Age-related Macular Degeneration

Model of care assessment and recommendations

31 August 2017

Building a better working world

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1. Executive summary

With a prevalence of ~5%, age-related macular degeneration (AMD) directly and indirectly impacts a large number of New Zealanders. Building on prior work, the Ministry of Health (the Ministry) has requested EY to assess the three major components of the model of care for people with AMD, as follows:

- Prevention and detection
- Treatment
- Low vision rehabilitation.

In assessing these components, EY has been asked to:

- Assess the overall model of care for AMD to identify whether there should be changes in the current model that would deliver some material improvements to patient outcomes, both within existing resources and within defined additional investment(s)
- Assess the feasibility of adoption, and the economics of the proposed model of care and potential options if relevant, and inform key stakeholders of considerations for their strategic directions and funding models
- Make recommendations to the Ministry on the introduction or otherwise of aspects of prevention, detection, treatment, and low vision rehabilitation in New Zealand, within the overall model of care for AMD.

In undertaking the above, EY has:

- Analysed relevant and available New Zealand data
- Analysed the international literature and assessed relevant international models of care (*see: Appendix D & Appendix E)*
- Conducted interviews and workshops to understand the current models of care for AMD and future options (*Appendix B*)
- Examined the current state, and potential future impact by DHB (*Appendix C*)
- Developed an economic Markov model using a Monte Carlo approach to assess health gains and cost implications of the current system and proposed changes (*Appendix F*)
- Assessed each component of the AMD model of care and drafted a report for Ministry consultation.

This report aims to aid understanding of current models of care for AMD in New Zealand; proposes a new system-level model of care including care pathways and key modelling assumptions; and indicates implementation considerations.

AMD

AMD is the leading cause of blindness in New Zealand. AMD is characterised by age-related changes to the macula - the central region of the retina which is the light-

sensitive tissue at the back of eye involved in detailed central vision. Risk factors include smoking, genetics, and diet. Two main forms of the disease exist, 'dry' AMD, and 'wet' AMD, with the main difference being the rapid proliferation of blood vessels in the wet form. The dry form is slowly progressive and has no specific treatment as yet, apart from a vitamin formulation (termed AREDS2[1]) that may slow the progression to wet AMD. The major change in care over the past 10 years has been the introduction of anti-VEGF[2] agents for the treatment of 'wet' AMD. This involves regular injections into the eye ('intravitreal'), and has been a startling success in up to 90% of cases, preventing what was otherwise a rapid slide to blindness over a 1-2 year period. Key to this is a rapid initiation (within two weeks of onset of symptoms) and regular planned follow-up injections.

Current model of care

The current model of care for AMD in New Zealand has evolved to meet the challenge of delivering timely intravitreal injections for wet AMD to suit local DHB circumstances. Elements of the injection process work well across many districts, with nurse and other injectors to support ophthalmologists, and many wet AMD patients seen for an initial injection within one week of referral. The widespread use of bevacizumab[3] as the first-line anti-VEGF, despite its 'off-label' status, has led to a strongly cost-effective approach. As the New Zealand public system was operating in 2016, we estimate the direct (secondary care) cost of intravitreal injections for wet AMD treatment at $6.1m, with 2,100 QALYs gained, and a cost per QALY of $2,900.

Issues identified with the current system include:

- Relatively low public understanding of the disease, with many people delaying coming forward upon the onset of symptoms
- Relative isolation of community eye practitioners from their hospital-based colleagues, with some unclear referral pathways
- Low uptake of AREDS2 to delay onset of wet AMD
- Difficulties with scheduling follow-up injections in busy clinics, leading to increased injection intervals and sub-optimal vision outcomes
- Potential for a better response with aflibercept as the second-line agent if no response with bevacizumab, rather than the current ranibizumab
- Significant variation in public-system access and treatment rates across the country, due to differences in models of care
- Lack of availability of low vision rehabilitation, with only three DHB-funded clinics operating.

[1] So-named after the *Age-Related Eye Disease Study 2* where its effectiveness was demonstrated.
[2] VEGF = vascular endothelial growth factor – a protein than encourages blood vessel growth. The main anti-VEGF agents available are bevacizumab (Avastin), ranibizumab (Lucentis) and aflibercept (Eylea).
[3] Trade name Avastin, requires re-formulation before being used in the eye.

As demand for eye services grows alongside the ageing population, availability of the ophthalmologist workforce is expected to become further constrained, and some current district models of care for AMD are likely to become unsustainable.

Proposed model of care

A strong stakeholder consensus developed throughout the project such that a single model of care option is proposed in this assessment. It has been designed on the premise that DHBs should use the most cost-effective resourcing mix, care setting and operating principles to deliver optimal care for patients who either have or are at risk of having AMD (Figure 1). The model provides a nationally consistent high-level view, with the understanding that detailed planning and implementation will occur at the district level, considering the following flexible elements:

- Workforce mix
- Funding arrangements
- Treatment approach (either treat and extend or strict PRN approach[4])
- Low vision rehabilitation approach.

Specifically, the proposed model is intended to:

- Support preventive activities
- Enable timely access to diagnosis, treatment and rehabilitation for people most likely to benefit
- Enable care to be delivered closer to home
- Make best use of health professionals' skills and time
- Make best use of technology and other infrastructure within the New Zealand health system.

Aspects of this proposed model of care do not deviate significantly from what is already being done in some districts, but no district is doing all parts, and for some it will be a significant change.

