Appendix C: Review protocols

	Details
Review question 1	What signs and symptoms should prompt a healthcare professional to suspect AMD in people presenting to healthcare services?
Objectives	To establish what signs and/or symptoms should raise suspicions about age-related macular degeneration in a person presenting to healthcare services
What the GC can recommend with this review	A list of signs and symptoms that should increase a healthcare professional's suspicion of a person having age related macular degeneration
What the GC will not be able to recommend	A list of signs and symptoms that will serve as a replacement for clinical judgement. The diagnostic accuracy of investigations or tests.
Type of review	Diagnostic
Language	English only
Study design	Systematic review Diagnostic cross-sectional study If insufficient evidence is available progress to: Case-control study
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) suspected of having AMD
Index test	Symptoms - development of: • Straight lines appearing crooked (distortion, metamorphosia) • Painless loss or blurring of central vision • Scotoma • Difficulty reading • Difficulty driving • Difficulty seeing fine detail (such as facial expressions and features and the need for brighter light than previously to read small print.). • Light glare. • Loss of (or decreased) contrast sensitivity (the ability to discern between different shades or 'luminances'). • Size or colour of objects appearing different with each eye (micropsia). • Delayed dark and light adaption (e.g. difficulty adjusting from bright to dim lighting) • Visual hallucinations (Charles Bonnet syndrome). Signs: • Reduced visual acuity (uniocular) • Breaks, waviness, or missing portions of the lines when looking at graph paper or Amsler grid (metamorphosia) On fundus examination (handheld diagnostic lens, biomicroscopy, slit lamp fundoscopy, ophthalmoscopy): • Drusen • Pigmentary, exudative, haemorrhagic, or atrophic changes affecting the macula.

	Details
	• Cystoid macular oedema and (rarely) choroidal polyps • Pigment epithelial detachment • Breaks in Bruch's membrane (angioid streaks, lacquer cracks, choroidal splits) • Pseudo-vitelliform degeneration
Reference standard	Confirmed diagnosis of AMD – early AMD or geographic atrophy diagnosis based on colour photos or fundoscopy, neovascular AMD diagnosed based on FFA.
Outcomes	Diagnostic accuracy of any one feature or group of features for AMD, neovascular AMD or geographic atrophy: • Accuracy metrics (Sensitivity, Specificity, PPV (positive predictive value), NPV (negative predictive value), likelihood ratios (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender Visual acuity Refractive myopia AMD disease stage Comorbidities affecting the eye (e.g. cataracts) Other co-morbidities

	Details
Review question 2	What risk factors increase the likelihood of a person developing AMD or progressing to late AMD?
Objectives	1) To determine which risk factors increase the likelihood of a person developing AMD 2) To determine which risk factors increase the likelihood of progressing to late AMD in an eye that already has AMD.
What the GC can recommend with this review	The GC will be able to recommend a list of risk factors that are useful in raising suspicion of AMD and the progression of AMD
What the GC will not be able to recommend	The GC will not be able to recommend risk stratification models or scores.
Type of review	Prognostic
Language	English only
Study design	Any observational study that presents multivariate adjustment using regression analysis
Status	Published papers only (full text) No date restrictions
Population	1) Adults (18 years and older) at risk of developing AMD. 2) Adults (18 years and older) who have been diagnosed with AMD in either eye who have not yet progressed to late AMD.
Variable	Ocular risk factors: • Refractive status (may be hard to interpret as neovascularisation could be as a result of myopia) • Iris colour

	Details
	• Cataract surgery (including lens replacement surgery) • Presence of AMD in the other eye • Drusen • Pseudo reticular drusen • Angioid streaks • Other pigmentary changes (RPE- retinal pigment epithelium) • Pseudovitelliform macular dystrophy • Pigment epithelial detachment (PED) • Cystoid macular oedema • Atrophy • Lifestyle: • Smoking • Diet and nutrition • Obesity (BMI) • Alcohol consumption • Exercise • Sunlight exposure Medical risk factors: • Hypertension • Hypercholesterolemia • Hypertriglyceridemia • Coronary/vascular disease • Cerebrovascular disease • Diabetes • Family history of AMD • Anticoagulant medication • Anti-platelet medication Other: • Gender • Race • Age • Socio-economic status
Outcomes	The risk of development of: • Any AMD • Early AMD • Geographic atrophy • Neovascular AMD
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Conference abstract • Grey literature
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender

	Details
Review question 3a	What information do people with suspected or confirmed AMD and their family members or carers find useful, and in what format (for example written or oral), and when?
Objectives	To establish what information people with suspected AMD and their family members or carers find useful and when. To establish what format of information people with suspected AMD and their family members or carers find useful and when.
What the GC can recommend with this review	A bullet pointed list of information that people with suspected AMD and their family members or carers should receive.
What the GC will not be able to recommend	What kinds of information people with confirmed AMD and their family members or carers should receive (to be covered below in part b)
Type of review	Qualitative
Language	English only
Study design	Qualitative studies Mixed-methods studies Survey studies
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) suspected of having first presentation of AMD
Themes	Salient Information needs might include: • Signs and symptoms of AMD • Pre-existing risk factors for the development of AMD, including genetic risk factors • What is AMD and the difference between wet, dry and early forms of the disease • Causes of AMD • Behavioural and therapeutic strategies available to reduce the risk of AMD or slow the progression of the disease • Investigations used for the diagnosis of AMD • Who to contact if deterioration in vision is suspected e.g. GP, eye clinic, optometrist Formats might include: • Written information • Font size, format and paper type • Accessible language • Video • Audio • Websites and apps
Outcomes	Qualitative evidence summary (thematic analysis): • Quotes, and authors analysis • Summary of themes
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age

	Details
	Gender Visual acuity AMD disease stage Comorbidities affecting the eye (e.g. cataracts) Other co-morbidities

