

# 1 Appendix L: Research recommendations

## L.1 Anti-oxidant supplements to slow AMD progression

Research recommendation 1	What is the effectiveness of antioxidant and zinc supplements on AMD progression for people with early AMD at high risk?
Population	People with early AMD at high risk (see recommendation in AMD classification)
Intervention	Anti-oxidant supplement (AREDS 2 formula)
Comparator	Placebo (normal diet)
Outcomes	<ul style="list-style-type: none"> <li>• Probability of progression to advanced AMD (late AMD)</li> <li>• Visual acuity (change in visual acuity, visual gain at least a 15-letter increase, visual loss at least a 15-letter decrease)</li> </ul>
Study design	Randomised controlled trials

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Potential criterion	Explanation
Importance to patients, service users or the population	There is evidence (from the AREDS1 study) reporting an overall positive effect of anti-oxidant supplements on slowing AMD progression. However, the effects of each of the formula components in the AREDS1 formula on AMD progression are unclear, and one of ingredients (carotene) is associated with lung cancer amongst smokers. The AREDS research group introduced a new formulation which excluded beta carotene in the AREDS2 study, but the effect of the AREDS2 formulation on AMD disease progression is difficult to estimate due to the complicated AREDS2 study design, involving a secondary randomisation. There is therefore the need for randomised controlled trials looking at the treatment effect of current anti-oxidant supplements (AREDS 2 formula) for slowing the progression of AMD.
Relevance to NICE guidance	High priority: it is currently not possible to provide recommendations about nutritional interventions for healthcare professionals to modify AMD progression amongst people with early AMD. These studies would enable this gap to be filled, and would allow for recommendations to be possible in future guideline updates.
Current evidence base	There is the AREDS 1 study assessing the effectiveness and anti-oxidant supplement on AMD progression, but this does not contain a formulation that is likely to be used in the UK.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible

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## L.2 Amsler chart in diagnosing people with suspected AMD

Research recommendation 2	What is diagnostic utility of the Amsler chart or other similar tools (digital or otherwise) for AMD?
Population	People presented with symptoms of AMD but not being diagnosed AMD
Index test	The Amsler chart (or other similar tools)
Reference standard	Ophthalmologist diagnosis
Outcomes	<ul style="list-style-type: none"> <li>• Sensitivity</li> <li>• Specificity</li> <li>• Positive/negative predictive value</li> <li>• Positive/negative likelihood ratios</li> </ul>
Study design	Prospective diagnostic accuracy studies

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Potential criterion	Explanation
Importance to patients, service users or the population	The guideline committee noted that people with signs and symptoms who presented in general practice sometimes were evaluated using the Amsler chart, but the diagnostic accuracy of the chart in people with suspected but not diagnosed AMD is not possible to judge from the currently available case-control studies. An evaluation of the diagnostic utility of the Amsler chart or similar tools would help to inform how or whether they can be used in the future diagnostic processes.
Relevance to NICE guidance	Low priority: the research would fill relevant gaps in the evidence base, but it is possible to make recommendations for diagnosing of people presenting with visual change or visual disturbance on the available evidence.
Current evidence base	There were case-control studies that reported the diagnostic utility of the Amsler chart, but no prospective evaluations in a population with suspected but not diagnosed AMD.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that cohort or cross sectional diagnostic studies in this area should be feasible

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## L13 Indocyanine green angiography (ICG) for people with polypoidal choroidal vasculopathy (PCV)

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Research recommendation 3	What is diagnostic utility of the indocyanine green angiography (ICG) for diagnosing people with polypoidal choroidal vasculopathy (PCV)?
Population	People diagnosed with polypoidal choroidal vasculopathy (PCV)
Index test	Indocyanine green angiography (ICG)
Reference standard	Fluorescein angiography (FA)
Outcomes	<ul style="list-style-type: none"> <li>• Sensitivity</li> <li>• Specificity</li> <li>• Positive/negative predictive value</li> <li>• Positive/negative likelihood ratios</li> </ul>
Study design	Prospective diagnostic accuracy studies

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Potential criterion	Explanation
Importance to patients, service users or the population	Indocyanine green angiography (ICG) as an imaging tool has been used for identifying PCV and guiding the treatment for PCV in some areas of clinical practice, but there is a lack of available data on the accuracy of ICG and the application of ICG-guided treatment for people who are diagnosed with PCV. This lack of evidence prevents the routine use of ICG in clinical practice. Therefore there is a need for research to evaluate the diagnostic utility of ICG would help to inform how it can be used as parts of both diagnostic and therapeutic processes for people with PCV.
Relevance to NICE guidance	Medium priority: there was no recommendations were made using ICG in this guideline due to the lack of evidence, and studies would allow for recommendations to be possible in future guideline updates.
Current evidence base	No evidence was identified about the diagnostic accuracy and the application of ICG for identifying and treating people with PCV, and an important gap in the evidence base as this is one of the situations it is felt likely to have the greatest benefits.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that cohort or cross sectional diagnostic studies in this area should be feasible

