Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Age-related Macular Degeneration: objectives, participants, interventions, and conclusions of the reliable systematic reviews, sorted by reverse chronological order of publication within intervention type

Study ID	PMID	Objective(s)	Participants	Intervention Comparisons	Number of Studies; Participants (or eyes)	Conclusion(s)
Anti-VEGF interventions						
Nguyen 2018	29843663	"To evaluate the relative efficacy and safety of anti-vascular endothelial growth factor (anti-VEGF) agents for the treatment of neovascular age-related macular degeneration."	Neovascular (wet or exudative) AMD	Pegaptanib; ranibizumab; bevacizumab; aflibercept; control	15; 8,479	"Bevacizumab and ranibizumab had equivalent efficacy for BCVA, while ranibizumab had greater reduction in central macular thickness and less rate of serious systemic adverse events. Aflibercept and ranibizumab had comparable efficacy for BCVA and central macular thickness."
Okada 2018	29885297	"To assess outcomes of the treat-and-extend (T&E) injection regimen for neovascular age-related macular degeneration (AMD) as compared to either a monthly or a pro re nata (PRN) treatment strategy."	Neovascular (wet or exudative) AMD	Ranibizumab treat & extend regimen; ranibizumab monthly; ranibizumab PRN	4; 940	"Despite the growing preference for the T&E regimen, there is limited head-to-head evidence comparing dosing strategies. The evidence available, however, suggests that at 12 months, T&E is comparable to monthly and superior to PRN dosing for both efficacy and safety outcomes when using ranibizumab."
Su 2018	29753123	"To evaluate the efficacy and safety between photodynamic therapy (PDT) combined with intravitreal ranibizumab (IVR) and ranibizumab monotherapy in treating wet age-related macular degeneration (AMD)."	Neovascular (wet or exudative) AMD	Ranibizumab; photodynamic therapy + ranibizumab	8; 922	"Combination therapy decreased the number of injections of ranibizumab, although its BCVA improvement was inferior to that of monotherapy over 12 months of follow-up."

Zhang 2018	29902977	"To assess the efficacy and safety of conbercept in the treatment of wet AMD."	Neovascular (wet or exudative) AMD	Conbercept; conservative treatment; ranibizumab; transpupillary thermotherapy; triamcinolone	18; 1,285	"Current evidence shows that conbercept is a promising option for the treatment of wet AMD. Nevertheless, further studies are required to compare the efficacy, long-term safety and cost-effectiveness between conbercept and other anti-VEGF agents in different populations."
Xie 2017	28596285	"To determine whether vitreomacular adhesion (VMA) or vitreomacular traction (VMT) has an influence on the outcomes of antivascular endothelium growth factor (anti-VEGF) treatment neovascular age-related macular degeneration (nAMD)."	Neovascular (wet or exudative) AMD	Anti-VEGF agent, non-specific	9; 2,212	"In using anti-VEGF drugs to treat neovascular AMD, clinicians should take into account the fact that concurrent vitreomacular adhesion (VMA) or vitreomacular traction (VMT) might antagonise the efficacy of anti-VEGF drugs during the early stage of treatment."
Chin-Yee 2016	26516125	"To evaluate the relative efficacy of as needed versus treat and extend regimen for the treatment of neovascular age-related macular degeneration (AMD)."	Neovascular (wet or exudative) AMD	Anti-VEGF agents, treat & extend regimen; anti-VEGF agents, as needed regimen	70; 11,789	"Though our study suggests superiority of the treat and extend regimen to PRN treatment in a 12-month period, this review demonstrates the need for randomised clinical trials to confirm our findings and to evaluate long-term efficacy outcomes with these regimens compared with monthly therapy."
Sarwar 2016	26857947	"To assess and compare the effectiveness and safety of intravitreal injections of aflibercept versus ranibizumab, bevacizumab, or sham for treatment of patients with neovascular AMD."	Neovascular (wet or exudative) AMD	Aflibercept; ranibizumab	2; 2,412	"Current available information on adverse effects of each medication suggests that the safety profile of aflibercept is comparable with that of ranibizumab; however, the number of participants who experienced adverse events was small, leading to imprecise estimates of absolute and relative effect sizes."

Chen 2015	25105318	"To evaluate the relative efficacy and safety of bevacizumab versus ranibizumab for the treatment of the neovascular form of age-related macular degeneration."	Neovascular (wet or exudative) AMD	Bevacizumab; ranibizumab	6; 2,612	"Bevacizumab and ranibizumab had equivalent efficacy for best-corrected visual acuity in the treatment of neovascular age-related macular degeneration. Ranibizumab tended to have a better anatomical outcome."
Schmid 2015	25271911	"To quantify the gain in visual acuity and serious side effects of ranibizumab, bevacizumab and aflibercept in age-related macular degeneration (AMD)."	Neovascular (wet or exudative) AMD	Ranibizumab; bevacizumab; aflibercept	11; 8,341	"The study revealed only a modest superiority of aflibercept 2 mg and ranibizumab 0.5 mg over other formulations and dosages."
Schmucker 2015	26368921	"To investigate whether treatment as required 'pro re nata' (PRN) versus regular monthly treatment regimens lead to differences in outcomes in neovascular age-related macular degeneration (nAMD)."	Neovascular (wet or exudative) AMD	Monthly anti-VEGF treatment; PRN anti-VEGF treatment	3; 1,844	"PRN treatment resulted in minor but statistically significant decrease in mean BCVA which may not be clinically meaningful. There is a small increase in risk of systemic adverse events for PRN treated patients. Overall, the results indicate that an individualized treatment approach with anti-VEGF using visual acuity and OCT-guided re-treatment criteria may be appropriate for most patients with neovascular AMD."
Kodjikian 2014	25142373	"To review systematically the effect of bevacizumab compared to ranibizumab in patients with AMD at 1 year."	Neovascular (wet or exudative) AMD	Bevacizumab; ranibizumab	5; 2,686	"The pooled evidence confirmed that, compared with ranibizumab, bevacizumab was associated with equivalent effects on visual acuity at 1 year and with a higher risk of systemic serious adverse events."

Moja 2014	25220133	"To assess the systemic safety of intravitreal bevacizumab (brand name Avastin®; Genentech/Roche) compared with intravitreal ranibizumab (brand name Lucentis®; Novartis/ Genentech) in people with neovascular AMD."	Neovascular (wet or exudative) AMD	Bevacizumab; ranibizumab	9; 3,665	"This systematic review of non-industry sponsored RCTs could not determine a difference between intravitreal bevacizumab and ranibizumab for deaths, all serious systemic adverse events (SSAEs), or specific subsets of SSAEs in the first two years of treatment, with the exception of gastrointestinal disorders. The current evidence is imprecise and might vary across levels of patient risks, but overall suggests that if a difference exists, it is likely to be small. Health policies for the utilization of ranibizumab instead of bevacizumab as a routine intervention for neovascular AMD for reasons of systemic safety are not sustained by evidence."
Si 2014	24967206	"To compare the efficacy and safety of combination of ranibizumab with photodynamic therapy (PDT) ranibizumab monotherapy in the treatment of age-related macular degeneration (AMD)."	Neovascular (wet or exudative) AMD	Photodynamic therapy + ranibizumab; ranibizumab	7; 742	"For the maintenance of vision, the comparison of the combination of ranibizumab with PDT ranibizumab monotherapy shows no apparent difference. Compared with the combination of ranibizumab and PDT, patients treated with ranibizumab monotherapy may gain more visual acuity (VA) improvement."

Solomon 2014 (Results also published in part or in full in: 26477843)	25170575	"To investigate: (1) the ocular and systemic effects of, and quality of life associated with, intravitreally injected anti-VEGF agents (pegaptanib, ranibizumab, and bevacizumab) for the treatment of neovascular AMD compared with no anti-VEGF treatment; and (2) the relative effects of one anti-VEGF agent compared with another when administered in comparable dosages and regimens."	Neovascular (wet or exudative) AMD	Pegaptanib; ranibizumab; bevacizumab; sham treatment or injection	12; 5,496	"The results of this review indicate the effectiveness of anti-VEGF agents (pegaptanib, ranibizumab, and bevacizumab) in terms of maintaining visual acuity; ranibizumab and bevacizumab were also shown to improve visual acuity."
Ueta 2014	25023760	"[To conduct] a meta-analysis of randomized trials of ranibizumab for age-related macular degeneration (AMD) to elucidate systemic vascular risk."	Neovascular (wet or exudative) AMD	Ranibizumab; different dosages of ranibizumab against each other; placebo	11; 6,596	"In ranibizumab treatment for patients with AMD, a possible relationship of more intensive treatment to more systemic vascular adverse events was identified, but no relationship with mortality was identified."
Schmucker 2012	22880086	"To evaluate whether off-label bevacizumab is as safe as licensed ranibizumab, and whether bevacizumab can be justifiably offered to patients as a treatment for age-related macular degeneration with robust evidence of no differential risk"	Neovascular (wet or exudative) AMD	Ranibizumab; bevacizumab; any control	11; 5,631	"Evidence from head-to-head trials raises concern about an increased risk of ocular and multiple systemic adverse effects with bevacizumab."
Schmucker 2011	20971791	"To conduct a systematic review in order to compare adverse effects (AE) and the reporting of harm in randomized controlled trials (RCTs) and non-RCTs evaluating intravitreal ranibizumab and bevacizumab in age-related macular degeneration."	Neovascular (wet or exudative) AMD	Bevacizumab; ranibizumab; no arm evaluated; any agent	25; NR	"The bevacizumab studies show too many methodological limitations to rule out any major safety concerns. Higher evidence from ranibizumab trials suggests signals for an increased ocular and systemic vascular and hemorrhagic risk which warrants further investigation."

Schmucker 2010	20393293	"To evaluate whether the existing evidence justifies the intravitreal use of bevacizumab in comparison to ranibizumab in age-related macular degeneration."	Neovascular (wet or exudative) AMD	Photodynamic therapy; ranibizumab; bevacizumab; photodynamic therapy + triamcinolone; no arm evaluated; sham treatment or injection; standard of care/Usual care	33; 2,519	"Given the lack of controlled data, the widespread off-label use of bevacizumab is not justified in clinical practice. On the other hand, a major challenge in the management of patients who require repeated anti-vascular endothelial growth factor injections is the high cost of ranibizumab."
Schouten 2009	18843500	"To provide evidence for the effect of bevacizumab on visual acuity (VA) and central retinal thickness (CRT) in exudative age-related macular degeneration"	Neovascular (wet or exudative) AMD	Photodynamic therapy; bevacizumab; photodynamic therapy + triamcinolone; photodynamic therapy + reduced triamcinolone; photodynamic therapy + bevacizumab	26; 1,435	"Visual acuity improves and central retinal thickness decreases in patients with exudative AMD after bevacizumab. There is no reasonable doubt that this is caused by bevacizumab."

Colquitt 2008	18462575	"To assess the clinical effectiveness and cost-effectiveness of ranibizumab and pegaptanib for subfoveal choroidal neovascularisation (CNV) associated with wet age-related macular degeneration (AMD)."	Neovascular (wet or exudative) AMD	Pegaptanib; ranibizumab; PDT + ranibizumab; ranibizumab + sham PDT; PDT + sham injection; sham treatment or injection	5; NR	"Patients with AMD of any lesion type benefit from treatment with pegaptanib or ranibizumab on measures of visual acuity when compared with sham injection and/or PDT. Patients who continued treatment with either drug appeared to maintain benefits after 2 years of follow-up. When comparing pegaptanib and ranibizumab, the evidence was less clear due to the lack of direct comparison through head-to-head trials and the lack of opportunity for indirect statistical comparison due to heterogeneity. The cost-effectiveness analysis showed that the two drugs offered additional benefit over the comparators of usual care and PDT but at increased cost."
Takeda 2007	17475698	"To assess the clinical effectiveness of pegaptanib sodium and ranibizumab for neovascular age-related macular degeneration (AMD)."	Neovascular (wet or exudative) AMD	Pegaptanib; ranibizumab; PDT + ranibizumab; PDT + sham injection; ranibizumab + sham PDT; sham treatment or sham injection	5; 1,524	"Pegaptanib and ranibizumab appear to slow or stop the progression of neovascular AMD. Uncertainty remains over the relative benefits of pegaptanib compared with ranibizumab and other unlicensed drugs (e.g., Avastin), due to the nature of the evidence."

Screening						
Chou 2016	26934261	"To update a 2009 systematic review on screening for impaired visual acuity among older adults for the US Preventive Services Task Force (USPSTF)."	Asymptomatic adults 65 years or older without known impaired visual acuity who have not sought care for evaluation of vision problems	Vision screening; delayed screening; no screening; usual care	3; NR	"Direct evidence found no significant difference between vision screening in older adults in primary care settings vs no screening for improving visual acuity or other clinical outcomes."

Vitamins, nutritional supplements, or behavioral interventions						
Evans 2017b (Results also published in part or in full in: 18425071)	28756618	"To assess the effects of antioxidant vitamin or mineral supplementation on the progression of AMD in people with AMD."	AMD (non specific)	Multivitamin supplement; zinc; vitamin E; any multivitamin or single component antioxidant supplement; lutein; zeaxanthin; placebo	19; 11,162	"People with AMD may experience delay in progression of the disease with antioxidant vitamin and mineral supplementation. This finding is drawn from one large trial conducted in a relatively well-nourished American population. The generalizability of these findings to other populations is not known. Although generally regarded as safe, vitamin supplements may have harmful effects."
Evans 2017a (Results also published in part or in full in: 18425071 & 2269317)	28756617	"To determine whether or not taking antioxidant vitamin or mineral supplements, or both, prevent the development of AMD."	AMD (non specific)	Vitamin E; beta-carotene; vitamin C; multivitamin; placebo	5; 77,493	"Taking vitamin E or beta-carotene supplements will not prevent or delay the onset of AMD. The same probably applies to vitamin C and the multivitamin (Centrum Silver) investigated in the one trial reported to date. There is no evidence with respect to other antioxidant supplements, such as lutein and zeaxanthin. Although generally regarded as safe, vitamin supplements may have harmful effects, and clear evidence of benefit is needed before they can be recommended."
Gaffney 2014	24735182	"To establish if eccentric viewing and steady eye strategy training improves outcomes in people with central vision loss in comparison to (1) performance before training or (2) another type of intervention/control group, in studies of any design."	Non-neovascular (non-exudative) AMD	Eccentric viewing training; steady eye strategy training	34; 1,046	"There is no conclusive evidence to show that a particular model of eccentric viewing training is superior to another, little clear evidence of a relationship between participant characteristics and training outcomes and no data regarding the cost effectiveness of training."

Evans 2013	23440785	"To determine the effect of Ginkgo biloba extract on the progression of AMD"	AMD (non specific)	Ginkgo biloba; placebo	2; 119	"The question as to whether people with AMD should take ginkgo biloba extract to prevent progression of the disease has not been answered by research to date. Two small trials have suggested possible benefit of Gingko biloba on vision and further trials are warranted."
Vishwanathan 2013	23652490	"To examine the evidence on zinc intake from foods and supplements in the primary prevention and treatment of AMD."	AMD (non specific)	Zinc; placebo	10; 90,819	"Current evidence on zinc intake for the prevention of AMD is inconclusive. Based on the strength of Age-Related Eye Disease Study, we can conclude that zinc treatment may be effective in preventing progression to advanced AMD. Zinc supplementation alone may not be sufficient to produce clinically meaningful changes in visual acuity."
Lawrenson 2012	23152282	"To review the evidence that increasing the levels of omega 3 long chain polyunsaturated fatty acids in the diet (either by eating more foods rich in omega 3 or by taking nutritional supplements) prevents AMD or slows the progression of AMD."	AMD (non specific)	Increased dietary intake of omega 3 fatty acids; placebo; no treatment/observation/no intervention	0; 0	"Until data from RCTs become available for analysis, there is currently no evidence to support increasing levels of omega 3 long chain polyunsaturated fatty acids in the diet for the explicit purpose of preventing or slowing the progression of AMD."
Chong 2008	18541848	"To systematically review the evidence on dietary ω-3 fatty acid and fish intake in the primary prevention of age-related macular degeneration (AMD)."	AMD (non specific)	ω-3 fatty acids and/or fish intake	9; 88,974	"Although this meta-analysis suggests that consumption of fish and foods rich in ω-3 fatty acids may be associated with a lower risk of AMD, there is insufficient evidence from the current literature, with few prospective studies and no randomized clinical trials, to support their routine consumption for AMD prevention."