	Details
Review question 3b	What information do people with suspected or confirmed AMD and their family members or carers find useful, and in what format (for example written or oral), and when?
Objectives	To establish what information people with confirmed AMD and their family members or carers find useful. To establish what format of information people with confirmed AMD and their family members or carers find useful.
What the GC can recommend with this review	A bullet pointed list of information that people with confirmed AMD and their family members or carers should receive.
What the GC will not be able to recommend	What kinds of information people with suspected AMD and their family members or carers should receive (covered above in part a).
Type of review	Qualitative
Language	English only
Study design	Topical survey Thematic survey Conceptual thematic description Interpretive explanation Mixed-methods studies
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) with diagnosed AMD
Intervention	Salient Information needs might include: • Signs and symptoms of AMD; • What is AMD and the difference between wet, dry and early forms of the disease; • Causes of AMD • Behavioural and therapeutic strategies available to reduce the risk of AMD or slow the progression of the disease. • Investigations used for the diagnosis of AMD • Who to contact if deterioration in vision is suspected e.g. retinal clinic, optometrist; • Management strategies available if early/indeterminate or geographic atrophy occurs • Therapeutic strategies available if neovascular AMD occurs and information about treatment experience • Adverse effects and who to contact • Success rates of treatment • Patient experience of treatment • Low vision support (strategies, tools, daily living advice, access to work employment)

	Details
	• signposting to other services and sources of information (for instance helplines, financial support, support groups) • Driving and DVLA laws • Possible effect on other activities of daily living. • Purpose and value of CVI registration and definitions of legal blindness • Smoking cessation advice and support • Psychological support • Prognosis and treatment plan (including frequency of administration required) • Information about progress of treatment (success/failure) • Home monitoring, how to do it and how often. Local pathways to re-referral if vision changes. • Possible complications, their likelihood and who to contact (for example Charles Bonnet Syndrome) Formats might include: • Written information • Font size, format and paper type • Accessible language • Video • Audio • Websites and apps
Comparator	Usual care, or not applicable for qualitative studies
Outcomes	Qualitative evidence summary: • Quotes, and authors analysis • Summary of themes
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender Visual acuity AMD disease stage Comorbidities affecting the eye (e.g. cataracts) Other co-morbidities Time since diagnosis

	Details
Review question 4a	What tools are useful for triage, diagnosis, informing treatment and determining management in people with suspected AMD?
Objectives	To establish the risks, benefits and accuracy of tools to assess and diagnose early AMD
What the GC can recommend with this review	The most appropriate tool for use in confirming the diagnosis of early AMD in people with suspected AMD.
What the GC will not be able to recommend	The most appropriate tool for use in confirming the diagnosis of geographic atrophy AMD in people with suspected or diagnosed AMD. (part b)

	Details
	The most appropriate tool for use in confirming the diagnosis of neovascular AMD in people with suspected or diagnosed AMD. (part c) The most appropriate tool for use in the self-monitoring of people with AMD (covered in a different question) The most appropriate tool for use in the monitoring of people with neovascular AMD (covered in a different question)
Type of review	Diagnostic
Language	English only
Study design	Systematic review Diagnostic cross-sectional study
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) with suspected AMD
Index test	Focus fundoscopy (slit lamp fundoscopy, biomicroscopy (dilated or non-dilated))
Reference standard	Ocular coherence tomography [including Fourier, spectral domain (OCT)]
Outcomes	Clinical utility or diagnostic test accuracy (critical) including: • Sensitivity • Specificity • Positive predictive value • Negative predictive value • Likelihood ratios, diagnostic odds ratio • Area under the ROC analyses. Safety and adverse events (important) Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published • Self-administered tests
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender Visual acuity AMD disease stage Comorbidities affecting the eye (e.g. cataracts)

	Details
Review question 4b	What tools are useful for triage, diagnosis, informing treatment and determining management in people with suspected AMD?
Objectives	To establish the risks, benefits and accuracy of tools to assess and diagnose geographic atrophy
What the GC can recommend with this review	The most appropriate tool for use in confirming the diagnosis of geographic atrophy in people with suspected or diagnosed AMD.
What the GC will not be able to recommend	The most appropriate tool for use in confirming the diagnosis of early AMD in people with suspected AMD. (part a)

	Details
	The most appropriate tool for use in confirming the diagnosis of neovascular AMD in people with suspected or diagnosed AMD. (part c) The most appropriate tool for use in the self-monitoring of people with AMD (covered in a different question) The most appropriate tool for use in the monitoring of people with neovascular AMD (covered in a different question)
Type of review	Diagnostic
Language	English only
Study design	Systematic review Diagnostic cross-sectional study
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) with AMD
Index test	• Fundus autofluorescence, • Focus fundoscopy (slit lamp fundoscopy, biomicroscopy (dilated or non-dilated)) • FFA • ICG
Reference standard	Ocular coherence tomography (OCT) (for example, spectral domain OCT)
Outcomes	Clinical utility or diagnostic test accuracy (critical) including: • Sensitivity • Specificity • Positive predictive value • Negative predictive value, • Likelihood ratios, • Diagnostic odds ratio • Area under the ROC analyses. Safety and adverse events (important) Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published
Baseline characteristics to be extracted in evidence tables	Ethnic group Age Gender Visual acuity AMD disease stage Comorbidities affecting the eye (e.g. cataracts)

	Details
Review question 4c	What tools are useful for triage, diagnosis, informing treatment and determining management in people with suspected AMD?
Objectives	To establish the risks, benefits and accuracy of tools to assess and diagnose neovascular AMD
What the GC can recommend with this review	The most appropriate tool for use in confirming the diagnosis of neovascular AMD in people with suspected or diagnosed AMD.

	Details
What the GC will not be able to recommend	The most appropriate tool for use in confirming the diagnosis of early AMD in people with suspected AMD. (part a) The most appropriate tool for use in confirming the diagnosis of geographic atrophy in people with suspected or diagnosed AMD. (part b) The most appropriate tool for use in the self-monitoring of people with AMD (covered in a different question) The most appropriate tool for use in the monitoring of people with neovascular AMD (covered in a different question)
Type of review	Diagnostic
Language	English only
Study design	Systematic review Diagnostic cross-sectional study
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) with suspected AMD
Variable	• Slit lamp fundoscopy, (biomicroscopy) (dilated or non-dilated) • Fundus autofluorescence, • Ocular coherence tomography (OCT) (for example, spectral domain OCT) • Indocyanine green angiography. (ICG angiography) • FFA plus OCT
Comparator	• Fundus fluorescein angiography (FFA) for classic and mixed nvAMD • ICG angiography reference standard for occult nvAMD and polyps • OCT for PED [if there are any studies that give long term follow up confirmation of nvAMD this is an acceptable reference standard]
Outcomes	Clinical utility or diagnostic test accuracy (critical) including: • Sensitivity • Specificity • Positive predictive value • Negative predictive value, • Likelihood ratios • Diagnostic odds ratio • Area under the ROC analyses. Safety and adverse events (important) Resource use and costs (criticial)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published
Baseline characteristics to be extracted in evidence tables	Ethnic group Age Gender Visual acuity AMD disease stage Comorbidities affecting the eye (e.g. cataracts)

