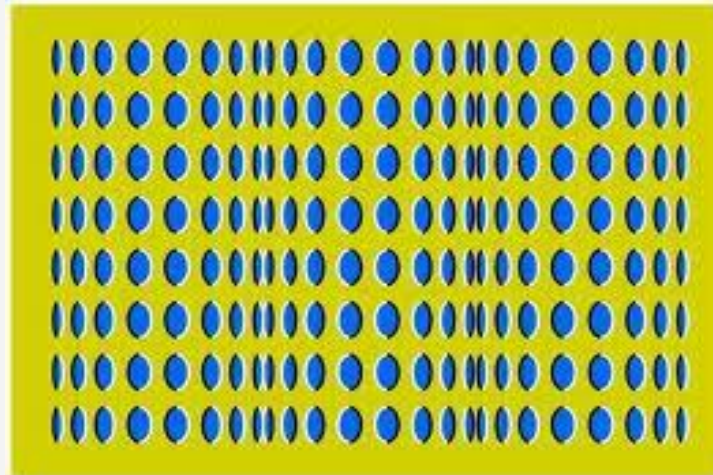


Seeing is believing – the case for carotenoids

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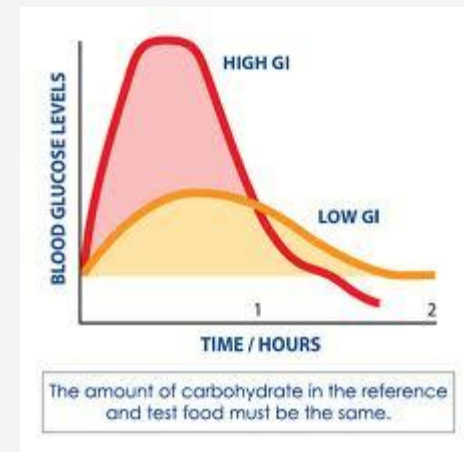


