HTA15.09.10 Systematic review of treatment of dry age-related macular degeneration and Stargardt disease.

Supplementary file 6. Summary tables of studies and excluded studies.

Table SF6.1 Characteristics

Non pharmacological treatments			
Study	**Summary of Intervention Details**	**Participant details and key eligibility criteria**	**Summary of Relevant Outcomes**
Acupuncture			
Krenn et al., 2008{#635} *Country:* Austria *Design:* Before and After study *Number of centres:* one *Funding:* none *Trial ID:* NR	*Intervention* *1.* Acupuncture *Dose details:* two times per day, 5 days per week, minimum time of 60 minutes between treatments, each participant was acupunctured at the same points. *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* 2 weeks	*Number of Participants*: total 328 of 344 willing participants (16 were not eligible, see below) *Number of eyes* 656 *Sample attrition/dropout*: none Included: consecutive patients with dry AMD diagnosed by their ophthalmologist, given one acupuncture treatment and enrolled if vision improved. Excluded*:* After one acupuncture treatment, the eye test was repeated. Participants whose vision had not improved were classified as nonresponders and were not eligible for enrolment.	*Outcomes* • Visual acuity score (0% no letter correctly read to 100 % (all letters correctly read). *Length of follow-up:* 2 weeks
Blue light filter			
Pipis et al., 2015{#223} *Country:* Germany *Design:* retrospective cohort study	*Intervention* *1.* blue light–filtering, UV-blocking intraocular lens *2.* no colour filter, UV-blocking intraocular lens	*Number of Participants*: Total 40 *Number of eyes:* Total 66 1. Blue-light filter, n=39 2. No colour filter, n=27	*Outcomes* • GA progression *Length of follow-up:* one year

Number of centres: one *Funding:* States none. *Trial ID:* NR	Mean time between cataract surgery and baseline measurement for the sample was 31.8 (29.8) months. *Dose details:* Not applicable *Dose modifications:* Not applicable *Concurrent treatment:* NR *Duration of treatment:* NR	6 patients had a blue light filter in one eye and no colour filter on the other eye. *Sample attrition/dropout*: NR Included: pseudophakic AMD (following an uncomplicated cataract extraction and implantation of a posterior chamber intraocular lens) with GA. Excluded*:* scans to monitor 1-year progression of GA unavailable or of low quality, history of any other ocular disease, wet AMD, and following vitreoretinal surgery including intravitreal injections	
Lavric & Pompe 2014{#997} *Country:* Slovenia *Design:* cohort study *Number of centres:* one *Funding:* not reported *Trial ID:* not reported	*Intervention* *1.* Intraocular lens (IOL) after cataract extraction with UV-light and blue-light filter (study eye) *2.*IOL UV-light filter (fellow eye) *Dose details:* not applicable *Dose modifications:* not applicable *Concurrent treatment:* not reported *Duration of treatment:* at least up to follow-up	*Number of Participants*: total 30 *Number of eyes* total 60 *Sample attrition/dropout*: not reported Included: uncomplicated age-related cataract, phacoemulsification, intraocular lens implantation at least 2 years before. Interval between first and contralateral cataract operation ≤3 months. Excluded*:* any known ocular pathology (other than cataract) such as corneal disease, inflammation, glaucoma, amblyopia, diabetic retinopathy.	*Outcomes (state if primary)* • BCVA (ETDRS, converted to logMAR) • Contrast Sensitivity • Macular findings • QOL (NEI-VFQ-25, score 0-100) *Length of follow-up:* mean 31.93 (SD 8.11) months blue light filter, 33.75 (8.4) months UV filter.
Nagai *et al.*, 2015{958} *Country:* Japan and Switzerland *Design:* cohort study *Number of centres:* 2	*Intervention* *1.* blue-light filtering intraocular lens (IOL) (yellow-tinted) at cataract extraction *2.* colourless IOL at cataract extraction *Dose details:* not applicable *Dose modifications:* not applicable	*Number of Participants*: total 131; 52 blue-light; 79 colourless *Number of eyes* total 131; 52 blue-light; 79 colourless *Sample attrition/dropout*: Of 174 eyes enrolled, total 43 eyes (blue-light IOL 22; colourless IOL 21) either no images obtained at follow-up; patient did not complete the visit or posterior capsule opacification	*Outcomes* • Development, progression or decrease in abnormal fundus autofluorescence (FAF) • Presence or absence of drusen • Development of wet AMD • Development of GA *Length of follow-up:* 2 years

Funding: not reported *Trial ID:* not reported	*Concurrent treatment:* not reported *Duration of treatment:* at least 2 years	Included: had uneventful cataract surgery with implantation of a blue-light IOL or colourless IOL and whose fundus autofluorescence images were obtainable immediately after surgery. If bilateral surgery, the first eye was included Excluded*:* presence of AMD, diabetic retinopathy, glaucoma or high myopia of -6.0 diopters or more.	
Chong *et al.*, 2011 (abstract){#907} *Country:* Not reported *Design:* Prospective cohort study (pilot) *Number of centres:* one *Funding:* Not reported *Trial ID:* Not reported	*Intervention* *1.* Blue blocking IOL *2.* Clear UV-filter IOL *Dose details:* N/A *Dose modifications:* N/A *Concurrent treatment:* Not reported *Duration of treatment:* up to 2 years, mean duration between consecutive cataract surgeries was 307 days	*Number of Participants*: 128 *Number of eyes:* 256 (blue blocking intraocular lens (IOL): 128, clear IOL: 128) *Sample attrition/dropout*: Not reported *Sample crossovers:* Not reported *Inclusion criteria:* patients undergoing consecutive bilateral cataract surgery with implantation of a clear IOL in one eye and a blue blocking IOL in the fellow eye within 1 year *Exclusion criteria:* Not reported	*Outcomes (state if primary)* • Progression of AMD, graded by clinical age-related maculopathy staging system (CARMS) *Length of follow-up:* mean 25.9 months
Haemopheresis			
Blaha et al., 2013{#372} Linked publication: Blaha et al 2012{#322} *Country:* Czech Republic *Design:* CCT (incorrectly described as randomised) *Number of centres:* one	*Intervention* *1.* rheohaemapheresis *2.* control *Dose details:* 8 procedures, 2 weekly with a 14-day pause, procedure repeated 4 times. *Dose modifications:* 1-2 procedures added after one year follow up if needed (if suspicion or symptoms of disease progression	*Number of Participants*: total 72: 38 rheohaemapheresis; 34 controls. Of these 12 and 13 patients had drusenoid retinal pigment epithelium detachment (DPED) *Number of eyes*: unclear for total group, for subgroup with DPED was 22 eyes in the rheohaemapheresis group and 18 in the control group. *Sample attrition/dropout*: 1 rheohaemapheresis participants withdrew after 2 treatments	*Outcomes* • BCVA (ETDRS) • Progression to wet AMD • DPED area. • Adverse events *Length of follow-up:* 2.5 years

Funding: non-commercial grant *Trial ID:* NR Possible overlap of participants from Studnilka et al 2013{#373} and Rencová et al., 2015 {#197}	discovered). *Concurrent treatment:* NR *Duration of treatment:* 10 weeks	Included: diagnosis of bilateral AMD, including dry AMD in one or both eyes, subgroup with late-stage, high-risk, preangiogenic form of AMD with soft drusen, confluent soft drusen and DPED Excluded*:* other retinal or choroidal disorder, optic nerve disorders, glaucoma, conditions limiting the examination of the fundus, and acute bleeding in the studied eye, general exclusion criteria for rheohaemapheresis	
Studnička et al 2013{#373} *Country:* Czech Republic *Design:* CCT *Number of centres:* one *Funding:* non-commercial grant *Trial ID:* NR Possible overlap of participants from Blaha et al., 2013{#371} and Rencova 2015 {#197)	*Intervention* *1*. rheohaemapheresis *2.* control *Dose details:* 8 procedures of 1.5 plasma volumes *Dose modifications:* not stated *Concurrent treatment:* not stated *Duration of treatment:* 10 weeks	*Number of Participants*: Total 37: 19 rheohaemapheresis; 18 controls. Of these 17 and 17 patients had drusenoid pigment epithelium detachment (DPED) *Number of eyes* rheohaemapheresis 35, control 27. For subgroup with DPED rheohaemapheresis 30; control 20 *Sample attrition/dropout*: NR Included: dry AMD, latestage, high-risk, preangiogenic form of AMD with soft drusen, confluent soft drusen, and DPED Excluded: other retinal or choroidal disorders, optic nerve disorders, glaucoma, conditions limiting the examination of the fundus, acute bleeding in the studied eye, general exclusion criteria for rheohaemapheresis. Eyes with neovascular AMD were not included in the subsequent evaluation.	*Outcomes* • BCVA (ETDRS) • Occurrence of wet AMD • Occurrence of DPED *Length of follow-up:* minimum 3.5 years (between 42 and 84 months)
Klingel et al., 2010 {#438} *Country:* Germany *Design:* Retrospective	*Intervention* *1*. Rheopheresis (double filtration plasmapheresis (DFPP)) *2.* Control (no treatment)	*Number of Participants*: 1110 with microcirculatory disorders for safety, total with Dry AMD 833. Total Dry AMD for efficacy 334 (279 treated; 55 controls) *Number of eyes* for efficacy assessments 513 (428	*Outcomes* • Adverse events (of treatments for variety of microcirculatory disorders) • BCVA

cohort study *Number of centres:* 65 *Funding:* Commercial funding *Trial ID:* not applicable	 *Dose details:* 8–10 rheopheresis treatments (average 8.1, SD 1.6) within a period of 10–17 (average 15, SD 14) weeks. *Dose modifications:* Patients with sudden sensorineural hearing loss, as an example of acute therapy, were treated twice within one week. *Concurrent treatment:* NR *Duration of treatment:* NR	treated, 85 controls) *Sample attrition/dropout*: efficacy data only available for 33% of AMD patients Included: having actually received a rheopheresis treatment. Dry AMD, soft drusen, pigmentary abnormalities or minor atrophy, visual acuity 0.1–0.63, or subjective or objective progression of vision loss with psychological strain. Control patients met the criteria but were not treated for different reasons, including unwilling to receive treatment. Excluded*:* NR	 *Length of follow-up:* mean of 6.75 (SD 5.25) months
Koss et al., 2009 {#479} *Country:* Germany *Design:* RCT *Number of centres:* one *Funding:* commercial funding *Trial ID:* NR	*Intervention* *1.* Rheopheresis *2.* Control (no treatment) *Dose details:* 10 treatments, treatments 1 and 2 were in the first week, with a 2–3 day interval, treatments 3-10 were performed as single therapies with a 1-week therapy-free interval between treatments. The target was to treat 100% of patient's plasma volume per treatment, estimated using the formula 40 ml x body weight (kg) of the patient. 99% (SE 0.08) of patients´ plasma volume was reached in 236 treatments of 25 patients. *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* within 17 weeks	*Number of Participants*: 52 (26 treatment, 26 control) *Number of eyes* 43 (22 treatment, 21 control) *Sample attrition/dropout*: 9 (4 treatment, 5 control) Included: 45-85 years; bilateral AMD, and dry AMD in the study eye; BCVA in study eyes 0.1-0.8 (by ETDRS charts); peripheral veins allowing vascular access to establish the extracorporeal circuit. Excluded: other retinal or choroidal disorders, optic nerve disease, glaucoma, conditions that limit the view of the fundus, acute bleeding in any eye, general exclusion criteria for rheopheresis .	*Outcomes* • mean logMar change in BCVA by ETDRS (primary outcome) • Proportion of eyes with loss or gain of BCVA • Safety *Length of follow-up:* 7.5 months
Pulido et al., 2006{#536}	*Intervention*	*Number of Participants*: 216 randomised, 198 treated	*Outcomes*

Linked publication of interim data Pulido et al., 2005{#535} *Country:* USA *Design:* RCT *Number of centres:* 13 *Funding:* not stated *Trial ID:* not stated	*1.* rheopheresis *2.* Placebo (sham treatment) *Dose details:* 8 treatments as paired sessions (1 plasma volume per session with a 2-day recovery interval between them) *Dose modifications:* those who experienced an "improvement" at 3-months but then later showed a decrease at 9-months were eligible to receive two additional treatments (either rheopheresis or placebo) 2 weeks after the 9-month post baseline visit. *Concurrent treatment:* Oral supplements of zinc, high-dose vitamins and antioxidants. *Duration of treatment:* 10 weeks	(rheopheresis 129; placebo 69) *Number of eyes* 198 (rheopheresis 129; placebo 69) *Sample attrition/dropout*: 18 did not complete 1 treatment and were not included in the analysis (group NR). 15 others were excluded from the rheopheresis group because of poor venous access (n=13) and no post baseline measurement (n=2). At 12 months, 10 rheopheresis and 6 placebo patients did not have follow-up. Included: 50-85 years, ≥50kg, dry AMD in study eye with ≥10 large, soft, semisoft, and/or confluent drusen within 3,000 nm of the foveal centre, BCVA (ETDRS) 20/32 - 20/125, GA allowed if N 3 disc diameters outside of 3,000 nm foveal centre, serous pigment epithelial detachment allowed if no neovascularisation present, ≤75 on VFQ-25 Visual Functioning Questionnaire, no conditions that limit the view of the fundus. If both eyes qualified, one eye was randomized to the study eye. Excluded*:* study eye with other retinal or choroidal disorder, significant central lens opacities, wet AMD, other ocular disease. Patient in poor health (various conditions stated but not extracted)	• BCVA change (primary outcome) • Decrease in drusen • Development of CNV • Adverse events • BCVA in fellow eye • Pepper Visual Skills for Reading Test • NEI VFQ-25. *Length of follow-up:* 12 months (initial data analysis of final data)
Rencová et al., 2015{#197} *Country:* Czech Republic *Design:* RCT *Number of centres:* one *Funding:* non-commercial	*Intervention* *1.* Rheohemapheresis *2.* Control (not specified) *Dose details:* 8 procedures (says standardised) *Dose modifications:* NR *Concurrent treatment:* NR	*Number of Participants*: Total 24 1. Rheohemapheresis 12 2. Control 12 *Number of eyes:* Total 40 (Rheohemapheresis 22, control 18) *Sample attrition/dropout*: NR Included*:* high-risk, preangiogenic form of AMD	*Outcomes* • BCVA (ETDRS letters) • DPED area *Length of follow-up:* 2.5 years

Trial ID: NR Possible overlap of participants from Blaha et al., 2013{#371} and Studnička et al 2013{#372}	*Duration of treatment:* 10 weeks	(dry) with soft drusen, reticular drusen, confluent soft drusen, and drusenoid pigment epithelium detachment (DPED) Excluded: other retinal or choroidal disorders, optic nerve disorders, glaucoma, conditions limiting the examination of the fundus, acute bleeding in study eye; general exclusion criteria for rheohaemapheresis.	
Brunner et al., 2000{#687} Widder et al., 2002 Country: Germany Design: RCT and Follow-up cohort study Number of centres: one Funding: Commercial support Trial ID: Not reported Cohort study (Widder et al) assumed by reviewers to be linked to Brunner, assumed that a subgroup from both groups who had Dry AMD (see Appendix X).	*Intervention* *1.* Membrane differential filtration *2.* Control (no treatment) *Dose details:* Treated 5 times (every 5 weeks). One treatment cycle was 2 treatments with a 2 day interval while patients were admitted to hospital. 120% of plasma volume processed during first treatment and 80% during second treatment *Dose modifications:* Smaller volumes of plasma, down to 60%, could be processed if the plasma protein values at the end of the first treatment were subnormal. *Concurrent treatment:* Anticoagulation of 4500 units of heparin and acid citrate dextrose formula A infused at a ratio of 1:16 *Duration of treatment:* 21 weeks	*Number of Participants*: Total 40 (membrane differential filtration 20, control 20) *Number of eyes* 40 (membrane differential filtration 20, control 20) *Sample attrition/dropout*: 3 after randomisation (membrane differential filtration 2, control 1) non treatment-related concomitant disease; replaced by 3 new patients. Included: Visual acuity between 20/160 and 20/32 in at least one eye, signs of AMD such as drusen, areolar atrophy, pigment clumping, pigment epithelium detachment or subretinal neovascularization (SRNV). If both eyes eligible, one eye was randomized by random numbers. Excluded: Dementia, severe cardiac disease, history of malignoma or infection with hepatitis, HIV or Treponema pallidum, suitability for laser coagulation.	*Outcomes* • Visual acuity, ETDRS charts, at 21 weeks (primary outcome) • Light responses • Central visual field • Adverse events *Length of follow-up:* treatment: 11 months (range 7-24), control 12 months (range 6-29)
Swartz et al., 1999{#686} *Country:* USA *Design:* RCT (pilot study)	*Intervention* *1.* Membrane Differential Filtration Apheresis *2.* Treatment without filtration *3.* No treatment	*Number of Participants*: total 30: Aphersis 10; treatment without filtration 10; no treatment 10 *Number of eyes* total 30: Apheresis 10; treatment without filtration 10; no treatment 10	*Outcomes* • BCVA (distance) (ETDRS) (primary outcome) • Reading speed (Pepper Visual Skills for Reading Test, PVSRT) (primary outcome)

Number of centres: assumed one *Funding:* not reported *Trial ID:* not reported	*Dose details:* apheresis 10 treatments, no other details *Dose modifications:* no details *Concurrent treatment:* no details *Duration of treatment:* 20 weeks	*Sample attrition/dropout*: not stated Included: non-exudative AMD characterised by large soft drusen and visual acuity 20/40 – 20/100 in one eye. Excluded: no details	*Length of follow-up:* 20 weeks assumed
Laser			
Figueroa et al., 1997{#780} *Country:* Spain *Design:* Case series and RCT *Number of centres:* One *Funding:* NR *Trial ID:* NR	*Intervention* Cohort 1: *1.* Laser photocoagulation *2.* Control Cohort 2: 1. Laser photocoagulation *Dose details:* Green argon laser applied a minimum of 500 microns from centre of the foveal avascular zone for 0.1 seconds with a spot size of 100 microns. Energy was sent at the minimum level to obtain a gray-white reaction. Average of 39 (range 18-47) laser spots applied. *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* One application	*Number of Participants*: Total n=46 Cohort 1, n=30 Cohort 2, n=16 *Number of eyes* Cohort 1, 60 eyes (one eye per patient assigned to intervention, n=30 and one eye assigned to control, n=30) Cohort 2, 32 eyes (both eyes per patient received intervention) *Sample attrition/dropout*: NR Included: Cohort 1: Bilateral confluent soft drusen and pigmentary changes. Cohort 2: High-risk drusen in one eye and choroidal neovascular membrane in fellow eye. Excluded: NR	*Outcomes* • Drusen disappearance • Visual acuity *Length of follow-up:* average 3 years (range 1.5 to 5 years)
Guymer et al., 2014{#239} *Country:* Australia *Design:* Prospective cohort	*Intervention* *1.* Ultra-low energy laser therapy *Dose details:* pulses to 12 spots around the macula of one eye (0.15–0.45 mJ), using 400	*Number of Participants*: total: 52 *Number of eyes*: 52 treated; 52 control eyes. *Sample attrition/dropout*: 1 participant did not receive	*Outcomes* • AMD risk factor questionnaire • BCVA • Macular sensitivity (flicker perimetry)

study (pilot), within participant controls *Number of centres:* 1 *Funding:* commercial and non-commercial grant *Trial ID:* ACTRN12609001056280 Linked study (Jobling et al 2015) compared these results to a natural history cohort, no details of these participants provided.	μm diameter spot, 3 nanosecond pulse length, 532 nm wavelength and energy titrated to each patient. The average laser energy at each treatment spot was 0.24 mJ (with a range of 0.15–0.45 mJ) with an average radiant exposure of 0.19 J/cm^2 (ranged 0.12–0.36). *Dose modifications:* at time unspecified the protocol was altered and treatment spots were moved out slightly further from the foveal centre (approximately 2000 μm), to just inside the arcades *Concurrent treatment:* NR *Duration of treatment:* NR	the intervention (unable to complete all tests required); 1 was lost to follow-up (died) Included: bilateral intermediate AMD (multiple drusen >125 μm in both maculae), aged over 49 years, BCVA (ETDRStudy logMAR chart) of at least 6/18 (60 letters). Excluded: evidence of GA on colour fundus photographic grading, presence of CNV, any past treatment for CNV in either eye or signs of any other ocular disease.	• Presence of GA or CNV • Drusen area (in a high risk subgroup) *Length of follow-up:* 12 months
Ivandic et al., 2008{#660} *Country:* Germany *Design:* before and after study (with control) (described as a case series) *Number of centres:* 1 *Funding:* NR *Trial ID:* NR	*Intervention* *1*. low-level laser therapy 2. control (mock treatment) *Dose details:* continuous emission at 780nm (7.5 mW, 292 Hz) fitted with collimating optics (spot diameter 3 mm) applied transconjunctivally to the macula for 40 sec (0.3 J/cm^2). *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* Four treatments (2 per week), total dose 1.2 J/cm^2.	*Number of Participants*: 203 total. 193 laser, 10 control *Number of eyes:* total 348 (laser group 328, control 20) *Sample attrition/dropout*: none Included: AMD at all stages (dry to wet exudative forms with or without cataracts); visual acuity ≤20/20. Excluded: concomitant diseases that would impair vision except for new cataracts, or received any prior treatment that could have affected vision.	*Outcomes* • Visual acuity (Snellen); • Colour vision; • Central scotomas • Safety. *Length of follow-up:* NR ('after therapy')
Luttrull et al., 2016{#70} *Country:* USA	*Intervention* *1*. Panmacular subthreshold diode micropulse laser (SDM)	*Number of Participants*: total 116: 108 AMD; 8 inherited photoreceptor degeneration (IPD) *Number of eyes* total 168: 158 AMD; 10 IPD	*Outcomes* • Visual function improvement; • Snellen visual acuity; • Adverse events.

Design: retrospective cohort study (pilot) *Number of centres:* 1 *Funding:* NR *Trial ID:* NR	*Dose details:* entire posterior retina circumscribed by the major vascular arcades was ‘‘painted’’ with 1800 to 3000 confluent spot applications of SDM (‘‘panmacular’’ treatment). *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* 0.15 second duration	*Sample attrition/dropout*: none Included: high-risk AMD and inherited photoreceptor degeneration Excluded: other ocular disease and pathology, poor pattern electroretinography test quality, subfoveal choroidal neovascular membrane in the treated eye, active choroidal neovascular membrane in the fellow eye requiring anti-VEGF treatment	*Length of follow-up:* within 1 month of treatment
Huang et al., 2011{#411} *Country:* China *Design:* non-random controlled trial (pilot) – eye unit of allocation *Number of centres:* one *Funding:* NR *Trial ID:* ChiCTR-TNRC-00000221	*Intervention* *1.* Prophylactic laser treatment *2.* control *Dose details:* argon green laser, 514 nm. Approximately 100 laser spots with 0.1 second in duration and 200 μm in spot size with lowest intensity (55 mW–100 mW) to produce a barely visible lesion. The laser spots were placed in a temporal horseshoe-shaped area more than 750 μm from the foveal centre, extending to the vascular arcades *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* single application (assumed)	*Number of Participants*: Total 10 1. 10 (same 10) 2. 10 (same 10) *Number of eyes:* Total 20 *Sample attrition/dropout*: mean follow-up period of 98.5 months Included: patients with bilateral soft drusen Excluded: exudative macular degeneration in either eye and macular or retinal diseases that would interfere with vision.	*Outcomes* • Number of soft drusen • BCVA • Retinal contrast sensitivity • Macular thickness • Complications (CNV) *Length of follow-up:* >8 years, mean 98.5 months
Prahs et al., 2010{#445} *Country:* Germany	*Intervention* *1.* Selective retina therapy laser (prototype) *2.* Control	*Number of Participants*: total: 6 *Number of eyes:*12 (6 intervention; 6 control)	*Outcomes* • Progression of atrophic area • Adverse events

Design: Non-randomised controlled study (pilot) *Number of centres:* 1 *Funding:* non-commercial funding *Trial ID:* NR	*Dose details:* short laser pulses, wavelength 527 nm. Duration of pulse adjusted from 200 ns up to 3 µs with 30 repetitive pulses at 100 Hz applied on each retinal spot. The treatment energies applied were 140–160µJ (200 ns) and 200–300µJ (1.7µs). *Dose modifications:* each patient received 5-16 test exposures with increasing energies up to the level where lesions became ophthalmoscopically visible or maximal laser energy was reached. *Concurrent treatment:* NR *Duration of treatment:* NR	*Sample attrition/dropout*: none Included*:* bilateral equally pronounced geographic atropy; eye with inferior visual acuity treated. Excluded: NR	*Length of follow-up:* 1 year
Merry et al., 2016{#681} *Country:* Canada *Design:* Before and after study (one group) *Number of centres:* Two *Funding:* NR *Trial ID:* NR	*Intervention* *1.* Photobiomodulation (PBM) *Dose details:* Multiwavelength light emitting diode (LED) light comprising of yellow (590 nm), red (670 nm) and near-infrared (790 nm) bandwidths. Two separate devices were required to provide the multiple wavelengths. All subjects were treated in both eyes with the two devices used sequentially at each treatment visit. 3 sessions per week, total 9 sessions. *Dose modifications:* NR *Concurrent treatment:* All subjects had been taking AREDS supplementation prior to the intervention, and no changes were made to their current dosing regimen during the observational period.	*Number of Participants*: Total 24 *Number of eyes:* 42 *Sample attrition/dropout*: NR Included: ≥50 years with dry AMD, AREDS grades (according to the American Academy of Ophthalmology) 2-4 [GA no CNV] and a BCVA of letter score ≥50 (logMAR 1.0, Snellen 20/200). Excluded*:* previous/active wet AMD, a history of epilepsy, other retinal diseases, significant media opacity and cataracts worse than grade 2 (LOCS III)	*Outcomes* • BCVA (primary outcome) • Contrast sensitivity (primary outcome) • Drusen volume • Central drusen thickness • Geographic atrophy area • Retinal volume • New CNV or geographic atrophy *Length of follow-up:* 3 months

	Duration of treatment: 3 weeks		
Microcurrent			
Shinoda et al., 2008{#643} *Country:* Japan *Design:* Prospective before and after study *Number of centres:* one *Funding:* NR *Trial ID:* NR	*Intervention* *1.* Transcutaneous Electrical Retinal Stimulation (microcurrent 800 μA transpalpebrally applied to both eyes) *Dose details:* each sessions 20 minutes (a monophasic pulse with a frequency of 290 Hz for 1 minute, 31 Hz for 2 minutes, 8.9 Hz for 10 minutes, and 0.28 Hz for 7 minutes), 4 times each day for up to 1 month *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* up to 4 weeks	*Number of Participants*: 21 (5 Dry AMD; 16 Wet AMD [not extracted]) *Number of eyes:* 34 (7 dry AMD; 27 wet AMD) *Sample attrition/dropout*: NR Included*:* Eyes with a wet-type or dry-type AMD lesion involving the geometric centre of the foveal avascular zone Excluded: any significant ocular disease affecting visual acuity, history of intraocular or laser surgery within 6 months, any medication for AMD within 6 months, criteria for photodynamic therapy or antiVEGF therapy of intravitreal pegaptanib injection, with pathologic myopia.	*Outcomes* • BCVA; • ETDRS score; • Mean deviation of the automated perimetry *Length of follow-up:* 4 weeks
Chaikin et al., 2015{#146} *Country:* USA *Design:* Prospective before and after study *Number of centres:* 2 *Funding:* NR *Trial ID:* NCT01790958.	*Intervention* *1.* Frequency-specific microcurrent stimulation applied in a transpalpebral manner. *Dose details:* states the number of treatments was determined by condition severity and patient response, each session 35 minutes, microcurrent was 150 μA. Frequency (Hz) was used in pairs and selected depending on disease process. *Dose modifications:* no details *Concurrent treatment:* no details *Duration of treatment:* ranged between 2-10,	*Number of Participants*: 17 *Number of eyes* 31 (25 with dry AMD; 6 wet AMD [not extracted]) *Sample attrition/dropout*: NR Included*:* ≥50 years, history of retinal disease involvement, no antivascular endothelial growth factor treatments (for ≤ 3 months), no new antioxidant / vitamin supplementation (for ≤6 months), no active bleeding for wet AMD Excluded: history of noncompliance, significant media opacities, presence of pigment epithelial tears or rips, diabetic retinopathy, serious allergies to fluorescein dye, presence of retinal	*Outcomes* • BCVA; • retinal thickness, • microperimetry. *Length of follow-up:* varied, up to 3 months

	mean 4.8 sessions.	neovascularization, treatment with investigation agents in the past 30 days.	
Kondrot et al., 2015{#174} *Country:* USA *Design:* retrospective before-and-after study (data collected over 10 years) *Number of centres:* one *Funding:* No external funding. Participants paid $3000 each. *Trial ID:* NR	*Intervention* Customised, Intravenous nutrition (Myer's cocktail), oxidative therapy, microcurrent stimulation, syntonic light therapy (all provided at least one to each participant) *Dose details:* Myer's cocktail: Oxidative therapy: minimum of 2 intravenous therapies. Ozone was mixed with blood and injected into body and provided as eye drops (no further details) Intravenous hydrogen peroxide given to some patients. Microcurrent stimulation: no details of frequency or duration of application Syntonic light therapy: 2 treatments per day *Dose modifications:* NR *Concurrent treatment:* Information about diet, nutrition, hydration and creation of balance in autonomic nervous system. Homeopathy prescribed but not started during 3 day programme. *Duration of treatment:* 3 days programme (microcurrent therapy initiated on day 2)	*Number of Participants*: Total 152. Dry AMD 70, Stargardt's disease 3 (79 with other eye diseases, not extracted) *Number of eyes:* Total 290. Dry AMD 140, Stargardt's disease 6 (144 with other eye diseases, not extracted) *Sample attrition/dropout*: NR Included*:* eye disease not responsive to traditional treatments, patients wanted to avoid surgery or side effects of medication, paid $3000 for 3-day treatment programme. Excluded: NR	*Outcomes* • Visual acuity (ETDRS) • Contrast sensitivity • Visual field *Length of follow-up:* 3-days (not clear)
Kondrot et al., 2002{#459} *Country:* USA	*Intervention* *1.* Microcurrent stimulation *Dose details:* Microstim 400 unit used for initial 8 treatments, then microstim 100 unit	*Number of Participants*: Total 28 (n=10 pilot study) *Number of eyes* 56 *Sample attrition/dropout*: NR	*Outcomes* • Visual acuity *Length of follow-up:* 3 months – 1 year

Design: Before-and-after study (also reports pilot study) *Number of centres:* one *Funding:* NR *Trial ID:* NR	twice a day for 5/7 days a week. 4 points above and 4 points below eye each treated with 4 frequency settings (292 HZ, 30 Hz, 9.1 Hz and 0.3 Hz) for 12 seconds each. The current was slowly turned up until a sensation was produced and then it was turned down until all sensation of electricity subsided. All treatments were conducted at this sub-threshold level. *Dose modifications:* NR *Concurrent treatment:* vitamin and nutritional supplementation consisting of Pure Focus sublingual spray (Biomax) and the Macular Degeneration Formula (Nutritional Research) *Duration of treatment:* minimum 3 months (unclear) also states 'every' three months for a year	Included*:* Dry AMD. No further details Excluded*:* glaucoma and previous retinal laser surgery	
Anastassiou et al., 2013{#343} *Country:* Germany *Design:* RCT *Number of centres:* 1 *Funding:* NR *Trial ID:* NR	*Intervention* *1.* Transpalpebral electrotherapy (microstimulation, TheraMac™) *2.* Placebo (sham treatment) *Dose details:* 2 sessions of 40 seconds on 5 consecutive days, *Dose modifications:* current varied between 150 and 220 µA. 8 contact points. Frequencies 5Hz to 80Hz in a pre-defined pattern. *Concurrent treatment:* NR *Duration of treatment:* 5 days	*Number of Participants*: 22 total (microstimulation: 12, placebo:10) of a total 31 eligible *Number of eyes:* NR *Sample attrition/dropout*: 9 of 31 eligible refused. 3 (1 microstimulation [capsulotomy]: 2 placebo [refused]) at the 6 month evaluation Included*:* Dry AMD, no history or signs of neovascular disease in either eye, visual acuity between 25 and 45 ETDRS letters. Excluded: current or history of heavy smoking, electrical implant such as a pacemaker, ocular comorbidities with significant influence on visual acuity, aged under 50 years.	*Outcomes* • Change in visual acuity (ETDRS letters) at 4 weeks (primary outcome); • change in contrast sensitivity; • macular sensitivity; • fixation stability; • adverse events. *Length of follow-up:* 6 months

Michael et al., 1993{#721} (study 1) Allen et al., 1998{#710} (study 2) (two linked studies, study 1 was ongoing, study 2 presented 2 studies, described here as cohorts) *Country:* USA *Design:* case series *Number of centres:* 3 *Funding:* not reported *Trial ID:* not reported	*Intervention* *1.* nutritional supplements and electrical stimulation *Dose details:* nutritional supplements taken twice daily. Microampere electricity applied to 8 points on the eye lid. Study 1: 200 micro amperes for a total time of treatment about 7 minutes per eye using the Electro-Acuscope 80. Study 2; cohort 1 treated once per week for 6 weeks and then monthly, with the Electro-Acuscope 80 (no longer available); cohort 2 'several' times per week with the Micro-Stim 400. Basic parameters are 200 micro-amperes at +/- 9 volts, alternating square wave current, 10 cycles per second. *Dose modifications:* participants in study 1 and the first cohort of study 2 received also nutritional supplements . *Concurrent treatment:* not reported *Duration of treatment:* study 1: 2-7 years; not reported for study 2	*Number of Participants*: total 71: study 1: 25; study 2: 46 (cohort 1 12; cohort 2: 34) *Number of eyes* total 71: study 1: 25; study 2: 46 (cohort 1 12; cohort 2: 34) *Sample attrition/dropout*: Study 1: 10 left the study (2 died, 3 had poor health, 2 had leakage, 2 had laser, 1 had a cardiac defibrillator). Study 2; cohort 2: 1 participant died, 1 left the state; 3 had cataract surgery; 2 had poor health but unclear if any of these dropped out as results were presented. Included: dry AMD (independently confirmed). Excluded: not reported	*Outcomes* • Visual acuity *Length of follow-up:* 2 years (study 1: 2-7 years)
Ozone			
Borrelli et al 2012{#323} *Country:* Italy *Design:* RCT *Number of centres:* one *Funding:* not stated	*Intervention* *1.* Oxygen Ozonetherapy (O_3-AHT) *2.* Control (oral supplementation of zinc and a high dose of vitamins and antioxidants) *Dose details:* O_3-AHT blood 225ml withdrawn from participant, missed with anticoagulant and ozone added which was mixed and then	*Number of Participants*: 140 (70 Oxygen Ozonetherapy (O_3-AHT); 70 control (multivitamins) *Number of eyes* 140 as state 1 study eye per participant (worst eye) *Sample attrition/dropout*: NR Included*:* between 59 and 82 years, diagnosis of bilateral AMD and dry AMD in the study eye with >	*Outcomes:* • mean change in log-MAR BCVA in study eyes (primary outcome); • proportioning of eyes with best-corrected ETDRS acuity loss or gain; • adverse events; NEI-VFQ (data not presented) *Length of follow-up:* 12 months

Trial ID: not stated	infused over 15-20 minutes. The entire procedure took approximately 40 minutes. Control: refers to a secondary publication for details of the supplements. *Dose modifications:* not stated *Concurrent treatment:* not stated *Duration of treatment:* O_3-AHT treatment was twice weekly for 7 weeks, twice monthly for 3 months and then monthly until the 12th month. Control not stated, assume for 12 months.	10 large, soft, semisoft and/or confluent drusen within 3mm of the foveal centre; BCVA with the ETDRS chart between 20/32 and 20/125 and no conditions limiting the view of the fundus. Excluded: study eye with concomitant retinal or choroidal disorder other than AMD, optic nerve pathology, glaucoma and bleeding.	
Bocci et al., 2011{674} *Country:* Italy *Design:* prospective controlled trial *Number of centres:* one *Funding:* NR (assume none) *Trial ID:* none	*Intervention* *1.* Ozonated AHT (undefined, assume autohaemotherapy) *2.* Oxygenated AHT (control) *Dose details:* ozonated AHT, a cycle of 12-13 treatments (elsewhere states 14-16) within 6.5-7.5 weeks *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* NR	*Number of Participants*: total 77: ozone 54; control 23 *Number of eyes:* not stated *Sample attrition/dropout*: not stated Included*:* not specified as such, states all presented with dry AMD, most commonly with soft confluent drusen followed by the geographic atrophy form Excluded*:* not stated	*Outcomes* • BCVA (Snellen chart) • Adverse events • Compliance *Length of follow-up:* 18 months
RPE transplant			
Schwartz *et al.*, 2015{#202} Schwartz *et al.*, 2016{#86} *Country:* USA	*Intervention* Subretinal transplantation of hESC derived retinal pigment epithelium (RP) *Dose details:* Injected 150 lL of resuspended	*Number of Participants*: Study 1: n= 9 with dry AMD Study 2: n=9 with Stargardt's macular dystrophy (STGD)	*Outcomes* • Safety and tolerability (primary outcome) • BCVA (ETDRS) • Quality of life.

