Appendix B: Guideline scope

B.1 Guideline title

Age-related macular degeneration: diagnosis and management

B.1.1 Short title

Age-related macular degeneration (AMD)

B.1.2 Topic

The Department of Health in England has asked NICE to develop a clinical guideline on the diagnosis and management of age-related macular degeneration.

B.1.3 Who the guideline is for

- People using services, families and carers and the public.
- Healthcare professionals in primary care.
- Healthcare professionals in secondary care.
- Social care practitioners.
- Local authorities.
- Commissioners of ophthalmic and optometric services.
- Providers of ophthalmic and optometric services.
- Practitioners in ophthalmic and optometric services.

It may also be relevant for:

- Private sector and voluntary organisations.
- People working in related services.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive.

B.2 Equality considerations

NICE has carried out an equality impact assessment during scoping. The assessment:

- lists equality issues identified, and how they have been addressed
- explains why any groups are excluded from the scope, if this was done.

B.3 What the guideline is about

B.3.1 Who is the focus?

Groups that will be covered

- Adults (18 years and older) at risk of, or diagnosed with, age-related macular degeneration (AMD).
- Specific consideration has been identified for people:
  - who smoke

- with a family history of AMD
- from low socio-economic status groups
- with other comorbidities that affect visual function, for example cataracts, glaucoma and retinal damage
- who have already had loss of vision in 1 eye
- with other forms of sensory loss, for example deafness
- who have difficulty in accessing care, for example, people with impaired cognitive function (such as dementia and learning disabilities), living in care settings, or with impaired mobility.

Groups that will not be covered

- People with juvenile macular degeneration.
- People with Sorsby's dystrophy.
- People with Stargardt's disease.
- People with Best's disease.
- People with Choroidal neovascularisation secondary to other causes.
- Young people (under 18) with other rare causes of macular degeneration.

B.4 Settings

Settings that will be covered

- All settings in which NHS funded care is received.

B.5 Activities, services or aspects of care

Key areas that will be covered

1. Information for people with suspected or diagnosed AMD and their family members or carers (as appropriate).
2. Service organisation:
   - Patient referral pathways, timescales, and service models for triage and diagnosis, treatment and ongoing management.
3. Risk of AMD:
   - Risk factors for the development and progression of AMD, including smoking, increasing age, family history of AMD, family origin, ocular factors and the presence of AMD in the other eye.
   - Strategies for reducing the risk of developing AMD in the unaffected eye or progressing to late AMD, including smoking cessation, increasing the intake of antioxidants, carotenoids and omega 3 fatty acids through dietary changes, high-dose vitamin and mineral supplementation, treatment with statins, and laser treatment of drusen.
4. Diagnosis:
   - Signs and symptoms of AMD.
   - Diagnosis and investigation of AMD. Investigations of interest include ophthalmological examination and photography, best corrected visual acuity, slit lamp fundoscopy, ocular coherence tomography, fundus autofluorescence, fluorescein angiography and indocyanine green angiography.
   - Classification systems for the staging of AMD.
5. Management strategies:

- Early and intermediate AMD: specific aspects that will be considered include strategies for slowing disease progression, strategies for optimising existing visual performance, laser treatment of drusen and psychological therapies.
- Late 'dry' AMD (advanced geographic atrophy): interventions of interest include psychological therapies and reablement services.
- Late 'wet' AMD (neovascular): interventions of interest include anti-angiogenic therapies (aflibercept, bevacizumab [aliquoted for use in the eye], pegaptanib sodium, ranibizumab), intravitreal steroids (dexamethasone, fluocinolone acetonide, triamcinolone acetonide), laser photocoagulation, photodynamic therapy, psychological therapies and reablement services.
- Frequency of administration and indications for stopping treatment will also be considered.
- Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a medicine's summary of product characteristics to inform decisions made with individual patients. Although bevacizumab is in use in the UK and elsewhere for the treatment of neovascular AMD, the Medicines and Healthcare Products Regulatory Agency regards it as unlicensed for this indication because its use requires the formulation of the licensed product to be divided into separate smaller doses (to produce multiple aliquots) for injection into the eye. Licensed alternatives (such as aflibercept, pegaptanib sodium, ranibizumab and verteporfin) are available. Although there is evidence (including research funded by the National Institute for Health Research) demonstrating the safety and efficacy of bevacizumab for treating AMD that will be referred to in the guideline, our ability to refer to its use in routine clinical practice for this condition is constrained by its licensing status. Therefore, while bevacizumab will be included in the evaluations carried out to develop the guideline, and information on its properties and use may be included in the final guideline, no recommendation for its use will be made in any case where there is a licensed alternative.

