



**A NEW HANDLE ON MACULAR PIGMENT MEASUREMENTS AND OCULAR NUTRITION**

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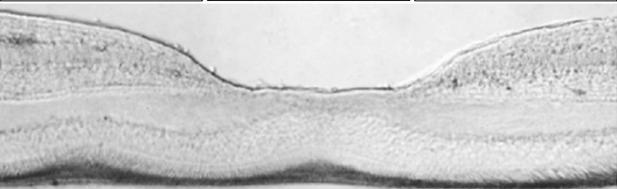
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Has a relevant financial relationship with  
Sanofi, Guardion Health, Thea Pharma and Innova systems as a  
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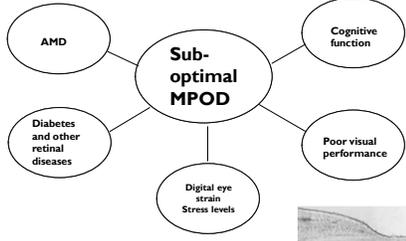
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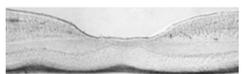
**CAN YOU DIRECTLY MEASURE EYES BLUE LIGHT ABSORPTION CAPACITY?**

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**MPOD IS A BIOMARKER**

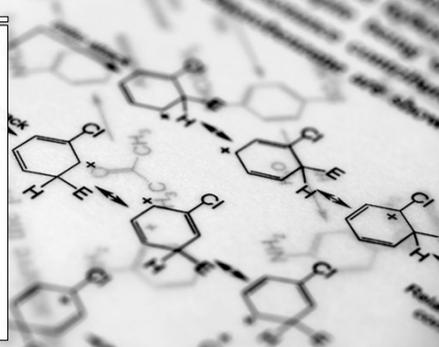



PG Davey et al. Differences in macular pigment optical density across ethnicities: A comparative study *The Advances in Ophthalmol* 2020



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**CAROTENOIDS- XANTHOPHYLLS THE BASICS**



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**WHILE ~750 CAROTENOIDS ARE FOUND IN NATURE, ONLY TWO ARE CONCENTRATED IN THE RETINA**



~750 Carotenoids

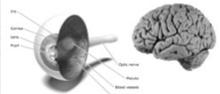


<50 Primary Carotenoids



~20 Carotenoids

Dietary carotenoids - Lutein and Zeaxanthin - are concentrated in the eye and brain

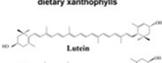


≈ 75 % of carotenoids in infant's brain is lutein and zeaxanthin

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## CAROTENOIDS IN RETINA-XANTHOPHYLLS

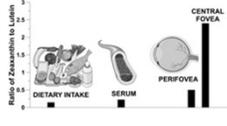
dietary xanthophylls



Lutein



Zeaxanthin



Ratio of Zeaxanthin to Lutein

DIETARY INTAKE    SERUM    CENTRAL FOVEA

Zeaxanthin to lutein ratio in central retina is 2.5:1



Photomicrograph courtesy of Dr. Joanne Curran-Coletano.

Nutrients 2020, 12, 1333; doi:10.3390/nu12051333

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### MACULAR XANTHOPHYLLS

- Two dietary carotenoids – lutein and zeaxanthin – make it to all over the body – eyes, brain, adrenal glands, skin.
- Only in the eye- RPE65 isomerase converts lutein to meso-zeaxanthin.
  - So don't need Meso if you have Lutein in diet
  - Everyone has it RPE65 if they have a functional retina that can see
  - In advanced stages of the disease if the RPE is broken down, lutein may have a tough time converting to meso-zeaxanthin but zeaxanthin is still absorbed
- Meso-zeaxanthin is not found in common foods – it is found in shrimp shells, turtle fat, and fish skin.

