

Ocular Nutrition Controversies

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Disclosure

- I have been on advisory boards/a consultant to/received honoraria from/ or been on speakers bureau list of the following:
 - Allergan, Apellis, Bausch & Lomb, Essilor, Genentech, LKC, MDA, Maculogix, Notal Vision, Novartis, Optos, Oyster Point, Regeneron, VSP, ZeaVision

All relevant relationships have been mitigated



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“Let Thy Food Be Thy Medicine”
Hippocrates

Maximus Diabeticus Triglicéridus
Hipertensus



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A quick tribute to Stuart Richer

- Is this really all that you need?



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And to Larry Alexander:
An egg a day keeps Anti-VEGF away



- Increasing diet to 1 egg/d in older adults can increase serum L & Z without affect on serum total cholesterol, HDL, LDL or triglycerides
 - Egg a day and L, Z and HDL/LDL and Cholest. J Nutr. 2006 Oct;136(10):2519-24.
- Increased MPOD w egg consumption: 31% increase w 2 yolks/d. Serum L and Z increased 16% and 36% at 5wks
 - Serum HDL increased 5% and no change in LDL
 - NOTE: These were elderly pts on lipid lowering meds
 - Egg yolks and MPOD. Am J Clin Nutr. 2009 Nov;90(5):1272-9.



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Why do we need to discuss?



- What is the leading source of Antioxidants in the average American's diet?¹
 - Coffee (2nd and 3rd are black tea and bananas)
- What percentage of Americans follow the 4 healthy lifestyle habits?
 - 3%
- What percentage of vege intake in the US is potato + ketchup
 - >50%
 - 2010-2015 F/V consumption down 7% compared to prior period measured
 - Leading "fruit" is OJ and leading "vege" is potato
 - 15% of tomato consumption is ketchup



Vinson et al. Polyphenols and US consumption. American Chem. Society 8/2005.


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SAFETY of VITAMINS: In the NEWS

Dietary Supplements and Mortality Rate in Older Women 2011

The Iowa Women's Health Study N=>20K women

Jaakko Miettinen, PhD; Kim Robison, PhD; Lisa J. Harnack, DrPH, MPH; Kyong Park, PhD; David R. Jacobs Jr., PhD



MV, Vit B6, folic acid, Mg, zinc, iron & copper may be associated with increase mortality rate

Background: Although dietary supplements are commonly taken to prevent chronic disease, the long-term health consequences of many compounds are unknown.

Methods: We assessed the use of vitamin and mineral supplements in relation to total mortality in 38,222 older women in the Iowa Women's Health Study; mean age was 61.6 years at baseline in 1986. Supplement use was self-reported in 1986, 1997, and 2004. Through December 31, 2008, a total of 4,123 deaths (48.2%) were identified through the State Health Registry of Iowa and the National Death Index.

Results: In multivariable adjusted proportional hazards regression models, the use of multivitamin (hazard ratio, 1.06; 95% CI, 1.02-1.10; absolute risk increase, 2.4%), vitamin B₆ (1.10; 1.01-1.21; 4.1%), folic acid (1.13; 1.00-1.32; 3.9%), iron (1.10; 1.03-1.17; 3.9%), magnesium (1.08; 1.01-1.15; 3.0%), zinc (1.08; 1.01-1.15; 3.0%), and copper (1.45; 1.20-1.75; 18.0%) were associated with increased risk of total mortality when compared with corresponding nonuse. Use of calcium was inversely related (hazard ratio, 0.91; 95% confidence interval, 0.88-0.94; absolute risk reduction, 3.8%). Findings for iron and calcium were replicated in separate, shorter-term analyses (10-year, 6-year, and 4-year follow-up), each with approximately 15% of the original participants being studied, starting in 1986, 1997, and 2004.

Conclusions: In older women, several commonly used dietary vitamin and mineral supplements may be associated with increased total mortality risk, this association is strongest with supplemental iron. In contrast to the findings of many studies, calcium is associated with decreased risk.

Arch Intern Med. 2011;171(18):1625-1631

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When does nutrition become important?

- Should everybody pay attention to it?
- Is nutrition preventative or should discussion be reserved for "active" disease?
- At what point in AMD do you start to discuss nutrition?
 - Subclinical disease?
- At what point in DM does nutrition become important?
- When do you discuss nutrition in OSD?

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Where is the best place to find nutrition?