6. Monitoring and review (including both the affected and unaffected eye):
   - Frequency of review for early AMD, intermediate AMD, and advanced geographic atrophy.
   - Frequency of review for neovascular AMD.
   - Strategies and tools for monitoring.

Areas that will not be covered

1. Access to optometric, emergency and GP services.
2. Training and certification for healthcare professionals.
3. Processes for assessing and implementing new technology.
4. Interventions that are not used in England, including experimental interventions such as stem cell therapy for advanced geographic atrophy.

B.6 Economic aspects

We will take economic aspects into account when making recommendations. We will develop an economic plan that states for each review question (or key area in the scope) whether economic considerations are relevant, and if so whether this is an area that should be prioritised for economic modelling and analysis. We will review the economic evidence and carry out economic analyses. The reference case used will be that for interventions with health outcomes in NHS settings; therefore, the preferred unit of effectiveness will be the quality-adjusted life year (QALY), and costs will be considered from an NHS and personal social services (PSS) perspective. As stipulated in Developing NICE guidelines: the manual, productivity costs will not be included in health economic analyses. However, it is possible

that the ability to work may be considered as a surrogate measure of broader functional capacity and this may contribute to estimates of health-related quality of life.

B.7 Review questions

While writing this scope, we have identified the following key issues, and key questions related to them. These questions are draft and may be subject to change during development of the guideline:

1. Information for people with suspected or diagnosed AMD and their family members or carers (as appropriate):
    - 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)?
2. Service organisation:
    - How do different organisational models and referral pathways for triage and diagnosis influence outcomes for people with suspected AMD (for example, correct diagnosis, errors in diagnosis, delays in diagnosis, process outcomes)?
    - How do different organisational models for ongoing treatment and follow up influence outcomes for people with neovascular AMD (for example, disease progression, time to treatment, non-attendance)?
    - What are the barriers to appointment attendance and uptake of treatment for people with AMD?
3. Risk of AMD:
    - Which risk factors increase the likelihood of a person developing AMD or progressing to late AMD?
    - What is the effectiveness of strategies to reduce the risk of developing AMD in the unaffected eye or slow the progression of AMD?
4. Diagnosis:
    - What signs and symptoms should prompt a healthcare professional to suspect AMD in people presenting to healthcare services?
    - What tools are useful for triage, diagnosis and informing treatment in people with suspected AMD?
    - What are the clinical utilities of disease stage classification tools for people with AMD?
5. Management strategies:
    - What is the effectiveness of different management strategies for neovascular AMD (for example, anti-angiogenic therapies, intravitreal steroids, laser photocoagulation, photodynamic therapy, psychological therapies and reablement services)?
    - What is the effectiveness of different anti-angiogenic regimens for the treatment of neovascular AMD?
    - What is the effectiveness of switching therapies for neovascular AMD if first-line therapy is contraindicated or has failed?
    - What is the effectiveness of early treatment of neovascular AMD in people with visual acuity greater than 6/12?
    - What is the effectiveness of adjunctive therapies for the treatment of neovascular AMD?
    - What factors indicate that treatment for neovascular AMD should be stopped?
    - What is the effectiveness of psychological therapies for AMD?

- 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)?

B.8 Main outcomes

The main outcomes that will be considered when searching for and assessing the evidence are:

1. Clinical outcomes and effectiveness:
   - visual acuity
   - disease stage progression
   - presence of anxiety and depression
   - reduced accidents, including falls
   - eligibility for Certificate of Vision Impairment
   - patient satisfaction.
2. Safety and adverse events of treatments and investigations.
3. Diagnostic accuracy and clinical utility.
4. Functional capacity, participation, independence and ability to carry out activities of daily living. Ability to work may be used as a measure of functional capacity. However, NICE guidance does not prioritise treatments most likely to benefit people of working age at the expense of other groups.
5. Health-related quality of life.
6. Service user experience and outcomes:
   - time to treatment
   - time to diagnosis
   - non-attendance
   - health and social care utilisation
   - number of hospital visits.
7. Behavioural outcomes and modifying risk factors, for example smoking cessation.
8. Impact on family members and carers (as appropriate).
9. Resource use and costs.

B.9 Links with other NICE guidance and NICE Pathways

B.9.1 NICE guidance

NICE guidance that will be updated by this guideline (subject to a Technology Appraisals review decision)

- Guidance on the use of photodynamic therapy for age-related macular degeneration (2003) NICE technology appraisal guidance 68

NICE guidance that will be incorporated unchanged in this guideline

- Aflibercept solution for injection for treating wet age-related macular degeneration (2013) NICE technology appraisal guidance 294
- Ranibizumab and pegaptanib for the treatment of age-related macular degeneration (2008) NICE technology appraisal guidance 155 (recommendations 1.1, 1.3 and 1.4 will be incorporated, however recommendation 1.2 is partly dependent on review work to be completed in this guideline and may not be incorporated verbatim)

NICE guidance about the experience of people using NHS services

NICE has produced the following guidance on the experience of people using the NHS. This guideline will not include additional recommendations on these topics unless there are specific issues related to age-related macular degeneration (AMD):

- Patient experience in adult NHS services (2012) NICE CG138
- Depression in adults with a chronic physical health problem (2009) NICE CG91
- Falls in older people (2013) NICE CG161
- Medicines adherence (2009) NICE CG76
- Medicines optimisation (2015) NICE NG5

NICE guidance in development that is closely related to this guideline

NICE is currently developing the following guidance that is closely related to this guideline:

- Cataracts NICE guideline. Publication expected June 2017.
- Macular degeneration NICE quality standard. Production will start in Autumn 2017.