Design: 2 before-after studies *Number of centres:* 4 *Funding:* Commercial and non-commercial funding *Trial ID:* NCT01345006 (STGD) NCT01344993 (dry AMD).	hESC-RPE. Three dose cohorts were used for each disorder with each cohort comprising three patients with STGD and three with AMD: cohort 1 received 50,000 cells, cohort 2 received 100,000 cells, and cohort 3 received 150,000 cells. *Dose modifications:* NR. *Concurrent treatment:* The immunosuppression regimen included tacrolimus (target blood concentrations 3–7 ng/mL) and mycophenolate mofetil (ranging from 0.25–2.00 g orally per day) a week before the surgical procedure and continued for 6 weeks. At week 6 the regimen called for discontinuation of tacrolimus and a continuation of mycophenolate mofetil for an additional 6 weeks. *Duration of treatment:* Single treatment with 12 weeks of immunosuppression.	*Number of eyes:* Study 1: 9 eyes (eye with worst vision) Study 2: 9 eyes (eye with worst vision) *Sample attrition/dropout*: Not stated Included*:* AMD: age >55 years, advanced dry AMD with >250 microns of GA involving central fovea. Stargadts: age > 18 years, end-stage disease, peripheral visual field constriction. Both diseases: BCVA of study eye 20/400 or worse; BCVA of fellow eye 20/400 or better, the ability to undergo a vitreoretinal surgical procedure under monitored anesthesia care, and psychological suitability to participate in a first-in-human clinical trial involving hESC-derived cells Excluded: other significant ophthalmic pathology, history of cancer, contraindications for systemic immunosuppression. Further details given in study appendix (not extracted).	*Length of follow-up:* Median follow-up 22 months (4 patients had <12 months follow-up, 12 patients had 12–36 months follow-up, and 2 patients had >36 months follow-up)
Song et al., 2015{#205} *Country:* Korea *Design:* Case series *Number of centres:* one *Funding:* commercial and non-commercial *Trial ID:* none	*Intervention* *1*. subretinal transplantation of human embryonic-stem-cell (hESC)-derived retinal pigment epithelium *Dose details:* details of the derivation of the RPE cells from the hESCs reported, not extracted. *Dose modifications:* not applicable *Concurrent treatment:* immunosuppression (no further details) *Duration of treatment:* 12 months	*Number of Participants*: 4 (2 dry AMD; 2 Stargardt's macular dystrophy). *Number of eyes* 4 *Sample attrition/dropout*: not applicable Included: none reported. Excluded: none reported	*Outcomes* • BCVA • Adverse events *Length of follow-up:* 12 months

Ho *et al.*, 2017{#971} *Country:* USA *Design:* cohort study, two phases 1) dose escalating, 2) 1 of 2 doses 'randomised'. Data for the two cohorts was combined. *Number of centres:* multicentre (number not stated) *Funding:* Commercial *Trial ID:* NCT01226628	*Intervention* *1.* subretinal administration of palucorcel (cell-based therapy) *2.* fellow eye control *Dose details:* human umbilical tissue–derived cells in a proprietary cryopreserved formulation. In phase 1 a single dose of palucorcel (ranging from 6.0 X 10^4 to 5.6 X 10^5 viable cells [12 received 6.0 X 10^4, 3 received 1.2 X 10^5, 15 received 3.0 X 10^5, 3 received 5.6 X 10^5 cells) In phase 2, single dose of 1 of the 2 doses of palucorcel (6.0 X 10^4 or 3 X 10^5 viable cells) *Dose modifications:* not applicable *Concurrent treatment:* standard postoperative care without systemic immunosuppression. *Duration of treatment:* not applicable	*Number of Participants*: total 35 enrolled; 33 treated: phase 1 29; phase 2 4 *Number of eyes* total 35 *Sample attrition/dropout*: 2 (in phase 1) underwent a partial surgical procedure but did not receive the cell implant because of retinal perforations; 3 (from phase 1) discontinued prior to 12 month follow-up. Included*:* ≥50 years of age with a confirmed diagnosis of bilateral GA caused by AMD (confirmed within 21 days prior to administration of the intervention); ≥1 GA lesion involving the centre of the macula, diameter of 360 μm, BCVA ≤20/200 in phase 1 and ≤20/80 in phase 2. The study eye was the eye with the worst visual acuity or selected by the investigator phase 1, and the worst eye in phase 2. Excluded*:* exudative AMD in either eye; evidence of other significant ophthalmic disease; any ophthalmic condition that reduced the clarity of the media (further details reported in the publication)	*Outcomes* • Adverse events (safety and tolerability primary outcome) • BCVA (ETDRS/logMAR/Snellen). • Contrast Sensitivity • Reading speed (not reported) • Reading acuity • Changes to area of GA • Quality of life (NEI VFQ-25) (states reported elsewhere, reference not provided) *Length of follow-up:* 4 years (ongoing), study endpoints 12 months Enrolment into phase 2 was suspended after 4 patients (for development of a more refined surgical technique for cell delivery).
Telescopes			
Hudson et al., 2006{#519} Linked publications: Boyer et al., 2015{#142} Hudson et al 2008{#618} Busbee et al., 2007{#551} Lane et al., 2006{#530} *Country:* USA	*Intervention* *1.* implantable miniature telescope *2.* non-implanted fellow eye *Dose details:* fixed-focus telescopic optical device, surgically implanted into the capsular bag, protruding through the pupil by 0.1-0.5mm. Two models implanted which differ in image enlargement only. Central visual	*Number of Participants*: total 217 enrolled; 206 implanted. *Number of eyes* total 434 (study eye 217; fellow eye 217) *Sample attrition/dropout*: 11 had aborted procedures (reasons provided); 2 required removal 1 month after implantation (condensation in the telescopic cylinder). At 12 months 14 were unavailable for	*Outcomes* • Gain of ≥ 2 lines of distance or near BCVA by ETDRS at 12 months (primary outcome) • ≥3 line improvement in BCVA (distance and near) • NEI VFQ-25 Activities of daily living scale. • Ocular complications from surgery • Adverse events (primary outcome)

Design: CCT *Number of centres:* 28 *Funding:* commercial funding *Trial ID:* NCT00976235 (for 5 year follow-up study).	field is enlarged 2.2 – 3 times that of an image normally projected by the cornea and lens, and the nominal forward field of view is 24° or 20°. *Dose modifications:* not reported *Concurrent treatment:* not reported *Duration of treatment:* up to 60 months	analysis (10 discontinued, reasons provided; 4 missing or lost to follow-up). At 24 months an additional 18 dropped out (numbers stated add to 32 assume double counting between 12 and 24 months: 10 died, 8 device removed [2 device failures, 2 cases of corneal oedema, 4 patient request], 13 lost to follow-up, 1 missed the two-year visit) At 60 months there were 63 participants with follow-up. Those aged 55–65 years (n=20) were excluded from the analysis. No other reasons for losses were reported. Included: aged ≥55 years, bilateral, central visual acuity loss by untreatable AMD (GA, disciform scar or both), phakic with cataract in the study eye, BCVA (distance) 20/80-20/800 (ETDRS), no ophthalmic pathologic features that could compromise functional peripheral vision in the fellow eye, ≥5 letter improvement with an external telescope for 3 days. Excluded: active CNV, treatment of CNV, intraocular or corneal surgery in the study eye, endothelial cell density <1600 cells/mm^2 and narrow angle.	• Vision loss • Telescope removal / malfunction *Length of follow-up:* up to 60 months (extension study Boyer, subgroup analyses only). Longest follow-up for whole population was 24 months (Hudson et al paper)
Qureshi et al., 2015{#196} *Country:* UK *Design:* Case series *Number of centres:* one *Funding:* commercial funding *Trial ID:* not reported	*Intervention* *1.* injectable telescopic intraocular lens (IOL) *Dose details:* consists of 2 soft hydrophobic acrylic IOLs, injected through a 3.0mm corneal incision, sits in the capsular bag and ciliary sulcus, provide a theoretical retical magnification of x1.25 to x1.3 with or without a prismatic effect. *Dose modifications:* not reported	*Number of Participants*: total 12 *Number of eyes* total 18 *Sample attrition/dropout*: not reported Included: bilateral, intermediate or advanced dry AMD with central scotomata, minimal cataract or pseudophakia, Snellen corrected distance visual acuity (CDVA) <0.25, improvement with extraocular simulation of the intervention	*Outcomes* • Corrected distance visual acuity (Snellen equivalent) • Corrected near visual acuity Snellen equivalent • Safety • Intraocular pressure *Length of follow-up:* 4 months

	Concurrent treatment: post-operative intracameral antibiotics, topical steroid and antibiotic for 1 month *Duration of treatment:* up to 4 months	Excluded*:* active CNV treated within 6 months, phacodonesis or corneal guttata, axial length of >24.5mm or <20.5mm, history of angle closure or pigment dispersion syndrome, retinal detachment, retinitis pigmentosa, optic neuropathy, uncontrolled glaucoma, intraocular surgery within 6 months.	

Pharmacological treatments			
Study	**Intervention Details**	**Participant details and key eligibility criteria**	**Relevant Outcomes**
Alprostadil			
Augustin et al 2013{#385} *Country:* Germany and Austria *Design:* RCT *Number of centres:* 6 *Funding:* commercial funding *Trial ID:* NR	*Intervention* *1.* alprostadil *2.* Placebo *Dose details:* once daily (5 days per week) intravenous infusions (15 infusions over 3 weeks) of 60 μg/day alprostadil (in 100ml sodium chloride) or 47.5mg lactose (placebo) in 100ml sodium chloride. Infusion took between 1.5 and 2 hours. *Dose modifications:* not stated *Concurrent treatment:* Treatments of diseases already present were continued, no further details. AREDS (reference given) medication, ophthalmologic dietary supplements, vasoactive medication, prostaglandins, any other dry AMD treatment were prohibited. *Duration of treatment:* 3 weeks	*Number of Participants*: 36 (18 alprostadil, 18 placebo) *Number of eyes* NR, assume 36 as refers to 'study eye' *Sample attrition/dropout*: 3 patients (2 alprostadil, 1 placebo) had no baseline measure and were excluded from full analysis. 12 had protocol deviations and were excluded from PPS (7 alprostadil, 5 placebo) Included: Adults over 50 years with dry AMD with hard drusen and possible early GA limited to the perifoveal area in one eye, visual acuity within 0.2 to 0.7 logMAR (ETDRS charts) Excluded*:* neovascular AMD in at least one eye, detachment of the retinal pigment epithelium, AREDS 3 with large soft drusen, glaucoma, uveitis, diabetic retinopathy, medical history of retinal vein occlusion, retinal haemorrhage, vitrectomy, cataract surgery, co-morbidities	*Outcomes:* • change from BCVA at 3 months (primary outcome). • Difference in BCVA immediately after treatment and at 6 months compared with baseline; • Differences in CS and colour vision immediately after as well as 3 and 6 months after the end of treatment; • State of dry AMD and presence of neovascular AMD (defined as Progression, Stabilization, or Amelioration) • Adverse events. *Length of follow-up:* 6 months after end of 3 week treatment phase
Ladewig et al., 2005{#529} *Country:* Germany	*Intervention* *1.* Prostaglandin E_1 (PGE_1) *2.* No treatment	*Number of Participants*: Total 21 (treated 11, not treated 10) *Number of eyes:* NR	*Outcomes:* • Visual acuity of the study eye (ETDRS chart) (primary outcome) • Contrast vision

Design: Controlled before and after study (pilot) *Number of centres:* one *Funding:* states financed independently *Trial ID:* NR	*Dose details:* intravenous infusion of PGE_1 (Prostavasin) 60µg, dissolved in 50 ml of sodium chloride once daily *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* 21 days	*Sample attrition/dropout*: NR Included: presence of dry form of AMD with ≥ 10 soft and/or hard drusen, atrophies and proliferations of the retinal pigment epithelium, early geographic atrophy and pigment epithelial detachment without indications of CNV. ETDRS acuity ≥0.2 and ≤0.8. Excluded*:* age < 50 years, other eye diseases, insufficiently treated heart failure or coronary heart disease, myocardial infarction (past 6 months), other comorbidities, anticipation of haemorrhagic complications	• Colour vision • Visual field • Drusen and atrophic areas • Adverse events *Length of follow-up:* 6 months
Dorzolamide			
Remky et al., 2005{#537} *Country:* Germany *Design:* RCT (pilot) *Number of centres:* 1 *Funding:* NR *Trial ID:* NR	*Intervention* *1.* Dorzolamide 0.2% eye drop *2.* Placebo, artificial tear. *Dose details:* 3 times daily for 12 weeks *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* 12 weeks	*Number of Participants*: total 40: dorzolamide 20; placebo 20 *Number of eyes:* total 40: dorzolamide 20; placebo 20 *Sample attrition/dropout*: 2 participants withdrew after recruitment and were replaced by 2 others. 2 participants withdrew after receiving allocated intervention, unclear which groups these came from. Included: AMD (any drusen, hyperpigmentation or small atrophic lesions) with visual acuity >0.4 (20/50). The eye with better visual acuity was selected, if equal, the eye with the lower refractive error was chosen. Excluded: any atrophic area >200 µm in diameter, any exudative lesions or history of eye disease that might have impact on retinal function, moderate and advanced nuclear opacities.	*Outcomes* • BCVA • Shortwavelength automated perimetry, mean and standard deviation sensitivity. *Length of follow-up:* 12 weeks (mean 96 (SD 9) days)
Complement inhibitors			
Eculizumab			

Yehoshua et al., 2014{#283} *Country:* USA *Design:* RCT *Number of centres:* one *Funding:* Commercial and non-commercial funding *Trial ID:* NCT00935883	*Intervention* *1.* Eculizumab *2.* Placebo (saline infusion) *Dose details:* The first 10 patients received low dose (600 mg via intravenous (iv) infusion for 4 weeks (induction) followed by 900 mg every 2 weeks until week 24 (maintenance)). The next 10 patients received high dose (900 mg iv for 4 weeks (induction) followed by 1200 mg every 2 weeks until week 24 (maintenance) *Dose modifications:* NR *Concurrent treatment:* All patients received a meningococcal vaccine at least 15 days before the initiation of treatment *Duration of treatment:* 24 weeks	*Number of Participants*: Total 30. Eculizumab n=20 (low dose 10, high dose 10); Placebo n=10 *Number of eyes:* Total 48 (30 study eyes, 18 fellow eyes) *Sample attrition/dropout*: 0 Included: age ≥50 years, total GA area of 1.25 to 18 mm^2, visual acuity of 20/63 or better; if both eyes eligible, 1 eye was chosen Excluded: GA contiguous with any peripapillary atrophy, any history of choroidal neovascularization in the study eye.	*Outcomes* • Change in area of GA at 26 weeks (primary outcome) • ETDRS visual acuity change from baseline in normal luminance and low luminance in both study and fellow eyes • Conversion rate from dry AMD to wet AMD in both study and fellow eyes. • Adverse events *Length of follow-up:* 12 months
Emixustat			
Dugal et al., 2015 {#152} *Country: USA* *Design:* RCT *Number of centres:* 12 *Funding:* commercial funding *Trial* NCT01002950	*Intervention* *1.* Emixustat (oral, once daily) *2.* Placebo *Dose details:* *1.* Emixustat 2mg once every morning (qAM) *2.* Emixustat 5mg qAM *3.* Emixustat 5mg once every evening (qPM) 4. Emixustat 7mg qAM *5.* Emixustat 10mg qAM *Dose modifications:* None stated	*Number of Participants*: N=72 1. Emixustat 2mg qAM (n=12) *2.* Emixustat 5mg qAM (n=12) *5.* Emixustat 5mg qPM (n=12) *4.* Emixustat 7mg qAM (n=12) *3.* Emixustat 10mg qAM (n=6) 6. Placebo (n=18) *Number of eyes:* one study eye – defined by it being either: (i) only eye, (ii) if both eyes qualified, then worse eye by largest lesion of GA; (iii) if both eyes qualified and same size lesion of GA and all inclusion criteria met, then right eye.	*Outcomes* • Modulation of visual cycle • Adverse events • Best corrected visual acuity • GA lesion size change • Compliance *Length of follow-up:* 90 days (7-mg and 10-mg emixustat groups received median exposure 25 days compared to 90 days for other groups)

	Concurrent treatment: None stated *Duration of treatment:* 90 days	*Sample attrition/dropout*: Overall: N=29 (Emixustat n=23; placebo n=6) due to ocular adverse events; Participant discontinuation: adverse events: N=8 (Emixustat n=8; placebo n=0); Sponsor discontinuation: 7mg and 10mg qAM doses discontinued due to adverse events: N=21 (Emixustat n=15; placebo n=6). Included: Adults, clinical diagnosis of GA (well-demarcated areas of partial or complete RPE depigmentation or loss); BCVA ≥20/400 in study eye. Excluded: GA in either eye associated with ocular disease other than AMD; known congenital/inherited colour vision abnormalities; exudative AMD in study eye; cataract or other intraocular surgery within 3 months; other eye surgery. (Note: 12 participants (10 emixustat, 2 placebo) exempt from inclusion criteria due to medication changes before study dosing.)	
Fenretinide			
Mata et al., 2013{#362} *Country:* USA *Design:* RCT *Number of centres:* 30 *Funding:* commercial funding *Trial ID:* NCT00429936	*Intervention* *1.* Fenretinide 100mg *2.* Fenretinide 300mg *3.* Placebo *Dose details:* oral fenretinide at either 100mg or 300mg after evening meal. No details of the placebo. *Dose modifications:* NR *Concurrent treatment:* also took vitamins without beta carotene.	*Number of Participants*: total 246; fenretinide 100mg: 80; fenretinide 300mg 84; placebo 82 *Number of eyes* NR (but refers to study eye and fellow eye) *Sample attrition/dropout*: total 68; fenretinide 100mg: 28 (12 withdrew consent, 2 lost to follow-up; 14 adverse event); fenretinide 300mg 26 (8 withdrew consent, 1 protocol violation, 17 adverse event); placebo 14 (8 withdrew consent, 1 protocol violation, 5 adverse events). Included: 50-89 years, GA (secondary to dry AMD) within 500 µm of fovea, total atrophic area 1-8 disk areas (2.54–20.32 mm^2) not characterized as either	*Outcomes* • change in aggregate lesion size growth (primary outcome) • BCVA • Contrast sensitivity • Onset of CNV • Night vision questionnaire (validated) – delayed dark adaptation (DDA) • Adverse events *Length of follow-up 25 months*

	Duration of treatment: NR (assume 2 years)	focal or patchy, BCVA 20/20 to 20/100. Excluded: active CNV in the study eye.	
Glatiramer acetate			
Landa et al., 2011{#412} Related publication of an earlier pilot study, Landa et al 2008{#633} reported here as few relevant outcomes and unclear if overlapping participants. *Country:* USA *Design:* CCT (pilot described as an RCT) *Number of centres:* one *Funding:* NR *Trial ID:* NR	*Intervention* *1.* glatiramer acetate *2.* placebo (sham injections) *Dose details:* weekly subcutaneous injections (pilot study states 20mg) *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* 12 weeks	*Number of Participants*: main analysis total 14; glatiramer acetate 7; placebo 7. Pilot study total 6; glatiramer acetate 4; placebo 2. *Number of eyes* main analysis total 26; glatiramer acetate 14; placebo 12. Pilot study total 12; glatiramer acetate 8; placebo 4. *Sample attrition/dropout*: NR Included: Dry AMD For the pilot study this was those aged over 50 years with bilateral intermediate dry AMD Excluded: NR in main publication. In the pilot study states excluded those with evidence of past or present exudative AMD in any eye.	*Outcomes* • Drusen changes (primary outcome) • Pilot study: total drusen area (primary outcome) *Length of follow-up:* 12 weeks
L-DOPA			
Brilliant et al., 2016{#18} *Country:* USA *Design:* Retrospective cohort study *Number of centres:* not applicable *Funding:* non-commercial grants	*Intervention* *1.* exposure to L-DOPA *2.* no exposure to L-DOPA *Dose details:* data on exposure captured by L-DOPA prescriptions *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* NR	*Number of Participants*: data from 3 registries. Marshfield Epidemiologic Study Area (approximately 17,500); Marshfield Clinic Personalized Medicine Research Project (PMRP, approximately 20,000); Truven MarketScan databases (15,215,458) *Number of eyes* NR *Sample attrition/dropout*: not applicable Included: those with long-term nearly complete electronic health records in the Marshfield Epidemiologic Study Area and those with an	*Outcomes* • incidence of AMD (any) *Length of follow-up:* NR

Trial ID: NR		ophthalmology record from the Truven MarketScan databases. Excluded: not stated	
NT-501			
Zhang et al., 2011{#691} *Country:* USA *Design:* RCT (pilot) *Number of centres:* 8 *Funding:* some funding from Neurotech USA (manufacturer) Trial ID: NCT00277134 (duplicate of record NCT00447954)	*Intervention* *1.* High dose intraocular NT-501 *2.* Low dose intraocular NT-501 (intended as placebo) 3. Sham *Dose details:* High dose: 20 ng per day Low dose: 5 ng per day *Dose modifications:* None *Concurrent treatment:* not reported *Duration of treatment:* 12 months	*Number of Participants*: Total n=51; *1.* High dose intraocular NT-501 n=27 *2.* Low dose intraocular NT-501 n=12 3. Sham n=12 *Number of eyes:* 51 (one eye per participant) *Sample attrition/dropout*: 0 Included: age ≥ 50 years, BCVA of 20/50–20/200 (Snellen equivalent, EDTRS) and presence of category 3 or 4:00 AMD geographic atrophy (defined by AREDS). Excluded: None stated.	*Outcomes* • Change in BCVA at 12 months after implant (primary outcome) • Retinal thickness and morphology • GA lesion size • Central vision visual field sensitivity *Length of follow-up:* 12 months
OT-551			
Wong et al., 2010{#454} *Country:* USA *Design:* RCT (phase II, pilot) *Number of centres:* one *Funding:* non-commercial funding *Trial ID:* NCT00306488	*Intervention* *1.* OT-551 (a lipophilic, disubstituted hydroxylamine) *2.* No treatment (observation) *Dose details:* 0.45%, eye drop with 40 µL, three times daily. *Dose modifications:* not reported *Concurrent treatment:* asked to refrain from using any medication into the no treatment eye.	*Number of Participants*: total 11 *Number of eyes* total 22; 11 OT-551; 11 no treatment (one eye from each participant randomly assigned to each arm) *Sample attrition/dropout*: 1 lost to follow-up at 3 months Included: bilateral GA, ≥ 60 years, area of GA in each eye not contiguous with areas of peripapillary atrophy and absence of evidence or history or exudative forms of AMD, adequate media clarity, good subjective tolerance, no signs of an allergic response.	*Outcomes* • BCVA (ETDRS) (primary outcome) • Changes in GA area • Progression to neovascular AMD • Drusen area • Contrast sensitivity • Safety *Length of follow-up:* 104 weeks (2 years + one month stated elsewhere)

	Duration of treatment: 2 years	Excluded: either eye with: history of other ocular disease, chronic ocular medication use for diseases that may affect study outcome, pseudovitelliform macular degeneration, vitreoretinal traction maculopathy, previous laser, photodynamic therapy, intravitral injections, other AMD treatments, ocular herpes simplex, cataract removal (previous 3 months).	
Prednisolone			
Vojniković et al., 2008{#631} *Country:* Croatia *Design:* Controlled before and after study *Number of centres:* NR *Funding:* NR *Trial ID:* NR	*Intervention* *1.* Prednisolone acetate *2.* Control *Dose details:* *1.* Prednisolone acetate 5 mg in parabulbar injections, 5 daily doses 2. multivitamin therapy (Lutein, Beta carotene, Vitamin E) in ordinary doses *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* 5 days for intervention, assume 6 months for control	*Number of Participants*: Total 475 (prednisolone 400, control 75) *Number of eyes* NR *Sample attrition/dropout*: NR Included: Dry AMD, no further details Excluded: NR	*Outcomes* • Visual acuity • Visual field *Length of follow-up:* 6 months
Ranibizumab			
Gallego-Pinazo et al., 2011{#903} *Country:* Spain *Design:* Before and after study *Number of centres:*1	*Intervention* *1.* intravitreal ranibizumab *Dose details:* a single intravitreal injection of 0.5 mg/0.05 mL of ranibizumab *Dose modifications: None* *Concurrent treatment:* topical gentamycin ointment following injection	*Number of Participants*: 6 patients *Number of eyes*: 6 eyes (1 per patient) *Sample attrition/dropout*: none Included: ≥50 years of age, study eye had ETDRS BCVA <20/30; drusenoid pigment epithelial detachment from AMD (defined).	*Outcomes* • ETDRS BCVA • Central macular thickness • Symptoms, including metamorphopsia • Number of treatments/re-treatments *Length of follow-up:*12 months (mean 66.7, SD 10.3, weeks)

Funding: NR *Trial ID:* NR	*Duration of treatment:* Patients were treated at baseline. Retreatment if persistence or recurrence of focal elevation of the retinal pigment epithelium contour or intraretinal fluid, or loss of ≥ five ETDRS letters compared with the prior examination. Mean number of re-treatments was 2.	Excluded: angiographic evidence of CNV; prior treatment with photodynamic therapy or other treatments ; history of uncontrolled glaucoma; retinal vascular disorder potentially related to macular oedema; and intraocular pressure of ≥25 mmHg.	
Sirolimus			
Petrou et al., 2015{#193} *Country:* USA *Design:* RCT *Number of centres:* one *Funding:* non-commercial grants (and investigational product donated by commercial company) *Trial ID:* NCT01445548	*Intervention* *1.* Sirolimus *2.* No treatment (observation) *Dose details:* 22 µg/lL (2%) solution in PEG 400 and 4% ethanol, 0.3ml injected as a 440 µg intravitreous injection in a 20 µL volume following anaesthetic. Given every 2 months. *Dose modifications:* not reported *Concurrent treatment:* not reported *Duration of treatment:* 12 months (aim was for 24 months).	*Number of Participants*: total 6 *Number of eyes* 12: one eye chosen randomly for the intervention group (n=6) and no treatment group (n=6) *Sample attrition/dropout*: one participant dropped out (adverse events); one participant had treatment discontinued (adverse events) Included: ≥56 years; bilateral GA; in each eye: area ≥ one-half disc area; ≥1 large drusen; BCVA 20/20 - 20/400; absence of evidence or history of exudative AMD Excluded: history of other ocular disease, intravitral injection (<4 months) or expectation of ocular surgery, lens removal or laser capsulotomy (<1 month), chronic ocular medication use for diseases that may affect study outcome, previous laser, photodynamic therapy, ocular herpes simplex virus, vitrectomy, history of cancer or receiving chemotherapy, other medical conditions or named medications (reported but not extracted)	*Outcomes* • Adverse events (primary outcome) • Changes in GA area (primary outcome) • BCVA (ETDRS) • Change in drusen area *Length of follow-up:* 1 year
Wong et al., 2013{#381} *Country:* USA	*Intervention* *1.* Sirolimus *2.* No treatment	*Number of Participants*: total 11 *Number of eyes* one eye chosen randomly for the intervention group (n=11) and no treatment group	*Outcomes* • Area of GA change (primary outcome) • BCVA

Design: RCT *Number of centres:* one *Funding:* non-commercial (and study drug donated by commercial entity) *Trial ID:* NCT00766649	*Dose details:* 2% solution in PEG 400 and 4% ethanol, injected into the subconjunctival space (20 µL volume with 440 µg sirolimus), administered at baseline and every 3 months. *Dose modifications:* not reported *Concurrent treatment:* not reported *Duration of treatment:* 24 months	(n=11) *Sample attrition/dropout*: 3 did not complete 24 months follow-up (2 withdrew for relocation and inability to travel; 1 died); all unrelated to study drug. Included: ≥55 years, bilateral GA, in each eye: GA in of area ≥ one-half disc area; ≥1 large drusen; BCVA 20/20 - 20/400; absence of evidence or history of exudative AMD Excluded: history of other ocular disease, topical treatment for advanced AMD (<1 month), intravitral injection (<4 months) or expectation of ocular surgery, lens removal (<3 months) or laser capsulotomy (<1 month), chronic ocular medication use, previous laser, photodynamic therapy, ocular herpes simplex virus, vitrectomy, history of cancer or receiving chemotherapy, other medical conditions or named medications (reported but not extracted)	• Area of drusen *Length of follow-up:* 24 months for efficacy, 27 months for safety
Statins			
Maguire et al., 2009{#481} *Country:* USA *Design:* Cross-sectional study (embedded within an RCT) *Number of centres:* 22 *Funding:* non-commercial grants *Trial ID:* none	*Intervention* *1.* Statins *Dose details:* no details *Dose modifications:* no details *Concurrent treatment:* no details but the focus of the trial was on laser treatment. *Duration of treatment:* starting year and ending year of statin use were recorded but not details provided	*Number of Participants*: 744 (of 764 in the trial). 296 had used statins, 187 started during commencement of the trial, 29 stopped using statins. *Number of eyes* 1477 *Sample attrition/dropout*: Not applicable Included: for original trial: ≥10 drusen ≥125 µm in diameter, visual acuity ≥20/40; no evidence of CNV, serous pigment epithelial detachment, GA within 500 µm of the foveal centre or >1 macular photocoagulation study disc area, or other ocular conditions or contraindication to laser treatment or follow-up; ≥50 years old. For this study, participants at the end of the trial were interviewed	*Outcomes* • Presence of endpoint GA. • Presence of CNV • Presence of advanced AMD *Length of follow-up:* between 5-6 years

		Excluded: NR	
Al-Holou 2015{#135} *Country:* USA *Design:* Prospective Cohort study *Number of centres:* 82 *Funding:* non-commercial and commercial grants *Trial ID:* NR	*Intervention* *1.* Statin use *Dose details:* NR *Dose modifications:* NR *Concurrent treatment:* AREDS2 trial participants either received placebo or lutein/zeaxanthin or docosahexaeonic acid (DHA) and eicosapentaenoic acid (EPA), or lutein/zeaxanthin and DHA plus EPA. *Duration of treatment:* NR	*Number of Participants*: 3791 *Number of eyes:* NR *Sample attrition/dropout*: NR Included: for AREDS2 trial: aged 50-85 years, bilateral large drusen or unilateral late AMD in one eye and large drusen in fellow eye. Excluded: NR	*Outcomes* • progression to late AMD *Length of follow-up:* median 5 years
Barbosa et al., 2014{#249} *Country:* USA *Design:* Cross sectional study *Number of centres:* not applicable (National Program) *Funding:* non-commercial grant (NIH) *Trial ID:* not applicable	*Intervention* *1.* Statin use (self-reported) *Dose details:* considered to be under statin therapy when reported the use of any type of statin such as lovastatin, pravastatin, simvastatin, fluvastatin, atorvastatin, cerivastatin, and rosuvastatin *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* mean length of time on statins 57.8 months, median 48 months (IQR: 24–96).	*Number of Participants*: 6797 participants eligible of which 5604 were included. 1231 were receiving statin therapy and 4873 were not. *Number of eyes:* 5604 *Sample attrition/dropout*: 1193 excluded (969 no complete ophthalmological examinations with retinal photographs, 224 unreadable photographs). Included: ≥ 40 years old, underwent both interview and examination of the National Health and Nutrition Examination Survey Excluded: NR	*Outcomes* Diagnosis of AMD in the worse eye: • Early AMD • Advanced or late AMD • Any AMD *Length of follow-up:* unclear, study used 2005-2008 data.
Vavvas et al., 2016{#94} *Country:* USA and Greece *Design:* Before and after	*Intervention* *1.* Atorvastatin *Dose details:* 80 mg, daily	*Number of Participants*: 26 *Number of eyes:* NR *Sample attrition/dropout*: 3 (1 cramps, 1 muscle	*Outcomes:* • reduction of drusenoid pigment epithelial detachment (PED) volume >50% (primary outcome) • Drusen volume

study, one group (pilot) *Number of centres:* 2 *Funding:* non-commercial funding *Trial ID:* none	*Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* minimum 12 months	aches, 1 hair loss) Included*:* >50 years of age, AMD, presence of many large (>300 μm in diameter, >100 μm in height) soft drusenoid pigment epithelial detachments (PED). Excluded: presence or history of significant GA or CNV, other eye diseases that could reduce visual acuity (excluding mild cataract), history of eye surgery, statin therapy (within the previous 2 years), history of liver disease.	*Length of follow-up:* minimum 12 months, average 1.5 years (average person years of follow-up were ~30)
McGwin et al., 2003{#897} *Country:* USA *Design:* Case-control study *Number of centres:* one *Funding:* non-commercial funding *Trial ID:* NR	*Intervention* *1.* Filled statin prescriptions (atorvastatin, cerivastatin, fluvastatin, pravastatin, simvastatin, lovastatin) and non-statin lipid lowering agents filled before the index date for each matched set of cases and controls *Dose details:* Not applicable *Dose modifications:* Not applicable *Concurrent treatment:* NR *Duration of treatment:* Reported in outcomes.	*Number of Participants*: Total 6050 (550 age related maculopathy (ARM) cases, 5500 controls) *Number of eyes* NR *Sample attrition/dropout*: NR Included: Men age ≥50 years who had at least one visit (inpatient or outpatient) to the medical centre 1 January 1997 and 31 December 2001; AMD defined using the ICD-9CM codes. Controls randomly selected from the study population without AMD. Ten controls were selected for each case and matched on age (plus or minus 1 year). Excluded: AMD diagnosis before the observation period	*Outcomes* • Proportion of patients with a statin prescription filled before the index date, • Current statin use, • Past statin use, • Duration of statin use, • Use of non-statin lipid lowering agents *Length of follow-up:* NR
Vanderbeek et al., 2013{#898} *Country:* USA *Design:* case-control *Number of centres:* one	*Intervention* *1.* Prescription of statins and other lipid-lowering medications (identified by National Drug Codes) *Dose details:* NR *Dose modifications:* NR	*Number of Participants*: 486,124 before exclusions due to diagnosis during initial 2 year period or missing laboratory values. Total for non-exudative AMD analysis: 107,007, Total for neovascular AMD analysis: 113,111; total for AMD progression analysis: 10753 *Number of eyes* NR	*Outcomes* • adjusted hazard ratios (HRs) of developing nonexudative AMD, exudative AMD, and conversion from nonexudative to exudative AMD *Length of follow-up:* duration in plan 4.2

Funding: non-commercial funding *Trial ID:* NR	*Concurrent treatment:* NR *Duration of treatment:* 751 (SD 634) days (nonexudative AMD analysis); 804 (SD 641) days (exudative AMD analysis); 797 (SD 649) days (progression from nonexudative to exudative AMD analysis)	*Sample attrition/dropout*: Not applicable Included: ≥ 60 year, in national insurance claims database ≥ 2 consecutive years and had ≥1 visits to an eye care provider during their time in the medical plan. Cases determined by ICD-9-CM codes, nonexudative AMD or exudative AMD Excluded: not in the medical plan continuously; exudative or nonexudative AMD in the first 2 years in the plan; for analysis on those already diagnosed with nonexudative AMD, those diagnosed with exudative AMD during this initial 2-year period; those without serum lipid levels recorded.	(SD 1.4) years
Kaiserman et al, 2009{#899} *Country:* Israel *Design:* Case control study (includes a second case control study with matched controls). *Number of centres:* 1 *Funding:* NR *Trial ID:* NR	*Intervention (same for both studies)* *1.* Any statin, e.g atorvastatin, cerivastatin, fluvastatin, lovastatin, pravastatin, and simvastatin. *Dose details:* standardised dose and potency by converting to World Health Organisation standard defined daily dose (DDD) per day (details reported but not extracted). The total DDDs taken by each patient were recorded. *Dose modifications:* no details. *Concurrent treatment:* no details.	*Number of Participants*: Study 1: 139,894 eligible; 283 had AMD meeting inclusion criteria (of 305 with AMD); 29417 had used statins. Study 2: 334 AMD cases and 1670 controls *Number of eyes:* NR *Sample attrition/dropout*: not applicable Included: aged >50 years; did not terminate membership to the health maintenance organisation before 31st May 2005. Having photodynamic therapy was a proxy for a diagnosis of neaovascular AMD. At least two-years of statin use prior to photodynamic therapy (for the with statin group). Control (second study only): 5 participants matched for each AMD case, on age, gender, hyperlipidemia, congestive heart failure, diabetes, and ischemic heart disease, place of birth and socioeconomic status. Also states ‘randomly selected’.	*Outcomes* • Association between prior statin use and diagnosis of AMD. *Length of follow-up:* NR as such, study looked at those diagnosed between a 53 month period (January 2001 to May 2005)