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## L24 26 **Optical coherence tomography angiography (OCT-A) for diagnosis people with late AMD (wet active)**

<b>Research recommendation 4</b>	<b>What is diagnostic utility of the optical coherence tomography angiography (OCT-A) for diagnosing people with late AMD (wet active)?</b>
Population	People with late AMD (wet active)
Index test	Optical coherence tomography angiography (OCT-A)
Reference standard	Fluorescein angiography (FA)
Outcomes	<ul style="list-style-type: none"> <li>• Sensitivity</li> <li>• Specificity</li> <li>• Positive/negative predictive value</li> <li>• Positive/negative likelihood ratios</li> </ul>
Study design	Prospective diagnostic accuracy studies

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<b>Potential criterion</b>	<b>Explanation</b>
Importance to patients, service users or the population	OCT-A has been becoming available more widely in clinical practice in recent years. As a non-invasive diagnostic technology, its diagnostic accuracy in detecting people with neovascular AMD is uncertain. Limited amounts of evidence reported the diagnostic utility of OCT-A, but the quality of evidence is low due to retrospective study designs and imprecisions of the estimated effects because of small sample sizes in the studies. Well conducted cohort or cross sectional study would provide value data to evaluate the accuracy of OCT-A and how it can be used in future diagnostic process.
Relevance to NICE guidance	Medium priority: it is currently not possible to provide recommendations about the diagnostic accuracy of OCT-A when detecting people with neovascular AMD due to limited amount of low quality evidence, and these studies would enable this gap to be filled and would allow for recommendations to be possible in future guideline updates.
Current evidence base	Only one retrospective study reported the diagnostic accuracy of OCT-A for identifying choroidal neovascularisation, and an important gap in high quality evidence base as this is one of the situations it is felt likely to have the greatest benefits for the application of OCT-A in clinical practice.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that cohort or cross sectional diagnostic studies in this area should be feasible

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## L25 Referrals

Research recommendation 5	What is diagnostic utility of providing an electronic image with the initial referral of people with suspected late AMD (wet active)?
Population	People with suspected late AMD (wet active)
Index test	The initial referral with electronic image attached
Reference standard	The initial referral with no image attached (ophthalmologist diagnosis)
Outcomes	<ul style="list-style-type: none"> <li>• Sensitivity</li> <li>• Specificity</li> <li>• Positive/negative predictive value</li> <li>• Positive/negative likelihood ratios</li> </ul>
Study design	Prospective diagnostic accuracy studies

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Potential criterion	Explanation
Importance to patients, service users or the population	Evidence on referrals with digital images attached from primary to secondary care have shown that patients could be triaged based on these images, and then referred directly for treatment at the appropriate hospital specialist clinic, avoiding unnecessary hospital appointments. This evidence was based on an observational study, and the quality was very low due to a retrospective study design and study population (not people with AMD specifically). Given the potential benefits on a patient's referral and subsequent treatment, there is a need for robust evidence base around the diagnostic accuracy of digital images attached with referral.
Relevance to NICE guidance	Medium priority: it is currently not possible to provide recommendations about the diagnostic accuracy of digital images attached with the initial referral of people with suspected AMD due to a lack of evidence. These studies would enable this gap to be filled and would allow for recommendations to be possible in future guideline updates.
Current evidence base	No evidence was found looking at the diagnostic accuracy of digital images attached with initial referral, and therefore it was not felt possible to make any recommendations.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently well-defined population available that cohort or cross sectional diagnostic studies in this area should be feasible.

