity (>308 mOsm/L) at baseline improved 25%**

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

Tear Osmolarity & MMP-9 Change from Baseline



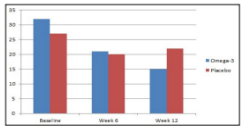
Tear Osmolarity (N=105)	Screening	Baseline (Week 0)	Week 6	Week 12	Change from Baseline
Omega-3	326	326	309	307	-19
Placebo	326	326	317	318	-8
p-value*			0.042	0.004	0.004



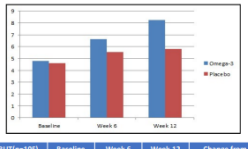
MMP-9 biomarker (N=105)	Baseline	Week 12
Omega-3	28	9*
Placebo	20	13
p-value*		0.024

* 68% reduction in MMP-9 Positivity

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

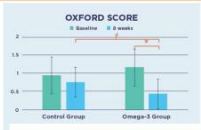
Meta Analysis – *Cornea* 2019

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

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.

Diabetic Eye Disease

Neuroprotective effect of oral omega-3 fatty acid supplementation in type 1 diabetes

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 [56,81], 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.J. Roberts, S. Braat, J.P. Craig, R.J. Maclaaac, *et al.* Investigating the neuroprotective effect of oral omega-3 fatty acid supplementation in type 1 diabetes (nPROOFS): a randomized placebo-controlled trial Diabetes, 70 (2021), pp. 1794-1806

58

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

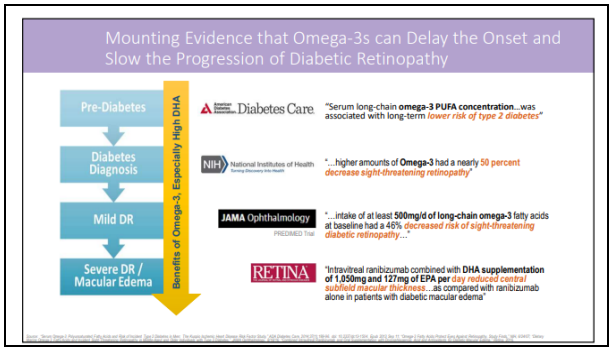
Alpha-lipoic acid

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.

59

Cataracts



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 vitamins supplements help maintain your vision? [Updated 2012 Nov 2]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK318312/

62

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 A.J, Donaldson C.I, Lim J.C, Donaldson P.J. Nutritional Strategies to Prevent Lens Cataract: Current Status and Future Strategies. Nutrients. 2019 May 27;11(5):1186. doi: 10.3390/nu11051186. PMID: 31137834; PMCID: PMC6566364.

63

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 findings

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

Rodella LI, 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: PMC10214144.

64

Age Related Macular Degeneration

Omega-3s and Maintaining Macular Health (2008)

ARCHIVES OF OPHTHALMOLOGY

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

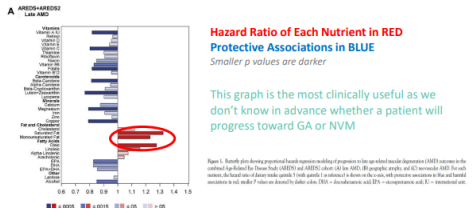
Be careful with ALA in supplements!!! (like flaxseed oil)

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.**

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

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

58

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.

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.

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

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

Elvira Agrón, MA,[1] Julie Mares, PhD,[1] Traci E. Clemons, PhD,[1] Anand Swaroop, PhD,[2] Emily Y. Chew, MD,[1] Tiarnan D.L. Keenan, BM BCh, PhD,[1] *for the AREDS and AREDS2 Research Groups*[3]

Purpose: To analyze associations between the dietary intake of multiple nutrients and risk of progression to late age-related macular degeneration (AMD), its subtypes, and large drusen.

Design: Post hoc analysis of 2 controlled clinical trial cohorts: Age-Related Eye Disease Study (AREDS) and AREDS2.

Participants: Eyes with no late AMD at baseline among AREDS participants (n = 4549) and AREDS2 participants (n = 3738) totaled 14 135 eyes. Mean age was 71.0 years (standard deviation, 6.7 years), and 56.5% of patients were women.

Methods: Fundus photographs were collected at annual study visits and graded centrally for late AMD. Dietary intake of multiple nutrients was calculated from food frequency questionnaires.

Main Outcome Measures: Progression to late AMD, geographic atrophy (GA), neovascular AMD, and separately analyzed large drusen.

Results: Over median follow-up of 10.2 years, of the 14 135 eyes, 32.7% progressed to late AMD. For 9 nutrients, quintiles 4 or 5 were associated significantly with decreased risk of progression to late AMD: vitamin A, vitamin B6, vitamin C, folate, β-carotene, lutein and zeaxanthin, magnesium, copper, and alcohol. For 3 nutrients, quintiles 4 or 5 were associated significantly with increased risk: saturated fatty acid, monounsaturated fatty acid, and oleic acid. Similar results were observed for GA. Regarding neovascular AMD, 8 nutrients were associated nominally with decreased risk – vitamin A, vitamin B6, β-carotene, lutein and zeaxanthin, magnesium, copper, docosahexaenoic acid, omega-3 fatty acid, and alcohol – and 3 nutrients were associated with increased risk – saturated fatty acid, monounsaturated fatty acid, and oleic acid. In separate analyses (n = 5399 eyes of 3154 AREDS participants), 12 nutrients were associated nominally with decreased risk of large drusen.

Conclusions: Higher dietary intake of some nutrients was associated with decreased risk of progression to late AMD, GA, and neovascular AMD. The same nutrients also tend to show protective associations against large drusen development. Strong genetic interactions exist for some nutrient–genotype combinations, particularly omega-3 fatty acids and CFH. These data may justify further research into underlying mechanisms and randomized trials of supplementation. *Ophthalmology 2021;128:425–442 Published by Elsevier on behalf of the American Academy of Ophthalmology*

Supplemental material available at www.aaojournal.org.


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

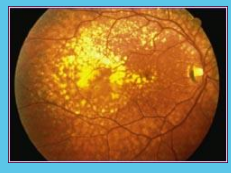
Association of plasma ω−3 fatty acids with early age-related macular degeneration in the Multi-Ethnic Study of Atherosclerosis (MESA)

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

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.

Protective Antioxidant Systems in the Macula

Primary Defenses

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

* Many enzymes contain 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.

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. 2013309(19):2005-2015.

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. 2013309(19):2005-2015.

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 photo or fluorescein angiography unless symptomatic • No fundus photo 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

*/TM are trademarks of Bausch & Lomb Incorporated or its affiliates. Any other brand names or logos are trademarks of their respective owners.

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: https://www.aao.org/ppp. Accessed July 10 2020.

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

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

*The marks of Bausch & Lomb Incorporated or its affiliates. Any other brand names or logos are trademarks of their respective owners.
AMD, age-related macular degeneration; AREDS2, Age-related Eye Disease Study 2; NEI, National Eye Institute

Got Questions?

www.pamtheriot.com

Pam@pamtheriot.com

Thank you

- Vision Expo East
- All of the Meeting Sponsors
- Attendees

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

Vision Expo Has Gone Green!

We have eliminated all paper session evaluation forms. Please be sure to complete your electronic session evaluations online when you login to request your CE Letter for each course you attended! Your feedback is important to us as our Education Planning Committee considers content and speakers for future meetings to provide you with the best education possible.

vision expo