		Excluded: NR	
Fong et al., 2010{#900} *Country:* USA *Design:* Case control study *Number of centres:* up to 11 *Funding:* none *Trial ID:* NR	*Intervention* *1.* Statins (atorvastin, ezetimibesimvastatin, lovastatin, pravastatin, and simvastatin) Also undertook analyses with all lipid-lowering agents, cholestyramine, colestipol, ezetimibe, fenofibrate, and gemfibrozil. 2. no statin use *Dose details:* Drug use defined as use before case determination. Recent use, defined as filled prescription in the year before the year of diagnosis, recent longer-term use defined as a filled prescription in each of 3 years before diagnosis. *Dose modifications:* NR *Concurrent treatment:* NR	*Number of Participants*: 79369 (cases 719; controls 78,650) of 86,635 who underwent an eye examination. *Number of eyes* NR *Sample attrition/dropout*: not applicable Included: all patients with a diagnosis of exudative AMD in 2007 who did not have exudative AMD in 2006, ≥ 60 years old, enrolled in Kaiser Permanente Southern California for at least 5 years. Cases were identified using outpatient diagnosis data. Controls had undergone an eye examination during the same year without the diagnosis of AMD. Excluded: NR	*Outcomes* • Association between statin use and new exudative AMD. *Length of follow-up:* NR
Etminan et al., 2008{#632} *Country:* Canada *Design:* nested Case-control *Number of centres:* Not applicable *Funding:* Not reported *Trial ID:* Not reported	*Intervention* *1.* Statin and ACE-I use *Dose details:* Not applicable *Dose modifications:* Not applicable *Concurrent treatment:* Not applicable *Duration of treatment:* Not applicable	*Number of Participants*: Total 14,335 (Wet AMD cases 2867, control 11,468) *Number of eyes* Not reported *Sample attrition/dropout*: Not applicable Included: People who had undergone revascularization interventions (percutaneous coronary angioplasty and or bypass grafting), data from health insurance and vital statistics databases, cohort members were ≥65 years. Cases had an ICD-9 code for the wet form of AMD. For each case, four controls were chosen randomly from the cohort and matched by age. A current user was defined as a person who was using	*Outcomes* • Association between statin and angiotensin-converting enzyme inhibitors (ACE-Is) and risk of AMD. *Length of follow-up:* Not reported

		a statin / ACE-Is prescription within 90 days of the index date (the date of diagnosis of AMD). Excluded: non-Quebec residents	
Tandospirone			
Jaffe et al., 2015{#167} *Country:* USA, Germany, Italy, Switzerland, Ireland, France, Australia, Israel, Austria, Belgium, United Kingdom, Japan, Portugal and Canada *Design:* RCT *Number of centres:* 48 *Funding:* commercial funding *Trial ID:* NCT00890097	*Intervention* *1.* Tandospirone 1.0% *2.* Tandospirone 1.75% *3.* Vehicle solution (placebo) *Dose details:* 1 drop into each eye twice daily (interval of approximately 12 hours between drops). Both eyes were treated but only one was designated as the study eye. *Dose modifications:* not reported *Concurrent treatment:* not reported *Duration of treatment:* 24 months	*Number of Participants*: total 772 randomised: tandospirone 1.0% 252; tandospirone 1.75% 259; vehicle solution 261 *Number of eyes* total 768 <u>treated</u> tandospirone 1.0% 250; tandospirone 1.75% 258; vehicle solution 260. Both eyes were treated but only one was designated as the study eye, either the one with the best BCVA or the dominant eye if BCVA was the same. *Sample attrition/dropout*: total 231; tandospirone 1.0% 68 (adverse events 21; unrelated to adverse events 15; withdrew consent 9; lost to follow-up 5; other 18) – figures shows 2 not treated but numbers do not add up; tandospirone 1.75% 86 (adverse events 32; unrelated to adverse events 12; withdrew consent 6; lost to follow-up 5; noncompliance 4; other 27) – figures shows 1 not treated but numbers do not add up; vehicle solution 77 (not treated 1; adverse events 28; unrelated to adverse events 17; withdrew consent 9; lost to follow-up 5; noncompliance 4; other 14). Included*:* ≥55 years, GA secondary to AMD, no evidence of CNV, well-demarcated area of atrophy, total lesion size of ≤20 mm^2, hyperautofluorescence adjacent to the area of atrophy, BCVA of ≥35 letters clear ocular media and adequate pupillary dilation. *Exclusion criteria:* other ocular disease that may confound assessment of GA lesions, or central visual acuity, history of cataract surgery or serious ocular trauma or intraocular surgery, use of serotonin	*Outcomes* • mean annualized lesion enlargement (primary outcome) • BCVA (ETDRS) • Near activity scores • Distance activity . *Length of follow-up:* 30 months (study terminated after 600 had completed the month 24 visit)

		receptor agonists or other treatments	
Trimetazidine			
Cohen et al, 2012{#324} *Country:* France, Belgium and Spain *Design:* RCT *Number of centres:* 324 *Funding:* commercial funding *Trial ID:* ISRCTN99532788	*Intervention* *1.* Trimetazidine (TMZ) one tablet twice a day *2.* Placebo, matched, one tablet twice a day *Dose details:* TMZ 35 mg modified release *Dose modifications:* NR *Concurrent treatment:* vitamins or antioxidants for at least 1 year: 36 TMZ and 36 placebo *Duration of treatment:* mean (SD) 37.6 (16.3) months.	*Number of Participants*: 1,192; TMZ 35mg 594; Placebo 598 Full analysis set: 1,086; TMZ 546; Placebo 540 *Number of eyes:* same as above *Sample attrition/dropout*: 299 withdrew; TMZ 135; Placebo 164 Included: AMD with unilateral CNV for 12 months, study eye was unaffected eye: ≥5 isolated soft drusen (Subgroup 1, N = 473), other types of drusen (hard, calcified, or serogranular) or RPE lesions (Subgroup 2 N = 545) or isolated RPE lesions excluding atrophy >1/3 DD (Subgroup 3 N = 68). White, aged 55-83 years. Excluded: (for study eye): CNV, chorioretinal atrophy in the central and/or the intermediate field (>1/3 DD), RPE detachment and other eye pathology, allergy to fluorescein, current treatment with TMZ, laser coagulation therapy.	*Outcomes* • Time to occurrence of CNV (primary outcome). • Incidence of atrophy larger than 1/3 DD (disk diameters), • number and area of drusen, • number and area of retinal pigment epithelium (RPE) lesions, • characteristics of CNV assessed by retinal fluorescein angiography, • adverse events. *Length of follow-up:* Minimum of 3 years, prolonged up to 5 years for those enrolled during the first 2 years. Follow-up assessments every 6 months.
Visaline			
Kaiser et al., 1995{#719} *Country:* Switzerland *Design:* RCT (pilot) *Number of centres:* one *Funding:* not reported *Trial ID:* not reported	*Intervention* *1.* Visaline *2.* Placebo *Dose details:* visaline contains buphenine HCI 1.5mg, beta-carotine 10mg, tocopherol acetate 10mg and ascorbic acid 50mg. Two tablets twice daily, 5 days per week. *Dose modifications:* none reported	*Number of Participants*: total 20; visaline 9; placebo 11 *Number of eyes* total 20; visaline 9; placebo 11 *Sample attrition/dropout*: none Included: >50 years, non-serous AMD (early AMD), corrected visual acuity between 20/100 – 20/25; distance correction <4.0 dpt spherical equivalent. If bilateral, the better eye was selected.	*Outcomes* • Far and near visual acuity • Contrast sensitivity • Visual function (subjective measure) *Length of follow-up:* 6 months

	Concurrent treatment: unable to take vitamin A containing substances, beta-blockers, sympathomimetics, sympatholytics, diuretics, vasoactive substances, chloroquine or tuberculostatics for 1 month prior to or during the study duration. *Duration of treatment:* 6 months	Excluded: serous AMD, diabetes mellitus, endocrine problems, cardiac dysrhythmia, status following cardiac infarction, uncontrolled hypertension, other ocular diseases	

Nutrient supplements			
Study	**Intervention Details**	**Participant details and key eligibility criteria**	**Relevant Outcomes**
AREDS			
AREDs study group 1{#844} *Country:* USA *Design:* RCT *Number of centres:* 11 *Funding:* commercial and non commercial *Trial ID:* not reported	*Intervention* *1.* Antioxidants *2.* Zinc *3.* Antioxidants and Zinc *4.* Placebo *Duration of treatment:* up to 6.3 years	*Number of Participants*: Total 3640; Antioxidants 945; Zinc 904; Antioxidants and Zinc 888; placebo 903 *Number of eyes:* Same *Sample attrition/drop out*: at 5 years 2.4% lost to follow-up (balanced across groups) Included: age 55-80, extensive small drusen, intermediate drusen, large drusen, noncentral GA or pigment abnormalities in 1 or both eyes, or advanced AMD or vision loss due to AMD in 1 eye. At least 1 eye with BCVA of 20/32 of better. Patients enrolled in 4 AMD categories.	*Outcomes* • Progression to or treatment for advanced AMD • BCVA *Length of follow-up:* 6.3 years
AREDs study group 2{#376} *Country:* USA *Design:* RCT *Number of centres:* 82	*Intervention – First Randomisation* *1.* Lutein + Zeaxanthin *2.* DHA + EPA *3.* Lutein + Zeaxanthin + DHA + EPA *4.* Placebo *Second randomisation* *1.* AREDs supplement *2.* AREDs and no beta carotene	*Number of Participants*: *First Randomisation* Total 4203; Lutein + Zeaxanthin 1044; DHA + EPA 1068; Lutein + Zeaxanthin + DHA + EPA 1079; placebo 1012 *Second Randomisation* Total 3036; AREDs 659; AREDs no beta carotene 863; AREDs low-dose zinc 689; AREDs no beta carotene + low-dose zinc 825 *Number of eyes: First Randomisation* Total 6916;	*Outcomes* • Development of advanced AMD • BCVA • Safety *Length of follow-up:* median 5 years

Funding: commercial and non commercial *Trial ID:* NCT00345176	*3.*AREDs with low-dose zinc *4.*AREDs with no beta carotene and with low-dose zinc *Duration of treatment:* at least 5 years	Lutein + Zeaxanthin 1714; DHA + EPA 1753; Lutein + Zeaxanthin + DHA + EPA 1754; placebo 1695 *Second Randomisation* Total 4987; AREDs 1101; AREDs no beta carotene 1410; AREDs low-dose zinc 1127; AREDs no beta carotene + low-dose zinc 1349 *Sample attrition/drop out*: 3% lost to follow-up and 9% died Included: 50 to 85 years at risk for progression to advanced AMD with bilateral large drusen or large drusen in 1 eye and advanced AMD in the fellow eye	
Carotenoids			
Berrow et al., 2013{#361} *Country:* UK *Design:* RCT *Number of centres:* one *Funding:* commercial funding *Trial ID:* ISRCTN 17842302	*Intervention* *1.* Lutein based supplement *2.* no supplement (control) *Dose details:* vitamin C 150 mg, cupric oxide 400 µg, vitamin E 15 mg, lutein 12 mg, zeaxanthin 0.6 mg, zinc 20 mg, omega-3 fatty acids 1,080 mg per day *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* 40 weeks	*Number of Participants*: 14 total; 8 lutein +; 6 controls *Number of eyes* 14 total; 8 lutein +; 6 controls (eye with the BCVA). *Sample attrition/dropout*: 2 (unclear which group). Included: ARM, BCVA ≥ 0·2 LogMAR (distance), clear optical media, no signs of other retinal or optic nerve disease in the study eye, good general health and no prescribed medication that can affect the retina. Excluded: moderate-to-dense lens opacities, intraocular lens, corneal opacities, glaucoma or ocular hypertension, previous history of other eye pathologies, trauma or surgery , diabetes, systemic hypertension, neurological disease, AMD in the studied eye, drugs causing retinal toxicity, epilepsy.	*Outcomes* • Contrast sensitivity • Visual acuity (logMAR) • Compliance *Length of follow-up:* 40 weeks (additional 20 weeks for the lutein supplement group)
Murray et al., 2013{#368} *Country:* UK and The Netherlands	*Intervention* *1.* Lutein *2.* Placebo	*Number of Participants*: total 84; lutein 42; placebo 42 *Number of eyes* one eye was analysed	*Outcomes* • MPOD • BCVA (ETDRS, logMAR) • Compliance (lutein serum

Design: RCT *Number of centres:* 2 *Funding:* commercial and non-commercial funding *Trial ID:* NCT01042860	*Dose details:* lutein 10mg capsules taken daily *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* 12 months	*Sample attrition/dropout*: total 11; lutein 6 (did not receive intervention 3, discontinued for medical reasons 3); placebo 5 (did not receive intervention 2, discontinued for medical reasons 1, unknown 2). Numbers reported suggest 1 additional participant discontinued in the placebo group. Included: aged 50-80 years, AMD grade 0 to 4 in one eye, BCVA (LogMAR) ≥ 0.5, minimal cataract Excluded: any ophthalmic disorder considered to be less typical of AMD, glaucoma, any dietary supplements containing lutein, zeaxanthin or meso-zeaxanthin within 3 months of the start of the study.	concentration) *Length of follow-up:* 12 months
Weigert et al., 2011{#418} *Country:* Austria *Design:* RCT *Number of centres:* one *Funding:* Commercial funding *Trial ID:* NCT00879671	*Intervention* *1.* Lutein *2.* Placebo *Dose details:* months 1 to 3: 20 mg once daily, months 4 to 6: 10 mg once daily *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* 6 months	*Number of Participants*: Total 126 (Lutein 84, placebo 42) *Number of eyes:* 126 (Lutein 84, placebo 42) *Sample attrition/dropout*: measurements could not be obtained in 1 patient, 9 dropped out after baseline visit (groups NR), a further 16 withdrew (10 lutein, 6 placebo), the reason was a serious adverse event in 2 lutein and 1 placebo. Included: AMD AREDS categories 2-4 with no CNV in the study eye, 50 -90 years, clear nonlenticular ocular media, visual acuity > 0.4, no previous lutein and/or zeaxanthin. If both eyes were eligible, one eye was selected randomly. Excluded: primary retinal pigment epithelium atrophy >125 µm, diabetic retinopathy (defined), participated in clinical trial in prior 3 weeks, ocular surgery (past 6 months), treatment with photosensitizing drugs	*Outcomes* • Macular pigment optical density (MPOD) (primary outcome) • Visual acuity (ETDRS) • Visual function: retinal sensitivity • Compliance • Serious adverse effects leading to withdrawal *Length of follow-up:* 6 months
Ma et al., 2012a {#331}	*Intervention*	*Number of Participants*: Total 108: Lutein 10 mg	*Outcomes*

Ma et al. 2012b{#329} Possibly linked to Huang et al., 2015a {#163} Huang et al., 2015b {#164} Country: China Design: RCT Number of centres: One Funding: non-commercial funding Trial ID: NCT01048476; NCT01528605	*1.* Lutein 10 mg *2.* Lutein 20 mg *3.* Lutein 10 mg and Zeaxanthin 10 mg *4.* Placebo *Dose details:* As above, taken daily *Dose modifications:* None *Concurrent treatment:* None *Duration of treatment:* 48 weeks	n=27; Lutein 20 mg n=27; Lutein and Zeaxanthin n=27; Placebo, n=27 *Number of eyes* NR *Sample attrition/dropout*: n=1 (lutein 10 mg group) *Sample crossovers:* one Included*:* 50-79 years, early AMD according to the AREDs classification system. Excluded*:* late AMD or other macular or choroidal disorders; other eye pathologies, laser or surgery ; unstable chronic illness; currently taking medications affecting macular function or consumed dietary supplements containing vitamins or carotenoids within prior 6 months.	• MPOD (primary outcome) • Best-corrected visual acuity (BCVA) • Contrast sensitivity • Photorecovery time • Amsler grid testing • Compliance • Adverse effects *Length of follow-up:* 48 weeks
Huang et al., 2015a {#163} Huang et al., 2015b {#164} Possible linked to et al., Ma 2012a {#331} and Ma et al. 2012b{#329} Country: China Design: RCT Number of centres: one Funding: Non-commercial funding Trial ID: NCT01528605 (incorrectly reported in	*Intervention* *1.* Lutein 10 mg *2.* Lutein 20 mg 3. Lutein 10 mg + zeaxanthin 10 mg 4. Placebo *Dose details:* NR *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* 2 years	*Number of Participants*: Total 112 (states 114 in the acknowledgements), 108 analysed *1.* Lutein 10 mg n=26 *2.* Lutein 20 mg n=27 3. Lutein 10 mg + zeaxanthin 10 mg n=27 4. Placebo n=28 *Number of eyes:* NR *Sample attrition/dropout*: 4 excluded from analysis (failed to attend examinations) Included*:* Age > 50 years, clinical diagnosis of early AMD according to the AREDs system, clear ocular media. Excluded: other ocular disorders or unstable systemic or chronic illness or consumed dietary supplements containing antioxidants or carotenoids within the	*Outcomes* • Macular pigment optical density (MPOD) (primary outcome); • Mean retinal sensitivity • BCVA • Contrast sensitivity • Flash recovery time • Vision-related quality of life (VFQ-25) • Adverse events *Length of follow-up:* 2 years

paper as NCT10528605)		previous 6 months.	
Kelly et al., 2014{#288} *Country:* The Netherlands *Design:* RCT *Number of centres:* one *Funding:* commercial funding *Trial ID:* NCT00527553	*Intervention* *1.* lutein egg yolk beverage *2.* lutein enriched egg *3.* zeaxanthin enriched egg *4.* normal egg *5.* control (no dietary modification) *Dose details:* eggs and beverage (equivalent of 1 egg yolk) taken once daily. Lutein beverage (970 µg lutein, 340µg zeaxanthin); Lutein egg (921.4 (SD 105) µg lutein and 137.3 (SD 14.0) µg per yolk); Zeaxanthin egg (174.3 (SD 14.5) µg lutein and 487.3 (SD 31.0) µg per yolk); normal egg (167.8 (SD 8.7) µg lutein and 85.0 (SD 1.7) µg per yolk). *Dose modifications:* not reported *Concurrent treatment:* asked not to make any other major modifications to diet *Duration of treatment:* assume 90 days	*Number of Participants*: total 100 (beverage 20; lutein egg 20; zeaxanthin egg 20; normal egg 20; control 20) *Number of eyes* total 100 (beverage 20; lutein egg 20; zeaxanthin egg 20; normal egg 20; control 20) *Sample attrition/dropout*: total 3 (beverage 0; lutein egg 1 moved away; zeaxanthin egg 0; normal egg 1 moved away; control 1 lost contact) Included*:* Healthy individuals aged at least 18 years Excluded: diabetes, heart disease, lipid metabolic diseases, AMD in both eyes (at least the eye studied in the trial had to be healthy), ocular media opacity or other ocular diseases, smokers, those taking supplements containing lutein and/or zeaxanthin in the past 6 months, BMI >30 kg/m^2, those with a MPOD score below 0.55.	*Outcomes* • Serum values of lutein and zeaxanthin (not data extracted) • MPOD *Length of follow-up:* 90 days
Kelly et al., 2017{#701} *Country:* Ireland *Design:* CCT *Number of centres:* 2 *Funding:* commercial and non-commercial funding *Trial ID:*	*Intervention* *1.* carotenoid-enriched eggs (lutein and meso-zeaxanthin in a 1:1 ratio) *2.* standard (placebo) egg *Dose details:* two-eggs daily, five days per week, prepared as scrambled eggs by the study investigators *Dose modifications:* if a participant did not attend they were given two eggs to prepare at	*Number of Participants*: total 50: carotenoid eggs 25; placebo eggs 25 *Number of eyes:* not reported *Sample attrition/dropout*: total 4: 2 carotenoid egg group (cholesterol exceeded upper threshold limit; personal reasons); 2 placebo egg group (cholesterol exceeded upper threshold limit; personal reasons). Included*:* age 18-65, no known allergy to eggs, no history of CVD, no ocular pathology, cholesterol	*Outcomes (state if primary)* • Macular Pigment measurement • BCVA (ETDRS charts, logMAR) • Contrast sensitivity • Adverse events *Length of follow-up:* 8 weeks

ISRCTN25867083	home, to ensure 100% compliance. *Concurrent treatment:* different side options served with the eggs (toast, croissants, muffins) *Duration of treatment:* 8 weeks	levels of ≤6·5 mmol/l. Excluded: current or recent history of supplementation with macular carotenoids and/or cholesterol-lowering statins.	
Richer et al., 2011{#414} *Country:* USA *Design:* RCT *Number of centres:* one *Funding:* commercial funding. *Trial ID:* NCT00564902	*Intervention* *1.* zeaxanthin *2.* zeaxanthin + lutein *3.* lutein ('Faux placebo') *Dose details:* *1.* 8 mg zeaxanthin, 1 capsule per day with a meal. *2.* 8 mg zeaxanthin + 9 mg lutein, 1 capsule per day with a meal. *3.* 9 mg lutein, 1 capsule per day with a meal. *Dose modifications:* none reported. *Concurrent treatment:* none stated. *Duration of treatment:* 12 months	*Number of Participants*: Total n= 60, *1.* 8 mg zeaxanthin, n=25 *2.* 8 mg zeaxanthin + 9 mg lutein, n=25 *3.* 9 mg lutein ('Faux placebo), n=10 *Number of eyes:* Not stated *Sample attrition/dropout*: n= 9, *1.* 8 mg zeaxanthin, n=4 *2.* 8 mg zeaxanthin + 9 mg lutein, n=4 *3.* 9 mg lutein ('Faux placebo), n=1 Included*:* Early and moderate AMD, retinopathy, symptoms and measurable deficits on the contrast sensitivity chart or glare disturbances, Amsler grid abnormalities, subjective functional night driving or reading disturbances. Excluded*:* high-risk retinal characteristics for advanced AMD or advanced AMD for which existing medical or surgical options were available. Consumption of lutein or zeaxanthin beyond 250 µg/d within 6 months, active comorbidities, use of retinotoxic medications.	*Outcomes* • Estimated central foveal one degree MPOD (primary outcome) • Colenbrander average eye near high-contrast visual acuity • Shape discrimination • Contrast sensitivity function • Glare recovery • Subjective visual function questionnaire (VQF25) • Adverse events • Compliance *Length of follow-up:* 12 months
Akuffo et al., 2015{#133} Sabour-Pickett 2014 *Country:* Ireland *Design:* RCT	*Intervention* *1.* Lutein 20 mg + zeaxanthin 2 mg (0.86 mg stated in 3 year follow-up paper) *2.* Meso-zeaxanthin 10 mg + Lutein 10 mg + zeaxanthin 2 mg	*Number of Participants*: Total 67 enrolled. Baselines given for n=52 with 12-month follow-up: 1. Lutein 20 mg + zeaxanthin 2 mg n=17 *2.* Meso-zeaxanthin 10 mg + Lutein 10 mg + zeaxanthin 2 mg n=21	*Outcomes* • Change in MPOD (primary outcome) • BCVA • letter contrast sensitivity • Grade of AMD.

Number of centres: one *Funding:* Non-commercial funding; commercial organisation provided the supplements. *Trial ID:* ISRCTN60816411	*3.* Meso-zeaxanthin 17 mg + Lutein 3 mg + zeaxanthin 2 mg *Dose details:* One tablet consumed daily with a meal. Discrepancies between label claim and measured values of the supplements used in this trial have been reported and in particular, Group 1 supplement contained small amounts of MZ (0.30 mg).	*3.* Meso-zeaxanthin 17 mg + Lutein 3 mg + zeaxanthin 2 mg n=14 3-year results for n=41 (study states 47 completed final study visit, numbers differ for each outcome reported, for primary outcome these were): 1. Lutein 20 mg + zeaxanthin 2 mg n=13 *2.* Meso-zeaxanthin 10 mg + Lutein 10 mg + zeaxanthin 2 mg n=16 *3.* Meso-zeaxanthin 17 mg + Lutein 3 mg + zeaxanthin 2 mg n=12 *Number of eyes:* 67 (47 at 3 year follow-up, one per participant) *Sample attrition/dropout*: n=20 (NB 15 were enrolled but not included in baselines). Drop out from total enrolled NR per group. Included*:* early AMD in at least 1 eye (the study eye); corrected distance visual acuity of ≥6/12 in the study eye, no other ocular pathology. Excluded*:* recent history of macular carotenoid supplementation; diabetes mellitus; any visually consequential ocular comorbidity	*Length of follow-up:* 3 years
Peng et al., 2016 {#80} *Country:* Taiwan *Design:* Before and after study (one group) (not RCT as described in title) *Number of centres:* one	*Intervention* *1.* Lutein complex: lutein 12g + zeaxanthin 2 mg *Dose details:* Lutein and zeaxanthin were extracted from a commercially prepared marigold flower and wolfberry to prepare lutein complex. Each serving (60 mL) contained 12 mg of lutein, 2 mg of zeaxanthin, 7 g of carbohydrate, 1 g of fat and 10 mg of sodium	*Number of Participants*: Total 56 1. Lutein complex n=56 *Number of eyes* NR *Sample attrition/dropout*: NR Included: Age 30-50 years, soft drusen, early stage AMD (AREDs classification stage 1) Excluded: chronic diseases, smoking, alcoholism,	*Outcomes* • BCVA • Intraocular pressure • Photostress recovery • Ocular comfort index • MPOD *Length of follow-up:* unclear as paper is contradictory; either 2 weeks or one month after end of intervention, i.e. 5.5 months or 6 months

Funding: Non-commercial funding. Lutein complex was provided by Standard Foods Corporation, Taipei *Trial ID:* NR	*Dose modifications:* NR *Concurrent treatment:* NR, a run-in period for 2-weeks unable to take any supplements *Duration of treatment:* 5 months	cataract, glaucoma or other disturbances at the anterior segment of the eyes	
Wu et al., 2015{#215} *Country:* USA *Design:* prospective cohort study *Number of centres:* not applicable *Funding:* Not commercial funding *Trial ID:* NR	*Intervention* *1.* Dietary intake of lutein, zeaxanthin and other carotenoids including any supplements of beta-carotene, multivitamins and lycopene – used to calculate an average predicted plasma score *Dose details:* Dietary intakes according to lutein/zeaxanthin quintile at middle of follow-up provided *Dose modifications:* Not applicable *Concurrent treatment:* Not applicable *Duration of treatment:* Not applicable	*Number of Participants*: Total 102,046 *Number of eyes:* unit of analysis = participant (worst eye used for classification) *Sample attrition/dropout*: Not applicable Included*:* Participants in the prospective cohort studies: Nurses' Health Study and the Health Professionals Follow-up study, age 50-90 years. Excluded*:* did not return the initial food frequency questionnaire or was incomplete, prevalent AMD, cancer, diabetes, cardiovascular disease, never reported an eye examination during follow-up. AMD case ascertainment: excluded cases with only small hard drusen (<63 μm in diameter)	*Outcomes* • Cases of intermediate AMD • Case of advanced AMD *Length of follow-up:* 26 years (NHS) and 24 years (HPFS)
Trieschmann et al., 2007{#592} *Country:* Germany *Design:* CCT *Number of centres:* assume one *Funding:* Commercial funding	*Intervention* *1.* Lutein and Zeaxanthin supplement *2.* no supplements (control) *Dose details:* 12 mg lutein and 1 mg zeaxanthin, both provided as ester, 120 mg vitamin C, 17.6 mg vitamin E, 10 mg zinc and 40 μg selenium. *Dose modifications:* NR *Concurrent treatment:* NR	*Number of Participants*: total 136 (Lutein and Zeaxanthin 108, control 28) *Number of eyes* total 136 (Lutein and Zeaxanthin 108, control 28) *Sample attrition/dropout*: 13 excluded from analysis in total, 11 in the lutein / zeaxanthin group and 2 in the control group. Failed to attend last follow-up visits. Included: age ≥50 years, no or minimal lens opacity, no lutein, zeaxanthin or co-antioxidant	*Outcomes* • MPOD • Compliance (supplement group) *Length of follow-up:* approximately 9 months

Trial ID: NR	*Duration of treatment:* 24 weeks	supplementation, good general health. One eye selected, the eye with higher quality autofluorescence image. If same in both eyes the eye with better visual acuity was selected. If no difference in visual acuity the right eye was selected. Excluded: eyes with central atrophic spots as well as those with central RPE proliferation or CNV.	
Arnold et al., 2013{#364} *Country:* Germany *Design:* RCT *Number of centres:* one *Funding:* Commercial funding *Trial ID:* NCT00763659	*Intervention* *1.* Supplement of lutein, zeaxanthin, and ω-3 long-chain polyunsaturated fatty acids (LCPUFAs) *2.* Supplement of lutein, zeaxanthin, and ω-3 long-chain polyunsaturated fatty acids (LCPUFAs), double dose *3.* Placebo *Dose details:* *1.* One capsule containing 10 mg of lutein, 1 mg of zeaxanthin, 100 mg of docosahexaenoic acid (DHA), and 30 mg of eicosapentaenoic acid (EPA) and one placebo capsule each day *2.* Two capsules (dose details as for group 1) each day 3. Two placebo capsules daily *Dose modifications:* NR *Concurrent treatment:* Participants instructed to abstain from dietary supplements containing carotenoids and fish oil	*Number of Participants*: Total 172 (Supplement group 1 60, supplement group 2 66, placebo 46) *Number of eyes:* Total 172 (Supplement group 1 60, supplement group 2 66, placebo 46) *Sample attrition/dropout*: Total 27. Supplement group 1: 10, supplement group 2: 11, placebo: 6. Reasons: exudative AMD, reduced mobility after prolonged illness, hospitalization, lack of time Included: nonexudative AMD classified according to AREDS. 1 eye of each patient was included. Excluded: central geographic atrophy, exudative forms of AMD, or pronounced opacity in the intended study eye	*Outcomes* • MPOD (primary outcome) *Length of follow-up:* 12 month

	Duration of treatment: 12 months		
Robman et al., 2007{#581} *Country:* Australia *Design:* cohort study *Number of centres:* assume one *Funding:* Non-commercial *Trial ID:* not reported	*Intervention* *1.* Dietary intake of lutein and zeaxanthin and fats *Dose details:* Not applicable (13 fruit and 25 vegetable items, each with 10 frequency options, were included in the food frequency questionnaire) *Dose modifications:* Not applicable *Concurrent treatment:* Not reported *Duration of treatment:* Not applicable	*Number of Participants*: Total 254 *Number of eyes* 254 (for progression definition 1; unclear for other outcomes) *Sample attrition/dropout*: 2 incomplete data on AMD grading and nutritional status Included: early AMD (intermediate drusen, soft drusen and [or] retinal pigment epithelium abnormalities) in the absence of GAor neovascular AMD in at least 1 eye. Participants were identified from 2 previous studies Excluded: None stated.	*Outcomes* • Progression of AMD using 3 definitions *Length of follow-up:* average 7 years
Vishwanathan et al., 2009{#494} *Country:* USA *Design:* before and after study *Number of centres:* *Funding:* commercial and non-commercial support *Trial ID:* not reported	*Intervention* *1.* Egg yolk consumption *Dose details:* 4 week lead in; daily foods containing 2 eggyolks for 5 weeks; 4 weeks egg-free period; daily food containing 4 egg yolks for 5 weeks. Food items were provided. Analysis of sample of eggs used (n=25) found lutein concentration was 243 (SE 24) µg and zeaxanthin 230 (SE 31) µg. *Dose modifications:* none *Concurrent treatment:* Those taking multivitamins containing lutein switched to multivitamins without lutein for 4 weeks before study initiation. No restriction of the consumption of lutein and zeaxanthin-containing vegetables or fruit. Instructed to refrain from eating eggs or egg yolk–rich	*Number of Participants*: 56 recruited; 52 completed study *Number of eyes* not reported *Sample attrition/dropout*: 4 unable to complete (2 unexpected vacation, 1 stopped taking cholesterol lowering medication, 1 gastrointestinal discomfort); only 37 had MPOD measurements, 3 of which were unable to undergo the measurements, remainder because the device was not calibrated. Included: >60 years, taking cholesterol lowering medication for at least 3 months, able to undergo blood collection and the willingness to consume foods containing the equivalent of 2 and 4 egg yolks per day for 5 weeks each. Excluded: not stated	*Outcomes* • MPOD *Length of follow-up:* 18 weeks

	products (other than study eggs or foods) during the entire study period; egg whites were allowed. *Duration of treatment:* 10 weeks (in a 14 week period)		
Olk et al., 2015{#675} *Country:* USA *Design:* Cohort study *Number of centres:* one *Funding:* Commercial *Trial ID:* NR	*Intervention* *1.* Triple therapy *2.* Triple therapy + zeaxanthin *Dose details:*Triple therapy: i) Intravitreal injection of 1.25 mg of bevacizumab at the initial visit ii) 1000 micrograms of intravitreal dexamethasone within 1 week iii) reduced-fluence photodynamic therapy with verteporfin (PDT), usually within 2 weeks from baseline. Group 2 also received oral zeaxanthin, 20 mg, daily *Dose modifications:* Retreatment based on the presence of any of: subretinal fluid/blood, intraretinal or subretinal fluid, decrease in vision, late leakage, or occult plaque. Overall, mean number of treatment cycles triple therapy: 2.1 over 1 year and 2.8 over 2 years; triple therapy + zeaxanthin: 1.6 at 1 year and 2.1 over 2 years. *Concurrent treatment:* All patients were taking a multi-vitamin and an AREDS I antioxidant regimen.	*Number of Participants*: Total 424 (triple therapy 210, triple therapy + zeaxanthin 214) *Number of eyes:* Total 543 (triple therapy 290, triple therapy + zeaxanthin 253) *Sample attrition/dropout*: NR Included: classic, minimally classic, and/or occult subfoveal CNV. Only eyes with macular blood, subretinal fluid, and/or retinal edema with characteristic CNV findings confirmed by fluorescein angiography, optical coherence tomography or indocyanine green angiography were included. Excluded: Eyes with >12 optic disc areas of CNV, eyes with less than 20/400 vision, presence of blood if covered greater than 12 disc areas.	*Outcomes* • Cost utility • Development of CNV in fellow eye *Length of follow-up:* 12 (90%-94%) to 24 (71%-72%) months

