

H.2.1 Strategies to slow the progression of age-related macular degeneration (AMD)

RQ7: What is the effectiveness of strategies to reduce the risk of developing AMD in the unaffected eye or slow the progression of AMD?

The GRADE tables in this section were produced as part of a collaboration between by the Cochrane Eyes and Vision group and the NICE Internal Clinical Guidelines Team.

Statin for age-related macular degeneration

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
AMD progression								
1 (Guymer 2013)	RCT	Serious ¹	N/A	Not serious	Serious ²	114	RR 0.78 (0.50, 1.02)	LOW
Adverse outcomes								
1 (Guymer 2013)	RCT	Serious ¹	N/A	Not serious	Serious ²	114	RR 0.64 (0.39, 0.92)	LOW
1. Downgraded one level for incomplete outcome data, data missing for 30% participants at 3 years follow-up 2. Downgraded one level for confidence interval crossing 1 lines of a defined minimal important difference								

Omega 3 fatty acids compared to placebo for slowing the progression of age-related macular degeneration

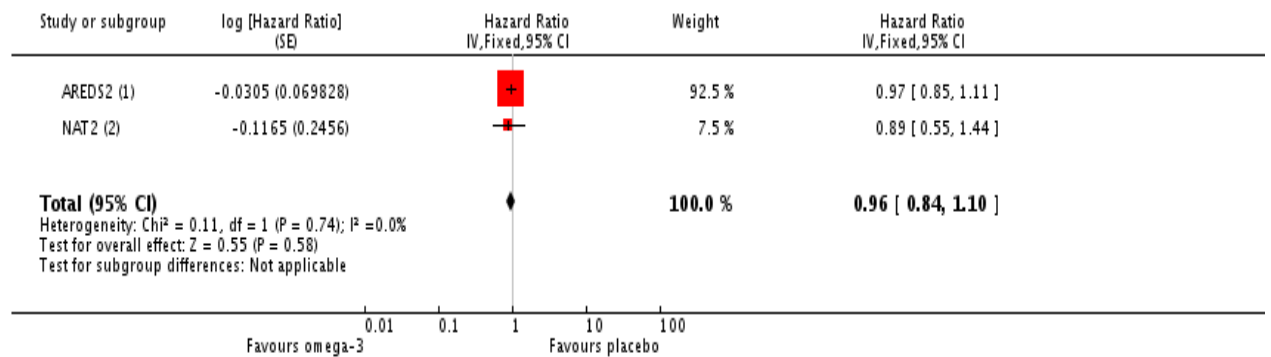
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
Loss of 3 or more lines of visual acuity at 24 months								
1 (ARES2)	RCT	Not serious	N/A	Not serious	Very serious ¹	236	RR 1.14, (0.53, 2.45)	LOW
Loss of 3 or more lines of visual acuity at 36 months								
1 (ARES2)	RCT	Not serious	N/A	Not serious	Very serious ¹	230	RR 1.25, (0.69, 2.26)	LOW
Incidence of CNV at 24 months								

Macular Degeneration
Appendix H: Grade tables and meta-analysis results

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
1 (NAT 2013)	RCT	Not serious	N/A	Not serious	Very serious ¹	224	RR 1.06, (0.47,2.40)	LOW
Incidence of CNV at 36 months								
1 (NAT 2013)	RCT	Not serious	N/A	Not serious	Very serious ¹	195	RR 1.12, (0.53 , 2.38)	LOW
Progression of AMD over 5 years								
2 (ARES and NAT)	RCT	Not serious	Not serious	Not serious	Not serious	2343	HR 0.96 (0.84, 1.1)	HIGH
Adverse effects								
2 (ARES and NAT)	RCT	Not serious	Not serious	Not serious	Not serious	2343	RR 1.01, (0.94 ,1.09)	HIGH
Visual acuity (ETDRS letters; higher is better)								
1 (Ute E K 2015)	RCT	Serious ³	N/A	Not serious	Not serious	79	MD 1.00 (-2.50 ,4.50)	MODERATE
1. Downgraded two levels for confidence interval crossing 2 lines of a defined minimal important difference 2. Downgraded one level for risk of bias due to study design (open label)								

Meta-analysis: Omega 3 fatty acids vs placebo: progression of AMD

Review: Omega 3 fatty acids for preventing or slowing the progression of age-related macular degeneration
Comparison: 1 Omega 3 fatty acids versus control
Outcome: 1 Progression of AMD



(1) Progression over 5 years; unit of analysis eye, adjusted for within person correlation.