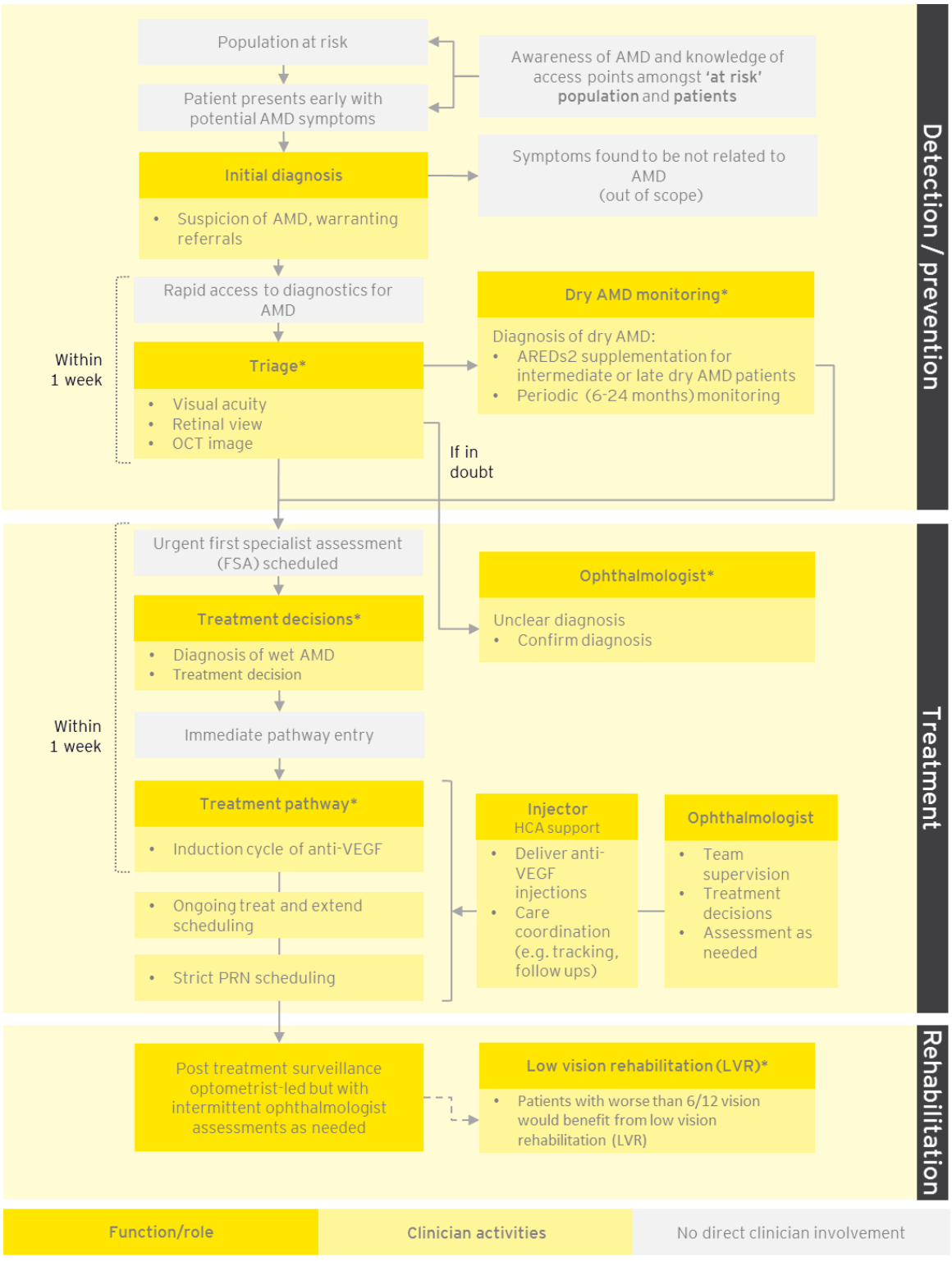
If the model of care had been what is proposed here, with a shift to credentialed nurse injectors with assistants, a less constrained treatment schedule, and aflibercept as the second line agent, we estimate that the secondary care cost in 2016 would have been between $4.5m and $5.5m, with between 2,190 and 2,220 QALYs gained, for a cost per QALY range of $2,020 to $2,510. While investment is going to be needed to undertake the changes proposed, once made service costs are likely to be able to be accommodated within the current funding levels going forward. Note that this difference in costs is at a national level – therefore individual DHB results will vary, with some likely to need to increase volumes more than others, and some will have higher implementation and training cost requirements. At the current nationwide cost of $6.1m, and ignoring inflationary costs, the projected growth of patients expected to need intravitreal injections would be

[4] Treat-and-extend follows a set injection schedule, adjusting over time, while strict PRN is similar, but involves active monitoring of the macula, with injections only administered as needed.

accommodated through to somewhere between 2020 and 2025 – that is, an additional 800 to 1,750 patients could be treated within that funding (*see further: Appendix E*).

Alongside this model of care is a set of recommendations to support implementation (*see: 1.1 - Recommendations*).

Figure 1: High-level proposed model of care



1.1 Recommendations

Recommendations have been made throughout the Future State (Section 5). For ease of access key recommendations were placed into call-out boxes and are aggregated here, listed according to the order in which they appear (*see: Section 5 – Future State*).[5] The "Investment" column represents time and effort, not just financial investment.