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## L36 Models of care

<b>Research recommendation 6</b>	<b>What is the long-term effectiveness, in terms of patient-relevant outcomes including BCVA and quality of life, of different models of care that aim to reduce time from initial presentation to referral, diagnosis, and treatment?</b>
Population	People with suspected or confirmed late AMD (wet active)
Intervention	Different models of care aim to reduce to time from initial presentation of symptoms to referral, diagnosis and treatment
Comparator	As above
Outcomes	<ul style="list-style-type: none"> <li>• Visual acuity and change in visual acuity</li> <li>• Vision related quality of life</li> </ul>
Study design	Randomised controlled trials

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<b>Potential criterion</b>	<b>Explanation</b>
Importance to patients, service users or the population	Evidence was identified supporting an association between visual loss and time delay in diagnosis and treatment pathway. However, no evidence was found looking at the impact of different models of care aiming to reduce diagnosis or treatment delay on patient-related outcomes such as visual acuity and quality of life for people with suspected or confirmed late AMD (wet active). There is therefore the need for randomised controlled trials looking at how different models of care affect people's visual acuity and their quality of life in the long-term.
Relevance to NICE guidance	High priority: it is currently not possible to provide recommendations about models of care that are potentially effective to minimise vision loss throughout referral pathway. These studies would enable this gap to be filled, and to identify the most effect models of care throughout the pathway to improve care.
Current evidence base	No evidence was found looking at the effectiveness of different models of care, and therefore it was not felt possible to recommend any model of care.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible

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## L37 Psychological therapies for the prevention of depression in people with AMD.

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Research recommendation 7	What is the effectiveness and cost-effectiveness of psychological therapies for the prevention of depression in people with AMD?
Population	People with AMD without depression
Intervention	Psychological therapies
Comparator	Usual care or not being treated with psychological therapies
Outcomes	<ul style="list-style-type: none"> <li>• Incidence and severity of anxiety and depression</li> <li>• Patient satisfaction</li> <li>• Mental and emotional wellbeing</li> <li>• Safety and adverse events (including suicide and parasuicide)</li> <li>• Resource use and costs</li> </ul>
Study design	Randomised controlled trials

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Potential criterion	Explanation
Importance to patients, service users or the population	Whilst very low-quality evidence was found looking at the effectiveness of psychological interventions in decreasing the risk of depression in people with AMD, no evidence was identified the preventative effect of psychological interventions for AMD people without depression, where it is believed there may be a positive effect. Therefore, if being referred to these intervention is going to be justified for preventing depression in people with AMD, well-conducted RCTs comparing psychological therapies to standard (or usual) care alone are needed, and would fill an important gap in the evidence base around the efficacy of psychological interventions preventing depression in people with AMD.
Relevance to NICE guidance	Medium priority: no recommendations were made in this guideline for the application psychological therapies for preventing depression in people with AMD due to a lack of robust evidence, and studies would allow for recommendations to be possible in future guideline updates.
Current evidence base	There was evidence reporting the impact of psychological intervention on the decreased severity of depression in people with AMD and depression at baseline, but its preventative effect on people at AMD without depression is unknown.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	The fact that similar studies already have been conducted for people with AMD implies it should be possible to have sufficiently large and well defined population available for the trial.

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## L48 Psychological therapy: emotional support strategies in people with AMD

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Research recommendation 8	What is the effectiveness and cost-effectiveness of emotional support strategies in people with AMD? (including mental and emotional wellbeing as outcomes)
Population	People with AMD
Intervention	Emotional support strategies
Comparator	Usual care or not being treated with psychological therapies
Outcomes	<ul style="list-style-type: none"> <li>• Incidence and severity of anxiety and depression</li> <li>• Patient satisfaction</li> <li>• Mental and emotional wellbeing</li> <li>• Safety and adverse events (including suicide and parasuicide)</li> <li>• Resource use and costs</li> </ul>
Study design	Randomised controlled trials

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Potential criterion	Explanation
Importance to patients, service users or the population	Evidence on psychological therapies found that such intervention were effective to decrease the severity of depression, anxiety and long term mental illness, but these interventions were usually multicomponent, including a number of therapeutic elements (CBT, peer support, counselling, information, even exercise therapy and rehabilitative equipment) and it was thus difficult to distinguish which of these components was producing the positive effect, if any. Additionally whilst some interventions showed positive results in some outcome domains, these effects were not consistent, and were often around or below the defined minimal important differences for these outcomes, where they were available. CBT interventions are expensive and access to the is not always available in the NHS, so there would be considerable value in evidence on whether lower cost and intensity emotional support interventions, which are much more widely available, would also be effective in people with AMD
Relevance to NICE guidance	Medium priority: no recommendations were made in this guideline for psychological therapies due to the lack of robust evidence, and studies would allow for recommendations to be possible in future guideline updates.
Current evidence base	During the development of this guideline specific, the effectiveness of psychological therapies with multiple components were identified for people with diagnosed AMD but their effects on people's mental and emotional well-being are unknown.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	The fact that similar studies already have been conducted for people with AMD implies. It should be possible to have sufficiently large and well defined population available for the trial.