Background



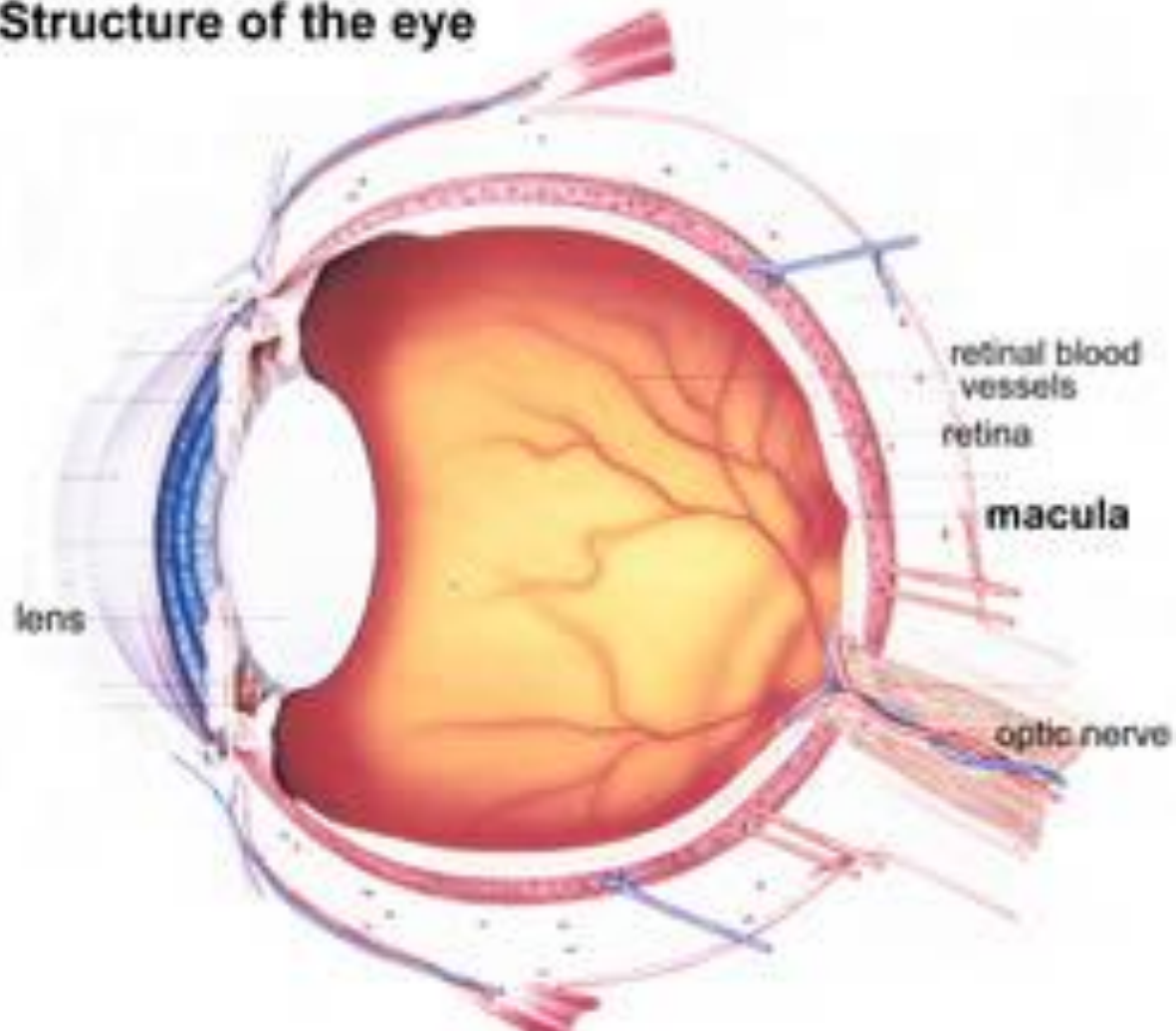
Key nutrients = Healthy balanced diet

- Lutein (and zeaxanthin)
- Vitamin C
- Vitamin E
- Zinc
- Omega-3 fatty acids (especially long-chain)
- Low Glycemic Index foods