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## CAROTENOIDS FOOD SOURCES

Foods	Serving Size	Lutein + Zeaxanthin Content (mg)
Spinach, frozen (cooked)	1 cup	29.8
Kale, frozen (cooked)	1 cup	25.6
Swiss chard (cooked)	1 cup	11.0
Collard greens, frozen (cooked)	1 cup	8.9
Summer squash (cooked)	1 cup	4.0
Peas, frozen (cooked)	1 cup	3.8
Brussel sprouts, frozen (cooked)	1 cup	2.4
Broccoli, frozen (cooked)	1 cup	2.0
Edamame, frozen	1 cup	1.6
Sweet yellow corn (boiled)	1 cup	1.5
Asparagus (boiled)	0.5 cup	0.7
Avocado, raw	1 medium-size	0.4
Egg yolk, raw	1 large	0.2



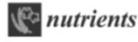
Meso-zeaxanthin is not found in common food : in shrimp shells, turtle fat, and fish skin

Lem, D.W.; Giehl, D.L.; Davy, P.G. A Systematic Review of Carotenoids in the Management of Diabetic Retinopathy. *Nutrients* **2021**, *13*, 2441. <https://doi.org/10.3390/nu13072441>

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## LUTEIN OR ZEAXANTHIN OR BOTH AND HOW MUCH?

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### Review Why is Zeaxanthin the Most Concentrated Xanthophyll in the Central Fovea?

Justyna Widomska <sup>1,\*</sup>, John Paul San Giovanni <sup>2,\*</sup> and Witold K. Subczynski <sup>3</sup>

- Very potent antioxidant-particularly in region of high oxygen tension and metabolism compared to lutein
- Zeaxanthin structure more stable in the lipid bilayer membranes
- Zeaxanthin is less predisposed to destruction than lutein when counteracting oxygen singlets

Nutrients 2020, 12, 1333; doi:10.3390/nu12051333

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### CAROTENOIDS INFLUENCE VISUAL FUNCTION

- Optical mechanisms
  - Glare Disability,
  - Color Contrast
  - Visual Range
  - Contrast Sensitivity
- Biological mechanisms
  - Glare Recovery
  - Neural Efficiency
  - Biomarker for Sleep Issues
  - Systemic Diseases

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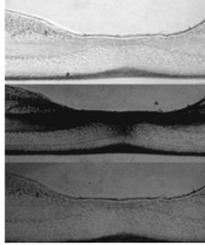
### WHY MEASURE THE MACULAR PIGMENT?

- Can predict your levels of carotenoid in brain!
- Is an indicator of health
- Is an indicator of eyes ability to fight disease
- Aids in evaluating benefits of supplements
- Best indicator of digital eye strain/computer vision syndrome
- Indicator of sleep health
- Blue light protection
- Because you need baseline!
- Do you expect to do blood work to lower a.c. cholesterol?
- Baseline data to know current status.
- Know what and how much is needed.
- Measure improvement
- Keep people compliant when they see their "eye health numbers" improve

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### MEASUREMENT OF MACULAR PIGMENT OPTICAL DENSITY

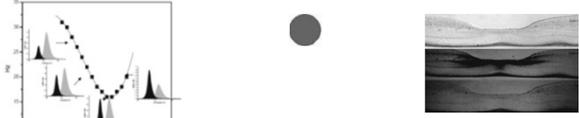
- Heterochromatic flicker Photometry- principle
- Macular pigment absorbs blue light (not green light)
- More macular pigment = longer time you see flicker
- Results are quantified via software



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### (SIMPLE EFFICIENT , APPROX 2 MINUTE TEST)

Centre Flickering Target



Heterochromatic flicker photometry is the most common form of technique used to measure MPOD  
It has excellent correlation with brain levels of coartenoids