Lee 2008	19032617	"To review the effectiveness of education programs to improve emotional status, daily living and self-efficacy in adults older than 60 years with age-related macular degeneration (AMD)."	AMD (non specific)	Health education program; control; no treatment/observation/no intervention	NR; 532	"Self-management programs appear effective for older adults with AMD. Small sample size, use of non- traditional statistics and methodological quality meant only a narrative analysis was possible."
Chong 2007	17923720	"To evaluate the effectiveness of dietary antioxidants in the primary prevention of age related macular degeneration (AMD)."	AMD (non specific)	Dietary supplements; zinc; vitamin E; beta-carotene; vitamin E + beta-carotene; alpha-carotene; placebo; no treatment/observation/no intervention	12; 149,203	"There is insufficient evidence to support the role of dietary antioxidants, including the use of dietary antioxidant supplements, for the primary prevention of early AMD."
Huang 2006	16880453	"To synthesize studies on the efficacy and safety of multivitamin/mineral supplement use in primary prevention of cancer and chronic disease in the general population."	AMD (non specific)	Vitamin and/or mineral supplements; placebo	15; 66,806	"Evidence is insufficient to prove the presence or absence of benefits from use of multivitamin and mineral supplements to prevent cancer and chronic disease."

Radiotherapy or laser therapy						
Virgili 2015	26493180	"To examine the effectiveness and adverse effects of laser photocoagulation of drusen in AMD."	AMD (non specific)	Laser photocoagulation; control	11; 2159 (3580 eyes)	"The trials included in this review confirm the clinical observation that laser photocoagulation of drusen leads to their disappearance. However, there is no evidence that this subsequently results in a reduction in the risk of developing choroidal neovascularization, geographic atrophy or visual acuity loss."
Geltzer 2013	23440797	"To examine effects of steroids with antiangiogenic properties in the treatment of neovascular AMD."	Neovascular (wet or exudative) AMD	Anecortave acetate; triamcinolone; photodynamic therapy; placebo	3; 809	"Based on the included trials, we found no evidence that antiangiogenic steroids prevent visual loss in patients with neovascular AMD. With the emergence of anti-vascular endothelial growth factor modalities, based on evidence summarized in this review, it is unclear what role steroids have in treating patients with neovascular AMD."
Evans 2010	20464726	"To examine the effects of radiotherapy on neovascular AMD."	Neovascular (wet or exudative) AMD	Radiotherapy; control	14; 1,242	"This review currently does not provide convincing evidence that radiotherapy is an effective treatment for neovascular AMD."
Hodge 2010	20628420	"To examine the economic implications of the Canadian health system of pharmacologic treatment of neovascular age-related macular degeneration (AMD)."	Neovascular (wet or exudative) AMD	Photodynamic therapy with verteporfin; ranibizumab; bevacizumab; pegaptanib	12; NR	"Although ranibizumab is effective for wet AMD, its cost is unacceptably high based on cost-utility theory."

Bekkering 2009	19370423	"To systematically review the effects and side effects of proton therapy for any indication of the eye."	AMD (non specific)	Proton radiotherapy; lower-dose proton radiotherapy; higher-dose proton radiotherapy; sham treatment or injection; no arm evaluated	37; NR	"There is limited evidence on the effectiveness and safety of proton radiation due to the lack of well-designed and well-reported studies. There is a need to lift evidence on proton therapy to a higher level by performing dose-finding randomized controlled trials (RCTs), comparative studies of proton radiation versus standard given alternatives and prospective case studies enrolling only patients treated with up-to-date techniques, allowing extrapolation of results to similar patient groups."
Oliva 2009	*Not available*	"To analyse the available scientific evidence regarding the effectiveness and safety of photodynamic therapy, pegaptanib and ranibizumab in the treatment of neovascular type AMD."	Neovascular (wet or exudative) AMD	Photodynamic therapy with verteporfin; ranibizumab; bevacizumab; pegaptanib	6; 3,090	"To prevent visual loss in patients with neovascular AMD, ranibizumab is effective and safe compared to placebo up to 2 years of treatment (Degree A of recommendation) and compared to photodynamic therapy up to one year (Degree B). Also, pegaptanib may be effective and safe compared to placebo during one year of treatment (Degree B). Photodynamic therapy is effective and safe in patients with predominantly classic neovascular AMD compared to placebo up to 2 years (Degree A). Finally, additional studies are required to assess the impact of the treatment by means of health-related quality of life tools and in terms of the treatments efficiency."
Eandi 2008	18843739	"[To assess] the effectiveness of macular translocation for preserving or improving vision in patients with neovascular age-related macular degeneration (AMD)."	Neovascular (wet or exudative) AMD	Macular translocation; photodynamic therapy	1; 50	"There is insufficient evidence from randomized controlled trials on the effectiveness of macular translocation, which is also not free of important risks. Furthermore, this technique is difficult to perform and a long surgical training is required."

Virgili 2007	17636773	"To examine the effects of laser photocoagulation for neovascular AMD."	Neovascular (wet or exudative) AMD	Laser photocoagulation; submacular surgery; no treatment/observation/ no intervention	15; 2,064	"In the medium to long term laser photocoagulation of choroidal neovascularization slows the progression of visual loss in people with neovascular AMD. However, it is associated with an increased risk of visual loss immediately after treatment and this period may be longer in people with subfoveal AMD. With the advent of modern pharmacological therapies, and concern for the impact of iatrogenic scotoma in subfoveal choroidal neovascularization, laser photocoagulation of subfoveal choroidal neovascularization is not recommended. No studies have compared photocoagulation with modern pharmacological agents for AMD for non-subfoveal choroidal neovascularization."
Wormald 2005	16235294	"To examine the effects of photodynamic therapy in the treatment of neovascular AMD."	Neovascular (wet or exudative) AMD	Photodynamic therapy with verteporfin; photodynamic therapy; photodynamic therapy + sham injection	6; 1,692	"Photodynamic therapy in people with choroidal neovascularisation due to AMD is effective in preventing clinically significant visual loss with a relative risk reduction of approximately 20%. Modified treatment regimens have not convincingly shown increased effectiveness. There was no evidence on quality of life and little on cost."
Meads 2003 (Results also published in part or in full in: 14736777)	12709292	"To establish the clinical and cost-effectiveness of photodynamic therapy for the neovascular form of wet AMD relative to current practice and in relation to current licensed indications."	Neovascular (wet or exudative) AMD	Photodynamic therapy with verteporfin; placebo	2; 948	"There is no indication of the relationship between benefits and costs where wet AMD affects the worse-seeing eye first."
Husereau 2002	*Notavailable*	"To assess the potential harms, benefits and economic implications of verteporfin photodynamic therapy (PDT) in patients with neovascular age-related macular degeneration (AMD)."	Neovascular (wet or exudative) AMD	Photodynamic therapy with verteporfin; placebo	3; 948	"The evidence from three high-quality RCTs suggested that verteporfin PDT treatment for 2 years reduces the number of cases of central blindness, compared with placebo, by slowing disease progression. However, this treatment is not aimed at restoring vision and the majority of treated patients will continue to lose visual acuity. Verteporfin treatment did not increase serious adverse events compared with placebo (angiography and sham treatment), however, some adverse events occurred with greater frequency in individuals treated with verteporfin."

Oliva 2002	*Not available*	"[To] analyze the scientific evidence available about effectiveness, efficacy, and safety of photodynamic therapy in the treatment of exudative AMD."	Neovascular (wet or exudative) AMD	Photodynamic therapy; placebo	2; 948	"The scientific evidence suggests that PDT may be effective and safe for subfoveal choroidal neovascularization secondary to AMD."

Surgical interventions						
Gupta 2018	29847689	"To assess the effectiveness and safety of the IMT [implantable miniature telescope] in improving visual acuity and quality of life in people with late or advanced AMD."	AMD (non specific)	Implantable miniature telescope (IMT); no IMT	0; 0	"We found no RCT or quasi-RCT and can draw no conclusion about the effectiveness and safety of the implantable miniature telescope (IMT) in improving visual acuity in individuals with late or advanced AMD. Since the IMT is typically implanted monocularly based upon which eye has better best-corrected distance visual acuity, randomization between eyes within an individual may not be acceptable."
Casparis 2009	19160299	"To evaluate the effectiveness and safety of cataract surgery in eyes with AMD."	AMD (non specific)	Cataract surgery; no treatment/observation/no intervention	0; 0	"At this time, it is not possible to draw reliable conclusions from the available data to determine whether cataract surgery is beneficial or harmful in people with AMD. Physicians will have to make practice decisions based on best clinical judgement until controlled trials are conducted and their findings published."
Giansanti 2009	19370663	"[To assess] the effectiveness of submacular surgery for preserving or improving vision in patients with AMD."	Neovascular (wet or exudative) AMD	Submacular surgery; laser photocoagulation; no treatment/observation/no intervention	3; 860	"There is no benefit with submacular surgery in most people with subfoveal choroidal neovascularization due to AMD in terms of prevention of visual loss. Furthermore, the risk of developing cataract and retinal detachment increases after surgery."
Hooper 2008	18347620	"To synthesize the research literature related to low vision secondary to AMD and its associated rehabilitative aspects when existing medical treatments have been unsuccessful or only partially successful for the patient."	AMD (non specific)	Low vision rehabilitation intervention; placebo	32; NR	"Additional randomized controlled trials with similar intervention comparisons and outcome measures are needed to form stronger conclusions for the most effective low-vision rehabilitation interventions for individuals with AMD"

Bockelbrink 2006	21289972 *see also 18572053*	"[To evaluate] the medical and health economic effects of cataract operations on the development and progression of an age related macular degeneration (AMD)"	AMD (non specific)	Cataract surgery; no treatment/observation/no intervention	8; NR	"The presentation of the evaluated literature made clear that only a small number of publications dealt with the development of age related macular degeneration in consequence of a cataract extraction. The overall scientific level of evidence of these articles was not very high. Therefore it was not possible to obtain a well-defined conclusion on the effect of a cataract extraction on the development or progression of an age related macular degeneration."
Waugh 2018	29846169	"To carry out a systematic review of treatments for dry AMD and STGD [Stargardt disease], and to identify emerging treatments where future NIHR research might be commissioned."	Non-neovascular (non-exudative) AMD; Stargardt Disease	Acupuncture; rheopheresis; microcurrent stimulation; lasers; ozone; intraocular telescopes or lenses; night-time light; control (Health Technology Assessment of all treatments for AMD and STGD)	104; NR	"There are some promising developments in dry AMD, but research studies are already under way in some of these, and we suggest waiting for their results. We have suggested some topics where the NIHR programs might consider primary research."
Gregg 2017	28399772	"To explore the development of the role of specialist ophthalmic nurses in delivering ranibizumab intravitreal injections to patients with wet age-related macular degeneration (AMD), and to evaluate their contribution to reducing capacity pressures in medical retina services, while maintaining safe and effective standards of care."	Neovascular (wet or exudative) AMD	Intravitreal injections delivered by trained ophthalmic nurse practitioners; intravitreal injections delivered by ophthalmologists	5; NR	"Role expansion, in which specialist ophthalmic nurses deliver intravitreal injections, has been shown to be economical, safe and effective. It enables timely delivery of the service, thereby preventing irreversible blindness for individuals with wet AMD."

Williams 2014	24431152	"To assess the effects and safety of complement inhibitors in the prevention or treatment of advanced AMD."	AMD (non specific)	Complement inhibitors	0; 0	"There is insufficient information at present to generate evidence-based recommendations on the potential safety and efficacy of complement inhibitors for prevention or treatment of AMD."
Gehlbach 2012	22419318	"To examine the effectiveness of statins compared with other treatments, no treatment, or placebo in delaying the onset and/or progression of AMD."	AMD (non specific)	Statins; placebo	2; 72	"Evidence from currently available RCTs was insufficient to conclude that statins have any role in preventing or delaying the onset or progression of AMD."
Reddy 2006	16437522	"To investigate interferon alpha as a treatment modality for neovascular age-related macular degeneration."	Neovascular (wet or exudative) AMD	Interferon alpha; placebo	1; 481	"At present there is not enough evidence to recommend the use of interferon alpha-2a for the treatment of age-related macular degeneration."

Abbreviations: AMD = age-related macular degeneration; anti-VEGF = anti-vascular endothelial growth factor; BCVA = best corrected visual acuity; DME = diabetic macular edema; DMO = diabetic macular oedema; DR = diabetic retinopathy; IOL = intraocular lens; IOP = intraocular pressure; PDT = photodynamic therapy; PRN = pro re nata; RCT = randomized controlled trial; T&E = treat and extend; T2DM = type II diabetes

eTable 2. Diabetic Retinopathy: objectives, participants, interventions, and conclusions of the reliable systematic reviews, sorted by reverse chronological order of publication within intervention type

Study ID	PMID	Objective(s)	Participants	Intervention Comparisons	Number of Studies; Participants (or eyes)	Conclusion(s) from the abstract
Anti-VEGF interventions						
Mehta 2018	29669176	"To assess the effects of intravitreal agents that block vascular endothelial growth factor activity (anti-VEGF agents) plus intravitreal steroids versus monotherapy with macular laser, intravitreal steroids or intravitreal anti-VEGF agents for managing DME."	Diabetic retinopathy, including diabetic macular edema	Anti-VEGF agent, non-specific; anti-VEGF + steroid; laser photocoagulation; steroid implantation	8; 566	"Combination of intravitreal anti-VEGF plus intravitreal steroids does not appear to offer additional visual benefit compared with monotherapy for DME; at present the evidence for this is of low-certainty."

He 2018	29784048	"[To evaluate] the effectiveness and safety of dexamethasone (DEX) implant and intravitreal anti-vascular endothelial growth factor (VEGF) treatment for diabetic macular edema (DME)."	Diabetic retinopathy, including diabetic macular edema	Dexamethasone intravitreal implant; anti-VEGF agent, non-specific	4; NR	"Compared with anti-VEGF, dexamethasone (DEX) implant improved anatomical outcomes significantly. However, this did not translate to improved visual acuity, which may be due to the progression of cataract."
Virgili 2017	28639415	"To compare the effectiveness and safety of the different anti-VEGF drugs in preserving and improving vision and quality of life using network meta-analysis methods"	Diabetic retinopathy, including diabetic macular edema	Any anti-VEGF agent; anti-VEGF plus laser; laser treatment; ranibizumab; bevacizumab; sham treatment or injection; no treatment/observation /no intervention	24; 6,007	"Anti-VEGF drugs are effective at improving vision in people with DME with three to four in every 10 people likely to experience an improvement of 3 or more lines visual acuity (VA) at one year. There is moderate-certainty evidence that aflibercept confers some advantage over ranibizumab and bevacizumab in people with DME at one year in visual and anatomic terms."

