Age-related macular degeneration

NICE guideline: short version

Draft for consultation, April 2017

This guideline covers diagnosing and managing age-related macular degeneration (AMD) in adults aged 18 and over. It aims to optimise service organisation and identification of risk factors, and improve diagnosis, management and review of this condition. It also aims to improve support and availability of information for people with AMD.

Who is it for?

- People with age-related macular degeneration, their families and carers
- Healthcare professionals in primary and secondary care
- Social care professionals
- Commissioners and providers of ophthalmic and optometric services

This version of the guideline contains the draft recommendations, context and recommendations for research. Information about how the guideline was developed is on the guideline's page on the NICE website. This includes the guideline committee's discussion and the evidence reviews (in the full guideline), the scope, and details of the committee and any declarations of interest.

Contents

1 Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

2 *1.1 Classifying age-related macular degeneration (AMD)*

3 1.1.1 Classify age-related macular degeneration (AMD) using table 1.

4 **Table 1. Age-related macular degeneration classification**

AMD classification	Definition
Normal	• No signs of age-related macular degeneration (AMD) • Small ('hard') drusen (less than 63 μm) only
Early AMD	• Low risk of progression: – medium drusen (63 μm or more and less than 125 μm), or – pigmentary abnormalities • Medium risk of progression: – large drusen (125 μm or more), or – reticular drusen, or – medium drusen with pigmentary abnormalities • High risk of progression: – large drusen (125 μm or more) with pigmentary abnormalities, or – reticular drusen with pigmentary abnormalities, or

AMD classification	Definition
	– adult vitelliform lesion without significant visual loss (best-corrected acuity better than 6/18), or – geographic atrophy smaller than 175 µm and not involving the fovea
Indeterminate AMD	• Retinal pigment epitheliopathy (presence of degenerative AMD changes with subretinal or intraretinal fluid in the absence of neovascularisation; similar to chronic central serous chorioretinopathy [CSCR]) • Serous pigment epithelial detachment (PED) without neovascularisation
Late AMD (wet active)	• Retinal angiomatous proliferation (RAP) • Classic choroidal neovascularisation (CNV) • Mixed (predominantly and minimally classic CNV with occult CNV) • Occult (fibrovascular PED and serous PED with neovascularisation) • Polypoidal choroidal vasculopathy (PCV)
Late AMD (dry)	• Geographic atrophy: larger than 175 µm, or affecting the fovea (in the absence of neovascular AMD) • Significant visual loss (6/18 or worse) associated with: – confluent drusen, or – advanced pigmentary changes or non-geographic atrophy, or – adult vitelliform lesion
Late AMD (wet inactive)	• Fibrous scar • Retinal pigment epithelial (RPE) tear • Atrophy (absence or thinning of RPE or retina) • Cystic degeneration (persistent intraretinal fluid or tubulations unresponsive to treatment)

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2 1.1.2 Do not refer to late AMD (wet inactive) as 'dry AMD'.

1.2 Information and support

1.2.1 Provide people with AMD, and their family members or carers (as appropriate), with information that is:

- available on an ongoing basis
- relevant to the stage of the person's condition
- tailored to the person's needs
- delivered in a caring and sensitive fashion.

For more guidance on providing information to people and discussing their preferences with them, see the NICE guideline on patient experience in adult NHS services.

1.2.2 Provide opportunities to discuss AMD with the person. Topics to cover should include:

- what AMD is and how common it is
- types of AMD
- causes of AMD
- stopping smoking and other lifestyle advice
- how AMD may progress and possible complications
- tests and investigations
- treatment options, including possible benefits and risks
- who to contact for practical and emotional support
- where the person's appointments will take place
- which healthcare professionals will be responsible for the person's care
- expected wait times for consultations, investigations and treatments
- potential benefits of certification and registration as sight impaired or severely sight impaired
- when, where and how to seek help with vision changes (see section 1.7)
- signposting to other sources of information and support.

1.2.3 Provide information in accessible formats to take away to people with AMD at their first appointment, and then whenever they ask for it. The information should cover the following:

- information about AMD and treatment pathways, including likely timescales
- key contact details (for example, who to contact if appointments need to be altered)
- advice about what to do and where to go if vision deteriorates
- available support (including transport and parking permits)
- links to local and national support groups.