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### THINGS I WANTED TO KNOW ABOUT MEASURING MPOD

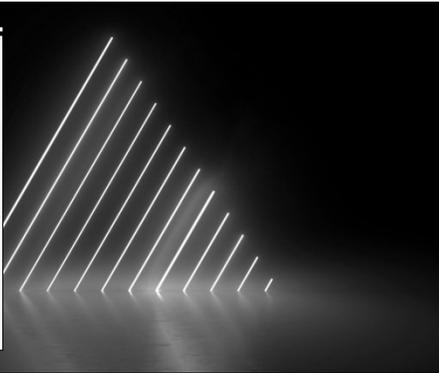
- Is it easy? Yes
- Do I need to perform in both eyes? No
- How long does it take? 2 minutes for testing
- Dominant eye? Any eye
- Can it measure changes? Yes



Davey PG et al. Clin Ophthalmol. 2016 Aug 29;10:1671-8. doi: 10.2147

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### MEASURING THE CAROTENOIDS - ZEAXANTHIN AND LUTEIN - THAT ARE CRITICAL TO THE EYE

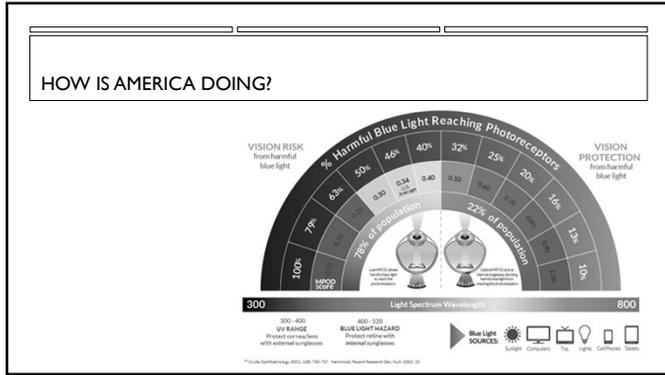


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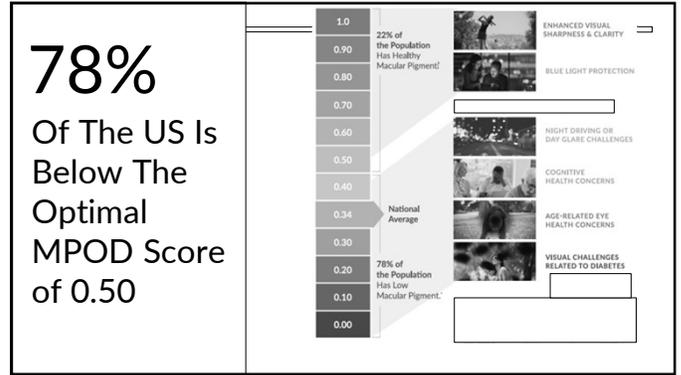
### DIRECT AND INDIRECT TECHNOLOGIES EXIST TO MEASURE CAROTENOIDS IN VIVO

	Raman Spectroscopy	Reflection Spectroscopy	Heterochromatic Flicker Photometry
Description	Measures skin carotenoids	Measures skin carotenoids	Directly measures macular pigment optical density (MPOD)
Products on the Market	Hand Scanner	Hand scanner	Eye measurements
Organ Tested	Skin	Skin	Eye
Carotenoids Measured	Skin Carotenoid Score	Skin Carotenoid Score	Zeaxanthin & Lutein
Carotenoids represented	Average of around 45	Average of around 45	Average of 3

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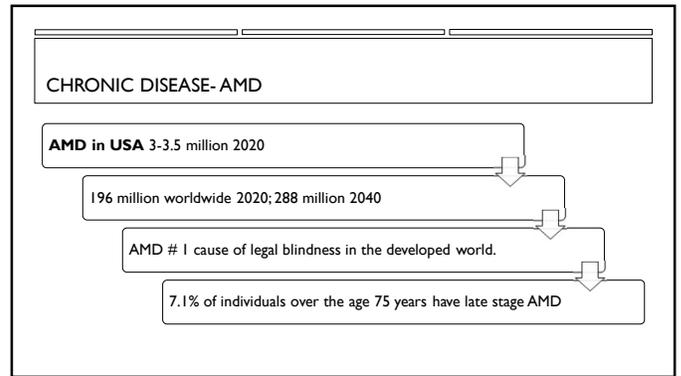
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### AMD CLASSIFICATION, HYPOTHESIS AND MORE