	Recommendation	Led by	Required involvement	Time horizon	Impact	Investment
1.	Encourage national consistency of intervention rates based on determined clinical criteria and patient outcomes, with flexibility in how services are delivered at a district level	Ministry	DHBs	*Short term*	*Moderate*	*Small (but see Recs 7 & 8)*
2.	Find the most cost-effective resourcing mix and settings of care to maximise patient benefit and efficiency of AMD diagnosis and care	DHBs	Ministry	*Short term*	*Moderate*	*Initial investment needed, potentially cost neutral*
3.	Encourage AMD community awareness, including Amsler grids visible in GP and optometrist clinic rooms.	DHBs, Ministry	New Zealand Association of Optometrists (NZAO), Royal NZ College of General Practitioners (RNZCGP), Macular	*Medium-term*	*Moderate*	*Small*

[5] Many of these recommendations represent standards to be reached by participants in the model of care. In some instances they will already be reached by certain participants, in which case they are able to maintain their current state in that area.

	Recommendation	Led by	Required involvement	Time horizon	Impact	Investment
			Degeneration New Zealand (MDNZ)			
4.	Use oculometrics in the community, closer to patients, where possible, with clear referral criteria (i.e., improving consistency)[6]	DHBs	Optometrists, general practitioners	*Short term*	*Moderate*	*Moderate*
5.	Review the evidence for funding of the AREDS2 vitamin regime in the New Zealand context to make preventive treatment easier for patients	RANZCO	PHARMAC; DHBs	*Medium term*	*Small*	*Small*
6.	If treatment is indicated, ensure that the first intravitreal injection for wet AMD takes place within one week of a referral for suspected wet AMD	DHBs	Ophthalmologists	*Short term*	*Moderate*	*Moderate*
7.	Treatment should follow a treat and extend or strict PRN approach, with timely availability of injections allowing the most cost-effective approach and maximal patient benefit	DHBs	Ophthalmologists	*Short term*	*Moderate*	*Large initially, should reduce*
8.	Given the health benefits able to be gained, and the strong cost-effectiveness of the treatment, consider the adequacy of volumes of treatment delivered based on these protocols	DHBs	Ministry	*Short term*	*Moderate*	*Will range by DHB*
9.	Develop a simpler, nationally consistent approach for ophthalmologists to follow with	RANZCO	Ministry; DHBs	*Medium*	*Small*	*Small*

[6] Oculometrics are AMD diagnostic tests, including an optical coherence tomography (OCT) scan, retinal viewing/photo and measurement of visual acuity.

	Recommendation	Led by	Required involvement	Time horizon	Impact	Investment
	patients when using bevacizumab and any future off-label treatments			*term*		
10.	Clarify the Medicines Act requirements around the reformulation of medicines in hospital pharmacies, including the potential to supply other hospitals	Medsafe	Ministry	*Short term*	*Small*	*Small*
11.	Explore the potential for DHBs to have a single contract for re-formulated bevacizumab	PHARMAC, DHBs		*Short term*	*Moderate*	*Small*
12.	Complete the process currently underway to investigate aflibercept as the second line agent for wet AMD treatment	PHARMAC, DHBs	Ministry; RANZCO	*Short term*	*Large*	*Moderate*
13.	Explore further utility and safety of ziv-aflibercept for ocular use	RANZCO	PHARMAC; DHBs; Ministry	*Medium term*	*Large*	*Large*
14.	Use nurse or other trained injectors, with assistants to support efficiency where demand is sufficient, under the supervision of ophthalmologists	DHBs	National Nursing Organisations group (NNO)	*Short term*	*Large*	*Training and revised protocols needed, should be cost saving*
15.	Develop a national AMD treatment protocol, including consistent criteria for starting / stopping / changing anti-VEGF treatment	RANZCO	DHBs, Ministry	*Medium term*	*Moderate*	*Small*

	Recommendation	Led by	Required involvement	Time horizon	Impact	Investment
16.	Offer a 1-2 hour low vision rehabilitation consultation with appropriate professionals to patients with 6/12 – 6/24 visual acuity	DHBs	Ministry, Optometrists, Blind Foundation	*Medium term*	*Moderate*	*Moderate*
17.	Design and implement a process for educating and training optometrists to conduct oculometrics, monitor dry AMD, and monitor patients post-treatment	NZAO	Ministry; RANZCO; DHBs	*Medium term*	*Moderate*	*Moderate*
18.	To support greater quality improvement for all responsible for delivering the AMD model of care, nationally consistent, measurable performance indicators should be developed and reported on	Ministry	DHBs, clinicians	*Medium term*	*Moderate*	*Small*
19.	Improve data collection and analysis according to nationally consistent specifications to allow monitoring of performance and measurement of patient gains made, and to provide a base to continue to improve the management of AMD in New Zealand	Ministry	DHBs	*Short term*	*Moderate*	*Small*
20.	A Clinical Working Group will be established with wide sector representation to oversee and guide eye services development	Ministry	DHBs; RANZCO; NZAO	*Short term*	*Moderate*	*Small*

2. Purpose of this document

The purpose of this assessment is to:

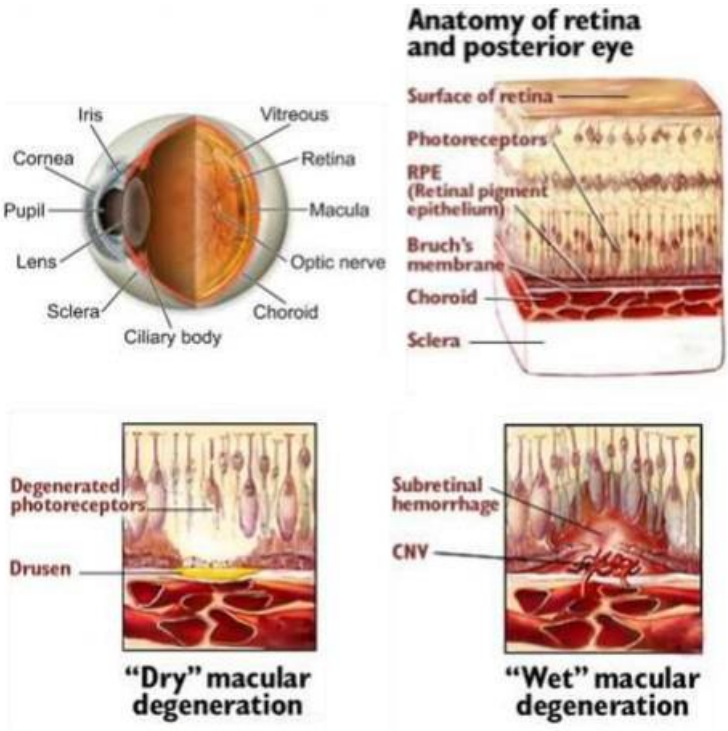
- Aid understanding of current models of care for AMD in New Zealand;
- Propose a new system-level model of care for AMD in New Zealand, including outlining proposed care pathways and key assumptions underpinning the model; and
- Outline considerations for DHBs and national entities when implementing the proposed model of care.

3. Background

3.1 Overview

AMD is the leading cause of blindness in New Zealand. AMD is characterised by age-related changes to the macula - the central region of the retina which is the light-sensitive tissue at the back of eye involved in detailed central vision (Figure 2). In AMD, deterioration of the macula causes progressive loss in the central field of vision, and can affect one or both eyes. There is no known cause of AMD other than age-related changes, but smoking and genetics[7] are risk factors. Other possible risk factors include diet and cardiovascular disease.

Figure 2: Changes in the eye as a result of AMD



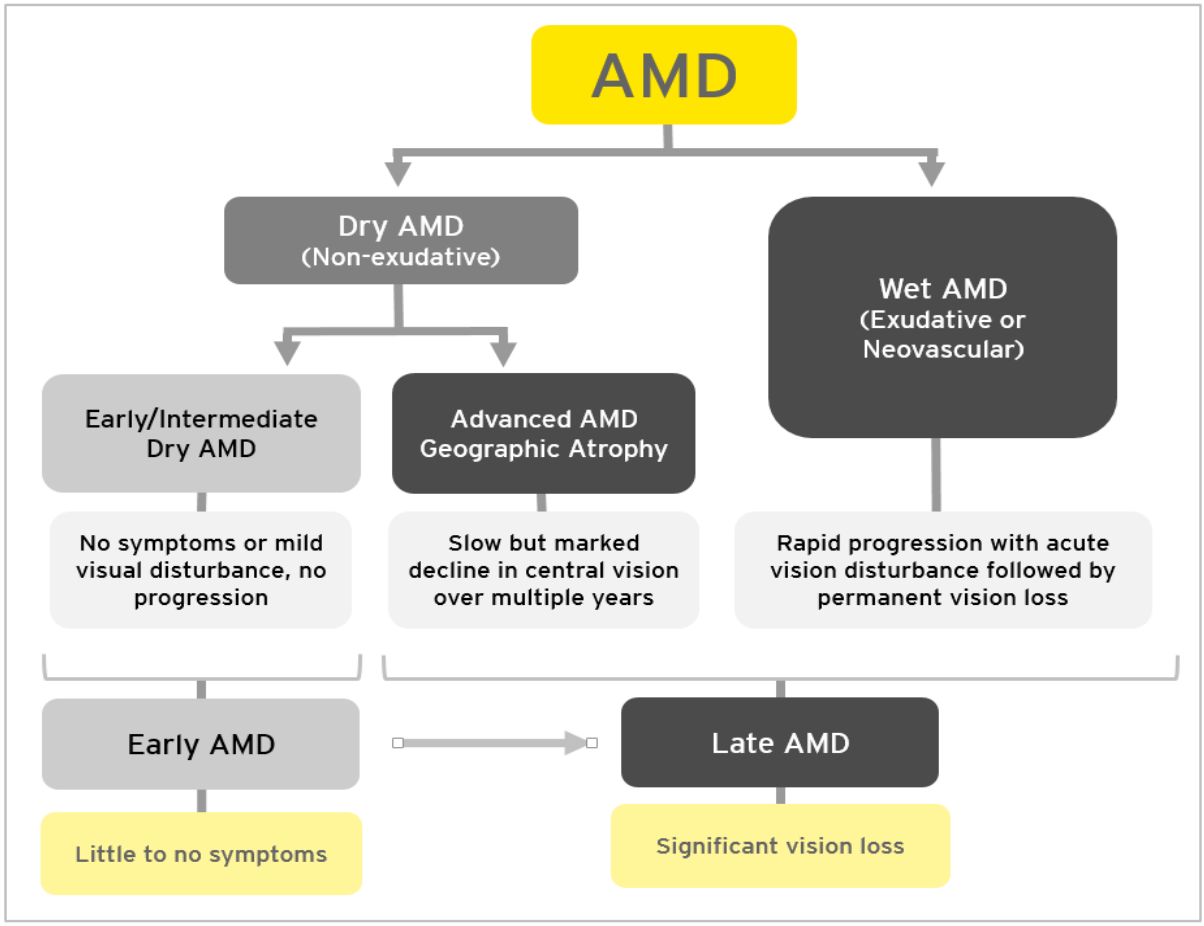
There are two distinct forms of AMD: early and late. Early AMD is the most common and less severe form, and is typically not associated with vision loss or impairment. Early AMD encompasses non-advanced 'dry' AMD, where abnormalities develop in the retinal pigment epithelium (RPE), and lipid deposits (drusen) form underneath the RPE. When dry AMD becomes advanced (geographic atrophy), it is classified as late AMD. Along with advanced dry AMD, late AMD also includes wet neovascular AMD (Figure 3). A glossary of terms used throughout the report is given in Appendix A.

Wet AMD is characterised by abnormalities in new choroidal blood vessel growth (choroidal neovascularisation) under the retina. These leak blood and proteins into the macular regions, causing thickening of the retina, which ultimately results in scarring and permanent damage to the photoreceptor retinal cells. Wet AMD is

[7] Note: genetic factors may explain up to 80% of cases. National Health Committee. Age-related macular degeneration. 2015. Wellington: National Health Committee. Available from: http://www.nhc.health.govt.nz/.

associated with rapid progression and permanent vision loss. There is currently no specific treatment for dry AMD, but intravitreal anti-VEGF injections are established as an effective treatment for wet AMD.

Figure 3: Overview of the various classifications within AMD



While AMD is not a primary cause of death, it is associated with a higher risk of mortality, and leads to a loss of disability-adjusted life-years (DALYs), which is a measure of health burden, factoring in both quality and quantity of life. Through its effect on visual acuity vision field loss, AMD can adversely affect quality of life and interfere with daily activities, which can result in people with AMD requiring formal publicly-funded supports such as home-based personal care and household management, or support from their families or carers. AMD is associated with an increased risk of depression, falls and injuries, as well as an earlier loss of independence and need for aged residential care.

The direct annual publicly-funded cost of delivering intravitreal injections for wet AMD in New Zealand is estimated at $6.1 million (*see: Appendix E*). EY time-series modelling suggests that at current treatment rates, over the next 10 years, AMD treatment will generate a 28,000 QALY gain at a direct[8] cost of ~$80m over that time (undiscounted), at ~ $2,900 per QALY (see*: Appendix G*).

[8] Cost of intravitreal injections (workforce, drug costs) and FSAs, public system only.

3.2 Incidence and prevalence

There are no recent comprehensive incidence or prevalence studies of AMD in New Zealand, meaning that estimates are based on extrapolation from international data, and current treatment rates. Internationally, reported rates vary depending on AMD definition criteria, oculometric accuracy, and the ethnicities and age ranges studied.

Incidence – number of new cases in a time period (e.g., one year)

Prevalence – number of cases overall in the population

In 2016 it was estimated that approximately 71,000 New Zealanders aged 65 years and over had AMD, with between:

- 58,000 and 60,000 cases of early to moderate dry AMD;
- 2,400 and 2,600 cases of late dry AMD;
- 5,500 and 5,700 cases of wet AMD.

In addition around 4,100 people were assessed as clinically blind[9], and therefore either no longer receiving treatment for wet AMD or suffering geographic atrophy through dry AMD.[10,11,12,13]

Based on the 2016 figures, there were approximately 2,000 to 2,500 new diagnoses of late AMD, and an estimated progression from dry to wet AMD of between 1,250 and 1,350 people in that year. The prevalence is then balanced out somewhat by mortality, and those completing their course of treatment remaining without active disease. The prevalence of AMD per head is around twice as high in European populations than in other groups such as Māori, Pacific and Asian.

There is likely to be an ongoing increase in crude incidence and thence prevalence over the next 20 years due to the population ageing. The underlying incidence per age group is likely to be stabilizing as smoking rates fall, and the effects of better detection is also likely to be stabilizing. In addition the prevalence of late AMD among people aged over 65 years is expected to increase through improving survival.

Approximately 50% of all cases of blindness in New Zealand are attributable to AMD, equating to between 6,000 and 7,000 people today. The incidence of low vision and blindness among people with AMD has reduced following the adoption of anti-VEGF therapy across New Zealand. A decline in membership with the New Zealand Blind Foundation for AMD-related vision loss was linked with the

[9] Blind Foundation, personal communication. Those with 6/24 vision or worse are termed 'clinically blind'.
[10] Seddon JM, Chen CA. The epidemiology of age-related macular degeneration. *Int Ophthalmol Clin*, 2004. 44(4): p.17-39.
[11] National Health Committee. *Age-related macular degeneration. 2015*. Wellington: National Health Committee. Available from: http://www.nhc.health.govt.nz/
[12] Deloitte Access Economics. *Socio-economic cost of macular degeneration in New Zealand*. Report for Macular Degeneration New Zealand, 2016.
[13] Geographic atrophy is considered the late stage of dry AMD, where initially central vision can still be good, though contrast is affected, glare an issue, and reading and seeing fine detail may become difficult. This progresses to a point where central vision is lost, resulting in significant impairment to quality of life, even though the person may not be classified as clinically blind.

introduction of anti-VEGF treatment, decreasing from membership rates of 19 to 14 memberships per 100,000 population from 2006 to 2012, but stabilising in recent years.[14]

The Blind Foundation estimates that it receives about 500 new cases each year as the result of AMD (dry and wet) which has caused a vision loss in the client of 6/24 or worse.[14] It estimates there is at least a 1:1 ratio of 6/12 to 6/24 cases, to cases 6/24 and worse. This suggests the incidence of AMD cases needing a first visit for vision rehabilitation is at least 1,000 per year, or around 2-3 per week at larger DHBs.

3.3 Our approach to this assessment

3.3.1 Scope

Building on prior work, the Ministry of Health determined the need to assess the three major components of the model of care for people with AMD as follows:

- Prevention and detection
- Treatment
- Low vision rehabilitation.

The Ministry commissioned EY to undertake an assessment of the model of care for AMD including *inter alia:*

- The overall model of care, to identify whether there could be change over a period of time that would deliver material improvements to patient outcomes
- Options for improving each component of the model of care, while also identifying the population served and the required investment, within currently available funding
- Assessing the feasibility of adopting the proposed model of care, including considering how the funding models and strategic directions identified by key stakeholders should be informed by the assessment
- Making recommendations to the Ministry on the following, within the overall model of care for AMD:
    - The use of genomic molecular oculometric tools to support prevention,[15] early identification and risk stratification of AMD;
    - Intravitreal anti-VEGF treatment in New Zealand; and
    - Low vision rehabilitation.

3.3.2 Process

In order to design an appropriate future model of care and make clear recommendations, EY engaged extensively with stakeholders (interviews and

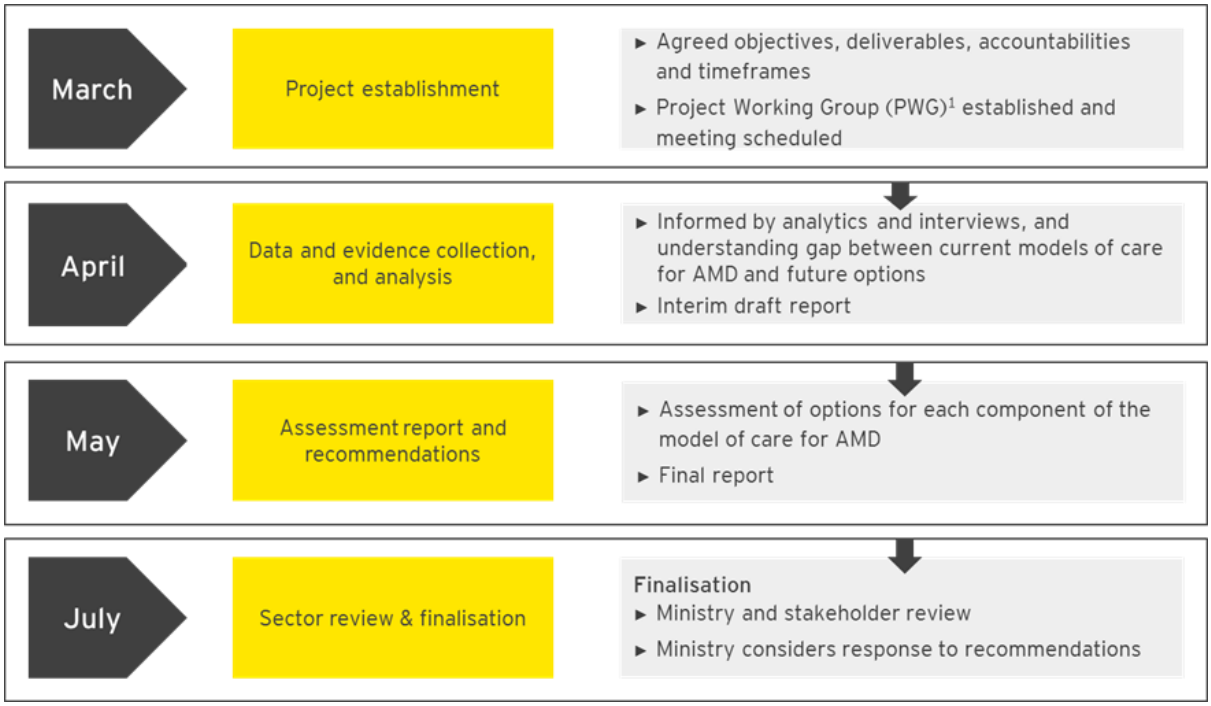
[14] Blind Foundation, personal communication.
[15] A review of the literature revealed that there is not currently sufficient evidence to justify pursuing the use of genomic molecular oculometric tools to support AMD prevention (see: Appendix E).

workshops) and conducted analysis (literature review and economic modelling), considering the following four domains:

- Clinical
- Societal and ethical
- Economic
- Feasibility of adoption.

Our process and timeline in 2017 is illustrated in Figure 4 below.

Figure 4: Process and timeline (2017)



Stakeholders engaged in the course of this work included ophthalmologists, optometrists, nurses, general practitioners (GPs), district health boards (DHBs), the Ministry of Health, the Macular Degeneration Society and the Blind Foundation (*see: Appendix B*). There is strong support for change, and movement towards a nationally consistent model of care for people with AMD in New Zealand.

For the project EY has:

- Analysed relevant and available New Zealand data
- Analysed the international literature and assessed relevant international models of care (*see: Appendix D & Appendix E)*
- Conducted interviews and workshops to understand the current models of care for AMD and future options (*Appendix B*)
- Examined the current state, and potential future impact by DHB (*Appendix C*)

- Developed an economic Markov model using a Monte Carlo approach to assess health gains and cost implications of the current system and proposed changes (*Appendix F*)
- Assessed each component of the AMD model of care and drafted this report for sector review.