1.2.4 Allow enough time to discuss the person's concerns and questions about their diagnosis, treatment and prospects for their vision. Assess the person's priorities when making management decisions.

1.2.5 Promote peer support for people with AMD, particularly for people who are beginning intravitreal injections, who may be reassured by discussion with someone who has previously had the same treatment.

1.3 Risk factors

1.3.1 If you suspect AMD, recognise that the following risk factors make it more likely that the person has AMD:

- older age
- presence of AMD in the other eye
- family history of AMD
- smoking
- hypertension
- BMI of 30 kg/m^2 or higher
- diet low in omega 3 and 6, vitamins, carotenoid and minerals
- diet high in fat
- lack of exercise.

1.4 Diagnosis and referral

1.4.1 Offer ophthalmoscopy (also called fundoscopy) as part of the ocular examination to people presenting with changes in vision (including micropsia and metamorphopsia) or visual disturbances.

Early AMD

1.4.2 Confirm a diagnosis of early AMD using slit-lamp biomicroscopic fundus examination alone.

1.4.3 Do not refer people with asymptomatic early AMD to hospital eye services for further diagnostic tests.

Late AMD (dry)

1.4.4 Confirm a diagnosis of late AMD (dry) using slit-lamp biomicroscopic fundus examination.

1.4.5 Only refer people with late AMD (dry) to hospital eye services

- for certification of sight impairment **or**
- if this is how people access low-vision services in the local pathway (see 1.6.3) **or**
- if they develop new visual symptoms that may suggest late AMD (wet active).

Late AMD (wet active)

1.4.6 Urgently refer people with suspected late AMD (wet active) to hospital eye services, whether or not they report any visual impairment.

1.4.7 Offer optical coherence tomography (OCT) to people with suspected late AMD (wet active).

1.4.8 Do not offer fundus fluorescein angiography (FFA) to people with suspected late AMD (wet active) if clinical examination and OCT exclude neovascularisation.

1.4.9 Offer FFA to people with suspected late AMD (wet active) to confirm the diagnosis if OCT does not exclude neovascular disease.

1.4.10 For eyes with confirmed late AMD (wet active) for which antiangiogenic treatment is recommended (see section 1.5), offer treatment as soon as possible (within 21 days of referral to the hospital eye service).

Referral pathway

1.4.11 Commissioners and providers should agree a clear local pathway for people with AMD, which should cover:

- referral from primary to secondary care, with direct referral preferred
- discharge from secondary to primary care, covering ongoing management and re-referral when necessary.

1.5 Pharmacological management of AMD

Antiangiogenic therapies

1.5.1 Offer intravitreal anti-vascular endothelial growth factor (VEGF) treatment for late AMD (wet active) for eyes with visual acuity within the range specified in recommendation 1.5.5.

1.5.2 In eyes with visual acuity of 6/96 or worse, only consider anti-VEGF treatment for late AMD (wet active) if a benefit in the person's overall visual function is expected (for example, if the affected eye is the person’s better-seeing eye).

1.5.3 Ensure intraocular injections are given by suitably trained healthcare professionals, for example:

- medical specialists, such as ophthalmologists
- nurse practitioners and technicians with experience in giving intraocular injections.

1.5.4 Bevacizumab is not licensed for intraocular use for AMD. Prescribers should be aware that:

- bevacizumab can only be prescribed for AMD if a person has a specific need and no other licensed product meets the need;
- bevacizumab may not be prescribed for intraocular use for AMD simply because it is cheaper or more cost effective than a licensed alternative;
- clinicians should consider relevant professional guidance if prescribing outside a licensed indication;
- no clinically significant differences in effectiveness and safety between aflibercept, ranibizumab and bevacizumab have been seen in the trials considered by the guideline committee.