	Duration of treatment: 2 years		
Beatty *et al*., 2013{#940} *Country:* Ireland (UK and Republic) *Design:* RCT *Number of centres:* 2 *Funding:* commercial *Trial ID:* ISRCTN94557601	*Intervention* *1*. lutein, zeaxanthin, vitamin E, vitamin C, zinc, copper (Ocuvite) *2.* Placebo *Dose details:* lutein 12mg, zeaxanthin 0.6mg, vitamin E 15mg, vitamin C 150mg, zinc oxide 20 mg, copper 0.4mg (daily dose) one tablet twice daily *Dose modifications:* not stated *Concurrent treatment:* not stated *Duration of treatment:* 3 years	*Number of Participants*: total 433; supplement 216; placebo 217 *Number of eyes* total 614; supplement 304; placebo 310 *Sample attrition/dropout*: 1 placebo participant deemed ineligible as CNV was present (remained in the analysis) 88 participants withdrew before the 12-month follow-up and these were reported to be distributed equally between the two groups (Figure 1 not available to reviewers). Most withdrew for personal reasons, 5 withdrew because of gastrointestinal disturbances, 7 died, 6 had late AMD in the sole study eye. Also states 252 contributed 1 study eye (group 1) and 181 contributed 2 study eyes (group 2) to the analysis. Included*:* ≥50 years. 2 groups: 1) any severity of early AMD in one eye (study eye) and late AMD (neovascular AMD or central GA) in the fellow eye. Visual acuity of at least 0.3 logMAR (≥70 ETDRS letters (equivalent to Snellen 20/40)) in the study eye; 2) features of early AMD in at least 1 eye when both eyes were free of late-stage AMD, minimum severity of 20 soft distinct or indistinct drusen in the central macular field, if fewer than 20 drusen, focal hyperpigmentation was required, same visual acuity as group 1. Both eyes included unless visual acuity didn't meet the criteria. Excluded: not stated	*Outcomes* • BCVA (primary outcome) • Contrast sensitivity • Progression of AMD • Macular pigment (raman counts, not extracted) • Serum levels of antioxidants (not extracted) States publication reports secondary outcomes but BCVA was reported. *Length of follow-up:* average 18.3 months, maximum 3 years (but 12 months was the minimum follow-up (and primary outcome) and when numbers were not affected by large numbers of withdrawals).
Carotenoids and other nutrients			
Bartlett et al., 2007{#548}	*Intervention* *1*. lutein combined with vitamins and	*Number of Participants*: total 30; lutein + vitamins 17; placebo 13	*Outcomes* • Contrast sensitivity (primary

Protocol published: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2400108/ *Country:* UK *Design:* RCT *Number of centres:* 2 *Funding:* non-commercial and commercial funds *Trial ID:* ISRCTN 78467674	minerals. *2.* placebo *Dose details:* 6mg lutein, 750µg retinol, 250mg vitamin C, 34mg vitamin E, 10mg zinc, 0.5mg copper. Placebo tablets contained cellulose. One tablet daily. *Dose modifications:* NR *Concurrent treatment:* encouraged not to alter their diets, or change their current supplementation regime *Duration of treatment:* 9 months	*Number of eyes* NR *Sample attrition/dropout*: total 5; lutein + vitamins 2; placebo 3 (reasons not stated) Included: no ocular pathology in at least one eye, or no ocular pathology other than ARM (soft or hard drusen and areas of increased or decreased pigment associated with these drusen) Excluded*:* type 1 or 2 diabetes, anti platelet or anti-coagulant medication, concurrent use of nutritional supplements, AMD in one or both eyes.	outcome) • Adverse events • Compliance *Length of follow-up:* 9 months
Richer et al 2004{#722} Linked publication, Richer et al., 2007{#723} reports secondary analyses on characteristics that increase MPOD *Country:* USA *Design:* RCT *Number of centres:* one *Funding:* commercial and non-commercial funding *Trial ID:* not reported	*Intervention* *1.* Lutein *2.* Lutein and carotenoids, antioxidants, vitamins, minerals (Lutein + others) *3.* Placebo *Dose details:* all 3 groups took 3 capsules twice per day with food. Contained: *1.* lutein 10mg. *2.* lutein + others (lutein 10mg, 2500 IU vitamin A, 15,000 IU natural beta carotene, 1,500-mg vitamin C, 400 IU vitamin D3, 500 IU natural vitamin E, 50mg vitamin B1, 10mg vitamin B2, 70mg vitamin B3, 50mg vitamins B5 and B6, 500mcg vitamin B12, 800mcg folic acid, 300mcg biotin, 500mg Calcium, 300mg magnesium, 75mcg iodine, 25mg zinc, 1mg copper, 2mg manganese, 200mcg selenium, 200mcg chromium, 75mcg molybdenum, 600mcg lycopene, 60mg	*Number of Participants*: total 90; Lutein 29; Lutein + others 30; placebo 31 *Number of eyes:* unclear, some results reported by eye (left or right) but unclear numbers. *Sample attrition/dropout*: at 12 months total 14; Lutein 4 (1 lost to follow-up, 1 died, 2 withdrew); Lutein + others 6 (2 lost to follow-up, 4 withdrew); placebo 4 (1 lost to follow-up, 2 died, 1 withdrew) Included: atrophic AMD, at least one vision-degrading visual-psychophysical abnormality (contrast sensitivity, photo-stress glare recovery deficits, Amsler grid deficits) in one or both eyes, clear non-lenticular ocular media, free of advanced glaucoma and diabetes or any other ocular or systemic disease that could affect central or parafoveal macular visual function.	*Outcomes* • Monocular visual acuity at distance (logMAR) • Visual acuity at near, letters • MPOD • Contrast sensitivity function • Compliance • NEI VFQ-14 (measures activities of daily living, night driving, glare recovery symptoms) • Adverse events *Length of follow-up:* 12 months

	bilberry extract, 150mg alpha lipoic acid, 200mg N-acetyl cysteine, 100mg quercetin; 100mg rutin, 250mg citrus bioflavonoids, 50mg plant enzymes, 5mg black pepper extract, 325mg malic acid, 900mg taurine, 100mg L-glycine,10mg L-glutathione, 2mg boron. *3.* Placebo maltodextrin *Dose modifications:* participants were encouraged not to alter their diets *Concurrent treatment:* not reported *Duration of treatment:* 12 months	Excluded*:* undergone recent (6 months) cataract or retinal surgery, taking photosensitizing drugs, taken lutein supplements (previous 6 months)	
Dawczynski et al., 2013{#712} *Country:* Germany *Design:* RCT *Number of centres:* one *Funding:* commercial funding *Trial ID:* NCT00763659	*Intervention* *1.* Dose 1 (10mg lutein, 1mg zeaxanthin, 225mg fish oil [of which 100mg docosahexaenoic acid, DHA, and 30mg eicosapentaenoic acid, EPA], antioxidants [60mg vitamin C, 20mg vitamin E, 10mg zinc, 0.25mg copper]) *2.* Dose 2 (20mg lutein, 2mg zeaxanthin, 500mg fish oil [of which 200mg DHA, and 60mg EPA], antioxidants [120mg vitamin C, 40mg vitamin E, 20mg zinc, 0.5mg copper]) *3.* Placebo capsule (no details). *Dose details:* As above *Dose modifications:* not reported *Concurrent treatment:* not reported	*Number of Participants*: total 172; dose 1 n=60; dose 2 n=66, placebo n=46 *Number of eyes* total 172; dose 1 n=60; dose 2 n=66, placebo n=46 *Sample attrition/dropout*: total 27; dose 1 n=10; dose 2 n=11, placebo n=6 Included: non-exudative AMD in at least in one eye, classified according to AREDS classification; aged 50-95 years, no lutein, zeaxanthin or omega-3 fatty acid supplementation in last 6 months. One eye only was included. Excluded: central geographic atrophy, exudative forms of AMDthe study eye; pronounced opacity in the intended study eye, subretinal haemorrhages, missing fixatino, optic nerve disease, unstable glaucoma, history of retina-vitreous surgery, advanced cataract.	*Outcomes* • BCVA (ETDRS, distance 4 metres, logMAR) • AREDS classification of reading letters • MPOD *Length of follow-up:* 12 months

	Duration of treatment: 12 months		
Garcia-Layana et al., 2013{#713} *Country:* Spain *Design:* RCT *Number of centres:* assume one *Funding:* commercial and non-commercial funding *Trial ID:* not reported	*Intervention* *1.* lutein, zeaxanthin, docosahexaenoic acid (DHA) *2.* placebo *Dose details:* intervention two tablets daily of 12 mg of lutein, 0.6 mg of zeaxanthin, 280 mg of DHA Placebo, containing sugar: two tablets daily. *Dose modifications:* not reported *Concurrent treatment:* not reported *Duration of treatment:* 12 months	*Number of Participants*: total 44; lutein + DHA 23; placebo 21 *Number of eyes:* not reported *Sample attrition/dropout*: assume none Included: early AMD (stage II-III AREDS classification: small/intermediate drusen and large drusen with/without pigment changes) Excluded: history of lactose intolerance, liver, kidney, or pancreatic disease, anaemia, insulin-dependent diabetes, hyperlipoproteinemia or alcoholism; current use of antihistamine drugs, steroids or nonsteroidal anti-inflammatory drugs; use of any nutrient supplement (< 2 months) or carotenoid supplements (< 6 months).	*Outcomes* • MPOD (primary outcome) • BCVA • Contrast sensitivity *Length of follow-up:* 12 months
Wolf-Schnurrbusch et al., 2015{#213} Country: Switzerland Design: RCT Number of centres: one Funding: commercial and non-commercial funding Trial ID: NCT00563979	*Intervention* *1.* Lutein 10 mg *2.* Lutein 10 mg + Omega-3 fatty acid (DHA/EPA) 160 mg (130 mg) *Dose details:* The ingredients of the supplement in both arms also included: vitamin C 10mg, vitamin E 20 mg, niacin / vitamin B3 10mg, copper 0.25 mg, zinc 10 mg, zeaxanthine 1 mg. *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* 6 months	*Number of Participants*: Total 79: Lutein n=40; Lutein + omega n=39 *Number of eyes* 79 *Sample attrition/dropout*: NR Included*:* age ≥50 years, early or intermediate AMD (reference provided). Only one eye of each patient included, the eye with more advanced AMD changes. Excluded*:* other eye disease in the study eye, opacities of optical media precluding fundus photography.	*Outcomes* • Contrast sensitivity (primary outcome) • MPOD (primary outcome) • BCVA (EDTRS charts); • Compliance *Length of follow-up:* 12 months
Piermarocchi et al.,	*Intervention*	*Number of Participants*: 145: Treatment group 103;	*Outcomes*

2012{#333} *Country:* Italy *Design:* RCT *Number of centres:* NR (multicentre) *Funding:* states none *Trial ID:* not stated	*1.* nutritional supplementation with carotenoids (lutein, zeaxanthin, astaxanthin), oligoelements and antioxidant vitamins *2.* no nutritional supplements (control) *Dose details:* vitamin C (180 mg), vitamin E (30 mg), zinc (22.5 mg), copper (1 mg), lutein (10 mg), zeaxanthin (1 mg), astaxanthin (4 mg). 1 tablet a day, concurrent with food intake at the same time every day. *Dose modifications:* encouraged not to alter diets or change supplementation regimen *Concurrent treatment:* NR *Duration of treatment:* 2 years	controls 42 (text also states 102 and 43) *Number of eyes* 145: Treatment group 103; controls 42 (or 102 and 43). States the eye with the best visual acuity was selected. When both eyes had the same visual acuity, the right eye was chosen for final analysis *Sample attrition/dropout*: withdrawals total 17: treatment group 14, control 3. Excluded from final analysis 35 (treatment group 19, control 16). Discontinued intervention (treatment group 20, control 17). Included: aged 55 – 80 years; dry AMD in at least one eye with extensive intermediate drusen; and at least one large drusen or GA not involving the macula centre ; BCVA in study eye ≥20/32 (74 ETDRS letters), no conditions that limit the view to the fundus, agree to take only the nutritional supplement provided. Excluded: advanced AMD in 1 or 2 eyes; ocular disease with irreversible reduction of visual acuity; significant opacity of the dioptrical media; cataract; lens opacity, surgery (<2 months); insufficient pupil dilation; previous laser treatment of the posterior pole; macular changes not attributable to AMD.	• mean changes in BCVA (primary outcome) • contrast sensitivity • NEI VFQ-25 score • Compliance • Adverse events *Length of follow-up:* 24 months
Fatty acids and antioxidants			
Reynolds et al., 2013{#363} *Country:* USA *Design:* cohort study *Number of centres:*	*Intervention* *1.* dietary omega-3 fatty acids and other fat intake *Dose details:* Diet details from food frequency questionnaires, measurements of total fat, saturated fat, total polyunsaturated fatty acids, monounsaturated fat,	*Number of Participants*: total 2531 (progressors 403; non-progressors 2128) *Number of eyes* total 4165 (progressors 525; non-progressors 4165) *Sample attrition/dropout*: not applicable	*Outcomes* • Progression to GA *Length of follow-up:* up to 12 years

Funding: non-commercial funding *Trial ID:* none reported	docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), combined long chain polyunsaturated fatty acids DHA and EPA, linolenic, and linoleic acid (an omega-6 fatty acid). *Dose modifications:* not applicable *Concurrent treatment:* antioxidant and/or zinc as per group allocation in the AREDs study *Duration of treatment:* not stated	Included: previously participated in the AREDs study; assigned a grade of no AMD, early AMD, intermediate AMD, or 2 forms of advanced or late stage AMD (GA and neovascular) – definitions for these five types were reported. Excluded: criteria for the original AREDs study would have applied. Also intake < 600 calories and ≥4200 (men) or ≥3200 (women) were excluded from the analysis. Eyes with the end point (grade 4 or 5) at baseline were excluded from the analysis.	
Feher et al., 2005{#513} *Country:* Hungary *Design:* RCT *Number of centres:* one *Funding:* not reported *Trial ID:* not reported	*Intervention* *1.* Phototrop (acetyl-L-carnitine, n-3 fatty acids, co-enzyme Q10) *2.* Placebo (soy oil) *Dose details:* two oral capsules per day. Phototrop: 100mg acetyl-L-carnitine, 530mg n-3 fatty acids, 10mg co-enzyme Q10). Placebo: equal quantities of soy oil. *Dose modifications: assume none* *Concurrent treatment:* any concomitant treatments were recorded. Not to take any AMD medications, corticosteroids, phenothiazine or antimalarial drugs (as above) *Duration of treatment:* 12 months	*Number of Participants*: total 106; 51 phototrop; 55 placebo *Number of eyes* used the most affected eye at baseline for the study eye (phototrop 48; placebo 53) but secondary analysis also undertaken on the fellow (less affected) eye (phototrop 43; placebo 45). *Sample attrition/dropout*: interrupted study medication total 5. Phototrop 3 (1 no post-baseline efficacy data, 2 adverse events unrelated to treatment); placebo 2 (1 no post-baseline efficacy data and 1 adverse events unrelated to treatment) Included: early bilateral AMD, BCVA between 0.8 – 0.4 (Snellen chart) in the most affected eye; 55-70 years, Caucasian origin; agree to discontinue current vitamin regimen. Excluded: late AMD (GA or macular scarring); exudative retinal diseases; other ocular pathologies; significant cardiovascular or cerebrovascular diseases; severe hepatic, renal, pulmonary, thyroid, HIV, hepatitis B or C or other immunosuppressive	*Outcomes* • Visual field mean defect (primary outcome) • Visual acuity (Snellen, ETDRS, logMAR) • Foveal sensitivity • Fundus alterations • Compliance *Length of follow-up:* 12 months

		disorders; other diets or treatments .	
Souied et al., 2013{#90} *Country:* France *Design:* RCT *Number of centres:* one *Funding:* commercial funding *Trial ID:* ISRCTN98246501.	*Intervention* *1.* docosahexaenoic acid (DHA) *2.* Placebo *Dose details:* 1. 3 oral capsules daily (280mg DHA, 90mg eicosapentaenoic acid, EPA, 2mg vitamin E). 2. Placebo (602mg olive oil). *Dose modifications:* not reported *Concurrent treatment:* Prohibited medication or use of any other drugs was checked at each visit and recorded in the case report form. *Duration of treatment:* 3 years	*Number of Participants*: total 300: DHA 150; placebo 150 *Number of eyes* total 300: DHA 150; placebo 150 *Sample attrition/dropout*: Total 63: DHA 29 (12 AE, 10 consent withdrawn, 4 disease worsening, 3 other), 3 of 29 were deaths unclear where these are counted); Placebo 34 (7 AE, 19 consent withdrawn, 1 disease worsening, 7 other), 6 of 34 were deaths unclear where these are counted); Included: early age-related maculopathy (any drusen or reticular pseudodrusen with or without pigmentary changes) in the study eye, neovascular AMD in the fellow eye; age ≥55 years to <85 years, visual acuity ≥ +0.4 logMAR units in the study eye Excluded: CNV in both eyes or no CNV in either eye, wide central subfoveal atrophy of the study eye, progressive ocular diseases, major corneal or lens opacities precluding retinal evaluation, serious systemic disease, known allergy to fish oil, fluorescein, indocyanine green, anticoagulant therapy or bleeding tendency, treatment (within 6 months) with nutritional supplements (containing longchain omega-3 fatty acids or α-tocopherol acetate), any concomitant nutritional supplement.	*Outcomes* • Time to occurrence of CNV (primary outcome) • Incidence of CNV • BCVA (logMAR) • Proportion with a visual acuity decrease of 15 letters on ETDRS charts • Safety • Compliance *Length of follow-up:* 3 years
Tao et al., 2016{#671} *Country:* China *Design:* RCT *Number of centres:* one	*Intervention* *1.* α -lipoic acid *2.* Vitamin C, stated as a placebo *Dose details:* α -lipoic acid 0.2 g orally daily. Vitamin C 1.0 g daily	*Number of Participants*: Total 100 (α -lipoic acid 50, placebo 50) *Number of eyes* not reported *Sample attrition/dropout*: not reported	*Outcomes* • BCVA • Contrast sensitivity • Chinese-Version Low Vision Quality of Life (CLVQOL) *Length of follow-up:* 3 months

Funding: non-commercial *Trial ID:* Not reported	*Dose modifications:* Not reported *Concurrent treatment:* Not reported *Duration of treatment:* 3 months	Included: Dry AMD, no diabetes or hypertension that may affect to retinal function; transparent lens opacity and ocular media; no family history of glaucoma, intra-ocular pressure normal and cyc / degree ≤ 0.4; no high myopia, uveitis and retinal detachment which may affect the macular function Excluded: no additional criteria reported	
Cougnard-Grégoire et al., 2016{#306} Linked to Delcourt 2010 *Country:* France *Design:* Cohort study *Number of centres:* 3 *Funding:* commercial and non-commercial funding *Trial ID:* Not reported	*Intervention* *1.* Olive oil consumption, 'regular users' *2.* 'Non users' of olive oil (also described as 'occasional users' *Dose details:* not applicable (typical foods consumed reported) *Dose modifications:* not applicable *Concurrent treatment:* not applicable *Duration of treatment:* not applicable	*Number of Participants*: Total 963; 654 analysed *Number of eyes* 1269 *Sample attrition/dropout*: 309 with incomplete data for AMD status or potential confounders Included: community-dwelling persons aged ≥65 years from three French cities (recruited from ongoing population-based study on risk factors for dementia) Excluded: Not stated	*Outcomes* • Early and late AMD prevalence. • Early AMD soft distinct drusen and/or soft indistinct drusen (>125 μm in diameter) and/or reticular drusen and/or pigmentary abnormalities, in the absence of late AMD. • Late AMD neovascular AMD or geographic atrophy *Length of follow-up:* approx. 7 years
Homocysteine levels, folic acid and B vitamins			
Christen et al., 2009{#499} *Country:* USA *Design:* RCT (secondary aim from a cardiovascular risk factor trial) *Number of centres:* not reported *Funding:* non-commercial	*Intervention* *1.* Folic acid, vitamin B6, Vitamin B12 *2.* Placebo *Dose details:* folic acid (2.5 mg/day), vitamin B6 (50 mg/day), and vitamin B12 (1 mg/day) *Dose modifications:* not reported *Concurrent treatment:* not reported *Duration of treatment:* 7.3 years	*Number of Participants*: total 5205; folic acid + vitamins 2607; placebo 2598 *Number of eyes*: total 5205; folic acid + vitamins 2607; placebo 2598 (individuals were the unit of analysis, classified according to status of the worst eye) *Sample attrition/dropout*: not reported Included: women included in the Women's Antioxidant and Folic Acid Cardiovascular Study (included those at high risk of cardiovascular disease)	*Outcomes* • Total AMD (includes neovascular) • Visually-significant AMD (BCVA loss to 20/30 or worse) • Compliance *Length of follow-up:* 7.3 years

funding. Investigational agents provided by commercial entity. *Trial ID:* not reported		without a diagnosis of AMD. Excluded: those with a diagnosis of AMD at baseline	
Merle et al., 2016 {#6} *Country:* USA *Design:* Prospective cohort study *Number of centres:* 11 *Funding:* various non-commercial grants *Trial ID:* For feeder RCT: NCT00594672	*Intervention* *1.* Folate and vitamin B (all) *Dose details:* Median quintiles consumed per day were reported as log-transformed, calorie-adjusted rates, for males (M) and females (F) in supplementary tables. These ranged as follows: Thiamin (M: 1.10-1.90; F: 0.85-1.43) Riboflavin (M: 1.24-2.41; F: 0.94-1.93) Niacin (M: 14.01-24.44; F: 10.30-18.46) Vitamin B6 (M: 1.22-2.46; F: 0.90-1.89) Folate (M: 260.37-571.66; F: 202.99 – 423.7) Vitamin B12 (M: 2.63-8.3; F: 1.95 - 6.14) *Dose modifications:* NR *Concurrent treatment:* participants either on Age-Related Eye Disease Study (AREDs) intervention (antioxidant and mineral supplements) or placebo. *Duration of treatment:* NR	*Number of Participants*: 4757 enrolled, 2525 in analysis (405 progressed; 2120 unprogressed) *Number of eyes* 4663 of the 2525 participants included in the analysis *Sample attrition/dropout*: 2232 (618 eye research consent only; 995 no genetic specimen; 111 lost to follow up; 39 advanced bilateral AMD; 343 incomplete genetic profile; 126 invalid total energy intake) Included: Participants of AREDs RCT, 55-80 years, ≥ one eye with a visual acuity ≤20/32, at least one eye free from disease that could complicate assessment of AMD, no previous ocular surgery in that eye (except cataract or photocoagulation for AMD). Excluded*:* conditions that would have made long-term follow-up or compliance with study protocol unlikely or difficult. Eyes with advanced AMD excluded from analysis	*Outcomes* • Progression to GA *Length of follow-up:* mean 8.7 years (range 0.5-13 years). 13 years in the survival analysis. Follow-up ended when an eye progressed to GA, or were censored when reached grade 5 clinical age-related maculopathy staging (CARMS)
Gopinath et al., 2013{#952} *Country:* Australia *Design:* Prospective cohort study *Number of centres:* not	*No intervention as such, is an exposure study* *1.* assessment of serum tHcy, folate, and vitamin B-12 levels *2.* intake of folate and vitamin B-12 (by food frequency questionnaire) *Dose details:* serum levels of exposures reported; total intakes recorded; proportion	*Number of Participants*: 2334 in total sample at baseline, 1760 with follow-up. 1390 of whom had the exposure and an assessment of the outcome of interest. *Number of eyes* NR *Sample attrition/dropout*: 574	*Outcomes* • Incidence of any AMD • Early AMD • Late AMD *Length of follow-up:* 5 or 10 years

applicable *Funding:* non-commercial grants *Trial ID:* none	consuming supplements recorded (details in results below) *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* Not applicable	Included: noninstitutionalized residents aged >49 years who were invited to attend a detailed baseline eye examination after a door-to-door census of the study area. Excluded: NR	
Antioxidant effect of vitamins			
Christen et al., 2007{#557} *Country:* USA *Design:* RCT *Number of centres:* NR *Funding:* non-commercial funding *Trial ID:* NR	*Intervention* *1.* Beta carotene *2.* Placebo *Dose details:* Beta carotene, 50-mg supplement every other day *Dose modifications:* NR *Concurrent treatment:* in beta-carotene arm only: low-dose aspirin, 325 mg every other day (terminated early in 1988) *Duration of treatment:* 12 years (range, 11.6 to 14.2)	*Number of Participants*: Total 21,142 (from 22,071 initially randomised) 1. Beta carotene 10,585 2. Placebo 10,557 *Number of eyes* unclear; participants not eyes were unit of analysis *Sample attrition/dropout*: 99.2% were providing information on morbidity at end of 11 years follow-up. 6% crossed over if placebo group reported taking supplemental beta carotene or vitamin A. Included: Healthy male physicians age 40-82 years in 1982. Excluded: Not explicitly reported. States worse eye could be excluded due to other ocular abnormalities. Physicians who died during the first seven years of follow-up were excluded.	*Outcomes* • Incident ARM responsible for a reduction in BCVA to 20/30 or worse (primary endpoint). • ARM with or without vision loss • Advanced ARM Participants were classified according to the status of the worse eye as defined by disease severity *Length of follow-up:* ≥7 years (average 12 years)
Christen et al., 2010{#425} *Country:* USA *Design:* RCT (substudy of RCT of cardiovascular prevention)	*Intervention* *1.* vitamin E (natural-source) and low dose aspirin *2.* Placebo *Dose details:* vitamin E 600 IU on alternate days	*Number of Participants*: total 39421: vitamin E 19,697; Placebo 19,724 *Number of eyes* total 39421: vitamin E 19,697; Placebo 19,724 (individuals were the unit of analysis, classified according to the worst eye) *Sample attrition/dropout*: 455 were excluded as had a	*Outcomes* • visually-significant AMD, BCVA reduced to 20/30 or worse (primary outcome) • Advanced AMD (includes exudative and GA) • AMD with or without vision loss (incident AMD)

Number of centres: not reported *Funding:* non-commercial grants and pills and packaging from commercial entities *Trial ID:* NCT00000161	*Dose modifications:* not reported *Concurrent treatment:* not reported *Duration of treatment:* 10 years	diagnosis of AMD (vitamin E 240; placebo 215). No details of any exclusions after baseline. Included: Women's Health Study participants, ≥45 years; postmenopausal or no intention of becoming pregnant; no history of specific illnesses or other serious illness precluding participation; no history of serious side effects to the study treatments; not currently taking aspirin, aspirin containing medication, or nonsteroidal anti-inflammatory drugs >1 day per week; not taking supplements of vitamin E or beta carotene >1 day per week; not taking anticoagulants or corticosteroids. Excluded: those with a diagnosis of AMD	• Compliance *Length of follow-up:* 10 years
Christen et al., 2014{#304} *Country:* USA *Design:* RCT (substudy of RCT of cancer and cardiovascular prevention) *Number of centres:* not stated *Funding:* non-commercial grants and pills and packaging from commercial entities *Trial ID:* NCT00270647	*Intervention* *1.* multivitamin *2.* Placebo *Dose details:* daily multivitamin, no details *Dose modifications:* not reported *Concurrent treatment:* not reported *Duration of treatment:* average 11.2 years	*Number of Participants*: total 14,233; multivitamin 7,111; placebo 7122 *Number of eyes* total 14,233; multivitamin 7,111; placebo 7122 (individuals were the unit of analysis, classified according to status of the worst eye) *Sample attrition/dropout*: those with cataract or AMD at baseline were excluded (n=3552). No details of any attrition after baseline. Included: healthy male physicians, aged ≥50 years, no history of serious illness that would preclude study participation, no history of significant adverse events attributed to study agents, no other concurrent vitamin and/or multivitamin supplementation, no concurrent vitamin K-depleting anticoagulants (e.g., warfarin). Excluded: those with cataract or AMD at baseline.	*Outcomes* • Visually-significant AMD, BCVA reduced to 20/30 or worse (co-primary outcome) • Total AMD with or without vision loss. • Advanced AMD (includes GA and exudative neovascular AMD) • Compliance • Adverse events *Length of follow-up:* mean 11.2 years
Cangemi et al., 2007{#552}	*Intervention* **RCT** *1.* microcurrent stimulation and nutritional	*Number of Participants*: RCT: Total 73 (microstimulation + supplement 36; sham + supplement 37).	*Outcomes* • Change in BCVA (ETDRS) (primary outcome)

Country: USA *Design:* 1. RCT (of microstimulation) 2. Cohort with historical controls (overlapping patients) *Number of centres:* 5 *Funding:* Commercial funding *Trial ID:* Not reported	supplement (data not reported) *2.* sham microcurrent stimulation and nutritional Supplement **Cohort study** *1.* sham microcurrent stimulation and nutritional supplement (arm from RCT) *2.* Placebo arm from MIRA-1 study (Pulido et al., 2002, in file) *Dose details:* microcurrent. Supplement: Vitamin A (total) 28,640 IU; Vitamin C 452 mg; Vitamin E 200 IU; Zinc Oxide 69.6 mg; Copper 1.6 mg; Taurine 400 mg; EPA Omega-3 Fatty Acids 180 mg; DHA Omega-3 Fatty Acids 120 mg; Lutein (free, not esterified) 8 mg; Zeaxanthin 400 mcg. 2 capsules three times per day *Dose modifications:* Not reported *Concurrent treatment:* Not reported *Duration of treatment:* 6 months	Cohort (sham + supplement): 37, historical control 15 *Number of eyes* analysis performed with patients and eyes as unit of analysis (not reported) *Sample attrition/dropout*: 3 from nutrition group withdrawn, reasons not provided. Included: age 50-90 years, at least 1 eye diagnosed with dry AMD having > 10 large soft drusen 63 μm in diameter, within 3,000 um of the fovea centre, , BCVA in the trial eye(s) of 20/32 to 20/125 inclusive (ETDRS), no conditions that limit the view to the fundus Excluded: Eyes with concomitant macular or choroidal disorders other than AMD and with indefinite signs of AMD, exudative AMD, significant ocular lens opacities causing vision decrease, other ocular pathologies and treatments, uncontrolled hypertension, stroke, epilepsy, any tobacco use.	• Contrast sensitivity • Macular function • Adverse events • Compliance • Visual function questionnaire-25 *Length of follow-up:* 6 months
Taylor et al., 2002{#725} *Country:* Australia *Design:* RCT *Number of centres:* one *Funding:* commercial and non-commercial funding *Trial ID:* not reported	*Intervention* *1.* Vitamin E *2.* Placebo *Dose details:* 1. vitamin E, 500 international units (335 mg d-α tocopherol) in a soybean oil suspension in gelatin capsule, daily. 2. Placebo: matched capsule with soybean oil only. *Dose modifications:* not reported	*Number of Participants*: total 1204 randomised (groups not specified); total after exclusion of 11: 1193, vitamin E 595; placebo 598 *Number of eyes* not reported *Sample attrition/dropout*: 11 participants were excluded after randomisation (outside the required age range, group not specified). Withdrawals total 150; Vitamin E 78 (died 11; adverse event 4; cataract extraction 1; relocated 4; health related 24; personal 23; taken own vitamin E 4; contraindication to	*Outcomes* • Development of early AMD (primary outcome), • AMD progression • Late AMD development • Incidence of drusen • Incidence of hypo and hyperpigmentation • Visual acuity (letters, logMAR) • Changes in visual function (VF-14 score) • Compliance

	Concurrent treatment: not reported *Duration of treatment:* 4 years	vitamin E 4; unknown 3); Placebo 72 (died 7; adverse event 7; cataract extraction 1; relocated 5; health related 21; personal 24; taken own vitamin E 1; contraindication to vitamin E 3; unknown 3). In addition, 144; Vitamin E 74 and placebo 70 discontinued treatment (reasons reported). Excluded from final analysis 14: Vitamin E 8 (diabetic retinopathy 6, myopic degeneration 1, missing data 1); Placebo 6 (adult vitelliform macular degeneration 4, missing data 2) Included: healthy volunteers, aged 55-80 years; lens and retina of at least one eye could be photographed. Excluded*:* bilateral cataract surgery, advanced bilateral cataract, other serious disease, sensitivity to vitamin E, taking steroids or anticoagulant treatment.	• Adverse events *Length of follow-up:* varied up to 4 years
Teikari et al., 1998{#726} *Country:* Finland *Design:* RCT (subgroup analysis of an RCT for lung cancer prevention) *Number of centres:* two *Funding:* non-commercial funding *Trial ID:* not reported	*Intervention* *1*. alpha-tocopherol *2*. beta-carotene *3.* alpha-tocopherol and beta-carotene *4.* Placebo *Dose details:* daily supplements. Alpha-tocopherol (50mg); beta-carotene (20mg) *Dose modifications:* not reported (see below for compliance) *Concurrent treatment:* not reported *Duration of treatment:* 6.6-6.7 years	*Number of Participants*: total sample 941: alpha-tocopherol 237; beta-carotene 234; alpha-tocopherol + beta-carotene 257; placebo 213 *Number of eyes:* assume total sample 1882: alpha-tocopherol 474; beta-carotene 468; alpha-tocopherol + beta-carotene 514; placebo 426 *Sample attrition/dropout*: none (as sample were those that agreed to participate in the substudy) Included: male, ≥65 years, smoking ≥5 cigarettes per day. Excluded: history of cancer or serious disease, taking supplements of vitamin E, vitamin A, or beta-carotene in excess of predefined doses, being treated with anticoagulants.	*Outcomes* • Incidence of AMD • Compliance *Length of follow-up:* 5-8 years (median 6.1)
HESA-A			
Ahmadi et al., 2009{#463}	*Intervention*	*Number of Participants*: total 280; HESA-A 140;	*Outcomes*

Country: Iran *Design:* RCT *Number of centres:* not stated, > 1 *Funding:* not stated *Trial ID:* NR	*1.* HESA-A (a drug of herbal-marine origin) *2.* Placebo *Dose details:* oral tablet 25mg/kg twice daily *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* 4 weeks	control 140 *Number of eyes* total: 280; HESA-A 140; control 140 *Sample attrition/dropout*: NR Included: clinical diagnosis of wet or dry AMD Excluded: diagnosis of cataract, glaucoma, corneal lesions and other macular pathologies	• BCVA (ETDRS charts converted to logMAR score). • Adverse events • Compliance *Length of follow-up:* 6 months (5 months after end of treatment period)
Saffron			
Riazi *et al.,* 2017 *Country:* Iran *Design:* RCT *Number of centres:* one *Funding:* not reported *Trial ID:* not reported	Intervention 1. Saffron supplement 2. Placebo (300mg starch, also states 200mg) Dose details: 50 mg saffron extract and 250 mg of starch in gelatin (also states 150mg starch), one per day Dose modifications: none reported Concurrent treatment: telephoned twice in month 1 and 2 to ensure compliance and for any adverse events. Duration of treatment: 3 months	*Number of Participants*: total 69 randomised; completing study 54; saffron 29, placebo 25 *Number of eyes* not stated if one or both eyes were assessed *Sample attrition/dropout*: 15 did not continue 'for various reasons' mainly lack of satisfaction with the impact of the capsules during month 1 and medical problems. Included*:* >50 years, with dry AMD mild (small drusen or a few medium-sized drusen) to moderate (many medium or at least one big drusen or GA without any sub-foveal involvement), confirmed by a retinal specialist. Excluded*:* wet and severe dry type AMD, systemic diseases such as hypertension, diabetes, or glaucoma, AMD secondary to retinal diseases, taking any other dietary supplements.	*Outcomes* • Quality of life and related activities (Melbourne low vision index), score up to 36 (no problems with daily activities) • Adverse events • BCVA • Contrast Sensitivity • Central macular thickness (not extracted) *Length of follow-up:* 3-months
Falsini et al., 2010{#431} Potential overlap with of participants with Piccardi	*Intervention* *1.* Saffron 20mg *2.* Placebo	*Number of Participants*: Total 25 1. Saffron then placebo, n=11 2. Placebo then saffron, 14	*Outcomes* • visual acuity *Length of follow-up:* 90 days on each

2012 cohort study *Country:* Italy *Design:* Randomised crossover trial (pilot) *Number of centres:* one *Funding:* States no sponsor but also reports non-commercial grants *Trial ID:* NCT00951288	*Dose details:* saffron 20 mg, no further details *Dose modifications:* NR. *Concurrent treatment:* None was taking medications known to affect macular function or to interfere with carotenoid absorption. No other systemic pharmacologic treatments were given. *Duration of treatment:* 90 days of first randomised intervention (saffron or placebo), 15 days washout period, then 90 days of second intervention	*Number of eyes* Total 25 *Sample attrition/dropout*: None. Included*:* bilateral early AMD; BCVA ≥0.3 in the study eye, central fixation, normal colour vision, no signs of other retinal or optic nerve disease and clear optical media. One eye, (typically with best visual acuity), was selected as the study eye. Excluded*:* no explicit criteria reported but confirmation of no geographic atrophy or retinal pigment epithelium detachment was required	treatment
Lashay *et al.*, 2016{#739} *Country:* Iran *Design:* RCT *Number of centres:* one *Funding:* none (saffron donated by manufacturer) *Trial ID:* IRCT 201205219820N1	*Intervention* *1*. Saffron *2.* Placebo *Dose details:* 2 oral capsules, 15mg saffron extract. Placebo was shaped similarly with the same dose and duration. *Dose modifications:* Not reported *Concurrent treatment:* other nutrients or supplements not permitted. No other systemic pharmacological agents were administered. *Duration of treatment:* 6 months	*Number of Participants*: total 30 with dry AMD; saffron 15; placebo 15 (30 with wet AMD also randomised, subgroup not extracted) *Number of eyes:* total 30; saffron 15; placebo 15 *Sample attrition/dropout*: lost to follow-up dry AMD saffron 3; placebo 8. *Sample crossovers:* none *Inclusion criteria:* age ≥ 65 years, physical status class of I-II based on the American Society of Anaesthesiologists classification system, a clinical diagnosis of dry (or wet) AMD confirmed by fluorescein angiography, BCVA 20/400-20/40 in the study eye, clear optical media. *Exclusion criteria:* cataracts, glaucoma, corneal opacities, any sign of retinal or optic nerve disease other than AMD, or systemic disease.	*Outcomes* • Macular thickness (primary outcome) • ERG amplitude (primary outcome) *Length of follow-up:* 6 months