Structure of the eye

Structure of the eye

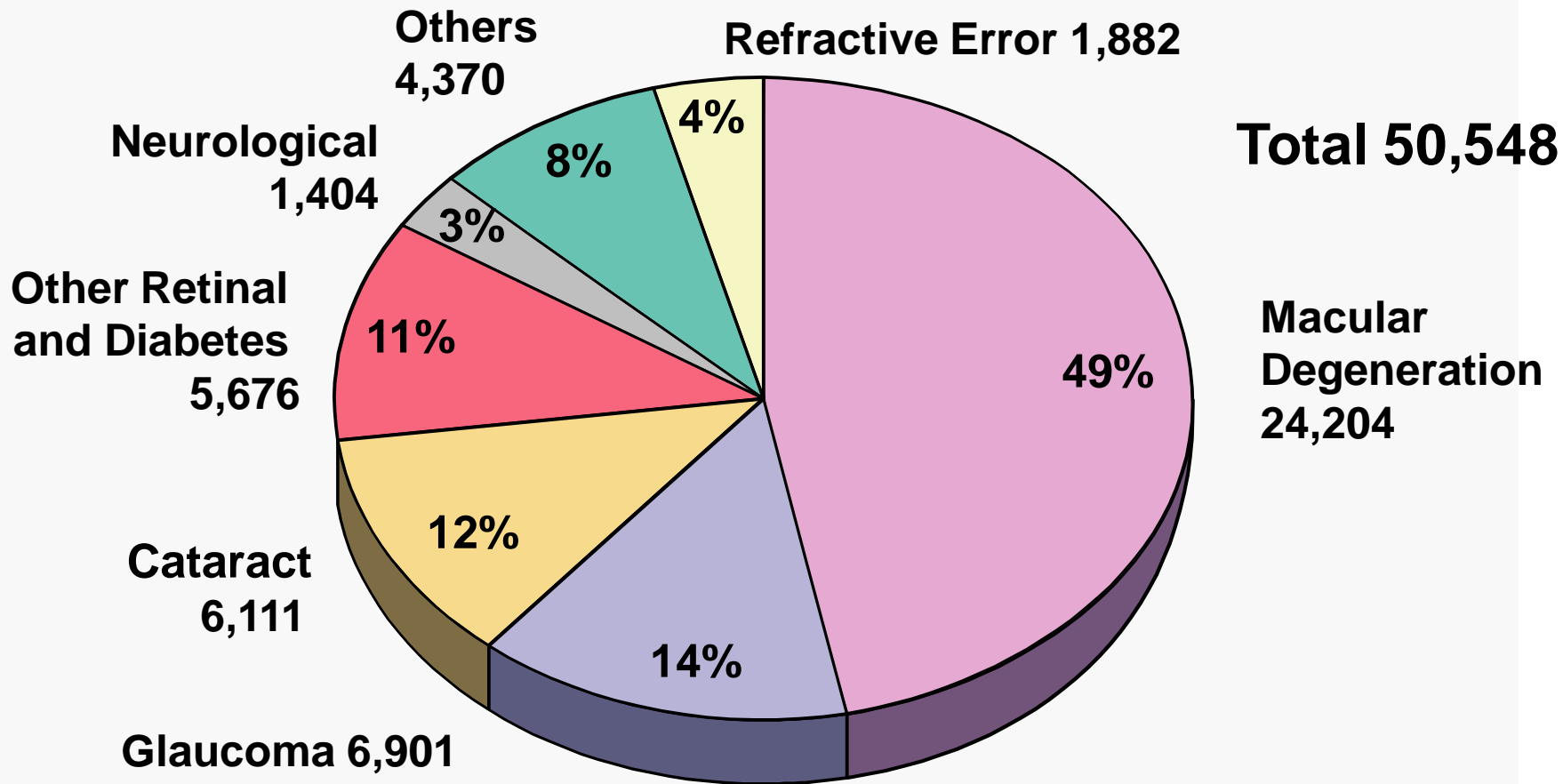


Age-related Macular Degeneration

- Two recognised **Late** forms:
- more frequent (2/3) **neovascular** – new blood vessels invade inner retina – haemorrhage and cause a scar on the retina
- less frequent (1/3) **atrophic** – progressive loss of macular pigment



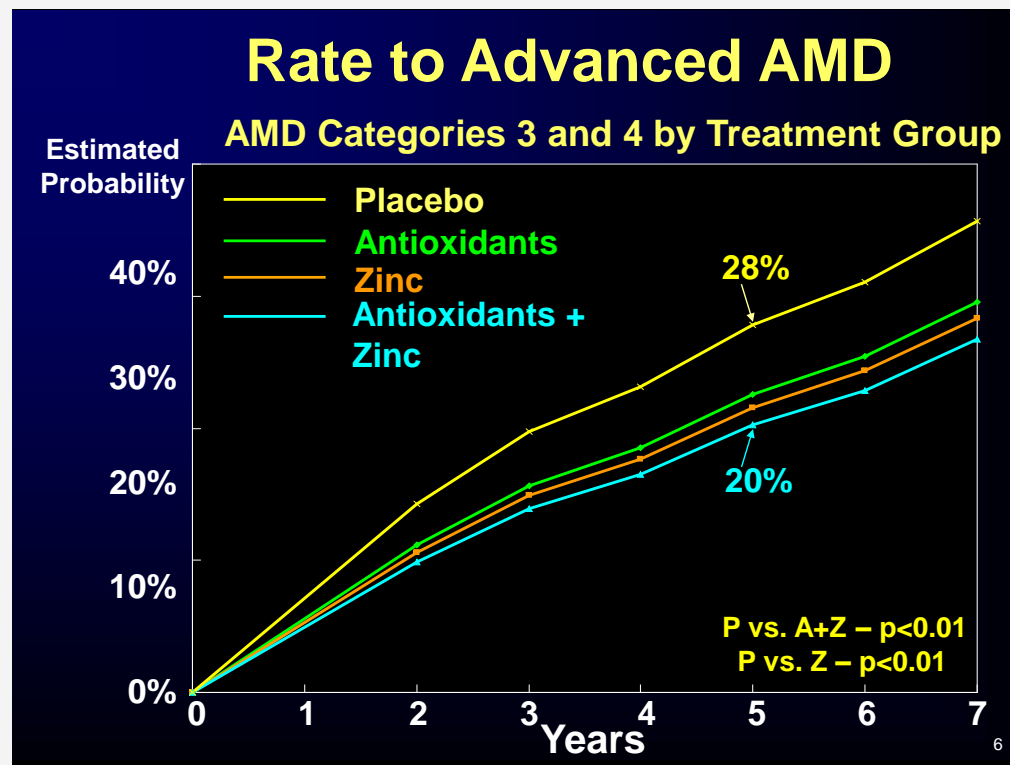
Blindness: <6/60 in Australia



MVIP and BMES

Blue Mountains Eye Study/ Visual Impairment Project data, incorporating contribution from nursing home residents, pooled & standardised to 2004 Australian population. Prevalence early ARM 4%; after 5 years follow-up (incidence): 8% AMD.

AREDS: Randomised Controlled Trial of antioxidants and zinc



Antioxidants: Vit C (500mg), B-carotene 15mg, Vit E 400 IU, Zinc 80mg



Rotterdam Cohort Study, n=4765 at baseline with dietary data

Table 4. Risk of Age-Related Macular Degeneration by Category of Combined Intake of 4 Predefined Antioxidant Nutrients (Vitamins C and E, Beta Carotene, and Zinc)

	Category of Dietary Intake*		
	Low (n = 466)	Middle (n = 3270)	High (n = 434)
Cases of age-related macular degeneration, No. (%)	76 (16.3)	442 (13.5)	42 (9.7)
Hazard ratio (95% confidence interval)			
Unadjusted	1.31 (1.03-1.67)	1.00	0.65 (0.48-0.89)
Age- and sex-adjusted	1.23 (0.97-1.58)	1.00	0.65 (0.49-0.93)
Fully adjusted†	1.20 (0.92-1.56)	1.00	0.65 (0.46-0.92)

*Categories were defined by using the median energy-adjusted daily intake per nutrient as a cutoff value and classifying above-median intake of all nutrients as high intake and below-median intake of all nutrients as low intake. Cutoff values were 114 mg for vitamin C, 13 mg for vitamin E, 3.6 mg for beta carotene, and 9.6 mg for zinc.

