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| **Author, YearStudy Name** | **Study Design** | **CountrySetting** | **Inclusion criteria** | **Randomized AnalyzedAttrition** | **Intervention**  |
| Chew, 201399 AREDS (Report #35) | RCT (long-term observational followup) | United StatesMulticenter | Age 55 to 80 years with AMD and BCVA ≥20/32 in at least one eye | n=2,459, focusing on AREDS categories 3 and 4 for vision-related outcomes; 3,476 for categories 2, 3, and 4; total sample 4,753Attrition: NA | A. Antioxidant supplement (vitamin C 500 mg + vitamin E 400 IU + beta-carotene, 15 mg/day)B. Zinc 80 mg/day C. Antioxidant supplement + zinc D. Placebo |
| Chew, 2009112 AREDS (Report #25) | RCT (long-term observational followup) | United StatesMulticenter | Age 55 to 80 years with AMD and BCVA ≥20/32 in at least one eye | Randomized: 4,757Analyzed (post-trial followup): 4,577Attrition: NA | A. Any AREDS active treatment B. Placebo  |
| Ma, 2012106 | RCT | ChinaSingle center | Age 50-79 years with early AMD used AREDS classification | Randomized: 108Analyzed: 107Attrition: 0.9% (1/108) | A. Lutein 10 mg/day B. Lutein 20 mg/day C. Lutein 10 mg/day + zeaxanthin 10 mg/day D. Placebo  |
| Murray, 2013105CLEAR | RCT | United KingdomMulticenter | Age 50-80 years with AMD grade 0 to 4 (Rotterdam criteria); BCVA logMAR ≥0.5, with minimal cataract | Randomized: 84Analyzed: 73Attrition: 13% (11/84) | A. Lutein 10 mg/day B. Placebo  |
| Souied, 2013107NAT2 | RCT | FranceSingle hospital-based ophthalmology clinic | Age ≥55 to <85 years with visual acuity >0.4 logMAR in study eye with early age-related maculopathy (presence of drusen or reticular pseudodrusen) in study eye and AMD in the fellow eye | Randomized: 300Analyzed: 263 for efficacy analysis, 300 for safety analysisAttrition: 21% (63/300) | A. Fish oil capsules (DHA 280 mg + EPA 90 mg + vitamin E 2 mg) 3x/day B. Placebo (olive oil 602 mg)  |

| **Author, YearStudy Name** | **Study Participants** | **Duration of Followup** | **Results** |
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| Chew, 201399 AREDS (Report #35) | A vs. B vs. C vs. D\*Median age 69 vs. 70 vs. 69 vs. 69 years55% vs. 57% vs. 56% vs. 56% femaleRace: 97% vs. 96% vs. 97% vs. 96% white2% vs. 3% vs. 3% vs. 4% black1% vs. 1% vs. <1% vs. <1% otherAMD category:2: 28% vs. 30% vs. 28% vs. 30%3: 40% vs. 41% vs. 42% vs. 40%4: 24% vs. 22% vs. 22% vs. 22% | 10 years | **A + C (antioxidant) vs. B+D (no antioxidant)***(Participants with AMD category 2, 3 or 4 at baseline)*All-cause mortality: 24.0% (439/1831) vs. 23.6% (427/1806); aHR\* 1.06 (95% CI 0.93 to 1.21)CV mortality: aRR 1.20 (95% CI 0.97 to 1.49)Cancer mortality: aRR 1.07 (95% CI 0.83 to 1.38)Non-CV, non-cancer mortality: aRR 0.94 (95% CI 0.74 to 1.20)**B + C (zinc) vs. A + D (no zinc)**All-cause mortality: 22.4% (401/1790) vs. 25.2% (465/1847); aHR 0.83 (95% CI 0.73 to 0.95)CV mortality: aRR 0.80 (95% CI 0.64 to 0.99)Cancer mortality: aRR 0.84 (95% CI 0.65 to 1.08)Non-CV, non-cancer mortality: aRR 0.93 (95% CI 0.73 to 1.18)**A vs. D**Loss of visual acuity ≥15 letters ETDRS: OR 0.88 (95% CI 0.73 to 1.06)Visual acuity <20/100: OR 0.87 (95% CI 0.68 to 1.11)Progression to advanced AMD: OR 0.74 (95% CI 0.59 to 0.92)**B vs. D**Loss of visual acuity ≥15 letters ETDRS: OR 0.89 (95% CI 0.74 to 1.08)Visual acuity <20/100: OR 0.91 (95% CI 0.71 to 1.15)Progression to advanced AMD: OR 0.87 (95% CI 0.70 to 1.07)**C vs. D**Loss of visual acuity ≥15 letters ETDRS: OR 0.76 (95% CI 0.63 to 0.93)Visual acuity <20/100: OR 0.75 (95% CI 0.58 to 0.97)Progression to advanced AMD: C vs D: OR 0.69 (95% CI 0.56 to 0.86)*Participants with AMD category 3 or 4 at baseline***A vs. D**Loss of visual acuity ≥15 letters ETDRS: OR 0.83 (95% CI 0.67 to 1.02)Visual acuity <20/100: OR 0.82 (95% CI 0.64 to 1.07)Progression to advanced AMD: OR 0.70 (95% CI 0.56 to 0.88)**B vs. D**Loss of visual acuity ≥15 letters ETDRS: OR 0.86 (95% CI 0.70 to 1.07)Visual acuity <20/100: OR 0.88(95% CI 0.69 to 1.14)Progression to advanced AMD: OR 0.82 (95% CI 0.66 to 1.02)**C vs. D**Loss of visual acuity ≥15 letters ETDRS: OR 0.71 (95% CI 0.57 to 0.88)Visual acuity <20/100: OR 0.72 (95% CI 0.56 to 0.94)Progression to advanced AMD: C vs D: OR 0.66 (95% CI 0.53 to 0.83)*Participants with AMD category 4 at baseline***A vs. D**Loss of visual acuity ≥15 letters ETDRS: OR 0.75 (95% CI 0.53 to 1.06)Visual acuity <20/100: OR 0.76 (95% CI 0.52 to 1.12)Progression to advanced AMD: OR 0.64 (95% CI 0.46 to 0.91)**B vs. D**Loss of visual acuity ≥15 letters ETDRS: OR 0.68 (95% CI 0.48 to 0.96)Visual acuity <20/100: OR 0.66 (95% CI 0.45 to 0.98)Progression to advanced AMD: OR 0.68 (95% CI 0.49 to 0.96)**C vs. D**Loss of visual acuity ≥15 letters ETDRS: OR 0.54 (95% CI 0.38 to 0.78)Visual acuity <20/100: OR 0.58 (95% CI 0.38 to 0.86)Progression to advanced AMD: C vs D: OR 0.56 (95% CI 0.40 to 0.79) |
| Chew, 2009112 AREDS (Report #25) | Not reported by treatment group for this analysis (see Chew 2013 for characteristics for the entire AREDS cohort) | Up to 11 years (mean followup not reported) | **A vs. B**Incident cataract surgery: 25.4% (798/3137) vs. 25.2% (369/1467); RR 1.01 (95% CI 0.01 to 1.13) |
| Ma, 2012106 | A vs. B vs. C vs. DMean age 70 vs. 69 vs. 69 vs. 69 years62% vs. 56% vs. 56% vs. 60% femaleRace not reportedBCVA 0.30 vs. 0.28 vs. 0.28 vs. 0.31 logMAR89% vs. 89% vs. 85% vs. 89% non-smoker | 48 weeks | **A vs. D**BCVA, mean change from baseline: -0.04 (95% CI -0.11 to 0.03) vs. -0.00 (95% CI -0.06 to 0.05); p=NS **B vs. D**BCVA, mean change from baseline: -0.02 (95% CI -0.11 to 0.06) vs. -0.00 (95% CI -0.06 to 0.05); p=NS**C vs. D**BCVA, mean change from baseline: -0.04 (95% CI -0.10 to 0.01) vs. -0.00 (95% CI -0.06 to 0.05); p=NS |
| Murray, 2013105CLEAR | A vs. BMean age 71.9 vs. 69.1 years56% vs. 65% femaleRace not reportedVisual acuity 0.10 vs. 0.05 logMAR | 1 year | **A vs. B**Visual acuity, mean change from baseline: 0.01 v.s -0.04; p<0.05 |