Piccardi et al., 2012{#332} *Country:* Italy *Design:* Before and after study (one group) *Number of centres:*1 *Funding:* Commercial support *Trial ID:* NR	*Intervention* *1.* Saffron oral supplementation *2.* None *Dose details:* Saffron oral supplementation (20mg/day) *Dose modifications:* Not stated *Concurrent treatment:* None *Duration of treatment (mean):* 14 months (SD 2)	*Number of Participants*: N=29 *Number of eyes:* N=29 (1 per participant, typically the eye with the best visual acuity) *Sample attrition/dropout*: Note reported Included: bilateral early AMD, BCVA of ≥0.5 in the study eye, central fixation, normal colour vision with Farnsworth D-15 testing, no signs of other retinal or optic nerve disease and clear optical media. Excluded: NR	*Outcomes* • Focal-electroretinograms (fERG) macular (18◦) flicker sensitivity (primary outcome). • Visual acuity • Compliance • Adverse effects *Length of follow-up:*15 months
Marangoni et al., 2013{#374} Likely overlap of participants from Piccardi 2012 (and potentially Falsini 2010) *Country:* Italy *Design:* Prospective cohort study *Number of centres:* one *Funding:* Saffron tablets provided by manufacturer Hortus Novus; non-commercial grant also *Trial ID:* not reported	*Intervention* *1.* Saffron *Dose details:* Saffron oral supplementation 20 mg/day *Dose modifications:* not reported *Concurrent treatment:* None was taking medications (e.g., chloroquine) that are known to affect macular function or to interfere with carotenoid absorption. No other systemic pharmacologic treatments *Duration of treatment:* average 11 months (range, 6–12)	*Number of Participants*: Total 33 *Number of eyes* 33 *Sample attrition/dropout*: none Included*:* bilateral early AMD; BCVA ≥0.5 in the study eye, central fixation, normal colour vision, no signs of other retinal or optic nerve disease and clear optical media. One eye, (typically with the best visual acuity), was selected as the study eye. Excluded: No additional criteria	*Outcomes* Focal electroretinogram (fERG) amplitude and macular sensitivity from estimated response amplitude thresholds (primary outcomes) Visual acuity (data not reported) Compliance Adverse events *Length of follow-up:* average 11 months (range, 6–12)

ALT: alanine aminotransferase; AMD: age-related macular degeneration; AREDs: Age-Related Eye Disease Study; ARM: Age-related maculopathy; BCVA: best corrected visual acuity; CNV: choroidal neovascularization; CS: Contrast Sensitivity; ETDRS: Early Treatment Diabetic Retinopathy Study; GA: Geographic Atrophy; NR: not reported; RCT: Randomised controlled trial; RPE: retinal pigment epithelium; STGD Stargardt's macular dystrophy

Stargardt's

Study	Intervention Details	Participant details and key eligibility criteria	Relevant Outcomes
Aleman et al., 2007{#544} *Country:* USA *Design:* Before-after study, no control (pilot) *Number of centres:* assume one *Funding:* not reported *Trial ID:* Non-commercial funding	*Intervention* *1.* Lutein *Dose details:* Oral lutein supplementation 20mg /day *Dose modifications:* Not reported *Concurrent treatment:* Not reported *Duration of treatment:* 6 months	*Number of Participants*: Total 11 (10 analysed: 8 Stargardt, 2 cone-rod dystrophy) (compared with 8 healthy controls, not extracted) *Number of eyes* 16 analysed *Sample attrition/dropout*: 1 excluded due to no serum response to lutein Included: Stargardt disease or cone-rod dystrophy with foveal fixation and known or suspected disease-causing mutations in the ABCA4 gene; relatively spared foveal function in ≥one eye. Excluded: No additional criteria stated.	*Outcomes* • MPOD *Length of follow-up:* 6 months
Querques et al., 2010{#447} *Country:* France *Design:* Case series *Number of centres:* one *Funding:* not reported *Trial ID:* not reported	*Intervention* *1.* docosahexaenoic acid (DHA) supplementation *Dose details:* 840 mg per day *Dose modifications:* not reported *Concurrent treatment:* not reported *Duration of treatment:* 6 months	*Number of Participants*: 20 *Number of eyes:* 40 *Sample attrition/dropout*: none Included: late onset Stargardt's disease (reported onset >18 years); >18 years old; evidence of hypo-autofluorescence from areas of macular atrophy; presence of hyperautofluorescent; diagnosis of dark choroid on fluorescein angiography	*Outcomes* • BCVA (ETDRS charts) • Adverse events • Progression in size of central atrophy • Progression to CNV *Length of follow-up:* 6 months

		Excluded: not reported	
Röck et al. 2013{#390} Röck et al., 2011{#757} *Country:* Germany *Design:* RCT *Number of centres:* 1 *Funding:* commercial funding *Trial ID:* NCT00804102	*Intervention* *1.* Sham-stimulation *2.* Transcorneal electrical Stimulation with 66% of the individual electrically stimulated phosphene threshold *3.* Transcorneal electrical Stimulation with 150% of the individual electrically stimulated phosphene threshold *Dose details:* modified neurostimulator with rectangular biphasic pulses (5 ms positive, directly followed by 5 ms negative) at 20 Hz; the threshold current for triggering phosphenes was determined for every patient several times at every visit. *Dose modifications:* NR *Concurrent treatment:* NR *Duration of treatment:* 30 minutes once per week for 6 consecutive weeks	*Number of Participants*: total 12, 66% TES 4; 150% TE 4; Sham 4 *Number of eyes* 12, 66% TES 4; 150% TE 4; Sham 4 *Sample attrition/dropout*: none Included: Stargardt's disease, age >18 years, visual acuity 0.02 to 0.9, evaluable full field ERG, multifocal ERG and static visual field; eye with worse visual acuity was selected (appears to be a subgroup of a larger study for those with various retinal diseases) Excluded: other eye diseases (e.g. advanced diabetic retinopathy, choroidal neovascularisation, exudative age-related macular degeneration), silicone oil tamponade, serious other diseases, aged >99 years	*Outcomes* • visual acuity (EDTRS), • visual field mean defect, • BCVA • Adverse events *Length of follow-up:* 8 weeks (?), 9 measurements: baseline, weekly measurements during stimulation period (measurements 2-7), 2 follow-up visits
Kondrot et al., 2015{#174} (details repeated from above) *Country:* USA *Design:* retrospective before-and-after study (data collected over 10 years) *Number of centres:* one	*Intervention* Customised, Intravenous nutrition (Myer's cocktail), oxidative therapy, microcurrent stimulation, syntonic light therapy (all provided at least one to each participant) *Dose details:* Myer's cocktail Oxidative therapy: minimum of 2 intravenous therapies. Ozone was mixed with blood and injected into body and provided as eye drops	*Number of Participants*: Stargardt's disease 3 *Number of eyes:* Stargardt's disease *Sample attrition/dropout*: NR Included*:* eye disease not responsive to traditional treatments, patients wanted to avoid surgery or side effects of medication, paid $3000 for 3-day treatment programme. Excluded: NR	*Outcomes* • Visual acuity (ETDRS), • Contrast sensitivity • Visual field *Length of follow-up:* 3-days (not clear)

Funding: No external funding. Participants paid $3000 each. *Trial ID:* NR	(no further details) Intravenous hydrogen peroxide given to some patients. Microcurrent stimulation: no details of frequency or duration of application Syntonic light therapy: 2 treatments per day *Dose modifications:* NR *Concurrent treatment:* Information about diet, nutrition, hydration and creation of balance in autonomic nervous system. Homeopathy prescribed but not started during 3 day programme. *Duration of treatment:* 3 days programme (microcurrent therapy initiated on day 2)		
Teussink et al., 2015{#208} *Country:* The Netherlands *Design:* Case series *Number of centres:* one *Funding:* non-commercial *Trial ID:* not reported	*Intervention* *1.* Light exposure protection *Dose details:* best eye had a black contact lens which covered the entire cornea and blocked >90% of light in the visible spectrum. *Dose modifications:* not reported *Concurrent treatment:* were previously advised of the potential benefits of wearing sunglasses, avoiding direct light exposure, and limiting dietary intake of vitamin A. Complete protection from light exposure was suggested as a treatment option. *Duration of treatment:* worn for waking hours for a year	*Number of Participants*: total 5 *Number of eyes* total 5 *Sample attrition/dropout*: none Included: Stargardt disease, at least 1 ABCA4 mutation, typical clinical symptoms associated with Stargardt's retinal dystrophy. Best eye included. Excluded*:* any medical concerns regarding the use of contact lenses	*Outcomes* • BCVA • Compliance • Adverse events • Presence of GA *Length of follow-up:* 17.8 months (range 11-26)
Schwartz et al., 2015	*Intervention*	*Number of Participants*:	*Outcomes*

{#202} Schwartz et al., 2016 {#86} (Details repeated from above) *Country:* USA *Design:* 2 before-after studies *Number of centres:* 4 *Funding:* Commercial and non-commercial funding *Trial ID:* NCT01345006 (STGD)	ubretinal transplantation of hESC derived retinal pigment epithelium (RP) *Dose details:* Injected 150 lL of resuspended hESC-RPE. Three dose cohorts were used for each disorder with each cohort comprising three patients with STGD and three with AMD: cohort 1 received 50,000 cells, cohort 2 received 100,000 cells, and cohort 3 received 150,000 cells. *Dose modifications:* NR. *Concurrent treatment:* The immunosuppression regimen included tacrolimus (target blood concentrations 3–7 ng/mL) and mycophenolate mofetil (ranging from 0.25–2.00 g orally per day) a week before the surgical procedure and continued for 6 weeks. At week 6 the regimen called for discontinuation of tacrolimus and a continuation of mycophenolate mofetil for an additional 6 weeks. *Duration of treatment:* Single treatment with 12 weeks of immunosuppression.	Study 2: n=9 with Stargardt's macular dystrophy (STGD) *Number of eyes:* Study 2: 9 eyes (eye with worst vision) *Sample attrition/dropout*: Not stated Included: age > 18 years, end-stage disease, peripheral visual field constriction. BCVA of study eye 20/400 or worse; BCVA of fellow eye 20/400 or better, the ability to undergo a vitreoretinal surgical procedure under monitored anesthesia care, and psychological suitability to participate in a first-in-human clinical trial involving hESC-derived cells Excluded: other significant ophthalmic pathology, history of cancer, contraindications for systemic immunosuppression. Further details given in study appendix (not extracted).	• Safety and tolerability (primary outcome) • BCVA (ETDRS) • Quality of life *Length of follow-up (includes AMD patients:* Median follow-up 22 months (4 patients had <12 months follow-up, 12 patients had 12–36 months follow-up, and 2 patients had >36 months follow-up)

Table SF6.2 Risk of bias summary tables

RCTs and CCTs:

Study Reference Intervention	Random sequence	Allocation concealment	Blinding participants and personnel (objective / subjective)	Blinding outcome assessors (objective / subjective)	Incomplete outcome data (objective / subjective)	Selective reporting	Other bias

Physical therapies							
Blaha et al. 2013{#372} Haemophoresis **CCT**	High	High	High / NA	Low / NA	High / NA	Low	Low
Studnička et al. 2013{#373} Haemophoresis **CCT**	High	High	High / NA	Low / NA	Unclear / NA	Low	Low
Koss et al., 2009 {#479}Haemophoresis	Low	Low	High / NA	High / NA	High / NA	Low	Low
Pulido et al., 2006{#536} Haemophoresis	Low	Unclear	Low / NA	Low / NA	High / NA	High	Low
Rencová *et al.* 2015 {#197} Haemophoresis	Unclear	Unclear	Unclear / NA	Unclear / NA	Unclear / NA	Unclear	Low
Brunner et al., 2000{#687} Haemophoresis	Unclear	Unclear	Unclear / NA	Unclear / NA	Unclear / NA	Low	Low
Swartz et al., 1999{#686} Haemophoresis	Unclear	Unclear	Unclear / NA	Unclear / NA	Unclear / NA	High	Unclear
Huang et al., 2011{#411} Laser	High	High	Unclear / NA	Unclear / NA	Unclear / NA	High	Low
Prahs et al., 2010{#445} Laser	High	High	High / NA	High / NA	Low / NA	Unclear	Low
Anastassiou et al., 2013{#343} Microcurrent	Unclear	Unclear	Low / NA	High / NA	Low / NA	Unclear	Low
Borrelli et al. 2012{#323} Ozone	Low	Low	Low / NA	Unclear / NA	Low / NA	High	Low
Bocci et al., 2011{#674}**CCT** Ozone	High	High	Unclear / NA	Unclear / NA	Unclear / NA	Unclear	Low
Hudson et al., 2006{#519} Telescopes **CCT**	High	High	High / High	Unclear / Unclear	Unclear / Unclear	Low	Low
Pharmacological agents							
Augustin et al. 2013{#385} Alprostadil	Unclear	Unclear	Low / NA	Unclear / NA	High / NA	Unclear	Low
Remky et al., 2005{#537} Dorzolamide	Unclear	Unclear	Low / NA	Unclear / NA	High / NA	Unclear	Unclear

Yehoshua et al. 2014{#283} Eculizumab	Low	Unclear	Unclear / NA	Unclear / NA	Low / NA	High	Low
Dugal et al., 2015 {#152} Emixustat	Low	Unclear	Low / NA	Unclear / NA	High / NA	High	Low
Mata et al. 2013{#362} Fenretinide	Unclear	Unclear	Unclear / NA	Low / NA	High / NA	High	Low
Landa et al. 2011{#412} Glatiramer acetate	Unclear	Unclear	Unclear / NA	Unclear / NA	Unclear / NA	High	Low
Zhang et al., 2011{#691} NT-501	Unclear	Unclear	Low / NA	Low / NA	Low / NA	High	Low
Wong et al., 2010{#454} OT-551	Unclear	Unclear	High / NA	Unclear / NA	Low / NA	Low	Low
Petrou et al. 2015{#193} Sirolimus	Unclear	Unclear	High / NA	Unclear / NA	Low / NA	Low	Unclear
Wong et al. 2013{#381} Sirolimus	Low	Unclear	High / NA	Unclear / NA	Low / NA	Low	Low
Jaffe et al. 2015{#167} Tandospirone	Low	Unclear	Low / Low	Unclear / Unclear	Low / Low	High	Unclear
Cohen et al. 2012{#324} Trimetazidine	Low	Low	Low / NA	Low / NA	High / NA	High	Low
Kaiser et al., 1995{#719} Visaline	Unclear	Unclear	Unclear / Unclear	Unclear / Unclear	Unclear / Unclear	Unclear	Low
Nutritional supplements							
Berrow et al. 2013{#361} Lutein	Low	Unclear	Unclear / NA	Unclear / NA	Unclear / NA	High	Low
Murray et al. 2013{#368} Lutein	Unclear	Unclear	Low / NA	Unclear / NA	High / NA	Low	Unclear
Weigert et al. 2011{#418} Lutein, lutein + zeaxanthin	Unclear	Unclear	Unclear / NA	Unclear / NA	High / NA	High	Low
Ma et al. 2012a {#331} Lutein, Zeaxanthin	Low	Unclear	Low / NA	Low / NA	Low / NA	Low	Low
Huang et al. 2015a {#163} Lutein, Zeaxanthin	Low	Unclear	Low / Low	Low / Low	Unclear / Unclear	Low	Low
Kelly et al., 2014{#288} Lutein, Zeaxanthin	Low	Unclear	High / NA	Unclear / NA	Low / NA	High	Low
Kelly et al., 2017{#701}	High	High	Unclear / NA	Unclear / NA	Low / NA	Low	Low

Lutein, Zeaxanthin							
Richer et al. 2011{#414} Lutein, Zeaxanthin	Low	Unclear	Low / Low	Low / Low	Low / Low	Unclear	Low
Akuffo et al. 2015 {#133} Lutein, Zeaxanthin	Unclear	Unclear	Unclear / NA	Unclear / NA	High / NA	Low	Low
Trieschmann et al., 2007{#592} **CCT** Lutein, Zeaxanthin	High	High	High / NA	Low / NA	Unclear / NA	Low	Low
Arnold *et al.* 2013{#364} Lutein, Zeaxanthin	Low	Low	Low / NA	Low / NA	High / NA	Low	Low
Beatty et al., 2013{#940} Lutein, Zeaxanthin + others	Low	Unclear	Low / NA	Unclear / NA	High / NA	Low	Low
Bartlett et al., 2007{#548} Lutein, Vitamins	Low	Unclear	Low / NA	Unclear / NA	High / NA	High	Low
Richer et al 2004{#722} Lutein, Vitamins	Unclear	Unclear	Low / Low	Unclear / Unclear	Low / Low	High	Low
Dawczynski et al., 2013{#712} Lutein, Vitamins	Unclear	Unclear	Unclear / NA	Unclear / NA	High / NA	Low	Low
Garcia-Layana et al., 2013{#713} Lutein, Vitamins	Low	High	Low / NA	Unclear / NA	Low / NA	Low	Low
Wolf-Schnurrbusch et al. 2015{#213} Lutein, Omega	Unclear	Unclear	High / NA	High / NA	Unclear / NA	Low	Low
Piermarocchi et al. 2012{#333} Carotenoids, oligoelements and antioxidant	Low	Low	High / Low	Low / Unclear	High / High	Low	Low
Feher et al., 2005{#513} Fatty acids	Low	Unclear	Low / NA	Unclear / NA	Low / NA	Low	Low
Souied et al., 2013{#90} DHA	Low	Unclear	Low / NA	Unclear / NA	Unclear / NA	Low	Low
Tao et al., 2016{#671} α -lipoic acid	Unclear	Unclear	Unclear / Unclear	Unclear / Unclear	Unclear / Unclear	Low	Low

Christen et al., 2007{#557} Vitamins (various)	Unclear	Unclear	Unclear / NA	Unclear / NA	High / NA	Low	Low
Christen et al., 2009{#499} Vitamins (various)	Unclear	Unclear	Unclear / NA	Unclear / NA	Unclear / NA	Low	Low
Christen et al., 2010{#425} Vitamins (various)	Unclear	Unclear	Unclear / NA	Unclear / NA	Unclear / NA	Low	Low
Christen et al., 2014{#304} Vitamins (various)	Unclear	Unclear	Unclear / NA	Unclear / NA	Unclear / NA	Low	Low
Taylor et al., 2002{#725} Vitamin E	Low	Unclear	Low / Low	Low / Low	High / High	High	Low
Teikari et al., 1998{#726} Alpha-tocopherol / beta-carotene	Unclear	Unclear	Unclear / NA	Low / NA	Low / NA	Low	Low
Ahmadi et al., 2009{#463} HESA-A	Unclear	Unclear	Unclear / NA	Unclear / NA	Unclear / NA	Low	Low
Riazi *et al.*, 2017{#1108} Saffron	Unclear	Unclear	Unclear / Unclear	Unclear / Unclear	Unclear / Unclear	Low	Low
Falsini et al., 2010{#431} Saffron	Unclear	Unclear	Unclear / NA	Unclear / NA	Low / NA	Low	Low
Lashay *et al.*, 2016{#739} Saffron	Low	Unclear	Low/NA	Low/NA	High/NA	Unclear	Low

CCT: Controlled Clinical Trial; NA: Not applicable

AREDS studies

Study Reference **Intervention**	**Random sequence**	**Allocation concealment**	**Blinding participants and personnel (objective / subjective)**	**Blinding outcome assessors (objective / subjective)**	**Incomplete outcome data (objective / subjective)**	**Selective reporting**	**Other bias**
AREDS 1 2001 {#844}	Low	Low	Low / NA	Low / NA	Low / NA	Low	Low
AREDS 2 {#376}	Low	Low	Low / NA	Low / NA	Low / NA	Low	Low

Before and After studies:

Criteria	Krenn et al., 2008{#635} Acupuncture	Merry et al. 2016{#681} Laser	Shinoda et al. 2008{#643} Microcurrent	Chaikin et al. 2015{#146} Microcurrent	Kondrot et al. 2015{#174} Microcurrent[a]	Kondrot et al, 2002{#459} Microcurrent	Schwartz et al. 2015{#202} RPE transplant	Gallego-Pinazo et al. 2011{#903} Ranibizumab
1. Study question clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Eligibility/selection criteria clearly described?	No	Yes	Yes	Yes	No	No	Yes	Yes
3. Participants representative?	CD	CD	CD	CD	No	CD	CD	CD
4. All eligible participants enrolled?	No	CD	CD	CD	CD	CD	CD	Yes
5. Sample size sufficiently large?	Yes	CD	No	No	Yes	No	No	No
6. Intervention clearly described and delivered consistently?	Yes	Yes	Yes	No	No	No	Yes	Yes
7. Outcome measures prespecified, defined, valid, reliable, assessed consistently?	No	Yes	CD	Yes	CD	No	Yes	Yes
8. Outcome assessors blinded?	No	No	Yes	No	No	No	No	No
9. Loss to follow-up ≤ 20% and losses accounted for in analysis?	Yes	CD	CD	CD	CD	CD	Yes	Yes
10. Pre-post changes measured? Statistical tests?	No	Yes	Yes	Yes	No	No	Yes	Yes
Overall quality assessment	**Poor**	**Fair**	**Fair**	**Poor**	**Poor**	**Poor**	**Fair**	**Fair**

CD: Cannot determine; NA: not applicable; NR: not reported. [a]had a small subgroup with Stargardt's disease

Before and After studies, cont:

Criteria	Peng et al., 2016 {#80} Lutein,	Vishwanathan et al., 2009{#494}	Vavvas et al. 2016{#94}	Piccardi et al. 2012{#332}

	Zeaxanthin	Lutein, Zeaxanthin	Statins	Saffron
1. Study question clearly stated?	Yes	Yes	Yes	Yes
2. Eligibility/selection criteria clearly described?	Yes	Yes	Yes	Yes
3. Participants representative?	CD	CD	CD	CD
4. All eligible participants enrolled?	Yes	No	CD	Yes
5. Sample size sufficiently large?	Yes	No	No	Yes
6. Intervention clearly described and delivered consistently?	Yes	Yes	Yes	Yes
7. Outcome measures prespecified, defined, valid, reliable, assessed consistently?	Yes	No	Yes	Yes
8. Outcome assessors blinded?	No	No	No	No
9. Loss to follow-up ≤ 20% and losses accounted for in analysis?	Yes	No	No	Yes
10. Pre-post changes measured? Statistical tests?	Yes	Yes	No	Yes
Overall quality assessment	**Good**	**Poor**	**Poor**	**Good**

CD: Cannot determine; NA: not applicable; NR: not reported

Cohort and cross-sectional studies

Criteria	Pipis *et al.* 2015 {#223} Blue light filters	Lavric & Pompe 2014{#997} Blue light filters	Nagai *et al.*, 2015{#958} Blue light filters	Chong *et al.*, 2011 (abstract){#907} Blue light filters	Klingel et al., 2010 {#438} Haemophoresis	Guymer et al. 2014{#239} Laser	Luttrull et al. 2016{#70} Laser	Ivandic et al., 2008{#660} Laser
1. Research question clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Study population specified and defined?	Yes	No	Yes	No	Yes	Yes	Yes	Yes
3. Participation rate ≥ 50%?	CD	CD	CD	CD	CD	Yes	CD	CD
4. Recruitment from similar populations? Eligibility criteria prespecified and applied uniformly?	CD	Yes	CD	CD	CD	Yes	Yes	CD
5. Sample size justification?	No	No	No	No	No	No	No	No
6. Exposure(s) measured prior to outcome(s) measured?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Timeframe sufficient?	Yes	Yes	Yes	Yes	Yes	CD	CD	CD
8. Different levels of the examined?	NA	NA	NA	NA	No	No	No	NR
9. Exposure measures defined, valid, reliable, implemented consistently?	Yes	Yes	Yes	CD	No	CD	CD	Yes
10. Exposure(s) assessed more than once over time?	No	No	No	No	No	Yes	No	No
11. Outcome measures defined, valid, reliable, implemented consistently?	Yes	Yes	Yes	Yes	CD	Yes	CD	CD
12. Outcome assessors blinded?	No	No	Yes	CD	No	Yes	No	No
13. Loss to follow-up ≤20%?	NA	CD	No	CD	Yes	Yes	Yes	Yes
14. Confounding variables	No	No	No	No	No	No	No	No

measured and adjusted for?								
Overall quality	**Poor**	**Poor**	**Fair**	**Poor**	**Poor**	**Fair**	**Poor**	**Poor**

CD: Cannot determine; NA: not applicable; NR: not reported

Cohort and cross-sectional studies, cont.

Criteria	Ho et al., 2017{#971} Cell transplant	Ladewig et al., 2005{#529} Alprostadil	Brilliant et al. 2016{#18} L-DOPA	Vojniković et al., 2008{#631} Prednisolone	Maguire et al., 2009{#481} Statins	Al-Holou 2015{#135} Statins	Barbosa et al. 2014{#249} Statins	Wu et al. 2015{#215} Lutein, Zeaxanthin
1. Research question clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Study population specified and defined?	Yes	Yes	No	No	Yes	Yes	Yes	Yes
3. Participation rate ≥ 50%?	CD	NR	NA	CD	Yes	CD	Yes	CD
4. Recruitment from similar populations? Eligibility criteria prespecified and applied uniformly?	Yes	CD	No	CD	Yes	Yes	Yes	Yes
5. Sample size justification?	No	No	No	No	No	No	No	No
6. Exposure(s) measured prior to outcome(s) measured?	Yes	Yes	No	Yes	No	Yes	CD	CD
7. Timeframe sufficient?	Yes	Yes	CD	Yes	Yes	Yes	CD	Yes
8. Different levels of the examined?	No	NA	No	No	No	No	Yes	Yes
9. Exposure measures defined, valid, reliable, implemented consistently?	No	Yes	CD	No	CD	No	No	Yes
10. Exposure(s) assessed more than once over time?	No	No	CD	No	No	Yes	No	Yes
11. Outcome measures defined, valid, reliable, implemented consistently?	Yes	Yes	CD	No	Yes	Yes	Yes	Yes
12. Outcome assessors	No	No	No	No	No	Yes	No	No

blinded?								
13. Loss to follow-up ≤20%?	Yes	NR	NA	CD	Yes	CD	NA	Yes
14. Confounding variables measured and adjusted for?	No	No	Yes	No	Yes	Yes	Yes	Yes
Overall quality	**Fair**	**Poor**	**Poor**	**Poor**	**Fair**	**Fair**	**Fair**	**Good**

CD: Cannot determine; NA: not applicable; NR: not reported

Cohort and cross-sectional studies, cont. 2

Criteria	Olk et al., 2015{#675} Zeaxanthin	Robman et al., 2007{#581} Lutein, Zeaxanthin	Reynolds et al., 2013{#363} Fatty acids	Cougnard-Grégoire et al. 2016{#306} Olive Oil	Merle et al. 2016{#6} Vitamins (various)	Gopinath et al. 2013{#952} Vitamins (various)	Cangemi et al., 2007{#552}[a] Vitamins (various)	Marangoni et al., 2013{#374} Saffron
1. Research question clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Study population specified and defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Participation rate ≥ 50%?	CD	CD	CD	CD	Yes	Yes	CD	CD
4. Recruitment from similar populations? Eligibility criteria prespecified and applied uniformly?	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
5. Sample size justification?	No	No	No	No	Yes	No	Yes	No
6. Exposure(s) measured prior to outcome(s) measured?	Yes	Yes	CD	Yes	Yes	Yes	Yes	Yes
7. Timeframe sufficient?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	CD
8. Different levels of the examined?	No	Yes	Yes	No	Yes	Yes	No	NA
9. Exposure measures defined, valid, reliable, implemented consistently?	Yes	CD	CD	CD	Yes	Yes	Yes	Yes
10. Exposure(s) assessed more than once over time?	No	No	No	No	No	No	Yes	NA
11. Outcome measures defined,	CD	CD	CD	Yes	Yes	Yes	CD	CD

valid, reliable, implemented consistently?								
12. Outcome assessors blinded?	No	No	No	No	No	No	No	No
13. Loss to follow-up ≤20%?	CD	Yes	CD	No	No	Yes	Yes	CD
14. Confounding variables measured and adjusted for?	No	Yes	Yes	Yes	Yes	Yes	No	No
Overall quality	**Poor**	**Fair**	**Poor**	**Fair**	**Good**	**Good**	**Fair**	**Poor**

CD: Cannot determine; NA: not applicable; NR: not reported

[a]also had an element of an RCT, see Appendix X

Case control studies: (5)

Criteria	McGwin et al. 2003{#897} Statins	Vanderbeek et al. 2013{#898} Statins	Kaiserman et al. 2009{#899} Statins	Fong et al. 2010{#900} Statins	Etminan et al. 2008{632} Stain + ACE-I
1. Research question clearly stated?	Yes	Yes	Yes	Yes	Yes
2. Study population clearly defined?	Yes	Yes	Yes	Yes	Yes
3. Sample size justification?	No	No	No	No	No
4. Controls selected from similar population to the cases?	Yes	Yes	Yes	Yes	Yes
5. Methods for selection of cases and controls valid, reliable, and implemented consistently?	Yes	CD	CD	CD	Yes
6. Cases clearly defined and differentiated from controls?	Yes	Yes	Yes	Yes	Yes
7. If <100% of eligible cases/controls were selected, were cases/controls randomly selected?	NA	NA	NA[a]	NA	CD
8. Use of concurrent controls?	Yes	Yes	Yes	Yes	Yes
9. Confirmation that exposure occurred prior to development of the condition?	No	No	Yes	Yes	Yes

10. Measures of exposure defined, valid, reliable, and implemented consistently?	Yes	CD	Yes	CD	Yes
11. Assessors of exposure blinded?	No	No	No	No	No
12. Confounding variables measured and adjusted for? Was matching accounted for (if applicable)?	No	Yes	No[b]	Yes	Yes
Overall quality	**Fair**	**Fair**	**Fair**	**Fair**	**Fair**

[a] For study 2 – 5 matched controls were randomly selected

[b]reported that not significant when adjusted but no results for adjusted analysis were reported to check

CD: Cannot determine; NA: not applicable; NR: not reported

Case series (2)

Criteria	Figueroa *et al.* 1997[a]{#780} Laser	Qureshi et al. 2015{#196} Telescopes	Michael et al., 1993{#721} Microcurrent	Song et al., 2015{#205} Stem cell transplant
1. Was the study question or objective clearly stated?	Yes	Yes	Yes	Yes
2. Was the study population clearly and fully described, including a case definition?	No	Yes	No	No
3. Were the cases consecutive?	NR	CD	CD	CD
4. Were the subjects comparable?	NR	CD	CD	No
5. Was the intervention clearly described?	Yes	Yes	No	Yes
6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	CD	Yes
7. Was the length of follow-up adequate?	Yes	CD	Yes	Yes
8. Were the statistical methods well-described?	No	NA	NA	NA
9. Were the results well-described?	No	Yes	No	Yes
Overall quality	**Poor**	**Fair**	**Poor**	**Fair**

CD: Cannot determine; NA: not applicable; NR: not reported

[a]also had a small element of an RCT, see Appendix X.