	Details
Review question 5	How do different organisational models and referral pathways for triage, diagnosis, ongoing treatment and follow up influence outcomes for people with suspected AMD (for example correct diagnosis, errors in diagnosis, delays in diagnosis, process outcomes)?
Objectives	To establish what models of service organisation are most effective for the triage, diagnosis, treatment and follow up of people with suspected AMD.
What the GC can recommend with this review	The committee can recommend an organisational model that will help to reduce inappropriate referrals, reduce patient waiting time and reduce burden on the retinal clinic.
What the GC will not be able to recommend	N/A
Type of review	Intervention
Language	English only
Study design	RCT Cohort study design If insufficient evidence progress to Non-randomised studies including retrospective case-control study, Implementation studies) Before and after observational study (case series)
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) suspected of AMD
Intervention	Telemedicine and virtual retinal clinics Triage through fast track clinics Triage through optometrist services Two stop and one stop models of care. Direct referral from GP, Optometrist or emergency services to retinal clinic Alternative referral pathways: including Optometrist to GP to retinal clinic, referral to the general hospital eye services
Comparator	Any of the above
Outcomes	• Clinical outcomes (visual acuity (LogMAR), disease stage progression) (critical) • Safety and adverse events (important) • Error in diagnosis (important) • Time to diagnosis/treatment/follow up (important) • Number of people seen (i.e. number of people being referred) (important) • Patient satisfaction • Appointment attendance and non-attendance (important) • Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Case studies • Abstract/non-published

	Details
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender Visual acuity Comorbidities affecting the eye (e.g. cataracts) Other co-morbidities

	Details
Review question 6	What effective classification tool should be used to classify different types of AMD?
Objectives	To establish the best available classification system or grading scale for people with diagnosed AMD.
What the GC can recommend with this review	A classification system or grading scale that should be applied following the diagnosis of people with AMD for the information of people with AMD.
What the GC will not be able to recommend	A risk stratification or prediction system for people who have not yet developed AMD or have early AMD.
Type of review	Prognostic and validation studies.
Language	English only
Study design	Any descriptive study that presents a classification of AMD as a whole or the subtypes of late wet (neovascular) AMD. Any observational study that presents multivariate adjustment using regression analysis (hazard ratios and time adjusted odds ratios).
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) with AMD
Variable	Classification and stratification tools for age related macular degeneration, including: • Wisconsin Age-Related Maculopathy Grading Scheme (WARMGS) • Early age-related maculopathy international classification system (ARM) • Age Related Eye Disease Study (AREDS) • Clinical Age-Related Maculopathy Staging System (CARMS) • International Classification for age related macular degeneration (IC) • Other classification systems used for the subtyping of late wet (neovascular) AMD • Other prediction models based on retinal, choroidal and/or functional features.
Comparator	Not applicable
Outcomes	Risk outcomes: time-adjusted odds ratios , adjusted hazard ratios • The risk of progression (developing geographic atrophy or developing neovascularisation) • The risk of developing end stage vision problems (for example eligibility for certificate of vision impairment) Validation outcomes Patient understanding
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published

	Details
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender Visual acuity AMD disease stage Comorbidities affecting the eye (e.g. cataracts) Current or previous treatment

	Details
Review question 7a	What is the effectiveness of strategies to reduce the risk of developing AMD in the unaffected eye or slow the progression of AMD?
Objectives	To determine whether strategies to reduce the risk of developing AMD can prevent the development of AMD in the unaffected eye.
What the GC can recommend with this review	A list of strategies that help prevent the development of AMD in an unaffected eye in those who have already developed AMD in the fellow eye. A list of strategies that will not prevent the development of AMD in the unaffected eye.
What the GC will not be able to recommend	A list of strategies for the primary prevention of AMD. Whether certain effective strategies are “more effective” than others.
Type of review	Intervention
Language	English only
Study design	RCT Systematic review of RCTs
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) with AMD in one eye and an eye without AMD
Intervention	Comparative or head to head trials of: • Smoking cessation • Antioxidant and carotenoids rich diet • Omega 3 fatty acids rich diet or supplementation • Vitamin supplementation • Mineral supplementation • Statins • Exercise • Weight loss interventions
Comparator	Placebo or usual care (including basic advice to stop smoking)
Outcomes	Clinical outcomes (critical): • Development of neovascular AMD • Development of geographic atrophy • Development of VA loss due to AMD (LogMAR: for example, loss of 3 or more lines of visual acuity) Safety and adverse events (important) Health related quality of life (important) Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language

	Details
	• Length of follow-up less than 1 year • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender Visual acuity Comorbidities affecting the eye (e.g. cataracts, cancer all types) Smokers and non-smokers

	Details
Review question 7b	What is the effectiveness of strategies to reduce the risk of developing AMD in the unaffected eye or slow the progression of AMD?
Objectives	To determine whether strategies to slow the progression of AMD can prevent the development of late AMD in an eye with an earlier stage of the disease.
What the GC can recommend with this review	A list of strategies that can slow the progression of AMD in an eye with early AMD. A list of strategies that will not slow the progression of AMD in an eye with early AMD.
What the GC will not be able to recommend	Whether certain effective strategies are “more effective” than others.
Type of review	Intervention
Language	English only (translated studies will be accepted where available)
Study design	RCT Systematic review of RCTs
Status	Published papers only (full text) No date restrictions
Population	b) Adults (18 years and older) with early AMD in one or both eyes.
Intervention	Comparative or head to head trials of: • Smoking cessation, • Antioxidant and carotenoids rich diet, • Omega 3 fatty acids rich diet or supplementation, • Vitamin supplementation, • Mineral supplementation, • Statins • Laser treatment of drusen. • Exercise • Weight loss interventions
Comparator	Placebo or usual care (including basic advice to stop smoking)
Outcomes	Clinical outcomes (critical): • Development of neovascular AMD • Development of geographic atrophy • Development of VA loss due to AMD (for example, loss of 3 or more lines of visual acuity) Safety and adverse events (important) Functional capacity, participation, independence and ability to carry out activities of daily living (important) Health related quality of life (important)

