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Commissioning Guidance

Age Related Macular Degeneration Services: Executive Summary

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1. Introduction

The macula is the centre of the retina that is responsible for high quality central vision. Age related macular degeneration (AMD) is a chronic progressive degenerative disease of the macula typically affecting people over the age of 50 years. There are two types of advanced forms of the disease, commonly called dry and wet AMD. Whilst the dry form is a slowly deteriorating condition with no treatment at present, the wet form presents acutely and need both urgent and chronic treatment over years.

This condition is the most common cause of visual impairment in the older population significantly affecting their quality of life and independence. Other than the cost incurred by social services, the cost of providing care for wet AMD is very high due to the cost of the drugs and the treatment burden of frequent visits to ophthalmology departments over several years. Moreover, as treatment must be initiated urgently, fast-track services need to be implemented. The demand for this service has already affected the capacity of several ophthalmology departments and is projected to rise as the ageing population increases, highlighting the need to continually plan for the chronic management and the growing need. New and existing drugs are being evaluated to reduce burden, ensure cost effectiveness, and improve outcomes.

People with advanced forms of AMD also require low visual aids, counselling on coping with their vision, advice on available support and have associated conditions and risk of falls that may also require treatment. Most patients with AMD are elderly, and many have other chronic diseases and mobility issues. Therefore, transport needs should be considered, and services should be readily accessible in terms of location, parking, public transport, and hours of opening. Stable treated AMD patients may be evaluated in the community. Psychological counselling regarding the loss of vision is also required. Eye Clinic Liaison Officers (ECLOs) are essential throughout a patient journey and people need the help of family/friends to attend appointments.

It is important to establish joint care with optometry services for diagnosis, referral, and monitoring of stable patients. However, a patient focused approach should be the overarching principle when designing local pathways. New ways of delivering care such as telemedicine, clinical decision tools incorporating artificial intelligence and diagnostic hubs and treatment centres are to be evaluated to benefit the patients, NHS, and the wider society.

This guidance sets out the principles and minimum standards of care for AMD to decrease variations of care across AMD services in England and Wales. It also provides information that can support the current and future capacity planning of AMD services. This guidance is intended for use by commissioners, providers, social care and users of the AMD services, including their families and carers. In this document, the term HCP refers to nurses, optometrists, and orthoptists.

The guidance follows the RCOphth guidance development process and is based on best available evidence obtained from systematic review of the literature (see appendix A in the main document) and is compliant with the National Institute for Health and Care Excellence (NICE) Clinical Guideline on AMD NG82 dated 23-01-2018[1]. NICE quality standard QS180

(standards 3 and 4) dated February 2019 has also been considered in compiling this statement[2].

There are several classification systems that describe the disease progression in AMD. The staging of severity of AMD is important because visual impairment increases with severity of AMD. The NICE guidance NG82 dated 23-01-2018 is the most recent classification of AMD. However, the frequently used terminologies to describe the various stages are based on previous classifications. Table 1 describes both NICE guidelines and the more commonly used terminology used to describe the changes.

Table 1: NICE guidelines-based classification of Age related macular degeneration[1]

AMD Classification in NICE Guidance	Definition in NICE Guidance	Frequently Used Terminology
Normal Eyes	No signs of age-related macular degeneration (AMD) Small ('hard') drusen (less than 63 micrometres) only	No AMD
Early AMD	Low risk of progression: • medium drusen (63 micrometres or more and less than 125micrometres) or pigmentary abnormalities Medium risk of progression: • large drusen (125micrometres or more) or • reticular drusen or • medium drusen with pigmentary abnormalities High risk of progression: • large drusen (125 micrometres or more) with pigmentary abnormalities or • reticular drusen with pigmentary abnormalities or • vitelliform lesion without significant visual loss (best-corrected acuity better than 6/18) or • atrophy smaller than 175 micrometres and not involving the fovea	Early AMD or Age-related maculopathy Intermediate AMD
Late AMD (indeterminate)	Retinal pigment epithelial (RPE) degeneration and dysfunction (presence of degenerative AMD changes with subretinal or intraretinal fluid in the absence of detectable neovascularisation) Serous pigment epithelial detachment (PED) without neovascularisation	

1.1 Prevalence of AMD in the UK

In 2012, it was estimated that there were 513K cases of late AMD, 276,000 cases of geographic atrophy, and 263,000 cases of neovascular AMD in the UK. When these figures are applied to updated 5 yearly population estimates for the UK, published by the United Nations for males and females combined, for years 2020 and 2050, the prevalence in 2020 is estimated to be 645,000 cases of late AMD, 354,000 cases of geographic atrophy and 339,000 cases of neovascular AMD. In 2050, these figures are projected to increase to 1.3 million late AMD, 720,000 geographic atrophy and 683,000 neovascular AMD (Personal communication with Dr Alicja R Rudnicka and Professor Christopher G Owen)[3,4].

1.2 Incidence of AMD in the UK

Based on the estimations made from the 2007-2009 UK population data, the annual incidence per year of new cases of late AMD is 71 000, equating to 4.1 cases per 1000 women and 2.6 per 1000 men. The incidence of geographic atrophy is 2.4 per 1000 women and 1.7 per 1000 men. For nAMD, these figures were 2.3 per 1000 women and 1.4 per 1000 men[3].

1.3 Cost of visual impairment

The Time to Focus report by Fight for Sight in 2020 revealed that the annual societal costs of AMD related visual impairment is £2.6 billion, of which 47% of costs fall within the health and social care sector. The estimated costs include £1.2billion on healthcare; £0.036 billion on devices; £0.14 billion on productivity; £0.002 billion on welfare; £0.5 billion on informal care; £0.69 billion on intangible costs. It was also estimated that more than 11,000 new cases of late AMD already have at least moderate visual impairment. Overall, the total lifetime costs for this cohort was estimated at almost £818 million with an average cost per patient of £73,350.

2. Risk Factors for development and progression of AMD

This includes all stages of AMD

2.1 Non-modifiable risk factors	
Increasing drusen area and volume	Patients with a drusen volume over 0.03 mm3 in the 3mm circle of the macula centred at the fovea has a greater than 4-fold increased risk for developing late AMD compared with those with lower drusen volumes [16,17].
Subretinal Drusenoid Deposits (SDD)	Subretinal Drusenoid Deposits (also known as reticular pseudodrusen) are an independent risk factor for AMD development progression [18,19].
Genetics	Although 52 genetic variants have been identified for AMD, almost 15% of patients with AMD have no risk variants [20,21]. Additionally, no genetic score has been defined to assess risk for AMD [22].
Fellow eye of wet AMD eyes	There is a 10% per year risk of developing wet AMD in the fellow eyes in people with unilateral wet AMD [23,24].