| Souied, 2013107NAT2 | A vs BMean age 74 vs. 73 years69% vs. 61% femaleRace not reportedMean visual acuity in study eye 0.14 vs. 0.12 logMARCataracts 61% vs. 62%Drusen:Absent: 0.7% vs. 0%<5: 0.7% vs. 2%5-20: 17% vs. 22%>20: 81% vs. 76%Pigmentary changes: 23% vs. 22%Stage of maculopathy: Stage 1: 78% vs. 78% Stage 2: 22% vs. 22%Smoking history: Current: 7% vs. 9% Former: 14% vs. 17% Nonsmoker: 79% vs. 74%CVD: 93% vs. 80%Metabolic and nutrition disorders: 53% vs. 59%Musculoskeletal and connective tissue disorders: 45% vs. 49%GI disorder: 30% vs. 33%Concomitant medications: Lipid-lowering agents: 49% vs. 53%Renin-angiotensin system agents: 42% vs. 36%Anti-inflammatory and anti-rheumatic agents: 16% vs. 29%Diabetes: 12% vs. 10% | 3 years | **A vs. B**All-cause mortality: 2.2% (3/134) vs. 4.7% (6/129); RR 3.00 (95% 0.33 to 28)Best-corrected visual acuity, mean change from baseline (logMAR): 6 months: 0.040 (SD 0.122) vs. 0.007 (SD 0.118)1 year: 0.0037 (SD 0.173) vs. 0.0008 (SD 0.122)2 years: 0.086 (SD 0.231) vs. 0.057 (SD 0.201)3 years: 0.155 (SD 0.297) vs. 0.116 (SD 0.258); p=0.311Loss of visual acuity, proportion of subjects with decrease >15 letters on ETDRS chart: 6 months: 3.1% (4/131) vs. 1.6% (2/126); RR 1.92 (95% CI 0.36 to 10)1 year: 5.3% (7/131) vs. 0.8% (1/123); RR 6.57 (95% CI 0.82 to 53)2 years: 10.8% (13/120) vs. 9.5% (11/116); RR 1.14 (95% CI 0.53 to 2.45)3 years: 17.8% (21/118) vs. 14.3% (16/112); RR 1.25 (95% CI 0.69 to 2.26)  |

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| **Author, YearStudy Name** | **Adverse Events** | **Sponsor** | **Quality** | **Comments** |
| Chew, 201399 AREDS (Report #35) | Not reported by treatment group; narrative report of no significant increase in incidence of hospitalization after adjustment for age, sex, smoking and treatment group | National Eye Institute/National Institutes of Health | Good | Hazard ratios for mortality outcomes adjusted for age, sex, race, education, smoking status, BMI, diabetes, angina, cancer, hypertension |
| Chew, 2009112 AREDS (Report #25) | Not reported | National Eye Institute/National Institutes of Health | Good | None |
| Ma, 2012106 | Not reported by treatment group; narrative report of no adverse events related to interventions | Not reported | Good | None |
| Murray, 2013105CLEAR | A vs. BWithdrawals due to adverse events: 7.1% (3/42) vs. 2.3% (1/42); RR 3.00 (95% 0.33 to 28) | BASF, UK Medical Research Council, Manchester Biomedical Research Center, Greater Manchester Comprehensive Local Research Network | Good | None |
| Souied, 2013107NAT2 | A vs. BAny adverse event: 93.3% (125/134) vs. 89.1% (115/129); RR 1.05 (95% CI 0.97 to 1.13)Any serious AE: 31.3% (42/134) vs. 30.2% (39/129); RR 1.04 (95% CI 0.72 to 1.49)Treatment-related AE (investigator-determined): 3.7% (5/134) vs. 1.6% (2/129); RR 2.41 (95% CI 0.48 to 12)Serious ocular AE: 8.2% (11/134) vs 7.0% (9/129); RR 1.18 (95% CI 0.50 to 2.75)Ocular AE: 65.7% (88/134) vs 57.4% (74/129); RR 1.14 (95% CI 0.94 to 1.39)Cataract development, worsening or need for cataract surgery: 50% (67/134) vs. 62.5% (81/129); RR 0.80 (95 % CI 0.64 to 0.99)Serious non-ocular AE: 23.1% (31/134) v.s 23.2% (30/129); RR 0.99 (95% CI 0.64 to 1.54) | Bausch & Lomb | Good | None |

**Abbreviations:** AMD = age-related macular degeneration, aHR = adjusted hazard ratio, aRR = adjusted risk ratio, BCVA = best corrected visual acuity, CV = cardiovascular, DHA = docosahexaenoic acid, EPA = eicosapentaenoic acid, ETDRS = Early Treatment Diabetic Retinopathy Study, IU = international units, mg = milligrams, NA = not applicable, OR = odds ratio, RCT = randomized controlled trial, RR = risk ratio, UK = United Kingdom.