	Details
	Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Length of follow-up less than 1 year • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender Visual acuity Comorbidities affecting the eye (e.g. cataracts, cancer all types) Smokers and non-smokers

	Details
Review question 8	What is the effectiveness of psychological therapies for AMD?
Objectives	To establish the effective psychological therapies to manage the mental wellbeing of people with AMD.
What the GC can recommend with this review	What psychological therapies are effective in people with AMD.
What the GC will not be able to recommend	Which effective psychological therapy provides the most benefit.
Type of review	Intervention
Language	English only
Study design	RCT and systematic review only If insufficient evidence (or very low quality RCT evidence) progress to cohort evidence.
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) with AMD
Intervention	Comparative trials of psychological and psychosocial interventions: • CBT (cognitive behavioural therapy including computerised CBT), mindfulness • Self-management • Problem solving treatment • Peer support • Befriending services (formalised, volunteer) • Sight loss counselling
Comparator	Usual care, or being on a waiting list for psychological therapy (deferred treatment).
Outcomes	• Clinical outcomes (critical): ○ Anxiety and depression ○ Patient satisfaction • Functional capacity, participation, independence and ability to carry out activities of daily living (important) • Health related quality of life (important) • Impact on carers (important) • Safety and adverse events (including suicide and parasuicide) • Resource use and costs (critical)

	Details
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender Visual acuity Comorbidities affecting the eye (e.g. cataracts) Other co-morbidities (people with other sensory loss) Time since diagnosis of AMD Time since visual impairment due to AMD Disease stage

	Details
Review question 9	What is the effectiveness of support strategies for people with visual impairment and AMD (for example reablement services and strategies for optimising existing visual performance)?
Objectives	To establish the risks and benefits of support strategies for people with visual loss and AMD.
What the GC can recommend with this review	Support strategies that would be appropriate for the support of people with AMD and vision loss.
What the GC will not be able to recommend	Psychological or psychosocial therapies that would be appropriate for the support of people with AMD. (covered in a separate question)
Type of review	Intervention
Language	English only
Study design	Systematic review Randomised controlled trial If no evidence is available progress to: Cohort study
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) with AMD and vision impairment
intervention	Low vision services including: • Sensory impairment team (including rehabilitation officers, sight loss advisor, ECLO) or low vision services at home, in the community or in secondary care. • Orientation and mobility programmes • Magnifiers, optical devices and low vision aids. • Daily living aids or assistive technologies
Comparator	Usual care (or waiting list)
Outcomes	• Clinical outcomes (critical): ○ Anxiety and depression ○ Patient satisfaction • Functional capacity, participation, independence and ability to carry out activities of daily living (important) • Health related quality of life (important)

	Details
	• Impact on carers (important) • Safety and adverse events (important) • Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender Baseline visual acuity AMD disease stage (including first or second eye) Comorbidities affecting the eye (e.g. cataracts)

	Details
Review question 10	What is the effectiveness of treatment of neovascular AMD in people presenting with visual acuity better than 6/12?
Objectives	To determine the effectiveness of first-line anti-angiogenic therapy in people presenting with visual acuity better than 6/12
What the GC can recommend with this review	Whether to offer first-line antiangiogenic therapy (as recommended in review question 12 and 18) in people presenting with neovascular AMD and visual acuity better than 6/12
What the GC will not be able to recommend	The type and frequency of anti-angiogenic therapy to be given (to be agreed in review questions 12 and 18) The benefit of adjunctive or combination therapy compared to monotherapy (covered in another question) When treatment should be stopped or switched (covered in another question) The most effective second line therapy (covered in another question)
Type of review	Intervention
Language	English only
Study design	Systematic review RCT Cohort study
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) diagnosed with neovascular AMD presenting with visual acuity better than 6/12
Intervention	First-line therapy (as recommended in review question 12 and 18
Comparator	Placebo No treatment (monitoring)
Outcomes	• Clinical outcomes (critical): visual acuity (LogMAR) • Safety and adverse events (important) • Functional capacity, participation, independence and ability to carry out activities of daily living (important) • Health related quality of life (important) • Impact on carers (important) • Resource use and costs (critical)

	Details
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Age Gender Ethnic group Comorbidities affecting the eye, e.g. cataracts, myopia, diabetes, mixed vascular dementia Blood pressure Anticoagulant treatment Statins Baseline visual acuity in study and fellow eye Status of fellow eye (ie first or second) Other general health co morbidities Smoking Subgroups: retinal angiomatous proliferation, classic, occult, mixed classic/occult, pigment epithelial detachment

	Details
Review question 11	What are the factors that suggest treatment should be switched or stopped for people diagnosed with neovascular AMD? a) What are the indicators for treatment failing and switching?
Objectives	a) To describe the clinical features associated with treatment failure b) To describe the clinical features associated with treatment futility c) To describe the clinical features associated with treatment remission
What the GC can recommend with this review	A list of clinical features that suggest that treatment should be switched A list of clinical features that suggest treatment should be stopped A list of clinical features that suggest that some one has gone into remission and should be monitored
What the GC will not be able to recommend	The most effective agent to switch on to when treatment has failed or is contraindicated (covered in another review question).
Type of review	Intervention Guidelines
Language	English only
Study design	RCT Cohort studies Reviews and guidance describing stopping rules and switching rules (citation search of these studies)
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) being treated for neovascular AMD
Intervention	Different criteria for: • Remission and monitoring • Switching treatment • Stopping treatment or discharge
Comparator	Not stopping or switching treatment in someone with one or more of the above clinical features.