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## L49 Low vision service for people with AMD

Research recommendation 9	What is the impact of optimising low vision services on people with AMD?
Population	People with AMD
Intervention	Low vision service
Comparator	Usual care or not being referred to low vision service
Outcomes	<ul style="list-style-type: none"> <li>• Anxiety and depression</li> <li>• Patient satisfaction</li> <li>• Functional capacity, participation, independence and ability to carry out activities of daily living</li> <li>• Health related quality of life</li> <li>• Resource use and costs</li> </ul>
Study design	Randomised controlled trials

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Potential criterion	Explanation
Importance to patients, service users or the population	The committee noted that, there are published studies reporting the effectiveness of low-vision services (for instance improved quality of life), but these studies either did not exclusively include people with AMD, or were not designed as randomised trials. The lack of robust evidence base makes it difficult to make a strong recommendation for low-vision services. Well conducted trials should ensure to evaluate the effectiveness of low vision services on people with AMD, and should include outcome measures such as visual acuity, functional performance of daily activities, as well as vision and health-related quality of life to enable the results to be used to assess the impact of low vision service on people being referred for the service.
Relevance to NICE guidance	Medium priority: A consensus-based recommendation was made to consider low vision service for people with AMD when visual problems occurs. Future studies would provide robust evidence on the effectiveness of low vision service for people with AMD specifically, and would enable this gap to be filled.
Current evidence base	Current evidence from one UK study showed compared different models of low-vision rehabilitation, and found no difference in people's functional capacity between models. The committee indicated that the main components of rehabilitation models outlined in the study did not reflect typical low-vision rehabilitation provided in everyday clinical practice in the UK, as many component were not routinely available and provided in the practice. Therefore it was not felt possible to make any strong recommendations.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

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## L.10 Anti-VEGF treatment frequency

Research recommendation 10	What is the effectiveness and cost-effectiveness of treatment by a 'treat-and-extend' regimen compared with alternative regimens (dosing frequencies)?
Population	People being treated with anti-VEGF for late AMD (wet active)
Intervention	Treat-and extend treatment regimen
Comparator	Alternative treatment frequencies including: <ul style="list-style-type: none"> <li>• PRN</li> <li>• Routine injection (monthly, bimonthly)</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Visual acuity</li> <li>• Number of injections</li> <li>• Safety and adverse events</li> <li>• Functional capacity, participation, independence and ability to carry out activities of daily living</li> <li>• Health related quality of life</li> <li>• Impact on carers</li> <li>• Resource use and costs</li> </ul>
Study design	Randomised controlled trials

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Potential criterion	Explanation
Importance to patients, service users or the population	Of different treatment frequencies, only one trial evaluated the effectiveness of a treat-and-extend regimen, comparing it with monthly routine treatment. The quality of the evidence was low due to the risk of bias and imprecision, which is likely to be explained by the relatively small sample size in the study. Only 60 people were included (40 people on a treat-and-extend regimen and 20 on routine injections). This introduced an uncertainty in the estimated effect of treat-and-extend regimen. The lack of high quality evidence makes it not possible to make any recommendation on this regimen, although indirect evidence from network meta-analysis indicated a possible positive benefit.
Relevance to NICE guidance	High priority: it was not possible to recommend treat-and-extend regimens when treating people with late AMD (wet active). Research would fill the gap in evidence and would be useful to evaluate whether treat-and-extend is effective comparing with alternative treatment regimens that currently in practice.
Current evidence base	Currently the evidence base around the effectiveness and cost-effectiveness of treat-and-extend regimen for treating encounter people with late AMD (wet active) is limited.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

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## L.11 Adjunctive therapy: polypoidal choroidal vasculopathy

<b>Research recommendation 11</b>	<b>What is the long-term effectiveness and cost effectiveness of photodynamic therapy (PDT) as an adjunct to anti-VEGF as first-line treatment for PCV (at least 2 years)?</b>
Population	People with polypoidal choroidal vasculopathy (PCV) who are starting anti-VEGF treatment
Intervention	Photodynamic therapy combined with anti-VEGF or steroid
Comparator	Anti-VEGF monotherapy
Outcomes	<ul style="list-style-type: none"> <li>• Visual acuity</li> <li>• Number of injections</li> <li>• Safety and adverse events</li> <li>• Functional capacity, participation, independence and ability to carry out activities of daily living</li> <li>• Health related quality of life</li> <li>• Impact on carers</li> <li>• Resource use and costs</li> </ul>
Study design	Randomised controlled trials