2.2 Modifiable risk factors for progression to more advance forms of AMD	
Smoking history	Smoking is an established strong modifiable risk factor for AMD [25]. Being a current smoker quadruples the risk of progression to late AMD [26,27]. A synergistic effect has been documented between smoking and genetic factors [28]. Current smokers develop late wet AMD at an average of 5.5 years younger than those who never smoked and 4.4. years younger than past smokers [29]. The risk of AMD goes back to that of a non-smoker wth 10 years of quitting, therefore smoking cessation should be recommended to these patients [30].
Body Mass Index	A higher body mass index (BMI) (>30) increases the risk for progression to advanced AMD (RR 2.35). A wider waist circumference is associated with a two-fold increased risk for progression[31]. There is a direct association with higher BMI leading to higher risk of AMD[32].
Nutrition	A diet low in omega-3 and -6 fatty acids, antioxidant vitamins, carotenoids and minerals are a risk factors for AMD. Adherence to a Mediterranean diet is associated with a 41% reduced risk of incident late AMD. The effect is due to the increased consumption of fruits and diet rich in antioxidants that aid in prevention of AMD[33]. A diet of 200 grams per day of vegetables, fruit two times per day, and fish two times per week is associated with a significantly reduced risk of AMD[34]. The original Age-Related Eye Disease Study (AREDS) showed that supplements containing vitamin C, vitamin E, beta carotene, and zinc reduced the 5-year likelihood of developing late AMD by an estimated 25% in at risk individuals[35]. These individuals were those with bilateral large drusen or fellow eyes with large drusen with late AMD in the first eye. The primary analysis of Age-Related Eye Disease Study 2 (AREDS 2) showed no additional value of adding lutein and Zeaxanthin, omega-3 long-chain polyunsaturated acid or the combination on the progression to advanced AMD or changes in visual acuity compared with placebo. However, secondary exploratory analyses suggest that due to the risk in smokers lutein/zeaxanthin is more appropriate than beta carotene in the AREDS supplementation[36]. These supplements may be obtained over the counter; and is an item not routinely prescribed in primary care (NHS England, *Items which should not be routinely prescribed in primary care: Guidance for CCGs* (2019).
Sunlight exposure	Meta-analysis on the association between sunlight exposure and AMD indicated no relationship between exposure to sunlight and increased risk of AMD[37].

2.3 Associations of AMD

Systemic comorbidities in patients with AMD may present a challenge for on-going care of this long-term condition due to difficulties in accessing care and maintaining compliance. Key co-morbidities include hearing loss, poorer cognitive function, established dementia, Alzheimer's disease, depression, and anxiety related to both the diagnosis and therapy[28.29].

Charles Bonnet syndrome (CBS) may be a secondary effect of AMD. It affects visually impaired patients and is characterized by the occurrence of chronic visual hallucinations, not attributable to other neurologic causes such as Alzheimer's disease, or use of drugs and the patients are aware of the unreality of these images[30]. The prevalence of CBS in nAMD patients ranges from 11% to as high as 40% and mainly affects older individuals with poor visual acuity[31,32]. It is useful to make this condition known to all patients with visual impairment. Misdiagnosis in patients with mental health issues is also a concern.

3. Diagnostic modalities of AMD

3.1 Clinical examination

Clinical examination should include:

- recording symptoms of AMD
- smoking and family history
- visual acuity assessment - ideally be measured using a LogMAR chart and recorded in Early Treatment Diabetic Retinopathy Study (ETDRS) letters for all cases of AMD and in all cases of nAMD initiated on treatment. Snellen visual acuity is acceptable if ETDRS is not available during the first consultation, however conversion of Snellen visual acuity to LogMar should be avoided due to high level of inaccuracy[33].
- fundoscopy
- examination of both eyes

3.2 Diagnostic tests

Optical Coherence tomography (OCT) is the first diagnostic test for patients with AMD[34] and has high sensitivity and specificity in detecting late AMD. In the indeterminate form of late AMD, it may identify subretinal or intraretinal fluid or serous pigment epithelial detachment (PED) without detectable choroidal neovascularisation. These cases require regular monitoring with multimodal imaging as they are at increased risk of developing late nAMD.

OCT should be acquired in both eyes. Fellow eyes of unilateral nAMD patients under treatment are at risk of conversion to nAMD and the progression of disease is best captured on OCT as patients may be asymptomatic at point of conversion. OCT is also the most sensitive tool to assess response to treatment including reactivation of disease.

Optical coherence tomography –angiography (OCT-A) has become more widely accepted as a rapid, sensitive, and non-invasive imaging test used for detection and management of nAMD[35]. When the structural OCT shows features suggestive of the nAMD, evidence of choroidal neovascularization on OCT-A is considered adequate evidence to initiate therapy. However, the technique requires high specification computers for data storage, analysis, and expert interpretation of scans due to presence of artefacts (such as motion, blink, projection). A negative OCT-A scan, however, does not exclude the diagnosis of CNV. In such cases, when the structural OCT suggests the nAMD, but OCT-A imaging does not confirm the presence of CNV, invasive tests may need to be performed to confirm nAMD. Fundus fluorescein angiography (FFA) is the recommended invasive test but indocyanine angiography (ICG) may add value to the interpretation especially when there is a suspicion of polypoidal choroidal vasculopathy[36,37].

3.3 Recommendations

1. The order of examination is shown above and most diagnosis can be made by clinical examination, OCT and OCTA.
2. OCT can be employed as sole investigation to detect nAMD in rare scenarios:
   a. when there is no ready access to confirmatory tests such as OCTA or FFA to avoid delay in receiving first treatment within 2 weeks of diagnosis; or
   b. due to patient factors such as difficulty in obtaining informed consent, allergy to fluorescein dye contraindicating FFA or inconclusive OCTA and/or FFA.

3. FFA in combination with ICG is indicated specifically in cases with equivocal scans on OCT-A, partial or poor responders to anti-VEGF therapy and in patients where any other retinal signs might be confounders.
4. Centres that do not have ICG facility may need to refer to those with services.

4. Care Pathway

4.1 General Recommendations for all AMD patients

1. Advice on smoking cessation services and the information on it has to be made available to patients by local services.
2. Nutrition and supplements – A healthy diet, rich in fresh fruit, vegetables, eggs and oily fish is recommended. Licensed formulations of multivitamin supplements containing the AREDS2 formulation are not available on prescription within the NHS. Patients may choose to source these over-the-counter supplements independently.
3. Genetic screening is not recommended[38,39].
4. Need for low vision aids should be assessed in those who meet the definition of low vision at any point throughout the patient journey. The definition of 'low vision' applies when a person's vision affects their daily lives and cannot be improved with spectacles or contact lenses.
5. Prescription for health – Eye Clinic Liaison Officers (ECLOs), ophthalmic nurses and GPs support is required to promote health-seeking behaviour, physical activity and signposting to other services. Social prescribing is recommended.
6. Screening of fellow eyes - Monitoring of fellow eyes with OCT should be done while the affected eye is undergoing treatment or is being monitored (NICE Quality Standard QS180)[2]. The evidence on monitoring of fellow eyes once the patient is discharged from the service is limited and continues to remain an unmet research need.
7. Whilst patients are undergoing treatment or are being monitored, continued attendance at their regular optometrist should be encouraged. This allows early identification of co-morbidities and correction of refractive errors.
8. Information on natural history and risk factors should be provided to patients (refer section 3).
9. Written information leaflets are recommended either locally developed or sourced from national organisations such as Royal Colleges or patient support charities. ECLO services should be commissioned for every clinic. Where this is not done commissioners need to be clear who will be providing these essential services, for example:
    a. Provision of emotional support for the patient and family
    b. Rapid referral to counselling or to medical care for depression/anxiety
    c. Early falls intervention
    d. Consistent and timely referral for CVI
    e. Timely referral to low vision support
    f. Signposting to services outside the clinic such as further information and advice, peer support, free services provided by third sector organisations.
10. When patients are discharged to primary care for ongoing monitoring it is essential that they are discharged with a report of the last findings at discharge, through communication between practitioners is essential to ensure patients receive safe and appropriate care.

4.2 Recommendations for patients with early AMD

The population with early AMD at any risk of progression may be diagnosed and managed by primary care optometrists working in the community. As minimal pre-requisites, diagnosis should be based on history, symptoms, visual acuity assessment and fundus assessment.

OCT can be helpful if available. In suspected cases of wet AMD or where diagnosis is uncertain, the patients must be referred to secondary eye care within a day.

1. Do not refer to secondary care when the diagnosis is confirmed as early AMD.
2. If confirmed as early AMD within secondary care, patients can be discharged and advised to have regular sight tests with their primary care optometrist. General ophthalmic services (GOS) only funds sight tests every 2 years. It is imperative that the primary care optometrist is kept updated of the diagnosis and management. This will allow for improved referrals and lower likelihood of unnecessary re-referrals.
3. Self-monitoring with Amsler chart is often recommended. Patients need to report if they notice distortion, sudden drop in vision or scotoma in central visual field. However, the diagnostic accuracy of Amsler chart is inferior to OCT screening. Any move towards routine OCT monitoring would require additional infrastructure and resources. Home monitoring devices are being evaluated. However, further evidence is required.
4. Subthreshold nanosecond laser or any other forms of laser is not recommended for early AMD.
5. General recommendations for AMD patients apply (refer section 4.1).

4.3 Recommendations for patients with Late dry AMD (Geographic Atrophy)

Currently, there are no treatment options for this condition.

1. General recommendations for AMD patients apply (refer section 4.1).
2. If patients with late dry AMD develop nAMD (wet active), they should be treated as late nAMD (wet active) unless there is no potential for visual improvement.
3. Depending on the visual acuity of both eyes, consider refraction, low visual aids or CVI and counselling regarding DVLA standards for driving eligibility.
4. Ophthalmic nursing support, trained health care professionals (HCP) and ECLO services are highly recommended as they play a useful, key role in terms of supporting, providing education, and making appropriate MDT and/or third sector referrals for these patients.
5. Optometrists and Dispensing Opticians in primary care practice are also able provide these support services, if commissioned.
6. Considerable support is provided by third sector and cover both visual and psychological challenges faced by individuals with this condition including those with Charles Bonnet Syndrome.
7. They may be discharged from secondary care to be monitored by local optometrists for routine sight tests and patient self-management.
8. These patients may be offered any clinical research on new treatments for late dry AMD.

4.4 Recommendations for patients with Late wet AMD (neovascular AMD /nAMD)

4.4.1 Population to whom care pathway applies

This population is defined as the group of patients with nAMD in one or both eyes who will be at risk of rapid decline in vision in the affected eye, if not treated promptly and efficiently. Early diagnosis, prompt referral and protocol-based treatment help to stabilise visual function in the majority of cases. However, the main issue faced by providers is a lack of adequate capacity in the face of increasing numbers of affected patients (due to increasing age of the population) who need prompt initiation of treatment and ongoing therapy over

several years. For commissioners, the increasing cost of ongoing therapy is a growing concern.

Patient suspected with nAMD must be referred to hospital eye service (HES) within a one working day[1]. There needs to be a dedicated robust rapid access referral system, either via direct referral to the HES (face to face or virtual clinics) or via a referral refinement system through primary care optometrists (optometrist decision maker or virtual opinion by HES on the optometrist collected data may be an option).

Table 2 referral source and requirements for AMD services

Referral source	Requirements
Primary care optometrist	Referral should include history and symptoms, visual acuity and fundoscopy findings. OCT is becoming more widely available in primary care and commissioners should work with providers to agree a clear pathway to include electronic direct referral, allow sharing the full volumetric OCT where available to avoid duplication of care.
General Practitioner	Referral should include history and symptoms indicating a suspicion of nAMD as a minimum. Optional referral to optometrists may be made first for diagnostic confirmation of nAMD prior to referral to rapid access clinic but this should not delay treatment.
Self-referral to eye casualty	Patients may notice distortion or central visual impairment and these patients should be fast-tracked for OCT evaluation to rule out nAMD.
Diabetic retinopathy services	Referral from should have minimum standards of colour fundus photograph findings and visual acuity record.
Telemedicine and virtual retinal clinics run in HES	May diagnose nAMD by reviewing visual acuity, OCT +/- colour fundus photograph.

Monitoring of second eye must be done at all visits while the first eye is being treated or monitored by OCT. Asymptomatic fellow eyes with active disease defined as new macular haemorrhage and/or OCT features of nAMD should be referred for treatment.

4.4.2 Referrals

Referral methods may include:

- A dedicated phone line for urgent referrals or a secure email service approved for information transfer of clinical information.
- If the option is available and compatible with local rapid access services, eRS helps optimise dialogue and feedback.
- Images may also be sent by email however a single OCT scan as part of an imaging dataset may not be adequate to prioritise timely review.

As a result of the COVID-19 pandemic, COVID-19 red flags are incorporated into urgent eye care service pathways developed by the national outpatient transformation programme of NHS England and NHS improvement. Please refer to the Community of Practice NHS website for updates https://future.nhs.uk/home/grouphome. It is envisaged that these transformations in services will be incorporated to routine care after the pandemic.

4.4.3 Booking of referrals in Hospital Eye Service

- Dedicated referral route – a fast track or rapid access assessment service should be available for these patients.
- Direct booking by administrative team into the Rapid Access clinic or virtual clinic as soon as the patient presents.
- If nAMD is suspected, a rapid access route to the medical retina service for evaluation and treatment needs to be available. These clinics may be face-to-face or virtual and provided by medical staff or allied health professionals, under the supervision of a medical retina consultant.

4.4.4 Assessment within Rapid Access Clinic in HES

Minimum standards to be met:

- Medical retina consultant led service providing governance structure.
- History and symptoms: medical history should include medication and allergies.
- Visual acuity assessment preferably in ETDRS letters
- Imaging: OCT for initial assessment. If clinical examination and OCT confirms no nAMD, the pathway stops, and patients may be discharged back to optometrists.
- OCT findings confirmed by OCT-A and/or FFA/ICG if OCT shows signs of nAMD.
- Assessment and offer of treatment within 2 weeks of date of referral after discussing the pros and cons of the treatment regimen.

4.4.5 Referral refinement of Rapid Access

OCT is becoming more widely available in primary care and commissioners should work with providers to agree a clear pathway to include electronic direct referral, allow sharing the full volumetric OCT where available and so avoid duplication of care.

Until OCT scanning is commissioned consistently, referral for further diagnostics is to be expected. Not all primary care optometrists have access to OCT scanning so in cases with a lower suspicion of wet AMD but a need to rule this out with OCT, a triaging or referral refinement approach may therefore be an effective way of managing the demand on the service.

Methods include:

1. Tele-ophthalmology where visual acuity and OCT images may be sent to the HES for further grading and refinement. There is emerging evidence on the

effectiveness of teleophthalmology, however its application to the service would require additional IT support and infrastructure [40-42].

2. HES governed virtual clinics where health care professionals document the visual acuity and obtain OCT images of both eyes for grading by retina trained HCP delegated to manage this clinic under the guidance of retinal specialists.
3. Traditional HES Face to face retinal clinic where decision is made on the outcome of the referral by medical or non-medical trained HCP.
4. Services for referral refinement should be developed with device agnosticism so that all primary care providers are able to feed into the service.

4.4.6 Referral Outcomes

Table 3 referral outcomes for AMD services

Outcome	Action
No AMD	Discharge
Early AMD	Follow recommendation for AMD in section 4.2
Late indeterminate AMD	Monitoring with visual acuity and OCT assessment; treatment initiated if nAMD is confirmed
nAMD present and symptomatic presenting VA better 6/96 or better	Follow recommendation for anti-VEGF in nAMD in section 6.
nAMD with or without disciform scar and poor visual potential (presenting visual acuity Snellen 6/96 or worse or ETDRS letters less than 25 letters)	Clinicians' discretion to initiate treatment or monitor. NICE guidance advises only consider treatment if the patient's visual function could improve e.g., if the better seeing eye is affected. Discharge if no treatment is expected.
Geographic atrophy (Late dry AMD)	Discharge and recommendations see section 4.3
Non-AMD causes of fluid at macula	Referral to Medical or Surgical Retina Service for diagnosis confirmation and appropriate treatment.
Other pathology	Refer to subspecialty depending on pathology identified.

Feedback on referral to be sent to the referrer and copied to the GP.

5. Pharmacological management of nAMD (late wet active AMD)

Table 4 Pharmacological management of nAMD (late wet active AMD)

Management option	Recommendations
No AMD	Intravitreal injections of anti-VEGF agents are the first line treatment options for nAMD. Available anti-VEGF agents are ranibizumab, aflibercept, brolucizumab and bevacizumab. Both ranibizumab and aflibercept are licensed for this indication and recommended by NICE. Bevacizumab is not licensed for this indication and its off-label use requires pre-requisites to be met (refer to main document). Brolucizumab is approved by European Medicines Agency and was approved by NICE in February 2021. Similarly, anti-VEGF biosimilars are also being evaluated at present. Full detail of the evidence on these agents are in Appendix B of the main document.
Verteporfin photodynamic therapy (vPDT)	vPDT is a treatment option for patients with polypoidal choroidal vasculopathy (PCV), that are not responding to anti-VEGF.
Non-pharmacological agents	There is no evidence that any treatment options such as photobiomodulation, laser or radiotherapy are effective for any stages of AMD[43,44].

5.1 Relative merits of the available anti-VEGF drugs

Ranibizumab was the first licensed anti-VEGF to be used for treating nAMD, approved by NICE in 2008. The current treatment posology is to treat optimally to maintain initial visual acuity gains after the loading phase. The treat and extend approach using ranibizumab advises extension at two weekly intervals when the macula is stable up to a maximum of twelve weeks.

Aflibercept was approved for use by NICE in 2013. Many units have adopted this as the first line approach because of a fixed treatment schedule of bimonthly treatment in the first year after the three loading doses. The most recent posology advises an initial extension to 8 weeks after three loading doses and then further extension if stable at two- or four-week intervals up to a maximum of sixteen weeks.

Bevacizumab is widely used outside the UK as an off-label option for the treatment of late active wet AMD. Lower cost per dose of treatment is achieved by aliquoting a full vial of the drug. Available trials comparing ranibizumab to bevacizumab show that equivalent efficacy can be achieved either through monthly dosing (CATT study) or if a treat and extend regimen is used (LUCAS study) if monthly monitoring is achieved[45,46].More injections are required overall with bevacizumab versus ranibizumab based on the individualised regimen in the LUCAS study. This increases the treatment burden (and hence the treatment risk) for the individual patient and also the capacity burden for intravitreal services as a whole. There are no clinical trials comparing bevacizumab and aflibercept in nAMD.

If bevacizumab is preferred to licensed NICE approved agents, patient information on bevacizumab would need to include the off-label status, the use of this drug instead of other available licensed NICE approved agents, mode of production, any added risks associated with this and the likelihood of a greater number of treatments overall to achieve equivalent efficacy. Such consent would need to be obtained without prejudicing availability and access to licensed treatment options.

Brolucizumab was approved by NICE in February 2021. The clinical trials on brolucizumab suggest some potential for greater anatomical efficacy versus aflibercept. Further evidence from clinical trials and real-world usage is required to validate the potential benefits and safety profile of this agent.

The choice of first line agent may be further guided by service setup, capacity, locally agreed costs and results of local audit of results of treatment. At the time of writing achieving a longer interval between appointments and treatments is also an important goal to facilitate social distancing.

6. High-value management pathway for nAMD

Given the large number of follow-up examinations and treatment required for the significant and increasing number of people with nAMD, a high value care pathway will need to include medical and other suitably trained and experienced non-medical HCPs in the hospital, and primary care optometry settings. A significant number of injections are provided by HCPs especially nurses. Development of current and future services necessitates identifying the population eye health needs, capacity and demand tools, use of electronic medical records, robust information technology (IT) support with secure clinical data and communication systems and strong infrastructure across the system.

Some patients may also have good visual acuity in the early stages of nAMD and these patients are likely to have a better than average long-term prognosis if treated early[47-50]. So, close monitoring is recommended.

6.1 Initiation of anti-VEGF therapy

Patients should be provided sufficient information to assist them to reach an informed decision about anti-VEGF therapy and to give informed consent.

Information and Consent

1. The patient information specified in NICE guidelines should be explained to the patient by all healthcare professionals involved in the care of the patients and opportunities should be provided to discuss all aspects of the AMD pathway. Topics to be covered include:
    a. what is AMD and its prevalence; types of AMD;
    b. causes of AMD; smoking cessation and other lifestyle advice;
    c. progression and complications of AMD;
    d. the possibility of developing visual hallucinations associated with retinal dysfunction (CBS) including signposting support services;
    e. vision standards for driving; required tests and investigations;
    f. treatment options, including possible benefits and risks;
    g. the importance of probable repeated injections should be discussed; the likely frequency at which these will be required, and long-term nature of therapy.
    h. who to contact for practical and emotional support including signposting third sector organisations;
    i. where the person's appointments will take place;
    j. which healthcare professionals will be responsible for the person's care;
    k. expected wait times for consultations, investigations and treatments and transport requirements;
    l. treatment options and licensing status;
    m. the benefits and entitlements for CVI when sight impaired or severely sight impaired;
    n. when, where and how to seek help with vision changes;
    o. consideration should be given to the needs of family and care givers.

Time should be allocated to discuss the patient’s concerns about their diagnosis, treatment, long term nature of treatment and prospects for their vision. Ophthalmic nurses and ECLO

are well-placed to identify and respond to the patient's emotional needs and refer as appropriate for support.

2. Pre injection consultation should cover the following aspects: the importance of treatment; the treatment options, differences in terms of burden and durability of each option; why the intravitreal (IVT) procedure is appropriate for the patient; what the treatment involves/what to expect/what the risks are; and who is likely to give the injection; risks to vision if patient non-compliant with treatment advice. Potentially serious risks quoted in relation to IVT should include endophthalmitis, retinal detachment, vitreous haemorrhage, central retinal artery occlusion and cataract. Additional risks should be explained for specific products e.g., anti VEGF therapy and the theoretical risk of thrombo-embolic events, floaters may occur following IVT and silicone floaters from syringes.

3. The information should be provided in accessible formats for people with AMD at their first appointment and to their accompanying caregivers, and then offered again on return to clinic or whenever asked for. The information should cover the information about AMD and treatment pathways, including likely timescales, key contact details; 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.

4. Patient's priorities should be assessed when making management decisions. ECLO support as a supplementary role to assess patient's situation holistically.

5. Additional peer support often facilitated by third sector organisations should be promoted particularly for people who are beginning intravitreal injections, as they may feel reassured by discussion with someone who has previously had the same treatment.

6. Valid consent must be obtained from the patient prior to first IVT procedure; this will normally suffice for a series of treatments over several months when the drug is licensed for IVT. However, it is recommended that local hospital consent policies are consulted for the time period a consent form for a course of treatment is considered valid. If consent is taken in advance, before every injection the patient must be asked about any changes to their medical condition and consent should be briefly re-confirmed.
7. Repeat written consent to be taken in the following scenarios:
    a. If there is a change to the treatment plan; drug used; the clinical condition and/or the perceived benefit/risk to the patient
    b. If the drug used is unlicensed for this condition.

6.2 Recommendations on initiation of treatment

1. Offer treatment within 2 weeks of referral (an audit standard for AMD service). Treatment on same day of diagnosis is an option especially if the better-seeing eye is affected.
2. Minimum standards to be met: visual acuity recorded in ETDRS letters and utilising OCT to diagnose and treat patients. Treatment is recommended in patients with a visual acuity of 6/96 (logMAR 1.20, 25 ETDRS letters) or higher. In patients with advanced disease, specialist assessment is required of the degree of

structural damage and potential benefit from treatment especially if the patient has excellent vision in the unaffected eye and is unlikely to gain functional benefit. In patients with visual acuity worse than 6/96, treatment may be considered if it is the only functional or better seeing eye.

3. Initiate anti VEGF therapy: Mandatory loading dose monthly for 3 injections
4. Choice of anti-VEGF: aflibercept, ranibizumab or brolucizumab may be used as first line therapy. Please see section 5.1 for potential use of bevacizumab as first line.
5. Monitoring of fellow eyes: Fellow eyes should be monitored with OCT while the patient is being treated or monitored for unilateral nAMD. However, there is an unmet need to explore continued access to regular OCT monitoring for patients who have been discharged from HES.

6.3 Medicines Management

Liaise closely with your local pharmacy department to ensure that an adequate supply can be maintained. Recognise that obtaining a timely supply must be balanced against ensuring that relevant patient information is collated to enable adequate payment. This may include but is not limited to keeping the relevant medication as stock and using an electronic record, implementing an automated dispensing system, investing in the pharmacy team to help manage supplies.

Treatment regimen

1. A loading phase of 3 injections is recommended irrespective of the anti-VEGF used.
2. A treat and extend regimen based on visual acuity and OCT is recommended.
3. Extend by 2 – 4 weeks to a maximum of 12-16 weeks based on disease activity and drug posology.
4. Option to monitor and extend if dry macula after maximum extension is reached and maintained at this interval for a further 2-3 visits. Patients may be kept on OCT monitoring which may be most efficient within virtual review clinics within HES or the community depending on local infrastructure.
5. nAMD is a lifelong disease and approximately 40% can reactivate and so the patients can very rarely be discharged from monitoring unless disease has been stable without requiring injections for at least two years[51].
6. There is a growing trend towards injecting indefinitely to improve long-term outcomes. An average of 5 injections per year on a treat and extend protocol is recommended to sustain the initial VA gains[52]. Long term injections may be a preferred option if treating an only functional or better seeing eye.
7. There are several intravitreal therapies in development that will not necessarily be labelled to follow this treatment regimen and the guidance will be updated if deemed necessary before.

6.4 Stability

Stable disease is defined clinically as 2-3 visits at maximal extension based on posology of the drug used (12 or 16 weeks) with dry retina and stable VA. However, this is subject to clinician discretion and varies with individual patient. After a treatment free monitoring interval of 12 months 34% of patients will still reactivate and need to restart treatment in the subsequent 12 months of further monitoring[53]. Self-monitoring using Amsler chart is not a sensitive tool. Home monitoring devices are not validated in the NHS yet. We await the

results of the MONARCH study to explore whether such devices are feasible for this age-group[54]. Meanwhile, OCT is the only sensitive monitoring tool for assessing reactivation.

Monitoring of stable patients:

1. Monitoring should be done with visual acuity and OCT: These may be done in virtual clinics or face to face clinic. Monitoring with visual acuity assessment or visual function devices alone is not appropriate.
2. Monitoring using visual acuity and OCT may be done closer to home by optometrists to avoid burden on hospitals, but the optometrists will need access to training to identify reactivation if they do not have the relevant higher qualification. Care pathways should support fast track referral to hospital, ophthalmology advice and guidance and joined up care with appropriate local quality assurance processes and training.
3. There is insufficient evidence at the current time to implement monitoring using artificial intelligence.
4. If reactivation occurs, re-treatment should be initiated as soon as possible on pro re nata or a treat and extend protocol or re-initiate on loading dose until stability criteria is met. The choice of treatment regimen is based on clinician discretion and individualised per patient.

6.5 Treatment discontinuation

The NICE guidelines indicate that it was appropriate to stop anti-VEGF treatment if an eye met the defined criteria of late AMD wet inactive (defined in section 1, Table 1), and/or if it was determined that there was no prospect of visual improvement as a result of continued treatment. Inefficient treatment, for example provided too infrequently, might cause a loss in visual acuity that leads to treatment discontinuation. However, treatment should be given as recommended in the guideline prior to determining whether it should be discontinued. These patients may be discharged from the Hospital Eye Service. Fellow eyes of those eyes that have discontinued treatment due to wet inactive disease would be discharged from HES. Refer to section 7 for recommendations on monitoring of these patients.

Premature treatment discontinuation and inefficient treatment are important causes of visual loss and should be avoided. On an average, a patient initiated on treatment would require 8 injections in the first year and 6 injections in the second year. From the third year, an average of 5 injections are required to prevent decrease in vision due to inadequate treatment. However, individualised care is recommended with some requiring more and others requiring less number of injections.

6.6 Non responders

A non-responder is defined as a patient whose visual acuity declines due to persistent activity of the neovascular complex despite optimally delivered treatment regimen.

1. The diagnosis should be re-evaluated as very few patients with active wet AMD do not respond to anti-VEGF therapy. This may require additional imaging with FFA and/or ICG angiography where applicable.
2. The most likely reason for non-response is inadequate therapy due to protocol deviations. Therefore, to avoid further loss, adhere strictly to a re-loading followed by treat and extend protocol[55]. Failsafe admin processes should be available to track patients with poor compliance due to co-morbidities.

3. A switch to another anti-VEGF agent is recommended in cases of allergy or presumed tachyphylaxis and for practical reasons. For example, it may be easier to switch to a fixed regimen rather than a treat and extend protocol in some individuals to aid adherence to treatment.
4. As new treatments emerge it would be worth evaluating the effectiveness based on efficacy (improved visual or anatomical outcomes) or decrease in treatment burden. Agents with a reduced treatment burden are particularly helpful for patients with co-morbidities affecting compliance and are also useful to allow timely service delivery of care.

6.7 Special clinical scenarios

Submacular haemorrhage

Some eyes may present with submacular haemorrhage with poor visual acuity.

The current evidence is to initiate on anti-VEGF therapy on a monthly basis until the haemorrhage improve or futility to treatment is established[56]. An FFA/ICG is recommended as PCV is more likely to bleed compared to active CNV.

A referral to vitreo-retinal team is recommended for possibility of pneumatic displacement and/or recombinant tissue plasminogen activator (tPA). Some patients may benefit from vitrectomy with subretinal tPA and air tamponade[57,58].

Polypoidal choroidal vasculopathy (PCV)

PCV may occur anywhere in the fundus. Peripapillary PCV may cause fluid to track to the macula and cause visual impairment. PCV may also present at the macula and is usually associated with visual impairment. These eyes need to be initiated on anti VEGF monotherapy if macula is affected by fluid due to PCV. PDT may be offered if there is insufficient response to anti-VEGF.

Retinal Pigment Epithelium (RPE) rip

RPE rips may occur in patients with large pigment epithelial detachments at the time of diagnosis or any time point during the course of therapy or in untreated eyes due to natural history. Intravitreal injections need to be continued unless there is foveal involvement of rip with no potential for visual acuity improvement as per decision of the treating clinician.

6.8 Complications

In services where an HCP has been delegated by a named consultant Ophthalmologist or SAS doctor with autonomous practice rights to deliver intravitreal agents, it is essential that the HCP has immediate access to advice from an ophthalmologist at all times whilst giving injections and an appropriately trained clinician is available on site to deal with any very urgent complications[59].

Endophthalmitis

The risk of endophthalmitis after anti-VEGF therapy is approximately 0.02-0.09% from randomized controlled trial data whereas real-world evidence from large cohorts suggests 0.028%[60-64]. The cumulative risk per individual increases with increasing number of injections.

1. The precautions to avoid endophthalmitis include use of topical Povidone Iodine 5% pre-injection as the most effective step. It is rare for patients to have a true allergy to Povidone Iodine and so alternate approach such as a pledget soaked with Povidone Iodine at the injection site should be attempted in patients who do

not tolerate topical Povidone Iodine rather than use an alternate antiseptic agent. This precaution should be supported by the use of surgical hand disinfection with sterile gloves (changed for each injection) and a “no lid touch” technique. The use of a lid speculum and face mask are mandatory. A sterile drape over the patient’s face may also be helpful or a “no-talking” technique whilst the injection is performed. Additionally, there are also injector devices available which may combine the functions of drape, caliper and speculum. Bilateral cases can be treated but separate equipment must be used for each eye and preferably different drug batches. Peri-operative or take home topical antibiotics are not recommended. Intravitreal injections should be performed in a designated clean room compliant with RCOphth standards[59].

2. Services should report each endophthalmitis case to the service risks management team as part of an incident reporting system so that early recognition of clusters of cases is undertaken[59]. Collective annual incidence should also be reported as part of an audit pathway.

Cataracts

Patients undergoing anti-VEGF may have increased risk of age related cataract with frequent injections. A very rare complication is iatrogenic cataract[65]. Zonular dehiscence is more common in people with repeated anti VEGF injections and extra caution should be taken[65,66]. Iatrogenic cataract is best managed by the vitreo-retinal team.

Glaucoma

There is a risk of ocular hypertension with increasing number of injections[67]. Eyes with ocular hypertension or glaucoma should have controlled IOP prior to injections. Post injection all patients get an initial spike in IOP, however only a small percentage may get sustained rise in IOP requiring treatment. The initial pressure spike may be reduced to a small degree in higher risk patients with the use of apraclonidine before injection.

1. Patients with persistent ocular hypertension should be referred to the glaucoma team for further management.
2. Routine IOP testing post injection is not recommended but annual IOP monitoring is required to identify sustained IOP rise from repeated injections.

Central Retinal Artery Occlusion (CRAO)

Immediate care such as anterior chamber paracentesis, acetazolamide and digital massage is indicated if there is a potential for vision improvement as determined by the clinician[59].

7. Monitoring

7.1 General Recommendations

Do not routinely monitor people with early AMD or late dry AMD at hospital eye services unless in clinical research.

Patients with late dry AMD, or people with AMD who have been discharged from hospital eye services should:

- Self-monitor their AMD
- Consult their eye-care professional as soon as possible if their vision changes
- Continue to attend routine sight-tests with their primary care optometrist.
- OCT is the most sensitive monitoring tool. For community provision, OCT should be used to monitor patients that are at high risk of new wet AMD or being monitored for stable wet AMD.
- Be provided information about sources of support for living with sight loss including local and national charities.
- Be made aware of the local ECLO service, and how to re-access emotional and practical support. This would include advice on Certification and Registration.

For people being monitored for late AMD (wet active), both eyes should be assessed at their monitoring appointments.

7.2 Self – Monitoring

Patients with AMD should be counselled by a trained HCP regarding the strategies available. Patients should be reminded that none of the strategies for home monitoring of visual function are currently sufficiently sensitive to detect disease recurrences and that OCT is the most sensitive detection tool.

Patients with AMD should report any new symptoms or changes with regard to their central vision to their eye-care professional as soon as possible:

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

It is essential to encourage and support patients with AMD who may lack confidence to self-monitor their symptoms. They should be advised to seek assistance from peer support groups or supporting organisations such as the Macular Society.

If patients are not able to self-manage their AMD, AMD monitoring techniques should be discussed with their family members or carers (as appropriate).

7.3 Monitoring nAMD

- Patients with nAMD (wet active) should be offered ongoing monitoring with OCT for both eyes whilst within the Hospital Eye Services.
- Offer fundus examination or colour photography if OCT appearances are stable, if there is a decline in visual acuity or the patient reports a decline in visual function.

- Consider FFA to identify unrecognised neovascularisation if OCT appearances are stable but there is a decline in visual acuity or the patient reports a decline in visual function.
- If OCT results suggest macular abnormalities but the abnormalities are not responding to treatment, consider alternate diagnosis.

7.4 Monitoring co-existent ocular pathology

- Diabetic retinopathy: Patients with co-existent diabetes should still continue attending their diabetic retinopathy screening appointment.
- Glaucoma: Patients with co-existent glaucoma should continue their management with the glaucoma team.

8. Support services

8.1 Low Vision Aid (LVA) service

1. Patients with late AMD usually experience difficulty with visual impairment and ought to maintain regular sight tests. However, planning of the timing of refraction studies is best evaluated by the service.
2. Patients may benefit from low visual aids especially for reading and should have access to low vision aid appointments. Option of electronic devices as LVA should be presented to the patient as well.
3. Those who qualify to for visual impairment registration should be informed about this eligibility and should be registered in a timely manner.
4. Some patients may benefit from eccentric viewing training and this should be encouraged in the LVA setting itself.
5. Group based rehabilitation programme is also recommended.
6. Patients who do not meet the requirements to hold a driving license due to their visual impairment should be informed that they must inform the DVLA and stop driving pending DVLA evaluation.
7. National LVA service that is primary care based and fee at the point of access has been proven successful in Wales. Practitioners providing this service are able to make appropriate social care and third sector referrals and undertake registration for CVI.
8. Referral to third sector organisations such as Macular Society, RNIB, SeeAbility etc. provide support and advice on technology

8.2 Eye Clinic Liaison Officers

All ophthalmic departments providing AMD services should have at least one ECLO to provide on-going holistic support for these patients and signposting to other services. Large services may require more than one ECLO to deal with the volume of patient assessments required. ECLO support should be provided to all patients with AMD and especially those with co-morbidities to improve patient engagement, help ensure timely treatment and follow-up and support registration and information provision. ECLO support may be needed at multiple time points during the care pathway of an individual patient.

8.3 Allied health professional (AHPs) with specialist role

We recommended in that stable patients be monitored via stable virtual review clinics. AHPs including specialist optometrists, Ophthalmic nurse specialists and orthoptists may undergo or lead on training of staff and the development of such services; working alongside medical staff at all stages of the patient pathway. AHP involvement is particular necessary with the volume of patients anticipated in the future. The RCOphth "Ophthalmic Common Clinical Competency Framework" may be used to guide training and development of relevant staff. (See Section 14 of the main document).

8.4 Charles Bonnet syndrome

Patients with CBS should be offered the opportunity to access psychological support. These patients require referral by GP, optometrist, ophthalmic nurse or ophthalmologist to the local low vision service for an assessment and support from trained ophthalmic nurses and ECLOs. All patients with AMD should be provided with dedicated literature from and signposted to contacts with high quality information and support e.g. NHS choices, the Macular Society and Esme's Umbrella (a campaign group to build awareness around CBS and NHS choices) have information and advice on CBS[68].

8.5 Depression and anxiety

These patients may require support from ophthalmic nurse counsellors and ECLO and referral to their GP for further management. Information and practical advice is also available from Macular Society and RNIB.

8.6 People with learning disabilities

Reasonable adjustments in eye care, treatment and surgery should be instituted. This includes good communication such as easy read information and proper consideration of capacity and consent issues and Best Interest meetings. They also need regular eye care and visits to the optometrists due to higher prevalence of refractive errors and co-morbid ocular conditions.

9. Governance and Administrative structure for an Anti VEGF service

- The service requires dedicated administrative staff available for booking patients, answering telephone calls, changes in appointments, tracking down patients who fail to attend clinic appointments.
- There should be senior fail-safe administrative support available within the remit of the medical retina services.
- Governance of the service should be led by a Consultant Ophthalmologist with Medical Retina expertise or a nominated SAS doctor with similar expertise and autonomous practice in this area.

10. Auditing– quality assurance

The 2018 AMD Feasibility Audit, commissioned by the Healthcare Quality Improvement Partnership, identified significant variation in clinical outcomes and processes between NHS sites. (Available at https://www.hqip.org.uk/resource/age-related-macular-degeneration-amd-feasibility-report/#.Xl0y2aj7TIU). As a result, providers are encouraged to audit a range of outcomes and key processes against local, national and international benchmarks to ensure that outcomes are comparable and to aid the delivery of a cost-effective service.

Until the National AMD Audit gives providers the opportunities to compare local outcomes and processes against national benchmarks, the results of clinical audit should be shared with local commissioners and neighbouring units. Real-world clinical outcomes rarely achieve similar outcomes to randomised clinical trials and comparison of visual acuity outcomes between units will need to take account of differences in baseline characteristics.

Suggested quality measures for providers of AMD treatment are shown below:

- Percentage of patients with confirmed Late AMD (wet active) being treated (or offered treatment) within 14 days of referral. (Actual interval versus planned interval) defined as time from referral to first treatment
- Follow-up delays for on-going injection appointments.
- Visual acuity change following initial three loading doses and at months 12 and 24, with adjustment for baseline visual acuity. Greater stability following initial visual gain is expected if treatment is continued at optimal intervals following loading doses.
- Proportion of patients with a loss of visual acuity of 10 or more ETDRS letters post loading at 12 months and 24 months from initiation of treatment. A change of 10 ETDRS letters is defined as a clinically meaningful change.
- Percentage of eyes with VA better or equal to 70 letters at month 12. This will be strongly influenced by the starting visual acuity of the local population and understanding of the need for urgent presentation and therefore may not directly be within the control of the treating service.
- Outcomes based on drug used and their long-term effectiveness annually.
- Annual incidence of presumed infectious endophthalmitis after intra-vitreal injection. This will be influenced by patient co-morbidities e.g., the prevalence of chronic diseases such as blepharitis within a population. Not all these co-

morbidities can be controlled and delaying injections in their presence can lead to visual loss.

- Percentage of patients with Late AMD given written, accessible information at their first appointment and whenever requested on the disease, treatment options and pathways, key local contacts, and available supports.
- Percentage of patients with AMD offered certification of visual impairment (CVI) as soon as they become eligible, even if they are still receiving active treatment.
- Percentage of patients with access to an ECLO during their treatment pathway
- Monitoring of “did not attend” (DNA) and appointment cancellation rates at yearly intervals.
- Percentage of patients that drop off the pathway every year of the patient journey.

Additional information on service quality from the following should also be made available to staff involved in the service provision:

- Friends and family Test
- Complaints and compliments
- Feedback from the Macular Society, RNIB and local patient groups
- Patient satisfaction questionnaires are also recommended.

It is recommended that standardized audit metrics to assess AMD service performance be used and audit results be shared with commissioners and regional eye care working groups. Electronic Medical Records systems are recommended for efficient auditing.

11. Workforce development and Training

Non-medical healthcare professionals (HCPs) are subject to statutory regulation. As registered practitioners, they are responsible and accountable for practising within their personal scope of practice and competence at any one time. They are responsible for the decisions and actions that they take (including decisions not to act), and for engaging in continuing education and professional development to maintain and update their knowledge and skills.

All HCPs should have the appropriate theoretical knowledge of anatomy and physiology, assessment and examination, disease, investigations, and management. Their individual education and training needs will vary, subject to the following: their specific contribution to managing patient caseload within a particular service set-up and multi-disciplinary team (including the team's skill mix and job role configuration) their profession's education and scope of practice their personal scope of practice, post-registration professional experience and opportunities for professional development to date.

For HCPs involved in treatment decisions within components of patient pathways managed within Hospital Eye Services, the Ophthalmic Practitioner Training (OPT) programme (based Ophthalmic Common Clinical Competency Framework; https://www.hee.nhs.uk/our-work/advanced-clinical-practice/ophthalmology-common-clinical-competency-framework-curriculum) can help to identify both their existing professional competence (gained and demonstrated through their pre- and post-registration education and professional experience) and their individual areas of learning need.

For HCPs involved in the diagnosis, referral and management of stable patients, accredited medical retina courses are available to support and recognise their professional development and competence. These include the CoO higher qualifications, delivered under CoO accreditation by universities; https://www.college-optometrists.org/cpd-and-cet/training-and-qualifications/higher-qualifications/courses-and-providers/higher-qualifications-in-medical-retina.html. OPT recognition of HCPs' successful completion of CoO higher qualifications, and other relevant HEI provision, is currently being pursued (supported by Health Education England).

The UK Ophthalmic Alliance (2019) has devised a policy document detailing the operating procedures for HCPs undertaking intravitreal injections (see https://uk-oa.co.uk/wp-content/uploads/2020/03/UKOA_Intravitreal_Injection_Policy_Pack_Oct-2019.docx.pdf). In summary, the HCP should have the appropriate theoretical knowledge of anatomy and physiology, assessment and examination, disease, investigations and management. Training and assessment may be undertaken as part of the OPT Medical Retina competency framework. Employers are responsible for ensuring practitioners are trained and working at the appropriate level of competence.

12. Information and Support

12.1 Links to patient information

Name	Published	Link
Royal National Institute of Blind People	RNIB	https://www.rnib.org.uk/eye-health/eye-conditions
NHS Choices conditions information	NHS	https://www.nhs.uk/conditions/age-related-macular-degeneration-amd/
Understanding Macular Disease	Macular Society	https://www.macularsociety.org/
Moorfields patient information	Moorfields Eye Hospital NHS Foundation Trust	https://www.moorfields.nhs.uk/content/patient-leaflets

12.2 Links to clinical information, clinical guidelines, decision support tools

Name	Published	Link
The Way Forward for AMD Services	The Royal College of Ophthalmologists	https://www.rcophth.ac.uk/standards-publications-research/the-way-forward/
NICE Serious Eye Disorders Quality Standard	NICE	https://www.nice.org.uk/guidance/qs180
Commissioning Standards	The Royal College of Ophthalmologists	https://www.rcophth.ac.uk/standards-publications-research/ophthalmic-services-guidance-2/ https://www.rcophth.ac.uk/standards-publications-research/commissioning-in-ophthalmology/age-related-macular-degeneration
Quality Standard for Medical Retina Disease Services	The Royal College of Ophthalmologists	Quality Standard for Medical Retina Disease Services
SAFE - Systems and Assurance Framework for Eye health	Clinical Council for Eye Health Commissioning	https://www.college-optometrists.org/the-college/ccehc/safe-systems-assurance-framework-for-eye-health.html
NHS England Eye Care Restoration and Transformation project resources	NHS England	https://future.nhs.uk/connect.ti/ECDC/view?objectId=22317360 Registration required to access

13. Service Model Options

Table 5 Service Model Options

Service model	Description
Artificial Intelligence	This has shown great promise in classifying two-dimensional photographs and OCTs of some common diseases and typically relies on databases of millions of annotated images. The technology has not been implemented in clinics yet.
Virtual Clinics	The use of the term "Virtual clinic" with respect to the management of AMD refers to a process where acquisition of data from the patient (e.g. visual acuity measurements and OCT images (including colour fundus photographs) occurs at a separate point in time to the assessment of that data to formulate a plan for treatment within secondary care including their diagnostic hubs.