	Details
Outcomes	• Clinical outcomes (critical): Visual acuity (LogMAR), [for example, dichotomous outcomes (such as loss of 15 or more letters) • Safety and adverse events (important) • Functional capacity, participation, independence and ability to carry out activities of daily living (important) • Health related quality of life (important) • Impact on carers (important) • Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Age Gender Ethnic group Comorbidities affecting the eye, e.g. cataracts, myopia, diabetes, mixed vascular dementia Blood pressure Anticoagulant treatment Statins Baseline visual acuity in study and fellow eye Status of fellow eye (ie first or second) Other general health co morbidities Smoking Subgroups analysis will be performed if heterogeneity is found, including following subgroups: retinal angiomatous proliferation, classic, occult, mixed classic/occult, pigment epithelial detachment, polyps, CSR pattern/ CSR-like AMD

	Details
Review question 12	What is the effectiveness of different anti-angiogenic therapies (including photodynamic therapy) for the treatment of neovascular AMD?
Objectives	To determine the most effective anti-angiogenic therapy for the treatment of neovascular AMD.
What the GC can recommend with this review	The comparative effectiveness of different anti-angiogenic monotherapy for treatment of neovascular AMD (also using evidence from the review on frequency of administration). Which anti-angiogenic therapies should not be used.
What the GC will not be able to recommend	The best frequency of administration or schedule with which to deliver these treatments. (covered in another question) The benefit of adjunctive or combination therapy compared to monotherapy (covered in another question) When treatment should be started, stopped or switched (covered in another question) The best second line therapy (covered in another question)

	Details
Type of review	Intervention
Language	English only (translated studies will be accepted where available)
Study design	RCT and systematic review of RCTs
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) diagnosed with neovascular AMD (treatment naïve)
Intervention	Comparative trials of: • Aflibercept • Bevacizumab • Ranibizumab • Photodynamic therapy • Placebo • No treatment
Comparator	Any of the above
Outcomes	• Clinical outcomes (critical): Visual acuity (LogMAR) • Safety and adverse events (important) • Functional capacity, participation, independence and ability to carry out activities of daily living (important) • Health related quality of life (important) • Impact on carers (important) • Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Studies without follow-up of at least 1 year • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Age Gender Ethnic group Comorbidities affecting the eye, e.g. cataracts, myopia, diabetes, mixed vascular dementia Blood pressure Anticoagulant treatment Statins Baseline visual acuity in study and fellow eye Status of fellow eye (ie first or second) Other general health co morbidities Smoking Subgroups: retinal angiomatous proliferation, classic, occult, mixed classic/occult, pigment epithelial detachment

	Details
Review question 13	What is the effectiveness of adjunctive therapies for the treatment of late wet active AMD?
Objectives	To determine the benefit of adjunctive therapies over monotherapy for late wet active AMD in first line treatment.

	Details
What the GC can recommend with this review	Effective adjunctive therapies to be used alongside monotherapy for first line treatment of late wet active AMD Which adjunctive therapies should not be used.
What the GC will not be able to recommend	When treatment should be started, stopped or switched (covered in another question)
Type of review	Intervention
Language	English only
Study design	RCT and systematic review of RCTs
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) diagnosed with late wet AMD (treatment naïve)
Intervention	Comparative and head to head trials of: Combination therapies (adding in photodynamic therapy (PDT), or steroids (dexamethasone, fluocinolone acetonide, triamcinolone acetonide)) along with the following anti-VEGF agents: • Aflibercept • Bevacizumab • Ranibizumab
Comparator	• Anti-VEGF monotherapy alone • Anti-VEGF monotherapy and placebo
Outcomes	• Clinical outcomes (critical): Visual acuity (LogMAR); number of injections • Safety and adverse events (important) • Functional capacity, participation, independence and ability to carry out activities of daily living (important) • Health related quality of life (important) • Impact on carers (important) • Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Studies without follow-up of at least 1 year • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Age Gender Ethnic group Comorbidities affecting the eye, e.g. cataracts, myopia, diabetes, mixed vascular dementia Blood pressure Anticoagulant treatment Statins Baseline visual acuity in study and fellow eye Status of fellow eye (ie first or second) Other general health co morbidities Smoking Subgroups: retinal angiomatous proliferation, classic, occult, mixed classic/occult, pigment epithelial detachment

	Details
Review question 14	a) What are the factors that suggest treatment should be switched or stopped for people diagnosed with neovascular AMD? b) What factors indicate that treatment for neovascular AMD should be stopped?
Objectives	a) To describe the clinical features associated with treatment failure b) To describe the clinical features associated with treatment futility c) To describe the clinical features associated with treatment remission
What the GC can recommend with this review	A list of clinical features that suggest that treatment should be switched A list of clinical features that suggest treatment should be stopped A list of clinical features that suggest that some one has gone into remission and should be monitored
What the GC will not be able to recommend	The most effective agent to switch on to when treatment has failed or is contraindicated (covered in another review question).
Type of review	Intervention Guidelines
Language	English only
Study design	RCT Cohort studies Reviews and guidance describing stopping rules and switching rules (citation search of these studies)
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) being treated for neovascular AMD
Intervention	Different criteria for: • Remission and monitoring • Switching treatment • Stopping treatment or discharge
Comparator	Not stopping or switching treatment in someone with one or more of the above clinical features.
Outcomes	• Clinical outcomes (critical): Visual acuity (LogMAR), [for example, dichotomous outcomes (such as loss of 15 or more letters) • Safety and adverse events (important) • Functional capacity, participation, independence and ability to carry out activities of daily living (important) • Health related quality of life (important) • Impact on carers (important) • Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Age Gender Ethnic group Comorbidities affecting the eye, e.g. cataracts, myopia, diabetes, mixed vascular dementia Blood pressure Anticoagulant treatment Statins

	Details
	Baseline visual acuity in study and fellow eye Status of fellow eye (ie first or second) Other general health co morbidities Smoking Subgroups analysis will be performed if heterogeneity is found, including following subgroups: • Retinal angiomatous proliferation • Classic, occult • Mixed classic/occult • Pigment epithelial detachment • Polyps • CSR pattern/CSR-like AMD

	Details
Review question 15	What is the effectiveness of switching therapies for late wet (neovascular) AMD if the first-choice therapy is contraindicated or has failed?
Objectives	To determine the most effective treatment of late wet (neovascular) AMD for those in whom first-choice therapy has failed.
What the GC can recommend with this review	The comparative effectiveness of different treatments for late wet (neovascular) AMD in those for whom first-choice therapy has failed or is contraindicated. Which therapies should not be used.
What the GC will not be able to recommend	First choice therapy and adjunctive therapies in treatment naïve people (covered in another question) When treatment should be started, stopped or switched (covered in another question)
Type of review	Intervention
Language	English only
Study design	RCT and systematic review of RCTs Cohort studies If insufficient evidence revert to before and after studies
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) diagnosed with late wet (neovascular) AMD in whom first-choice (anti-VEGF agent monotherapy only) treatment has failed
Intervention	Comparative trials of: • Aflibercept • Bevacizumab • Ranibizumab • Anti-VEGF drug in combination with photodynamic therapy or intravitreal steroids (dexamethasone, fluocinolone acetonide, triamcinolone acetonide) • Placebo (or sham injections) • No treatment
Comparator	Any of the above
Outcomes	• Clinical outcomes (critical): visual acuity (LogMAR) • Safety and adverse events (important)