Stargardt's – see also ROB for Kondrot{174} (microstimulation) and Schwartz et al{#202}{#86} RPE transplant

RCTs

Study Reference **Intervention**	**Random sequence**	**Allocation concealment**	**Blinding participants and personnel (objective / subjective)**	**Blinding outcome assessors (objective / subjective)**	**Incomplete outcome data (objective / subjective)**	**Selective reporting**	**Other bias**
Röck *et al.* 2013{#390} Microcurrent	Unclear	Unclear	Unclear / NA	Unclear / NA	Low / NA	Low	Low

Before and After studies

Criteria	Aleman et al., 2007{544} Lutein
1. Study question clearly stated?	Yes
2. Eligibility/selection criteria clearly described?	Yes
3. Participants representative?	CD
4. All eligible participants enrolled?	No
5. Sample size sufficiently large?	No
6. Intervention clearly described and delivered consistently?	Yes
7. Outcome measures prespecified, defined, valid, reliable, assessed consistently?	Yes
8. Outcome assessors blinded?	No
9. Loss to follow-up ≤ 20% and losses accounted for in analysis?	Yes
10. Pre-post changes measured? Statistical tests?	Yes
Overall quality assessment	**Fair**

CD: Cannot determine

See also above for Kondrot et al. 2015 {174} Microcurrent which had a small subgroup with Stargardt's disease

Case series

Criteria	Querques *et al.*,	Teussink et al.,

	2010{#447} docosahexaenoic acid	2015{#208} Light exposure protection
1. Was the study question or objective clearly stated?	Yes	Yes
2. Was the study population clearly and fully described, including a case definition?	Yes	No
3. Were the cases consecutive?	CD	No
4. Were the subjects comparable?	CD	CD
5. Was the intervention clearly described?	Yes	Yes
6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	No
7. Was the length of follow-up adequate?	Yes	Yes
8. Were the statistical methods well-described?	Yes	NA
9. Were the results well-described?	No	No
Overall quality	**Fair**	**Poor**

CD: Cannot determine; NA: not applicable; NR: not reported

Table SF6.3 Baseline characteristics of participants

Study	Arm, N	Age	Male (%)	Ethnic origin % White	BCVA, mean (SD) letters or LogMAR	Smoking history, (%)	Classification (as reported) (%)	Other reported baselines
Non pharmacological treatments								
Acupuncture								
Krenn et al., 2008{#635}	Acupuncture, n=328	77.4 (8.6)	30.8	100	22 (0, 55)[a]	NR	NR	
Blue light filter								
Pipis et al., 2015 {#223}	Blue-light filter, n=39 eyes	82.3 years (range 71-94)	27.5	NR	NR	NR	NR	Area of GA Visual acuity reading from 40cm distance
	No colour filter, n=27 eyes			NR	NR	NR	NR	
Lavric & Pompe 2014{#997}	Blue light filter IOL, n=30 eyes	74.8 (8.0)	36.7	NR	NR	NR	NR	
	UV filter IOL, n=30 eyes							

Nagai *et al.*, 2015{#958}	blue-light filtering IOL, n=52	73.9 (8.9)	36.5	NR	NR	*Never* 57.7 *Past* 7.7 *Current* 11.5 *Unknown* 23.1	NR	
	colourless IOL, n=79	75.5 (6.9)	34.2	NR	NR	*Never* 45.6 *Past* 36.7 *Current* 11.4 *Unknown* 6.3	NR	
Chong *et al.*, 2011 (abstract){#907}	Blue blocking IOL, n=128 eyes	74	NR	NR	NR	NR	NR	
	Clear IOL, n=128 eyes							
Haemopheresis								
Blaha et al., 2013{#372}	Rheohaemapheresis, n=38	66 (range 54-85)	36.8	NR	0.61 (range[b] 0.06 – 1.00)	NR	NR	DPED area
	Control, n=34	76 (range 65-83)	13.4	NR	0.60 (range[b] 0.05 – 1.00)	NR	NR	
Studnička et al 2013{#373}	Rheohaemapheresis, n=19	67.6 (range 55-76)	21.1	NR	0.74 (95% CI 0.36, 1.0)	NR	Bilateral soft drusen 100 Neovascular AMD in 1 eye 5.3	DPED area
	Control, n=18	72.8 (range 64–81)	11.1	NR	0.71 (95% CI 0.15, 1.0)	NR	Neovascular AMD in 1 eye 16.7	
Klingel et al., 2010 {#438}	Rheopheresis, n=279	NR	39.5	NR	NR	NR	NR	
	Controls, n=55	NR	NR	NR	NR	NR	NR	
Koss et al., 2009 {#479}	Rheopheresis, n=22	70	23	NR	0.58	NR	NR	
	Control, n=21	73	33	NR	0.66	NR	NR	
Pulido et al., 2006{#536}	Rheopheresis, n=129	75.0 (6.51)	48.1	96.1	-0.4 (0.16), n=114	NR	NR	
	Placebo, n=69	74.2 (5.79)	52.2	100	-0.4 (0.16) n=69	NR	NR	
Rencová et al., 2015{#197}	Rheohemapheresis, n=12	64.3 (range 64-93)	NR	NR	74.0 (95% CI 56.2, 81.3)	NR	NR	DPED
	Control, n=12	65.6 (range 64-	NR	NR	74.0 (95% CI	NR	NR	

		83)			25.2, 82.6)			
Brunner et al., 2000{#687}	Membrane differential filtration, n=20	72 (6)	NR	NR	0.47 (0.13)	NR	Subfoveal subretinal neovascularization 45	Light rise
	Control, n=20	70 (8)	NR	NR	0.39 (0.24)	NR	Subfoveal subretinal neovascularization 45	
Swartz et al., 1999{#686}	Apheresis, n=10	NR	NR	NR	NR	NR	NR	
	No filtration, n=10	NR	NR	NR	NR	NR	NR	
	No treatment, n=10	NR	NR	NR	NR	NR	NR	
Laser								
Figueroa et al., 1997{#780}	Laser photocoagulation, 1) n=30, 2) n=16	69 (62-74)	NR	NR	NR	NR	NR	
	Control, n=30 eyes		NR	NR	NR	NR	NR	
Guymer et al., 2014{#239}	Laser, n=52	68 (49-86)	30.1	NR	Range 93 (6/4.8) to 60 (6/18)	NR	NR	Flicker sensitivity
Ivandic et al., 2008{#660}	Laser, n=193	64.6 (4.3)	44.6	NR	NR	NR	% eyes (n=328) Cataract 55 Drusen or depigmented 70.1 Geographic atrophy 3.7 Progressive, exudative AMD 26.2	
	Control, n=10	62.3 (6.4)	40	NR	NR	NR	NR 'all stages of AMD'	
Luttrull et al., 2016{#70}	Subthreshold diode micropulse laser, n=108	NR	NR	NR	NR	NR	NR	
Huang et al., 2011{#411}	Prophylactic laser treatment, n=10	70.1 (range 55.0-80.0)	NR	NR	≥ 20/25	NR	NR	
Prahs et al., 2010{#445}	Selective retina therapy laser, n=6	72 (6)	NR	NR	NR	NR	NR	Number of lesions
Merry et al.,	Photobiomodulation,	78 (7.83)	37.5	NR	86.29 (11.36)	NR	% of eyes	Contrast

2016{#681}	n=24,						AREDS 2 21 AREDS 3 48 AREDS 4 31 Geographic atrophy 31 Reticular pseudodrusen, 67	sensitivity Drusen vol, GA area, central retinal thickness retinal volume
Microcurrent								
Shinoda et al., 2008{#643}	Transcutaneous Electrical Retinal Stimulation, n=5	75.7 (9.2)	100	NR	39.8 (SE 4.7)	NR	NR	deviation of the automated perimetry
Chaikin et al., 2015{#146}	Frequency-specific microcurrent stimulation, n=17	82.9 years (range 67-95)	NR	NR	NR	NR	NR	
Kondrot et al., 2015{#174}	Intravenous nutrition (Myer's cocktail), oxidative therapy, microcurrent stimulation, syntonic light therapy, n=70, n=3 (Stargardts)	NR	NR	NR	NR	NR	NR	
Kondrot et al., 2002{#459}	Microcurrent stimulation, n=28	NR	NR	NR	20/25 to 1/400	NR	NR	
Anastassiou et al., 2013{#343}	Microstimulation, n=12	76.2	NR	NR	36.0 (7.5)	NR	AREDs Stage 2 33.3 AREDs Stage 3 50 AREDs Stage 4 16.7	Contrast Sensitivity Macular sensitivity
	Placebo, n=10	76.5	NR	NR	37.3 (4.2)	NR	AREDs Stage 2 0 AREDs Stage 3 90 AREDs Stage 4 10	
Michael et al., 1993{#721} Allen et al., 1998{#710}	Microcurrent + nutritional supplements N=71 study 1: 25; study 2: 46 (cohort 1 12; cohort 2: 34)	Study 1: range 48-79	Study 1 24 Study 2a 8.3 Study 2b 41.2	NR	NR	NR	NR	

Ozone								
Borrelli et al 2012{#323}	Oxygen Ozonetherapy, n=70	70.6 (6.4)	76	NR	0.36 (0.12)	NR	NR	
	Control, n=70	71.4 (7)	84	NR	0.38 (0.18)	NR	NR	
Bocci et al., 2011{#674}	Ozonated AHT, n=54	63-81	NR	NR	1.27 (0.49)	NR	NR	
	Oxygenated AHT, n=23		NR	NR	0.95 (0.5)	NR	NR	
RPE transplant								
Schwartz et al., 2015{#202} 2016{#86}	Dry AMD, n=9	77 (70-88)	33.3	100	NR	NR	NR	
	STGD, n=9	50 (20-71)	44.4	88.9	NR	NR	NR	
Song et al., 2015{#205}	Dry AMD, n=2 STGD, n=2	65-79 40-45	100	NR	See Appendix	NR	NR	
Ho et al., 2017{#971}	Cell implant, n=33	82.0 (66-94), n=35	45.7, n=35	100	Median 1.10 (0.7 – 1.6)	NR	NR	
Telescopes								
Hudson et al., 2006{#519} (linked publications)	Implanted eye, n=217	75.6 (7.3)	52.5	95.9	NR	NR	ICD-9 visual impairment, % Moderate 9.7 Severe 57.6 Profound 32.7	
	Fellow eyes, n=217				NR	NR	NR	
Qureshi et al., 2015{#196}	Telescope n=12	77 (65-85)	33.3	NR	distance 0.120 (SE 0.08)	NR	WHO definition of visual impairment Moderate 8 eyes Severe 7 eyes Profound 3 eyes	

[a]Median (IQR) visual acuity reading from 3m distance, % lines correctly read. [b] assume range, not stated.

Study	**Arm, N**	**Age**	**Male (%)**	**Ethnic**	**BCVA, mean**	**Smoking**	**Classification (as**	**Other reported**

				origin % White	(SD) letters or LogMAR	history, (%)	reported) (%)	baselines
Pharmacological treatments								
Alprostadil								
Augustin et al 2013{#385}	Alprostadil, n=18	76.5 (8.3)	56	NR	7.81 (1.28), n=16	11	NR	Contrast sensitivity + colour vision
	Placebo, n=18	71.8 (7.8)	44	NR	7.29 (1.16), n=17	0	NR	
Ladewig et al., 2005{#529}	Prostaglandin E1 (PGE1), n=11	76 (4)	9.1	NR	NR	NR	NR	
	No treatment, n=10	73 (6)	3	NR	NR	NR	NR	
Dorzolamide								
Remky et al., 2005{#537}	Dorzolamide, n=20	70.6 (6.6)	70	NR	0.13 (0.1)	NR	Pseudophakic 1	Metric acuity, Shortwavelength automated perimetry
	Placebo, n=20	70.1 (6.4)	60	NR	0.12 (0.13)	NR	Pseudophakic 1	
Complement inhibitors								
Eculizumab								
Yehoshua et al., 2014{#283}	Eculizumab, n=20 eyes	79 (7)	NR	NR	71.3 (7.8)	NR	NR	Area of GA
	placebo, n=10 eyes	81 (6)	NR	NR	78.6 (5.2)	NR	NR	
Emixustat								
Dugal et al., 2015 {#152}	Emixustat 2mg qAM (n=12)	78 (55-88)[b]	16.7	91.7	68.0 (33-83)	NR	NR	Lesion size
	Emixustat 5mg qAM (n=12)	75.5 (60-89) [b]	33.3	83.3	74.0 (34-85)	NR	NR	
	Emixustat 5mg qPM (n=12)	82.0 (67-91) [b]	33.3	91.7	58.5 (30-84)	NR	NR	
	Emixustat 7mg qAM (n=12)	79.0 (65-95) [b]	41.7	100	52.5 (19-74)	NR	NR	
	Emixustat 10mg qAM (n=6)	77.0 (73-85) [b]	33.3	100	60.0 (18-85)	NR	NR	
	Placebo (n=18)	82.0 (55-87) [b]	44.4	94.4	65.0 (40-79)	NR	NR	
Fenretinide								

Mata et al., 2013{#362}	fenretinide 100mg, n=80	79.5 (58-89) [b]	35	100	68.59	NR	NR	Lesion size by photography Lesion size by AF
	fenretinide 300mg, n=84	79 (53-90) [b]	46.4	98.8	68.12	NR	NR	
	Placebo, n= 82	80 (55-89) [b]	36.6	98.8	66.57	NR	NR	
Glatiramer acetate								
Landa et al., 2011{#412}	glatiramer acetate, n=7	NR	NR	NR	NR	NR	NR	Numbers of drusen with convex / concave shape
	Placebo, n= 7	NR	NR	NR	NR	NR	NR	
L-DOPA								
Brilliant et al., 2016{#18}	exposure to L-DOPA, n=15,252,958	NR	NR	NR	NR	NR	NR	
NT-501								
Zhang et al., 2011{#691}	High dose NT-501, n=27	74.9 (7.5)	37.0	100	53.5 (9.0)	NR	NR	Area of GA Macular volume Field sensitivity
	Low dose NT-501, n=12	78.3 (5.6)	58.3	100	49.9 (10.2)	NR	NR	
	Sham 2, n=12	74.5 (6.0)	58.3	100	55.3 (7.3)	NR	NR	
Wong et al., 2010{#454}	OT-551, n=10 (eyes)	76.8 (8.27)	40	100	46.1 (20.8)	NR	NR	Area of GA Area of drusen Contrast sensitivity
	No treatment, n=10 (eyes)				57.1 (12.0)	NR	NR	
Prednisolone								
Vojniković et al., 2008{#631}	Prednisolone acetate, n=400	39-80	NR	NR	NR	NR	NR	
	Control, n=75		NR	NR	NR	NR	NR	
Ranibizumab								

Gallego-Pinazo et al., 2011{#903}	Intravitreal ranibizumab, n=6	69 (2.9)	33.3	NR	0.40 (0.15)	NR	drusenoid pigment epithelial detachment, 100%	Central macular thickness
Sirolimus								
Petrou et al., 2015{#193}	Sirolimus, n=6 (eyes)	74.33 (8.45)	66.7	83.3	52.7 (14.5)	NR	NR	Total GA area
	No treatment, n=6 (eyes)				39.2 (20.0)	NR	NR	
Wong et al., 2013{#381}	Sirolimus, n=8 (eyes)	77.88 (8.15)	62.5	100	62.4 (12.7)	NR	NR	Total GA area Area of drusen
	No treatment, n=8 (eyes)				55.1 (20.6)	NR	NR	
Statins								
Maguire et al., 2009{#481}	Statins, n=744	70 (7.4)	36.6	99.5	NR	*Never* 46.1 *Quit* 48.7 *Current: 5.2*	NR	% global area with drusen; focal hyperpigmentation, + depigmentation of RPE; Comorbidities
Al-Holou 2015{#135}	Statin use, 1659	73.5 (7.3)	48.9	96.1	NR	*Never* 40.3 *Former* 53.0 *Current* 6.6	Bilateral large drusen 61.8 Unilateral late AMD 38.2	Comorbidities
	No statin use, n=2132	72.3 (8.1)	38.9	96.9	NR	*Never* 46.2 *Former* 47.4 *Current* 6.4	Bilateral large drusen 67.4 Unilateral late AMD 32.6	
Barbosa et al., 2014{#249}	Statin use, n=1231	With AMD 68 (SE 0.9) Without AMD 55.6 (SE 0.36)	54	82.1	NR	*Current* 15.1 *Past* 42.1 *Never* 42.9	NR	Comorbidities
	No statin use, n=4374		46	76	NR	*Current* 22 *Past* 28.2 *Never* 49.9	NR	

Vavvas et al., 2016{#94}	Atorvastatin, n=23	68.1 (6.0)	30.4	100	77.6 (8.3)	NR	NR	Comorbidities
McGwin et al., 2003{#897}	Cases of ARM, n=550	72.9 (6.8)	100	83.5	NR	NR	NR	Comorbidities
	Controls, n=5500	73.2 (6.7)	100	45.6	NR	NR	NR	
Vanderbeek et al., 2013{#898}	All participants, n=unclear	65.6	45.6	69.0	NR	NR	NR	
Kaiserman et al, 2009{#899}	All members taking statins, n=29,417	68.67 (9.26)	44.7	NR	NR	NR	NR	Comorbidities
	All members not taking statins, n=110,477	63.51 (11.16)	46.3	NR	NR	NR	NR	
Fong et al., 2010{#900}	Wet AMD, n=719	78.6	45.5	70.1	NR	NR	NR	Comorbidities
	Controls, n=78,650	72.7	42.7	48.8	NR	NR	NR	
Etminan et al., 2008{#632}	Cases, n=2867	70.2 (8.5)	55.4	NR	NR	NR	NR	Comorbidities, Prescriptions, diabetic medications
	Controls, n=11,468	70.2 (8.4)	58.6	NR	NR	NR	NR	
Tandospirone								
Jaffe et al., 2015{#167}	tandospirone 1.0% n=252	77.9 (8.0)	48	96	NR	NR	NR	Lesion size
	tandospirone 1.75% n=259	78.3 (7.7)	37	98	NR	NR	NR	
	vehicle solution n=261	78.8 (7.1)	44	96	NR	NR	NR	
Trimetazidine								
Cohen et al, 2012{#324}	Trimetazidine, n=546	73.5 (5.6)	38	100	NR	Former 25 Current 11	NR	Distance VA >0.5 snellen equivalent Hypo/hyperpimentation. Duration of diagnosis, Family history, Comorbidities
	Placebo, n=540				NR			
Visaline								
Kaiser et al.,	Visaline, n=9	72 (6.2)	55.6	NR	Far: 0.60 (0.15)	NR	100% Regional	

1995{#719}					Near: 0.57 (0.19)		atrophy of the pigment epithelium.	
	Placebo, n=11	74 (7.6)	9.1	NR	Far: 0.55 (0.15) Near: 0.45 (0.13)	NR	100% Regional atrophy of the pigment epithelium.	

Study	**Arm, N**	**Age**	**Male (%)**	**Ethnic origin % White**	**BCVA, mean (SD) letters or LogMAR**	**Smoking history, (%)**	**Classification (as reported) (%)**	**Other reported baselines**
Nutrient supplements								
AREDs								
AREDs study group 1{#844}	Total: 3640	Median 69 years	44	96	NR	8% current 49% former	NR	
AREDs study group 2{#376}	Total 4203 (first randomisation)	73.1	43	96	NR	7% current 49% former	NR	
Carotenoids								
Berrow et al., 2013 {#361}	Lutein, n=8	65.5 (9.27)	NR	100	NR	*Pack-yrs* 7.04 (SD 9.42)	NR	
	Control, n=6	69.67 (7.52)	NR	100	NR	*Pack-yrs* 13.5 (SD 15.86)	NR	
Murray et al., 2013{#368}	Lutein, n=36	71.9 (8.7)	44.4	NR	0.10 (0.17)	NR	NR	MPOD
	Placebo, n=36	69.1 (8.6)	33.3	NR	0.05 (0.13)	NR	NR	
Weigert et al., 2011{#418}	Lutein, n=84	71.6 (8.6)	39.7	NR	83.9 (6.0)	NR	AREDS staging, n, 2/3/4: 50/23/43	AREDS stage 2/3/4 MPOD MDLT
	Placebo, n=42							
Ma et al., 2012a {#331} Ma et al.	Lutein 10 mg, n=26	69.9 (8.4)	38.5	NR	0.30 (0.23)	*Never* 88.5 *Former* 7.7 *Current* 3.8	NR	Early cataracts, MPOD, contrast sensitivity,

2012b{#329}	Lutein 20 mg, n=27	69.0 (6.8)	44.4	NR	0.28 (0.23)	*Never* 88.9 *Former 7.4* *Current* 3.7	NR	photorecovery time, amsler grid defects
	Lutein + Zeaxanthin, n=27	68.6 (7.0)	44.4	NR	0.28 90.24)	*Never* 85.2 *Former* 3.7 *Current* 11.1	NR	
	Placebo, n=27	68.9 (7.6)	40.7	NR	0.31 (0.19)	*Never* 88.9 *Former* 3.7 *Current* 7.4	NR	
Huang et al., 2015a{#163} 2015b{#164}	Lutein 10 mg, n=26	69.7 (8.3)	34.6	NR	0.31 (0.21)	*Never 84.6* *Former 11.5* *Current 3.8*	NR	Early cataracts MPOD Contrast sensitivity Photorecovery time VFQ25 score
	Lutein 20 mg, n=27	69.3 (6.9)	51.9	NR	0.31 (0.21)	*Never 88.9* *Former 7.4* *Current 3.7*	NR	
	Lutein +zeaxanthin, n=27	68.5 (6.9)	44.4	NR	0.32 (0.25)	*Never 85.2* *Former 3.7* *Current 11.1*	NR	
	Placebo, n=28	69.0 (7.5)	39.3	NR	0.34 (0.19)	*Never 89.3* *Former 3.6* *Current 7.1*	NR	
Kelly et al., 2014{#288}	Lutein beverage, n=20	43 (16)	40	NR	NR	NR	NR	MPOD
	Lutein egg, n=20	45 (19)	40	NR	NR	NR	NR	
	Zeaxanthin egg, n=20	48 (17)	45	NR	NR	NR	NR	
	Normal egg, n=20	53 (12)	45	NR	NR	NR	NR	
	Control, n=20	44 (16)	45	NR	NR	NR	NR	
Kelly et al., 2017{#701}	Carotenoid-enriched eggs, n=25	35 (8)	84	NR	106 (5.6)	*Never 68* *Past 20* *Current 12*	NR	MPOD
	Placebo eggs, n=25	41 (10)	40	NR	105 (4.5)	*Never 64* *Past 16* *Current 20*	NR	
Richer et al.,	Zeaxanthin, n=25	74.4 (11)	96	NR	95.4 (7)	*pack/d/5y* 0.7	NR	near VA, low

2011{#414}					distance	(0.2)		luminance, MPOD, contrast sensitivity, glare recovery, shape discrimination, BMI, AMD duration, AREDs retinal grade, Comorbidities
	Zeaxanthin + Lutein, n=25	75.8 (9)	96	NR	93.7 (9) distance	*pack/d/5y* 0.2 (0.7)	NR	
	Lutein (faux placebo), n=10	73.9 (9)	96	NR	98.5 (5) distance	*pack/d/5 y* 0.3 (0.5)	NR	
Akuffo et al., 2015 {#133}	Lutein 20 mg + zeaxanthin 2 mg, n=17	65 (7)	29	NR	99 (7) CDVA	*Current* 12 *Past* 47 *Never* 41	NR	Contrast sensitivity, MPOD
	Meso-zeaxanthin 10 mg + Lutein 10 mg + zeaxanthin 2 mg, n=21	64 (9)	38	NR	99 (8) CDVA	*Current* 10 *Past* 33 *Never* 57	NR	
	Meso-zeaxanthin 17 mg + Lutein 3 mg + zeaxanthin 2 mg, n=14	70 (8)	36	NR	98 (6) CDVA	*Current* 0 *Past* 71 *Never* 29	NR	
Peng et al., 2016 {#80}	Lutein complex, n=56	NR	37.5	NR	0.14 (0.09)	NR	NR	Frequency of eye useage; Intraocular pressure; Intraocular pressure; Photostress Recovery; Ocular comfort; Index MPOD
Wu et al., 2015{#215}	Lutein, zeaxanthin and other carotenoids, n=102,046	NR	37.8	c.97	NR	Current c.8	NR	Comorbidities
Trieschmann et al., 2007{#592}	Lutein and Zeaxanthin, n=108	71.5 (7.1)	62.6	NR	NR	Current 4.7	Features of AMD 92.6 Drusen 60	Comorbidities MPOD

							Non-central retinal pigment epithelium proliferation 33 Atrophic changes 7 Healthy maculae 7.4	
	Control, n=28	71 (8.1)	57	NR	NR	NR	Features of AMD 89.2 Drusen 62 Non-central retinal pigment epithelium proliferation 32 Atrophic changes 6 Healthy maculae 10.7	
Arnold et al., 2013{#364}	lutein, zeaxanthin, and ω-3 LCPUFAs, n=50	69 (11)	42	NR	NR	NR	NR	
	lutein, zeaxanthin, and ω-3 LCPUFAs, double dose, n=54	70 (9)	48.1	NR	NR	NR	NR	
	Placebo, n=40	68 (9)	47.5	NR	NR	NR	NR	
Robman et al., 2007{#581}	Dietary intake of lutein, zeaxanthin, fats, n=252	N=254 74 (7)	47	NR	NR	Former or current 46		Family history
Vishwanathan et al., 2009{#494}	Egg consumption, n=52	69 (SE 0.8)	40	98	NR	Never 31 Past 40 NR 29	AMD 15	MPOD Comorbidities
Olk et al., 2015{#675}	Triple therapy, n=210	82 (range 50-99)	27.6	NR	1.12	NR	Bilateral CNV 38.1 Unilateral CNV 61.9 CNV in first eye and drusen in fellow eye 76	
	Triple therapy + zeaxanthin, n=214	80 (range 53-97)	40.7	NR	1.00	NR	CNV in first eye and drusen in fellow eye 37.4	

Beatty et al., 2013{#940}	lutein, zeaxanthin, vitamin E, vitamin C, zinc, copper, n=216	NR	42.6	NR	79.7 (6.6) in 304 eyes	Never 37.5 Ever 50.0 Current 11.6	NR	
	Placebo, n=217	NR	42.9	NR	79.9 (6.5) in 310 eyes	Never 42.9 Ever 40.6 Current 16.1	NR	
Carotenoids and other nutrients								
Bartlett et al., 2007{#548}	Lutein + vitamins, n=15	69.2 (7.8)	47	100	0.20 (0.28)	NR	NR	Contrast senstitivity, previous vit c supp
	Placebo, n=10				0.08 (0.15)	NR	NR	
Richer et al 2004{#722}	Lutein, n=29	74.4 (6.4)	93.1	NR	0.279	*pack-years* 5.2 (14.1)	NR	Contrast sensitivity
	Lutein + other, n=30	73.5 (8.5)	96.7	NR	0.303	*pack-years* 7.1 (1 7.3)	NR	
	Placebo, n=30	76.1 (6.4)	96.8	NR	0.286	*pack-years* 9.2 (22.6)	NR	
Dawczynski et al., 2013{#712}	Lutein + dose 1, n=60	70 (10)	45.3	NR	0.134 (0.17)	31.4	*AREDS stage III: 40.1%* *AREDS stage IV: 15.1%*	Comorbidities
	Lutein + dose 2, n=66			NR	0.104 (0.14)			
	Placebo, n=46			NR	0.129 (0.16)			
Garcia-Layana et al., 2013{#713}	Lutein/zeaxanthin/DHA, n=23	69.2 (7.8)	43.5	NR	76.4 (8.7)	NR	NR	Contrast sensitivity, MPOD
	Placebo, n=21	67.8 (9.2)	38.1	NR	78.3 (6.2)	NR	NR	
Wolf-Schnurrbusch et al., 2015{#213}	Lutein, n=40	75.2 (range 54–88)	45	NR	79.7 (7.4)	NR	Early AMD 55 Intermediate AMD 45	Reports contrast sensitivity, MPOD
	Lutein + Omega, n=39	72.5 (range 54–88)	39	NR	78.6 (10.5)	NR	Early AMD 46 Intermediate AMD 54	
Piermarocchi et al., 2012{#333}	Supplementation, n=103	72.5 (6.8)	39.8	NR	82 (5.7)	Current 16.5 Former 42.7 Never 40.7	NR	Contrast sensitivity NEI VFQ-25 Comorbidities
	Control, n=42	72.6 (7.5)	40.7	NR	81.5 (5.9)	Current 16.6	NR	

						Former 28.5 Never 54.7		
Fatty acids and antioxidants								
Reynolds et al., 2013{#363}	Progressors, n=403	< 70: 46 ⩾70: 54	48	NR	NR	Never 43 Past 50 Current 6	grade in eye 1,1/1,2/2,2: 5 1,3/2,3/3,3: 72 1,4/2,4/3,4: 10 1,5/2,5/3,5: 13	
	Non-progressors, n=2128	< 70: 61 ⩾70: 39	44	NR	NR	Never 47 Past 47 Current 5.5	grade in eye 1,1/1,2/2,2: 57 1,3/2,3/3,3: 30 1,4/2,4/3,4: 1 1,5/2,5/3,5: 12	
Feher et al., 2005{#513}	Phototrop, n=51	63.5 (2.45)	33	100	0.55	15.1	NR	Foveal sensitivity
	Placebo, n=55	63.0 (2.95)			0.55		NR	
Souied et al., 2013{#90}	DHA, n=134	73.9 (6.6)	31.3	NR	0.41 (0.14)	Current 6.7 Former 14.2 Nonsmoker 79.1	See Appendix X	Comorbidities
	Placebo, n=129	73.2 (6.8)	39.5	NR	0.12 (0.15)	Current 8.5 Former 17.1 Nonsmoker 74.4	See Appendix X	
Tao et al., 2016{#671}	α -lipoic acid, n=50	70.86 (7.74)	52	NR	0.64 (0.34)	24	NR	Lesioned disk area, Contrast sensitivity, CLVQOL
	Placebo, n=50	72.06 (7.38)	56	NR	0.61 (0.39)	32	NR	
Cougnard-Grégoire et al., 2016{#306}	Olive oil, n=479	72.8 (4.4)	38.2	NR	NR	None 64.7	Early AMD 28.9 Late AMD 5.5	Comorbidities
	No olive oil, n=175	73.5 (4.2)	40	NR	NR	None 64.6		
Homocysteine levels, folic acid and B vitamins								
Christen et al., 2009{#499}	Folic acid/B6/B12 (n=2,607)	62.6	0	NR	NR	Current 11.4 Past 43.6 Never 45.0	NR	Comorbidities
	Placebo (n=2,598)	62.6	0	NR	NR	Current 12.2 Past 45.0	NR	

						Never 42.7		
Merle et al., 2016 {#6}	Folate and vitamin B, n=4757 (progressors/non-progressons)	≤ 64: 14.6/18.4 65-74: 58.8/66.9 >74: 26.6/14.7	48.6/43.7	NR	NR	NR	NR	Smoking pack years, CARMS grades in each eye, previous tx
Gopinath et al., 2013{#952}	serum tHcy, folate, and vitamin B-12 levels, with AMD n=219 / without AMD n=1171	71.6 (6.7) / 66.7 (7.4)	31.5 / 43.5	NR	NR	Current 8.2 / 7.7	NR	
Antioxidant effect of vitamins								
Christen et al., 2007{#557}	Beta-carotene, n=10,585	52.8	NR	NR	NR	Never 50.2 Past only 39.1 Current 10.7	NR	Comorbidities
	Placebo, n=10,557	52.8	NR	NR	NR	Never 50.0 Past only 39.4 Current 10.6	NR	
Christen et al., 2010{#425}	Vitamin E, n=19,697	54.5	NR	NR	NR	Current 13.1 Past/Never 86.9	NR	Comorbidities
	Placebo, n=19,724	54.5	NR	NR	NR	Current 13.3 Past/Never 86.7	NR	
Christen et al., 2014{#304}	Multivitamin, n=7111	63.9 (8.9)	100	NR	NR	Never 57.1 Former 39.4 Current 3.5	NR	Comorbidities
	Placebo, n=7122	64.0 (9.0)	100	NR	NR	Never 56.4 Former 39.9 Current 3.6	NR	
Cangemi et al., 2007{#552}	Sham + supplement (RCT and cohort study) n=37	76.3 (7.8)	45.9	91.9	0.41 (0.17)	Current 0 Never 67.6 Former 29.7	NR	Cataract surgery Glaucoma Comorbidities
	Placebo (cohort study, matched from Pulido), n=15	74.7 (5.9)	33.0	100	0.39 (0.17)	NR	NR	

Taylor et al., 2002{#725}	Vitamin E n=595	65.72	46	NR	99	Current 2.3 Ever 48	Early AMD 17.5 Late AMD 0.5	Comorbidities, Family history.
	Placebo n=598	65.73	42	NR	99	Current 1.7 Ever 49	Early AMD 18 Late AMD 0.5	
Teikari et al., 1998{#726}	alpha-tocopherol n=237	68.8	100	NR	See Appendix	n/day: 15	NR	Comorbidities
	beta-carotene n=234	68.7	100	NR	See Appendix	n/day: 15	NR	
	alpha-tocopherol + beta-carotene n=257	68.6	100	NR	See Appendix	n/day: 15	NR	
	placebo n=213	68.1	100	NR	See Appendix	n/day: 15	NR	
HESA-A								
Ahmadi et al., 2009{#463}	HESA-A, n=140	69.41 (8.98)	45.7	NR	1.69 (0.65)	NR	NR	
	Control, n=140	68.72 (7.99)	42.1	NR	1.71 (0.65)	NR	NR	
Saffron								
Riazi *et al.*, 2017{#ID}	Saffron, n=29	70.04 (8.5)	65.2	NR	0.46 (0.41)	NR	NR	
	Placebo, n=25	68.9 (8.26)	34.8	NR	0.62 (0.55)	NR	NR	
Falsini et al., 2010{#431}	Saffron then placebo, n=11	65 (5)	48	NR	0.7 (22)	NR	Intermediate AMD 100	Focal RPE abnormalities Drusen Comorbidities
	Placebo then saffron, 14							
Lashay *et al.*, 2016{#739}	Saffron, n=12	68.4 (4.7)	NR	NR	NR	NR	NR	
	Placebo, n=7	63.0 (6.8)	NR	NR	NR	NR	NR	
Piccardi et al., 2012{#332}	Saffron, n=29	69.3 (7)	55.2	NR	0.75	NR	NR	
Marangoni et al., 2013{#374}	Saffron, n=33	68.4 (15-85)	45.5	NR	NR	NR	NR	Comorbidities

BCVA: best corrected visual acuity; c.: Circa; CDVA: corrected distance visual acuity; CVD: cardiovascular disease

[b] median (range)

Table SF6.4: Baseline characteristics of participants – Stargardt's

Study	Arm, N	Age	Male (%)	Ethnic origin % White	BCVA, mean (SD) letters or LogMAR	Smoking history, (%)	Classification (as reported) (%)	Other reported baselines
Aleman et al., 2007{#544}	Lutein, n=11	30 (11)	64	82	NR	Smoker 27	Stargardts 73 Cone-rod dystrophy 27	MPOD Foveal absolute sensitivity
Querques et al., 2010{#447}	Docosahexaenoic acid, n=20	45 (15)	55	NR	NR	NR	NR	
Röck et al. 2013{#390}	Stimulation 66%, n=4	40.0 (9.07)	NR	NR	0.65 (0.24)	NR	NR	
	Stimulation 150%, n=4		NR	NR	0.88 (0.79)	NR	NR	
	Sham, n=4		NR	NR	0.74 (0.25)	NR	NR	
Teussink et al., 2015{#208}	Light protection, n=5	22.6 (range 10-46)	40	100	IPD only	NR	NR	

See also above as Kondrot 2015{#174} subgroup with Stargardt's disease (no baselines reported) for microstimulation, and Schwartz et al{#202}{#86} RPE transplant

Table SF6.5 Studies excluded or not used.

All studies of treatment of wet AMD were excluded, but any studies of prevention of development of wet AMD were eligible. Many of the studies listed below were not used, rather than excluded. For example, there are many reviews and it was not necessary to use them all. Space constraints were also an issue.

First author and Year	Citation	Reason
Abraham 2010	Abraham P, Yue H, Wilson L. Randomized, double-masked, sham-controlled trial of ranibizumab for neovascular age-related macular degeneration: PIER study year 2. *Am J Ophthalmol* 2010;**150**:315-24.e1.	Wet
Aguilà 2016	Aguila M, Cheetham ME. Hsp90 as a Potential Therapeutic Target in Retinal Disease. *Advances in Experimental Medicine & Biology* 2016;**854**:161-7.	Pre-clinical science
Ahmadieh 2011	Ahmadieh H, Taei R, Riazi-Esfahani M, Piri N, Homayouni M, Daftarian N, *et al.* Intravitreal bevacizumab versus combined intravitreal bevacizumab and triamcinolone for neovascular age-related macular degeneration: six-month results of a randomized clinical trial. *Retina* 2011;**31**:1819-26.	Wet AMD
Ahmed 2016	Ahmed CM, Biswal MR, Li H, Han P, Ildefonso CJ, Lewin AS. Repurposing an orally available drug for the treatment of geographic atrophy. *Molecular Vision* 2016;**22**:294-310.	Basic science, xaliproden
Alguere 2016	Algvere PV, Kvanta A, Seregard S. Drusen maculopathy: a risk factor for visual deterioration. *Acta Ophthalmologica* 2016;**94**:427-33.	Not used
Alvarez Palomo 2015	Alvarez Palomo AB, McLenachan S, Chen FK, Da Cruz L, Dilley RJ, Requena J, *et al.* Prospects for clinical use of reprogrammed cells for autologous treatment of macular degeneration. *Fibrogenesis & tissue repair* 2015;**8**:9.	Not used iSPC review
Amadio 2016	Amadio M, Govoni S, Pascale A. Targeting VEGF in eye neovascularization: What's new?: A comprehensive review on current therapies and oligonucleotide-based interventions under development. *Pharmacological Research* 2016;**103**:253-69.	wet
Anand 2014	Anand A, Sharma K, Chen W, Sharma NK. Using current	Review of research needs

	data to define new approach in age related macular degeneration: need to accelerate translational research. *Current Genomics* 2014;**15**:266-77	
Andretta 2014	Andreatta W, El-Sherbiny S. Evidence-based nutritional advice for patients affected by age-related macular degeneration. *Ophthalmologica* 2014;**231**:185-90.	Superseded review
Apte 2016	Apte RS. Targeting Tissue Lipids in Age-related Macular Degeneration. *EBioMedicine* 2016;**5**:26-7.	Editorial
AREDS Report No 3	Age-Related Eye Disease Study Research Group. Risk factors associated with age-related macular degeneration. A case-control study in the age-related eye disease study: Age-Related Eye Disease Study Report Number 3. *Ophthalmology* 2000;**107**:2224-32.	Case control study risk factors
AREDS Report No 7	Age-Related Eye Disease Study Research Group. The effect of five-year zinc supplementation on serum zinc, serum cholesterol and hematocrit in persons randomly assigned to treatment group in the age-related eye disease study: AREDS Report No. 7. *J Nutr* 2002;**132**:697-702.	Zinc serum levels
AREDS Report No 17	Davis MD, Gangnon RE, Lee LY, Hubbard LD, Klein BE, Klein R, *et al.* The Age-Related Eye Disease Study severity scale for age-related macular degeneration: AREDS Report No. 17. *Arch Ophthalmol* 2005;**123**:1484-98.	Severity scales
AREDS Report No 18	Ferris FL, Davis MD, Clemons TE, Lee LY, Chew EY, Lindblad AS, *et al.* A simplified severity scale for age-related macular degeneration: AREDS Report No. 18. *Arch Ophthalmol* 2005;**123**:1570-4.	Severity scales
Arend 2015	Arend N, Wertheimer C, Laubichler P, Wolf A, Kampik A, Kernt M. Idebenone Prevents Oxidative Stress, Cell Death and Senescence of Retinal Pigment Epithelium Cells by Stabilizing BAX/Bcl-2 Ratio. *Ophthalmologica*	Pre-clinical science of idebenone

	2015;**234**:73-82.	
Bandello 2016	Bandello F, Corvi F, La Spina C, Benatti L, Querques L, Capuano V, *et al.* Outcomes of intravitreal anti-VEGF therapy in eyes with both neovascular age-related macular degeneration and diabetic retinopathy. *Br J Ophthalmol* 2016;**100**:1611-6	wet
Barar 2016	Barar J, Aghanejad A, Fathi M, Omidi Y. Advanced drug delivery and targeting technologies for the ocular diseases. *Bioimpacts* 2016;**6**:49-67.	New methods of drug delivery
Bartlett 2007	Bartlett HE, Eperjesi F. Effect of lutein and antioxidant dietary supplementation on contrast sensitivity in age-related macular disease: a randomized controlled trial. *European Journal of Clinical Nutrition* 2007;**61**:1121-7.	Small RCT, 9 month duration, 6mg lutein
Bartlett 2003	Bartlett H, Eperjesi F. Age-related macular degeneration and nutritional supplementation: a review of randomised controlled trials. *Ophthalmic Physiol Opt* 2003;**23**:383-99.	Superseded review
Battaglio-Parodi 2009	Battaglia-Parodi M, Sheth S, Papayannis A, Bandello F. Treatment of serous pigment epithelium detachment with subthreshold micropulse diode laser photocoagulation: a case report. *Eur J Ophthalmol* 2009;**19**:887-9.	Single case report
Bennett 2016	Bennett J, Wellman J, Marshall KA, McCague S, Ashtari M, DiStefano-Pappas J, *et al.* Safety and durability of effect of contralateral-eye administration of AAV2 gene therapy in patients with childhood-onset blindness caused by RPE65 mutations: a follow-on phase 1 trial. *Lancet* 2016;**388**:661-72.	Not STGD
Berner 2016	Berner AK, Kleinman ME. Therapeutic Approaches to Histone Reprogramming in Retinal Degeneration. *Advances in Experimental Medicine & Biology* 2016;**854**:39-44.	Basic science
Biswal 2015	Biswal MR, Ahmed CM, Ildefonso CJ, Han P, Li H, Jivanji H, *et al.* Systemic treatment with a 5HT1a agonist induces anti-oxidant protection and preserves the retina from mitochondrial oxidative stress. *Experimental Eye*	Basic science

	Research 2015;**140**:94-105.	
Black 2016	Black JR, Clark SJ. Age-related macular degeneration: genome-wide association studies to translation. *Genetics in Medicine* 2016;**18**:283-9.	Basic Science
Bloch 2013	Bloch SB, Lund-Andersen H, Sander B, Larsen M. Subfoveal fibrosis in eyes with neovascular age-related macular degeneration treated with intravitreal ranibizumab. *Am J Ophthalmol* 2013;**156**:116-24.e1.	wet
Bojke 2008	Bojke L, Claxton K, Sculpher MJ, Palmer S. Identifying research priorities: the value of information associated with repeat screening for age-related macular degeneration. *Medical Decision Making* 2008;**28**:33-43.	VOI
Brandsetter 2016	Brandstetter C, Patt J, Holz FG, Krohne TU. Inflammasome priming increases retinal pigment epithelial cell susceptibility to lipofuscin phototoxicity by changing the cell death mechanism from apoptosis to pyroptosis. *Journal of Photochemistry and Photobiology B: Biology* 2016;**161**:177-83.	Basic science
Brantley 2012	Brantley MA, Jr., Osborn MP, Sanders BJ, Rezaei KA, Lu P, Li C, *et al.* The short-term effects of antioxidant and zinc supplements on oxidative stress biomarker levels in plasma: a pilot investigation. *Am J Ophthalmol* 2012;**153**:1104-9.e2.	Anti-oxidants and zinc. Only 7 days follow-up
Bressler 2013	Bressler NM, Chang TS, Varma R, Suner I, Lee P, Dolan CM, *et al.* Driving ability reported by neovascular age-related macular degeneration patients after treatment with ranibizumab. *Ophthalmology* 2013;**120**:160-8.	wet
Brown 2009	Brown DM, Michels M, Kaiser PK, Heier JS, Sy JP, Ianchulev T. Ranibizumab versus verteporfin photodynamic therapy for neovascular age-related macular degeneration: Two-year results of the ANCHOR study.	wet

	Ophthalmology 2009;**116**:57-65.e5.	
Brown 2014	Brown MM, Brown GC, Lieske HB, Lieske PA. Financial return-on-investment of ophthalmic interventions: a new paradigm. *Current Opinion in Ophthalmology* 2014;**25**:171-6.	Not relevant
Brucker 2009	Brucker AJ. Age-related macular degeneration. *Retina* 2009;**29**:S2-4.	Superseded review
Brunel 2005	Brunel JM, Salmi C, Loncle C, Vidal N, Letourneux Y. Squalamine: a polyvalent drug of the future? *Current Cancer Drug Targets* 2005;**5**:267-72.	Squalamine in wet AMD
Brunner 1996	Brunner R, Widder R, Fischer RA, Walter P, Bartz-Schmidt KU, Heimann K, *et al.* Clinical efficacy of haemorheological treatment using plasma exchange, selective adsorption and membrane differential filtration in maculopathy, retinal vein occlusion and uveal effusion syndrome. *Transfusion Science* 1996;**17**:493-8.	Mixed wet and dry with no separate results
Brunner 1995	Brunner R, Widder RA, Walter P, Borberg H, Oette K. Change in hemorrheological and biochemical parameters following membrane differential filtration. *Int J Artif Organs* 1995;**18**:794-8.	"Various macular diseases" and only 10 patients.
Byrne 2003	Byrne S, Beatty S. Current concepts and recent advances in the management of age-related macular degeneration. *Ir J Med Sci* 2003;**172**:185-90.	Superseded review
Cia 2016	Cai X, McGinnis JF. Nanoceria: a Potential Therapeutic for Dry AMD. *Adv Exp Med Biol* 2016;**854**:111-8.	Basic science, nanoceria
Calejo et al 2016	Calejo MT, Ilmarinen T, Jongprasitkul H, Skottman H, Kellomaki M. Honeycomb porous films as permeable scaffold materials for human embryonic stem cell-derived retinal pigment epithelium. *Journal of Biomedical Materials Research Part A* 2016;**104**:1646-56.	Basic science of scaffolds
Calton 2016	Calton MA, Vollrath D. The mTOR Kinase Inhibitor	Pre-clinical science

	INK128 Blunts Migration of Cultured Retinal Pigment Epithelial Cells. *Advances in Experimental Medicine & Biology* 2016;**854**:709-15.	
Cao 2016a	Cao S, Wang JC, Gao J, Wong M, To E, White VA, *et al*. CFH Y402H polymorphism and the complement activation product C5a: effects on NF-kappaB activation and inflammasome gene regulation. *British Journal of Ophthalmology* 2016;**100**:713-8.	Basic science
Cao 2016b	Cao J, Murat C, An W, Yao X, Lee J, Santulli-Marotto S, *et al*. Human umbilical tissue-derived cells rescue retinal pigment epithelium dysfunction in retinal degeneration. *Stem Cells* 2016;**34**:367-79.	Basic science
Caramoy 2011	Caramoy A, Fauser S, Kirchhof B. Retinal stimuli can be restored after autologous transplant of retinal pigment epithelium and choroid in pigment epithelium tears. *Acta Opthalmologica* 2011;**89**:e490-5.	Basic science
Cardelli 2016	Cardelli M, Giacconi R, Malavolta M, Provinciali M. Endogenous retroelements in cellular senescence and related pathogenic processes: Promising drug targets in age-related diseases. *Current Drug Targets* 2016;**17**:416-27.	Basic science
Carver 2016	Carver KA, Yang D. N-Acetylcysteine Amide Protects Against Oxidative Stress-Induced Microparticle Release From Human Retinal Pigment Epithelial Cells. *Investigative Ophthalmology & Visual Science* 2016;**57**:360-71.	Basic science
CATT Research Group 2012	Comparison of Age-related Macular Degeneration Treatments Trials (CATT) Research Group. Ranibizumab and bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. *Ophthalmology* 2012;**119**:1388-98.	wet

CATT Research Group 2011	CATT Research Group. Ranibizumab and bevacizumab for neovascular age-related macular degeneration. *N Engl J Med* 2011;**364**:1897-908.	wet
Chaikitmongkol 2016	Chaikitmongkol V, Tadarati M, Bressler NM. Recent approaches to evaluating and monitoring geographic atrophy. *Current Opinion in Ophthalmology* 2016;**27**:217-23.	Not used
Chan 2015	Chan CK, Gangwani RA, McGhee SM, Lian J, Wong DS. Cost-Effectiveness of Screening for Intermediate Age-Related Macular Degeneration during Diabetic Retinopathy Screening. *Ophthalmology* 2015;**122**:2278-85	On screening for AMD
Chandramohan 2016	Chandramohan A, Stinnett SS, Petrowski JT, Schuman SG, Toth CA, Cousins SW, *et al.* Visual Function Measures in Early and Intermediate Age-Related Macular Degeneration. *Retina* 2016;**36**:1021-31.	Visual functions tests
Chang 2016	Chang P, Tan A, Jaffe GJ, Fleckenstein M, Holz FG, Schmitz-Valckenberg S. Analysis of Peripapillary Atrophy in Relation to Macular Geographic Atrophy in Age-Related Macular Degeneration. *Investigative Ophthalmology & Visual Science* 2016;**57**:2277-82.	Basic science of atrophy
Chang 2014	Chang YC, Chang WC, Hung KH, Yang DM, Cheng YH, Liao YW, *et al.* The generation of induced pluripotent stem cells for macular degeneration as a drug screening platform: identification of curcumin as a protective agent for retinal pigment epithelial cells against oxidative stress. *Frontiers in aging neuroscience* 2014;**6**:191.	Basic science – cells and turmeric
Charbel Issa 2015	Charbel Issa P, Barnard AR, Herrmann P, Washington I, MacLaren RE. Rescue of the Stargardt phenotype in Abca4 knockout mice through inhibition of vitamin A dimerization. *Proceedings of the National Academy of Sciences of the United States of America* 2015;**112**:8415-	Basic science in mice

	20.	
Chen 2012	Chen J, Smith LE. Protective inflammasome activation in AMD. *Nat Med* 2012;**18**:658-60.	Basic science
Chen 2016	Chen L, Bai Y, Zhao M, Jiang Y. TLR4 inhibitor attenuates amyloid-beta-induced angiogenic and inflammatory factors in ARPE-19 cells: Implications for age-related macular degeneration. *Molecular Medicine Reports* 2016;**13**:3249-56	Basic science
Cheng 2005	Cheng CY, Chung WY, Szeto YT, Benzie IF. Fasting plasma zeaxanthin response to Fructus barbarum L. (wolfberry; Kei Tze) in a food-based human supplementation trial. *British Journal of Nutrition* 2005;**93**:123-30.	Plasma levels only
Chew 2015	Chew EY, Clemons TE, Agron E, Launer LJ, Grodstein F, Bernstein PS, *et al.* Effect of Omega-3 Fatty Acids, Lutein/Zeaxanthin, or Other Nutrient Supplementation on Cognitive Function: The AREDS2 Randomized Clinical Trial. *JAMA* 2015;**314**:791-801.	Cognitive function
Chong 2007	Chong EW, Wong TY, Kreis AJ, Simpson JA, Guymer RH. Dietary antioxidants and primary prevention of age related macular degeneration: systematic review and meta-analysis. *BMJ* 2007;**335**:755.	Dietary anti-oxidants - too old
Choudary 2016	Choudhary M, Malek G. A Brief Discussion on Lipid Activated Nuclear Receptors and their Potential Role in Regulating Microglia in Age-Related Macular Degeneration (AMD). *Advances in Experimental Medicine & Biology* 2016;**854**:45-51.	Basic science
Choudary 2016	Choudhary P, Whiting PJ. A strategy to ensure safety of stem cell-derived retinal pigment epithelium cells. *Stem Cell Res Ther* 2016;**7**:127.	Pre-clinical
Choudary 2016	Choudhary P, Gutteridge A, Impey E, Storer RI, Owen	Basic science

	RM, Whiting PJ, *et al.* Targeting the cAMP and Transforming Growth Factor-beta Pathway Increases Proliferation to Promote Re-Epithelialization of Human Stem Cell-Derived Retinal Pigment Epithelium. *Stem Cells Translational Medicine* 2016;**5**:925-37.	
Chuo 2007	Chuo JY, Wiens M, Etminan M, Maberley DA. Use of lipid-lowering agents for the prevention of age-related macular degeneration: a meta-analysis of observational studies. *Ophthalmic Epidemiology* 2007;**14**:367-74.	Superseded review
Colby 2007	Colby KA, Chang DF, Stulting RD, Lane SS. Surgical placement of an optical prosthetic device for end-stage macular degeneration: the implantable miniature telescope. *Archives of Ophthalmology* 2007;**125**:1118-21.	Old
Coleman 2007	Coleman H, Chew E. Nutritional supplementation in age-related macular degeneration. *Curr Opin Ophthalmol* 2007;**18**:220-3.	Superseded review
Corso 2016	Corso L, Cavallero A, Baroni D, Garbati P, Prestipino G, Bisti S, *et al.* Saffron reduces ATP-induced retinal cytotoxicity by targeting P2X7 receptors. *Purinergic signalling* 2016;**12**:161-74.	Basic science
Complications of Age-Related Macular Degeneration Prevention Trial Research Group 2006	Complications of Age-Related Macular Degeneration Prevention Trial Research Group. Laser treatment in patients with bilateral large drusen: the complications of age-related macular degeneration prevention trial. *Ophthalmology* 2006;**113**:1974-86.	In Cochrane review
Cugati 2007	Cugati S, Cumming RG, Smith W, Burlutsky G, Mitchell P, Wang JJ. Visual impairment, age-related macular degeneration, cataract, and long-term mortality: the Blue Mountains Eye Study. *Archives of Ophthalmology* 2007;**125**:917-24.	Not relevant
Cukras 2010	Cukras C, Agron E, Klein ML, Ferris FL, 3rd, Chew EY,	Not used

	Gensler G, *et al*. Natural history of drusenoid pigment epithelial detachment in age-related macular degeneration: Age-Related Eye Disease Study Report No. 28. *Ophthalmology* 2010;**117**:489-99.	
Damdimopoulou 2016	Damdimopoulou P, Rodin S, Stenfelt S, Antonsson L, Tryggvason K, Hovatta O. Human embryonic stem cells. *Best Practice & Research in Clinical Obstetrics & Gynaecology* 2016;**31**:2-12.	Not used
Damico 2012	Damico FM, Gasparin F, Scolari MR, Pedral LS, Takahashi BS. New approaches and potential treatments for dry age-related macular degeneration. *Arq Bras Oftalmol* 2012;**75**:71-6.	Superseded
Dang 2015	Dang Y, Zhang C, Zhu Y. Stem cell therapies for age-related macular degeneration: the past, present, and future. *Clinical Interventions In Aging* 2015;**10**:255-64.	Not used
Danner 2016	Danner M, Vennedey V, Hiligsmann M, Fauser S, Gross C, Stock S. How Well Can Analytic Hierarchy Process be Used to Elicit Individual Preferences? Insights from a Survey in Patients Suffering from Age-Related Macular Degeneration. *Patient* 2016;**9**:481-92.	Not relevant
Delcourt 2007	Delcourt C, Carriere I, Cristol JP, Lacroux A, Gerber M. Dietary fat and the risk of age-related maculopathy: the POLANUT study. *European Journal of Clinical Nutrition* 2007;**61**:1341-4.	Superseded short report on fat intake
den Hollander 2010	Den Hollander AI, Black A, Bennett J, Cremers FPM. Lighting a candle in the dark: Advances in genetics and gene therapy of recessive retinal dystrophies. *Journal of Clinical Investigation* 2010;**120**:3042-53	genomics
den Hollander 2016	den Hollander AI. Omics in Ophthalmology: Advances in Genomics and Precision Medicine for Leber Congenital Amaurosis and Age-Related Macular Degeneration.	Not used

	Investigative Ophthalmology & Visual Science 2016;**57**:1378-87.	
Do 2014	Do DV, Pieramici DJ, van Lookeren Campagne M, Beres T, Friesenhahn M, Zhang Y, *et al.* A phase ia dose-escalation study of the anti-factor D monoclonal antibody fragment FCFD4514S in patients with geographic atrophy. *Retina* 2014;**34**:313-20.	Phase 1 study for safety and dosage of a Genentec anti –complement factor drug FCFO4515S, now known as lampalizumab. Superseded by Mahalo trial.
Dong 2015	Dong LF, Yao J, Wang XQ, Shan K, Yang H, Yan B, *et al.* Lenalidomide, an anti-tumor drug, regulates retinal endothelial cell function: Implication for treating ocular neovascular disorder. *Biochemical & Biophysical Research Communications* 2015;**465**:678-84.	Possible use of lenalidomide in eye diseases
Dong LM 2015	Dong LM, Stark WJ, Jefferys JL, Al-Hazzaa S, Bressler SB, Solomon Sd et al. Progression of age-related macular degeneration after cataract surgery. *Arch Ophthalmology 2009;127:1412-19*	Only 12 months follow-up.
Dornstauder 2012	Dornstauder B, Suh M, Kuny S, Gaillard F, Macdonald IM, Clandinin MT, *et al.* Dietary docosahexaenoic acid supplementation prevents age-related functional losses and A2E accumulation in the retina. *Investigative Ophthalmology & Visual Science* 2012;**53**:2256-65.	Mice and no relevant outcomes
Doyle 2012	Doyle SL, Campbell M, Ozaki E, Salomon RG, Mori A, Kenna PF, *et al.* NLRP3 has a protective role in age-related macular degeneration through the induction of IL-18 by drusen components. *Nat Med* 2012;**18**:791-8.	Basic science
Duan 2007	Duan Y, Mo J, Klein R, Scott IU, Lin HM, Caulfield J, *et al.* Age-related macular degeneration is associated with incident myocardial infarction among elderly Americans. *Ophthalmology* 2007;**114**:732-7.	Epidemiology
Dubuc 2009	Dubuc S, Wittich W, Gomolin JE, Kapusta M, Overbury	Not used

	O. Beyond visual acuity: functional outcome and patient satisfaction following treatment for age-related macular degeneration. *Canadian Journal of Ophthalmology* 2009;**44**:680-5.	
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Duvvari 2016	Duvvari MR, van de Ven JP, Geerlings MJ, Saksens NT, Bakker B, Henkes A, *et al.* Whole Exome Sequencing in Patients with the Cuticular Drusen Subtype of Age-Related Macular Degeneration. *PLoS ONE* 2016;**11**:e0152047.	Basic science
Dysli 2016	Dysli C, Wolf S, Hatz K, Zinkernagel MS. Fluorescence Lifetime Imaging in Stargardt Disease: Potential Marker for Disease Progression. *Investigative Ophthalmology & Visual Science* 2016;**57**:832-41.	Diagnostics
Eells 2016	Eells JT, Gopalakrishnan S, Valter K. Near-Infrared Photobiomodulation in Retinal Injury and Disease. *Advances in Experimental Medicine & Biology* 2016;**854**:437-41.	Review of photobiomodulation, not relevant
Ehmann 2016	Ehmann D, Shahlaee A, Ho AC. Cell therapy for retinal disease. *Current Opinion in Ophthalmology* 2016;**27**:185-90.	Not used
Eidet 2016	Eidet JR, Reppe S, Pasovic L, Olstad OK, Lyberg T, Khan AZ, *et al.* The Silk-protein Sericin Induces Rapid Melanization of Cultured Primary Human Retinal Pigment Epithelial Cells by Activating the NF-kappaB Pathway. *Scientific Reports* 2016;**6**:22671.	Basic science
El Mollayess 2012	El-Mollayess GM, Mahfoud Z, Schakal AR, Salti HI, Jaafar D, Bashshur ZF. Fixed-interval versus OCT-guided variable dosing of intravitreal bevacizumab in the	wet

	management of neovascular age-related macular degeneration: a 12-month randomized prospective study. *Am J Ophthalmol* 2012;**153**:481-9.e1.	
Elshout 2016	Elshout M, van der Reis MI, de Jong-Hesse Y, Webers CA, Schouten JS. Distinguishing between Better and Worse Visual Acuity by Studying the Correlation with Quality of Life in Neovascular Age-Related Macular Degeneration. *Ophthalmology* 2016;**123**:2408-12	wet
Erie 2009	Erie JC, Good JA, Butz JA, Pulido JS. Reduced zinc and copper in the retinal pigment epithelium and choroid in age-related macular degeneration. *American Journal of Ophthalmology* 2009;**147**:276-82.e1.	Basic science
Evans 2103	Evans JB, Syed BA. New hope for dry AMD? *Nature Reviews Drug Discovery* 2013;**12**:501-2.	Short non-systematic review, superseded
Evans 2010	Evans JR, Sivagnanavel V, Chong V. Radiotherapy for neovascular age-related macular degeneration. *Cochrane Library*	wet
Fadda 2011	Fadda V, Maratea D, Trippoli S, Messori A. Treatments for macular degeneration: summarising evidence using network meta-analysis. *Br J Ophthalmol* 2011;**95**:1476-7.	wet
Fernando 2016	Fernando N, Natoli R, Valter K, Provis J, Rutar M. The broad-spectrum chemokine inhibitor NR58-3.14.3 modulates macrophage-mediated inflammation in the diseased retina. *Journal of Neuroinflammation* 2016;**13**:47.	Basic science
Ferrington 2016	Ferrington DA, Kapphahn RJ, Leary MM, Atilano SR, Terluk MR, Karunadharma P, *et al.* Increased retinal mtDNA damage in the CFH variant associated with age-related macular degeneration. *Experimental Eye Research* 2016;**145**:269-77.	Basic science
Fields 2015	Fields MA, Bowrey HE, Gong J, Ablonczy Z, Del Priore LV. Retinoid Processing in Induced Pluripotent Stem Cell-	Basic science

	Derived Retinal Pigment Epithelium Cultures. *Progress in molecular biology and translational science* 2015;**134**:477-90.	
Fini 2016	Fini ME, Bauskar A, Jeong S, Wilson MR. Clusterin in the eye: An old dog with new tricks at the ocular surface. *Experimental Eye Research* 2016;**147**:57-71.	Basic science of clusterin
Fisher 2016	Fisher DE, Klein BE, Wong TY, Rotter JI, Li X, Shrager S, *et al.* Incidence of Age-Related Macular Degeneration in a Multi-Ethnic United States Population: The Multi-Ethnic Study of Atherosclerosis. *Ophthalmology* 2016;**123**:1297-308.	Epidemiology
Flaxel 2012	Flaxel C, Schain MB, Hamon SC, Francis PJ. Prospective randomized controlled trial of combination ranibizumab (Lucentis) and bromfenac (Xibrom) for neovascular age-related macular degeneration: a pilot study. *Retina* 2012;**32**:417-23	Wet
Folgar 2016	Folgar FA, Yuan EL, Sevilla MB, Chiu SJ, Farsiu S, Chew EY, *et al.* Drusen Volume and Retinal Pigment Epithelium Abnormal Thinning Volume Predict 2-Year Progression of Age-Related Macular Degeneration. *Ophthalmology* 2016;**123**:39-50.e1	Not used
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Foster 2010	Foster WJ, Tufail W, Issa AM. The quality of pharmacoeconomic evaluations of age-related macular degeneration therapeutics: a systematic review and quantitative appraisal of the evidence. *British Journal of Ophthalmology* 2010;**94**:1118-26.	Not used
Frenneson 2009	Frennesson CI, Bek T, Jaakkola A, Nilsson SE, Prophylactic Laser Treatment Study G. Prophylactic laser	In Cochrane review

	treatment of soft drusen maculopathy: a prospective, randomized Nordic study. *Acta Opthalmologica* 2009;**87**:720-4.	
Friberg 2007	Friberg TR, Huang L, Palaiou M, Bremer R. Computerized detection and measurement of drusen in age-related macular degeneration. *Ophthalmic Surgery, Lasers & Imaging* 2007;**38**:126-34.	Diagnostics, drusen
Friberg 2006	Friberg TR, Musch DC, Lim JI, Morse L, Freeman W, Sinclair S, *et al.* Prophylactic treatment of age-related macular degeneration report number 1: 810-nanometer laser to eyes with drusen. Unilaterally eligible patients. *Ophthalmology* 2006;**113**:622.e1.	In Cochrane review
Friberg 2009	Friberg TR, Brennen PM, Freeman WR, Musch DC, Group PS. Prophylactic treatment of age-related macular degeneration report number 2: 810-nanometer laser to eyes with drusen: bilaterally eligible patients. *Ophthalmic Surgery, Lasers & Imaging* 2009;**40**:530-8.	In Cochrane review
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Fusco 2014	Fusco S, Ullrich F, Pokki J, Chatzipirpiridis G, Ozkale B, Sivaraman KM, *et al.* Microrobots: A new era in ocular drug delivery. *Expert Opinion on Drug Delivery* 2014;**11**:1815-26.	Drug delivery methods
Galvin 2016	Galvin O, Srivastava A, Carroll O, Kulkarni R, Dykes S, Vickers S, *et al.* A sustained release formulation of novel quininib-hyaluronan microneedles inhibits angiogenesis and retinal vascular permeability in vivo. *Journal of Controlled Release* 2016;**233**:198-207.	Basic science
Gangon 2104	Gangnon RE, Lee KE, Klein BE, Iyengar SK,	Diagnostics

	Sivakumaran TA, Klein R. Misclassification can explain most apparent regression of age-related macular degeneration: results from multistate models with misclassification. *Investigative Ophthalmology & Visual Science* 2014;**55**:1780-6.	
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Garg 2013	Garg SJ, Federman J. Optogenetics, visual prosthesis and electrostimulation for retinal dystrophies. *Curr Opin Ophthalmol* 2013;**24**:407-14.	Retinitis pigmentosa
Gekeler 2013 and 2015	Gekeler F. Transcorneal electrostimulation. [German, English]. *Ophthalmologe* 2012;**109**:129-35; Gekeler F, Gosheva M, Naycheva L, Pach J, Willmann G, Zrenner E, *et al.* Transcorneal electrical stimulation for retinitis pigmentosa-a prospective shamcontrolled follow-up study over 1 year in 63 patients. *Investigative Ophthalmology and Visual Science* 2015;**56 (7)**:3801	Electrotherapy for retinitis pigmentosa
Gelfand 2016	Gelfand BD, Ambati J. A Revised Hemodynamic Theory of Age-Related Macular Degeneration. *Trends Mol Med* 2016;**22**:656-70.	Hypothesis on causation
Genead 2009	Genead MA, Fishman GA, Stone EM, Allikmets R. The natural history of stargardt disease with specific sequence mutation in the ABCA4 gene. *Investigative Ophthalmology & Visual Science* 2009;**50**:5867-71.	Not used
Gerstenblith 2013	Gerstenblith AT, Baskin DE, Shah CP, Wolfe JD, Fineman MS, Kaiser RS, *et al.* Electroretinographic effects of	Small case series of omega-3 supplements in dry AMD but only 17

	omega-3 Fatty Acid supplementation on dry age-related macular degeneration. *JAMA Ophthalmol* 2013;**131**:365-9.	patients followed for 6 months. No effect seen.
Giacolone 2016	Giacalone JC, Wiley LA, Burnight ER, Songstad AE, Mullins RF, Stone EM, *et al.* Pluripotent stem cells pluripotent stemcells concise review: Patient-specific stem cells to interrogate inherited eye disease. *Stem Cells Translational Medicine* 2016;**5**:132-40.	Basic science
Giddabasappa 2016	Giddabasappa A, Lalwani K, Norberg R, Gukasyan HJ, Paterson D, Schachar RA, *et al.* Axitinib inhibits retinal and choroidal neovascularization in in vitro and in vivo models. *Experimental Eye Research* 2016;**145**:373-9.	Basic science axitinib
Giustolisi 2011	Giustolisi R, Fantozzi N, Staltari M, Marchiori J, Mastrangelo O, Marcucci R, *et al.* Combined intravitreal ranibizumab and verteporfin photodynamic therapy versus ranibizumab alone for the treatment of age-related macular degeneration. *Digit J Ophthalmol* 2011;**17**:23-30.	wet
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Gomi 2012	Gomi F, Sawa M, Tsujikawa M, Nishida K. Topical bromfenac as an adjunctive treatment with intravitreal ranibizumab for exudative age-related macular degeneration. *Retina* 2012;**32**:1804-10.	Wet
Grob 2016	Grob S, Finn A, Papakostas T, Eliott D. Clinical trials in retinal dystrophies. *Middle East African Journal of Ophthalmology* 2016;**23**:49-59.	Review, not used
Grunwald 2015	Grunwald JE, Pistilli M, Ying GS, Maguire MG, Daniel E, Martin DF. Growth of geographic atrophy in the comparison of age-related macular degeneration treatments	Not used

	trials. *Ophthalmology* 2015;**122**:809-16.	
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Guo 2016	Guo X, Zhu D, Lian R, Han Y, Guo Y, Li Z, *et al.* Matrigel and Activin A promote cell-cell contact and anti-apoptotic activity in cultured human retinal pigment epithelium cells. *Experimental Eye Research* 2016;**147**:37-49.	Basic science
Gupta 2007	Gupta SK, Murthy GV, Morrison N, Price GM, Dherani M, John N, *et al.* Prevalence of early and late age-related macular degeneration in a rural population in northern India: the INDEYE feasibility study. *Investigative Ophthalmology & Visual Science* 2007;**48**:1007-11.	Prevalence in India
Guymer 2007	Guymer R, Robman L. Chlamydia pneumoniae and age-related macular degeneration: a role in pathogenesis or merely a chance association? *Clinical & Experimental Ophthalmology* 2007;**35**:89-93.	Aetiology, not used.
Hammond 2016	Hammond BR, Jr., Renzi-Hammond LM. Perspective: A Critical Look at the Ancillary Age-Related Eye Disease Study 2: Nutrition and Cognitive Function Results in Older Individuals with Age-Related Macular Degeneration. *Advances in Nutrition* 2016;**7**:433-7.	AREDS but cognition
Han 2014	Han Z, Conley SM, Naash MI. Gene therapy for Stargardt disease associated with ABCA4 gene. *Advances in Experimental Medicine & Biology* 2014;**801**:719-24.	Not used
Handa 2016 BBA	Handa JT, Cano M, Wang L, Datta S, Liu T. Lipids, oxidized lipids, oxidation-specific epitopes, and Age-related Macular Degeneration. *Biochim Biophys Acta* 2016; 10.1016/j.bbalip.2016.07.013.	Not used

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Hayashi 2006	Hayashi K, Hayashi H. Visual function in patients with yellow tinted intraocular lenses compared with vision in patients with non-tinted intraocular lenses. *Br J Ophthalmol* 2006;**90**:1019-23.	Blue filter lenses but no data relevant to AMD
He 2014	He L, Marneros AG. Doxycycline inhibits polarization of macrophages to the proangiogenic M2-type and subsequent neovascularization. *Journal of Biological Chemistry* 2014;**289**:8019-28.	Basic science
Heier 2012	Heier JS, Brown DM, Chong V, Korobelnik JF, Kaiser PK, Nguyen QD, *et al.* Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. *Ophthalmology* 2012;**119**:2537-48.	wet
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Hodge 2006	Hodge WG, Schachter HM, Barnes D, Pan Y, Lowcock EC, Zhang L, *et al.* Efficacy of omega-3 fatty acids in preventing age-related macular degeneration: a systematic review. *Ophthalmology* 2006;**113**:1165-72;	Superseded review
Hodge 2010	Hodge W, Brown A, Kymes S, Cruess A, Blackhouse G, Hopkins R, *et al.* Pharmacologic management of neovascular age-related macular degeneration: systematic review of economic evidence and primary economic evaluation. *Can J Ophthalmol* 2010;**45**:223-30.	wet
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	acuity-driven ranibizumab treatment regimen in age-related macular degeneration: outcomes of a drug and disease model. *Invest Ophthalmol Vis Sci* 2010;**51**:405-12.	
Hotta 2015	Hotta A, Yamanaka S. From Genomics to Gene Therapy: Induced Pluripotent Stem Cells Meet Genome Editing. *Annual Review of Genetics* 2015;**49**:47-70.	Not used
Huang 2008	Huang LL, Coleman HR, Kim J, de Monasterio F, Wong WT, Schleicher RL, *et al.* Oral supplementation of lutein/zeaxanthin and omega-3 long chain polyunsaturated fatty acids in persons aged 60 years or older, with or without AMD. *Investigative Ophthalmology & Visual Science* 2008;**49**:3864-9.	No relevant outcomes
Hulleman 2016	Hulleman JD. Malattia Leventinese/Doyne Honeycomb Retinal Dystrophy: Similarities to Age-Related Macular Degeneration and Potential Therapies. *Advances in Experimental Medicine & Biology* 2016;**854**:153-8.	Not relevant
Huynh 2013	Huynh TP, Mann SN, Mandal NA. Botanical compounds: effects on major eye diseases. *Evidence-Based Complementary & Alternative Medicine: eCAM* 2013;**2013**:549174.	Not used
Hytti 2016	Hytti M, Tokarz P, Maatta E, Piippo N, Korhonen E, Suuronen T, *et al.* Inhibition of BET bromodomains alleviates inflammation in human RPE cells. *Biochemical Pharmacology* 2016;**110-111**:71-9.	Basic science
Ibrahim 2009	Ibrahim NMS, Hashem HA, Helal AY. Evaluation of the acute effect of Sildenafil citrate on visual function in patients with early-stage age-related macular degeneration. *International Journal of Ophthalmology* 2009;**9**:824-7.	Could not open PDF
Ibrahim 2016	Ibrahim AS, Mander S, Hussein KA, Elsherbiny NM, Smith SB, Al-Shabrawey M, *et al.* Hyperhomocysteinemia disrupts retinal pigment epithelial structure and function	Basic science

	with features of age-related macular degeneration. *Oncotarget* 2016;**7**:8532-45.	
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Ildefonso 2016b	Ildefonso CJ, Jaime H, Brown EE, Iwata RL, Ahmed CM, Massengill MT, *et al.* Targeting the Nrf2 signaling pathway in the retina with a gene-delivered secretable and cell-penetrating peptide. *Investigative Ophthalmology and Visual Science* 2016;**57**:372-86.	Basic science
Iloki-Assanga 2015	Iloki-Assanga SB, Lewis-Lujan LM, Fernandez-Angulo D, Gil-Salido AA, Lara-Espinoza CL, Rubio-Pino JL. Retino-protective effect of Bucida buceras against oxidative stress induced by H2O2 in human retinal pigment epithelial cells line. *BMC Complementary & Alternative Medicine* 2015;**15**:254.	In vitro study
IVAN Study Investigators 2012	IVAN Study Investigators. Ranibizumab versus bevacizumab to treat neovascular age-related macular degeneration: one-year findings from the IVAN randomized trial. *Ophthalmology* 2012;**119**:1399-411.	wet
Izawa 2016	Izawa H, Shimazawa M, Inoue Y, Uchida S, Moroe H, Tsuruma K, *et al.* Protective effects of NSP-116, a novel imidazolyl aniline derivative, against light-induced retinal damage in vitro and in vivo. *Free Radical Biology & Medicine* 2016;**96**:304-12.	Mice
Jack 2016	Jack LS, Sadiq MA, Do DV, Nguyen QD. Emixustat and Lampalizumab: Potential Therapeutic Options for Geographic Atrophy. *Developments in Ophthalmology* 2016;**55**:302-9.	Non-systematic review

Jee 2016	Jee D, Kang S, Yuan C, Cho E, Arroyo JG, Epidemiologic Survey Committee of the Korean Ophthalmologic S. Serum 25-Hydroxyvitamin D Levels and Dry Eye Syndrome: Differential Effects of Vitamin D on Ocular Diseases. *PLoS ONE [Electronic Resource]* 2016;**11**:e0149294.	Vitamin D and dry eyes
Jeung 2016	Jeung IC, Jee D, Rho CR, Kang S. Melissa Officinalis L. Extracts Protect Human Retinal Pigment Epithelial Cells against Oxidative Stress-Induced Apoptosis. *International Journal of Medical Sciences* 2016;**13**:139-46.	Basic science
Jin 2016	Jin HL, Lee SC, Kwon YS, Choung SY, Jeong KW. A novel fluorescence-based assay for measuring A2E removal from human retinal pigment epithelial cells to screen for age-related macular degeneration inhibitors. *Journal of Pharmaceutical & Biomedical Analysis* 2016;**117**:560-7	Basic science
Jo 2016	Jo YJ, Kim WJ, Shin IH, Kim JY. Longitudinal Changes in Retinal Nerve Fiber Layer Thickness after Intravitreal Anti-vascular Endothelial Growth Factor Therapy. *Korean Journal of Ophthalmology* 2016;**30**:114-20.	Wet, basic science
Jobling 2015	Jobling AI, Guymer RH, Vessey KA, Greferath U, Mills SA, Brassington KH, *et al.* Nanosecond laser therapy reverses pathologic and molecular changes in age-related macular degeneration without retinal damage. *FASEB Journal* 2015;**29**:696-710.	Partly in mice, partly in removed human eyes, and partly a pilot for the LEAD trial. Not used.
Joussen 2007	Joussen AM, Lehmacher W, Hilgers RD, Kirchhof B. Is significant relevant? Validity and patient benefit of randomized controlled clinical trials on age-related macular degeneration. *Survey of Ophthalmology* 2007;**52**:266-78.	Not used
Jyothi 2010	Jyothi S, Chowdhury H, Elagouz M, Sivaprasad S.	Wet, Avastin

