

Age-Related Eye Disease Study 2
The Lovon, Zeaxanthin and Omega 3 Supplementation Trial

What have the Age-Related Eye Disease Study (AREDS) and AREDS2 Taught Us?

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On Behalf of the AREDS and AREDS2 Research Groups

Presenter has No Financial Disclosures



The Age-Related Eye Disease Study

AREDS

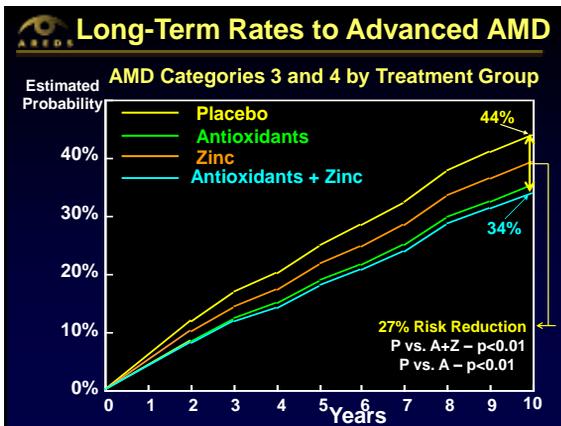
Supplements Studied

Antioxidants – Daily Oral Dose

- Vitamin C – 500 mg
- Vitamin E – 400 IU
- Beta-carotene – 15 mg (25,000 IU vit A)

Zinc

- Zinc – 80 mg
- Copper – 2 mg



AREDS

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AREDS Formulation Recommended:

- patients with intermediate AMD (bilateral large drusen)
- patients with advanced AMD in one eye
- NOT for current smokers

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AREDS Formulation Adverse Effects:

- Beta-carotene increased the risk of lung cancer and its associated mortality
- High levels of zinc resulted in increased hospitalizations for genitourinary causes (mostly hypertrophy of the prostate)

Who should take the AREDS formulation?

Should offsprings of affected individuals with AMD take the AREDS formulation?

- No, unless they have bilateral large drusen or advanced AMD in one eye
- AREDS formulation does not prevent early AMD from progressing along the mild to the moderate severity of AMD

Who should take the AREDS formulation?

Should the AREDS formulation be taken for general eye health?

- No, unless they have bilateral large drusen or advanced AMD in one eye
- AREDS formulation does not prevent cataract progression or early AMD progression

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Lutein/Zeaxanthin



Spinach, Kale and Collard Greens

Omega-3 Long-chain Polyunsaturated Fatty Acids (LCPUFAs) (DHA/EPA)



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Study Design

Primary Objective:

- Test effects of adding
 - Lutein/Zeaxanthin (10mg/2 mg)
 - Omega-3 Long-Chain Polyunsaturated Fatty Acids (DHA & EPA=1 g total)
 - Combination

Adding to the AREDS Formulation on AMD outcomes

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Study Design

Inclusion Criteria

- Bilateral Large Drusen or Late AMD in One Eye



Large Drusen



GA

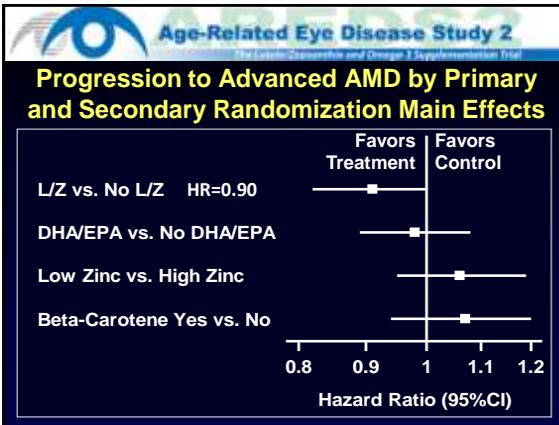
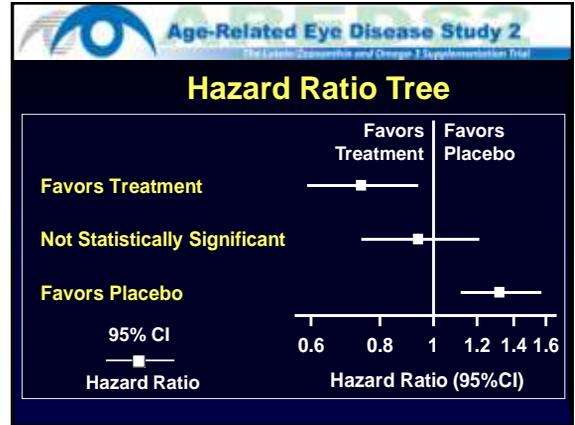


NV AMD

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AREDS Formulation

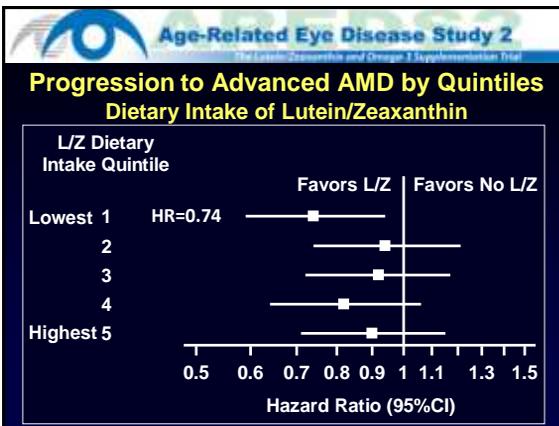
- Vitamin C (500 mg)
- Vitamin E (400 IU)
- Beta Carotene (15 mg)
- Zinc (80 mg zinc oxide)
- Copper (2 mg cupric oxide)



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Comparison of Lutein/Zeaxanthin vs. no Lutein/Zeaxanthin

Advanced AMD: HR: 0.90 P=0.04
10% additional reduction in the risk of progression to AAMD with lutein/zeaxanthin
Other HRs were not statistically significant



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Lutein/Zeaxanthin vs. no Lutein/Zeaxanthin Lowest Quintile of Dietary Lutein/Zeaxanthin

- Lowest Quintile – 26% Reduction in Risk (p<0.01)
- Higher Quintiles – Not Statistically Significant

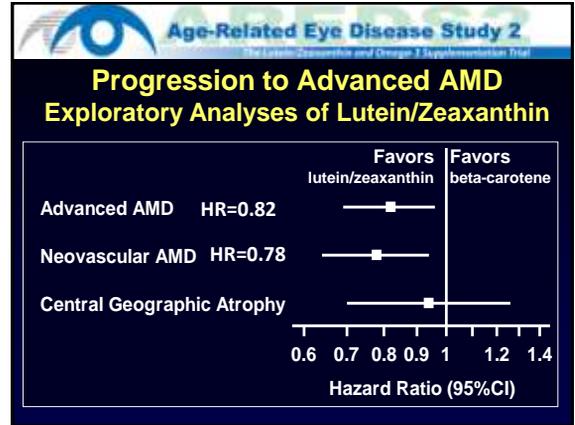
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Compare AREDS formulation with lutein/zeaxanthin substituted for beta-carotene vs. AREDS formulation

Lutein/Zeaxanthin plus AREDS Formulation minus Beta-Carotene
N = 1114 eyes

vs.

AREDS Formulation with Beta-Carotene
N = 1117 eyes



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L/Z plus AREDS Minus Beta-Carotene vs. AREDS (with Beta-Carotene)

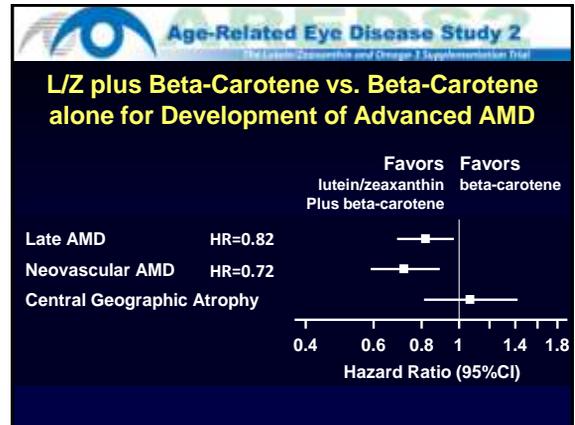
Lutein/Zeaxanthin vs. Beta-carotene

Advanced AMD: HR: 0.82 P=0.02
18% reduction in the risk of progression to AAMD with lutein/zeaxanthin

Neovascular AMD: HR: 0.78 P=0.01
22% reduction in the risk of progression to neovascular AMD with lutein/zeaxanthin

Not statistically significant for CGA

Favors Lutein/Zeaxanthin



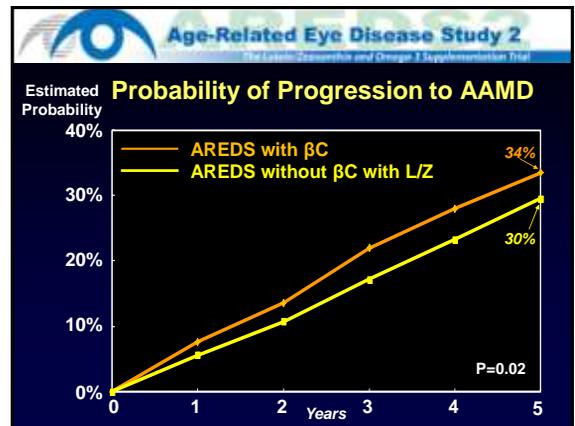
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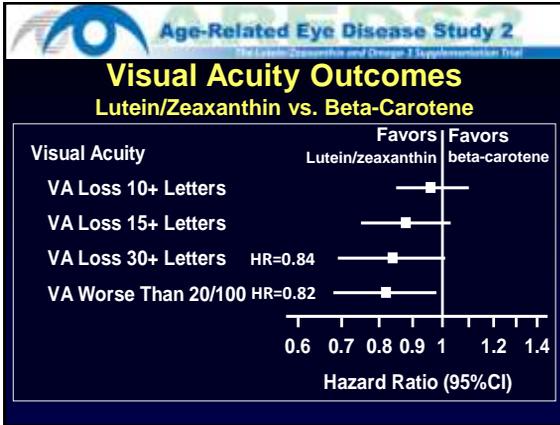
Lutein/Zeaxanthin plus Beta-carotene vs. Beta-carotene

Advanced AMD: HR: 0.82 P=0.02
18% reduction in the risk of progression to AAMD with lutein/zeaxanthin + beta-carotene

Neovascular AMD: HR: 0.72 P=0.002
28% reduction in the risk of progression to neovascular AMD with lutein/zeaxanthin + b-carotene

Not statistically significant for CGA





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L/Z plus AREDS Minus Beta-Carotene vs. AREDS with Beta-Carotene for Vision

Vision loss of 30+ letters compared with baseline: HR: 0.84 P=0.06
16% reduction in the risk of progression to AAMD with lutein/zeaxanthin

Visual Acuity <20/100: HR: 0.82 P=0.03
18% reduction in the risk of progression to neovascular AMD with lutein/zeaxanthin

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Safety Outcome: Lung Cancer

Beta-carotene Main Effect

β-Carotene (N = 1348)	No β-Carotene (N = 1341)	P-value
23 Cases (2.0%)	11 Cases (0.9%)	0.04

Increased risk of lung cancer with β-Carotene
91% former smokers (quit > 1 year prior to randomization)

Analysis excludes smokers

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Safety Outcome: Lung Cancer

Lutein/Zeaxanthin Main Effect

Lutein/Zeaxanthin (N = 2123)	No Lutein/Zeaxanthin (N = 2080)	P-value
33 Cases (1.5%)	31 Cases (1.5%)	0.80

No increased risk of lung cancer
62% were former smokers, equal in both arms

Analysis includes smokers

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Conclusions

- Although no statistically significant results from primary analyses, the main effect of lutein/zeaxanthin demonstrated 10% reduction of AAMD
- ~ 20% reduction in the risk of progression to AAMD of L/Z beyond the effects of AREDS supplement for 1) the lowest dietary intake of L/Z, 2) for neovascular AMD, 3) especially in the head-to-head comparison L/Z vs. beta-carotene

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Conclusions

- No effect with DHA/EPA (omega-3 fatty acids) main effect or primary analyses—still consider a diet replete with fish
- Secondary randomization suggests no differences in the progression to AAMD for elimination of beta-carotene or lowering zinc dose

Conclusions

- Improve the safety of the AREDS supplements by removing beta-carotene to decrease the risk of lung cancer in smokers and former smokers who compose 2/3 of persons with AMD.
- Considering the totality of evidence, lutein/zeaxanthin may be an appropriate carotenoid substitution for beta-carotene in the AREDS formulation

AREDS2 Formulation

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

Recognition

We want to thank the following:

- AREDS2 Participants
- AREDS2 Research Team