1.5.5 Ranibizumab, within its marketing authorisation, is recommended as an option for the treatment of wet age-related macular degeneration if:

- all of the following circumstances apply in the eye to be treated:
  - the best-corrected visual acuity is between 6/12 and 6/96
  - there is no permanent structural damage to the central fovea
  - the lesion size is less than or equal to 12 disc areas in greatest linear dimension
  - there is evidence of recent presumed disease progression (blood vessel growth, as indicated by fluorescein angiography, or recent visual acuity changes)

  and

- the manufacturer provides ranibizumab with the discount agreed in the patient access scheme (as revised in 2012). [This recommendation is from Ranibizumab and pegaptanib for the treatment of age-related macular degeneration (NICE technology appraisal guidance 155).]

1.5.6 Pegaptanib is not recommended for the treatment of wet age-related macular degeneration. [This recommendation is from Ranibizumab and pegaptanib for the treatment of age-related macular degeneration (NICE technology appraisal guidance 155).]

1.5.7 People who are currently receiving pegaptanib for any lesion type should have the option to continue therapy until they and their clinicians consider

it appropriate to stop. [This recommendation is from Ranibizumab and pegaptanib for the treatment of age-related macular degeneration (NICE technology appraisal guidance 155).]

1.5.8 Aflibercept solution for injection is recommended as an option for treating wet age-related macular degeneration only if:

- it is used in accordance with the recommendations for ranibizumab in NICE technology appraisal guidance 155 (re-issued in May 2012 [see recommendation 1.5.5]) and
- the manufacturer provides aflibercept solution for injection with the discount agreed in the patient access scheme. [This recommendation is adapted from Aflibercept solution for injection for treating wet age-related macular degeneration (NICE technology appraisal guidance 294).]

1.5.9 People currently receiving aflibercept solution for injection whose disease does not meet the criteria in 1.5.8 should be able to continue treatment until they and their clinician consider it appropriate to stop. [This recommendation is from Aflibercept solution for injection for treating wet age-related macular degeneration (NICE technology appraisal guidance 294).]

1.5.10 Do not offer photodynamic therapy alone for late AMD (wet active).

Adjunctive therapies

1.5.11 Do not offer photodynamic therapy as an adjunct to anti-VEGF as first-line treatment for late AMD (wet active).

1.5.12 Only offer photodynamic therapy as an adjunct to anti-VEGF as second-line treatment for late AMD (wet active) in the context of a randomised controlled trial.

1.5.13 Do not offer intravitreal corticosteroids as an adjunct to anti-VEGF for late AMD (wet active).

Switching and stopping antiangiogenic therapy for late AMD (wet)

1.5.14 Consider switching therapy for people with wet AMD if there are practical reasons for doing so (for example, if a different medicine can be given in a regimen the person prefers), but be aware that clinical benefits are likely to be limited.

1.5.15 Consider stopping anti-VEGF treatment if the eye experiences severe, progressive loss of visual acuity despite treatment.

1.5.16 Stop anti-VEGF treatment if the eye develops late AMD (wet inactive).

1.5.17 Consider observation without giving anti-VEGF treatment if disease appears stable (in this event, see 1.7 for recommendations on monitoring and self-monitoring).

1.5.18 Ensure that patients are actively involved in all decisions about the stopping or switching of treatment (see section 1.2 on patient information).

1.6 Non-pharmacological management of AMD

Strategies to slow the progression of AMD

1.6.1 Do not offer thermal laser therapy (for example, argon, diode) for treating drusen in people with early AMD.

Supporting people with AMD and visual impairment

1.6.2 Be aware that people with AMD are at an increased risk of depression. Identify and manage the depression according to the NICE guideline on depression in adults with a chronic physical health problem.

1.6.3 Consider referring people with AMD causing visual impairment to low-vision services.

1.6.4 Consider a group-based rehabilitation programme in addition to a low-vision service to promote independent living for people with AMD.

1.6.5 Consider eccentric viewing training for people with central vision loss in both eyes.

1.7 Monitoring AMD

1.7.1 Do not routinely monitor people with early AMD or late AMD (dry) through hospital eye services.

1.7.2 Advise people with late AMD (dry), or people with AMD who have been discharged from hospital eye services to:

- self-monitor their AMD
- consult their healthcare professional as soon as possible if their vision changes (see recommendation 1.8.5).