	Details
	• Functional capacity, participation, independence and ability to carry out activities of daily living (important) • Health related quality of life (important) • Impact on carers (important0 • Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Age Gender Ethnic group Comorbidities affecting the eye, e.g. cataracts, myopia, diabetes, mixed vascular dementia Blood pressure Anticoagulant treatment Statins Baseline visual acuity in study and fellow eye Status of fellow eye (ie first or second) Other general health co morbidities Smoking Subgroups: retinal angiomatous proliferation, classic, occult, mixed classic/occult, pigment epithelial detachment

	Details
Review question 16	How do different organisational models for ongoing treatment and follow up influence outcomes for people with diagnosed neovascular AMD (for example disease progression, time to treatment, non-attendance)?
Objectives	To establish what models of service organisation are most effective for treatment and follow up of people with diagnosed neovascular AMD.
What the GC can recommend with this review	The committee can recommend an organisational model that will help to reduce inappropriate referrals, reduce patient waiting time and reduce burden on the retinal clinic.
What the GC will not be able to recommend	N/A
Type of review	Intervention
Language	English only
Study design	RCT Cohort study design If insufficient evidence progress to Non-randomised studies including retrospective case-control study, Implementation studies) Before and after observational study (case series)
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) diagnosed with neovascular AMD
Intervention	• Telemedicine and virtual retinal clinics • Triage through fast track clinics

	Details
	• Triage through optometrist services • Two stop and one stop models of care. • Optometrist/optician provision of treatment • Optometrist/optician provision of follow up • Optometrist/optician provision of monitoring • Specialist nurse/technician provided injections • Direct referral from GP, Optometrist or emergency services to retinal clinic • Community based ophthalmology care • Alternative referral pathways: including Optometrist to GP to retinal clinic, referral to the general hospital eye services • Treatment delay
Comparator	Any of the above
Outcomes	• Clinical outcomes (visual acuity (LogMAR), disease stage progression) (critical) • Safety and adverse events (important) • Error in diagnosis (important) • Time to treatment/follow up (important) • Number of people seen (important) • Patient satisfaction (important) • Appointment attendance and non-attendance (important) • Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Case studies • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender Visual acuity AMD disease stage Comorbidities affecting the eye (e.g. cataracts) Other co-morbidities

	Details
Review question 17	What are the barriers and facilitators to appointment attendance and uptake of treatment for people with AMD?
Objectives	To understand the perspectives, priorities and important experiences of people being treated for AMD
What the GC can recommend with this review	Methods of managing patient care throughout the care pathway that reflect the priorities of people with AMD
What the GC will not be able to recommend	The most effective treatments for AMD. The most effective models of service delivery for AMD.
Type of review	Qualitative
Language	English only
Study design	Qualitative studies Mixed-methods studies

	Details
	Survey studies
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) being treated for AMD
Variable	Salient beliefs and barriers may include: • The difficulty of frequent visits to hospital (including length of time at hospital) • Painful injections into the eye and discomfort • Travel and expense (including hospital transport) • Travelling in the dark • Structural issues (communication, appointment organisation, signposting, hospital environment) • Mental health and lack of motivation • Fear and lack of confidence • Immobility e.g. in care settings • Co-morbidity and poor health • Lack of perceived danger e.g. complications of condition • Lack of perceived benefit e.g. importance of treatment • Lack of understanding e.g. importance how to of self-monitoring • Lack of local services e.g. low vision clinics
Outcomes	Qualitative evidence summary: • Quotes, and authors analysis • Summary of themes
Other criteria for inclusion / exclusion of studies	Exclusion: • People who are being treated for AMD • Non-English language • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender Visual acuity AMD disease stage (including first or second eye) Comorbidities affecting the eye (e.g. cataracts)

	Details
Review question 18	What is the effectiveness of different frequencies of administration of antiangiogenic therapies for the treatment of neovascular AMD?
Objectives	To determine the comparative effectiveness of different frequencies of administration for the treatment of neovascular AMD with antiangiogenic therapies.
What the GC will be able to recommend	The GC will be able to recommend the most effective frequency of administration for each of the below medicines.
What the GC will not be able to recommend	The GC will not be able to make recommendations comparing frequencies of administration of different drugs (this would come out of a larger network meta-analysis, also using evidence from another review question)
Type of review	Intervention
Language	English only (translated studies will be accepted where available)

	Details
Study design	RCT and systematic review of RCTs
Status	Published papers only (full text)
Population	Adults (18 years and older) diagnosed with neovascular AMD
Intervention	Different frequencies of administration for: • Aflibercept • Bevacizumab • Ranibizumab • Photodynamic therapy For example: • Ranibizumab - treat and extend, PRN • Aflibercept - dosing as described in SPC • Pregaptanib sodium - dosing as described in BNF • Bevacizumab - dosing as described in trial evidence • Other frequencies of administration found in trial evidence
Comparator	Any of the above
Outcomes	• Clinical outcomes (critical): visual acuity (LogMAR) • Safety and adverse events (important) • Functional capacity, participation, independence and ability to carry out activities of daily living (important) • Health related quality of life (important) • Impact on carers (important) • Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Studies without follow-up of at least 1 year • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Age Gender Ethnic group Comorbidities affecting the eye, e.g. cataracts, myopia, diabetes, mixed vascular dementia Blood pressure Anticoagulant treatment Statins Baseline visual acuity in study and fellow eye Status of fellow eye (ie first or second) Other general health co morbidities Smoking Subgroups: retinal angiomatous proliferation, classic, occult, mixed classic/occult, pigment epithelial detachment

	Details
Review question 19	How often should people with early AMD, indeterminate AMD, or advanced geographic atrophy be reviewed?
Objectives	To establish the risks and benefits of different frequencies of monitoring for the following groups; People with early AMD,