(2) Incidence of CNV in fellow eye over 3 years; unit of analysis study eye, one per person; adjusted for age, smoking and stage of maculopathy.

Laser treatment of drusen to prevent progression of advanced age-related macular degeneration

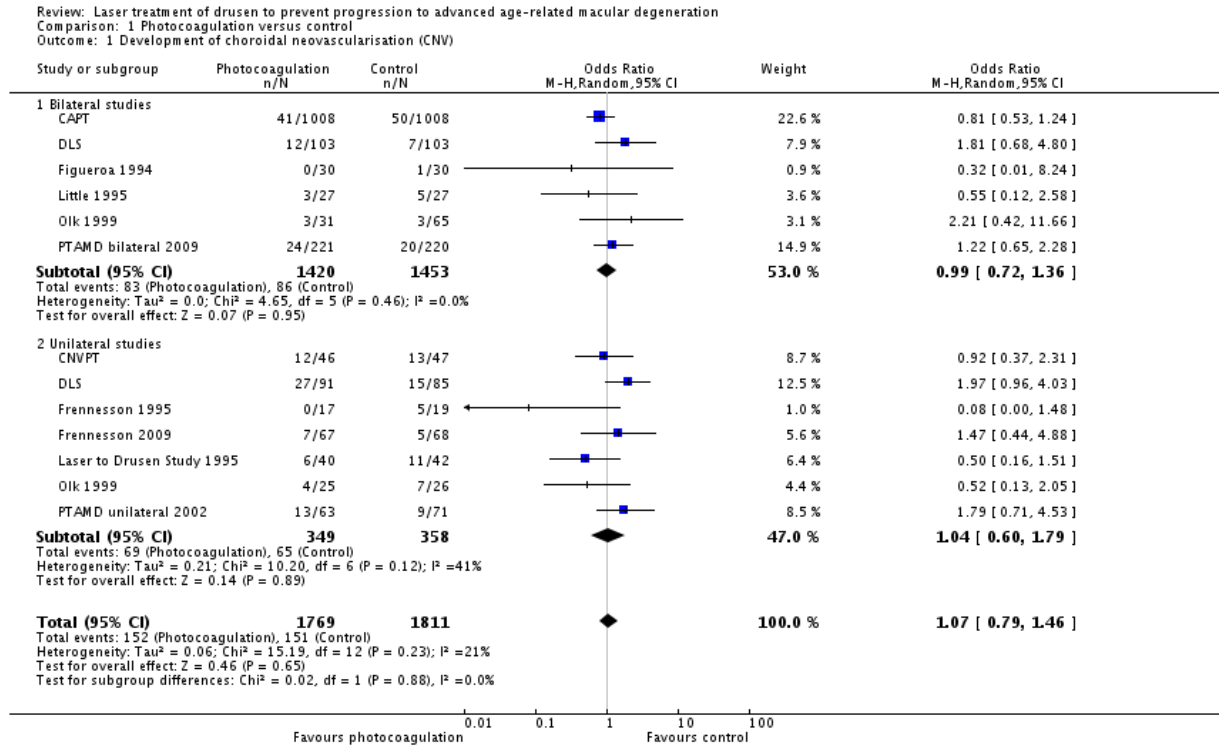
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
Development of CNV								
11 (CAPT, DLS, Figueroa 1994, Little 1995, Oik 1999, PTAMD bilateral 2009, CNVPT, Fremensson 1995, Fremesson 2009, Laser to Drusen study 1995, PTAMD unilateral 2002)	RCT	Not serious	Not serious	Not serious	Serious ¹	2159 (3580 eyes)	RR* 1.03, (0.83, 1.27)	MODERATE
Development of geographic atrophy								
2 (CNVPT, laser to Drusen study 1995)	RCT	Not serious	Not serious	Not serious	Very serious ²	148 (148 eyes)	RR* 1.27 (0.41, 3.94)	LOW
Visual loss of 2-3+ lines of visual acuity at 3-year follow-up								
9 (CAPT, DLS, Figueroa 1994, PTAMD bilateral 2009, CNVPT, Laser to Drusen Study 1995, Oik 1999, PTAMD unilateral 2002)	RCT	Serious ³	Not serious	Not serious	Not serious	2002 (3486 eyes)	RR* 0.99 (0.83, 1.18)	MODERATE
Drusen reduction								