Avery 2016	26513684	"To evaluate the systemic safety of intravitreous anti-VEGF injections in high-risk patients with DME and to investigate separately the subgroup of these patients with the highest level of exposure to anti-VEGF monthly treatment for 2 years."	Diabetic retinopathy, including diabetic macular edema	Aflibercept; ranibizumab; sham treatment or injection	4; 1,328	"In this meta-analysis of anti-VEGF agents for patients with DME, assessment of the highest-level exposure group (those high-risk patients with DME who received 2 years of monthly treatment) revealed a possible increased risk for death and potentially for cerebrovascular accidents."
Zhang 2016	27434498	"To compare the efficacy and safety of current treatments in diabetic macular edema (DME)."	Diabetic retinopathy, including diabetic macular edema	Dexamethasone implant; intravitreal aflibercept; intravitreal bevacizumab; intravitreal ranibizumab; intravitreal ranibizumab + laser; dexamethasone implant + laser; intravitreal bevacizumab + intravitreal triamcinolone; intravitreal bevacizumab + laser; intravitreal triamcinolone + laser; laser; placebo	21; 4,307 (eyes)	"Our analysis confirms that intravitreal aflibercept is most favorable with both BCVA improvement and central macular thickness decrease than other current therapies in the management of DME within 12 months. Vascular endothelial growth factor inhibitors for DME should be used with caution due to systemic adverse effects. Combined intravitreal triamcinolone with laser has a stronger efficacy in decreasing central macular thickness than the other interventions in the early stages after injection."

Korobelnik 2015	25975823	"[To compare] the effectiveness of intravitreal afilbercept 2 mg every 8 weeks after 5 initial monthly doses and other diabetic macular edema therapies at doses licensed outside the USA."	Diabetic retinopathy, including diabetic macular edema	Intravitreal aflibercept; laser treatment; intravitreal bevacizumab (IVB) + laser; intravitreal ranibizumab (IVR); IVR + laser; IVR + prompt laser; IVR + deferred laser; intravitreal triamcinolone acetonide (IVTA) + laser; dexamethasone	11; NR	"Studies of IVT-AFL 2q8 showed improved 12-month visual acuity measures compared with studies IVR 0.5 mg PRN and dexamethasone 0.7 mg implants based on indirect comparisons. These analyses are subject to a number of limitations which are inherent in indirect data comparisons."

Simunovic 2015	26398553	"To systematically review and perform meta-analysis on the available randomized controlled trial data for anti-vascular endothelial growth factor (anti-VEGF) agents in the management of proliferative diabetic retinopathy and its complications."	Diabetic retinopathy, including diabetic macular edema	Ranibizumab; pegaptanib; bevacizumab; panretinal photocoagulation (PRP); intravitreal ranibizumab + panretinal photocoagulation; pars plana vitrectomy (PPV); intravitreal bevacizumab + pars plana vitrectomy; saline	22; 1,397 eyes	"The use of anti-VEGF agents before panretinal photocoagulation results in superior functional and structural outcomes at 3 months to 4 months. The use of anti-VEGF agents before pars plana vitrectomy results in decreased duration of surgery, fewer breaks, and less intra-operative bleeding. Although there is evidence for a decreased incidence of early postoperative vitreous hemorrhage, the quality of evidence is low. The available data therefore support the use of anti-VEGF agents as adjuncts to panretinal photocoagulation and pars plana vitrectomy in patients with complicated proliferative diabetic retinopathy primarily as a means of facilitating, and potentially minimizing the iatrogenic damage resulting from, these procedures."

Smith 2015	26250103	"To summarize the effects of anti-VEGF use to reduce the occurrence of posterior vitreous cavity hemorrhage after vitrectomy surgery for proliferative diabetic retinopathy."	Diabetic retinopathy, including diabetic macular edema	Bevacizumab; sham treatment or injection; no treatment/observation /no intervention	12; 645	"The use of pre- or intraoperative bevacizumab lowers the incidence of early posterior vitreous cavity hemorrhage. The reported complications from its use appear to be low."
Martinez-Zapata 2014	25418485	"To assess the effectiveness and safety of anti-VEGFs for proliferative diabetic retinopathy"	Diabetic retinopathy, including diabetic macular edema	Anti-VEGF with or without panretinal photocoagulation; panretinal photocoagulation (PRP); anti-VEGF + vitrectomy; vitrectomy	18; 1,005	"There was very low or low quality evidence from RCTs for the efficacy and safety of anti-VEGF agents when used to treat proliferative diabetic retinopathy over and above current standard treatments. However, the results suggest that anti-VEGFs can reduce the risk of intraocular bleeding in people with proliferative diabetic retinopathy."
Yanagida 2014	24667549	"To evaluate systemic safety of ranibizumab for diabetic macular edema."	Diabetic retinopathy, including diabetic macular edema	Ranibizumab; laser treatment; triamcinolone; ranibizumab + laser; sham + laser; sham treatment or injection	6; 2,459	"Ranibizumab for diabetic macular edema is considered safe when the patients are carefully selected based on systemic vascular conditions and it is used on pro re nata basis."

Ford 2013	23457327	"To appraise the evidence for the use of anti-VEGF drugs and steroids in diabetic macular oedema (DMO) as assessed by change in best corrected visual acuity (BCVA), central macular thickness and adverse events."	Diabetic retinopathy, including diabetic macular edema	Ranibizumab; laser photocoagulation; ranibizumab + laser; bevacizumab; pegaptanib; VEGF trap-eye; dexamethasone; dexamethasone + laser; no treatment/observation /no intervention; sham treatment or injection	29; 6,587	"The anti-VEGFs ranibizumab and bevacizumab have consistently shown good clinical effectiveness without major unwanted side effects. Steroid results have been mixed and are usually associated with cataract formation and intraocular pressure increase. Despite the current wider spectrum of treatments for DME, only a small proportion of patients recover good vision (≥20/40)."
Fortin 2012	24279000	"To evaluate the effects of intravitreal bevacizumab for the treatment of diabetic macular edema."	Diabetic retinopathy, including diabetic macular edema	Bevacizumab; laser treatment; bevacizumab + triamcinolone; laser treatment; bevacizumab + laser; intravitreal triamcinolone; sham treatment or injection	10; 923	"There is insufficient evidence to draw conclusions on the effects of bevacizumab on mortality, serious morbidity, activities of daily living, and quality of life."

Ollendorf 2012	*Not available*	"To conduct a systematic review of the evidence on the clinical effectiveness and potential harms of intravitreal agents which inhibit vascular endothelial growth factor (VEGF) in patients with diabetic macular edema."	Diabetic retinopathy, including diabetic macular edema	Ranibizumab; intravitreal triamcinolone; laser treatment; bevacizumab; intravitreal triamcinolone; aflibercept; pegaptanib; sham treatment or injection	23; NR	"Evidence accumulated to date suggests that anti-VEGF therapy improves visual acuity in patients with diabetic macular edema relative to macular laser treatment or sham injection. Our analyses suggest no significant difference in clinical performance among the anti-VEGF agents, however. The systemic side effect profile of Avastin relative to Lucentis or other anti-VEGF agents remains the greatest element of uncertainty."
Goyal 2011	20665044	"To evaluate the effect of bevacizumab (Avastin) in diabetic macular edema (DME)."	Diabetic retinopathy, including diabetic macular edema	Bevacizumab; intravitreal bevacizumab + macular photocoagulation; macular photocoagulation; intravitreal bevacizumab + intravitreal triamcinolone acetide (IVT); sham treatment or injection	4; 484 eyes	"Intravitreal bevacizumab (IVB) is an effective short-term treatment for diabetic macular edema, and that its efficacy wanes after 6 weeks."

Yilmaz 2011	20645926	"To compare intravitreal bevacizumab (IVB) injection versus macular photocoagulation (MPC) or a combination of intravitreal bevacizumab and intravitreal triamcinolone acetonide (IVB⁄IVTA) injection in improving visual acuity (VA) of patients with primary diabetic macular oedema (DMO)."	Diabetic retinopathy, including diabetic macular edema	Bevacizumab; macular photocoagulation (MPC); combination of intravitreal bevacizumab and intravitreal triamcinolone acetonide	4; 445	"Intravitreal bevacizumab injection is effective in improving visual acuity (VA) in patients with primary DME for 6 weeks, but the benefits are no longer present 12 weeks following the injection."
Mohamed 2007	17712074	"To review the best evidence for primary and secondary intervention in the management of DR, including diabetic macular edema."	Diabetic retinopathy, including diabetic macular edema	Glycemic control; blood pressure control; lipid-lowering therapy; pan-retinal laser photocoagulation; focal laser; vitrectomy; intravitreal steroids; any anti-VEGF agent; aspirin	44; NR	"Tight glycemic and blood pressure control remains the cornerstone in the primary prevention of DR. Pan-retinal and focal retinal laser photocoagulation reduces the risk of visual loss in patients with severe DR and macular edema, respectively. There is currently insufficient evidence to recommend routine use of other treatments."

Screening						
Echouffo-Tcheugui 2013	23819487	"[To review] the published literature on the relationship between screening intervals for diabetic retinopathy and the incidence of visual loss."	Diabetic retinopathy, including diabetic macular edema	Various screening intervals	25; NR	"This review of evidence suggests that a 2-year screening interval for people with diabetes and no diabetic retinopathy at diagnosis may be safely adopted. However, this is contingent upon the availability of facilities to conduct appropriate eye examinations and deliver appropriate care to people detected."
Zhang 2007	17888859	"To assess the effectiveness of interventions aimed to increase retinal screening among people with diabetes."	Diabetes (non specific)	Interventions to improve screening	48; 162, 157	"Increasing patient awareness of diabetic retinopathy, improving provider and practice performance, and improving healthcare system infrastructure and processes, can significantly increase screening for diabetic retinopathy."
Harris 2003	12558362	"To examine the evidence that screening and earlier treatment are effective in reducing morbidity and mortality associated with diabetes."	Diabetes (non specific)	Interventions to improve screening	0; 0	"The interventions that are most clearly beneficial during the preclinical phase are those that affect the risk for cardiovascular disease. The magnitude of additional benefit of initiating tight glycemic control during the preclinical phase is uncertain but probably small."
Vitamins, nutritional supplements, or behavioral interventions						

Xie 2016	26559744	"To assess the efficacy and safety of intensive blood pressure-lowering strategies."	Diabetic retinopathy, including diabetic macular edema	Intensive blood pressure lowering; less intensive blood pressure lowering	19;444,989	"Intensive blood pressure lowering provided greater vascular protection than standard regimens. In high-risk patients, there are additional benefits from more intensive blood pressure lowering, including for those with systolic blood pressure below 140 mmHg. The net absolute benefits of intensive blood pressure lowering in high-risk individuals are large."
Do 2015	25637717	"To summarize the existing evidence regarding the effect of interventions to control or reduce blood pressure levels among diabetics on incidence and progression of diabetic retinopathy, preservation of visual acuity, adverse events, quality of life, and costs. A secondary aim was to compare classes of anti-hypertensive medications with respect to the same outcomes"	Diabetes (non specific)	Blood pressure control; lifestyle modification + anti-hypertensive medication; ACE inhibitor; calcium channel blockers, angiotensin receptor blockers, beta-blockers, or a combination of an agent + ACE inhibitors; no treatment/observation/no intervention; placebo	12;13,669	"The available evidence supports a beneficial effect of intervention to reduce blood pressure with respect to preventing diabetic retinopathy for up to 4 to 5 years. However, the lack of evidence to support such intervention to slow progression of diabetic retinopathy or to prevent other outcomes considered in this review, along with the relatively modest support for the beneficial effect on incidence, weakens the conclusion regarding an overall benefit of intervening on blood pressure solely to prevent diabetic retinopathy."

Virk 2015	26210869	"To systematically review the effectiveness of systemic interventions for diabetic retinopathy (DR) in type 1 diabetes."	Diabetic retinopathy, including diabetic macular edema	Intensive insulin therapy; blood pressure control; islet cell transplant; pancreas transplant; combined pancreas-kidney transplant; kidney transplant; pulsatile insulin; standard basal-bolus regime; cholesterol control + triglyceride control + diet; somatostatin analogue octreotide; aldose reductase inhibitor sorbinil; vitamin E + insulin; insulin injections; cyclosporin A + insulin; conventional insulin therapy; diet alone; placebo; standard of care/usual care; no treatment/observation/no intervention	24;9,3002	"Intensive insulin therapy, and specifically insulin pump therapy vs multiple daily injections, prevents DR in both adults and adolescents with type 1 diabetes. Antihypertensive agents provide protection in normotensive, normoalbuminuric adults. In patients with type 1 diabetes of longer duration, islet cell transplantation may be more effective than medical therapy. There is insufficient evidence for antilipid therapy or other systemic interventions."
Fullerton 2014	24526393	"To assess the effects of intensive versus conventional glycaemic targets in patients with type 1 diabetes in terms of long-term complications and determine whether very low, near normoglycaemic values are of additional benefit."	Diabetes (type I)	Intensive glucose control; conventional glucose control	12;2,230	"The effects of tight blood sugar control seem to become weaker once complications have been manifested... Furthermore, there is a lack of evidence from RCTs on the effects of tight blood sugar control in older patient populations or patients with macrovascular disease. There is no firm evidence for specific blood glucose targets and treatment goals need to be individualised taking into account age, disease progression, macrovascular risk, as well as the patient's lifestyle and disease management capabilities"
Kähler 2014	25138801	"To assess the benefits and harms of targeting intensive versus conventional glycaemic control in patients with type 1 diabetes mellitus."	Diabetes (type I)	Intensive glycemic control; conventional glycemic control	18;2,254	"The data for retinopathy and ketoacidosis were inconsistent. There was a severe lack of reporting on patient relevant outcomes, and all trials had poor bias control."

Buehler 2013	22212249 99	"To examine the effects of tight versus conventional glucose control in total mortality, cardiovascular and microvascular events, and hypoglycemia in patients with type 2 diabetes."	Diabetes (type II)	Tight glucose control; standard of care/usual care	6;27,654	"Tight blood glucose control reduces the risk for some macrovascular and microvascular events, without effect on all-cause mortality and cardiovascular mortality. Tight glucose control increases the risk of severe hypoglycemia."
Hemmingsen 2011	22115901	"To assess the effect of targeting intensive glycaemic control versus conventional glycaemic control on all cause mortality and cardiovascular mortality, non-fatal myocardial infarction, microvascular complications, and severe hypoglycaemia in patients with type 2 diabetes."	Diabetes (type II)	Intensive glycaemic control; conventional glycaemic control	14;28,614	"Data available from randomized clinical trials remain insufficient to prove or refute a relative risk reduction for cardiovascular mortality, non-fatal myocardial infarction, composite microvascular complications, or retinopathy at a magnitude of 10%. Intensive glycemic control increases the relative risk of severe hypoglycemia by 30%."
Sumamo 2011	25473696	"To synthesize evidence from randomized controlled trials (RCTs) on the effectiveness of lifestyle interventions to control progression of type 2 diabetes, progression to diabetes from metabolic syndrome, or recurrence of breast cancer and prostate cancer."	Diabetes (type II)	Lifestyle intervention; standard of care/usual care	20;NR	"Comprehensive lifestyle interventions that include exercise, dietary changes, and at least one other component are effective in decreasing the incidence of type 2 diabetes mellitus in high risk patients and the benefit extends beyond the active intervention phase. In patients who have already been diagnosed with type 2 diabetes, there is some evidence to suggest long-term benefit on microvascular and macrovascular outcomes, although the evidence is from one trial of high risk diabetic patients and included pharmacotherapy."