	Details
	People with indeterminate AMD People with advanced geographic atrophy.
Type of review	Intervention
Language	English only
Study design	Systematic review Randomised controlled trial If no RCT evidence is available progress to: Cohort study
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) with non-neovascular AMD
Intervention	Review schedules of varying frequency
Comparator	Standard care (can include self-presenting) Different frequencies of review
Outcomes	Visual acuity (LogMAR) Functional capacity, participation, independence and ability to carry out activities of daily living. Health related quality of life Impact on carers Resource use and costs Service user experience and outcomes: time from symptomatic to diagnosis to treatment
Other criteria for inclusion / exclusion of studies	Exclusion: Non-English language Abstract/non-published
Baseline characteristics to be extracted in evidence tables. (a study can be rated down for quality for not reporting enough of these baseline characteristics)	Ethnic group Age Gender Baseline visual acuity AMD disease stage (including first or second eye) Comorbidities affecting the eye (e.g. cataracts)
Search strategies	Databases searched included Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), HTA, Database of Abstracts of Reviews of Effect (DARE), Embase (Ovid), MEDLINE (Ovid), MEDLINE In-Process (Ovid). There were no date restrictions.
Review strategies	Appropriate NICE recommended Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect with sub-groups by diagnosis as above. All GC selected outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements. Subgroup analysis will be undertaken for people with other co-morbidities affecting the eye, where appropriate

	Details
Review question 20	How often should people with early AMD, indeterminate AMD, or advanced geographic atrophy have their non-affected eye reviewed?
Objectives	To establish the risks and benefits of different frequencies of monitoring of the unaffected eye for the following groups; People with early AMD, People with indeterminate AMD People with advanced geographic atrophy.
Type of review	Intervention
Language	English only
Study design	Systematic review Randomised controlled trial If no RCT evidence is available progress to: Cohort study
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) with non-neovascular AMD in one eye
Intervention	Review schedules of varying frequency
Comparator	Standard care (can include self-presenting) Different frequencies of review
Outcomes	Visual acuity (LogMAR) Functional capacity, participation, independence and ability to carry out activities of daily living. Health related quality of life Impact on carers Resource use and costs Service user experience and outcomes: time from symptomatic to diagnosis to treatment
Other criteria for inclusion / exclusion of studies	Exclusion: Non-English language Abstract/non-published
Baseline characteristics to be extracted in evidence tables. (a study can be rated down for quality for not reporting enough of these baseline characteristics)	Ethnic group Age Gender Baseline Visual acuity AMD disease stage (including first or second eye) Comorbidities affecting the eye (e.g. cataracts)
Search strategies	Databases searched included Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), HTA, Database of Abstracts of Reviews of Effect (DARE), Embase (Ovid), MEDLINE (Ovid), MEDLINE In-Process (Ovid). There were no date restrictions.
Review strategies	Appropriate NICE recommended Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect with sub-groups by diagnosis as above..

	Details
	All GC selected outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements. Subgroup analysis will be undertaken for people with other co-morbidities affecting the eye, where appropriate

	Details
Review question 21	In people with neovascular AMD who are not being actively treated, how often should they be reviewed?
Objectives	To establish the risks and benefits of different frequencies of monitoring for people with neovascular AMD in whom treatment has been deferred.
Type of review	Intervention
Language	English only
Study design	Systematic review Randomised controlled trial If No evidence is available progress to: Cohort study
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) with neovascular AMD in whom treatment has been deferred. Adults (18 years and older) with neovascular AMD who have been discharged because of quiescent neovascular disease.
Intervention	Review schedules of varying frequency
Comparator	Standard care (can include self-presenting) Different frequencies of review
Outcomes	Visual acuity (LogMAR) Functional capacity, participation, independence and ability to carry out activities of daily living. Health related quality of life Impact on carers Resource use and costs Service user experience and outcomes: time from symptomatic to diagnosis to treatment
Other criteria for inclusion / exclusion of studies	Exclusion: Non-English language Abstract/non-published
Baseline characteristics to be extracted in evidence tables. (a study can be rated down for quality for not reporting enough of these baseline characteristics)	Ethnic group Age Gender Visual acuity AMD disease stage (including first or second eye) Comorbidities affecting the eye (e.g. cataracts)
Search strategies	Databases searched included Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), HTA, Database of Abstracts of Reviews of Effect (DARE), Embase (Ovid), MEDLINE (Ovid), MEDLINE In-Process (Ovid). There were no date restrictions.

	Details
Review strategies	Appropriate NICE recommended Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All GC selected outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements. Subgroup analysis will be undertaken for people with other co-morbidities affecting the eye, where appropriate Subgroup analysis will be undertaken for people in whom treatment has been deferred, where appropriate. Subgroup analysis will be undertaken for people whom have been discharged with quiescent, where appropriate.

	Details
Review question 22	How often should people with neovascular AMD have their non-affected eye reviewed?
Objectives	To establish the risks and benefits of different frequencies of monitoring of the unaffected eye for people with neovascular AMD.
Type of review	Intervention
Language	English only
Study design	Systematic review Randomised controlled trial If no evidence is available progress to: Cohort study
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) with neovascular AMD in one eye
Intervention	Review schedules of varying frequency
Comparator	Standard care (can include self-presenting) Different frequencies of review
Outcomes	Visual acuity (LogMAR) Functional capacity, participation, independence and ability to carry out activities of daily living. Health related quality of life Impact on carers Resource use and costs Service user experience and outcomes: time from symptomatic to diagnosis to treatment
Other criteria for inclusion / exclusion of studies	Exclusion: Non-English language Abstract/non-published
Baseline characteristics to be extracted in evidence tables. (a study can be rated down for quality for not reporting enough of these baseline characteristics)	Ethnic group Age Gender Baseline visual acuity AMD disease stage (including first or second eye) Comorbidities affecting the eye (e.g. cataracts)

	Details
Search strategies	Databases searched included Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), HTA, Database of Abstracts of Reviews of Effect (DARE), Embase (Ovid), MEDLINE (Ovid), MEDLINE In-Process (Ovid). There were no date restrictions.
Review strategies	Appropriate NICE recommended Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements. Subgroup analysis will be undertaken for people with other co-morbidities affecting the eye, where appropriate