1.7.3 For people being monitored for late AMD (wet inactive), review both eyes at their monitoring appointments.

Self-monitoring

1.7.4 Discuss self-monitoring with people with AMD, and explain the strategies available.

1.7.5 Advise people with AMD to report any new symptoms or changes in the following to their healthcare professional as soon as possible:

- blurred or grey patch in their vision
- straight lines appearing distorted
- objects appearing smaller than normal.

1.7.6 Encourage and support people who may lack confidence to self-monitor their AMD.

1.7.7 If people are not able to self-manage their AMD, discuss AMD monitoring techniques with their family members or carers (as appropriate).

Monitoring for late AMD (wet active)

1.7.8 Offer people with late AMD (wet active) ongoing monitoring with OCT for both eyes.

1.7.9 Offer ophthalmoscopy (fundoscopy) or colour photography if OCT appearances are stable, but:

- there is a decline in visual acuity **or**
- the person reports a decline in visual function.

1.7.10 Consider FFA to identify unrecognised neovascularisation if OCT appearances are stable, but:

- there is a decline in visual acuity **or**
- the person reports a decline in visual function.

1.7.11 If OCT results suggest macular abnormalities but the abnormalities are not responding to treatment, think about:

- using alternative imaging
- alternative diagnoses.

Terms used in this guideline

Low vision

People with low vision have visual impairments that cause restriction in their everyday lives and that cannot be corrected by surgery, medicine, or glasses or contact lenses. This definition includes, but is not limited to those who are registered as sight impaired or severely sight impaired. It can include blurred vision, blind spots or tunnel vision. A **low-vision service** provides a range of services for people with low vision to enable them to make use of their eyesight to achieve maximum potential.

Hospital eye services

Services set in secondary care providing diagnosis or treatment of the eye or vision-related conditions.

Putting this guideline into practice

[This section will be finalised after consultation]

NICE has produced tools and resources [link to tools and resources tab] to help you put this guideline into practice.

[Optional paragraph if issues raised] Some issues were highlighted that might need specific thought when implementing the recommendations. These were raised during the development of this guideline. They are:

- [add any issues specific to guideline here]
- [Use 'Bullet left 1 last' style for the final item in this list.]

Putting recommendations into practice can take time. How long may vary from guideline to guideline, and depends on how much change in practice or services is needed. Implementing change is most effective when aligned with local priorities.

Changes recommended for clinical practice that can be done quickly – like changes in prescribing practice – should be shared quickly. This is because healthcare professionals should use guidelines to guide their work – as is required by professional regulating bodies such as the General Medical and Nursing and Midwifery Councils.

Changes should be implemented as soon as possible, unless there is a good reason for not doing so (for example, if it would be better value for money if a package of recommendations were all implemented at once).

Different organisations may need different approaches to implementation, depending on their size and function. Sometimes individual practitioners may be able to respond to recommendations to improve their practice more quickly than large organisations.

Here are some pointers to help organisations put NICE guidelines into practice:

1. **Raise awareness** through routine communication channels, such as email or newsletters, regular meetings, internal staff briefings and other communications with all relevant partner organisations. Identify things staff can include in their own practice straight away.

2. **Identify a lead** with an interest in the topic to champion the guideline and motivate others to support its use and make service changes, and to find out any significant issues locally.

3. **Carry out a baseline assessment** against the recommendations to find out whether there are gaps in current service provision.

4. **Think about what data you need to measure improvement** and plan how you will collect it. You may want to work with other health and social care organisations and specialist groups to compare current practice with the recommendations. This may also help identify local issues that will slow or prevent implementation.

5. **Develop an action plan**, with the steps needed to put the guideline into practice, and make sure it is ready as soon as possible. Big, complex changes may take longer to implement, but some may be quick and easy to do. An action plan will help in both cases.

6. **For very big changes** include milestones and a business case, which will set out additional costs, savings and possible areas for disinvestment. A small project group could develop the action plan. The group might include the guideline champion, a senior organisational sponsor, staff involved in the associated services, finance and information professionals.

7. **Implement the action plan** with oversight from the lead and the project group. Big projects may also need project management support.