Lopes 2008	18254110	"To review the literature in a standard systematic way in order to assess the effects of vitamin C and superoxide dismutase on diabetic retinopathy in methodologically robust trials."	Diabetic retinopathy, including diabetic macular edema	Vitamin C; superoxide dismutase; vitamin C + superoxide dismutase; no treatment; placebo	0; 0	"No research to date has adequately examined the treatment of diabetic retinopathy with vitamin C or superoxide dismutase (SOD) in such a way as to indicate whether this form of intervention has a significant impact on the progress of this clinical condition."
Hodge 2005 (Results also published in part or in full in: 16815401 and 17290205)	16111433	"To conduct a systematic review of the scientific medical literature to identify, appraise and synthesize the evidence for the effects of omega-3 fatty acids on eye health."	Diabetic retinopathy, including diabetic macular edema	Omega-3 fatty acids; any agent	16; NR	"There was insufficient evidence to draw firm conclusions."

Radiotherapy and laser interventions						
Moutray 2018	29543992	"To assess the effects of different types of laser, other than argon laser, and different laser protocols, other than those established by the Early Treatment of Diabetic Retinopathy Study (ETDRS), for the treatment of proliferative diabetic retinopathy (PDR)."	Diabetic retinopathy, including diabetic macular edema; diabetes (non specific)	Standard argon laser pan-retinal photocoagulation; alternative laser pan-retinal photocoagulation strategy	11; 1,069	"There is limited evidence available with respect to the efficacy and safety of alternative laser systems or strategies compared with the standard argon laser as described in Early Treatment Diabetic Retinopathy Study (ETDRS)."
Wu 2018	29091878	"To assess the effects of laser photocoagulation as monotherapy or adjuvant therapy for the treatment of DME."	Diabetic retinopathy, including diabetic macular edema	Conventional laser photocoagulation (CLP) + ranibizumab; subthreshold diode micropulse laser photocoagulation (SDMLP); CLP + bevacizumab	18; 1,746	"There was no apparent difference on improving vision between subthreshold diode micropulse laser (SDMLP) monotherapy and conventional laser photocoagulation (CLP) monotherapy. The most effective treatment in the network was ranibizumab therapy combined with CLP followed by SDMLP monotherapy, Bevacizumab therapy combined with CLP, and CLP monotherapy in rank order."

Royle 2015	26173799	"To assess the clinical effectiveness and cost-effectiveness of pan-retinal photocoagulation (PRP) given at the non-proliferative stage of diabetic retinopathy (NPDR) compared with waiting until the high-risk proliferative diabetic retinopathy (HR-PDR) stage was reached."	Diabetic retinopathy, including diabetic macular edema	Argon photocoagulation; xenon photocoagulation; laser photocoagulation; laser photocoagulation + anti-VEGF	25; NR	"There is, as yet, no convincing evidence that modern laser systems are more effective than the argon laser used in Early Treatment Diabetic Retinopathy Study (ETDRS), but they appear to have fewer adverse effects."
Evans 2014	25420029	"To assess the effects of laser photocoagulation for diabetic retinopathy compared to no treatment or deferred treatment."	Diabetic retinopathy, including diabetic macular edema	Laser treatment; deferred laser treatment; no treatment/observation/no intervention	5; 4,786	"This review provides evidence that laser photocoagulation is beneficial in treating proliferative diabetic retinopathy. We judged the evidence to be moderate or low, depending on the outcome. This is partly related to reporting of trials conducted many years ago, after which panretinal photocoagulation has become the mainstay of treatment of proliferative diabetic retinopathy."

Régnier 2014	25029255	"[To] compare the efficacy of ranibizumab, aflibercept, laser, and sham in the first-line treatment of diabetic macular edema (DME) to inform technology assessments such as those conducted by the UK National Institute for Health and Care Excellence (NICE)."	Diabetic retinopathy, including diabetic macular edema	Laser treatment; ranibizumab + laser; ranibizumab; aflibercept; sham treatment or injection	8; 1,978	"Ranibizumab was non-significantly superior to aflibercept and both anti-VEGF therapies had statistically superior efficacy to laser."
Milne 2012	25356446	"To assess the effectiveness of interventions for DR to improve HRQL."	Diabetic retinopathy, including diabetic macular edema	Laser photocoagulation; vitrectomy; panretinal photocoagulation; phacoemulsification; pegaptinib; ranibizumab; ranibizumab + laser photocoagulation	16; NR	"Two tools developed specifically for patients with DR are currently undergoing evaluation. In general, health-related quality of life was improved following interventions for DR. ... The current research on the impact of other interventions for DR on health-related quality of life is insufficient to draw conclusions about the relative effect of one intervention versus another."

Lopes de Jesus 2008	18425965	"To review the literature in a systematic way in order to assess the effects of pentoxyfilline for diabetic retinopathy in methodologically robust trials."	Diabetic retinopathy, including diabetic macular edema	Pentoxifylline + photocoagulation; no treatment + photocoagulation; placebo	0; 0	"No sound research to date has examined the treatment of diabetic retinopathy with pentoxyfilline in such a way as to indicate whether this form of intervention has a significant impact on the natural history of this clinical condition. The potential role of this substance in the treatment of diabetic retinopathy remains open to debate, and it is suggested that future research focusing on patient-relevant outcomes takes the opportunity of addressing this important issue directly."
Other interventions						
Shi 2018	29487821	"To provide evidence for application of lipid lowering agents in treatment of diabetic retinopathy (DR)."	Diabetic retinopathy, including diabetic macular edema	Statins; fibrate + simvastatin; fenofibrate; atorvastatin; simvastatin; no treatment/observation/no intervention; placebo + simvastatin; placebo	8; 13,454	"In DR patients, lipid-lowering agents show a protective effect on DR progression and might be associated with reduced risk in the development of DME. However, lipid-lowering agents have no effects on vision loss and hard exudates aggravation. Further clinical trials in larger scale are required to confirm the conclusion of this study and thus justify the use of intensive control lipids with anti-lipid agents at the early stages of DR."

Larun 2016	26983145	"[To investigate] whether the use of forms by general practitioners for recording clinical data contributes to lower mortality and morbidity for this patient group."	Diabetes (non specific)	Clinical data form; follow-up without use of a diabetes form (e.g., normal use of electronic patient records)	7; 20,370	"Published data at present provide no clear answers, but show that use of forms in the follow-up of patients with diabetes in general practice may tend to contribute to lower mortality and morbidity."
Health Quality Ontario 2015	26644812	"To determine the clinical effectiveness of islet transplantation in patients with type 1 diabetes, with or without kidney disease."	Diabetes (type I)	Islet transplantation; insulin injections; pancreas transplantation	17; NR	"For patients with type 1 diabetes with difficult-to-control blood glucose levels, islet transplantation may be a beneficial B-cell replacement therapy to improve glycemic control and secondary complications of diabetes. However, there is uncertainty in the estimates of effectiveness because of the generally low to very low quality of evidence for all outcomes of interest."
Sahoo 2015	25686158	"To assess the effects of topical non-steroidal anti-inflammatory drugs (NSAIDs) for diabetic cystoid macular oedema (CMO)"	Diabetic retinopathy, including diabetic macular edema	Topically applied NSAIDs	0; 0	"The review did not identify any RCTs investigating the effects of topical NSAIDs in the treatment of diabetic cystoid macular oedema. Most of the studies identified through the electronic searches had been conducted to analyse the effect of topical NSAIDs for pseudophakic cystoid macular oedema. In the absence of high quality evidence, clinicians need to use their clinical judgement and other low level evidence, such as observational non-randomised trials, to decide whether to use topical NSAIDs in cases of diabetic cystoid macular oedema."

Lv 2012	22927798	"To assess the effects of intensive blood pressure lowering on vascular, eye, and renal outcomes."	Diabetes (non specific)	Intensive blood pressure lowering with meds; standard blood pressure lowering with meds	15; 37,348	"Intensive blood pressure lowering regimens provided greater vascular protection than standard regimens that was proportional to the achieved difference in systolic blood pressure, but did not have any clear impact on the risk of death or serious adverse events."
Qaseem 2012	22312141	"To present the evidence and provide clinical recommendations on the comparative effectiveness and safety of type 2 diabetes medications."	Diabetes (type 2)	Monotherapy; combination therapy	NR; NR	"The evidence shows that most diabetes medications reduced HbA1c levels to a similar degree. Metformin was more effective than other medications as monotherapy as well as when used in combination therapy with another agent for reducing HbA1c levels, body weight, and plasma lipid levels. It was difficult to draw conclusions about the comparative effectiveness of type 2 diabetes medications on all-cause and cardiovascular mortality, cardiovascular and cerebrovascular morbidity, and microvascular outcomes because of low-quality or insufficient evidence."

Tricco 2012	22683130	"To assess the effects of quality improvement strategies on glycated haemoglobin (HbA1c), vascular risk management, microvascular complication monitoring, and smoking cessation in patients with diabetes."	Diabetes (non specific)	Audit and feedback; case management; team changes; electronic patient registry; clinician education; clinician reminders; facilitated relay; patient education; promotion of self management; patient reminders; continuous quality improvement; financial incentives; control	142; 123,529	"Many trials of quality improvement strategies showed improvements in diabetes care. Interventions targeting the system of chronic disease management along with patient-mediated quality improvement strategies should be an important component of interventions aimed at improving diabetes management. Interventions solely targeting health-care professionals seem to be beneficial only if baseline HbA1c control is poor."
Yilmaz 2009	19410949	"To compare intravitreal triamcinolone acetonide (IVTA) injection versus no treatment or sub-Tenon triamcinolone acetonide (STTA) injection in improving visual acuity (VA) of patients with refractory diabetic macular edema (DME; unresponsive to focal laser therapy)."	Diabetic retinopathy, including diabetic macular edema	Intravitreal triamcinolone; sub-Tenon triamcinolone; cotton tip; no treatment/observation/no intervention; placebo	6; 207	"Intravitreal triamcinolone acetonide injection is effective in improving visual acuity (VA) in patients with refractory DME in the short-term, but the benefits do not seem to persist in the long-term."

Grover 2008	18254088	"[To evaluate] the effectiveness and safety of intraocular steroids in treating diabetic macular edema (DME)."	Diabetic retinopathy, including diabetic macular edema	Intravitreal triamcinolone acetonide injection; intravitreal fluocinolone acetonide implantation; no treatment/observation/no intervention	7; 632 eyes	"RCTs included in this review suggest that steroids placed inside the eye by either intravitreal injection or surgical implantation may improve visual outcomes in eyes with persistent or refractory DME."
Mukhopadhyay 2007	17678864	"To study the effects of continuous subcutaneous insulin infusion (CSII) vs multiple-dose insulin (MDI) therapy on glycemic control and pregnancy outcome in diabetic women."	Diabetes (non specific)	Continuous subcutaneous insulin infusion; multiple-dose insulin	6; 213	"This systematic review does not show any advantage or disadvantage of using continuous subcutaneous insulin infusion (CSII) over multiple-dose insulin (MDI) in pregnant diabetic women."
De Schryver 2003	12535415	"To assess the efficacy and safety of dipyridamole versus control in the secondary prevention of vascular events in patients with vascular disease."	Diabetic retinopathy, including diabetic macular edema	Dipyridamole; other antiplatelet drug; dipyridamole + aspirin; aspirin; control; placebo	29; 23,019	"For patients who presented with arterial vascular disease, there was no evidence that dipyridamole, in the presence or absence of another antiplatelet drug reduced the risk of vascular death, though it reduces the risk of further vascular events. This benefit was found only in patients presenting after cerebral ischemia. There was no evidence that dipyridamole alone was more efficacious than aspirin."

Abbreviations: AMD = age-related macular degeneration; anti-VEGF = anti-vascular endothelial growth factor; BCVA = best corrected visual acuity; DME = diabetic macular edema; DMO = diabetic macular oedema; DR = diabetic retinopathy; IOL = intraocular lens; IOP = intraocular pressure; PDT = photodynamic therapy; PRN = pro re nata; RCT = randomized controlled trial; T&E = treat and extend; T2DM = type II diabetes

eTable 3. Idiopathic Epiretinal Membrane & Vitreomacular Traction: objectives, participants, interventions, and conclusions of the reliable systematic reviews, sorted by reverse chronological order of publication within intervention type

Study ID	PMID	Objective(s)	Participants	Intervention Comparisons	Number of Studies; Participants (or eyes)	Conclusion(s) from the abstract
Surgical interventions						
Fang 2017	28314834	"To determine whether internal limiting membrane (ILM) peeling improves anatomical and functional outcomes in idiopathic macular pucker (IMP)/epiretinal membrane (ERM) surgery."	Idiopathic epiretinal membrane & vitreomacular traction	Internal limiting membrane (ILM) peeling; non internal limiting membrane (ILM) peeling	13; 359	"Internal limiting membrane (ILM) peeling yielded greater anatomical success, but no improvement in functional outcomes as the treatment of choice for patients undergoing idiopathic macular pucker surgery."
Hatef 2015	25950286	"To assess the effectiveness and safety of pneumatic retinopexy versus scleral buckle or pneumatic retinopexy versus a combination treatment of scleral buckle and vitrectomy	Rhegmatogenous retinal detachment (RRD)	Pneumatic retinopexy; scleral buckle	2; 216	"[P]neumatic retinopexy may result in lower rates of reattachment and higher rates of recurrence than scleral buckle for eyes with rhegmatogenous retinal detachment (RRD), but does not rule out no difference between procedures. The relative safety of the procedures is uncertain and the relative effects of these procedures in terms of other patient-important

		for people with rhegmatogenous retinal detachment (RRD). The secondary objectives were to summarize any data on economic measures and quality of life."				outcomes, such as visual acuity and quality of life, is unknown."
Soni 2013	23511114	"To examine possible differences in clinical outcomes between pars plana vitrectomy (PPV) and scleral buckling (SB) for uncomplicated rhegmatogenous retinal detachment (RRD)."	Rhegmatogenous retinal detachment (RRD)	Pars plana vitrectomy	6; 523	"There were no significant differences in the proportions of primary reattachment in the pars plana vitrectomy (PPV) and scleral buckle (SB) groups in phakic eyes. The SB-treated phakic eyes had better postoperative BCVA at 6 months or more. This is most likely related to higher rates of cataract progression in PPV-treated phakic eyes. There were no significant differences in proportions of primary reattachment and postoperative BCVA at 6 months or more in pseudophakic/aphakic eyes."
Other interventions						
Neffendorf 2017	29040800	"To assess the efficacy and safety of ocriplasmin compared to no treatment, sham or placebo for the treatment of symptomatic vitreomacular adhesion."	Symptomatic vitreomacular adhesion (sVMA)	Ocriplasmin; placebo	4; 932	"[O]criplasmin is useful in the treatment of symptomatic vitreomacular adhesion (sVMA). However, up to 20% of eyes treated with ocriplasmin will still require additional treatment with pars plana vitrectomy (PPV) within six months. There were more ocular adverse events in eyes treated with ocriplasmin than control (sham or placebo injection) treatment. Many of these adverse events, particularly vitreous floaters and photopsia, are known to be associated with posterior vitreous detachment."
CADTH 2014	*Not available*	"To perform a systematic review of the beneficial and harmful effects of ocriplasmin for the treatment of symptomatic vitreomacular adhesion (sVMA)."	Symptomatic vitreomacular adhesion (sVMA)	Ocriplasmin (125 mcg intravitreal injection);	3; 712	"Overall, treatment with ocriplasmin was superior to placebo for the resolution of VMA and total posterior vitreous detachment (PVD). Although there was a greater overall incidence of adverse events for patients treated with ocriplasmin compared with placebo, many events were transient and possibly related to the procedure instead of the drug itself. There is uncertainty regarding the efficacy of ocriplasmin for the treatment of full-thickness macular holes (FTMHs),

				placebo		avoidance of vitrectomy, and improvement in best-corrected visual acuity (BCVA). Moreover, no data were available on whether ocriplasmin prevents VMA-related vision loss or blindness, a key outcome according to patient groups."