Macular Degeneration
Appendix H: Grade tables and meta-analysis results

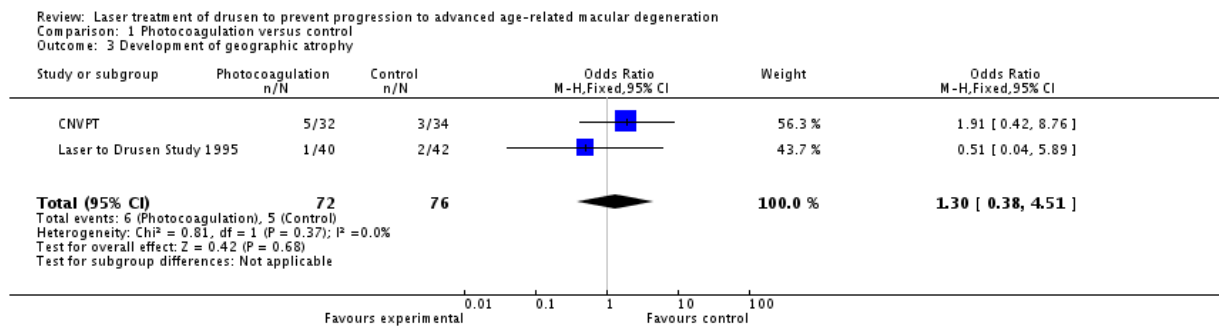
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
3 (CNVPT, PTAMD bilateral 2009, PTAMD unilateral 2002)	RCT	Not serious	Serious ⁴	Not serious	Not Serious	570 (944 eyes)	RR* 4.47 (1.64, 12.19)	MODERATE
<ol style="list-style-type: none"> 1. Downgraded one level for confidence interval crossing 1 line of a defined minimal important difference 2. Downgraded two levels for confidence interval crossing 2 lines of a defined minimal important difference 3. Downgraded one level for risk of bias due to visual acuity examiners were masked in less than half of studies 4. Downgraded one level for heterogeneity ($i^2=89\%$) <p>*Converted from odds ratios reported in included Cochrane review</p>								