	Intravitreal bevacizumab (Avastin) for age-related macular degeneration: a critical analysis of literature. *Eye (Lond)* 2010;**24**:816-24.	
Kaewkhaw 2016	Kaewkhaw R, Swaroop M, Homma K, Nakamura J, Brooks M, Kaya KD, *et al.* Treatment Paradigms for Retinal and Macular Diseases Using 3-D Retina Cultures Derived From Human Reporter Pluripotent Stem Cell Lines. *Investigative Ophthalmology & Visual Science* 2016;**57**:ORSFl1-ORSFl11.	Basic science stem cells
Kannan 2016	Kannan R, Sreekumar PG, Hinton DR. Alpha crystallins in the retinal pigment epithelium and implications for the pathogenesis and treatment of age-related macular degeneration. *Biochimica et Biophysica Acta* 2016;**1860**:258-68	Basic science crystallins
Kasier 2012	Kaiser PK, Boyer DS, Cruess AF, Slakter JS, Pilz S, Weisberger A. Verteporfin plus ranibizumab for choroidal neovascularization in age-related macular degeneration: twelve-month results of the DENALI study. *Ophthalmology* 2012;**119**:1001-10.	wet
Karampelas 2013	Karampelas M, Sim DA, Keane PA, Papastefanou VP, Sadda SR, Tufail A, *et al.* Evaluation of retinal pigment epithelium-Bruch's membrane complex thickness in dry age-related macular degeneration using optical coherence tomography. *Br J Ophthalmol* 2013;**97**:1256-61	Diagnostics
Karnon 2008	Karnon J, Czoski-Murray C, Smith K, Brand C, Chakravarthy U, Davis S, *et al.* A preliminary model-based assessment of the cost-utility of a screening programme for early age-related macular degeneration. *Health Technology Assessment* 2008;**12**:iii-iv, ix-124.	Cost-effectiveness of screening
Karthikeyan 2016	Karthikeyan B, Arun A, Harini L, Sundar K, Kathiresan T. Role of ZnS Nanoparticles on Endoplasmic Reticulum	Basic science

	Stress-mediated Apoptosis in Retinal Pigment Epithelial Cells. *Biological Trace Element Research* 2016;**170**:390-400.	
Keenan 2013	Keenan TD, Kelly SP, Sallam A, Mohamed Q, Tufail A, Johnston RL. Incidence and baseline clinical characteristics of treated neovascular age-related macular degeneration in a well-defined region of the UK. *Br J Ophthalmol* 2013;**97**:1168-72.	wet
Kernt 2010	Kernt M, Neubauer AS, Liegl RG, Hirneiss C, Alge CS, Wolf A, *et al.* Sorafenib prevents human retinal pigment epithelium cells from light-induced overexpression of VEGF, PDGF and PlGF. *British Journal of Ophthalmology* 2010;**94**:1533-9.	Basic science, sorafenib and cells
Kessel 2015	Kessel L, Erngaard D, Flesner P, Andresen J, Tendal B, Hjortdal J. Cataract surgery and age-related degeneration. An evidence-based update. *Acta Ophthalmologica 2015;93:593-600*	Examined AMD 6-12 months after cataract surgery which is too soon
Khan 2006	Khan JC, Shahid H, Thurlby DA, Bradley M, Clayton DG, Moore AT, *et al.* Age related macular degeneration and sun exposure, iris colour, and skin sensitivity to sunlight. *British Journal of Ophthalmology* 2006;**90**:29-32.	Aetiology, sunshine
Kim 2006	Kim LS, Fishman GA. Comparison of visual acuity loss in patients with different stages of Stargardt's disease. *Ophthalmology* 2006;**113**:1748-51.	Not used
Kimbrel 2015	Kimbrel EA, Lanza R. Current status of pluripotent stem cells: Moving the first therapies to the clinic. *Nature Reviews Drug Discovery* 2015;**14**:681-92.	Not used
Kiser 2008	Kiser AK, Deschler EK, Dagnelie G. Visual function and performance with blue-light blocking filters in age-related macular degeneration. *Clinical & Experimental Ophthalmology* 2008;**36**:514-20.	Not about AMD

Klein 2007	Klein R, Klein BE, Knudtson MD, Meuer SM, Swift M, Gangnon RE. Fifteen-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study. *Ophthalmology* 2007;**114**:253-62.	Old Beaver Dam study paper
Klettner 2013	Klettner A, Kauppinen A, Blasiak J, Roider J, Salminen A, Kaarniranta K. Cellular and molecular mechanisms of age-related macular degeneration: from impaired autophagy to neovascularization. *Int J Biochem Cell Biol* 2013;**45**:1457-67.	Review of pathology
Klettner 2014	Klettner A, Tahmaz N, Dithmer M, Richert E, Roider J. Effects of aflibercept on primary RPE cells: toxicity, wound healing, uptake and phagocytosis. *British Journal of Ophthalmology* 2014;**98**:1448-52.	Wet AMD
Knudston 2007	Knudtson MD, Klein R, Klein BE. Alcohol consumption and the 15-year cumulative incidence of age-related macular degeneration. *American Journal of Ophthalmology* 2007;**143**:1026-9.	Aetiology, alcohol
Kompella 2010	Kompella U, Amrite A, Pugazhenthi V, Cheruvu N. Delivery of celecoxib for treating diseases of the eye: influence of pigment and diabetes. *Expert Opin Drug Deliv* 2010;**7**:631-45.	Basic science, celicoxib
Kothary 2016	Kothary PC, Rossi B, Del Monte MA. Valproic Acid Induced Human Retinal Pigment Epithelial Cell Death as Well as its Survival after Hydrogen Peroxide Damage is Mediated by P38 Kinase. *Advances in Experimental Medicine & Biology* 2016;**854**:765-72.	Basic science, valproate and cells
Kowluro 2011	Kowluru RA, Zhong Q. Beyond AREDS: is there a place for antioxidant therapy in the prevention/treatment of eye disease? *Invest Ophthalmol Vis Sci* 2011;**52**:8665-71	Beyond AREDS review
Krebs 2013	Krebs I, Schmetterer L, Boltz A, Told R, Vecsei-Marlovits V, Egger S, *et al.* A randomised double-masked trial	wet

	comparing the visual outcome after treatment with ranibizumab or bevacizumab in patients with neovascular age-related macular degeneration. *Br J Ophthalmol* 2013;**97**:266-71.	
Kumar-Singh 2008	Kumar-Singh R. Barriers for retinal gene therapy: separating fact from fiction. *Vision Research* 2008;**48**:1671-80.	Gene therapy, superseded
Kuno 2010	Kuno N, Fujii S. Biodegradable intraocular therapies for retinal disorders: progress to date. *Drugs & Aging* 2010;**27**:117-34.	Drug delivery
Lambros 2016	Lambros ML, Plafker SM. Oxidative Stress and the Nrf2 Anti-Oxidant Transcription Factor in Age-Related Macular Degeneration. *Advances in Experimental Medicine & Biology* 2016;**854**:67-72.	Basic science
Larsen 2012	Larsen M, Schmidt-Erfurth U, Lanzetta P, Wolf S, Simader C, Tokaji E, *et al.* Verteporfin plus ranibizumab for choroidal neovascularization in age-related macular degeneration: twelve-month MONT BLANC study results. *Ophthalmology* 2012;**119**:992-1000	wet
Li 2012	Li X, Hu Y, Sun X, Zhang J, Zhang M. Bevacizumab for neovascular age-related macular degeneration in China. *Ophthalmology* 2012;**119**:2087-93.	Wet
Liegl 2014	Liegl R, Koenig S, Siedlecki J, Haritoglou C, Kampik A, Kernt M. Temsirolimus inhibits proliferation and migration in retinal pigment epithelial and endothelial cells via mTOR inhibition and decreases VEGF and PDGF expression. *PLoS ONE [Electronic Resource]* 2014;**9**:e88203.	Basic science temsorilimus
Lindblad 2009	Lindblad AS, Lloyd PC, Clemons TE, Gensler GR, Ferris FL, 3rd, Klein ML, *et al.* Change in area of geographic atrophy in the Age-Related Eye Disease Study: AREDS	Not used

	report number 26. *Archives of Ophthalmology* 2009;**127**:1168-74.	
Liu 2016a	Liu X, Zhu M, Yang X, Wang Y, Qin B, Cui C, *et al*. Inhibition of RACK1 ameliorates choroidal neovascularization formation in vitro and in vivo. *Experimental & Molecular Pathology* 2016;**100**:451-9.	Basic science
Liu 2016b	Liu X, Chen J, Liu Z, Li J, Yao K, Wu Y. Potential Therapeutic Agents Against Retinal Diseases Caused by Aberrant Metabolism of Retinoids. *Investigative Ophthalmology & Visual Science* 2016;**57**:1017-30.	Basic science
Liu 2016c	Liu X, Ward K, Xavier C, Jann J, Clark AF, Pang IH, *et al*. The novel triterpenoid RTA 408 protects human retinal pigment epithelial cells against H2O2-induced cell injury via NF-E2-related factor 2 (Nrf2) activation. *Redox Biology* 2016;**8**:98-109.	Basic science
Lu 2014	Lu B, Tai YC, Humayun MS. Microdevice-based cell therapy for age-related macular degeneration. *Developments in Ophthalmology* 2014;**53**:155-66.	Artificial Bruch's membrane
Ma 2016	Ma J, Sun Y, Lopez FJ, Adamson P, Kurali E, Lashkari K. Blockage of PI3K/mTOR Pathways Inhibits Laser-Induced Choroidal Neovascularization and Improves Outcomes Relative to VEGF-A Suppression Alone. *Investigative Ophthalmology & Visual Science* 2016;**57**:3138-44.	Basic science
Maclaren 2015	MacLaren RE. Gene therapy for age-related macular degeneration. *The Lancet* 2015;**386**:2369-70.	editorial
Mainolfi 2016	Mainolfi N, Karki R, Liu F, Anderson K. Evolution of a New Class of VEGFR-2 Inhibitors from Scaffold Morphing and Redesign. *ACS Medicinal Chemistry Letters* 2016;**7**:363-7.	Basic science
Malek 2014	Malek G. Nuclear receptors as potential therapeutic targets for age-related macular degeneration. *Advances in*	Review of possible drug targets

	Experimental Medicine & Biology 2014;**801**:317-21.	
Maneros 2016	Marneros AG. VEGF-A and the NLRP3 Inflammasome in Age-Related Macular Degeneration. *Advances in Experimental Medicine & Biology* 2016;**854**:79-85.	Basic science
Manikandan 2016	Manikandan R, Thiagarajan R, Goutham G, Arumugam M, Beulaja M, Rastrelli L, *et al.* Zeaxanthin and ocular health, from bench to bedside. *Fitoterapia* 2016;**109**:58-66.	Another review zeaxanthin
Mariotti 2015	Mariotti C, Lazzarini R, Nicolai M, Saitta A, Orsini E, Orciani M, *et al.* Comparative study between amniotic-fluid mesenchymal stem cells and retinal pigmented epithelium (RPE) stem cells ability to differentiate towards RPE cells. *Cell & Tissue Research* 2015;**362**:21-31.	Basic science of stem cells
Meagher 2013	Meagher KA, Thurnham DI, Beatty S, Howard AN, Connolly E, Cummins W, *et al.* Serum response to supplemental macular carotenoids in subjects with and without age-related macular degeneration. *British Journal of Nutrition* 2013;**110**:289-300.	No outcomes of interest
Mohan 2016	Mohan S, Nare S, Natarajan S, Kumaramanickavel G. Regenerative medicine in retina: The future cure. *Current Tissue Engineering* 2016;**5**:45-51.	Not used
Montserrat-de la Paz 2016	Montserrat-de la Paz S, Naranjo MC, Bermudez B, Lopez S, Moreda W, Abia R, *et al.* Postprandial dietary fatty acids exert divergent inflammatory responses in retinal-pigmented epithelium cells. *Food & Function* 2016;**7**:1345-53.	Basic science
Morris 2007a	Morris B, Imrie F, Armbrecht AM, Dhillon B. Age-related macular degeneration and recent developments: new hope for old eyes? *Postgrad Med J* 2007;**83**:301-7.	Old review
Morris 2007b	Morris MS, Jacques PF, Chylack LT, Hankinson SE, Willett WC, Hubbard LD, *et al.* Intake of zinc and antioxidant micronutrients and early age-related	Not used

	maculopathy lesions. *Ophthalmic Epidemiology* 2007;**14**:288-98.	
Mucke 2010	Mucke HA, Mucke PM. Current drug patenting for retinal diseases: beyond VEGF inhibitors. *Idrugs* 2010;**13**:30-7.	Patents
Nagai 2014	Nagai N, Kubota S, Tsubota K, Ozawa Y. Resveratrol prevents the development of choroidal neovascularization by modulating AMP-activated protein kinase in macrophages and other cell types. *Journal of Nutritional Biochemistry* 2014;**25**:1218-25.	Basic science in mice
Nagineni 2014	Nagineni CN, Raju R, Nagineni KK, Kommineni VK, Cherukuri A, Kutty RK, *et al.* Resveratrol Suppresses Expression of VEGF by Human Retinal Pigment Epithelial Cells: Potential Nutraceutical for Age-related Macular Degeneration. *Aging & Disease* 2014;**5**:88-100.	Basic science resveratrol in cells
Newman 2016	Newman DK. Photodynamic therapy: current role in the treatment of chorioretinal conditions. *Eye* 2016;**30**:202-10.	Wet
Nguyen 2012	Nguyen QD, Schachar RA, Nduaka CI, Sperling M, Klamerus KJ, Chi-Burris K, *et al.* Evaluation of the siRNA PF-04523655 versus ranibizumab for the treatment of neovascular age-related macular degeneration (MONET Study). *Ophthalmology* 2012;**119**:1867-73	Wet
North 2014	North V, Gelman R, Tsang SH. Juvenile-onset macular degeneration and allied disorders. *Developments in Ophthalmology* 2014;**53**:44-52.	Superseded by more detailed reviews
Novac 2016	Novack GD. Eyes on new product development. *Journal of Ocular Pharmacology and Therapeutics* 2016;**32**:1-2.	Review
Novikova 2014	Novikova YP, Gancharova OS, Eichler OV, Philippov PP, Grigoryan EN. Preventive and therapeutic effects of SkQ1-containing Visomitin eye drops against light-induced retinal degeneration. *Biochemistry-Russia* 2014;**79**:1101-10..	Visomitin eye drops in albino rats

Nussenblatt 2010	Nussenblatt RB, Byrnes G, Sen HN, Yeh S, Faia L, Meyerle C, *et al.* A randomized pilot study of systemic immunosuppression in the treatment of age-related macular degeneration with choroidal neovascularization. *Retina* 2010;**30**:1579-87	wet
Ogawa 2014	Ogawa K, Kuse Y, Tsuruma K, Kobayashi S, Shimazawa M, Hara H. Protective effects of bilberry and lingonberry extracts against blue light-emitting diode light-induced retinal photoreceptor cell damage in vitro. *BMC Complementary & Alternative Medicine* 2014;**14**:120.	In vitro study
Ontario HTA	Health Quality Ontario. Optical Coherence Tomography for Age-Related Macular Degeneration and Diabetic Macular Edema: An Evidence-Based Analysis. *Ontario Health Technology Assessment Series* 2009;**9**:1-22.	OCT screening
Parodi 2012	Parodi MB, Cascavilla M, Papayannis A, Kontadakis DS, Bandello F, Iacono P. Intravitreal bevacizumab in advanced-stage neovascular age-related macular degeneration with visual acuity lower than 20/200. *Arch Ophthalmol* 2012;**130**:934-5.	wet
Patel 2008	Patel PJ, Bunce C, Tufail A. A randomised, double-masked phase III/IV study of the efficacy and safety of Avastin(R) (Bevacizumab) intravitreal injections compared to standard therapy in subjects with choroidal neovascularisation secondary to age-related macular degeneration: clinical trial design. *Trials* 2008;**9**:56.	wet
Patel 2012	Patel PJ, Chen FK, Da Cruz L, Rubin GS, Tufail A. Contrast sensitivity outcomes in the ABC Trial: a randomized trial of bevacizumab for neovascular age-related macular degeneration. *Invest Ophthalmol Vis Sci* 2011;**52**:3089-93	Contrast sensitivity
Patterson 2007	Patterson DM, Rustin GJS, Serradell N, Rosa E, Bolos J.	Basic science combretastatin

	Combretastatin A-4 phosphate: Vascular disrupting agent oncolytic treatment of age-related macular degeneration. *Drugs of the Future* 2007;**32**:1025-32.	
Pauleikhoff 2005	Pauleikhoff D. neovascular age-related macular degeneration: Natural History and Treatment Outcomes. *Retina* 2005;**25**:1065-84.	wet
Payne 2103	Payne AJ, Kaja S, Sabates NR, Koulen P. A case for neuroprotection in ophthalmology: developments in translational research. *Missouri Medicine* 2013;**110**:429-36.	Review of neuroprotection
Pennington 2016	Pennington BO, Clegg DO. Pluripotent Stem Cell-Based Therapies in Combination with Substrate for the Treatment of Age-Related Macular Degeneration. *Journal of Ocular Pharmacology & Therapeutics* 2016;**32**:261-71.	Review of stem cell basic science
Pikkel 2013	Pikkel J, Chassid O, Sharabi-Nov A, Beiran I. A retrospective evaluation of the effect of hydroxyquinine on RPE thickness. *Graefes Archive for Clinical & Experimental Ophthalmology* 2013;**251**:1687-90.	No relevant outcomes
Pinna 2016	Pinna A, Zaccheddu F, Boscia F, Carru C, Solinas G. Homocysteine and risk of age-related macular degeneration; a systematic review and meta-analysis. *Acta Ophthalmologica 2016: doi; 10.1111/aos.13343*	Mainly concerned with wet AMD
Puntel 2015	Puntel A, Maeda A, Golczak M, Gao SQ, Yu G, Palczewski K, *et al.* Prolonged prevention of retinal degeneration with retinylamine loaded nanoparticles. *Biomaterials* 2015;**44**:103-10.	Mice only
Ramos 2014	Ramos De Carvalho JE, Willig A, Chung R, Peiretti E, Mura M. Current surgical treatment of age-related macular degeneration. *Expert Review of Ophthalmology* 2014;**9**:235-45.	Not used
Rasmussen 2013	Rasmussen A, Bloch SB, Fuchs J, Hansen LH, Larsen M,	Wet

	Lacour M, *et al.* A 4-year longitudinal study of 555 patients treated with ranibizumab for neovascular age-related macular degeneration. *Ophthalmology* 2013;**120**:2630-6.	
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Rezai 2008	Rezai KA, Gasyna E, Seagle BL, Norris JR, Jr., Rezaei KA. AcrySof Natural filter decreases blue light-induced apoptosis in human retinal pigment epithelium. *Graefes Archive for Clinical & Experimental Ophthalmology* 2008;**246**:671-6.	Not used
Richer 2009	Richer S, Stiles W, Thomas C. Molecular medicine in ophthalmic care. *Optometry (St Louis, Mo)* 2009;**80**:695-701.	Resveratrol single case report
Richer 2013	Richer S, Stiles W, Ulanski L, Carroll D, Podella C. Observation of human retinal remodeling in octogenarians with a resveratrol based nutritional supplement. *Nutrients* 2013;**5**:1989-2005.	Resveratrol case report, 3 patients, wet AMD
Rohrer 2016	Rohrer B, Bandyopadhyay M, Beeson C. Reduced Metabolic Capacity in Aged Primary Retinal Pigment Epithelium (RPE) is Correlated with Increased Susceptibility to Oxidative Stress. *Advances in Experimental Medicine & Biology* 2016;**854**:793-8.	Basic science review
Saad 2016	Saad L, Washington I. Can Vitamin A be Improved to Prevent Blindness due to Age-Related Macular Degeneration, Stargardt Disease and Other Retinal Dystrophies? *Advances in Experimental Medicine &*	Not used

	Biology 2016;**854**:355-61.	
Sadda 2016	Sadda SR, Chakravarthy U, Birch DG, Staurenghi G, Henry EC, Brittain C. Clinical endpoints for the study of geographic atrophy secondary to age-related macular degeneration. *Retina* 2016;**36**:1806-22	Diagnostics
Sahel 2013	Sahel JA, Roska B. Gene therapy for blindness. *Annual Review of Neuroscience* 2013;**36**:467-88.	genes
Sarezky 2016	Sarezky D, Raquib AR, Dunaief JL, Kim BJ. Tolerability in the elderly population of high-dose alpha lipoic acid: a potential antioxidant therapy for the eye. *Clin Ophthalmol* 2016;**10**:1899-903.	Phase 1 study of alpha lipoic acid
Sarraf 2016	Sarraf D, London NJ, Khurana RN, Dugel PU, Gune S, Hill L, *et al.* Ranibizumab Treatment for Pigment Epithelial Detachment Secondary to Neovascular Age-Related Macular Degeneration: Post Hoc Analysis of the HARBOR Study. *Ophthalmology* 2016;**123**:2213-24	wet
Saskai 2012	Sasaki M, Shinoda H, Koto T, Uchida A, Tsubota K, Ozawa Y. Use of micronutrient supplement for preventing advanced age-related macular degeneration in Japan. *Archives of Ophthalmology* 2012;**130**:254-5.	Survey of supplement use in Japan
Schatz 2011	Schatz A, Rock T, Naycheva L, Willmann G, Wilhelm B, Peters T, *et al.* Transcorneal electrical stimulation for patients with retinitis pigmentosa: a prospective, randomized, sham-controlled exploratory study. *Invest Ophthalmol Vis Sci* 2011;**52**:4485-96	Retinitis pigmentosa
Schmidt-Erfurth 2011	Schmidt-Erfurth U, Eldem B, Guymer R, Korobelnik JF, Schlingemann RO, Axer-Siegel R, *et al.* Efficacy and safety of monthly versus quarterly ranibizumab treatment in neovascular age-related macular degeneration: the EXCITE study. *Ophthalmology* 2011;**118**:831-9.	Wet
Schmuker 2011	Schmucker C, Loke YK, Ehlken C, Agostini HT, Hansen	wet

	LL, Antes G, *et al.* Intravitreal bevacizumab (Avastin) versus ranibizumab (Lucentis) for the treatment of age-related macular degeneration: a safety review. *Br J Ophthalmol* 2011;**95**:308-17	
Schouten 2009	Schouten JS, La Heij EC, Webers CA, Lundqvist IJ, Hendrikse F. A systematic review on the effect of bevacizumab in exudative age-related macular degeneration. *Graefes Arch Clin Exp Ophthalmol* 2009;**247**:1-11.	wet
Schwartz 2016	Schwartz SG, Hampton BM, Kovach JL, Brantley MA, Jr. Genetics and age-related macular degeneration: a practical review for the clinician. *Clin Ophthalmol* 2016;**10**:1229-35.	Review of genetic testing
Schoenberger 2013	Schoenberger SD, Kim SJ. Nonsteroidal anti-inflammatory drugs for retinal disease. *International Journal of Inflammation* 2013;**2013**:281981.	Reviews of NSAIDS in wet AMD
Shen 2016	Shen J, He J, Wang F. Association of lipids with age-related macular degeneration. *Discov Med* 2016;**22**:129-45.	Not used
Silva 2013	Silva R, Axer-Siegel R, Eldem B, Guymer R, Kirchhof B, Papp A, *et al.* The SECURE study: long-term safety of ranibizumab 0.5 mg in neovascular age-related macular degeneration. *Ophthalmology* 2013;**120**:130-9	wet
Silvan 2016	Silvan JM, Reguero M, de Pascual-Teresa S. A protective effect of anthocyanins and xanthophylls on UVB-induced damage in retinal pigment epithelial cells. *Food & Function* 2016;**7**:1067-76.	Review of oxidative damage in cells
Singer 2012	Singer MA, Awh CC, Sadda S, Freeman WR, Antoszyk AN, Wong P, *et al.* HORIZON: an open-label extension trial of ranibizumab for choroidal neovascularization secondary to age-related macular degeneration.	wet

	Ophthalmology 2012;**119**:1175-83.	
Sivan 2016	Sivan PP, Syed S, Mok PL, Higuchi A, Murugan K, Alarfaj AA, *et al.* Stem Cell Therapy for Treatment of Ocular Disorders. *Stem Cells International* 2016;**2016**	Review stem cells in eye diseases
Sivaprasad 2013	Sivaprasad S, Hykin P. What is new in the management of wet age-related macular degeneration? *Br Med Bull* 2013;**105**:201-11.	Not used
Smailhodzic 2014	Smailhodzic D, van Asten F, Blom AM, Mohlin FC, den Hollander AI, van de Ven JP, *et al.* Zinc supplementation inhibits complement activation in age-related macular degeneration. *PLoS ONE [Electronic Resource]* 2014;**9**:e112682.	Zinc No relevant outcomes
Solinis 2015	Solinis MA, del Pozo-Rodriguez A, Apaolaza PS, Rodriguez-Gascon A. Treatment of ocular disorders by gene therapy. *European Journal of Pharmaceutics & Biopharmaceutics* 2015;**95**:331-42	genes
Soudaver 1998	Soudavar F, Widder RA, Brunner R, Walter P, Bartz-Schmitz K, Borberg H. Changes of retinal haemodynamics after elimination of high molecular weight proteins and lipids in patients with age-related macular degeneration [abstract] The Association for Research in Vision and Ophthalmology (ARVO) annual meeting. Fort Lauderdale, Florida, USA. May 10-15, 1998. Abstracts. *Invest Ophthalmol Vis Sci* 1998;**39**:S386.	Abstract only with sparse detail. 13 patients but type of AMD not specified
Sreekumar 2013	Sreekumar PG, Chothe P, Sharma KK, Baid R, Kompella U, Spee C, *et al.* Antiapoptotic properties of alpha-crystallin-derived peptide chaperones and characterization of their uptake transporters in human RPE cells. *Invest Ophthalmol Vis Sci* 2013;**54**:2787-98.	Basic science of chaperones
Sreekumar 2016	Sreekumar PG, Ishikawa K, Spee C, Mehta HH, Wan J, Yen K, *et al.* The Mitochondrial-Derived Peptide Humanin	Basic science

	Protects RPE Cells From Oxidative Stress, Senescence, and Mitochondrial Dysfunction. *Investigative Ophthalmology & Visual Science* 2016;**57**:1238-53.	
Strauss 2016	Strauss RW, Ho A, Munoz B, Cideciyan AV, Sahel JA, Sunness JS, *et al.* The Natural History of the Progression of Atrophy Secondary to Stargardt Disease (ProgStar) Studies: Design and Baseline Characteristics: ProgStar Report No. 1. *Ophthalmology* 2016;**123**:817-28.	Good but baseline data only
Subramian 2009	Subramanian ML, Ness S, Abedi G, Ahmed E, Daly M, Feinberg E, *et al.* Bevacizumab vs ranibizumab for age-related macular degeneration: early results of a prospective double-masked, randomized clinical trial. *Am J Ophthalmol* 2009;**148**:875-82.e1	wet
Suner 2009	Suner IJ, Kokame GT, Yu E, Ward J, Dolan C, Bressler NM. Responsiveness of NEI VFQ-25 to changes in visual acuity in neovascular AMD: validation studies from two phase 3 clinical trials. *Invest Ophthalmol Vis Sci* 2009;**50**:3629-35	wet
Sur 2014	Sur A, Kesaraju S, Prentice H, Ayyanathan K, Baronas-Lowell D, Zhu D, *et al.* Pharmacological protection of retinal pigmented epithelial cells by sulindac involves PPAR-alpha. *Proceedings of the National Academy of Sciences of the United States of America* 2014;**111**:16754-9.	Sulindac and RPE cells
Takeda 2007	Takeda AL, Colquitt J, Clegg AJ, Jones J. Pegaptanib and ranibizumab for neovascular age-related macular degeneration: a systematic review. *Br J Ophthalmol* 2007;**91**:1177-82	SHTAC article
TAP Study Group	Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) Study Group. Verteporfin therapy of subfoveal choroidal neovascularization in	wet

	patients with age-related macular degeneration: additional information regarding baseline lesion composition's impact on vision outcomes-TAP report No. 3.	
TAP Study Group	Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) Study Group. Verteporfin therapy for subfoveal choroidal neovascularization in age-related macular degeneration: three-year results of an open-label extension of 2 randomized clinical trials--TAP Report no. 5. *Arch Ophthalmol* 2002;**120**:1307-14.	Wet
Tochitsky 2015	Tochitsky I, Kramer RH. Optopharmacological tools for restoring visual function in degenerative retinal diseases. *Current Opinion in Neurobiology* 2015;**34**:74-8.	Basic science, optopharmacological tools
Trounson 2016	Trounson A, DeWitt ND. Pluripotent stem cells progressing to the clinic. *Nature Reviews Molecular Cell Biology* 2016;**17**:194-200	Not used
Tufail 2010	Tufail A, Patel PJ, Egan C, Hykin P, da Cruz L, Gregor Z, *et al.* Bevacizumab for neovascular age related macular degeneration (ABC Trial): multicentre randomised double masked study. *BMJ* 2010;**340**:c2459	Wet, bevacizumab
Van der Made 2014	van der Made SM, Kelly ER, Berendschot TT, Kijlstra A, Lutjohann D, Plat J. Consuming a buttermilk drink containing lutein-enriched egg yolk daily for 1 year increased plasma lutein but did not affect serum lipid or lipoprotein concentrations in adults with early signs of age-related macular degeneration. *Journal of Nutrition* 2014;**144**:1370-7.	No useful outcomes
Vasireddy 2010	Vasireddy V, Wong P, Ayyagari R. Genetics and molecular pathology of Stargardt-like macular degeneration. *Progress in Retinal & Eye Research* 2010;**29**:191-207.	genes
Veerappan 2016	Veerappan M, El-Hage-Sleiman AM, Tai V, Chiu SJ,	Diagnostic

	Winter KP, Stinnett SS, *et al.* Optical Coherence Tomography Reflective Drusen Substructures Predict Progression to Geographic Atrophy in Age-related Macular Degeneration. *Ophthalmology* 2016;**123**:2554-70.	
Vertoporforin Study Group 2001	Verteporfin In Photodynamic Therapy Study Group. Verteporfin therapy of subfoveal choroidal neovascularization in age-related macular degeneration: two-year results of a randomized clinical trial including lesions with occult with no classic choroidal neovascularization--verteporfin in photodynamic therapy report 2. *Am J Ophthalmol* 2001;**131**:541-60.	wet
Viringipurampeer 2013	Viringipurampeer IA, Bashar AE, Gregory-Evans CY, Moritz OL, Gregory-Evans K. Targeting inflammation in emerging therapies for genetic retinal disease. *International Journal of Inflammation* 2013;**2013**:581751.	Review of role of inflammation
Vujosevic 2011	Vujosevic S, Smolek MK, Lebow KA, Notaroberto N, Pallikaris A, Casciano M. Detection of macular function changes in early (AREDS 2) and intermediate (AREDS 3) age-related macular degeneration. *Ophthalmologica* 2011;**225**:155-60	Diagnostics
Waheed 2016	Waheed NK, Moult EM, Fujimoto JG, Rosenfeld PJ. Optical Coherence Tomography Angiography of Dry Age-Related Macular Degeneration. *Dev Ophthalmol* 2016;**56**:91-100.	Diagnostics of dry AMD
Wang 2016	Wang Q, Stern JH, Temple S. Regenerative Medicine: Solution in Sight. *Advances in Experimental Medicine & Biology* 2016;**854**:543-8.	Not used
Weber 2014	Weber BH, Charbel Issa P, Pauly D, Herrmann P, Grassmann F, Holz FG. The role of the complement system in age-related macular degeneration. *Deutsches Arzteblatt International* 2014;**111**:133-8.	Review of complement system in AMD

Wei 2016	Wei CX, Sun A, Yu Y, Liu Q, Tan YQ, Tachibana I, *et al.* Challenges in the Development of Therapy for Dry Age-Related Macular Degeneration. *Advances in Experimental Medicine & Biology* 2016;**854**:103-9	Not considered a systematic review
Weiss 2010	Weiss JN. Hyperbaric oxygen therapy and age-related macular degeneration. *Undersea & Hyperbaric Medicine* 2010;**37**:101-5.	Case series with no data on which if any had patients had dry AMD
Westenskow 2014	Westenskow PD, Kurihara T, Friedlander M. Utilizing stem cell-derived RPE cells as a therapeutic intervention for age-related macular degeneration. *Advances in Experimental Medicine & Biology* 2014;**801**:323-9.	Review stem cells
Wilson 2004	Wilson HL, Schwartz DM, Bhatt HR, McCulloch CE, Duncan JL. Statin and aspirin therapy are associated with decreased rates of choroidal neovascularization among patients with age-related macular degeneration. *Am J Ophthalmol* 2004;**137**:615-24.	Aetiology, aspirin
Woo 2010	Woo SJ, Kim JH, Yu HG. Ursodeoxycholic acid and tauroursodeoxycholic acid suppress choroidal neovascularization in a laser-treated rat model. *Journal of Ocular Pharmacology & Therapeutics* 2010;**26**:223-9.	Wet, rats
Yang 2016	Yang J, Cai B, Glencer P, Li Z, Zhang X, Li X. Induced pluripotent stem cells and outer retinal disease. *Stem Cells International* 2016;**2016**	Not used
Xu 2016	Xu XR, Yu HT, Yang Y, Hang L, Yang XW, Ding SH. Quercetin phospholipid complex significantly protects against oxidative injury in ARPE-19 cells associated with activation of Nrf2 pathway. *European Journal of Pharmacology* 2016;**770**:1-8.	Basic science quercetin
Xuan 1999	Xuan B, Zhou YH, Li N, Min ZD, Chiou GC. Effects of crocin analogs on ocular blood flow and retinal function. *J Ocul Pharmacol Ther* 1999;**15**:143-52.	Old review crocin analogues and blood flow

Yang 2016	Yang PM, Wu ZZ, Zhang YQ, Wung BS. Lycopene inhibits ICAM-1 expression and NF-kappaB activation by Nrf2-regulated cell redox state in human retinal pigment epithelial cells. *Life Sciences* 2016;**155**:94-101	Basic science lycopene
Yildirim 2011	Yildirim Z, Ucgun NI, Yildirim F. The role of oxidative stress and antioxidants in the pathogenesis of age-related macular degeneration. *Clinics (Sao Paulo)* 2011;**66**:743-6.	Review of pathology
Zehetner 2013	Zehetner C, Kirchmair R, Huber S, Kralinger MT, Kieselbach GF. Plasma levels of vascular endothelial growth factor before and after intravitreal injection of bevacizumab, ranibizumab and pegaptanib in patients with age-related macular degeneration, and in patients with diabetic macular oedema. *Br J Ophthalmol* 2013;**97**:454-9.	wet
Zeng 2012	Zeng S, Hernandez J, Mullins RF. Effects of antioxidant components of AREDS vitamins and zinc ions on endothelial cell activation: implications for macular degeneration. *Invest Ophthalmol Vis Sci* 2012;**53**:1041-7	Basic science
Zhou 2016	Zhou X, Wei Y, Qiu S, Xu Y, Zhang T, Zhang S. Propofol Decreases Endoplasmic Reticulum Stress-Mediated Apoptosis in Retinal Pigment Epithelial Cells. *PLoS ONE* 2016;**11**:e0157590.	Basic science propofol
Zhu 2009	Zhu D, Deng X, Xu J, Hinton DR. What determines the switch between atrophic and neovascular forms of age related macular degeneration? - the role of BMP4 induced senescence. *Aging* 2009;**1**:740-5.	Not used
Zhu 2012	Zhu XF, Zou HD, Yu YF, Sun Q, Zhao NQ. Comparison of blue light-filtering IOLs and UV light-filtering IOLs for cataract surgery: a meta-analysis. *PLoS One* 2012;**7**:e33013.	Blue filters but not about AMD