8. **Review and monitor** how well the guideline is being implemented through the project group. Share progress with those involved in making improvements, as well as relevant boards and local partners.

NICE provides a comprehensive programme of support and resources to maximise uptake and use of evidence and guidance. See our into practice pages for more information.

Also see Leng G, Moore V, Abraham S, editors (2014) Achieving high quality care – practical experience from NICE. Chichester: Wiley.

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Context

Age-related macular degeneration (AMD) is the term given to ageing changes without any other obvious cause that occurs in the central area of the retina (macula), sometimes with new blood vessel formation (wet AMD). It is the most common form of macular degeneration.

AMD is a painless condition that generally leads to the gradual impairment of vision, but can sometimes cause a rapid reduction in vision. It predominantly affects the central vision, which is used for reading and recognising faces. Normal macular ageing changes are a common incidental finding on a routine visit to the optometrist, but AMD may also be detected this way before it is symptomatic, or people may present with difficulty in performing daily activities such as driving, reading and recognising faces.

Various ways of classifying AMD have been proposed. This guideline considers the best approach and recommends that a distinction is drawn between 'early' and 'late' disease (with an additional category – 'indeterminate AMD' – reflecting rarer subtypes). Within 'late' disease, distinction should be drawn between disease that is 'wet active' (neovascular lesions that may benefit from treatment), 'wet inactive' (neovascular disease with irreversible structural damage) and 'dry' (non-neovascular disease, including geographic atrophy). For more details, see recommendation 1.1.1.

The consequences of this condition for vision can be severe. AMD is the most common cause of visual impairment in the developed world, and the Royal National Institute of Blind People (RNIB) reports that AMD is the most common cause of certification for vision impairment. In an Australian cohort study of people with early stage AMD, the risk of progression to intermediate or advanced AMD within 5 years was 17%. However early AMD is not always significantly progressive as 83% did not and AMD lesions appeared to have improved and regressed in 8% of people.

The prevalence of late AMD in the UK among people aged 50 years or over is 2.4% (from a meta-analysis applied to UK 2007–09 population data). This increases to 4.8% in people aged 65 years or over, and 12.2% in people aged 80 years or over. The same study found the prevalence of geographic atrophy to be 1.3 to 6.7%, and

the prevalence of neovascular AMD to be 1.2 to 6.3%. Estimates indicate there may be 26,000 people with neovascular AMD now suitable for treatment in the UK each year; given a total UK population of 60 million. This equates to 450 new cases per million per year.

There has been a significant increase in hospital activity in England for episodes with a primary diagnosis of AMD, from less than 10,000 episodes in the years 2005/06 to over 75,000 episodes in the years 2013/14. The most common primary procedure administered in hospital to people with a primary diagnosis of macular degeneration involves intravitreal injection. The cost of aflibercept and ranibizumab, medicines for the treatment of late AMD (wet active), is significant. In 2015−16, ranibizumab was second and aflibercept was fourth in the list of medicines with positive NICE technology appraisals on which the NHS spent most money, between them accounting for a total of around £450 million expended (although some of these costs relate to use for other licensed indications).

More information

[The following sentence is for post-consultation versions only – editor to update hyperlink with guideline number]You can also see this guideline in the NICE pathway on [pathway title]. [Note: this should link to the specific topic pathway, not to the overarching one.]

To find out what NICE has said on topics related to this guideline, see our web page on [developer to add and link topic page title or titles; editors can advise if needed].

[The following sentence is for post-consultation versions only – editor to update hyperlink with guideline number]See also the guideline committee's discussion and the evidence reviews (in the full guideline), and information about how the guideline was developed, including details of the committee.

Recommendations for research

The guideline committee has made the following recommendations for research. [If there are more than 5 in the full guideline, add:] The committee's full set of research recommendations is detailed in the full guideline.

