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| **Study, Year** | **Aims** | **Literature Searches** | **Patients/Trials** | **Interventions** |
| Evans, 200898 *Antioxidant vitamin and mineral supplements* | To assess the effects of antioxidant vitamin or mineral supplementation, alone or in combination, on the progression of AMD | CCRCT, MEDLINE, EMBASE, National Research Register through 2007, PubMed in process through 24 January 2006, AMED 1985-January 2006, SIGLE 1980-March 2005 | 9 trials (18 publications) Primary publications: Richer 1996, AMDSG (n=71); Age-Related Eye Disease Study Research Group 2001, AREDS (n=3640); Holz 1993 (n=58); Kaiser 1995 (n=20); Newsome 1988 (n=174); Stur 1996 (n=112); Garrett 1999, VECAT study (n=1204); Richer 2004, LAST study (n=90); Wang 2004 (n=400); total n=5769 | 3 trials: zinc 200 mg QD vs. placebo 2 trials: broad-spectrum antioxidant compound vs. placebo 1 trial: vitamin E 500 mg QD vs. placebo 1 trial: zinc 80 mg QD vs. antioxidant combination vs. zinc + antioxidants vs placebo 1 trial: lutein 10 mg QD vs. lutein + broad-spectrum antioxidant 1 trial: zinc oxide 80 mg QD, vitamin C, vitamin E vs. placebo |
| Evans, 200849 *Ginkgo biloba* | To determine the effect of ginkgo biloba extract on the progression of AMD | CCRCT (Quarter 4, 2005), MEDLINE (1966-January 2006, week 3), EMBASE (1980-January 2006), SIGLE (1980-2005/03), AMED (1985-January 2006), NRR (2005, Issue 4); reference lists, Science Citation Index; expert recommendation | 2 trials: Fies 2002 (n=99); Lebuisson 1986 (n=20); total n=119 | Gingko biloba extract EGb 761, doses 60-160 mg QD; placebo |
| Vedula, 2008120 | To investigate the effects of anti-VEGF modalities for treating neovascular AMD | CCRCT, MEDLINE, EMBASE, LILACs through February 2008; hand search of Association for Research in Vision & Ophthalmology meeting abstracts | 5 trials (15 publications)  Primary publications: Brown 2006, ANCHOR Trial (n=423); Macugen 2007, EOP 1003 Trial (n=578); Leys 2007, EOP 1004 Trial (n=612); Heier 2006, FOCUS Trial (n=162); Rosenfeld 2006, MARINA Trial (n=716) | Pegaptanib 0.3, 1.0 or 3.0 mg  Ranibizumab 0.3 or 0.5 mg  Verteporfin PDT  Sham injection/sham PDT |
| Virgili, 2007113 | To examine the effect of laser photocoagulation on neovascular (wet) AMD | CCRCT, MEDLINE, EMBASE, LILACS, NRR, ZETOC through March 2007 | 15 trials; 12 of which compared laser photocoagulation to no treatment | Laser photocoagulation  No treatment |
| Wormald, 2008114 | To examine the effects of photodynamic therapy in the treatment of AMD | CCRCT, MEDLINE, EMBASE through March 2007; Science Citation Index (no date specified); expert recommendation | 3 trials (7 publications)  Primary publications: Treatment of Age-Related Macular Degeneration with Photodynamic Therapy Study Group, TAP 1999 (n=609); Visudyne in Minimally Classic Choroidal Neovascularization Study, VIM 2005 (n=117); Verteporfin in Photodynamic Therapy Study Group, VIP 2001 (n=2001); total n=1065 | IV verteporfin (2 trials: 6 mg/m2; 1 trial dose NR) + cold laser vs placebo + cold laser |

| **Study, Year** | **Results** | **Conclusion** | **Quality** |
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| Evans, 200898 *Antioxidant vitamin and mineral supplements* | **All comparisons** *Any multivitamin or antioxidant vs placebo*  Change in visual acuity, defined as a loss of ≥3 lines (≥15 letters) on a logMAR chart (AREDS, Newsome 1988, VECAT; I²=27.7%): random effects model pooled OR 0.83 (CI 0.63 to 1.09; p=0.18); fixed effects model pooled OR 0.81 (CI 0.67 to 0.98; p=0.03)  Mean difference visual acuity (AMDSG, Kaiser 1995, Newsome 1988, Stur 1996, LAST; I²=0%): pooled SMD 0.02 (CI -0.21 to 0.26) AMD progression as a dichotomous variable (AREDS, Holz 1993, Stur 1996. VECAT; I²=64.2%): OR range: 0.50 to 2.31; no pooled analysis due to heterogeneity of studies AMD progression as a continuous variable (AMDSG): mean difference -0.06 (CI -0.62 to 0.50)  **Individual comparisons**  *Multivitamin supplements vs placebo (AREDS, Kaiser 1995, Richer 1996, Richer 2004)*  Change in visual acuity, defined as a loss of ≥3 lines (≥15 letters) on a logMAR chart (AREDS): OR 0.77 (CI 0.62 to 0.96) vs. placebo Mean difference visual acuity (Kaiser 1995, AMDSG, LAST; I²=0%): pooled SMD 0.16 (CI -0.19 to 0.51)  AMD progression as a dichotomous variable (AREDS): adjusted OR 0.68 (CI 0.53 or 0.87)  AMD progression as a continuous variable (AMDSG): mean difference -0.06 (CI -0.62 to 0.50)  *Vitamin E vs. placebo (VECAT)*  Change in visual acuity, defined as a loss of ≥3 lines (≥15 letters) on a logMAR chart: OR 1.05 (CI 0.70 to 1.57) AMD progression: OR 0.11 (CI 0.80 to 1.55)  *Zinc vs. placebo (AREDS, Holz 1993, Newsome 1988, Stur 1996)*  Change in visual acuity, defined as a loss of ≥3 lines (≥15 letters) on a logMAR chart (AREDS, Newsome 1988; I²=0%): OR 0.81 (CI 0.66 to 0.99)  Mean difference visual acuity (Newsome 1988, Stur 1996; I²=56.6%): results somewhat inconsistent but no statistically significant difference found between treatment and control groups in both trials  AMD progression as a dichotomous variable (AREDS, Holz 1993, Stur 1996; I²=29.0%): pooled OR 0.73 (0.58-0.93)  *Lutein vs. placebo (LAST)*  Mean difference visual acuity: 0.04 (-0.15 to 0.23) | Limited evidence, based primarily on AREDS, suggests a benefit in the use of antioxidant vitamins and minerals in slowing AMD progression (risk reduction ~20-25%.) The AREDS population was relatively well-nourished at the trial's initiation and this may have had some effect on the trial results. Prolonged antioxidant use had been found to be harmful in some other populations (e.g. smokers) | Good |
| Evans, 200849 *Ginkgo biloba* | *Gingko biloba 160 mg QD vs placebo (1 trial; n=20)*  Change in visual acuity: WMD 1.70 (CI 1.21 to 2.19)  Clinical improvement: OR 36.00 (2.72 to 476.28)  *Gingko biloba 60 mg QD vs. 240 mg QD (1 trial; n=99)*  Mean visual acuity: WMD 0.05 (CI -0.03 to 0.13)  >0.2 improvement in visual acuity score: OR 2.29 (CI 0.90 to 5.80)  No serious AEs reported in either trial (headache, blood in stool and abdominal pain reported in 3/99 patients) | There is inadequate evidence from 2 small, short-term trials to draw conclusions regarding the effect of gingko biloba on AMD progression. There may be harms associated with gingko biloba use, but they have been too inadequately reported. | Good |
| Vedula, 2008120 | *Change in visual acuity (% of patients losing ≥3 lines of acuity at 1 year)*  Pegaptanib (all doses) vs sham: RR 0.71 (CI 0.60 to 0.84); NSD for 3.0 mg dose vs sham; NNT 6.67 0.3 mg dose, 6.25 1.0 mg dose, 14.28 3.0 mg dose  Ranibizumab (both doses) vs sham: RR 0.14 (CI 0.08 to 0.25); NNT 3.13 (both doses)  *Blindness*  Pegaptanib: RR 0.69 (CI 0.59 to 0.82)  Ranibizumab: RR 0.28 (CI 0.21 to 0.37)  *Quality of life, mean change in NEI-VFQ score at 2-year followup*  ANCHOR Trial: 5.9 ranibizumab 0.3 mg vs. 8.1 ranibizumab 0.5 mg vs 2.2 verteprofin  MARINA Trial: 4.8 ranibizumab 0.3 mg vs. 4.5 0.5 mg ranibizumab vs -6.4 sham injection  Ranibizumab: similar rates of serious AEs, including mortality; unpublished data from SAILOR Trial reported by the drug's manufacturer showed a significantly higher stroke risk with 0.5 mg dose relative to 0.3 mg dose (p=0.02; no sham control in this trial)  Pegaptanib: Serious ocular AEs (endophthalmitis, retinal detachment, traumatic cataract) in tx groups, none in sham group | Both interventions effective a reducing visual acuity loss and progression to blindness with improved QoL outcomes | Good |
| Virgili, 2007113 | *Photocoagulation vs no treatment*  Visual acuity, loss of ≥6 lines at 3 months (5 trials): RR 1.41 (95% CI 1.08 to 1.82; I2=0%) Visual acuity, loss of ≥6 lines at 2 years (5 trials): RR 0.67 (95% CI 0.53 to 0.83; I2=58%) Visual acuity 20/200 or better at 1-3 years (3 trials): RR 0.73 (95% CI 0.61 to 0.86; I2=43%) Visual acuity 20/200 or better at 5 years followup (2 trials): RR 0.77 (95% CI 0.66 to 0.90; I2=21%) | Photocoagulation is effective for certain types of AMD (extrafoveal CNV). For juxta- or sub-foveal CNV patients, the benefit of laser photocoagulation is less clear. | Good |
| Wormald, 2008114 | *Laser photocoagulation vs sham*  Loss of >3 lines of visual acuity at 12 months (4 trials): RR 0.80 (95% CI 0.69 to 0.93; I2=30%)  Loss of >3 lines of visual acuity at 24 months (4 trials): RR 0.80 (95% CI 0.73 to 0.83; I2=0%)  Loss of ≥6 lines of visual acuity at 12 months (4 trials): RR 0.70 (95% CI 0.56 to 0.88; I2=0%)  Loss of ≥6 lines of visual acuity at 24 months (4 trials): RR 0.66 (95% CI 0.53 to 0.83; I2=31%)  Gain of ≥3 lines of visual acuity at 12 months (3 trials): RR 2.19 (95% CI 0.99 to 4.82; I2=0%)  Gain of ≥3 lines of visual acuity at 24 months (3 trials): RR 2.55 (95% CI 1.31 to 4.99; I2=0%)  *Harms*  Severe acute loss of visual acuity (3 trials): RR 3.75 (95% CI 0.87 to 16; I2=28%)  Visual disturbance (3 trials): RR 1.56 (95% CI 1.21 to 2.01; I2=7%)  Injection site reaction (3 trials): RR 2.09 (95% CI 1.29 to 3.39; I2=73%)  Infusion-related back pain (4 trials): RR 9.93 (95% CI 2.82 to 35; I2=0%  Allergic reaction (2 trials): RR 0.94 (95% CI 0.34 to 2.56; I2=0%)  Photosensitivity (2 trials): RR 5.37 (95% CI 1.01 to 29; I2=70%) | Photodynamic therapy is effective in preventing further visual loss due to AMRD, although the effect size is unclear. | Good |

**Abbreviations:** AE = adverse event; AMD = age-related macular degeneration; CI = confidence interval; IV = intravenous; logMAR = logarithmic minimum angle of resolution; NEI -VFQ = National Eye Institute Visual Functioning Questionnaire; NNH = number needed to harm; NNT = number needed to treat; NR = not reported; NRR = National Research Register; OR = odds ratio; PDT = photodynamic therapy; pts = patients; QD = daily; QoL = quality of life; RR = relative risk; VECAT = Vitamin E, Cataract and Age-Related Maculopathy Study; VEGF = vascular endothelial growth factor; WMD = weighted mean difference.