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AMD	
<p><b>Dry or non exudative</b></p> <p>Chronic visual acuity remains unchanged for long, some degree vn loss, may progress to severe blindness</p>	<p><b>Wet or exudative</b></p> <p>10-15% of AMD Vision dramatically reduced</p> <p><b>Advanced AMD</b> Geographic Atrophy Or choroidal neovascular growth</p>

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### CLASSIFICATION AND PATHOGENESIS

Although neat to classify as dry and wet

There is overlap of pathogenesis

The end stage of dry AMD continues into wet AMD

So important to understand that wet AMD pathogenesis continues in the background of dry AMD

Neovascular AMD-Anti VEGF

Dry AMD- Vitamins

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**Lutein + Zeaxanthin and Omega-3 Fatty Acids for Age-Related Macular Degeneration: The Age-Related Eye Disease Study 2 (AREDS2) Randomized Clinical Trial**

JAMA. 2013;309(19):2005-2015. Published online May 5, 2013. doi:10.1001/jama.2013.4997

- No true placebo- patients got AREDS formula
- Addition of lutein (10 mg)+zeaxanthin (2mg)+ EPA (650 mg) + DHA (350 mg) did not further reduce the risk of progression to Advanced AMD
- More lung cancer was noticed in β-carotene group compared to no β-carotene in current or past-smokers

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**POPULATION OF AREDS-2**

- Extremely educated
- Well nourished population

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**SUB-GROUP ANALYSIS**

Specialy lutein and zeaxanthin was most beneficial when the individuals were taking it had lowest level to begin with

Treatment	Main Effect	P Value
Lutein + zeaxanthin	Favors Treatment	.05
DHA + EPA	Favors Control	.74
Low-dose zinc	Favors Control	.32
Beta carotene	Favors Control	.31

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LOWER MPOD IS NOW ACCEPTED AS A MODIFIABLE RISK FACTOR TO AMD

**SUB-GROUP ANALYSIS**

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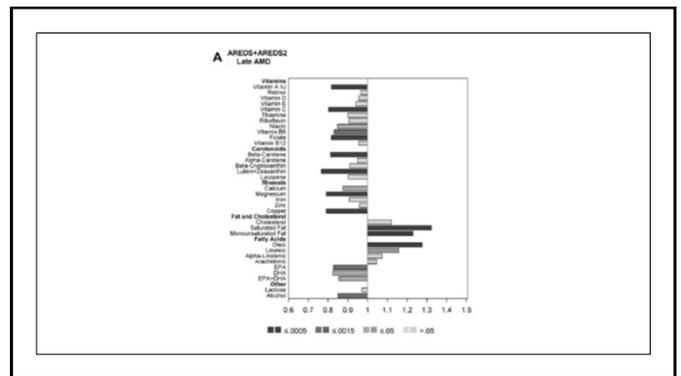
AMERICAN ACADEMY OF OPHTHALMOLOGY

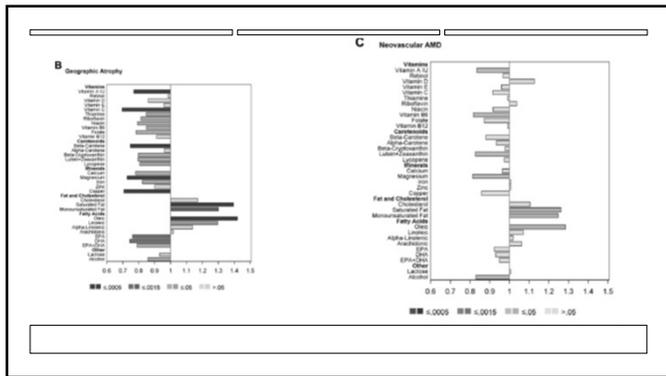
**Dietary Nutrient Intake and Progression to Late Age-Related Macular Degeneration in the Age-Related Eye Disease Studies 1 and 2**