[Add up to 5 high-priority research recommendations (for CGUT updates, up to 6 old and new recs). See 'Developing NICE guidelines: the manual' section 9.5 for guidance on formulating and selecting high-priority research recommendations for inclusion in the guideline. Use the following style for each recommendation:]

1 Strategies to slow the progression of age-related macular degeneration (AMD)

1. What is the effectiveness of antioxidant and zinc supplements on AMD disease progression for people with early AMD at high risk of progression in the context of an RCT

Why this is important

Age-related eye disease study (AREDS 2001) examined the effect of antioxidant supplementation on AMD progression using the AREDS formation, which included beta carotene, vitamin E, vitamin C and zinc. Although the study showed some beneficial effects of the combined antioxidant supplementation in a subgroup of participants, the effects of each of the formula components on AMD progression are unclear. Additionally 1 of the ingredients (beta carotene) in AREDS 2001 formulation is associated with a possible risk of lung cancer among smokers. The AREDS research group introduced a new formulation that excluded beta carotene in the AREDS2 study, but the effect of AREDS2 formulation on AMD disease progression is unknown because of a complicated study design involving secondary randomisation and no placebo control. Therefore, a well conducted randomised trial would provide an evidence base for the benefits and risks of individual components of the antioxidant supplements, and provide the ability to establish the treatment effect of antioxidant supplementation (the AREDS2 formula) on AMD progression by comparing AREDS2 formula with no treatment (for instance normal diet).

2 Organisational models for AMD diagnosis and management

What is the long-term effectiveness, in terms of patient-relevant outcomes including visual acuity and quality of life, of different models of care that aim to reduce time from initial presentation to referral, diagnosis, and treatment?

Why this is important

There is robust evidence showing that visual loss is linked with delays to diagnosis and/or treatment, but a lack of evidence which evaluates the impact of any particular model of care/services in reducing any of the time intervals throughout the referral and treatment process, plus the subsequent influence of different models of care on peoples' visual acuity and quality of life. A well conducted trial would, therefore provide the evidence base to assess the long-term effectiveness of different organisational models on referral, diagnosis and treatment for people with late AMD (wet active).

3 Antiangiogenic therapies and frequency of administration

What is the effectiveness and cost effectiveness of the 'treat-and-extend' regimen compared with alternative regimens (dosing frequencies)?

Why this is important

Only 1 trial was identified that evaluated the effectiveness of the treat-and-extend regimen, compared with routine monthly treatment. The quality of evidence reported was low because of risk of bias and imprecision, which is because of the small sample size in the study. Only 60 participants were recruited (40 participants receiving the treat-and-extend regimen and 20 receiving routine monthly injections). This introduced an uncertainty in the estimated effect of the treat-and-extend regimen. The lack of high quality evidence available means that it is not possible to make any recommendations on this regimen, although it is commonly used in practice and indirect evidence from a network meta-analysis indicates possible positive benefit.

4 Frequency of monitoring

What is the long-term cost effectiveness, in terms of patient-relevant outcomes including best-corrected visual acuity and quality of life, of different review frequencies/strategies for people at risk of progression to late AMD (wet active)?

Why this is important

There is currently no evidence on the different frequencies for monitoring people with AMD. This means that it is not possible to identify an optimum monitoring strategy for people at different stages of AMD, leading to uncertainty in how to correctly manage treatment for individuals or how to configure eye care services to support patients. A study of the needs of people at risk of progression to late AMD (wet active) to identify the optimum review arrangements would remove this uncertainty. Trials would need to measure visual outcomes and health service resource use to measure the trade-offs between the optimal management of people at risk of disease progression in relation to the use of resource.

5 Self-monitoring strategies

Does earlier detection of the incidence of late AMD (wet active) by self-monitoring in people diagnosed with early AMD, indeterminate AMD or late AMD (dry) lead to earlier treatment and better long-term outcomes?

Why this is important

A review of the evidence demonstrated that self-monitoring interventions 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, and also failed to capture potential negative effects of self-monitoring (including the potential for increased anxiety). A study designed to follow up a cohort of people diagnosed with early, indeterminate or late AMD (dry) to the time when the diagnosis of late AMD (wet active) is established, comparing time to diagnosis of late AMD (wet active), time to treatment, long-term visual acuity and participants' quality of life would establish the association between early detection and early treatment plus good long-term vision outcome, and enable the weighing of any such positive effects against the potential for harm.

1 ISBN: