

Appendix Table 3. Efficacy of Multivitamin and Mineral Supplement Use in Primary Prevention of Cataracts and Age-Related Macular Degeneration\*

Study (Reference)	Disease End Point	Study Supplement†	Participants, n‡				Disease Events, n‡			Prevalence of Disease End Point		Unadjusted Odds Ratio (95% or 99% CI) §	Change in Outcome Measure		Comment
			Total	Received Supplements with Specified Nutrients	Received Supplements without Specified Nutrients	All Participants	Received Supplements with Specified Nutrients	Received Supplements without Specified Nutrients	Received Supplements with Specified Nutrients	Received Supplements without Specified Nutrients	Treatment Group		Placebo Group		
Linxian General Population Trial: cataracts (22)	Prevalence of nuclear cataracts	Retinol + zinc	3249	1628	1621	–	–	–	0.120	0.151	0.77 (0.58–1.02)	–	–		
		Riboflavin + niacin		1623	1626	–	–	–	0.107	0.169	Overall, 0.59 (0.45–0.79); 0.99 (0.62–1.59) in persons age 55–64 y; 0.45 (0.31–0.64) in persons age 65–74 y	–	–		
		Vitamin C + molybdenum		1654	1595	–	–	–	0.121	0.150		0.78 (0.59–1.04)	–	–	
	β-Carotene + selenium + α-tocopherol		1617	1632	–	–	–	0.146	0.125	1.19 (0.90–1.59)		–	–		
	Prevalence of cortical cataracts	Retinol + zinc		1628	1621	–	–	–	0.342	0.325	1.08 (0.92–1.27)	–	–		
		Riboflavin + niacin		1623	1626	–	–	–	0.342	0.325	1.08 (0.92–1.27)	–	–		
		Vitamin C + molybdenum		1654	1595	–	–	–	0.325	0.342	0.92 (0.79–1.09)	–	–		
		β-Carotene + selenium + α-tocopherol		1617	1632	–	–	–	0.330	0.338	0.96 (0.82–1.13)	–	–		
		Prevalence of posterior subcapsular cataracts	Retinol + zinc		1628	1621	–	–	–	0.008	0.013	0.59 (0.31–1.14)	–	–	
Riboflavin + niacin				1623	1626	–	–	–	0.016	0.006	2.64 (1.31–5.35)	–	–		
Vitamin C + molybdenum			1654	1595	–	–	–	0.011	0.009	1.25 (0.65–2.38)	–	–			
	β-Carotene + selenium + α-tocopherol		1617	1632	–	–	–	0.013	0.008	1.56 (0.81–3.00)	–	–			

MONMD (26)	Acuity of left eyes, distance visual acuity [logMAR]	β-Carotene + vitamin E + vitamin C + zinc picolinate + selenium + vitamin B <sub>2</sub> + chromium + non-vitamin/mineral nutrients vs. placebo	71	39	32	–	–	–	–	–	–	–	From 0.17 to 0.19 logMAR	From 0.26 to 0.35 logMAR	No difference between randomized groups in refraction, metamorphosis, and Lens Opacities Classification System II readings on nuclear color, nuclear opalescence, and posterior subcapsular opacities; unexpected cortical cataractogenic effect for right eyes in the multivitamin group
	Acuity of left eyes, near visual acuity [M print]		71	39	32	–	–	–	–	–	–	–	From 0.77 M to 0.89 M¶	From 1.29 M to 2.03 M	
REACT (27)	Anterior percentage pixel opaque (primary end point)	β-Carotene + vitamin C + <i>all-rac</i> α-tocopherol vs. placebo	158	81	77	–	–	–	–	–	–	–	Baseline, 5.7 ± 1.6, last, 7.3 ± 2.0; mean change from baseline, 1.7 ± 1.0**	Baseline, 5.0 ± 1.4; last, 8.3 ± 2.2; mean change from baseline, 3.3 ± 1.4	Unfavorable changes in secondary outcomes were smaller in the active supplement group, but none was significantly different from placebo group.
AREDS: cataract (28)	Total lens events	Vitamin C + vitamin E + β-carotene	4596	2286	2310	1541	756	785	–	–	0.97 (0.84–1.11)	–	–	–	Adjustments for several potential confounders did not materially alter results
	Cataract surgery		4596	2286	2310	675	–	–	–	–	0.94 (0.77–1.14)	–	–	–	
	Severe lens event		4596	2286	2310	991	–	–	–	–	0.92 (0.76–1.12)	–	–	–	
	Nuclear event	Vitamin C + vitamin E + β-carotene	4331	–	–	1674	–	–	–	–	0.98 (0.84–1.14)	–	–	–	
		Vitamin C + vitamin E + β-carotene vs. placebo	2715	–	–	1027	–	–	–	–	1.00 (0.82–1.22)	–	–	–	
	Cortical event	Vitamin C + vitamin E + β-carotene	4329	–	–	1058	–	–	–	–	0.99 (0.82–1.19)	–	–	–	

		Vitamin C + vitamin E + β-carotene vs. placebo	2715	–	–	625	–	–	–	–	0.91 (0.71–1.15)	–	–	
	Posterior subcapsular event	Vitamin C + vitamin E + β-carotene	4329	–	–	888	–	–	–	–	0.94 (0.78–1.14)	–	–	
		Vitamin C + vitamin E + β-carotene vs. placebo	2715	–	–	535	–	–	–	–	0.91 (0.70–1.17)	–	–	
	Lens event in eyes without opacities	Vitamin C + vitamin E + β-carotene (comparison group not specified)	823	–	–	—	–	–	–	–	0.85 (0.55–1.33)	–	–	Among those with no or minimal opacity in at least one eye at enrollment
	Loss of visual acuity score of 15 letters or more	Vitamin C + vitamin E + β-carotene vs. placebo	–	537	580	172	–	–	–	–	1.03 (0.63–1.66)	–	–	Among those without age-related macular degeneration at enrollment
AREDS: age-related macular degeneration (29)	Progression to advanced age-related macular degeneration (among those in age-related macular degeneration categories 2, 3, or 4)	Vitamin C + vitamin E + β-carotene	3609	–	–	803	–	–	–	–	0.87 (0.70–1.09)	–	–	
		Vitamin C + vitamin E + β-carotene vs. placebo									0.80 (0.59–1.09)	–	–	Analysis adjusted for sex, age, race, and category, and smoking status at enrollment did not materially alter the size or direction of estimates
		Vitamin C + vitamin E + β-carotene + zinc vs. placebo									0.72 (0.52–0.98)††	–	–	

Loss of visual acuity score of $\geq 15$ letters from baseline (among those in age-related macular degeneration categories 2,3, or 4)	Vitamin C + vitamin E + $\beta$ -carotene	3597	-	-	1197	-	-	-	-	0.90 (0.74-1.09)	-	-
	Vitamin C + vitamin E + $\beta$ -carotene vs. placebo									0.88 (0.67-1.15)	-	-
	Vitamin C + vitamin E + $\beta$ -carotene + zinc vs. placebo									0.79 (0.60-1.04) <sup>††</sup>	-	-
Progression to advanced age-related macular degeneration (among those in age-related macular degeneration categories 3 or 4)	Vitamin C + vitamin E + $\beta$ -carotene	2556	-	-	775	-	-	-	-	0.83 (0.66-1.06) <sup>§§</sup>	-	-
	Vitamin C + vitamin E + $\beta$ -carotene vs. placebo	2549	-	-	1022	-	-	-	-	0.76 (0.55-1.05) <sup>††</sup>	-	-
	Vitamin C + vitamin E + $\beta$ -carotene + zinc vs. placebo									0.66 (0.47-0.91)	-	-
Loss of visual acuity score of $\geq 15$ letters from baseline (among those in age-related macular degeneration categories 3 or 4)	Vitamin C + vitamin E + $\beta$ -carotene									0.86 (0.70-1.07)	-	-
	Vitamin C + vitamin E + $\beta$ -carotene vs. placebo									0.85 (0.63-1.14)	-	-

Vitamin C +  
vitamin E + β-  
carotene +  
zinc vs.  
placebo

0.73 (0.54–  
0.99)¶¶

\*\_ = not reported; AREDS = Age-related eye disease study; MONMD = Multicenter Ophthalmic and Nutritional Age-Related Macular Degeneration Study; REACT= Roche European American Cataract Trial.

†Unless otherwise specified, comparisons were made between groups receiving the combination of the listed nutrients and groups receiving combinations of placebo or nutrients other than the nutrients listed.

‡Total number was presented (when available) if the number in each comparison group was not reported.

§95% CIs are reported for the Linxian General Population Trial, and 99% CIs are reported for AREDS.

|| Difference from placebo, -0.7 logMAR ( $P = 0.03$ ).

¶| Difference from placebo, -0.62 ( $P = 0.07$ ).

\*\* Difference between groups: -1.6 ( $P = 0.05$ ).

††  $P = 0.007$ .

‡‡  $P = 0.03$ .

§§  $P = 0.05$ .

|||  $P = 0.001$ .

¶¶  $P = 0.008$ .