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<b>Potential criterion</b>	<b>Explanation</b>
Importance to patients, service users or the population	Photodynamic therapy (PDT) is still commonly used alone or as an adjunct to anti-VEGF when treating polypoidal choroidal vasculopathy (PCV). The application of PDT can seal polyps, which should reduce fluid leakage and haemorrhage, and help to reduce anti-VEGF burden. A limited amount of evidence (2 studies) compared PDT adjunctive therapy and anti-VEGF monotherapies for the treatment of PCV.
Relevance to NICE guidance	Medium priority: it is currently not possible to provide recommendations about combined PDT treatment for healthcare professionals likely to encounter people with PCV, and these studies would enable this gap to be filled.
Current evidence base	The Current evidence base around the effectiveness and cost-effectiveness of PDT combined therapies for treating people with PCV is limited.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

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## L.12 Adjunctive therapy: second-line treatment

Research recommendation 12	What is the effectiveness and cost-effectiveness of photodynamic therapy as an adjunct to anti-VEGF as second-line treatment for late AMD (wet active)?
Population	People with late age-related macular degeneration who have been previously treated with anti-VEGF monotherapy
Intervention	Photodynamic therapy combined with anti-VEGF or steroid
Comparator	Anti-VEGF monotherapy
Outcomes	<ul style="list-style-type: none"> <li>• Visual acuity</li> <li>• Number of injections</li> <li>• Safety and adverse events</li> <li>• Functional capacity, participation, independence and ability to carry out activities of daily living</li> <li>• Health related quality of life</li> <li>• Impact on carers</li> <li>• Resource use and costs</li> </ul>
Study design	Randomised controlled trials

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Potential criterion	Explanation
Importance to patients, service users or the population	Current evidence showed no visual acuity benefit among treatment naïve people who received combination therapies adding in photodynamic therapy or steroids along with anti-VEGF drugs, and therefore the committee agreed that adjunctive therapies should not be used as part of first-line treatment. A number of studies (2) included people with previous treatment but the visual effect of adjunctive therapies was not consistent or possible to estimate with any precision. Well conducted randomised controlled trials comparing PDT plus anti-VEGF to anti-VEGF alone would fill an important gap in the evidence base around whether PDT combined interventions is effective when being used as second-line treatment for people with late AMD (wet active).
Relevance to NICE guidance	Medium priority: the research would fill relevant gaps in the evidence for using adjunctive therapies as second-line treatment when treating people with late AMD (wet active).
Current evidence base	Currently evidence base around the effectiveness and cost-effectiveness of PDT combined therapies for treating people with late AMD (wet active) who had been treated previously is limited.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

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## L.13 Switching therapies: preference of people with AMD

Research recommendation 13	How does patient preference impact on switching treatments, and how does switching affect quality of life?
Population	People being treated with anti-VEGF for late AMD (wet)
Intervention	People's preferred treatment decision for: <ul style="list-style-type: none"> <li>• Remission and monitoring</li> <li>• Switching treatment</li> <li>• Stopping treatment</li> </ul>
Comparator	Assigned treatment (based on clinician or imaging assessment) for: <ul style="list-style-type: none"> <li>• Remission and monitoring</li> <li>• Switching treatment</li> <li>• Stopping treatment</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Visual acuity</li> <li>• Number of injections</li> <li>• Safety and adverse events</li> <li>• Functional capacity, participation, independence and ability to carry out activities of daily living</li> <li>• Health related quality of life</li> <li>• Impact on carers</li> <li>• Resource use and costs</li> </ul>
Study design	Randomised controlled trials or cohort studies

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Potential criterion	Explanation
Importance to patients, service users or the population	A number of factors such as changes in visual acuity, structural damages in eyes, adverse events and people's quality of care were considered affecting treatment decision-making in practice. Currently there is no evidence on the value of people's preferences when switching or stopping their treatment, and how or whether patient's preferences would affect decision-making when switching therapies. Additionally little is known about subsequent influence on their quality of life.
Relevance to NICE guidance	Low priority: the research would fill relevant gaps in the evidence base, but it is possible to make recommendations for switching and sequencing based on the available clinical evidence.
Current evidence base	Low-quality evidence were found looking at the effectiveness of switching or augmenting treatment when first-line treatment is not providing adequate vision improvement, but no evidence evaluates the impact of patients' preference and their involvement on treatment decision-making.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently number and well defined population available that randomised controlled trials and/or cohort studies in this area should be feasible.

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## L.14 Stoppage of therapies: clinical indicators

Research recommendation 14	What clinical features are indicative of a lack of benefit or prognosis from anti-VEGF therapy?
Population	People being treated with anti-VEGF for late AMD (wet)
Predictive features	Clinical features that potentially indicate a lack of benefit from anti-VEGF therapy
Outcomes	<ul style="list-style-type: none"> <li>• Visual acuity</li> <li>• Number of injections</li> <li>• Safety and adverse events</li> <li>• Functional capacity, participation, independence and ability to carry out activities of daily living</li> <li>• Health related quality of life</li> <li>• Impact on carers</li> <li>• Resource use and costs</li> </ul>
Study design	Prospective cohort studies

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Potential criterion	Explanation
Importance to patients, service users or the population	There was no evidence found identifying any robust criteria that indicate that anti-VEGF treatment has failed and should therefore be stopped, and therefore it was not possible to make any strong, evidence based recommendations in this area. In practice, people with AMD are likely to be over-treated in the later stages of the condition due to a lack of clinical criteria for treatment stoppage. To maximise the benefit-risk balance from anti-VEGF, it is necessary to identify in clinical features that will indicative of potential lack of benefit to avoid treating people with late AMD (wet active) unnecessarily.
Relevance to NICE guidance	Medium priority: it was not possible to recommend any clinical features such as functional and structural changes that are useful to indicate potential benefit of or prognosis from anti-VEGF. Studies would filled in an important gap in evidence base and would enable recommendations to be made in future updates of the guideline.
Current evidence base	Low-quality evidence were found looking at the effectiveness of switching or augmenting treatment when first-line treatment is not providing adequate vision improvement, but no evidence identifies any clinical features that can be used to indicate prognosis from anti-VEGF treatment.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that cohort studies in this area should be feasible.

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## L.15 Frequency of monitoring

Research recommendation 15	What is the cost-effectiveness of different review frequencies/ strategies for people at risk of progression to late AMD (wet active)?
Population	People at risk of progression to late AMD (wet active)
Intervention	Difference frequencies monitoring people with <ul style="list-style-type: none"> <li>• Late AMD (wet active) in one eye</li> <li>• Late AMD (wet active) in whom treatment has been deferred</li> <li>• Late AMD (wet active) who have been discharged because of quiescent phase of disease</li> </ul>
Comparator	<ul style="list-style-type: none"> <li>• Standard care (self-presenting)</li> <li>• Different frequencies of review</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Visual acuity</li> <li>• Number of injections</li> <li>• Safety and adverse events</li> <li>• Functional capacity, participation, independence and ability to carry out activities of daily living</li> <li>• Health related quality of life</li> <li>• Impact on carers</li> <li>• Resource use and costs</li> </ul>
Study design	Randomised controlled trials

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Potential criterion	Explanation
Importance to patients, service users or the population	Currently there is no evidence about different frequencies when monitoring people with AMD. This means that it is not possible to identify or follow the optimum monitoring strategy for people at different stages of AMD, as these will be different, leading to uncertainty in correct and appropriate management for that individual as well as demands on eye services.
Relevance to NICE guidance	High priority: consensus based recommendations have been made to recommend how patients at different stages of AMD can be reviewed and what service can be used, but future updates of the guideline would benefit from prospectively collected data on different frequencies when reviewing people with AMD.
Current evidence base	No evidence was identified about varying frequency of monitoring for people at different stages of AMD , an important gap in the evidence base as this is one of the situations it is felt likely to have the greatest benefits.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

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## L.16 Self-monitoring interventions

<b>Research recommendation 16</b>	<b>What is the effectiveness and cost-effectiveness of self-monitoring strategies in improving the long-term visual, functional and quality of life outcomes of people with early, indeterminate or late-dry age-related macular degeneration?</b>
Population	People with early, indeterminate or late AMD (dry)
Intervention	Self-monitoring interventions for instance <ul style="list-style-type: none"> <li>• Environmental Amsler Grid or computerised Amsler</li> <li>• Preferential hyperacuity perimetry (PHP) (for example, ForeSeeHome device)</li> <li>• Journals (keep sight journal for instance)</li> </ul>
Comparator	<ul style="list-style-type: none"> <li>• Standard care (not using self-monitoring tools)</li> </ul>
Outcomes	<ul style="list-style-type: none"> <li>• Visual acuity</li> <li>• Number of injections</li> <li>• Safety and adverse events</li> <li>• Functional capacity, participation, independence and ability to carry out activities of daily living</li> <li>• Health related quality of life</li> <li>• Impact on carers</li> <li>• Resource use and costs</li> </ul>
Study design	Randomised controlled trial

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<b>Potential criterion</b>	<b>Explanation</b>
Importance to patients, service users or the population	Currently available evidence on self-monitoring interventions failed to establish a link between early detection and better long-term visual acuity, with only one RCT which measured visual acuity at the time of diagnosis, with no long-term follow up.
Relevance to NICE guidance	Medium priority: consensus-based recommendations were made to ensure people with AMD were made aware of the availability of self-monitoring tools, and to encourage people to monitor their visual changes themselves. However, it was not possible to recommend specific self-monitoring tools due to a lack of evidence on the potential benefits for patient relevant outcomes including visual acuity and quality of life.
Current evidence base	There is currently little robust evidence available to address questions around the effectiveness and cost-effectiveness of self-monitoring strategies in improving the long-term visual, functional and quality of life outcomes for people with AMD.
Equality	Some people are unable to monitor their own vision (for example, those with comorbidities such as impaired cognitive function). The role of family members and carers are specifically acknowledged for this group of people, and it is important to provide advice for carers/family members on how to monitor changes in people's vision.
Feasibility	There is a sufficient number and well defined population available that randomised controlled trials in this area should be feasible

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## L.17 Self-monitoring strategies: detection and treatment

<b>Research recommendation 17</b>	<b>Does earlier detection of the incidence of late age-related macular degeneration (wet active) in people diagnosed with early, indeterminate or late-dry age-related macular degeneration lead to earlier treatment and better long-term outcomes?</b>
Population	People with early, indeterminate or late AMD (dry)
Intervention	Length of time when incidence of late AMD (wet active) is detected
Comparator	Different length of time to be treated for late AMD(wet active)
Outcomes	<ul style="list-style-type: none"> <li>• Visual acuity</li> <li>• Time to treatment</li> <li>• Health related quality of life</li> <li>• Impact on carers</li> <li>• Resource use and costs</li> </ul>
Study design	Prospective cohort studies

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Potential criterion	Explanation
Importance to patients, service users or the population	Self-monitoring interventions were found to result in earlier diagnosis for people with late AMD (wet active). However, the evidence failed to demonstrate that earlier diagnosis would result in improvements in long-term outcomes such as visual acuity. Prospective cohort studies following up a cohort of people with AMD could help to evaluate the impact of earlier detection on people's visual acuity and time to being treated.
Relevance to NICE guidance	High priority: the research would fill relevant gaps in the evidence base, but it is possible to make recommendations on the self-monitoring tools based on consensus.
Current evidence base	No evidence available to address questions around whether earlier detection of the incidence of late age-related macular degeneration (wet active) in people diagnosed with early, indeterminate or late-dry age-related macular degeneration leads to earlier treatment and better long-term outcomes.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that cohort studies in this area should be feasible

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## L.18 Monitoring: optical coherence tomography angiography

Research recommendation 18	What is the relative accuracy and cost of OCT-A compared with the reference standard of multimodal imaging?
Population	People being treated for late AMD (wet active)
Index test	Optical coherence tomography angiography (OCT-A)
Reference standard	Multimodal imaging including OCT, FFA and ICGA
Outcomes	<ul style="list-style-type: none"> <li>• Sensitivity</li> <li>• Specificity</li> <li>• Positive/negative predictive value</li> <li>• Positive/negative likelihood ratios</li> <li>• Resource use</li> </ul>
Study design	Prospective diagnostic accuracy studies

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Potential criterion	Explanation
Importance to patients, service users or the population	Optical coherence tomography angiography (OCT-A) has been increasingly becoming available and used in monitoring disease activity in people with late AMD (wet active). OCT-A is considered closer to fundus fluorescein angiography in its ability to provide information on patterns of blood and leakage to identify vascular change in people with late AMD (wet active). As a new imaging tool, OCT is an expensive procedure. Currently only limited amounts of evidence report the accuracy of OCT-A, and there is therefore the need of studies of OCT-A, compared with multimodal imaging (such as OCT and FFA) as reference standard to assess its accuracy in monitoring AMD progression and treatment response and to provide an evidence base for its wide application in clinical practice. The optimal study design for this question would be a cohort or cross-sectional study of people being treated for late AMD (wet active).
Relevance to NICE guidance	Medium priority: it is currently not possible to provide recommendations about the application of OCT-A as a monitoring tool when reviewing neovascular activities for people being treated for late AMD (wet active). The research would fill relevant gaps in the evidence base, and enable recommendations to be made in future updates of the guideline
Current evidence base	There was evidence identified around the accuracy of standard OCT, however only one retrospective study reported the diagnostic accuracy of OCT-A for identifying leakage compared with FFA. There is thus a need for studies of OCT-A to provide an evidence base for the clinical effectiveness and cost effectiveness of OCT-A when monitoring neovascular activity.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	The fact that similar studies have been conducted for people being treated with late AMD (wet active), and there is a sufficient number and well defined population available that diagnostic studies in this area should be feasible