Meta-analysis: Laser treatment of drusen to prevent progression to advanced AMD

Development of CNV¹

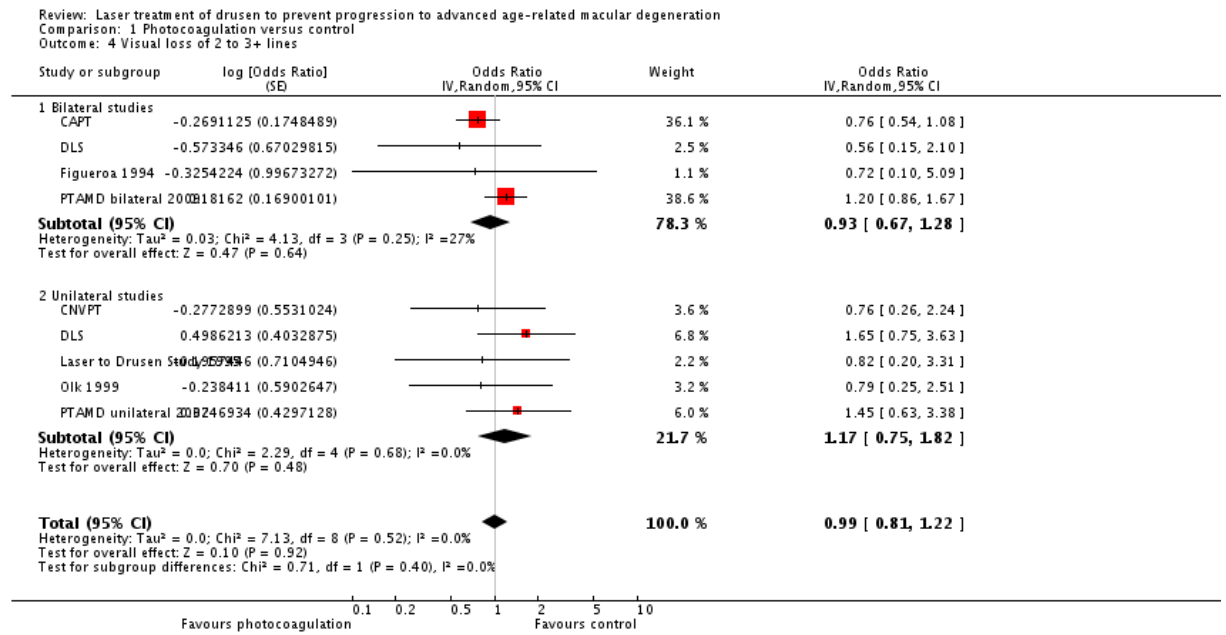


Development of geographic atrophy

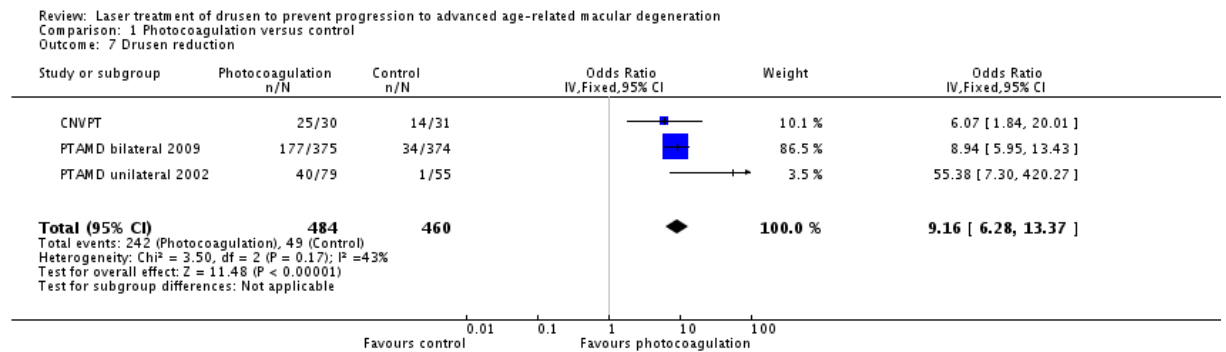


¹ Meta-analysis were extracted from the Cochrane review, and odds ratios were reported in Cochrane review.
© NICE 2018. All rights reserved. See [Notice of rights](#).

Visual acuity (loss of at least 2 lines)



Drusen reduction



Antioxidant vitamin or mineral supplement for slowing the progression of age-related macular degeneration

Multivitamin supplement

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
Progression to Late AMD (wet active or geographic atrophy)								
3 (AREDS 2001, CARMA 2013, CARMIS 2011)	RCT	Not serious	Not serious	Not serious	Serious ¹	2140	RR* 0.77 (0.67, 0.89)	MODERATE
Progression to Late AMD (wet active)								
1 (AREDS 2001)	RCT	Not serious	N/A	Not serious	Serious ¹	1206	RR* 0.67 (0.53, 0.85)	MODERATE
Progression to Late AMD (geographic atrophy)								
1 (AREDS 2001)	RCT	Not serious	N/A	Not serious	Serious ¹	1206	RR* 0.76 (0.53, 1.10)	MODERATE
Progression to visual loss (loss of 3 or more lines on logMAR chart)								
1 (AREDS 2001)	RCT	Not serious	N/A	Not serious	Serious ¹	1807	RR* 0.83 (0.70, 0.97)	MODERATE
Quality of life assessed with change in NEI-VFQ score (higher scores indicate better QoL)								
1 (CARMIS 2011)	RCT	Serious ²	N/A	Not serious	Serious ¹	110	MD=12.30 (4.24, 20.36)	LOW
Visual acuity (logMAR score) (lower values indicate better vision)								
4 (AMDSG 1996, CARMA 2013, Bartlett 2007, Veterans)	RCT	Serious ²	Not serious	Not serious	Serious ¹	979	SMD=0.01 ² (-0.12, 0.13)	LOW