Abbreviations: AMD = age-related macular degeneration; anti-VEGF = anti-vascular endothelial growth factor; BCVA = best corrected visual acuity; DME = diabetic macular edema; DMO = diabetic macular oedema; DR = diabetic retinopathy; IOL = intraocular lens; IOP = intraocular pressure; PDT = photodynamic therapy; PRN = pro re nata; RCT = randomized controlled trial; T&E = treat and extend; T2DM = type II diabetes

eTable 4. Idiopathic Macular Holes: objectives, participants, interventions, and conclusions of the reliable systematic reviews, sorted by reverse chronological order of publication within intervention type

Study ID	PMID	Objective(s)	Participants	Intervention Comparisons	Number of Studies; Participants (or eyes)	Conclusion(s) from the abstract
Surgical interventions						
Hu 2016	26385613	"To evaluate the impact of postoperative posturing with or without face-down on the anatomical and functional outcomes of macular hole surgery."	Idiopathic macular hole	Face-down posturing; no face-down posturing	4; 251	"Our work found that no face-down posturing (FDP) was not inferior to its face-down counterpart for the success of macular hole surgery (MHS) when macular holes were smaller than 400 lm in size. For macular holes larger than 400 lm, statistical analysis proved that FDP might be necessary."
Rahimy 2016	26441264	"To assess the literature regarding macular hole reopening rates stratified by whether the internal limiting membrane (ILM) was peeled during vitrectomy surgery."	Idiopathic macular hole	Macular hole surgery with internal limiting membrane peeling; macular hole surgery without internal limiting membrane peeling	50; 5,480	"The results of this meta-analysis support the concept that internal limiting membrane (ILM) peeling during macular hole surgery reduces the likelihood of macular hole reopening."
Parravano 2015	25965055	"To examine the effects of vitrectomy for Idiopathic macular hole on visual acuity. A secondary objective was to investigate anatomic effects on hole closure and other dimensions of visual function, as well as to report on adverse effects recorded in included studies."	Idiopathic macular hole	Vitrectomy, non-specific; no treatment/no intervention/observation	3; 356	"Vitrectomy is effective in improving visual acuity, resulting in a moderate visual gain, and in achieving hole closure in people with macular hole. However, these results may not apply to modern surgery due to technological improvements in vitrectomy techniques."

Spiteri Cornish 2013	23740611	"To determine whether internal limiting membrane (ILM) peeling improves anatomical and functional outcomes of macular hole surgery compared with the no-peel ing technique and to investigate the impact of different parameters such as presenting vision, stage/size of the hole and duration of symptoms in the success of the surgery."	Idiopathic macular hole	Vitrectomy with internal limiting membrane peeling; vitrectomy without internal limiting membrane peeling	4; 317	"Although we found no evidence of a benefit of internal limiting membrane (ILM) peeling in terms of the primary outcome (visual acuity at six months), ILM peeling appears to be superior to its no-peeling counterpart as it offers more favorable cost effectiveness by increasing the likelihood of primary anatomical closure and subsequently decreasing the likelihood of further surgery, with no differences in unwanted side-effects compared with no peeling."
Solebo 2011	22161423	"To evaluate the evidence of the impact of postoperative face-down positioning on the outcome of surgery for macular hole."	Idiopathic macular hole	Facedown positioning; seated; no treatment/no intervention/obs ervation	3; 243	"There is currently insufficient evidence from which to draw firm conclusions about the impact of postoperative face-down positioning on the outcome of surgery for macular hole. Of three RCTs, two suggested a benefit in larger holes but none demonstrated evidence of a benefit in smaller holes. CONSORT adherent RCTs and large scale, well designed non-randomized observational studies are needed to determine with confidence the value of this intervention."

Abbreviations: AMD = age-related macular degeneration; anti-VEGF = anti-vascular endothelial growth factor; BCVA = best corrected visual acuity; DME = diabetic macular edema; DMO = diabetic macular oedema; DR = diabetic retinopathy; IOL = intraocular lens; IOP = intraocular pressure; PDT = photodynamic therapy; PRN = pro re nata; RCT = randomized controlled trial; T&E = treat and extend; T2DM = type II diabetes

eTable 5. PVD, retinal breaks, & lattice degeneration: objectives, participants, interventions, and conclusions of the reliable systematic reviews, sorted by reverse chronological order of publication within intervention type

Study ID	PMID	Objective(s)	Participants	Intervention Comparisons	Number of Studies; Participants (or eyes)	Conclusion(s) from the abstract
Surgical interventions						
Yuan 2017	29179705	"To evaluate the effects on vitrectomy with internal limiting membrane (ILM) peeling versus vitrectomy with inverted internal limiting membrane flap technique for macular hole-induced retinal detachment (MHRD)."	PVD, Retinal Breaks, & Lattice Degeneration	Vitrectomy with internal limiting membrane peeling; virectomy with inverted internal limiting membrane flap technique	4; 98	"Compared with internal limiting membrane (ILM) peeling, vitrectomy with inverted ILM flap technique resulted significantly higher of the rate of retinal reattachment and macular hole closure, but seemed does not improve postoperative best-corrected visual acuity."
Ang 2012	22336825	"To evaluate the effectiveness of prophylactic 360-degree interventions in the fellow eye of patients with unilateral giant retinal tear to prevent the occurrence of a giant retinal tear, a retinal detachment or both."	PVD, Retinal Breaks, & Lattice Degeneration	360-degree encircling scleral buckling; 360-degree transscleral cryotherapy; 360-degree laser photocoagulation; no treatment	0; 0	"No strong evidence in the literature was found to support or refute prophylactic 360-degree treatments to prevent a giant retinal tear or a retinal detachment in the fellow eye of patients with unilateral giant retinal tears."

Wilkinson 2014	25191970	"To assess the effectiveness and safety of techniques used to treat asymptomatic retinal breaks and lattice degeneration for the prevention of retinal detachment."	PVD, Retinal Breaks, & Lattice Degeneration	Any treatment of asymptomatic retinal breaks and lattice degeneration; control	0; 0	"No conclusions could be reached about the effectiveness of surgical interventions to prevent retinal detachment in eyeswith asymptomatic retinal breaks or lattice degeneration, or both."

eTable 6. Retinal Artery Occlusions: objectives, participants, interventions, and conclusions of the reliable systematic reviews, sorted by reverse chronological order of publication within intervention type

Study ID	PMID	Objective(s)	Participants	Intervention Comparisons	Number of Studies; Participants (or eyes)	Conclusion(s) from the abstract
Other interventions						
Fraser 2009	19160204	"To examine the effects of treatments used for acute non-arteritic central retinal artery occlusion (CRAO)."	Retinal and ophthalmic artery occlusions	Pentoxifylline; haemodilution; no EECP - haemodiluation only; placebo	2; 30	"The included studies in this review were small and from single centres. Neither study was completely clear about it's method of treatment allocation. One study described the use of pentoxifylline tablets (three 600 mg tablets daily) and the other the use of enhanced external counter pulsation (EECP) combined with haemodilution. Both studies indicated improved retinal perfusion in the non-control group but neither showed an improvement in vision.

Abbreviations: AMD = age-related macular degeneration; anti-VEGF = anti-vascular endothelial growth factor; BCVA = best corrected visual acuity; DME = diabetic macular edema; DMO = diabetic macular oedema; DR = diabetic retinopathy; IOL = intraocular lens; IOP = intraocular pressure; PDT = photodynamic therapy; PRN = pro re nata; RCT = randomized controlled trial; T&E = treat and extend; T2DM = type II diabetes

eTable 7. Retinal Vein Occlusions: objectives, participants, interventions, and conclusions of the reliable systematic reviews, sorted by reverse chronological order of publication within intervention type

Study ID	PMID	Objective(s)	Participants	Intervention Comparisons	Number of Studies; Participants (or eyes)	Conclusion(s) from the abstract
Anti-VEGF interventions						
Regnier 2015	26048209	"To compare the efficacy and safety of approved treatments for macular oedema secondary to branch retinal vein occlusion (BRVO)."	Retinal vein occlusions	Aflibercept; ranibizumab; dexamethasone; laser photocoagulation; placebo	8; 1,743	"There was no statistically significant difference between ranibizumab and aflibercept."
Ford 2014b	24513867	"To review systematically the randomised controlled trial (RCT) evidence for treatment of macular oedema due to central retinal vein occlusion(CRVO)."	Retinal vein occlusions	Aflibercept; bevacizumab; dexamethasone intravitreal implant; intravitreal injection of pegaptanib sodium; intravitreal triamcinolone; no treatment; sham injection	8; 1,714	"Bevacizumab, ranibizumab, aflibercept and triamcinolone appear to be effective in treating macular oedema secondary to central retinal vein occlusion."

Ford 2014a	25056974	"To indirectly compare aflibercept, bevacizumab, dexamethasone, ranibizumab and triamcinolone for treatment of macular oedema secondary to central retinal vein occlusion using a network meta-analysis (NMA)."	Retinal vein occlusions	Aflibercept; dexamethasone; ranibizumab; triamcinolone; sham injection; no treatment/no intervention/observation	7; 953	"We found no evidence of differences between ranibizumab, aflibercept, bevacizumab and triamcinolone for improving vision. The antivascular endothelial growth factors (VEGFs) are likely to be favoured because they are not associated with steroid induced cataract formation. Aflibercept may be preferred by clinicians because it might require fewer injections."
Braithwaite 2014	24788977	"To investigate the effectiveness and safety of anti-VEGF therapies for the treatment of macular oedema secondary to central retinal vein occlusion (CRVO)."	Retinal vein occlusions	Anti-VEGF agent, non-specific; no treatment/no intervention/observation ; placebo	6; 947	"Compared to no treatment, repeated intravitreal injection of anti-VEGF agents in eyes with central retinal vein occlusion (CRVO) macular oedema improved visual outcomes at six months. All agents were relatively well tolerated with a low incidence of adverse effects in the short term."

Glanville 2014	24447389	“To assess the efficacies of widely used treatments for macular oedema secondary to RVO and the feasibility of conducting indirect comparisons between these therapies”	Retinal vein occlusions	Ranibizumab; bevacizumab; dexamethasone IVT; laser photocoagulation; best supportive care; grid pattern photocoagulation; sham injections; mixed treatment comparisons	14; 2,633	“Data from RCTs for ranibizumab and dexamethasone IVT demonstrate that both new agents constitute significant improvements over the previously widely accepted standard of care (laser therapy) for the treatment of BRVO and CRVO. However, head-to-head studies are needed to assess the relative efficacies of licensed therapies for RVO”
Zhou 2014	24330277	"To evaluate the safety and efficacy of anti-VEGF therapy, thus providing high-quality evidence from a large sample for the clinical practice of anti-VEGF therapy in the treatment of macular oedema secondary to central retinal vein occlusion (CRVO)."	Retinal vein occlusions	Aflibercept; bevacizumab; ranibizumab; pegatanib; no treatment/no intervention/observation	6; 940	"Intravitreal anti-vascular endothelial growth factor injections were safe and effective for macular oedema secondary to central retinal vein occlusion. The efficacy was rapid and robust."

Mitry 2013	23440840	"To investigate the efficacy and safety of intravitreal anti-VEGF agents for preserving or improving vision in the treatment of macular edema (ME) secondary to branch retinal vein occlusion (BRVO)."	Retinal vein occlusions	Ranibizumab; bevacizumab; laser photocoagulation; sham injection	2; 427	"The available RCT evidence suggests that repeated treatment of non-ischaemic macular edema secondary to branch retinal vein occlusion (BRVO) with the anti-VEGF agent ranibizumab may improve clinical and visual outcomes at six and 12 months. However, the frequency of re-treatment has not yet been determined and the impact of prior or combined treatment with laser photocoagulation on the primary outcome is unclear. Results from ongoing studies should assess not only treatment efficacy but also, the number of injections needed for maintenance and longterm safety and the effect of any prior treatment."

Pielen 2013	24205253	"To evaluate efficacy and safety outcomes of intravitreal therapies for macular edema in CRVO and BRVO"	Retinal vein occlusions	Ranibizumab; bevacizumab; pegaptanib; aflibercept; triamcinolone; dexamethasone; fluocinolone; observation or sham injection in CRVO; sham injection and/or grid laser photocoagulation in BRVO	11; 3,352	"Anti-VEGF agents result in a promising gain of visual acuity, but require a high injection frequency. Dexamethasone implant might be an alternative, but comparison is impaired as the effect is temporary and it has not yet been tested in PRN regimen. The ocular risk profile seems to be favorable for anti-VEGF agents in comparison to steroids. Because comparative data from head-to-head trials are missing currently, clinicians and patients should carefully weigh the benefit-harm ratio."
Radiotherapy and laser interventions						

Lam 2015	25961835	"To examine the effects of macular grid laser photocoagulation in the treatment of macular oedema following branch retinal vein occlusion (BRVO)."	Retinal vein occlusions	Laser photocoagulation; pharmacologic treatment; no treatment/no intervention/observation	5; 108	"Moderate-quality evidence from one RCT supports the use of grid laser photocoagulation to treat macular oedema following branch retinal vein occlusion (BRVO).There was insufficient evidence to support the use of early gridlaser or subthreshold laser. There was insufficient evidence to show a benefit of intravitreal triamcinolone or anti-vascular endothelial growth factor (VEGF) over macular grid laser photocoagulation in BRVO."

McIntosh 2007	17397923	"To assess the evidence on interventions to improve visual acuity (VA) and to treat macular edema and/or neovascularization secondary to branch retinal vein occlusion (BRVO)."	Retinal vein occlusions	Laser photocoagulation; intravitreal triamcinolone-aflibercept (IVTA); intravitreal triamcinolone-aflibercept + macular grid laser therapy; hemodilution therapy; troxerutin therapy; no treatment/no intervention/observation ; placebo	12; 1,026	"There is limited level I evidence for any interventions for branch retinal vein occlusion (BRVO). The Branch Retinal Vein Occlusion Study (BVOS) showed that macular grid laser photocoagulation is an effective treatment for macular edema and improves vision in eyes with visual acuity (VA) of 20/40 to 20/200, and that scatter laser photocoagulation can effectively treat neovascularization. The effectiveness of many new treatments is unsupported by current evidence."
Other interventions						

Gewaily 2015	26352007	"To explore the effectiveness and safety of intravitreal steroids in the treatment of central retinal vein occlusion macular edema (CRVO-ME)."	Retinal vein occlusions	Intravitreal steroids; no treatment/no intervention/observation	2; 1,538	"The two RCTs reviewed herein provide insufficient evidence to determine the benefits of intravitreal steroids (IVS) for individuals with central retinal vein occlusion macular edema (CRVO-ME). The improvement in visual acuity noted in the SCORE trial should be interpreted with caution as outcome data were missing for a large proportion of the observation group. Adverse events were observed more often with IVS treatment compared with observation/no treatment."

Lazo-Langner 2010	20305141	"[To conduct] a systematic review and meta analysis of randomized trials evaluating the effect of low molecular weight heparin in patients with retinal vein occlusion."	Retinal vein occlusions	Low molecular weight heparin; aspirin	3; 238	"In patients with retinal vein occlusion treatment with low molecular weight heparin seems to be associated with improvement in the visual acuity and less adverse ocular outcomes. These benefits might differ in patients with central as opposed to branch retinal vein occlusion. Further studies are required to confirm these findings and clarify its benefits in specific subgroups of patients before definitive recommendations can be made."
Squizzato 2010	20126837	"To systematically summarize best available evidence on the acute treatment and on the secondary prevention of retinal vein occlusion (RVO) with antithrombotic and fibrinolytic drugs."	Retinal vein occlusions	Low-molecular-weight-heparin (LMWH); aspirin; ticlopidine; intravenous fibrinolytic therapy followed by warfarin or aspirin with either hemodilution or no treatment; no treatment/no intervention/observation ; placebo	6; 384	"[A]ntithrombotic therapy, in particular low-molecular-weight-heparin (LMWH), may be part of the therapeutic armamentarium for patients with recent onset RVO. No firm recommendation can be provided given the limited available evidence."

