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Optometry Australia's chairside reference for the diagnosis and management of age-related macular degeneration

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CLINICAL AND EXPERIMENTAL
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CHAIRSIDE REFERENCE

Optometry Australia's chairside reference for the diagnosis and management of age-related macular degeneration

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Age-related macular degeneration (AMD) is the leading cause of irreversible vision loss in people over the age of 50 years in Australia. Optometry Australia has developed this AMD chairside reference in consultation with a member-based working group comprised of experienced practitioners. It provides an evidence-based approach to current best practice in the diagnosis and management of AMD. Optometrists should be competent in assessing patients with or at risk of developing AMD, so that they are able to provide evidence-based management including appropriate communication, diagnosis and referral when indicated. This AMD chairside reference covers risk factors for the development of AMD or progression to late-stage AMD; the current clinical classification of AMD; common signs and symptoms; optometric assessment including ocular imaging and biomarkers; differential diagnoses; and management of early, intermediate and late AMD. Optometry Australia's chairside reference is intended as a general guide for optometrists, and is not a formal management protocol.

Key words: age-related macular degeneration, chairside reference, diagnosis, imaging, management, optometry, treatment

Late age-related macular degeneration (AMD) is the most common cause of irreversible vision loss in people over the age of 50 years in Australia. Approximately one in seven people over the age of 50 years have signs of AMD, but not all will progress to vision loss.[1] This is equivalent to approximately 1.3 million people, and is expected to rise to 1.7 million by 2030.[2] Globally, it is

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estimated that 8.4 million people had moderate or severe vision impairment from AMD in 2015, and it is the cause of 5.6 per cent of cases of legal blindness (almost two million people).[3]

The prevalence of late AMD in people of European ancestry is 1.4 per cent at the age of 70 years, 5.6 per cent at 80 years and 20 per cent by 90 years.[4] It is a multi-factorial eye disease, with a number of known and suspected risk factors. AMD described in this chairside reference refers to the phenotype associated with drusen and pigmentary abnormalities associated with progression to geographic atrophy (GA) and/or choroidal neovascularisation (CNV).

AMD has a significant socio-economic burden. In 2010, the total cost of AMD-related vision loss (including direct and indirect costs) in Australia was estimated at AUD$5.2 billion.[2] Since this time, the utilisation of anti-vascular endothelial growth factor (anti-VEGF) injections has increased dramatically. In addition, AMD has a high personal cost – including a loss of independence and social interaction,[5] decreased quality of life[6] and increased levels of depression (up to one in three people with AMD).[7,8] Caregivers of people with AMD are also at high risk of emotional distress and disruption to their own lives.[9]

It is important that optometrists are competent in assessing patients with or at risk of developing AMD, so that they are able to provide evidence-based management including appropriate communication, diagnosis and referral when indicated.

Methods

Optometry Australia developed this chairside reference by convening a working group of members who are experienced practitioners with a clinical and/or research interest in the area of AMD assessment and management.

The purpose of the working group was to support the development of a chairside reference for the diagnosis and management of optometric patients with AMD. This included providing advice on the best standards of clinical care in managing these patients. Working group members reviewed each phase of the chairside reference during development and a consensus position of the working group was sought. Finally, the chairside reference was circulated to state and territory organisations and the National Board of Optometry Australia for feedback and endorsement.

The authors acknowledge there are several limitations in the development of this chairside reference.[10] Due to resource constraints, the National Health and Medical Research Council (NHMRC) standard for clinical practice guide development was not adhered to strictly. In particular, a review of the evidence was undertaken, but not a complete critical appraisal and synthesis of the evidence. However, the authors followed a process that endeavoured to produce an evidence-based chairside reference that reflects best-practice and can be used as a source of practical support by all optometrists.

Risk factors for AMD

Risk factors that make it more likely that a person will either develop AMD or progress to late-stage AMD are detailed in Table 1. The factors have been divided into those with strong, moderate and weak evidence, as determined by a systematic review that looked at risk factors for progressing to late-stage AMD[11] and the recent National Institute for Health and Care Excellence (NICE) AMD guidelines (UK).[32] In the systematic review, data from 18 prospective and cross-sectional studies, and six case control studies were identified contributing a sample of 113,780 patients; 17,236 with late-stage AMD. Fixed-effects meta-analyses were conducted for each factor to combine odds ratio and/or relative risk outcomes across studies by study design. Overall raw point estimates of each risk factor and associated 95 per cent confidence intervals were calculated. In the NICE AMD guidelines, a very detailed review of all known and suspected risk factors, including effect sizes and an evaluation of the strength of the study was conducted.

A Melbourne-based study found that despite our knowledge of the relationship between diet and smoking with AMD, only one third of a sample of optometry patients had been routinely questioned about smoking status, diet and nutritional supplements.[33] Optometrists have a duty of care to raise the issue of smoking as the strongest modifiable risk factor in AMD development and progression.

Clinical classification

Historically, there has been considerable confusion over even basic terms in AMD, thus terminology consistency is important. For example, although the term 'age-related maculopathy' (ARM) is sometimes used to describe exaggerated 'normal' age-related changes at the macula, the exact distinction between ARM and early AMD varies. Similarly, dry AMD has been used in reference to presentations varying from drusen only to GA. To avoid confusion, the working group recommends limiting the use of these terms 'ARM', 'wet' and 'dry' AMD.

The most current clinical classification scheme for AMD is the Beckman classification[34] (Figure 1). This scheme arose from the Beckman Initiative for Macular Research Classification Committee, a panel of expert ophthalmologists, a neuro-ophthalmologist and a methodologist.[34] The classifications are determined based on clinical examination (using common ophthalmoscopy equipment, such as an ophthalmoscope or slitlamp with accessory lenses) or evaluation of a fundus photo. Classification is based on fundus lesions within two-disc diameters of the fovea in patients older than 55 years of age. Drusen size should be estimated based on their smallest diameter. Note, the average width of the central retinal vein at the optic disc margin is 125 µm, so drusen larger than this are considered large drusen. Medium drusen are between half and one-full width of the vein (63–125 µm), and small drusen are less than half the vein width (< 63 µm).[34,35]

The Beckman classification scheme was designed to reflect the fact that risk profiles can be linked to the clinical signs of drusen and pigmentary abnormalities (see Table 2). AMD pigmentary abnormalities are defined as any hyper-pigmentary or hypo-pigmentary abnormalities associated with medium or large drusen, but not associated with other known disease entities (for example, inherited retinal degenerations). The presence of large drusen is considered a risk factor for developing late stage AMD.[12] Observation of pigmentary abnormalities also means a higher risk of developing late stage disease.[34–36] In early AMD (medium drusen only), people have a 3.1 per cent chance of progressing to late AMD within five years.[35] However, once a person has large drusen and pigmentary abnormalities in both eyes (intermediate AMD), this risk increases to around 47.3 per cent.[35] If a patient presents with late AMD in one eye, the risk of progression in the other eye is slightly higher.[35]

A more detailed classification scheme based on newer imaging technologies is also

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Risk factor	Explanation	Level of evidence
Older age (> 60 years)	• The strongest risk factor for AMD.[11,12] • The risk of developing AMD increases more than threefold in patients older than 75 years compared to those aged between 65 and 74 years.[12,13]	Strong
Family history of AMD/genetics	• 34 different loci have been identified.[14,15]	Strong
Smoking	• The strongest modifiable risk factor. • Has been shown to at least double the risk of AMD.[16] • There is a direct correlation between current smoking and the number of cigarettes a person has smoked during their life and their risk of late AMD.[17,18] • Smokers, on average, develop AMD five to 10 years earlier than non-smokers.[3]	Strong
Hypertension	• Three case control studies have identified a significant association between hypertension and late AMD.[11,19]	Moderate
Cardiovascular disease	• A history of cardiovascular disease may approximately double the risk of late AMD.[11]	Moderate
BMI of 30 kg/m^2 or higher	• The Blue Mountains eye study and other major prospective studies have shown that being overweight/obese increases the risk of late AMD.[11,20–22]	Moderate
Diet low in omega-3 fatty acids, vitamins, carotenoid and minerals[23,24]	• There have been a number of studies showing interactions with diet and AMD, particularly from the Age-Related Eye Disease Studies 1 and 2 (AREDS).[25,26] • A diet high in macular carotenoids (zeaxanthin and lutein) and omega-3 long-chain essential fatty acids may be protective.[27]	Weak*
Diet high in fat (saturated fats, trans fats and omega-6 fatty acids)[28]	• A 2014 Melbourne study found that a diet high in fruits, vegetables, chicken and nuts, and a pattern low in red meat seems to be associated with a lower prevalence of late AMD.[29] • No particular food pattern seemed to be associated with the prevalence of the earliest stages of AMD.[29]	Weak*
Lack of exercise[30,31]	• A prospective study found that higher doses of vigorous exercise was associated with lower incident risk of AMD.[30]	Weak*

*Although a higher level of evidence is currently lacking, it may be nonetheless prudent for clinicians to advise patients of the potential risk of AMD associated with lifestyle factors, including diet and a lack of exercise.

Table 1. Risk factors for age-related macular degeneration (AMD)

emerging and will require a shift in terminology. GA will be re-termed complete retinal pigment epithelium (RPE) and outer retinal atrophy (cRORA) in the absence of CNV.[37]

Common signs and symptoms

Common signs and symptoms of AMD are summarised in Table 3. These signs and symptoms are stratified according to when they occur in the natural history of the disease process, or in some cases that are not stage specific.

Optometric assessment

Examination

A standard comprehensive optometry examination, including targeted history, high-contrast visual acuity, refraction, stereoscopic slitlamp examination and dilated fundus examination, should be performed. Table 4 provides more detail on some of these tests.

Ocular imaging

Ocular imaging tools for the diagnosis and assessment of AMD, if available, that are recommended for use by optometrists, are listed in Table 5.

Recent recommendations[53] from the expert Classification of Atrophy Consensus Group is that when detecting, quantifying and monitoring late AMD (GA), the assessment protocol should include colour fundus photography (CFP), fundus autofluorescence (FAF), confocal near-infrared reflectance (NIR) and high-resolution optical coherence tomography (OCT): multimodal imaging (MMI).

MMI can also help determine if a patient has a higher risk of progression from intermediate to late-stage AMD (see 'Prognostic biomarkers' section), so it is recommended to use these tools on patients with intermediate AMD.[54] If a practitioner does not have access to these imaging tools, referral to a colleague or ophthalmologist should be considered (Table 5 and Figure 2).

PROGNOSTIC BIOMARKERS

There are three key prognostic biomarkers – namely reticular pseudodrusen (RPD), hyperreflective foci, and nascent geographic atrophy (nGA) – that can be identified with MMI in some patients with intermediate AMD and have been shown to be risk factors for progression to late AMD.

RPD have been shown to be associated with a 2–6-fold increased risk of progression to late AMD.[40,41] They can be difficult to

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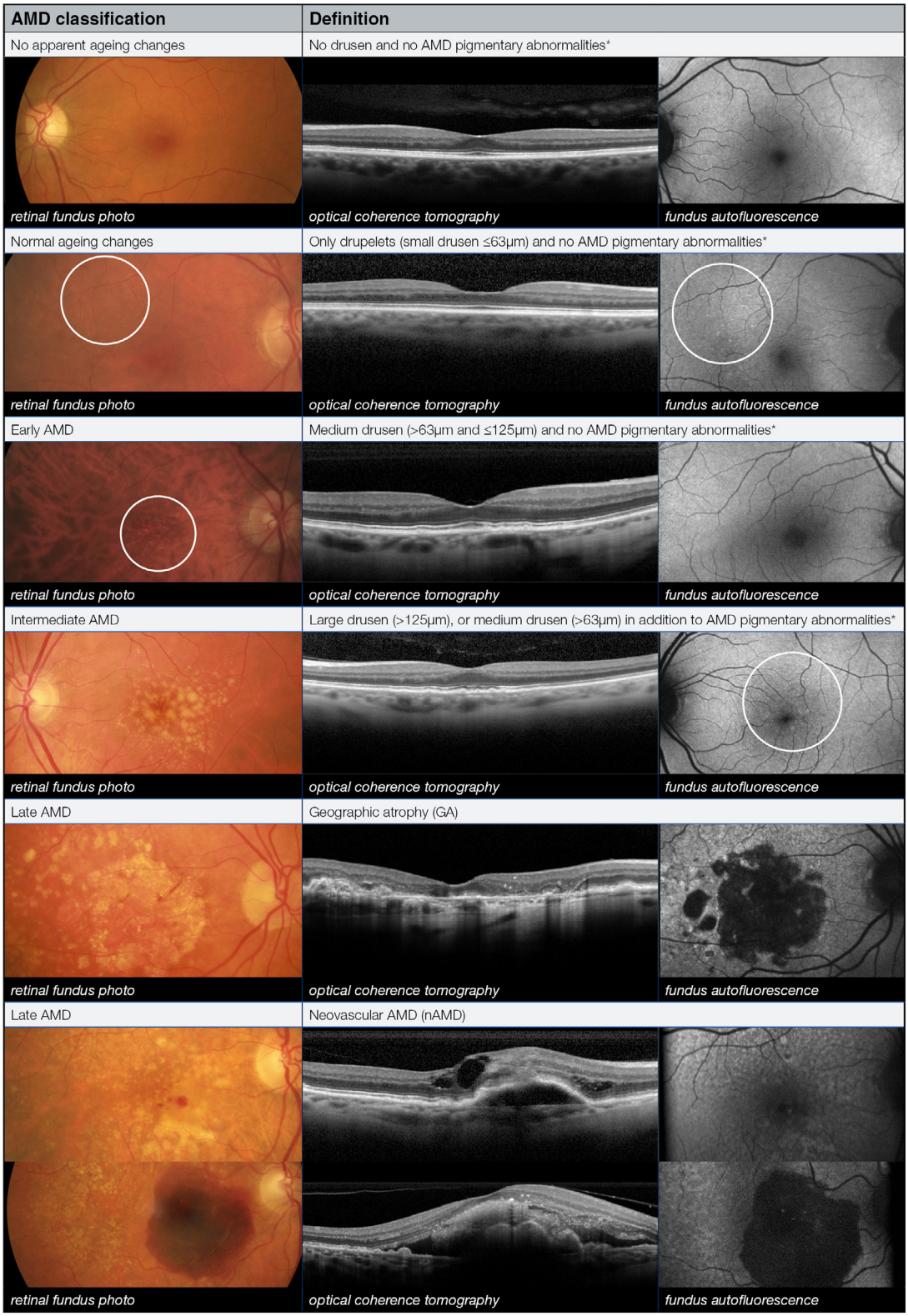

Figure 1. Beckman classification of age-related macular degeneration (AMD),[34] with corresponding example retinal fundus photos, optical coherence tomography (OCT) and fundus autofluorescence. Images kindly provided by Prof. Robyn Guymer, Centre for Eye Research Australia. *AMD pigmentary abnormalities are defined as any hyper-pigmentary or hypo-pigmentary abnormalities associated with medium or large drusen, but not associated with known disease entities.

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Risk factors	Risk of progression for patients without late AMD in either eye at baseline*	Risk of progression for patients with late AMD in one eye at baseline†
0	0.4%	-
1	3.1%	-
2	11.8%	14.8%
3	25.9%	35.4%
4	47.3%	53.1%

*Assign one risk factor: for each eye with large drusen, for each eye with pigment abnormalities, if neither eye has large drusen and both eyes have medium drusen (early AMD).

†Assign two risk factors for the eye that has late AMD. Assign an additional risk factor if the eye at risk has large drusen and an additional risk factor if the eye at risk also has pigmentary abnormalities.

Table 2. Five-year risk of progression to late age-related macular degeneration (AMD)[35]

assess with just one imaging modality, so it can be helpful to compare MMI to confirm findings (Figure 3). The appearance of RPD has been described in Table 3 and appear on OCT as deposits in the subretinal space above the RPE, unlike classical drusen which are below the RPE.[44] Using other modalities, such as FAF or NIR, they typically appear as collections of semi-regular, interlacing, hypo-autofluorescent or hypo-reflective ribbons or spots.

Hyper-reflective foci represent a five-fold increased risk of progression to late AMD.[44] They are best visualised using OCT as intra-retinal, hyper-reflective dots and often correspond with hyper-pigmentary abnormalities using fundoscopy (Figure 3).

Recently, an OCT-defined GA classification scheme has been proposed.[37] This scheme identifies two stages based upon OCT changes as incomplete RPE and outer retinal atrophy (iRORA; nGA), and complete RPE and outer retinal atrophy (cRORA) or GA[37] (Figure 4). The RPE band is present but interrupted in nGA, and the hypertransmission of light through the retinal layers appears more discontinuous. nGA is a proposed precursor to GA and causes decreased retinal sensitivity.[55] It was present in approximately seven per cent of patients with bilateral intermediate AMD in a small Australian sample[45] and is defined on OCT as the presence of (1) subsidence of the outer plexiform layer and inner nuclear layer, or (2) development of a hypo-reflective wedge-shaped band within the limits of the outer plexiform layer. By comparison, GA presents on OCT as clear absence of the RPE band spanning at least 250 µm in diameter (with overlying outer retinal thinning and dropout of the ellipsoid zone) and underlying homogeneous hypertransmission into the choroid. Larger studies are currently underway to assess the characteristics, prevalence, and prognostic nature of nGA. For now, optometrists should be aware that it is a biomarker for AMD.

Differential diagnoses

As the cardinal sign of AMD is the presence of drusen, it is possible for rarer drusen-associated retinal conditions to be misdiagnosed as AMD. Differences in drusen appearance (size and distribution), strong family history and patient age remain the

Stage of disease	Clinical symptoms	Clinical funduscopic signs
Early	• Usually asymptomatic.	Medium drusen (≤ 125 µm)
Intermediate	• May have reduced contrast sensitivity and difficulties with dark adaptation[38] e.g. difficulties reading in dim light or adjusting from different lighting conditions.	Large drusen (> 125 µm) and/or pigmentary abnormalities, pigment epithelial detachment due to confluence of large drusen
Late: geographic atrophy	• Decrease in vision that is not improved with refractive correction. • A central field defect or blur that may or may not affect fixation.	Area of photoreceptor and retinal pigment epithelium atrophy, forming a well-demarcated lesion of at least 250 µm in diameter, with choroidal vessels visible in its base[37]
Late: neovascular	• Visual distortions (scotoma, metamorphopsia, micropsia or macropsia). • Difficulties with visual tasks/activities of daily living, such as watching television, going down stairs, reading or recognising people. • Some people with late AMD and poor vision in both eyes will develop visual hallucinations in Charles Bonnet syndrome.[39] This can be distressing to patients, who will often require counselling.	Choroidal neovascularisation which may appear as a well-demarcated grey/green area of the retina, macular fluid (sub- or intra-retinal), lipid or haemorrhage, pigment epithelial detachment
Non-stage specific		Reticular pseudodrusen (subretinal drusenoid deposits) are yellowish, net-like deposits. They are not a unique phenotype to AMD, but they have been shown to be associated with an increased risk of progression to late-stage AMD[40,41]

Table 3. Common signs and symptoms of age-related macular degeneration (AMD)

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Clinical test	Notes
History	Screen for new symptoms suggestive of AMD (see Table 3). Establish risk factors (see Table 1), including family history of AMD, smoking history and status, as well as documentation of nutritional supplement use and driving status.
Visual acuity	Monocular best-corrected visual acuity. Include near monocular visual acuity.
Fundus examination	Dilated fundus examination (DFE), including stereoscopic biomicroscopic evaluation of the macula, is recommended at least annually for those exhibiting signs or symptoms of AMD. Careful consideration of a patient's risk profile (see Tables 1 and 2) should also help determine if the patient requires a DFE.
Amsler grid	Presentation of the grid at 30 cm leads to a retinal projection of 20°, with each square representing a 1° angle.[42] It has been shown that white lines on the black background is more sensitive and reliable than the white background.[42]
Contrast sensitivity	Some patients can have symptoms of poor vision, but good visual acuity; contrast sensitivity provides additional useful information.[43]
Photostress test	The photostress test assesses retinal function, so macular disease will cause a prolonged photostress recovery time, even in early stages of AMD.[43]

Table 4. Optometric assessment of a patient with age-related macular degeneration (AMD)

key distinguishing factors in these other drusen-associated diseases. In addition, conditions which present with central serous retinal detachments (such as central serous chorioretinopathy, adult-onset vitelliform dystrophy and Best disease) can be mistaken for AMD (Table 6).

Several conditions should be considered as a differential diagnosis to neovascular AMD. In these, CNV can form, but they will not typically present with related drusen. Examples include polypoidal choroidal vasculopathy, ocular histoplasmosis syndrome,[61] pathologic myopia,[62] choroidal rupture,[62] angioid streaks[62] and idiopathic CNV. Diabetic macular oedema may be another differential diagnosis to consider when macular haemorrhage, lipid, exudate, sub- or intra-retinal fluid are detected at the macula.

Management of early and intermediate AMD

The mainstay of optometric management for early and intermediate AMD is counselling on

Colour fundus photography (CFP)	Key indications: CFP is often used for monitoring drusen number, size, presence of pigmentary abnormalities and signs of late disease (for example, geographic atrophy [GA] is currently defined in most studies by a colour fundus photo[37]); however, may be limited by low contrast.
Optical coherence tomography (OCT)	Advances in OCT have enhanced our ability to detect structural retinal and retinal pigment epithelium (RPE) changes that may precede the development of late AMD[44] and vision loss, such as reticular pseudodrusen,[40] hyper-reflective foci[44] and nascent GA.[45] Refined phenotyping of macular atrophy is also possible.[37] See the 'Prognostic biomarkers' section for more detail. Key indications: OCT is one of the most valuable imaging tools for the detection and management of AMD.[37] It is often used for the detection of signs of active neovascular AMD (such as retinal fluid), and can also be used for monitoring drusen and pigment.
Fundus autofluorescence (FAF)	FAF can show areas of increased lipofuscin accumulation, such as cells in oxidative stress or in drusen (as hyper-fluorescent), and areas where the RPE cells have died (hypo-fluorescent).[46] A simplified interpretation is that atrophic areas of a retina will appear dark on an AF image, whilst the areas surrounding the lesion (junctional zones) will sometimes appear bright, as a sign of an unhealthy RPE.[47] The FAF pattern is also likely to be altered in intermediate and neovascular AMD and its pattern is associated with different rates of growth of GA. Increased background FAF in non-drusenoid location is a strong indicator of inherited retinal disease rather than AMD. Key indications: FAF provides better demarcation of areas of GA than a photo,[48,49] so is commonly used to measure the size and extent of atrophic lesions. Reticular pseudodrusen are more easily seen on FAF than in colour photography. See Figure 2A.
Near infrared imaging (NIR)	NIR light will be absorbed by molecules such as haemoglobin and water, meaning that any blood or fluid at the retina will be imaged as a dark area (including the normal retinal vasculature). In contrast, GA will appear as a bright patch on the IR image due to reflection off the sclera.[50,51] Key indications: NIR is especially useful for imaging of atrophic lesions (particularly those involving the fovea centre) and reticular pseudodrusen. See Figure 2B.
OCT-angiography (OCT-A)	OCT-A allows imaging of the retinal and superficial choroidal vasculature and blood flow without the need for dye injection.[52] However, OCT-A does not detect vessel leakage, meaning that standard fluorescein angiography still has a place in the diagnostic protocol. Key indications: OCT-A is useful for diagnosing choroidal neovascularisation and visualising retinal vascular abnormalities. See Figure 2C.

Table 5. Ocular imaging of a patient with age-related macular degeneration (AMD)

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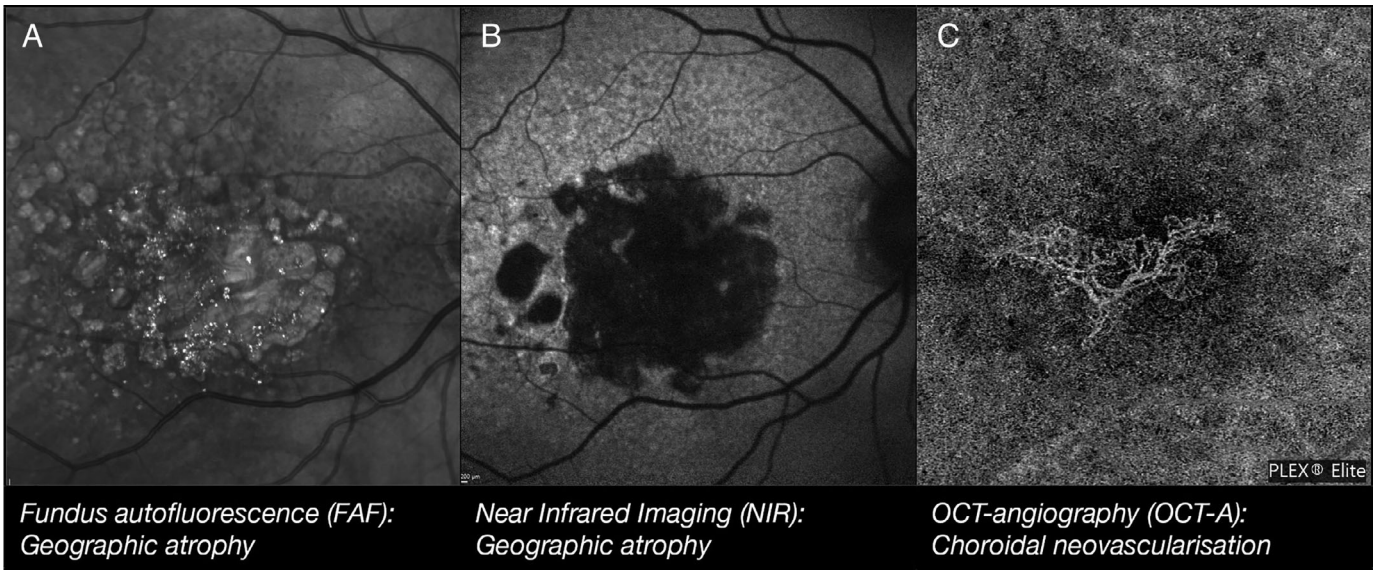

Figure 2. Ocular imaging showing examples of FAF, NIR, and OCT-A. Also refer to Table 5. Images kindly provided by Prof. Robyn Guymer, Centre for Eye Research Australia. OCT-A image also courtesy of Prof. Guymer as part of the Zeiss ARI network.

modifiable risk factors (Table 7), providing a home Amsler grid for self-monitoring and counselling on the appropriate course of action if the patient notices a change in their vision. The sensitivity of the Amsler grid has been shown to be less than 50 per cent, and experts in the field have called for a new home monitoring option.[65] Despite a number of computerised versions being tested,[66–68] the hardcopy grid is still a common form of home monitoring for AMD at this time.[69] Optometrists should consider liaising with a patient's general practitioner who can provide additional support to quit smoking and advice regarding diet, lifestyle and nutritional supplements.

Patients with early or intermediate AMD do not generally require referral to an ophthalmologist.[54] However, if the patient has: a young age of onset for AMD (< 50 years); a strong family history (in which case they may have a dominantly inherited disease which is being mistaken for AMD); abnormal structural, functional or historical clinical findings that require a second opinion; or wish to be involved in a research study or clinical trial, referral to an ophthalmologist is recommended.

For those with established AMD, it is important to emphasise the importance of

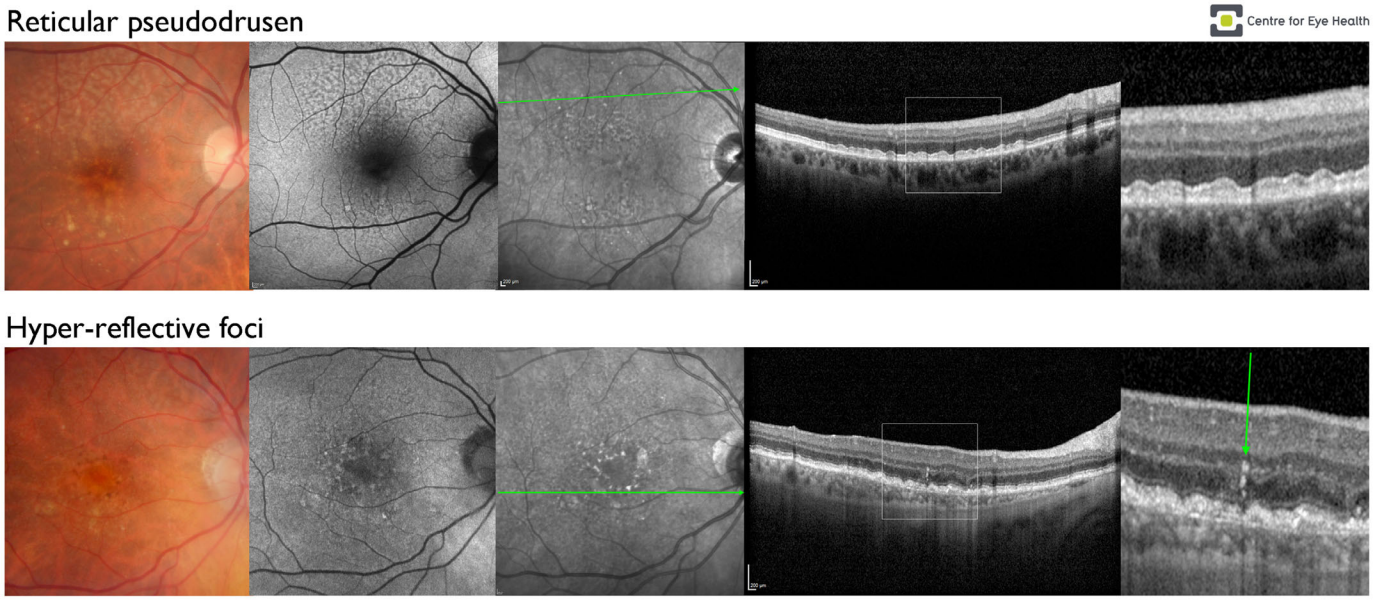

Figure 3. Case figures (CFP, FAF, NIR, OCT) illustrating the appearance of prognostic biomarkers. Images kindly provided by Angelica Ly, Centre for Eye Health.

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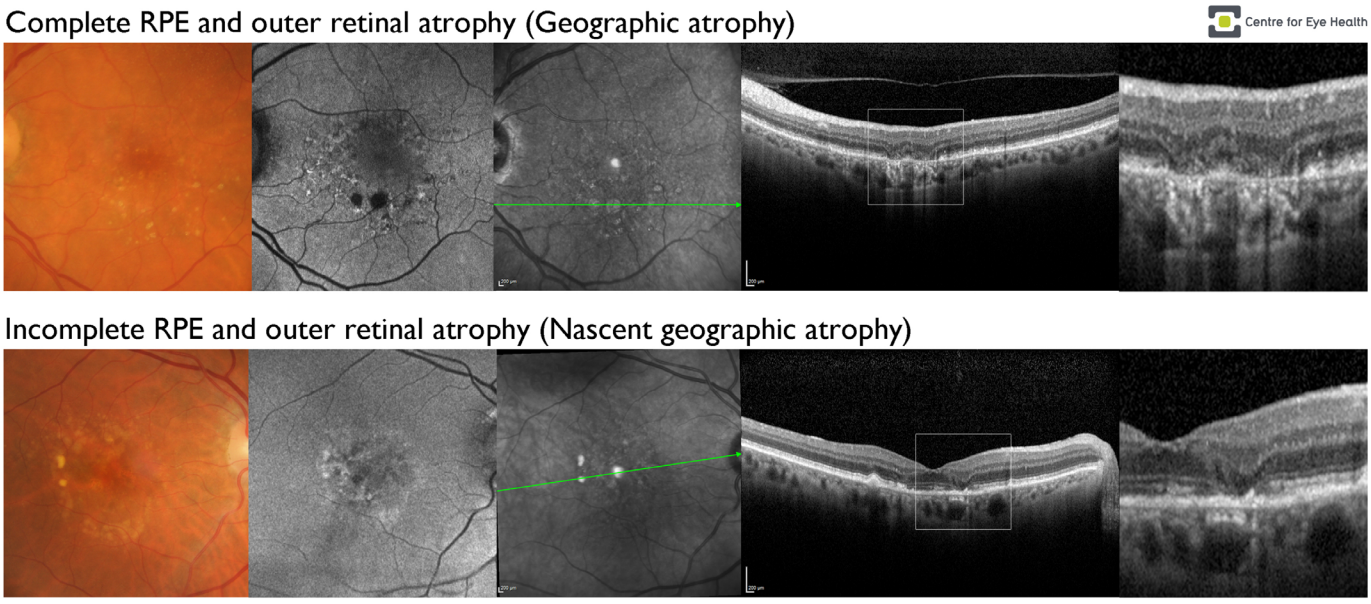

Figure 4. Case figures (CFP, FAF, NIR, OCT) illustrating the appearance of complete and incomplete RPE and outer retinal atrophy (cRORA). Images kindly provided by Angelica Ly, Centre for Eye Health.

vigilant self-monitoring with a home Amsler grid at each visit.[54] The patient should be advised to present for immediate review if symptoms suggestive of late AMD develop, for example, visual distortion, central blur or loss of vision. Fundus examination and OCT are advised[32] if new symptoms have developed, or if there is any suspicion that signs of neovascular AMD may be present. The patient should be referred to an ophthalmologist or colleague if needed.

Recommended management protocols for patients with no, early or intermediate AMD are presented in Figure 5.[54,70]

Disease	Notes
Chronic central serous chorioretinopathy (CSCR)[56]	A serous detachment of the neurosensory retina occurs over an area of leakage from the choriocapillaris. It most often occurs in young and middle-aged adults, and in men more often than women. Vision loss is usually temporary and acute, but in chronic CSCR the impact and signs can be longer lasting. CSCR has been linked to the use of corticosteroids, pregnancy, hypertension, Cushing's syndrome, sleep apnoea and to patients with emotional distress and/or 'Type A' personalities.
Adult-onset vitelliform dystrophy[56]	Similar features to Best disease, but a later onset age (usually mid-adulthood). It is characterised by a solitary, oval, slightly elevated yellowish subretinal lesion of the fovea typically spanning one third of a disc diameter in size that is similar in appearance to the vitelliform or egg-yolk stage of Best disease. Prognosis is more optimistic than for Best disease, with most patients retaining useful central vision throughout life.
Best disease[57]	Also known as Best vitelliform dystrophy, Best disease is a hereditary condition. Patients will often present in childhood or early adulthood with central vision loss and a characteristic bilateral yellow 'egg-yolk' appearance of the macula. The stage of the disease dictates the clinical appearance, which may progress through: vitelliform, pseudohypopyon, vitelliruptive and atrophic stages.
Stargardt's disease/Fundus flavimaculatus[58]	Stargardt's disease is the most common inherited macular dystrophy which typically presents with foveal atrophy surrounded by discrete, pale-yellow, fleck-like or round retinal deposits in childhood.
Familial dominant drusen[59]	The drusen have a radial and symmetrical appearance, and present very early in life (usually by the third decade via autosomal dominant inheritance although expressivity varies).
Epiretinal membrane (ERM)[60]	ERM is an acquired formation of a semitransparent fibrocellular membrane at the macular and often occurs after a posterior vitreous detachment, or secondary to retinal detachment surgery or a retinal break.

Table 6. Differential diagnosis of age-related macular degeneration (AMD)

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Modifiable factor	Evidence-based management
Smoking	Given the known correlation with smoking status and risk of AMD progression,[16–18] all patients who smoke, chew or consume tobacco should be advised to quit.
Diet and lifestyle	A diet rich in green leafy vegetables, fish and antioxidants should be encouraged.[24] Systemic conditions including hypertension and cardiovascular disease, as well as obesity should be discussed with the patient as risk factors for late AMD.[11]
Nutritional supplements	It has been shown that patients with intermediate AMD (large drusen and/or pigmentary changes) may benefit from certain nutritional supplements.[25,26] The current recommendation for the supplement ingredients is: • 500 milligrams (mg) of vitamin C • 400 international units of vitamin E • 80 mg zinc as zinc oxide* • 2 mg copper as cupric oxide • 10 mg lutein • 2 mg zeaxanthin Supplements are not currently recommended for patients with normal ageing changes, early AMD, late AMD in both eyes, or for those at risk of AMD without any signs of the disease.[63]

*This dosage of zinc exceeds the upper level of intake guidelines for Australia and New Zealand.[64] The use of supplements should be discussed in conjunction with the patient's general practitioner.

Table 7. Recommended management of early and intermediate age-related macular degeneration (AMD)

Referral to low vision services should be initiated as soon as AMD causes visual impairment.

Management of late AMD

Geographic atrophy (GA)

In GA, a slowly progressing degeneration of the photoreceptors and RPE occurs. Currently, there are no regulatory-approved treatments for GA, and the standard of care is monitoring every six to 12 months depending on vision/driving status and the individual's risk of progression (see Tables 1 and 2 and 'prognostic biomarkers' section). Low vision care – for example, magnifiers and/or referral to low vision services – is most likely indicated.

GA can progress to neovascular AMD, so patients should be instructed on Amsler grid use, modifiable lifestyle factors and to return for immediate review if new symptoms suggestive of neovascular AMD develop.

Neovascular AMD (nAMD)

It is recommended that optometrists refer to an ophthalmologist urgently, *within one week*, if there is suspected or definite new-onset choroidal neovascular membrane (CNVM). A telemedicine opinion may be sought via e-referral, *within one week*, if practising in a location with limited access to ophthalmology services.

A suggested 'urgent referral' criteria for nAMD is:

- a recent (within three months) history of vision loss, spontaneously reported distortion or onset of missing patch/blurring in central vision
- any of the following signs: suspected or definite new-onset CNVM, macular fluid (sub- or intra-retinal) or macular haemorrhage without other obvious cause.

In the past decade, the mainstay of nAMD treatment has been anti-VEGF agents.[71–73] The main drugs in use in Australia today are ranibizumab (Lucentis) and aflibercept (Eylea). Bevacizumab (Avastin) is used off-label. All drugs have similar efficacy, so drug availability, treatment frequency and cost are often key factors when choosing the treatment drug. Thermal laser photocoagulation and photodynamic therapy (PDT) are now only considered in rare cases or in a subset of AMD – polypoidal choroidal vasculopathy, where laser or PDT is sometimes used when the neovascular lesion is well defined and extrafoveal.

Generally, initial anti-VEGF treatment is commenced with a fixed monthly interval until there are no signs of ongoing activity (for example, fluid visible on the OCT).[74] More recently, individualising the treatment based upon response has gained popularity, such as using treat and extend protocols. In treat and extend, the period between treatments is increased by two weeks each time there are no signs of active CNV, such as fluid on the OCT or a loss of five Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity letters or fresh haemorrhage. Visual acuity outcomes in treat and extend are similar to monthly injections.[75] Ophthalmologists may also choose to treat on a *pro re nata* basis, monthly or bi-monthly basis, or an 'observe and plan' regime, but in general, results are not as good as treat and extend or monthly.[76]

One of the best predictors of long term visual acuity in nAMD is the presenting visual acuity; and generally, the earlier a person receives treatment, the better their chances of maintaining, or to a lesser degree, improving their vision.[77] This highlights the important role optometrists play in the prompt management of patients with nAMD.

Future directions

Recent advances in nAMD research have shown that early detection and treatment is vital for best patient outcomes.[77] As such, optometrists have a major role to play in the management of this condition. In particular, it is important that they are aware of the new imaging biomarkers, such as RPD and nGA, which can enable identification of those at highest risk of progression from intermediate to late AMD.

There are likely to be new AMD treatments in the future. In particular, there are currently clinical trials underway for new early AMD interventions and possible pharmaceuticals for GA, which will significantly change the management pathways.

Due to the rapid growth in the research of AMD, there are opportunities for patients to be involved in research studies (both natural history and treatment trials). A list of relevant trials can be found on the following website: https://clinicaltrials.gov/ct2/home.

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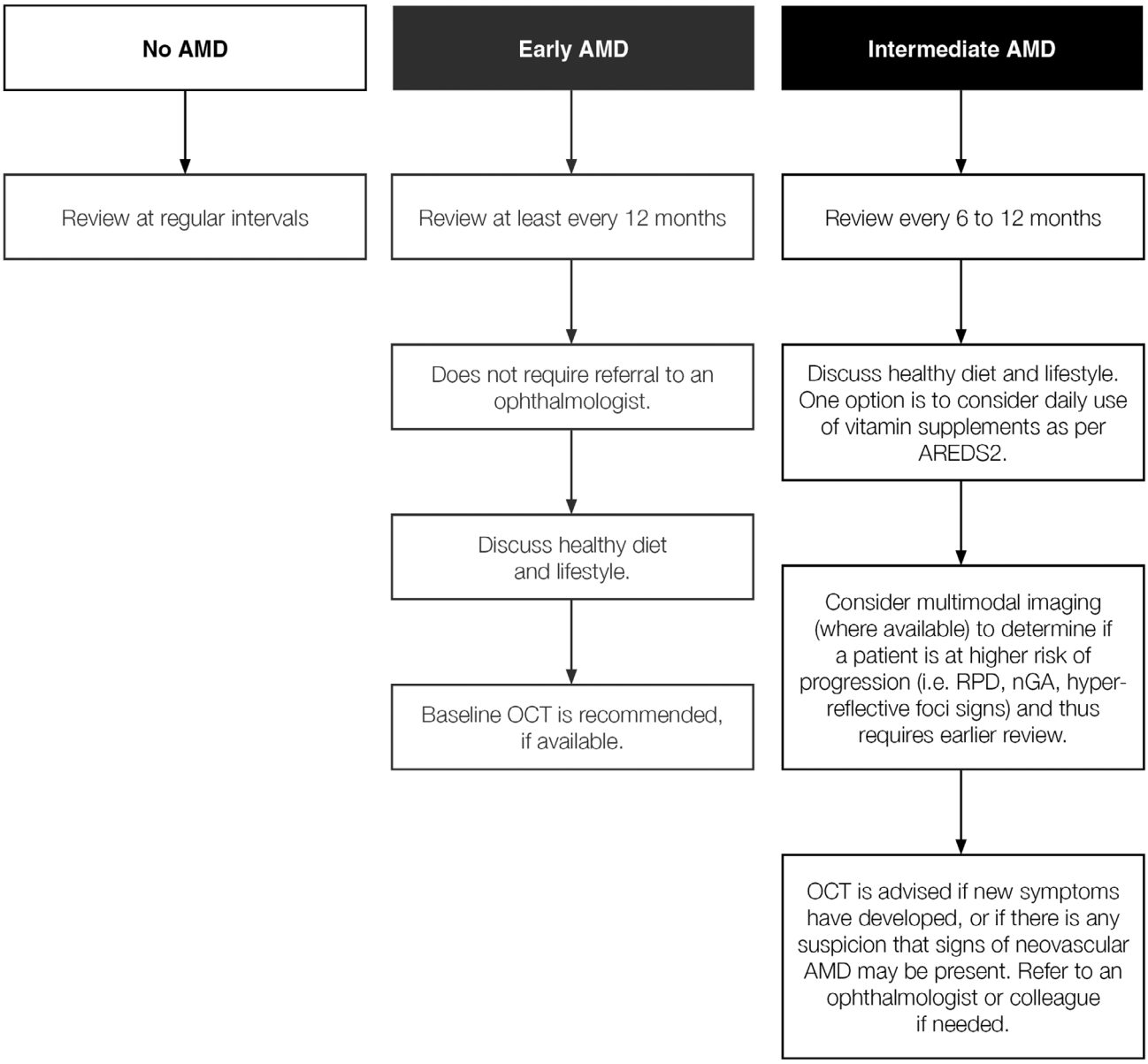

Figure 5. Management of no, early and intermediate age-related macular degeneration (AMD)

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