Elvira Agrón, MA,<sup>1</sup> Julie Mares, PhD,<sup>2</sup> Traci E. Clemons, PhD,<sup>3</sup> Anand Swaroop, PhD,<sup>4</sup> Emily Y. Chew, MD,<sup>1</sup> Tiaman D.L. Keenan, BM BCh, PhD,<sup>1</sup> for the AREDS and AREDS2 Research Groups\*

*Ophthalmology* 2021;128:425-442

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### Imaging lutein and zeaxanthin in the human retina with confocal resonance Raman microscopy

Blinov U<sup>1</sup>\*, Evan W. George<sup>1</sup>, Gregory T. Rogers<sup>1</sup>, Aneta Gorosavlac<sup>1</sup>, Anubhar Ranganathan<sup>1,2</sup>, Fu-Yen Chang<sup>1</sup>, Lingta Shi<sup>1</sup>, Jeanne M. Frederick<sup>1</sup>, and Paul S. Bernstein<sup>1,2</sup>

<sup>1</sup>Department of Ophthalmology and Visual Science, Wharton Eye Center, University of Utah School of Medicine, Salt Lake City, UT 84143

Zeaxanthin	Lutein
<ul style="list-style-type: none"> <li>Mainly accumulates in the IPL, OPL, and ONL at the center of the human foveal pit</li> <li>Concentrates highly in Fovea centralis</li> <li>Fovea high risk of Light induced oxidative damage, singlet oxygen produced by AZE and A2PE and lipofuscin- Zeaxanthin better at quenching</li> </ul>	<ul style="list-style-type: none"> <li>Distributed more diffusely across the retina at a much lower concentration relative to zeaxanthin</li> <li>Evenly and low concentration across macula</li> </ul>

Take home "the current AREDS2" formula's 10 mg of lutein and 2 mg of zeaxanthin may not be enough and greater amounts may be needed.

www.pnas.org/cgi/doi/10.1073/pnas.1502793117

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### antioxidants

*Systematic Review*  
**A Systematic Review of Carotenoids in the Management of Age-Related Macular Degeneration**

Drake W. Lem<sup>1,2</sup>, Pinakin Gunvant Davey<sup>1,2,3</sup>, Dennis L. Gierhart<sup>2</sup> and Richard B. Rosen<sup>3</sup>

Neutralize  
Free radical species & reduce oxidative damage, oxidative injury

Absorb  
High energy light, prevent photooxidation of peroxyl radicals

Modulate  
Free radical concentrations by the antioxidant response

Ameliorate  
Oxidative damage to retinal cells

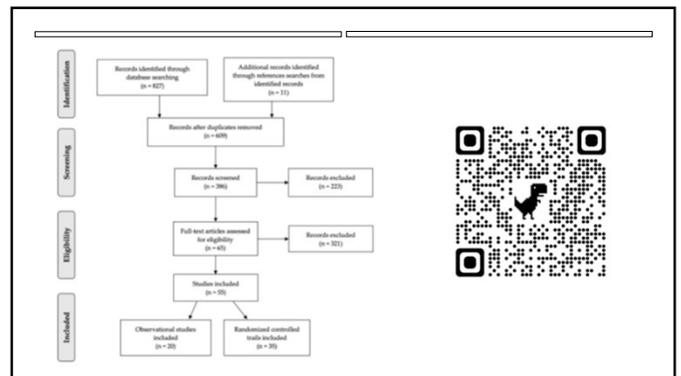
Protection  
Reduce oxidative damage to DNA, proteins & cell membranes

Macular carotenoids & neuroprotection

There is robust evidence all stages of AMD are helped by carotenoid vitamin therapy

Antioxidants 2021, 10, 1255. <https://doi.org/10.3390/antiox10081255>

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### SUMMARY OF BENEFITS OF CAROTENOIDS IN AMD

Increase in serum levels	Increase in MPOD	Enhanced central retinal functions mfERG	Slight benefits to BCVA
Contrast improvements	Glare improvements	Mesopic vision improvements	Risk reduction to progression

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### CASE 1

- Age 45, Vision 20/20 OU Family history of AMD. Ocular health normal, Fundus normal
- MPOD testing 0.22
- What next?

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### CASE 2

- Age 55 Vision 20/20 OU Family history of AMD. All ocular health normal except fundus OU small hard drusen OU
- MPOD testing 0.41
- What next?

- Would your management be different if MPOD 0.55 Why or Why not ?

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## APPROXIMATELY WHAT SHOULD A PERSON'S IMPROVEMENT LOOK LIKE?

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### WHAT CAN THE DOCTOR EXPECT?

- Herman study 2017
- Baseline and repeat measurements every six-months up to 24 months
- Carotenoid vitamin supplements
- Sample size 515 (98.8% completed the study)
- Absolute real-world clinical trial
  - Doctors decided 1 or two softgels on the basis of MPOD
  - Individuals with >0.5 MPOD one softgel

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### OVERALL RESULTS

Mean age 53.4 years	Baseline MPOD Reading	6m MPOD Reading	12m MPOD Reading	18m MPOD Reading	24m MPOD Reading
Mean	.2791	.3472	.4081	.4653	.5096
Std. Deviation	±.1260	±.1011	±.988	±.902	±.948
Range	.04 - .71	.10 - .72	.12 - .74	.13 - .73	.10 - .79
Mean % Increase	-	24.3%	46.2%	66.7%	82.6%

Initial MPOD Reading	6m MPOD Mean Increase	12m Mean Increase	18m Mean Increase	24m Mean Increase
<.20	171%	297%	421%	502%
.21-.30	91.2%	131.4%	166.6%	191.2%
.31-.40	29.2%	56.1%	72.6%	84.2%
.41-.50	9.4%	13.2%	31.1%	49.3%
Over .50	6.7%	11.9%	21.2%	20.4%
Overall Range	6.7%-171%	11.9%	12.2%	13.2%
Mean % Increase All Categories	24.3%	46.2%	66.7%	82.6%

An improvement of 0.12 MPOD is considered to be statistically significant

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### SO WHAT ELSE CAN YOU DO TO HELP YOURSELF

- Take the supplements with your large meal
- Make sure you have some healthy fats in your diet (carotenoids are fat soluble)
- Take your fish oil supplements at the same time (helps with absorption of carotenoids)
- Although not shown directly, individuals that have lower body fat percentage can have better MPOD uptake
- Exercise: increase HDL and may help with carotenoid transfer in blood stream

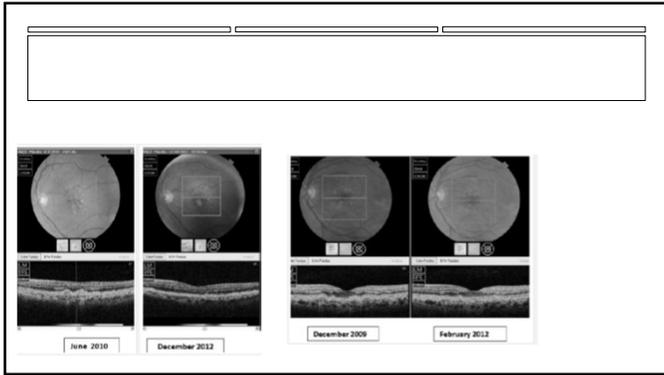
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### WHAT CAN DOCTORS EXPECT CLINICALLY?