Mohamed 2007	17324695	"To assess the evidence for the effectiveness of interventions to improve visual acuity (VA) and prevent or treat neovascularization secondary to central retinal vein occlusion (CRVO)."	Retinal vein occlusions	Medical treatment; hemodilution; intravitreal steroids; laser photocoagulation; chorioretinal venous anastomosis; surgical procedures	17; NR	"This review found limited level I evidence for any intervention to improve visual acuity (VA) in patients with central retinal vein occlusion (CRVO). Panretinal photocoagulation resulted in regression of neovascularization. Hemodilution may improve vision in some patients, but the data conflict."

Abbreviations: AMD = age-related macular degeneration; anti-VEGF = anti-vascular endothelial growth factor; BCVA = best corrected visual acuity; DME = diabetic macular edema; DMO = diabetic macular oedema; DR = diabetic retinopathy; IOL = intraocular lens; IOP = intraocular pressure; PDT = photodynamic therapy; PRN = pro re nata; RCT = randomized controlled trial; T&E = treat and extend; T2DM = type II diabetes

eTable 8. Multiple retina/vitreous conditions: objectives, participants, interventions, and conclusions of the reliable systematic reviews, sorted by reverse chronological order of publication within intervention type

Study ID	PMID	Objective(s)	Participants	Intervention Comparisons	Number of Studies; Participants (or eyes)	Conclusion(s) from the abstract
Anti-VEGF interventions						
Poku 2014	25034629	"To assess the safety of intravitreal bevacizumab (IVB) as a monotherapy and to evaluate the relationship between quality of treatment and adverse events."	AMD (non specific); diabetic retinopathy, including diabetic macular edema	Bevacizumab; sham; no treatment/no intervention/observation	89; NR	"Available evidence demonstrates low rates of serious local and systemic adverse events following treatment. However, the role of intravitreal bevacizumab (IVB) quality in the incidence of adverse events remains unclear."
Cheng 2012	22829940	"To investigate the effects of intravitreal anti-VEGF on the risk of arterial thromboembolic events"	Neovascular (wet or exudative) AMD; "patients with ocular neovascular diseases, such as age-related macular degeneration, diabetic retinopathy, and retinal vein occlusion"	Any intravitreal anti-VEGF agent; no intravitreal active agent	13 total; 6 AMD; 4942	"The strength [of the] evidence suggests that the intravitreal use of anti-VEGF antibodies is not associated with an increased risk of arterial thromboembolic events."

Abbreviations: AMD = age-related macular degeneration; anti-VEGF = anti-vascular endothelial growth factor; BCVA = best corrected visual acuity; DME = diabetic macular edema; DMO = diabetic macular oedema; DR = diabetic retinopathy; IOL = intraocular lens; IOP = intraocular pressure; PDT = photodynamic therapy; PRN = pro re nata; RCT = randomized controlled trial; T&E = treat and extend; T2DM = type II diabetes

eTable 9. Steps for Searching to Support a Systematic Review

STEP	Suggested Instructions
1 – Develop your concepts	Start by identifying the minimum number of concepts necessary to represent your research question. Concepts should represent the Population, Intervention (or Exposure), and Comparison for your study. *Tip: Depending on the question, the Outcomes, Timepoints, and Setting may also be included as concepts.*
2 – Identify terms to represent concepts	Use a combination of controlled vocabulary (standardized terminology, such as Medical Subject Headings [MeSH] terms) and natural language terms (key words) to best represent your concepts. *Tip: Tools such as the National Library of Medicine (NLM) MeSH Database(https://www.ncbi.nlm.nih.gov/mesh) and the Yale MeSH Analyzer (http://mesh.med.yale.edu/) can help you identify new controlled vocabulary and additional search terms that may be relevant.*
3 – Combine concepts using Boolean operators	Use Boolean operators such as "OR", "NOT" and "AND" to combine search terms. *Tip: Using "NOT" to exclude terms that retrieve "false" hits may inadvertently exclude relevant records from the search [e.g. (NOT children) will exclude records that may be about both children AND adults].*
4 – Use unique search syntax and tools	Each database has specific rules, or syntax, for how to structure a search, as well as tools for ensuring search quality.
5 – Apply validated search filters (if appropriate)	Use specially-designed and tested search filters where appropriate. Use only filters that have been assessed for the reliability, performance, and accuracy. Search strategies with inappropriate or inadequate filters may not locate relevant studies. *Tip: The Cochrane Handbook (https://training.cochrane.org/handbook) provides search filters for identifying randomized trials in MEDLINE and EMBASE.*
6 – Evaluate search terms	Examine a sample of titles and abstracts from the initial search results to see whether they fit the research question. *Tip: Look for additional controlled vocabulary or key word terms that may have been missed.*
7 – Adapt search strategy for other databases	Each database has different syntax and tools. MeSH terms may have to be translated into a different controlled vocabulary or vice versa.
8 – Assess the quality of your search strategy	Guidelines and checklists, such as the Peer Review of Electronic Search Strategies (PRESS) Checklist (https://www.cadth.ca/resources/finding-evidence/press), to help you assess the quality of your search strategies.

eTable 10. Search Strategy

PubMed:

((((("Amaurosis Fugax"[Mesh Terms] OR "Amblyopia"[Mesh Terms] OR "Asthenopia"[Mesh Terms] OR "Blindness"[Mesh Terms] OR "Blindness, Cortical"[Mesh Terms] OR "Color Vision Defects"[Mesh Terms] OR "Conjunctival Diseases"[Mesh Terms] OR "Corneal Diseases"[Mesh Terms] OR "Diplopia"[Mesh Terms] OR "Eye Abnormalities"[Mesh Terms] OR "Eye Burns"[Mesh Terms] OR "Eye Diseases"[Mesh Terms] OR "Eye Diseases, Hereditary"[Mesh Terms] OR "Eye Foreign Bodies"[Mesh Terms] OR "Eye Hemorrhage"[Mesh Terms] OR "Eye Infections"[Mesh Terms] OR "Eye Injuries"[Mesh Terms] OR "Eye Injuries, Penetrating"[Mesh Terms] OR "Eye Manifestations"[Mesh Terms] OR "Eye Neoplasms"[Mesh Terms] OR "Eyelid Diseases"[Mesh Terms] OR "Hemianopsia"[Mesh Terms] OR "Lacrimal Apparatus Diseases"[Mesh Terms] OR "Lens Diseases"[Mesh Terms] OR "Night Blindness"[Mesh Terms] OR "Ocular Hypertension"[Mesh Terms] OR "Ocular Hypotension"[Mesh Terms] OR "Ocular Motility Disorders"[Mesh Terms] OR "Optic Nerve Diseases"[Mesh Terms] OR "Orbital Diseases"[Mesh Terms] OR "Photophobia"[Mesh Terms] OR "Pupil Disorders"[Mesh Terms] OR "Refractive Errors"[Mesh Terms] OR "Retinal Diseases"[Mesh Terms] OR "Scleral Diseases"[Mesh Terms] OR "Scotoma"[Mesh Terms] OR "Uveal Diseases"[Mesh Terms] OR "Vision Disorders"[Mesh Terms] OR "Vitreoretinopathy, Proliferative"[Mesh Terms] OR "Vitreous Detachment"[Mesh Terms] OR "Ophthalmologic Surgical Procedures"[Mesh] OR Abnormal Accommodation[tiab] OR Abnormal Color Vision[tiab] OR Abnormal Colour Vision[tiab] OR Abnormal Lacrimation[tiab] OR Abnormal Vision[tiab] OR Accommodative Disorder*[tiab] OR Amblyopia[tiab] OR Ametropia[tiab] OR Anisocoria[tiab] OR Anophthalmia[tiab] OR Anterior Chamber Haemorrhage[tiab] OR Anterior Chamber Hemorrhage[tiab] OR Aphakia[tiab] OR Aqueous Outflow Obstruction[tiab] OR Asthenopia[tiab] OR Balint's Syndrome[tiab] OR Blepharitis[tiab] OR Blepharospasm[tiab] OR Blindness[tiab] OR Blurred Vision[tiab] OR Cataract*[tiab] OR chalazia[tiab] OR chalazion[tiab] OR Chorioretinal Disorder*[tiab] OR Chorioretinitis[tiab] OR Choroid Diseases[tiab] OR Choroidal[tiab] OR Choroiditis[tiab] OR Chromatopsia[tiab] OR Conjunctival Disease*[tiab] OR Conjunctival Haemorrhage*[tiab] OR Conjunctival Hemorrhage*[tiab] OR Conjunctival Injur*[tiab] OR Conjunctival Ulceration*[tiab] OR Conjunctivitis[tiab] OR Corneal abrasion*[tiab] OR Corneal Deposit*[tiab] OR Corneal Disease*[tiab] OR Corneal Disorder*[tiab] OR Corneal Erosion*[tiab] OR Corneal Injur*[tiab] OR Corneal Oedema*[tiab] OR Corneal Opacity[tiab] OR Corneal Opacification[tiab] OR Corneal Ulceration*[tiab] OR Decreased Lacrimation[tiab] OR Decreased Vision[tiab] OR Defective Vision[tiab] OR Delayed Visual Maturation[tiab] OR Difficulty Seeing[tiab] OR Difficulty With Vision[tiab] OR Dim Vision[tiab] OR Diminished Vision[tiab] OR Diplopia[tiab] OR Disturbed Vision[tiab] OR Dry eye[tiab] OR Endophthalmitis[tiab] OR Epiphora[tiab] OR Episcleritis[tiab] OR Equatorial Staphyloma[tiab] OR Esotropia[tiab] OR Exophthalmos[tiab] OR Eye Abnormalit*[tiab] OR Eye Burn*[tiab] OR Eye Disease*[tiab] OR Eye Disorder*[tiab] OR Eye Edema*[tiab] OR Eye Foreign Bod*[tiab] OR Eye Hemorrhage*[tiab] OR Eye Haemorrhage*[tiab] OR Eye Infection*[tiab] OR Eye Injur*[tiab] OR Eye Malformation*[tiab] OR Eye Manifestation*[tiab] OR Eye Muscle Paralysis[tiab] OR Eye Neoplasm*[tiab] OR Eye Pain[tiab] OR Eye Swelling[tiab] OR Eye transplant*[tiab] OR Eyelid Disease*[tiab] OR Eyelid Disorder*[tiab] OR Eyelid Pain[tiab] OR Eyelid Retraction[tiab] OR Fixed Pupil*[tiab] OR Fuchs endothelial dystrophy[tiab] OR Glaucoma*[tiab] OR Hazy Vision[tiab] OR

Hemianopia[tiab] OR Hemianopsia[tiab] OR Hepatolenticular Degeneration[tiab] OR Hordeola [tiab] OR Hordeolum[tiab] OR Horner's Syndrome[tiab] OR Hypopyon[tiab] OR Impaired Vision[tiab] OR Impaired Visual Acuity[tiab] OR Interference With Vision[tiab] OR Iritis[tiab] OR Keratitis[tiab] OR Keratoconjunctivitis[tiab] OR Keratoconus[tiab] OR LASIK[tiab] OR LASEK[tiab] OR Lacrimal Apparatus Disease*[tiab] OR Lacrimal Disorder*[tiab] OR Lacrimal Duct Obstruction*[tiab] OR Legally Blind[tiab] OR Legal Blindness[tiab] OR Lens Disease*[tiab] OR Lens Disorder*[tiab] OR Lens Opacit*[tiab] OR Lens Subluxation[tiab] OR Localized Anterior Staphyloma[tiab] OR Low Vision[tiab] OR Macular Degeneration[tiab] OR Macular hole*[tiab] OR Macular Oedema*[tiab] OR Meibomianitis[tiab] OR Metastases to Eye*[tiab] OR Miosis[tiab] OR Mydriasis[tiab] OR Myopia[tiab] OR Night Blindness[tiab] OR Nystagmus[tiab] OR Ocular Degeneration[tiab] OR Ocular Discomfort[tiab] OR Ocular Disease*[tiab] OR Ocular Haemorrhage*[tiab] OR Ocular Hemorrhage*[tiab] OR Ocular Herpes[tiab] OR Ocular Hypertension[tiab] OR Ocular Hypotension[tiab] OR Ocular Infection*[tiab] OR Ocular Inflammation*[tiab] OR Ocular Injur*[tiab] OR Ocular Motility Disorders*[tiab] OR Ocular cancer*[tiab] OR Ocular carcinoma*[tiab] OR Ocular Neoplasm*[tiab] OR Ocular tumor*[tiab] OR Ocular Tumour*[tiab] OR Oculopath*[tiab] OR Open Wound of Ocular Adnexa[tiab] OR Ophthalmic Disorder*[tiab] OR Ophthalmological Disorder*[tiab] OR Ophthalmopathy[tiab] OR Optic Atrophy[tiab] OR Optic Nerve Disease*[tiab] OR Optic Nerve Disorder*[tiab] OR Optic Nerve glioma*[tiab] OR Optic Nerve Injur*[tiab] OR Optic Neuritis[tiab] OR Orbital Disease*[tiab] OR Orbital cancer*[tiab] OR Orbital carcinoma*[tiab] OR Orbital neoplasm*[tiab] OR Orbital tumor*[tiab] OR Orbital tumour*[tiab] OR Papilloedema[tiab] OR Partial Sight[tiab] OR Partial Vision Loss[tiab] OR Partially Sighted[tiab] OR Penetrating Eye Injur*[tiab] OR Periorbital Fat Herniation[tiab] OR (Periocular[tiab] AND carcinoma*[tiab]) OR Photalgia[tiab] OR Photophobia[tiab] OR Photopsia[tiab] OR Pigment Precipitation[tiab] OR Poor Vision[tiab] OR Posterior capsule opacification[tiab] OR Posterior Dislocation Of Lens[tiab] OR Posterior Synechiae[tiab] OR Problem Seeing[tiab] OR Problems Seeing[tiab] OR Proliferative Vitreoretinopathy[tiab] OR Pupil Disorder*[tiab] OR (Eye*[tiab] AND Redness[tiab]) OR Discharge of Eye*[tiab] OR Reduced Ability to See[tiab] OR Reduced Vision[tiab] OR Refraction Error*[tiab] OR Refractive Disorder*[tiab] OR Refractive Error*[tiab] OR Retinal Defect*[tiab] OR Retinal Deposit*[tiab] OR Retinal Detachment*[tiab] OR Retinal Disease*[tiab] OR Retinal Disorder*[tiab] OR Retinal Edema[tiab] OR Retinal Haemorrhage*[tiab] OR Retinal Hemorrhage*[tiab] OR Retinal Oedema[tiab] OR Retinal tear*[tiab] OR Retinitis[tiab] OR Retinoblastoma[tiab] OR Retinopath*[tiab] OR Retrobulbar Neuritis[tiab] OR Scleral Disease*[tiab] OR Scleral Staphyloma[tiab] OR Scleritis[tiab] OR Scotoma[tiab] OR Sight Impair*[tiab] OR Staphyloma Posticum[tiab] OR Strabismus[tiab] OR Subnormal Vision[tiab] OR Sunken Eye*[tiab] OR Symblepharon[tiab] OR Thrombosis Retinal Vein[tiab] OR Traumatic Hyphema[tiab] OR Tunnel Vision[tiab] OR Uveal Diseases*[tiab] OR Uveal Disorder*[tiab] OR Uveitis[tiab] OR Vision Defect*[tiab] OR Vision Deficienc*[tiab] OR Vision Disorder*[tiab] OR Vision Disturbance*[tiab] OR Vision Impair*[tiab] OR Vision Problem*[tiab] OR Visual Agnosia[tiab] OR Visual Defect*[tiab] OR Visual Difficult*[tiab] OR Visual Disorder*[tiab] OR Visual Disturbance*[tiab] OR Visual Field Constriction*[tiab] OR Visual Field Defect*[tiab] OR Visual Field Disorder*[tiab] OR Visual Impair*[tiab] OR Visual Loss[tiab] OR Visual Pathway Disorder*[tiab] OR Visual System Disorder*[tiab] OR Vitrectomy[tiab] OR Vitreous Detachment*[tiab] OR Vitreous Haemorrhage*[tiab] OR Vitreous Hemorrhage*[tiab] OR Vitreous Membranes And Strands[tiab] OR Vitreous Prolapse*[tiab] OR Vitreous Syneresis[tiab] OR Wavefront Aberration*[tiab] OR Weak