†Adjusted for age, sex, body mass index, smoking status, pack-years of smoking, systolic blood pressure, atherosclerosis composite score, serum total cholesterol, and alcohol intake.



Antioxidants and eye disease

- Retina susceptible to oxidative stress: high exposure to oxygen, high concentration of PUFA's, exposure to light
- Phagocytosis of retinal pigment epithelium: oxidative stress
- Therefore antioxidants likely to be important for healthy cell function
- Macula also concentrated in carotenoids: lutein and zeaxanthin and zinc
- Zinc is a co-factor for antioxidant enzymes: superoxide dismutase and catalase



Relationship between AMD and CVD and stroke

Among people <75 years:

- early AMD predicted doubling of CVD mortality (RR 2.32, 95%CI 1.03-5.19)
- late AMD predicted fivefold CVD mortality (RR 5.57, 95%CI 1.35-22.99)
- late AMD predicted 10-fold higher stroke mortality (RR 10.21, 95%CI 2.39-43.6)

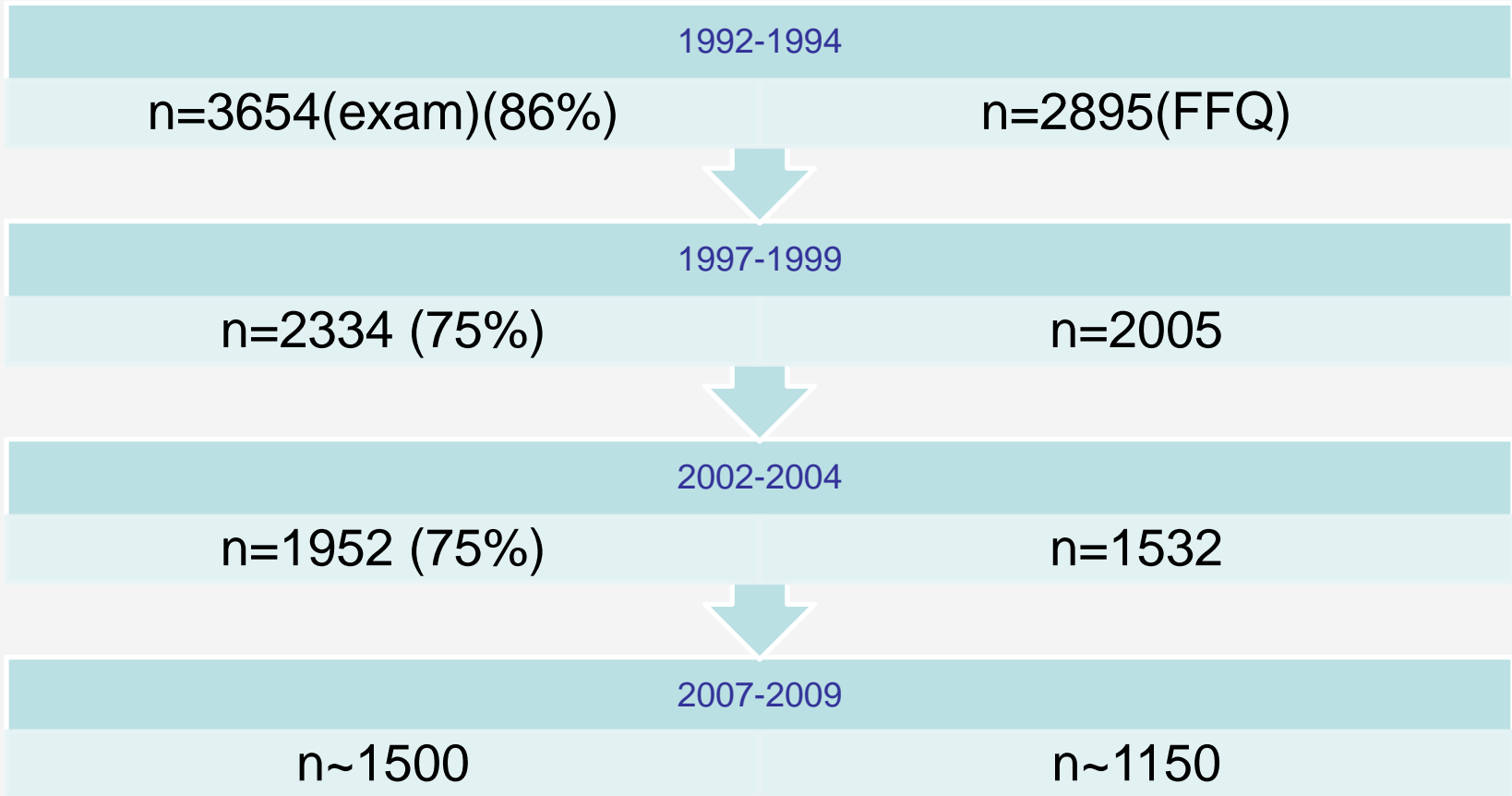
(Tan et al, BJOphtal, 2008)