	Details
Review question 23a	What strategies and tools are useful for monitoring and self-monitoring for people with AMD?
Objectives	To establish the risks and benefits of tools and strategies for the self-monitoring of people with AMD.
What the GC can recommend with this review	Self-monitoring tools and strategies that would be effective for the use of monitoring in people with AMD to aid the early detection of disease progression (progression to neovascular AMD).
What the GC will not be able to recommend	Monitoring tools and strategies that would be appropriate for the monitoring of treatment response in people with neovascular AMD. (covered in part b)
Type of review	Intervention
Language	English only
Study design	Systematic review RCT If insufficient evidence progress to Cohort evidence
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) with AMD
Intervention	• Amsler Grid or computerised Amsler • M-Charts • Visual acuity tests (for example, Snellen or LogMAR) (excluding low light/mesopic) • MCPT- Macular Computerized Psychophysical Test • Preferential hyperacuity perimetry (PHP) (for example, ForeSeeHome device) • Macular mapping test • Multibit Test (MBT) • Entopic perimetry (for example MyVision test) • Noise-field campimetry • Journals (keep sight journal for instance)
Comparator	No self-monitoring

	Details
Outcomes	• Clinical outcomes (critical): Visual acuity • Safety and adverse events (important) • Functional capacity, participation, independence and ability to carry out activities of daily living (important) • Health related quality of life (important) • Impact on carers (important) • Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published • Monitoring tests performed by healthcare professionals.
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender Visual acuity AMD disease stage (including first or second eye) Comorbidities affecting the eye (e.g. cataracts)

	Details
Review question 23b	What strategies and tools are useful for monitoring for people with neovascular AMD?
Objectives	To establish the accuracy of OCT for the monitoring of people with neovascular AMD for the features of: • RPE rip, Haemorrhage, exudate • leakage
What the GC can recommend with this review	Monitoring tools and strategies that would be appropriate for the use of monitoring in people being treated for neovascular AMD to assess disease progression and treatment success. [it was agreed that other measures of assessing response to treatment (fibrosis, oedema, subretinal fluid, retinal cysts and tubulations) were best visualised on OCT however it was unclear which diagnostic tests were best for the diagnosis of RPE rip, haemorrhage, exudate or leakage.]
What the GC will not be able to recommend	Self-monitoring tools and strategies that would be appropriate for the use of monitoring in people with AMD. (part a)
Type of review	Diagnostic
Language	English only
Study design	Systematic review Diagnostic cross-sectional study If insufficient evidence is available progress to: Case control study
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) with neovascular AMD
Index test	Ocular coherence tomography (OCT) (including, spectral domain OCT)
Reference standard	• Colour photographs (biomicroscopy, slit lamp fundoscopy, ophthalmoscopy) • FFA (Fundus fluorescein angiography)

	Details
Outcomes	Clinical utility or diagnostic test accuracy (if available) including: • Sensitivity • Specificity • Positive predictive value • Negative predictive value, • Likelihood ratios, • Diagnostic odds ratio and • Area under the ROC analyses
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender Visual acuity AMD disease stage (including first or second eye) Comorbidities affecting the eye (e.g. cataracts)

	Details
Review question 24	How soon should people with neovascular AMD be diagnosed and treated after becoming symptomatic?
Objectives	To establish what models of service organisation are most effective for the triage, treatment and follow up of people with neovascular AMD.
What the GC can recommend with this review	The committee can recommend an organisational model that will help to reduce inappropriate referrals, reduce patient waiting time and reduce burden on the retinal clinic.
What the GC will not be able to recommend	N/A
Type of review	Intervention
Language	English only
Study design	RCT Cohort study design If insufficient evidence progress to: Non-randomised studies including retrospective case-control study, implementation studies) Before and after observational study (case series)
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) diagnosed with AMD
Intervention	• Telemedicine and virtual retinal clinics • Triage through fast track clinics • Triage through optometrist services • Two stop and one stop models of care. • Optometrist/optician provision of treatment • Optometrist/optician provision of follow up • Optometrist/optician provision of monitoring

	Details
	• Specialist nurse/technician provided injections • Direct referral from GP, Optometrist or emergency services to retinal clinic • Community based ophthalmology care • Alternative referral pathways: including Optometrist to GP to retinal clinic, referral to the general hospital eye services • Treatment delay
Comparator	Any of the above
Outcomes	• Time to diagnosis/treatment/follow up (critical) • Clinical outcomes (visual acuity (LogMAR), disease stage progression) (critical) • Safety and adverse events (important) • Number of people being referral (important) • Patient satisfaction (important) • Appointment attendance and non-attendance (important) • Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Case studies • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Ethnic group Age Gender Visual acuity AMD disease stage Comorbidities affecting the eye (e.g. cataracts) Other co-morbidities

	Details
Review question 25	What is the effectiveness of treatment of neovascular AMD in people presenting with visual acuity worse than 6/96?
Objectives	To determine the effectiveness of first-line anti-angiogenic therapy in people presenting with visual acuity worse than 6/96
What the GC can recommend with this review	Whether to offer first-line antiangiogenic therapy (as recommended in review question 12 and 18) in people presenting with neovascular AMD and visual acuity worse than 6/96
What the GC will not be able to recommend	The type and frequency of anti-angiogenic therapy to be given (to be agreed in review questions 12 and 18) The benefit of adjunctive or combination therapy compared to monotherapy (covered in another question) When treatment should be stopped or switched (covered in another question) The most effective second line therapy (covered in another question)
Type of review	Intervention
Language	English only
Study design	Systematic review RCT Cohort study

	Details
Status	Published papers only (full text) No date restrictions
Population	Adults (18 years and older) diagnosed with neovascular AMD presenting with visual acuity worse than 6/96
Intervention	First-line therapy (as recommended in review question 12 and 18
Comparator	Placebo No treatment (monitoring)
Outcomes	• Clinical outcomes (critical): Visual acuity (LogMAR) • Safety and adverse events (important) • Functional capacity, participation, independence and ability to carry out activities of daily living (important) • Health related quality of life (important) • Impact on carers (important) • Resource use and costs (critical)
Other criteria for inclusion / exclusion of studies	Exclusion: • Non-English language • Abstract/non-published
Baseline characteristics to be extracted in evidence tables.	Age Gender Ethnic group Comorbidities affecting the eye, e.g. cataracts, myopia, diabetes, mixed vascular dementia Blood pressure Anticoagulant treatment Statins Baseline visual acuity in study and fellow eye Status of fellow eye (ie first or second) Other general health co morbidities Smoking Subgroups: retinal angiomatous proliferation, classic, occult, mixed classic/occult, pigment epithelial detachment