Vision[tiab] OR Wegener's granulomatosis[tiab] OR Wilson's Disease[tiab] OR Xerophthalmia[tiab]))
AND
(Cochrane Database Syst Rev[Ta] OR Search[tiab] OR Meta-Analysis[Pt] OR Medline[tiab] OR (Systematic[tiab] AND Review[tiab])))
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("animals"[MeSH Terms] NOT "humans"[MeSH Terms])))

Cochrane Library Search:
#1 "Abnormal Accommodation":ti,ab,kw or "Abnormal Color Vision":ti,ab,kw or "Abnormal Colour Vision":ti,ab,kw or "Abnormal Lacrimation":ti,ab,kw or "Abnormal Vision":ti,ab,kw or Accommodative:ti,ab,kw near/3 Disorder*:ti,ab,kw or Amblyopia:ti,ab,kw or Ametropia:ti,ab,kw or Anisocoria:ti,ab,kw or Anophthalmia:ti,ab,kw or "Anterior Chamber":ti,ab,kw near/3 Haemorrhage*:ti,ab,kw or "Anterior Chamber" Hemorrhage*:ti,ab,kw or Aphakia:ti,ab,kw or "Aqueous Outflow":ti,ab,kw near/3 Obstruction*:ti,ab,kw or Asthenopia:ti,ab,kw or "Balint's Syndrome":ti,ab,kw or Blepharitis:ti,ab,kw or Blepharospasm:ti,ab,kw or Blindness:ti,ab,kw or "Blurred Vision":ti,ab,kw or Cataract*:ti,ab,kw or chalazia:ti,ab,kw or chalazion:ti,ab,kw or Chorioretinal:ti,ab,kw near/3 Disorder*:ti,ab,kw or Chorioretinitis:ti,ab,kw or Choroid:ti,ab,kw near/3 Disease*:ti,ab,kw or Choroidal:ti,ab,kw or Choroiditis:ti,ab,kw or Chromatopsia:ti,ab,kw or Conjunctival:ti,ab,kw near/3 Disease*:ti,ab,kw or Conjunctival:ti,ab,kw near/3 Haemorrhage*:ti,ab,kw or Conjunctival:ti,ab,kw near/3 Hemorrhage*:ti,ab,kw or Conjunctival:ti,ab,kw near/3 Injur*:ti,ab,kw or Conjunctival:ti,ab,kw near/3 Ulceration*:ti,ab,kw or Conjunctivitis:ti,ab,kw or Corneal:ti,ab,kw near/3 abrasion*:ti,ab,kw or Corneal:ti,ab,kw near/3 Deposit*:ti,ab,kw or Corneal:ti,ab,kw near/3 Disease*:ti,ab,kw or Corneal:ti,ab,kw near/3 Disorder*:ti,ab,kw or Corneal:ti,ab,kw near/3 Erosion*:ti,ab,kw or Corneal:ti,ab,kw near/3 Injur*:ti,ab,kw or Corneal:ti,ab,kw near/3 Oedema*:ti,ab,kw or "Corneal Opacity":ti,ab,kw or "Corneal Opacification":ti,ab,kw or Corneal:ti,ab,kw near/3 Ulceration*:ti,ab,kw or "Decreased Lacrimation":ti,ab,kw or "Decreased Vision":ti,ab,kw or Defect*:ti,ab,kw near/3 Vision:ti,ab,kw or "Delayed Visual Maturation":ti,ab,kw or "Difficulty Seeing":ti,ab,kw or "Difficulty With Vision":ti,ab,kw or "Dim Vision":ti,ab,kw or "Diminished Vision":ti,ab,kw or Diplopia:ti,ab,kw or Disturb*:ti,ab,kw near/3 Vision:ti,ab,kw or "Dry eye":ti,ab,kw or Endophthalmitis:ti,ab,kw or Epiphora:ti,ab,kw 14335
#2 Episcleritis:ti,ab,kw or "Equatorial Staphyloma":ti,ab,kw or Esotropia:ti,ab,kw or Exophthalmos:ti,ab,kw or Eye:ti,ab,kw near/3 Abnormalit*:ti,ab,kw or Eye:ti,ab,kw near/3 Burn*:ti,ab,kw or Eye:ti,ab,kw near/3 Disease*:ti,ab,kw or Eye:ti,ab,kw near/3 Disorder*:ti,ab,kw or Eye:ti,ab,kw near/3 Edema*:ti,ab,kw or Eye:ti,ab,kw near/3 "Foreign Body":ti,ab,kw or Eye:ti,ab,kw near/3 "Foreign Bodies":ti,ab,kw or Eye:ti,ab,kw near/3 Hemorrhage*:ti,ab,kw or Eye:ti,ab,kw near/3 Haemorrhage*:ti,ab,kw or Eye:ti,ab,kw near/3 Infection*:ti,ab,kw or Eye:ti,ab,kw near/3 Injur*:ti,ab,kw or Eye:ti,ab,kw near/3 Malformation*:ti,ab,kw or Eye:ti,ab,kw near/3 Manifestation*:ti,ab,kw or "Eye Muscle":ti,ab,kw near/3 Paralysis:ti,ab,kw or Eye:ti,ab,kw near/3 Neoplasm*:ti,ab,kw or "Eye Pain":ti,ab,kw or Eye:ti,ab,kw near/3 Swelling:ti,ab,kw or Eye:ti,ab,kw near/3 transplant*:ti,ab,kw or Eyelid:ti,ab,kw near/3 Disease*:ti,ab,kw or Eyelid:ti,ab,kw near/3 Disorder*:ti,ab,kw or Eyelid:ti,ab,kw near/3 Pain:ti,ab,kw or Eyelid:ti,ab,kw near/3 Retraction:ti,ab,kw or Fixed:ti,ab,kw near/3 Pupil*:ti,ab,kw or "Fuchs endothelial dystrophy":ti,ab,kw or Glaucoma*:ti,ab,kw or "Hazy Vision":ti,ab,kw or Hemianopia:ti,ab,kw

or Hemianopsia:ti,ab,kw or "Hepatolenticular Degeneration":ti,ab,kw or Hordeola:ti,ab,kw or Hordeolum:ti,ab,kw or "Horner's Syndrome":ti,ab,kw or Hypopyon:ti,ab,kw or Impaired:ti,ab,kw near/3 Vision:ti,ab,kw or Impaired:ti,ab,kw near/3 "Visual Acuity":ti,ab,kw or "Interference With Vision":ti,ab,kw or Iritis:ti,ab,kw or Keratitis:ti,ab,kw or Keratoconjunctivitis:ti,ab,kw or Keratoconus:ti,ab,kw or LASIK:ti,ab,kw or LASEK:ti,ab,kw or "Lacrimal Apparatus":ti,ab,kw near/3 Disease*:ti,ab,kw or Lacrimal:ti,ab,kw near/3 Disorder*:ti,ab,kw or "Lacrimal Duct":ti,ab,kw near/3 Obstruction*:ti,ab,kw or "Legally Blind":ti,ab,kw or "Legal Blindness":ti,ab,kw or Lens:ti,ab,kw near/3 Disease*:ti,ab,kw or Lens:ti,ab,kw near/3 Disorder*:ti,ab,kw or Lens:ti,ab,kw near/3 Opacit*:ti,ab,kw or Lens:ti,ab,kw near/3 Subluxation:ti,ab,kw or "Localized Anterior Staphyloma":ti,ab,kw or "Low Vision":ti,ab,kw or "Macular Degeneration":ti,ab,kw or Macular:ti,ab,kw near/3 hole*:ti,ab,kw 13497

#3 Macular:ti,ab,kw near/3 Oedema*:ti,ab,kw or Meibomianitis:ti,ab,kw or Metastases:ti,ab,kw near/3 Eye*:ti,ab,kw or Miosis:ti,ab,kw or Mydriasis:ti,ab,kw or Myopia:ti,ab,kw or "Night Blindness":ti,ab,kw or Nystagmus:ti,ab,kw or "Ocular Degeneration":ti,ab,kw or "Ocular Discomfort":ti,ab,kw or Ocular:ti,ab,kw near/3 Disease*:ti,ab,kw or Ocular:ti,ab,kw near/3 Haemorrhage*:ti,ab,kw or Ocular:ti,ab,kw near/3 Hemorrhage*:ti,ab,kw or "Ocular Herpes":ti,ab,kw or "Ocular Hypertension":ti,ab,kw or "Ocular Hypotension":ti,ab,kw or Ocular:ti,ab,kw near/3 Infection*:ti,ab,kw or Ocular:ti,ab,kw near/3 Inflammation*:ti,ab,kw or Ocular:ti,ab,kw near/3 Injur*:ti,ab,kw or Ocular:ti,ab,kw near/1 Motility:ti,ab,kw near/3 Disorders*:ti,ab,kw or Ocular:ti,ab,kw near/3 cancer*:ti,ab,kw or Ocular:ti,ab,kw near/3 carcinoma*:ti,ab,kw or Ocular:ti,ab,kw near/3 Neoplasm*:ti,ab,kw or Ocular:ti,ab,kw near/3 tumor*:ti,ab,kw or Ocular:ti,ab,kw near/3 Tumour*:ti,ab,kw or Oculopath*:ti,ab,kw or "Ocular Adnexa":ti,ab,kw or Ophthalmic:ti,ab,kw near/3 Disorder*:ti,ab,kw or Ophthalmological:ti,ab,kw near/3 Disorder*:ti,ab,kw or Ophthalmopathy:ti,ab,kw or Optic:ti,ab,kw near/3 Atrophy:ti,ab,kw or "Optic Nerve":ti,ab,kw near/3 Disease*:ti,ab,kw or "Optic Nerve":ti,ab,kw near/3 Disorder*:ti,ab,kw or "Optic Nerve":ti,ab,kw near/3 glioma*:ti,ab,kw or "Optic Nerve":ti,ab,kw near/3 Injur*:ti,ab,kw or "Optic Neuritis":ti,ab,kw or Orbital:ti,ab,kw near/3 Disease*:ti,ab,kw or Orbital:ti,ab,kw near/3 cancer*:ti,ab,kw or Orbital:ti,ab,kw near/3 carcinoma*:ti,ab,kw or Orbital:ti,ab,kw near/3 neoplasm*:ti,ab,kw or Orbital:ti,ab,kw near/3 tumor*:ti,ab,kw or Orbital:ti,ab,kw near/3 tumour*:ti,ab,kw or Papilloedema:ti,ab,kw or "Partial Sight":ti,ab,kw or "Partial Vision Loss":ti,ab,kw or "Partially Sighted":ti,ab,kw or Penetrating:ti,ab,kw near/1 Eye:ti,ab,kw near/3 Injur*:ti,ab,kw or "Periorbital Fat Herniation":ti,ab,kw or Periocular:ti,ab,kw near/3 carcinoma*:ti,ab,kw or Photalgia:ti,ab,kw or Photophobia:ti,ab,kw or Photopsia:ti,ab,kw or "Pigment Precipitation":ti,ab,kw or "Poor Vision":ti,ab,kw or "Posterior capsule":ti,ab,kw near/3 opacification:ti,ab,kw or "Posterior Dislocation":ti,ab,kw near/3 Lens:ti,ab,kw or "Posterior Synechiae":ti,ab,kw or "Problem Seeing":ti,ab,kw or "Problems Seeing":ti,ab,kw or "Proliferative Vitreoretinopathy":ti,ab,kw or Pupil:ti,ab,kw near/3 Disorder*:ti,ab,kw or (Eye*:ti,ab,kw and Redness:ti,ab,kw) or Discharge:ti,ab,kw near/3 Eye*:ti,ab,kw or "Reduced Ability to See":ti,ab,kw or Reduc*:ti,ab,kw near/3 Vision:ti,ab,kw or Refraction:ti,ab,kw near/1 Error*:ti,ab,kw or Refractive:ti,ab,kw near/3 Disorder*:ti,ab,kw or Refractive:ti,ab,kw near/3 Error*:ti,ab,kw or Retina*:ti,ab,kw near/3 Defect*:ti,ab,kw or Retinal:ti,ab,kw near/1 Deposit*:ti,ab,kw or Retina*:ti,ab,kw near/3 Detachment*:ti,ab,kw or Retina*:ti,ab,kw near/3 Disease*:ti,ab,kw or Retina*:ti,ab,kw near/3 Disorder*:ti,ab,kw or Retina*:ti,ab,kw near/3 Edema*:ti,ab,kw or Retina*:ti,ab,kw near/3 Haemorrhage*:ti,ab,kw or Retina*:ti,ab,kw near/3 Hemorrhage*:ti,ab,kw or Retina*:ti,ab,kw near/3 Oedema*:ti,ab,kw or Retina*:ti,ab,kw near/3 tear*:ti,ab,kw or Retinitis:ti,ab,kw or Retinoblastoma:ti,ab,kw or Retinopath*:ti,ab,kw or