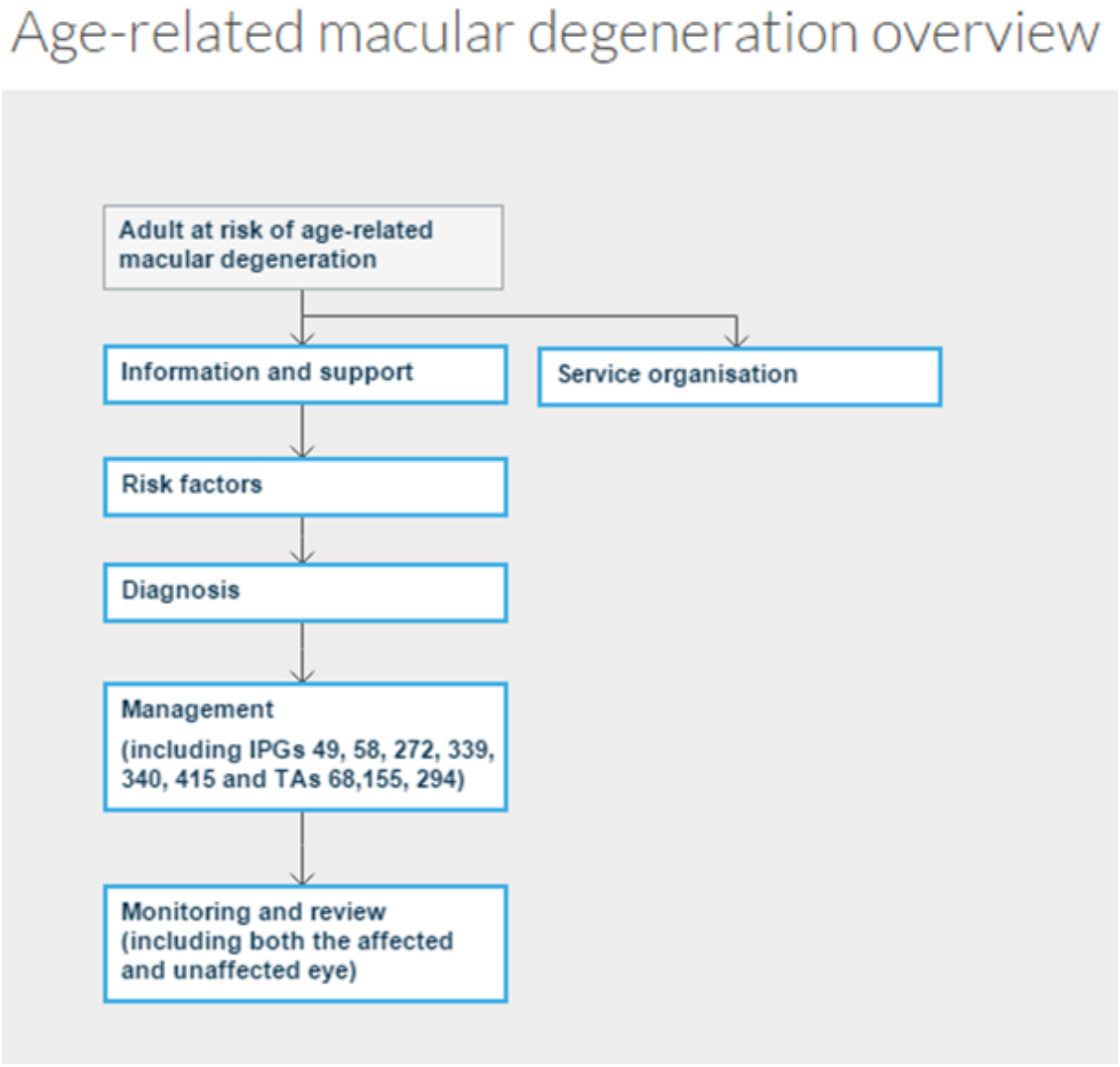
B.10.4 NICE Pathways

When this guideline is published, the recommendations will be added to NICE Pathways. NICE Pathways bring together all related NICE guidance and associated products on a topic in an interactive topic-based flow chart.

A draft pathway outline on AMD, based on the draft scope, is included below. It will be adapted and more detail added as the recommendations are written during guideline development. The AMD pathway will be accessible from the eye conditions pathway.

Other relevant NICE guidance will also be added to the NICE Pathway, including:

- Aflibercept solution for injection for treating wet age-related macular degeneration (2013) NICE technology appraisal guidance 294
- Epiretinal brachytherapy for wet age-related macular degeneration (2011) NICE interventional procedure guidance 415
- Macular translocation with 360° retinotomy for wet age-related macular degeneration (2010) NICE interventional procedure guidance 340
- Limited macular translocation for wet age-related macular degeneration (2010) NICE interventional procedure guidance 339
- Ranibizumab and pegaptanib for the treatment of age-related macular degeneration (2008) NICE technology appraisal guidance 155
- Implantation of miniature lens systems for advanced age-related macular degeneration (2008) NICE interventional procedure guidance 272
- Transpupillary thermotherapy for age-related macular degeneration (2004) NICE interventional procedure guidance 58
- Radiotherapy for age-related macular degeneration (2004) NICE interventional procedure guidance 49
- Guidance on the use of photodynamic therapy for age-related macular degeneration (2003) NICE technology appraisal guidance 68



B.11 Context

B.11.1 Key facts and figures

Age-related macular degeneration (AMD) is the most common form of macular degeneration and is the term given to ageing changes without any other obvious cause that occurs in the central area of the retina (macula). It is a painless eye condition that generally leads to the gradual impairment of vision, but can sometimes cause a rapid reduction in vision. AMD may be an incidental finding on a routine visit to the optometrist or people may present with difficulty in performing daily activities such as driving, reading and recognising faces.

AMD may be classified according to the stage of disease progression into early, intermediate and late. Late AMD can be further classified as either 'wet' AMD (neovascular) or 'dry' AMD (advanced geographic atrophy). Geographic atrophy may occur at the intermediate stage but is not considered to be late AMD until atrophic changes affect the fovea. Consequences of this condition 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 1 Australian cohort study of people with early stage AMD, the risk of progression to intermediate or advanced AMD within 5 years was 17%. Lesions appeared to have improved and regressed in 8% of people.

Neovascular AMD can develop very suddenly but can be treated if caught early; therefore fast referral to a hospital specialist is essential. In people with untreated neovascular AMD, who are not already visually impaired or blind, over half will become visually impaired or blind within 3 years. In American studies, more than 50% of patients treated for neovascular AMD failed to maintain near normal vision in their first affected eye after 2 years of treatment. People who developed neovascular AMD in their second affected eye maintained near normal vision in that eye over 90% of the time. The better outcome of the second affected eye is likely because of increased monitoring that occurs during treatment of the first affected eye. This finding reflects the importance of early detection and treatment.

Geographic atrophy is the more common type of AMD. It usually develops very slowly and causes a gradual change in the central vision. Geographic atrophy usually takes a number of years to get to its final stage and there is currently no proven treatment. Three lines of visual acuity are lost in 31% of people within 2 years of diagnosis, and in 53% of people within 4 years.

Currently, the exact cause for AMD is not known but factors such as age, family origin (prevalence is higher in people of white and Chinese family origin), diet and nutrition, genetics, and smoking are thought to affect the risk of developing the disease. Socioeconomic factors also may result in later presentation and poorer outcomes. A qualitative study found that cost was seen as a significant barrier to accessing sight tests.