13.1 Virtual clinics

Acquisition of data for these virtual clinics assessments often occurs by HCP in a high-throughput clinic in secondary care and is then commonly followed by a later asynchronous assessment of the data by trained clinicians, again facilitating the review of high volumes of patient data without interacting directly with the patient.

Benefits can include :

- At least double the number of patients' data could be reviewed and management plans made compared to the number of patients assessed in a traditional face-to face clinic format
- For new patient referrals increased throughput and ensures that the true positive diagnoses of nAMD can be fast-tracked into the rapid access clinic whilst false positive patients (e.g. with late dry AMD) can still be seen within a service but in a lower priority timescale
- Data acquisition can be delivered outside of routine working hours when equipment such as OCT scanners and VA charts lie unused so that other types of patient care episodes can be prioritized during normal working hours. This is beneficial to services where clinic infrastructure is inadequate to meet demand.
- An effective way of increasing throughput in assessment clinics for nAMD disease activity status without compromising quality of care in terms of decision making on hospital eye services
- It is possible for patients to be seen for initial consultation or monitoring in diagnostic hubs and primary care optometry where OCT is available, and the visual acuity record and the OCT images could be transferred securely to be read in a hospital eye service (teleophthalmology) if required.

Disadvantages:

- Can compromise patient care, in that a holistic face-to-face clinical interaction between patient and clinician does not then occur at every single patient episode. It is also not possible to give patients a treatment plan and next appointment on the day of their attendance

Mitigation:

- Ensure that whilst a majority of care episodes are virtual, regular infrequent face-to-face care episodes occur in parallel
- At virtual clinic data acquisition episodes there should be an opportunity for patients to report new concerns or request a face-to face visit
- Patients should also have access to a mechanism for reporting new symptoms or side effects outside of routine clinic episodes e.g. a designated telephone number staffed by staff with clinical training to triage patient reported problems into clinical priority. The same service providing treatment and assessments should provide this emergency support so that access to and review of care records is possible.

Service development should include provision of ECLOs in virtual clinics. This ECLO service needs to adhere to the UKOA/RNIB ECLO Quality Framework.

Decisions in teleophthalmology should not be based only on visual acuity and visual symptoms. OCT is the most sensitive test to diagnose new CNV or reactivation and must form part of the decision support provided by teleophthalmology.

14. Summary

This guidance is intended to apply to 80% of patients on 80% of occasions and this recommendation provides details of the optimum pathway for patient benefit. In clinical medicine, there will always be exceptions and uncertainties. It sets out principles and the minimum standards of care, to be moderated by well-informed clinical judgement and common sense for individual patient situations.

Patients with no or early low risk AMD do not require any monitoring or treatment and can be discharged to routine review by primary care optometrists.

Patients with medium or high-risk AMD should be advised to stop smoking, encouraged to have a healthy diet, with plenty of greens and monitor themselves for any central visual disturbances and report if they experience any visual symptoms. It is recommended that they be advised that OCT is the most sensitive tool to diagnose conversion. Visual symptoms and using Amsler charts are not sensitive measures to identify conversion to nAMD.

Genetic testing is not advocated at present.

Indeterminate AMD is challenging and best reviewed regularly at primary care optometrists or in secondary care either in virtual clinics with imaging facilities or directly in the medical retina clinics. These are challenging cases and would require secondary care oversight. Advanced AMD is associated with visual impairment and increased likelihood of depression, falls and cognitive impairment. Timely initiation and prompt repeated intravitreal anti-VEGF therapy is the first line evidence based cost-effective treatment option for active wet AMD. Access to this treatment should not be denied in eyes that meet NICE criteria.

Photodynamic therapy may be used in combination with anti-VEGF in the variant of AMD polypoidal vasculopathy.

A typical care pathway for anti-VEGF treatment is described in the document but this must be personalised to the patient and adaptable for patients with specific needs. Auditing of high value anti-VEGF pathway for nAMD should include time from referral to first injection, delays in planned assessments and treatments, and change in visual outcome over time stratified by baseline visual acuities, occurrence of significant complications should be recorded routinely and the data should be available to care providers and commissioners and regional eye care working groups.

Information required for the UK minimum dataset should be routinely collected locally for annual audit of the services and clinical outcomes.

Currently, there is no treatment available for late dry AMD. Patients with poor VA due to Late AMD should be offered visual rehabilitation such as low visual aid assessment. If eligible, subject to willingness, these patients should also be informed about the provision of CVI.

15. Abbreviations and Glossary

Abbreviation	Explanation
AHP	Allied Health Professional
AMD	Age-related macular degeneration
Anti-VEGF	Drugs that block the action of Vascular Endothelial Growth Factor. They are effective in the treatment of choroidal neovascularisation
AREDS	Age Related Eye Disease study
CBS	Charles Bonnet Syndrome
CoO	College of Optometrists
Community Ophthalmology Services (COS)	Commissioned by CCGs. These may involve the assessment and management of patients whose eye conditions are at low-risk of deterioration who are either referred by primary care for further assessment or discharged from secondary care for monitoring (Primary Eye Care, Community Ophthalmology and General Ophthalmology 2019)
CFP	Colour Fundus Photo
CNV	Choroidal neovascularisation
CI	Credible Interval
CVI	Certificate of Vision Impairment
DNA	Did Not Attend
ECLO	Eye Clinic Liaison Officer
Endophthalmitis	Infection that involves the internal structures of the eye. It usually poses a serious threat to the visual function of the eye and is a rare complication of intravitreal injection.
eRS	Electronic Referral System
ETDRS	Early Treatment Diabetic Retinopathy Study
FFA	Fundus Fluorescein Angiography
GA	Geographic Atrophy
GOS	General Ophthalmic Services
HCP	Health Care Professional. In this document, the term HCP refers to nurses, optometrists, and orthoptists. Each profession is regulated by a different regulatory body (respectively the Nursing and Midwifery Council, General Optical Council and Health Care Professions Council)
HES	Hospital Eye Service

ICG	Indocyanine Green Angiography
LVA	Low Vision Assessment
MDT	Multidisciplinary Team
MSVI	Moderate to Severe Visual Impairment (presenting visual acuity <6/18 to 3/60 inclusive)
nAMD	Neovascular or “wet” AMD
NICE	National Institute for Health and Care Excellence
NHS	National Health Service
NPSA	National Patient Safety Agency
OCT	Optical Coherence Tomography
OCTA	Optical Coherence Tomography Angiography
OPT	Ophthalmic Practitioner Training
PCV	Polypoidal Choroidal Vasculopathy
PDT	Photodynamic therapy
PED	Pigment Epithelial Detachment
Primary Care	GPs and pharmacists can provide non-specialist eye care including initial assessment and treatment of common low-risk conditions not requiring specialist expertise or equipment (e.g., conjunctivitis), but first contact eye care is a small part of their routine workload. (Primary Eye Care, Community Ophthalmology and General Ophthalmology 2019)
RAP	Retinal angiomatous proliferation
RPE	Retinal pigment epithelium
SAS Doctors	Staff and Associate Specialist Doctors
SD	Standard Deviation
SDD	Subretinal Drusenoid Deposits
SI	Sight Impairment
SMH	Sub Macular Haemorrhage
SSI	Severe Sight Impairment (presenting visual acuity < 3/60)
TREX or T&E	Treat and Extend
UI	Uncertainty interval
VA	Visual Acuity

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