Observed change in hard drusen	MPOD Change Categories			Totals n(%)
	< 15% change n(%)	15% - 30% change n(%)	> 30% change n(%)	
Improvement	3 (18.8%)	6 (35.3%)	44 (27.0%)	53 (27.0%)
Stable	13 (81.3%)	11 (64.7%)	116 (71.2%)	140 (71.4%)
Minor advancement	0 (0.0)	0 (0.0)	2 (1.2%)	2 (1.0%)
Notable advancement	0 (0.0)	0 (0.0)	1 (0.6%)	1 (0.5%)
Total stable or improved	16 (100%)	17 (100%)	163 (98.2%)	193 (98.5%)

Improvements in glare function  
Improvements in low contrast visual function

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### WHAT CAN WE DO DIFFERENT THAN AREDS?

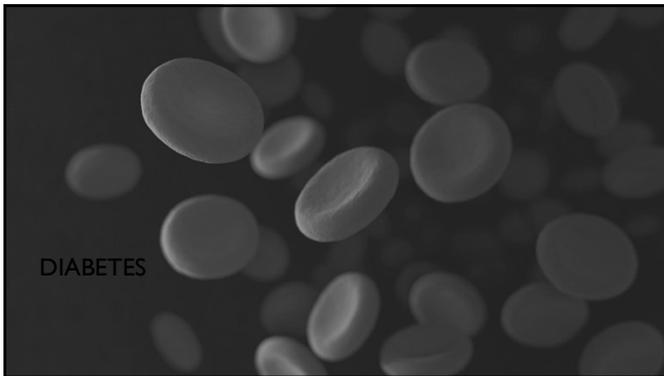
**Testing**

- Measure MPOD
- Measure functional tests
  - Contrast sensitivity
  - Color Contrast
  - Glare function

**Management**

- More amounts of carotenoids
- NSF certification
- Omega-3 Enhances carotenoid absorption
- Measure baseline MPOD Check it every 3 months
- Check Functional vision tests Monitor compliance  
Monitor uptake
- MPOD values greater than 0.5 du  
If baseline is already at .5 or higher increase it by 0.15 du

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### CASE: DIABETES EXAM-WHAT'S YOUR DIAGNOSIS?

Courtesy of Pinakin Davey OD, PhD

- 49 YO Asian male,
- HO DM type 2, 10 years "recently" not compliant with meds
- HO HTN x10 years
- Restarted metformin recently but has side effect of diarrhea
- Blood pressure today 168/96

What was his MPOD 0.28  
Dominant eye

Diabetic Eye Exam Standard of Care

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Patient worried enough about change in vision that he returned for 1 Month follow-up visit

Foveal Avascular Zone measurements OCT-A done 1 month later

OD

OS

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FAZ 0.341 mm<sup>2</sup>

FAZ 0.316 mm<sup>2</sup>

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### WHAT WOULD BE A GOOD PLAN FOR HIM

- Adding MPOD testing
- Revealed changes from early diabetic eye disease which otherwise would have been missed
- Motivated patient to follow-up with 1 month visit
- Allowed for detailed discussion about diet, lower blood pressure
- Patient began diabetes nutritional supplements

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### THE DIABETES VISUAL FUNCTION SUPPLEMENT STUDY (DIVFUSS)

The Diabetes Visual Function Supplement Study (DiV FuSS) was designed to test the effects of a novel, multi-component nutritional supplement on visual function. Participants included patients with both type 1 and type 2 diabetes.

- *British Journal of Ophthalmology*
  - six-months
  - placebo controlled

#### CLINICAL STUDY RESULTS WITH DVS

Randomized, placebo-controlled study demonstrated:

- 21% improvement in color vision\*\*
- 19% improvement in contrast sensitivity (easier to read ink on an newspaper)\*\*
- 12% improvement in central and peripheral vision\*\*

\*\*Measurements were made without significantly altering final blood glucose but

Carotenoid vitamin supplement benefits individuals with diabetes and diabetic eye disease

BJO 2016 Feb; 100(2):227-34

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### NIGHT VISION AND CAROTENOIDS