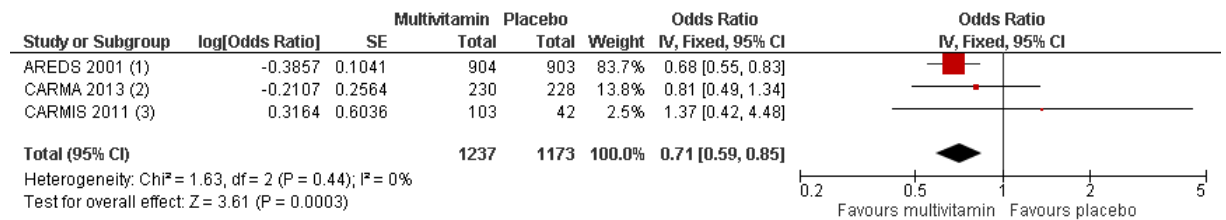
² 0.01 logMAR= - 0.5 letters, 95%CI -6.5 to 6 letters

Macular Degeneration
 Appendix H: Grade tables and meta-analysis results

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
LAST study (2004)								
1. Downgraded one level for confidence interval crossing 1 line of a defined minimal important difference 2. Downgraded for risk of bias (randomisation and allocation; blinding; incomplete outcome) *Converted from odds ratios reported in included Cochrane review								

Meta-analysis: Multivitamin antioxidant vitamin or mineral supplement

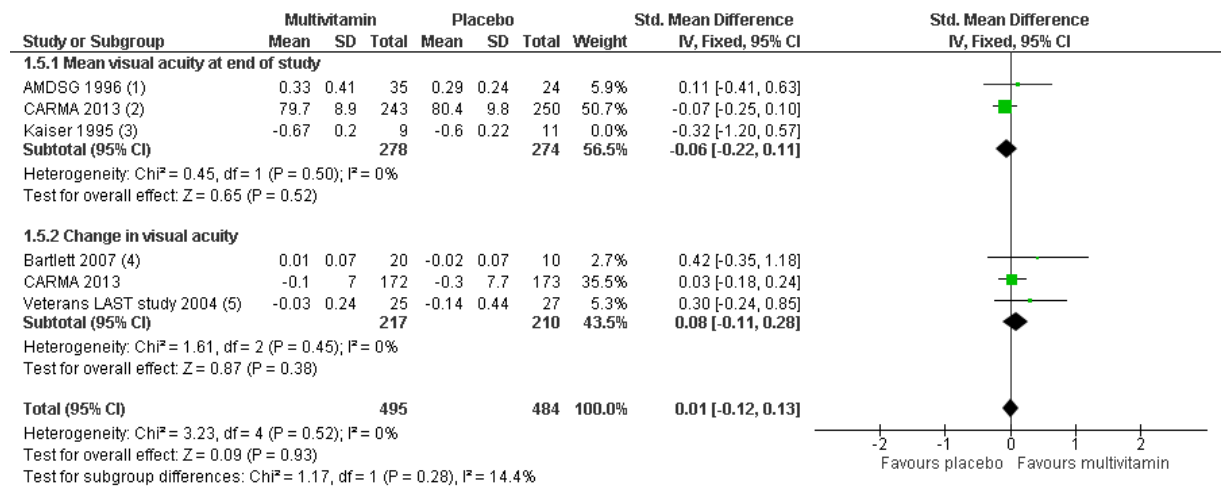
Progression to late AMD (wet active) or late AMD (geographic atrophy)



Footnotes

- (1) By person (event in at least one eye): progression to advanced AMD over average 6.3 years follow-up
- (2) Follow-up: 12 months
- (3) Follow-up: 24 months

Mean visual acuity



Footnotes

- (1) Right eye: LogMAR score (converted from Snellen decimal acuity) at 18 months
- (2) Number of letters read at 4m at 12 months
- (3) Study eye: Snellen acuity (expressed as decimal) at six months,
- (4) Study eye: Change in logMAR score (EDTRS chart) over 9 months
- (5) Right eye: Change in logMAR score (converted from Snellen decimal acuity) over 12 months

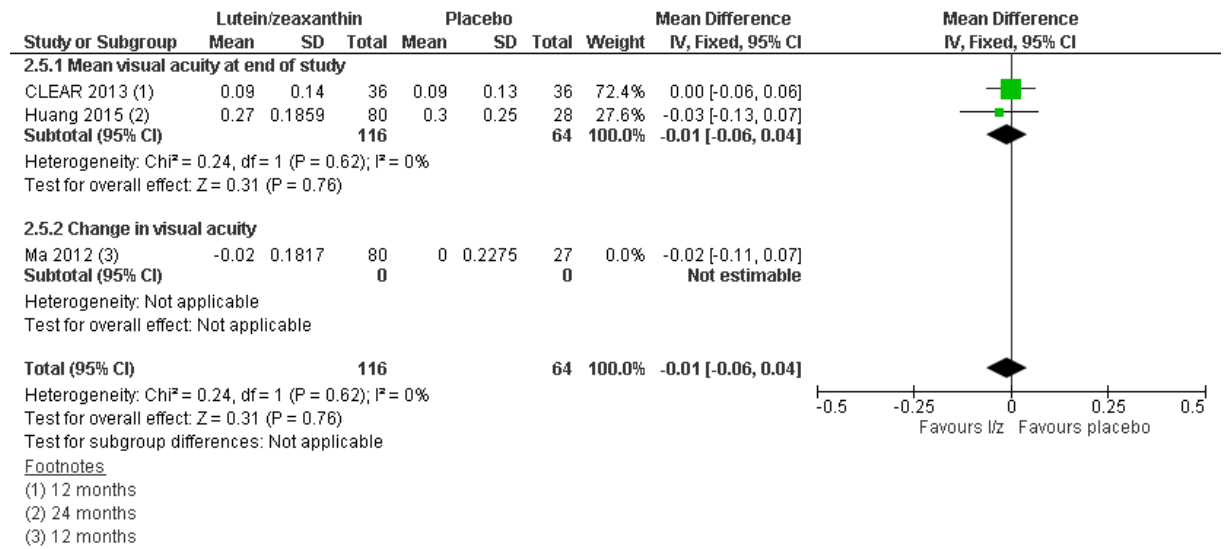
Lutein/zeaxanthin

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
Progression to Late AMD (wet active or geographic atrophy)								
1 (AREDS2 2013)	RCT	Not serious	N/A	Serious ¹	Serious ²	6891	RR 0.94 (0.87, 1.01)	LOW
Progression to Late AMD (wet active)								
1 (AREDS2 2013)	RCT	Not serious	N/A	Serious ¹	Serious ²	6891	RR 0.92 (0.84, 1.02)	LOW
Progression to Late AMD (geographic atrophy)								
1 (AREDS2 2013)	RCT	Not serious	N/A	Serious ¹	Serious ²	6891	RR 0.92 (0.80, 1.05)	LOW
Quality of life assessed with change in NEI-VFQ score (higher scores better)								
1 (Huang 2015)	RCT	Not serious	N/A	Not serious	Serious ²	108	MD 1.48 (-5.53, 8.49)	MODERATE
Visual acuity (logMAR score) (lower values better)								
2 (CLEAR 2013, Huang 2015)	RCT	Not serious	Not serious	Not serious	Not Serious	180	MD -0.01 ³ (-0.06, 0.04)	HIGH
1. Downgraded one level for indirectness as everyone in trial took AREDS formula which may have affected the estimate of effect 2. Downgraded one levels for confidence interval crossing 1 line of a defined minimal important difference								

³ -0.01 logMAR= + 0.5 letters, 95%CI -2 to 3 letters
© NICE 2018. All rights reserved. See [Notice of rights](#).

Meta-analysis: Lutein and zeaxanthin

Distance visual acuity mean (logMAR)



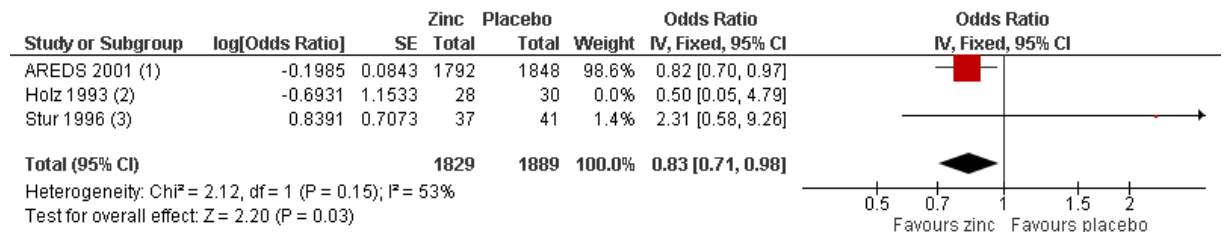
Zinc supplement

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
Progression to Late AMD (wet active or geographic atrophy)								
3 (AREDS 2001, Holz 1993, Stur 1996)	RCT	Not serious ¹	Not serious	Not Serious	Serious ²	3776	RR* 0.87 (0.77, 0.98)	MODERATE
Progression to Late AMD (wet active)								
1 (AREDS 2001)	RCT	Not serious	N/A	Not serious	Serious ²	3640	RR* 0.80 (0.67, 0.94)	MODEATE
Progression to Late AMD (geographic atrophy)								
1 (AREDS 2001)	RCT	Not serious	N/A	Not serious	Serious ²	3640	RR* 0.85 (0.66, 1.09)	MODERATE
Distance visual acuity (logMAR) (lower values better)								
2 (Stur 1996, Newsome 1998)	RCT	Not serious	Serious ³	Not serious	Serious ²	155	MD -0.09 ⁴ (-0.57, 0.39)	LOW
<ol style="list-style-type: none"> 1. Although there were risk of bias due to incomplete outcome data and selective reporting in Holz 1993 and Stur 1996, AREDS contributed to 98% of weight in pooled results, so not downgraded. 2. Downgraded one level for confidence interval crossing 1 line of a defined minimal important difference. 3. Downgraded one level for heterogeneity ($i^2 > 50\%$) <p>*Converted from odds ratios reported in included Cochrane review</p>								

⁴ -0.09logMAR=+4.5 letters, 95%CI: -11.5 to 20.5

Meta-analysis: Zinc supplements

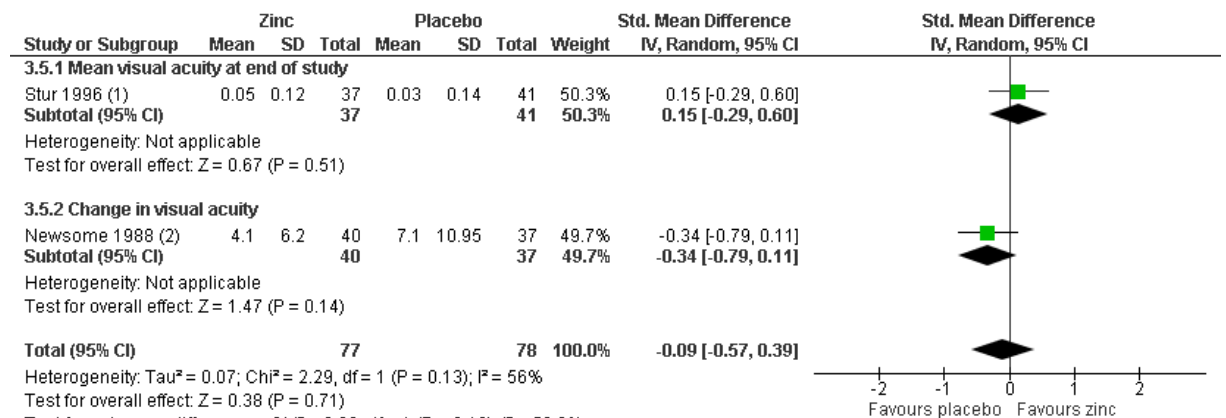
Progression to late AMD (wet active) or late AMD (geographic atrophy)



Footnotes

- (1) By person (event in at least one eye): progression to advanced AMD over average 6.3 years follow-up
(2) By person: "new exudative or dry macular lesions" over 12 to 24 months
(3) Study eye: incidence of exudative AMD over 24 months

Visual acuity



Footnotes

- (1) Study eye: LogMAR score (Bailey-Lovie chart) at 24 months
(2) Study eye: Change in number of correct letters (EDTRS chart) 19 to 24 months