"Retrobulbar Neuritis":ti,ab,kw or Scleral:ti,ab,kw near/3 Disease*:ti,ab,kw or "Scleral Staphyloma":ti,ab,kw or Scleritis:ti,ab,kw or Scotoma:ti,ab,kw or Sight:ti,ab,kw near/3 Impair*:ti,ab,kw	13548	
#4	"Staphyloma Posticum":ti,ab,kw or Strabismus:ti,ab,kw or "Subnormal Vision":ti,ab,kw or Sunken:ti,ab,kw near/1 Eye*:ti,ab,kw or Symblepharon:ti,ab,kw or Thrombosis:ti,ab,kw near/3 "Retinal Vein":ti,ab,kw or Traumatic:ti,ab,kw near/1 Hyphema*:ti,ab,kw or "Tunnel Vision":ti,ab,kw or Uvea*:ti,ab,kw near/3 Diseases*:ti,ab,kw or Uvea*:ti,ab,kw near/3 Disorder*:ti,ab,kw or Uveitis:ti,ab,kw or Vision:ti,ab,kw near/3 Defect*:ti,ab,kw or Vision:ti,ab,kw near/3 Deficienc*:ti,ab,kw or Vision:ti,ab,kw near/3 Disorder*:ti,ab,kw or Vision:ti,ab,kw near/3 Disturbance*:ti,ab,kw or Vision:ti,ab,kw near/3 Impair*:ti,ab,kw or Vision:ti,ab,kw near/3 Problem*:ti,ab,kw or "Visual Agnosia":ti,ab,kw or Visual:ti,ab,kw near/3 Defect*:ti,ab,kw or Visual:ti,ab,kw near/3 Difficult*:ti,ab,kw or Visual:ti,ab,kw near/3 Disorder*:ti,ab,kw or Visual:ti,ab,kw near/3 Disturbance*:ti,ab,kw or "Visual Field":ti,ab,kw near/3 Constriction*:ti,ab,kw or "Visual Field":ti,ab,kw near/3 Defect*:ti,ab,kw or "Visual Field":ti,ab,kw near/3 Disorder*:ti,ab,kw or Visual:ti,ab,kw near/3 Impair*:ti,ab,kw or Visual:ti,ab,kw near/3 Loss:ti,ab,kw or "Visual Pathway":ti,ab,kw near/3 Disorder*:ti,ab,kw or "Visual System":ti,ab,kw near/3 Disorder*:ti,ab,kw or Vitrectomy:ti,ab,kw or Vitreous:ti,ab,kw near/3 Detachment*:ti,ab,kw or Vitreous:ti,ab,kw near/3 Haemorrhage*:ti,ab,kw or Vitreous:ti,ab,kw near/3 Hemorrhage*:ti,ab,kw or "Vitreous Membranes and Strands":ti,ab,kw or Vitreous:ti,ab,kw near/3 Prolapse*:ti,ab,kw or "Vitreous Syneresis":ti,ab,kw or Wavefront next/1 Aberration*:ti,ab,kw or Weak:ti,ab,kw next/1 Vision:ti,ab,kw or "Wegener's granulomatosis":ti,ab,kw or "Wilson's Disease":ti,ab,kw or Xerophthalmia:ti,ab,kw	7108	
#5	#1 or #2 or #3 or #4	33338
#6	MeSH descriptor: [Amaurosis Fugax] explode all trees	2
#7	MeSH descriptor: [Amblyopia] explode all trees	189
#8	MeSH descriptor: [Asthenopia] explode all trees	35
#9	MeSH descriptor: [Blindness] explode all trees	228
#10	MeSH descriptor: [Blindness, Cortical] explode all trees	2
#11	MeSH descriptor: [Color Vision Defects] explode all trees	39
#12	MeSH descriptor: [Conjunctival Diseases] explode all trees	1376
#13	MeSH descriptor: [Corneal Diseases] explode all trees	1245
#14	MeSH descriptor: [Diplopia] explode all trees	36
#15	MeSH descriptor: [Eye Abnormalities] explode all trees	23
#16	MeSH descriptor: [Eye Burns] explode all trees	25
#17	MeSH descriptor: [Eye Diseases] explode all trees	13868
#18	MeSH descriptor: [Eye Diseases, Hereditary] explode all trees	210
#19	MeSH descriptor: [Eye Foreign Bodies] explode all trees	32
#20	MeSH descriptor: [Eye Hemorrhage] explode all trees	178
#21	MeSH descriptor: [Eye Infections] explode all trees	953
#22	MeSH descriptor: [Eye Injuries] explode all trees	179
#23	MeSH descriptor: [Eye Injuries, Penetrating] explode all trees	17
#24	MeSH descriptor: [Eye Manifestations] explode all trees	118
#25	MeSH descriptor: [Eye Neoplasms] explode all trees	142
#26	MeSH descriptor: [Eyelid Diseases] explode all trees	293
#27	MeSH descriptor: [Hemianopsia] explode all trees	28
#28	MeSH descriptor: [Lacrimal Apparatus Diseases] explode all trees	730
#29	MeSH descriptor: [Lens Diseases] explode all trees	899

#30	MeSH descriptor: [Night Blindness] explode all trees	33
#31	MeSH descriptor: [Ocular Hypertension] explode all trees	2784
#32	MeSH descriptor: [Ocular Hypotension] explode all trees	28
#33	MeSH descriptor: [Ocular Motility Disorders] explode all trees	606
#34	MeSH descriptor: [Optic Nerve Diseases] explode all trees	317
#35	MeSH descriptor: [Orbital Diseases] explode all trees	411
#36	MeSH descriptor: [Photophobia] explode all trees	28
#37	MeSH descriptor: [Pupil Disorders] explode all trees	96
#38	MeSH descriptor: [Refractive Errors] explode all trees	1457
#39	MeSH descriptor: [Retinal Diseases] explode all trees	3487
#40	MeSH descriptor: [Scleral Diseases] explode all trees	11
#41	MeSH descriptor: [Scotoma] explode all trees	36
#42	MeSH descriptor: [Uveal Diseases] explode all trees	1002
#43	MeSH descriptor: [Vision Disorders] explode all trees	1263
#44	MeSH descriptor: [Vitreoretinopathy, Proliferative] explode all trees	46
#45	MeSH descriptor: [Vitreous Detachment] explode all trees	14
#46	MeSH descriptor: [Ophthalmologic Surgical Procedures] explode all trees	5535
#47	#6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46	15588
#48	#5 or #47	34994 (446 in Cochrane Reviews, 563 Other Reviews, 454 HTAs and 300 Economic Evaluations)

Embase:

1. 'transitional blindness'/exp OR 'amblyopia'/exp OR 'asthenopia'/exp OR 'blindness'/exp OR 'cerebral blindness'/exp OR 'color vision defect'/exp OR 'conjunctiva disease'/exp OR 'cornea disease'/exp OR 'diplopia'/exp OR 'eye malformation'/exp OR 'eye burn'/exp OR 'eye disease'/exp OR 'intraocular foreign body'/exp OR 'eye infection'/exp OR 'eye injury'/exp OR 'perforating eye injury'/exp OR 'endocrine ophthalmopathy'/exp OR 'eye disease assessment'/exp OR 'eye tumor'/exp OR 'eyelid disease'/exp OR 'hemianopia'/exp OR 'homonymous hemianopia'/exp OR 'lacrimal gland disease'/exp OR 'lens disease'/exp OR 'night blindness'/exp OR 'intraocular pressure abnormality'/exp OR 'glaucoma'/exp OR 'intraocular hypotension'/exp OR 'eye movement disorder'/exp OR 'optic nerve disease'/exp OR 'orbit disease'/exp OR 'photophobia'/exp OR 'pupil disease'/exp OR 'refraction error'/exp OR 'retina disease'/exp OR 'sclera disease'/exp OR 'uvea disease'/exp OR 'visual disorder'/exp OR 'vitreoretinopathy'/exp OR 'vitreous body detachment'/exp OR 'eye surgery'/exp
2. 'abnormal accommodation':ab,ti OR 'abnormal color vision':ab,ti OR 'abnormal colour vision':ab,ti OR 'abnormal lacrimation':ab,ti OR 'abnormal vision':ab,ti OR accommodative NEAR/3 disorder* OR amblyopia:ab,ti OR ametropia:ab,ti OR anisocoria:ab,ti OR anophthalmia:ab,ti OR 'anterior chamber' NEAR/3 haemorrhage* OR 'anterior chamber' NEAR/1 hemorrhage* OR aphakia:ab,ti OR 'aqueous outflow' NEAR/3 obstruction* OR asthenopia:ab,ti OR 'balints syndrome':ab,ti OR blepharitis:ab,ti OR blepharospasm:ab,ti OR blindness:ab,ti OR 'blurred vision':ab,ti

OR cataract*:ab,ti OR chalazia:ab,ti OR chalazion:ab,ti OR chorioretinal NEAR/3 disorder* OR chorioretinitis:ab,ti OR choroid NEAR/3 disease* OR choroidal:ab,ti OR choroiditis:ab,ti OR chromatopsia:ab,ti OR conjunctival NEAR/3 disease* OR conjunctival NEAR/3 haemorrhage* OR conjunctival NEAR/3 hemorrhage* OR conjunctival NEAR/3 injur* OR conjunctival NEAR/3 ulceration* OR conjunctivitis:ab,ti OR corneal NEAR/3 abrasion* OR corneal NEAR/3 deposit* OR corneal NEAR/3 disease* OR corneal NEAR/3 disorder* OR corneal NEAR/3 erosion* OR corneal NEAR/3 injur* OR corneal NEAR/3 oedema* OR 'corneal opacity':ab,ti OR 'corneal opacification':ab,ti OR corneal NEAR/3 ulceration* OR 'decreased lacrimation':ab,ti OR 'decreased vision':ab,ti OR defect* NEAR/3 vision OR 'delayed visual maturation':ab,ti OR 'difficulty seeing':ab,ti OR 'difficulty with vision':ab,ti OR 'dim vision':ab,ti OR 'diminished vision':ab,ti OR diplopia:ab,ti OR disturb* NEAR/3 vision OR 'dry eye':ab,ti OR endophthalmitis:ab,ti OR epiphora:ab,ti

3. episcleritis:ab,ti OR 'equatorial staphyloma':ab,ti OR esotropia:ab,ti OR exophthalmos:ab,ti OR eye NEAR/3 abnormalit* OR eye NEAR/3 burn* OR eye NEAR/3 disease* OR eye NEAR/3 disorder* OR eye NEAR/3 edema* OR eye NEAR/3 'foreign body' OR eye NEAR/3 'foreign bodies' OR eye NEAR/3 hemorrhage* OR eye NEAR/3 haemorrhage* OR eye NEAR/3 infection* OR eye NEAR/3 injur* OR eye NEAR/3 malformation* OR eye NEAR/3 manifestation* OR 'eye muscle' NEAR/3 paralysis OR eye NEAR/3 neoplasm* OR 'eye pain':ab,ti OR eye NEAR/3 swelling OR eye NEAR/3 transplant* OR eyelid NEAR/3 disease* OR eyelid NEAR/3 disorder* OR eyelid NEAR/3 pain OR eyelid NEAR/3 retraction OR fixed NEAR/3 pupil* OR 'fuchs endothelial dystrophy':ab,ti OR glaucoma*:ab,ti OR 'hazy vision':ab,ti OR hemianopia:ab,ti OR hemianopsia:ab,ti OR 'hepatolenticular degeneration':ab,ti OR hordeola:ab,ti OR hordeolum:ab,ti OR 'horner syndrome':ab,ti OR hypopyon:ab,ti OR impaired NEAR/3 vision OR impaired NEAR/3 'visual acuity' OR 'interference with vision':ab,ti OR iritis:ab,ti OR keratitis:ab,ti OR keratoconjunctivitis:ab,ti OR keratoconus:ab,ti OR lasik:ab,ti OR lasek:ab,ti OR 'lacrimal apparatus' NEAR/3 disease* OR lacrimal NEAR/3 disorder* OR 'lacrimal duct' NEAR/3 obstruction* OR 'legally blind':ab,ti OR 'legal blindness':ab,ti OR lens NEAR/3 disease* OR lens NEAR/3 disorder* OR lens NEAR/3 opacit* OR lens NEAR/3 subluxation OR 'localized anterior staphyloma':ab,ti OR 'low vision':ab,ti OR 'macular degeneration':ab,ti OR macular NEAR/3 hole*
4. macular NEAR/3 oedema* OR meibomianitis:ab,ti OR metastases NEAR/3 eye* OR miosis:ab,ti OR mydriasis:ab,ti OR myopia:ab,ti OR 'night blindness':ab,ti OR nystagmus:ab,ti OR 'ocular degeneration':ab,ti OR 'ocular discomfort':ab,ti OR ocular NEAR/3 disease* OR ocular NEAR/3 haemorrhage* OR ocular NEAR/3 hemorrhage* OR 'ocular herpes':ab,ti OR 'ocular hypertension':ab,ti OR 'ocular hypotension':ab,ti OR ocular NEAR/3 infection* OR ocular NEAR/3 inflammation* OR ocular NEAR/3 injur* OR ocular NEAR/1 motility NEAR/3 disorders* OR ocular NEAR/3 cancer* OR ocular NEAR/3 carcinoma* OR ocular NEAR/3 neoplasm* OR ocular NEAR/3 tumor* OR ocular NEAR/3 tumour* OR oculopath*:ab,ti OR 'ocular adnexa':ab,ti OR

ophthalmic NEAR/3 disorder* OR ophthalmological NEAR/3 disorder* OR ophthalmopath*:ab,ti OR optic NEAR/3 atrophy OR 'optic nerve' NEAR/3 disease* OR 'optic nerve' NEAR/3 disorder* OR 'optic nerve' NEAR/3 glioma* OR 'optic nerve' NEAR/3 injur* OR 'optic neuritis':ab,ti OR orbital NEAR/3 disease* OR orbital NEAR/3 cancer* OR orbital NEAR/3 carcinoma* OR orbital NEAR/3 neoplasm* OR orbital NEAR/3 tumor* OR orbital NEAR/3 tumour* OR papilloedema:ab,ti OR 'partial sight':ab,ti OR 'partial vision loss':ab,ti OR 'partially sighted':ab,ti OR penetrating NEAR/1 eye NEAR/3 injur* OR 'periorbital fat herniation':ab,ti OR periocular NEAR/3 carcinoma* OR photalgia:ab,ti OR photophobia:ab,ti OR photopsia:ab,ti OR 'pigment precipitation':ab,ti OR 'poor vision':ab,ti OR 'posterior capsule' NEAR/3 opacification OR 'posterior dislocation' NEAR/3 lens OR 'posterior synechiae':ab,ti OR 'problem seeing':ab,ti OR 'problems seeing':ab,ti OR 'proliferative vitreoretinopathy':ab,ti OR pupil NEAR/3 disorder* OR eye* NEAR/1 redness OR discharge NEAR/3 eye* OR 'reduced ability to see':ab,ti OR reduc* NEAR/3 vision OR refraction NEAR/1 error* OR refractive NEAR/3 disorder* OR refractive NEAR/3 error* OR retina* NEAR/3 defect* OR retinal NEAR/1 deposit* OR retina* NEAR/3 detachment* OR retina* NEAR/3 disease* OR retina* NEAR/3 disorder* OR retina* NEAR/3 edema* OR retina* NEAR/3 haemorrhage* OR retina* NEAR/3 hemorrhage* OR retina* NEAR/3 oedema* OR retina* NEAR/3 tear* OR retinitis:ab,ti OR retinoblastoma:ab,ti OR retinopath*:ab,ti OR 'retrobulbar neuritis':ab,ti OR scleral NEAR/3 disease* OR 'scleral staphyloma':ab,ti OR scleritis:ab,ti OR scotoma:ab,ti OR sight NEAR/3 impair*

5. 'staphyloma posticum':ab,ti OR strabismus:ab,ti OR 'subnormal vision':ab,ti OR sunken NEAR/1 eye* OR symblepharon:ab,ti OR thrombosis NEAR/3 'retinal vein' OR traumatic NEAR/1 hyphema* OR 'tunnel vision':ab,ti OR uvea* NEAR/3 diseases* OR uvea* NEAR/3 disorder* OR uveitis:ab,ti OR vision NEAR/3 defect* OR vision NEAR/3 deficienc* OR vision NEAR/3 disorder* OR vision NEAR/3 disturbance* OR vision NEAR/3 impair* OR vision NEAR/3 problem* OR 'visual agnosia':ab,ti OR visual NEAR/3 defect* OR visual NEAR/3 difficult* OR visual NEAR/3 disorder* OR visual NEAR/3 disturbance* OR 'visual field' NEAR/3 constriction* OR 'visual field' NEAR/3 defect* OR 'visual field' NEAR/3 disorder* OR visual NEAR/3 impair* OR visual NEAR/3 loss OR 'visual pathway' NEAR/3 disorder* OR 'visual system' NEAR/3 disorder* OR vitrectomy:ab,ti OR vitreous NEAR/3 detachment* OR vitreous NEAR/3 haemorrhage* OR vitreous NEAR/3 hemorrhage* OR 'vitreous membranes and strands':ab,ti OR vitreous NEAR/3 prolapse* OR 'vitreous syneresis':ab,ti OR wavefront NEXT/1 aberration* OR weak NEXT/1 vision OR 'wegeners granulomatosis':ab,ti OR 'wilsons disease':ab,ti OR xerophthalmia:ab,ti
6. #1 OR #2 OR #3 OR #4 OR #5
7. 'meta analysis':ti,ab OR medline:ti,ab OR 'systematic review':ti,ab
8. #6 AND #7