- But what's the reality?
- What foods are good for Xanthophyll?
 - Kale (40mg/serving), Spinach (12mg), Romaine lettuce (2.3mg), Broccoli (1.7mg)
- Do you ever ask your patients about f/v consumption?
- What about Mediterranean diet?
 - Approx 47% less Adv AMD
 - More L/Z the better! Hogg. Ophthalmology 11/16.
- An apple a day keeps AMD away!
 - 15% decrease Ophthalmologica 2015: Coimbra Eye Study



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But....

- 2022 NHANES analysis shows daily consumption of 100% fruit juice was associated with a **21-fold** increased risk of advanced AMD after most adjustments!!
- No adjustment for genetics



Front. Nutr., 21 April 2022

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Is there a best diet?



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OCULAR Benefits of Mediterranean dietary habits

Following a Mediterranean diet has been associated with a decrease in plasma biomarkers for oxidative stress.

High consumption of fatty fish containing **omega-3 EFAs** and vegetables rich in **carotenoids** is beneficial for those at risk for AMD, while a Western dietary pattern has an increased association with AMD prevalence.

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The LXXVI Edward Jackson Memorial Lecture 2020
by Dr. Emily Chew



- Re-iterated results of AREDS1 and AREDS2
- Regarding Mediterranean diet: benefits in incident AMD and to late AMD (especially high fish consumption in AREDS 1&2)
- “This would suggest that it is never too early or too late to adopt a healthy diet, such as the Mediterranean diet.”
- Genetics seems to affect efficacy of Med diet to late AMD



AJO 9/2020

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Wine consumption

- People in the Mediterranean drink alcohol moderately and regularly. In fact, moderate drinkers outlive nondrinkers!
- 1 to 2 glasses per day with friends and/or with food.
- And no, you cannot save up all week and have 14 drinks on Saturday!

• Buettner D, Skemp S. Blue Zones: Lessons From the World's Longest Lived. *Am J Lifestyle Med.* 2016 Jul 7;10(5):318-321. doi: 10.1177/1559827616637066. PMID: 30202288; PMCID: PMC6125071.

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Carotenoids are not just for your eyes!

Association of Serum Antioxidant Vitamins and Carotenoids With Incident Alzheimer Disease and All-Cause Dementia Among US Adults

NHANES 2022 with over 7k over 26yrs

May A. Stephan, PhD, MPH, MEd, A. Stephan, PhD, MPH, Marie T. Farni-Akumara, PhD, Jordan Hwang, PhD, Shantel Healy, PhD, John Kishi, MD, Michael Kim, MD, and Alan B. Zaslavsky, PhD

Correspondence: Dr. Stephan stephan@mark.umh.gov

Abstract **MIND** THE BEST DIET FOR YOUR BRAIN

Dietary carotenoids related to risk of incident Alzheimer dementia (AD) and brain AD neuropathology: a community-based cohort of older adults

Changcheng Yuan,^{1,2,3} Hai Chen,⁴ Yamin Wang,⁵ Julie A Schneider,³ Walter C Willett,^{2,1,6} and Martha Clare Morris⁴

Conclusion: High dietary carotenoid consumption substantially lowers the risk of cognitive decline, dementia & brain neuropathology.

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What about lutein and zeaxanthin in the Alzheimer brain?

Low Xanthophylls, Retinol, Lycopene, and Tocopherols in Gray and White Matter of Brains with Alzheimer's Disease

Alzheimers Dis. 2022 Aug 16. doi: 10.3233/JAD-220460. Online ahead of print. PMID: 35988225

Key Findings:

- Showed remarkable decrease in xanthophylls – particularly 7X (not 001)

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The Rush Medical/Harvard Study 2021

Dietary carotenoids related to risk of incident Alzheimer dementia (AD) and brain AD neuropathology: a community-based cohort of older adults


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Multi-vitamins

- Are multivitamins worthwhile?
- Are they just a fairy-dust formulation?
- Are they true to label?
 - NY AG investigation of major retailers
- Frame of reference as to AREDS2...



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“True to label”

- You can't take for granted that things are what they say..
- NYT article in Nov. 2013 looking at 44 bottles from 12 companies of supplements
 - Bottles from 2 companies had 100% and 2 had 0% accuracy to label
 - 2 bottles of St John's wort contained NONE of the actual herb
 - 1/3 showed substitution (no trace of advertised)

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NY Attorney's General gets involved

- In Feb 2015 NYAG did sting with GNC, Target, Walgreens and Walmart
 - Ex: Walgreens Ginseng was only powdered garlic and rice
 - Walmart Ginkgo biloba was radish, houseplants and wheat (Despite being labeled gluten/wheat free)
 - 3/6 tested at Target had 0% of labeled claim
 - GNC: unlisted ingredients including legumes as fillers

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So...

- Use only brands you can trust
- PRESCRIBE to your patient as you would anything else
- Look for independent lab testing, production in NSF, follow BMP (best manufacturing practices) facilities and a company that will be there when you need them!

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Can you prescribe vitamins?

- Matter of perspective



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MPOD

- Does MPOD only relate to AMD **risk**?
- Are carotenoids important beyond AMD?

Remember what I said earlier about how to easily discuss with patients?

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Can we improve visual function

- ZVF, LAST, LAST2
 - What do we mean by visual function?



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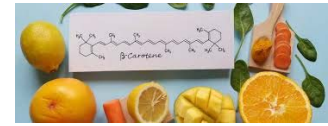
Which is better....2 or 3

- Carotenoids found in macula
 - Lutein
 - Zeaxanthin
 - Mesozeaxanthin
- Does something need to be dietary to be important?
- Does it need to be able to “perform” on it’s own?

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Beta Carotene

- What’s up doc?
- Is it helpful?
- Is it harmful?

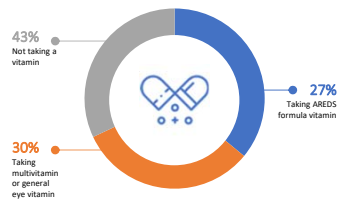


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64% of Patients with Moderate to Advanced AMD Are Not Taking an AREDS Formula Vitamin

Key Barriers

- Lack of awareness of vitamins based on the AREDS Study
- Lack of doctor recommendation



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AREDS2

- What did the abstract from AREDS2 tell us?
- What did AREDS2 really tell us?

National Eye Institute Recommended Formula:		
Nutrient	Amount (per day)	Percent Daily Value*
Vitamin C	500 mg	840%
Vitamin E	400 IU	1340%
Zinc	80 mg	840%
Copper	2 mg	100%
Lutein	10 mg	--
Zeaxanthin	2 mg	--

*Percent Daily Values (DV) listed on a 2,000-calorie diet
**Daily Values (DV) not established
Speak with your doctor to determine if the updated AREDS 2 formula is right for you.



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How many papers have there been from AREDS2???

- #1: Study design and baseline characteristics
- #12: OPERA: Peripheral retinal changes in AMD
- #13: Late AMD associated with lower survival (mortality)
- #15-17: Papers dealing with Geographic atrophy
- #19: If need anti-VEGF, vision declines with time
- #20: Aspirin not SS associated with advanced AMD
- There have been 24 (most recent 2/21)
- Separate subset: HOME Study for remote detection of wet AMD
- AND...there will be more!

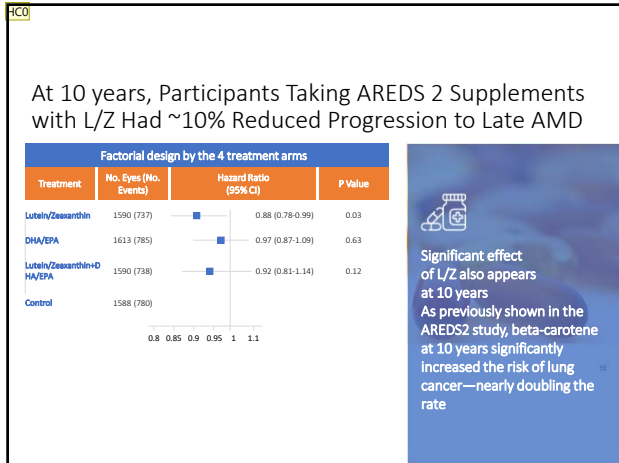
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The National Eye Institute Published the AREDS2 10 Year Follow-On Study Results

Published Online June 2, 2022
Jama Ophthalmology



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Nutrition for digital eye strain?

- Can nutrition be used to benefit eye strain / computer vision syndrome?
 - Recent article by Drake Lem, et al with over 330 references thinks so¹
 - From improving ocular surface (primarily Omega-3)
 - Anthocyanin for asthenopia relief
 - Carotenoids for photophobia, glare, contrast and fatigue
 - Astaxanthin for improved focusing ability and decrease in “tiredness”
- Do you ever talk to patients about nutrition and device use?

1. Lem et al. Can Nutrition Play a Role in Ameliorating Digital Eye Strain. *Nutrients*, 2022 Oct; 14(19): 4005.

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What about vitreous floaters?

Healthy Vitreous

Vitreous Antioxidants - Enzymatic & Non-enzymatic

- Ascorbic Acid
- Glutathione
- Cysteine
- Taurine
- Crystallin
- Silicic acid
- Human serum albumin
- Transferrin
- Pigment epithelium-derived factor
- Selenium
- Zinc
- Superoxide dismutase 3
- Glutathione peroxidase 3
- Glutathione peroxidase 4
- Catalase

Ankamaiah et al. Antioxidants. 2020;7

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Results: Micronutrient Formula vs. Placebo

Personalized Improvement (6 months)

Placebo vs. Micronutrient formula

* statistically significant at the p<0.05 level

Those participants taking the micronutrient formula experienced:

- 21.5% decrease in vitreous opacity area
- 46% decrease in visual discomfort
- 9% improvement in contrast sensitivity
- 47% improvement in daily visual experience
- 67% of patients on active supplement experience an improvement in visual comfort

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What about Fish Oil

- What did AREDS2 say?
- What have European studies said?
- What about other potential worries with fish oil?
 - What about DR specifically?
 - PREDIMED
 - 500mg for 48% less incident DR

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What about DREAM

- Dry Eye Assessment and Management Study Research Group
 - 3000mg fish oil (2000 EPA/1000 DHA) vs control (1000mg Olive oil)
 - WHAT DID IT SAY?
 - Both groups improved significantly on OSDI
 - Fish oil improved MORE than olive oil, but not statistically significantly

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Slide 31

HCO Updated data slightly based on Chew 2022 (JAMA Ophthalmol)
Hayley Clay, 2022-09-01T20:56:26.381

OK...what to think about Zinc?

- Is it friend or foe?
- It is necessary for general body function?
- What did AREDS1 say?
- What did AREDS2 say?
- What do we know about the genetics of zinc?



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The Accumulation of Zinc studies..

- Several by the Awh group: all same conclusion of efficacy of genetic testing and importance
- Several by the Chew group: All same conclusion of lack of efficacy and unimportant
- Seddon et al. 12/16 BJO: Some importance in genetics driving response
- Vavvas et al. 1/18 PNAS: Genetics drives response to nutraceuticals
- Assel et al. 3/18 Ophth: Genetics don't matter
- Kauffman et al. 8/2020: J VR Dz: Genetics matters

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-
-
-
-

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There is more to Diabetes than sugar!

Billy has 32 candy bars. He eats 28.
What does he have now?
Diabetes.
Billy has diabetes.

- Can we improve visual function in patients with diabetes through diet / nutritional intervention?
- Can we help treat macular edema through nutrition?

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Mean hsCRP diabetes

Contrast Color 5-2 MPOD LDL-C HDL-C TGs (r) hsCRP HbA1c Fovea DPNS

OPEN ACCESS

The Diabetes Visual Function Supplement Study (DVIUS)
A Fair Clous, Stuart F. Richer, Jeffrey D. Gerson, Rami A. Kibbi

ABSTRACT

Background: Visual function is a critical component of quality of life in patients with diabetes. The Diabetes Visual Function Supplement Study (DVIUS) is a randomized, controlled trial designed to evaluate the efficacy of a dietary supplement in improving visual function in patients with diabetes. The study is currently ongoing and will provide valuable insights into the role of nutrition in the management of diabetes-related visual impairment.

CONCLUSIONS

The DVIUS study is a significant contribution to the field of diabetes research, as it addresses the need for effective interventions to improve visual function in this population. The results of the study will help inform clinical practice and provide a better understanding of the underlying mechanisms of diabetes-related visual impairment.

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More on Diabetes

- Fish oil in prevention of vision loss
 - 2 servings per week to achieve approx 50% less vision loss
- Fish oil and antioxidants aiding anti-VEGF

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Do you sell supplements

- Pro vs con



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Too much of a good thing

- Is too much of a good thing an even better thing?
- Can you get to much?
What happens?

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Summary

- OD's can be a resource for patients regarding nutrition
- This can be an in-depth or only surface scratching endeavor
- Patients need help...they don't know what they don't know... (neither do we, by the way)
- Nutrition can be profitable (in several ways)

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Thank You!

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Which fruits/veggies should I eat?

- Historically, recommendations are made for green leafy veggies
 - Maize has highest % of lutein, and Orange pepper/Goji Berries has highest % of Zeaxanthin
 - High amounts were also found in: kiwi fruit, grapes, spinach, orange juice, zucchini and different kinds of squash
 - Note: different colors of f/v involved
 - F&V affecting MPOD: Br J Ophthalmol. 1998 Aug;82(8):907-10.
 - Note, Mesozexanthin is found in food sources, but not in meaningful quantities

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