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## L.19 Monitoring strategies

Research recommendation 19	What is the clinical effectiveness of OCT-A, evaluated using a test and treat approach (OCT(+/-FFA) -v- OCT+OCT-A)?
Population	People being treated for late AMD (wet active)
Intervention	AMD treatment guided by monitoring with OCT and OCT-A
Comparator	AMD treatment guided by monitoring with OCT and FFA
Outcomes	<ul style="list-style-type: none"> <li>• Visual acuity</li> <li>• Number of injections</li> <li>• Safety and adverse events</li> <li>• Functional capacity, participation, independence and ability to carry out activities of daily living</li> <li>• Health related quality of life</li> <li>• Impact on carers</li> <li>• Resource use and costs</li> </ul>
Study design	Test and treat randomised control trials

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Potential criterion	Explanation
Importance to patients, service users or the population	As well as evidence on the diagnostic accuracy of OCT-A, it is also important to know whether its uses results in differences in clinical decision, and therefore patient outcomes, compared to monitoring using standard OCT and FFA.
Relevance to NICE guidance	Medium priority: it is currently not possible to provide recommendations about the application of OCT-A as a monitoring tool when reviewing neovascular activities for people being treated for late AMD (wet active). Test and treated RCTs would enable this gap to be filled, and would allow for recommendations to be possible in future guideline updates.
Current evidence base	There were evidence around the accuracy of OCT, however only one retrospective study reported the diagnostic accuracy of OCT-A for identifying leakage comparing with FFA. The need of studies of OCT-A provides evidence based for clinical effectiveness of OCT-A as part of the monitoring regimen for people with late AMD (wet active)
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that test and treat RCTs in this area should be feasible

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## L.20 Information: terminology

Research recommendation 20	What terminology is clearest and most acceptable to patients to describe suspected or confirmed AMD throughout the pathway?
Population	People with AMD
Phenomena of interest	Standardised terminologies that are clearest and most acceptable when describing AMD to patients with suspected or confirmed AMD
Study design	Qualitative study

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Potential criterion	Explanation
Importance to patients, service users or the population	Being provided with clear information about the condition is important for people who are at risk of developing and/or are diagnosed with AMD, but there was inconsistent poorly chosen language identified as being used in practice, and this could lead to confusion and misconceptions amongst patients and carers. Qualitative studies of the choice of terminology and how to describe the condition to people at all stages of the disease and in different clinical settings (for instance both primary care and secondary care) would enable to optimisation of people's understanding about AMD and obtaining appropriate supports for people at different stages of the condition.
Relevance to NICE guidance	Medium priority: it is currently not possible to provide recommendations about the use of terminologies which are considered to be clear and acceptable when describing AMD to people with suspected or confirmed AMD. Qualitative studies would identify terminologies that are clear and acceptable from the patients' perspectives, would therefore enhance communication between healthcare professionals and patients throughout pathway.
Current evidence base	There is currently little evidence available to identify the use and the choice of terminology when and how to describe the condition to people at all stages of the disease and in different clinical settings (for instance both primary care and secondary care).
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently number and well defined population available that qualitative studies in this area should be feasible

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## L.21 Information: working people with AMD

<b>Research recommendation 21</b>	<b>What is the impact of AMD on working people (aged &lt;65 years or in paid/unpaid employment), and what information do they find useful and in what format and when?</b>
Population	People with AMD who aged <65 years or in paid/unpaid employment
Phenomena of interest	Information on living with AMD, including: <ul style="list-style-type: none"> <li>• What information are useful</li> <li>• How to live with AMD</li> <li>• When to contact a healthcare professional</li> <li>• Identification of visual changes</li> </ul>
Study design	Qualitative study

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<b>Potential criterion</b>	<b>Explanation</b>
Importance to patients, service users or the population	The incidence of AMD is known to be higher in older populations (particularly aged between 70-90 years), but it can also affected people at a younger age (such as 55 years onward). Little is known about the impact of AMD on this group of population, and what specific information that they consider useful may help them to live with the condition. Qualitative studies of experience living with AMD and information needs for people aged under 65 years would fill the gap in current evidence and would identify their specific needs to optimise support services for them.
Relevance to NICE guidance	Medium priority: it is currently not possible to provide recommendations specifically for people with AMD in younger age groups and/or those who are in employment. Qualitative studies would improve an understanding of specific information needs for this group of population, and enable recommendations to be made in future updates of the guideline.
Current evidence base	There is currently little evidence available to address questions around the information needs of people with AMD who are younger than 65 years and/or those who are still in employment.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently number and well defined population available that qualitative studies in this area should be feasible.

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