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**nutrients** MDPI

Communication

### Night Vision and Carotenoids (NVC): A Randomized Placebo Controlled Clinical Trial on Effects of Carotenoid Supplementation on Night Vision in Older Adults

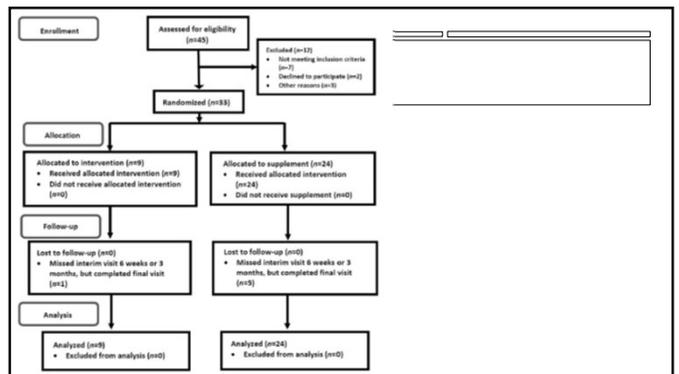
Stuart Richer <sup>1,2,\*</sup>, Steven Novil <sup>1</sup>, Taylor Gullett <sup>2</sup>, Avni Dervishi <sup>2</sup>, Sherwin Nassiri <sup>2</sup>, Co Duong <sup>2,3</sup>, Robert Davis <sup>3</sup> and Pinakin Guvant Davey <sup>4-6</sup>

**Aim:**  
Can carotenoid improve night vision and comfort in driving in individuals that complain of nighttime driving issues?

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Active Ingredients	Amount per Serving
Zeaxanthin	14 mg
Lutein	7 mg
Vitamin A	2500 IU
Vitamin C	60 mg
Vitamin D	1000 IU
Vitamin E	60 IU
Vitamin B6	2 mg
Folic Acid	400 mcg
Vitamin B12	6 mcg
Zinc	15 mg
Selenium	70 mcg
Manganese	2 mg
Fish Oil	150 mg
Coenzyme Q10	15 mg
Bilberry	15 mg
Berry Anthocyanin Extract	15 mg
Alpha Lipoic Acid	10 mg
Mixed Tocopherols	6 mg

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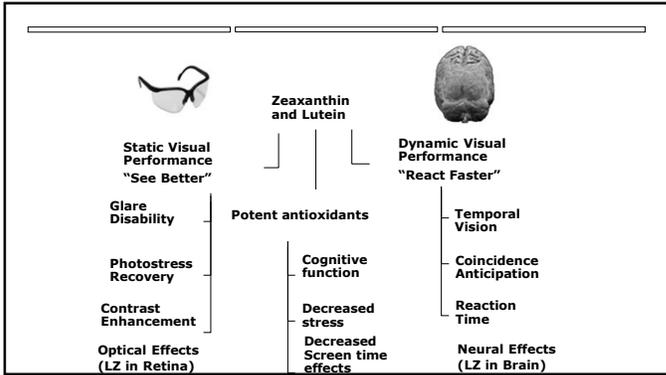


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**RESULTS**

- Improvements in contrast sensitivity with glare in both eyes
- Monocularly tested glare recovery time improved 2.76 and 2.54 s, respectively, ( $p = 0.008$  and  $p = 0.02$ ),
- decreased preferred luminance required to complete visual tasks
- Improvements in UFOV scores of divided attention ( $p < 0.001$ ) and improved composite crash risk score ( $p = 0.004$ ) were seen in the supplemented group.
- The placebo group remained unchanged.

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**GLOBAL SUMMARY**



- It is tough to get perfect nutrition everyday.
- Nutritional supplements can be a reliable way of augmenting your diet.
- Carotenoids are important for vision
- Maybe even more for health than we thought!
- Measuring MPOD allows for a trackable measure in various health and disease states- compliance and bioavailability measure.
- An ounce of prevention...

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**THANK YOU!**

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