The prevalence of late AMD in the UK amongst those aged 50 years or more is 2.4% (from a meta-analysis applied to UK 2007−2009 population data). This increases to 4.8% in people aged 65 years or more, and 12.2% in people aged 80 years or more. The same study using UK population data found the prevalence of geographic atrophy to be 1.3−6.7%, and the prevalence of neovascular AMD to be 1.2−6.3%. Estimates indicate there may be 26,000 people with neovascular AMD now eligible 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 2005−2006 to over 75,000 episodes in the years 2013−2014. The most common primary procedure in hospital episodes of people with a primary diagnosis of macular degeneration involves intravitreal injection. The cost of ranibizumab, a medicine for the treatment of neovascular AMD, is significant. In 2013−14 ranibizumab was second in the list of drugs by cost for medicines positively appraised by NICE. In the same year the cost of this medicine to the NHS was £244 million (although some of this cost will be for other licensed indications).

B.11.2 Current practice

A person with AMD will present to local healthcare services, usually self-referred because they are experiencing blurring or distortion of the central vision, or asymptomatic and referred after a routine examination. Presentation may be at a GP practice, optometrist, local eye unit, eye casualty or emergency department. People with difficulty accessing optometric services, low socioeconomic status, cognitive impairment or increasing age may have a higher risk of delayed presentation. This could lead to significant visual impairment, especially in the case of neovascular AMD which can develop quickly and is considered an urgent problem. The Royal College of Ophthalmologists' Age-related macular degeneration: guidelines for management state that referral from the optometrist to attendance at the fast track macular clinic should ideally take place within 1 week from presentation of neovascular AMD.

After attendance at the fast track macular clinic or medical retina clinic, the time for the person with neovascular AMD to receive treatment is recommended within 1 week "as an ideal to aim for". The basis for early referral is that there are treatments available in secondary care that should be given as soon as possible after neovascular AMD is confirmed in order to prevent visual impairment. People with suspected neovascular AMD

should initially receive investigations such as medical, family, social and medication history, ophthalmological examination, best corrected visual acuity, slit lamp examination and photography. After referral to secondary care people may receive more specialist investigations such as optical coherence tomography, fundus fluorescein angiography and indocyanine green angiography. These will help to confirm the diagnosis, classify the stage of neovascular AMD and image disease areas in order to direct treatment.

Depending on the type of AMD a person will be offered different treatment. People with early AMD or geographic atrophy will receive limited treatment that may consist of advice and information, low vision rehabilitation and psychological support where required. The treatment options for neovascular AMD are greater and include anti-angiogenic therapies, laser anticoagulation and photodynamic therapy. These treatments are given by the designated treatment provider. People with all types of AMD should also receive information about the risk to the second eye and the importance of presenting early if they develop symptoms. A study in 2001 found that 70% of newly-diagnosed blind and partially sighted people wanted someone to talk to about their fears and concerns but only 19% were offered this opportunity by their eye clinic. A further study in 2008 reported nearly 1 in 5 (17%) of blind and visually impaired people surveyed received no help or information in the eye clinic other than medical diagnosis and treatment. This rises to 1 in 3 (32%) for working age adults.

In terms of supportive care, people with AMD may be referred to a low vision clinic or community low vision service for assessment and issue or purchase of low vision equipment. These services should also notify social services in situations where a home visit or rehabilitation may be needed. People with AMD may need to be registered using the certificate of vision impairment. Fitness to drive should be assessed by a clinician. Signposting to other agencies such as The Macular Society, RNIB, and any local services for provision for the blind should also be provided. Variable access to these services should be taken into account when considering equality issues across populations in the UK.

B.11.3 Policy, legislation, regulation and commissioning

Policy

This guideline will address areas highlighted in the UK Vision Strategy 2013−2018, including improving awareness and understanding of eye health; access to eye care services to detect and prevent sight loss; the coordination, integration and effectiveness of eye health and care services and consideration of equality issues.

Legislation, regulation and guidance

The Royal College of Ophthalmologists' Age-related macular degeneration: guidelines for management provide guidance on many aspects of AMD management. This guideline will also consider guidance from the Driver and Vehicle Licensing Agency At a glance: guide to the current medical standards of fitness to drive.

Commissioning

This guideline will consider relevant documents relating to the commissioning of services by Clinical Commissioning Groups:

- Department of Health (2007) Commissioning toolkit for community based eye care services
- Department of Health (2007) Step-by-step guide to commissioning community eye care services
- Clinical commissioning guidance from The College of Optometrists and the Royal College of Ophthalmologists (2013) Commissioning better eye care: age-related macular degeneration

B.12 Further information

This is the final scope, incorporating comments from registered stakeholders during consultation.

Our website has information about how NICE guidelines are developed.