Blue Mountains Eye Study

- Population based cohort study of residents 49 years and older
- Complete census (door-knock) of 2 postcode areas in the Blue Mountains.
- Baseline: 1992-94 (n=3654)
- Population similar to Australian population older people, except higher SES and more Caucasians.
- FFQ used to measure dietary intake in ~ 80% of people with clinical examinations

Study population



15 year mortality: n=1047 (28.7%)



Survey questions

- Socio-demographic
- Medications
- Measured weight, height, BP
- SR health status (CVD, cancer, etc)
- Mini-mental
- Eye examination
- Blood assays: lipids, glucose, Hb, Hcyst
- Dietary data: FFQ



Analyses

- Nutrient analyses: NUTTAB , fatty acids (Man et al, US Carotenoid Database)
- Logistic regression: odds of AMD (and other health outcomes), by quintiles of diet intake at baseline, adjusted for confounding variables
- Data linked to Australian National Death Index

Dietary antioxidants and the long-term incidence of age-related macular degeneration

Main findings

- People with highest tertile of lutein and zeaxanthin had 65% reduced risk for neo-vascular AMD (RR 0.35; CI 0.13-0.92), compared to the remainder
- People with highest decile zinc intake reduced risk for early AMD (0.54; 95% CI 0.3-0.97) (Highest decile >15.8mg/day)
- People with highest tertile of vegetables, reduced risk of any AMD (0.64; 95% CI 0.41-0.98)





Fish and nuts

Incident cases of age-related macular degeneration (ARM) in BMES (5 yrs)

- People in highest quintile of n-3 PUFA vs the lowest quintile n-3 PUFA had 60% reduced risk of developing incident ARM over 5 years (OR 0.4, CI 0.2-0.8)

(Chua, Flood, Mitchell, Archives Ophthalmol 2006)

	Odds of 5-year incident	
	Early ARM	Late ARM
Total Fish* §		
<1 /month	1.00 (ref)	1.00 (ref)
≥1 /week	0.58 (0.37-0.90)	0.44 (0.16-1.21)
≥3 /week	0.62 (0.38-1.03)	0.25 (0.06-1.00)
Nuts §		
Never	1.00 (ref)	1.00 (ref)
<1 /week	0.80 (0.52-1.25)	0.82 (0.29-2.34)
≥1 /week	0.79 (0.46-1.34)	0.55 (0.14-2.16)

§ adjusted for age, sex, current smoking, antioxidants (diet & supplements) * Includes sardines, tuna, other fish



10-year cohort

(Tan, Wang, Flood, Mitchell; Arch Ophthal. 2009)

- 1 serve fish /wk and risk early AMD = 0.69 (0.49-0.96);
- <median linoleic acid RR=0.57 (0.49-0.98),
- not sig among >median linoleic acid

Quartiles of long-chains omega-3s	Early AMD	
Linoleic acid, Q1 and Q2 <i>P trend=0.01</i>	1	1.0
	2	0.76(0.46-1.25)
	3	0.50(0.29-0.86)
	4	0.48 (0.27-0.83)
Linoleic acid Q3 and Q4	1	1.0
	2	1.3(0.71-2.37)
	3	0.98(0.52-1.82)
	4	1.08 (0.59-1.97)



Nuts and AMD, 10 year cohort

Table 6. Associations Between Baseline Dietary Intake of Nuts and 10-Year Incident Early AMD in the BMES

AMD Stage/Lesion	Servings per Week ^a	No. of Outcomes/ No. at Risk	Adjusted RR (95% CI) ^b
Early AMD	<1	85/517	1 [Reference]
	1-2	76/818	0.65 (0.47-0.91)
	≥3	59/590	0.73 (0.51-1.06)
<i>P</i> value for trend			.43
Indistinct soft or reticular drusen	<1	76/521	1 [Reference]
	1-2	61/821	0.61 (0.42-0.87)
	≥3	46/595	0.66 (0.44-0.98)
<i>P</i> value for trend			.23
Pigmentary abnormality	<1	114/483	1 [Reference]
	1-2	135/772	0.74 (0.56-0.98)
	≥3	95/558	0.75 (0.56-1.02)
<i>P</i> value for trend			.28

Abbreviations: AMD, age-related macular degeneration; BMES, Blue Mountains Eye Study; CI, confidence interval; RR, relative risk.

^aMedian number of servings per week for each category was 0.14 serving/wk for less than 1; 1 serving/wk for 1 to 2; and 5 servings/wk for at least 3.

^bAdjusted for age, sex, and smoking. Boldface type indicates significant values.



Translating research into practice

- Review the evidence
- Consider current dietary guidelines and nutrient content of foods
- What's feasible / realistic?

Lutein and zeaxanthin

Food (serve)	Lutein and zeaxanthin (μg) (no current RDI; mean intake BMES 914 μg)
Spinach, cooked $\frac{1}{2}$ cup	5282
Broccoli, cooked, medium serve	1669
Green beans, $\frac{1}{2}$ cup	525
Egg, enriched, 1 medium*	179
Tomatoes, 75g	97
Egg, regular, 1 medium	28



USDA national nutrient database, release 1998

* based on Australian fortified product

Lutein and zeaxanthin, main food sources, BMES

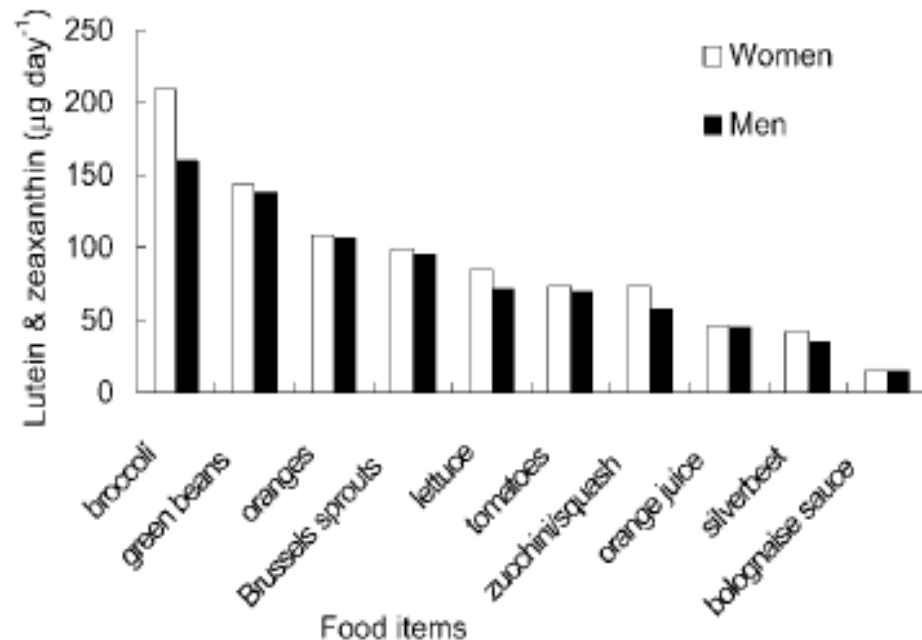
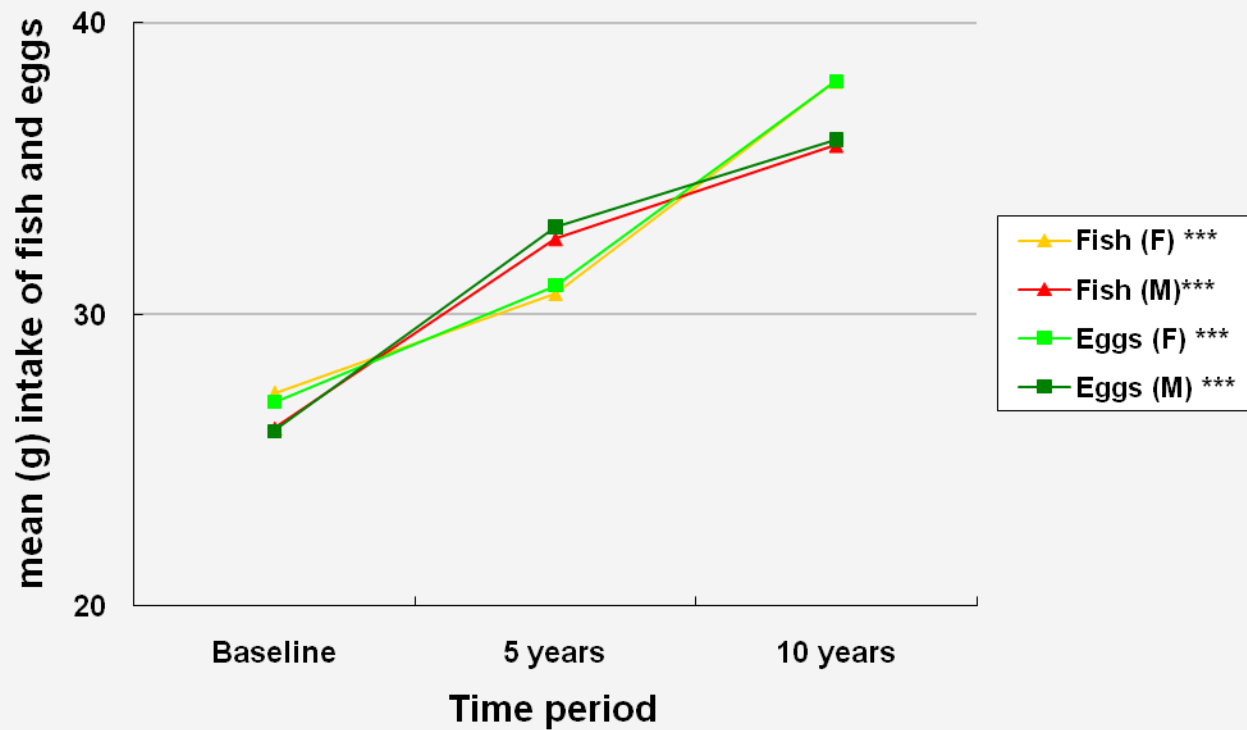


Fig. 4 The main contributors to mean intakes of lutein and zeaxanthin ($\mu\text{g day}^{-1}$) in women and men

Mean intake = 914ug

Fish and Eggs

- Both increased significantly

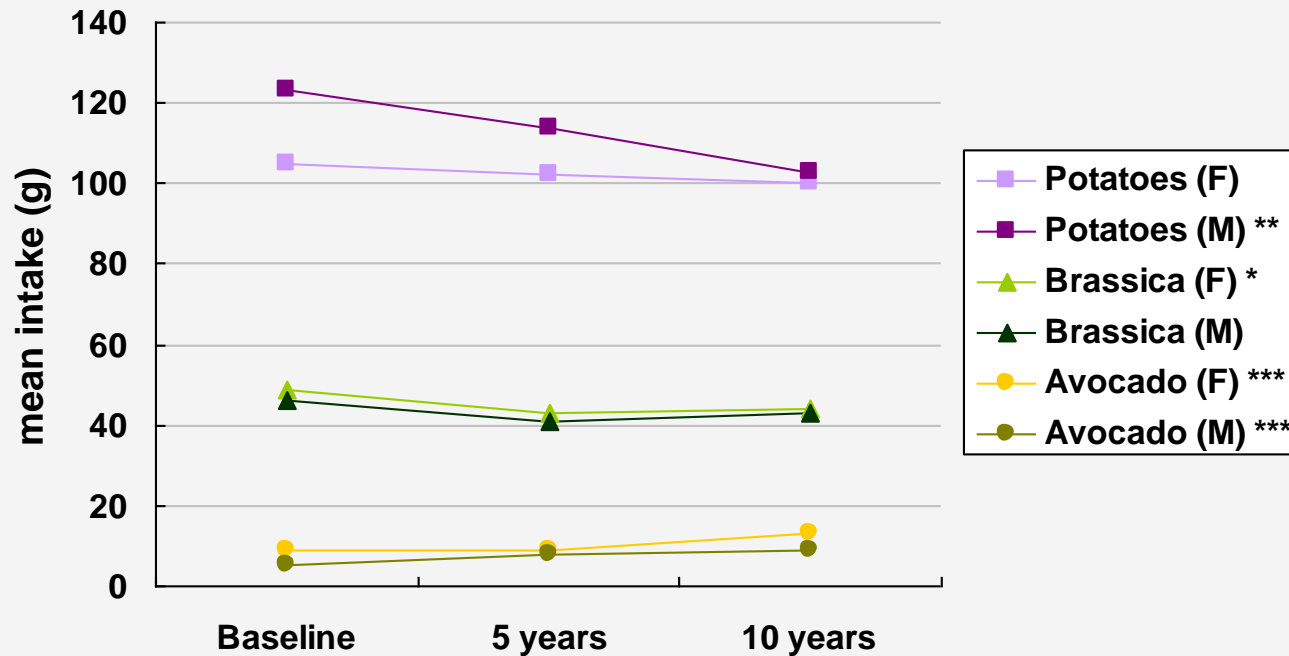


*** $p < 0.0001$



Vegetables

- No change in mean intake of veg's over 10 years



* $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$

Summary recommendations

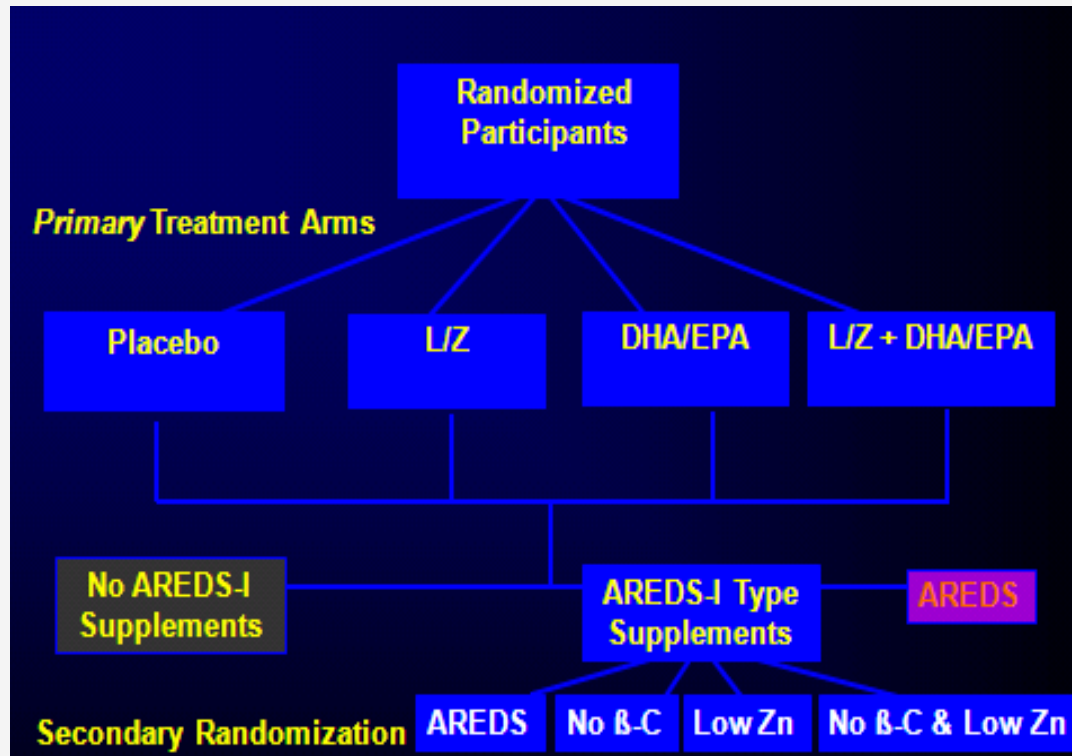
1. Eat **fish** regularly, about twice a week (especially oily fish types with higher omega-3 concentrations, such as salmon).
2. Consume plenty **of vegetables and fruit**. Follow the current dietary guidelines of 5 serves of vegetables and 2 fruit. Include a variety of vegetables, especially green leafy vegetables.
4. Include **nuts and seeds** 1-2 times per week, higher in PUFA and mono-unsaturated fatty acids.
5. Include 3-4 small serves of **lean red meat** in the diet as an excellent source of highly bioavailable zinc.
6. Choose **low GI, high fibre foods** in a balanced diet of moderate carbohydrate intake. Examples include wholegrain breads and cereals, dairy, legumes and most fruit.
7. Consider important sources of lutein in the diet. These include green leafy vegetables, and also found in enriched **eggs** (which also contain omega-3 PUFA).
8. And what about butter vs margarine? Butter increases the saturated fat concentration of the diet. **Use margarines / oils high in omega-3**, and include alternative sources of fat, such as olive oil or linseed (flaxseed oil).

Sustainable Public Health Messages

- Grow your own silverbeet
- Consume variety of veg's and fruit, in season
- Eat fresh foods, with limited processed foods (e.g. wholegrains)
- Eat small serves of lean red meat
- Include fish (canned ok)
- Include alternative sources of protein: eggs and nuts



Seeing is believing?



Lutein/zeaxanthin 10mg/2mg (or L/Z placebo) and two soft-gel capsules (DHA/EPA 350mg/650mg or DHA/EPA placebo).

Acknowledgments

Other investigators

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