4. Current state

4.1 Prevention and early detection

There are few known ways to prevent AMD, though current clinical guidelines recommend smoking cessation and the adoption of a Mediterranean-type diet as two options.16 Although no smoking cessation campaigns directly related to AMD are in place in New Zealand, 'better help for smokers to quit' is one of New Zealand's national Health Targets.[17] This reflects the wider emphasis on smoking cessation, that will prevent AMD through an overall reduction in smoking prevalence (a 4% reduction in smoking prevalence occurred between 2006/07 – 2015/16).[18]

In terms of detection, stakeholders cited a lack of public awareness of AMD as one of the reasons that many people are slow to access care, and that encouraging the use of Amsler grids by the at-risk population will be likely to improve early detection.[19] While Macular Degeneration NZ (www.mdnz.org.nz) has run campaigns, there has been no systematically funded awareness-raising work. There is an opportunity to increase awareness (particularly through general practice and community optometry), which is warranted as timely diagnosis and access to treatment is cost-effective, improving patient health outcomes.[20],[21] People presenting late require more treatment injections and are likely to finish with lower visual acuity (VA).

Initial detection using an Amsler grid is confirmed through optical coherence tomography (OCT), and VA and retinal photo oculometrics. These diagnostic checks are often referred by a GP and completed by an optometrist, but the testing may occur in a public hospital setting. No specific treatment for dry AMD exists at present. Those people diagnosed as having dry AMD are taught to monitor their vision using an Amsler grid, but are not referred to an ophthalmologist. Those with inconclusive or initial wet AMD diagnoses are referred to an ophthalmologist for a confirmatory diagnosis (see: Section 4.3 - Treatment).

There is no uniform approach to accreditation of providers of oculometrics. This limits the ability of the system to invest in consistent technology. For example, OCT machines are not uniform, meaning that scans need to be repeated by an ophthalmologist after referral from an optometrist, and future scans to show AMD progression need to be taken on the same OCT machine.

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[16] Carneiro Â, Andrade JP. Nutritional and lifestyle interventions for age-related macular degeneration: a review. *Oxidative Medicine and Cellular Longevity* 2017; 2017:1-13

[17] National performance measures reflecting significant government and public priorities.

[18] Ministry of Health. *New Zealand Health Survey: Annual Update of Key Results 2015/16*. Wellington: Ministry of Health, 2016.

[19] The at-risk population is defined as those over 65 years, and those with a genetic history of AMD are 50% more likely to have it (Dianne Sharp, workshop, 11 April 2017)

[20] Gillies MC, Campain A, Walton R, Simpson et al. Time to initial clinician-reported inactivation of neovascular age-related macular degeneration treated primarily with ranibizumab. *Ophthalmology2015*; 122(3), 589-594

[21] Andrew Thompson (Retinal Specialist, Bay of Plenty), General Stakeholder Workshop, 11 April 2017, Wellington (*see: Appendix B*).

Referral methods also vary, rather than communicating consistent information through a single channel. Inconsistent referral content combined with clerical staff lacking contextual understanding can result in delays in records being received for clinical triaging of suspected wet AMD cases. With process delays, or when these are not correctly triaged as urgent, time to confirmatory diagnosis and first treatment is extended, potentially resulting in added blood vessel growth causing avoidable visual acuity loss, and requiring more extensive treatment. Based on the 2016 cohort, it is estimated that over 10 years, up to 5,000 QALYs may be being lost. In addition initial treatment costs would increase by ~$1.2m due to more severe cases needing greater treatment[22] (see: Appendix G). On average the model suggests those people entering treatment late experience overall treatment costs that are 18% higher, with session frequency increasing by 12%, further increasing demand pressures (see: Section 4.3 - Treatment).

In terms of preventing the progression of AMD, the AREDS2 nutritional supplement regime is currently the most effective treatment available to slow the progression of intermediate and late dry to wet AMD.[23] Over-the-counter AREDS2 solutions are available, of which there is varied uptake across the country (with actual uptake and therefore effectiveness unknown).[24] This is not subsidised, and depends on clinicians recommending uptake. Currently there is an estimated approximate 10% uptake of AREDS2 for those who are looking likely to progress from moderate or late dry AMD to wet AMD.[25] The AREDS2 study suggested that 25% of participants received a positive effect of a 2-3 year delay in progression to wet AMD.23 Ideally one would have evidence from more than one trial, but based on these figures, and given the projected population change over the next 10 years, it is estimated that at a 10% uptake rate 80 QALYs would be gained at a cost of $0.8m, for a cost per QALY of $10,300. Each further 10% increment would gain a further 80 QALYs at a cost of $0.8m.[26]

A key issue in the current state of prevention and detection is the relative professional isolation of optometrists from other eye health practitioners.[27] This is not the case in all DHBs however, and in some cases where there have historically been issues, inroads are being made in relationship building. An example is employment by Waikato DHB of three optometrists, one full-time and two on a sessional basis (for children and people with diabetes), which is seen as a valuable

[22] Where blood vessel proliferation is more advanced more intravitreal injections are needed to get the growth under control, and the greater the risk of poor or no control being achieved

[23] Age-Related Eye Disease Study 2 Research Group. Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. *JAMA* 2013; 309(19), 2005-2015. AREDS2 formulation is: 500 mg vitamin C, 400 IU vitamin E, 25 mg zinc as zinc oxide (reduced from 80 mg in initial study following gastrointestinal side-effects), 2 mg copper as cupric oxide, 10 mg lutein, 2 mg zeaxanthin. In the study varying levels of zinc were trialled, with 40mg the most common. There was no strong indication that higher levels were any better than the 25 mg starting dose.

[24] Some patients purchase AREDS2 vitamins overseas at a lower cost

[25] Clinical Director Workshop, 04 April 2017, Wellington (*see: Appendix B*). Suggestions ranged from 5% to 25%, verbal consensus at 10%, noting that this does not include a number of people with early dry AMD who may be taking supplements but are not recommended to do so (only effective in intermediate and late dry)

[26] Note that the AREDS studies were carried out in USA. To the extent that New Zealander's general diet is better than that of the US expected benefits may be somewhat lower than is shown here. We have not attempted to quantify this.

[27] General Stakeholder Workshop, 11 April 2017, Wellington (*see: Appendix B*)

means of increasing public service capacity, upskilling and relationship building. Such progress is reported to be limited in some districts by a perception that although some optometrists are interested in eye disease, many are not and therefore are not open to additional training as might be required to take on an extended role in the diagnosis and treatment of AMD.[28]

Prevention and early detection: why change?

- Early detection (e.g., through use of the Amsler grid) and timeliness to and between treatments should improve outcomes and reduce treatment costs. Modelling suggests a potential 18% reduction in overall treatment costs and a 12% reduction in treatment frequency. Patient health would improve with the loss of 5,000 QALYs avoided, along with the need for an extra $1.2m required for more extensive treatment over the next 10 years
- Uptake of the AREDS2 nutritional supplement regime varies across the country. It may delay the progression of mid-late dry AMD patients to wet AMD by 2-3 years in some cases – though data is limited to two clinical trials. Modelling suggests a moderately cost-effective $10,300 per QALY gained at current pricing. It is likely that this price would drop if subsidised supplements were introduced
- Optometrists are relatively under-utilised, and represent a growing part of the future health workforce, with the skills and capacity to support prevention and detection

4.2 Current treatment

4.2.1 Diagnosis confirmation and initial treatment of wet AMD

Following an inconclusive or initial wet AMD diagnosis by a GP or optometrist, a first specialist assessment (FSA) by an ophthalmologist will confirm the diagnosis. A confirmatory diagnosis of wet AMD should result in an immediate appointment booking for administration of the first anti-VEGF injection, in some cases that same day (and sometimes during the FSA appointment) or within a week.[29] If the ophthalmologist's diagnosis is dry AMD, the patient will be referred back to the GP and optometrist for periodic monitoring, following the same process as other dry AMD patients (*see: Section 4.2 - Prevention and early detection*).

Following the first anti-VEGF injection for patients with wet AMD, treatment normally continues with the next two injections spaced one month apart (for further information on individual DHB treatment rates, see *Appendix C*). If initial injections are less than 5.3 weeks apart, patients retain a higher level of visual acuity than those with intervals of more than 5.3 weeks, which require an average of three additional injections and a longer course of treatment.[30]

[28] General Stakeholder Workshop, 11 April 2017, Wellington (*see: Appendix B*)
[29] Some funding arrangements are reported to disincentivise ophthalmologists from injecting during the FSA, which delays time to first injection and can result in avoidable VA loss. While it is noted that same day treatment is preferable, some patients require more time to decide upon the course of treatment.
[30] Gillies, MC, Campain A, Walton R, Simpson J M, Arnold JJ et al. Time to initial clinician-reported inactivation of neovascular age-related macular degeneration treated primarily with ranibizumab. *Ophthalmology* 2015 122(3), 589-594.

4.2.2 Approaches to ongoing treatment

- **Treat and extend** follows a set injection schedule, adjusted periodically depending on response – often at every third visit. This approach avoids having to make treatment decisions every visit.
- **Strict PRN** involves active monitoring of the macula, with injections only administered as needed, and each treatment interval assessed each visit. This reduces the risk of overtreatment and the disutility of receiving injections more frequently; however, it can be more resource-intensive than the treat and extend approach.

Treatment intensities currently vary between DHBs but averages ~four injections per patient per year. Although this accounts for patients who are advanced in their treatment and therefore require less frequent injections, a 13-week interval on average indicates that some patients are likely to fall outside the 5.3 week threshold needed for a good initial response.

4.2.3 Anti-VEGF medications

The anti-VEGF medications used are:

- **Bevacizumab** (Avastin) – this is the first-line agent, approved for use in colorectal and renal cell cancer in New Zealand. Bevacizumab is a recombinant humanized monoclonal antibody that selectively binds to and neutralises the biologic activity of human VEGF. It is produced by recombinant DNA technology in a Chinese hamster ovary cells in a nutrient medium containing the antibiotic gentamicin. It needs to be reformulated for use in the eye, a service offered privately (e.g., by Baxter New Zealand, based in Auckland) for ~$85 per dose.[31] More recently, DHB hospital pharmacies have developed this service internally (e.g. Auckland, Canterbury and Southern DHBs), at ~$35 per dose[31] excluding implementation costs. If this level of savings was possible nationally then total injections costs could be reduced by $12m over the next 10 years (excluding implementation costs). Use for the treatment of AMD in the hospital setting is funded by PHARMAC.[32]

Off-label

As the company involved has not applied to extend the approved use, bevacizumab has not been approved by Medsafe for treatment in the eye. Use in the eye is thus termed 'off-label', and requires a physician to take responsibility for this. In New Zealand there is no legal barrier to 'off label' medicine use providing that the Code of Health and Disability Services Consumers' Rights 1996 is followed.

See: www.medsafe.govt.nz/safety/EWS/q-and-a-hprofs.asp#off-label [accessed 28 May 2017].

[31] General Stakeholder Workshop, 11 April 2017, Wellington (*see: Appendix B*). At present DHBs negotiate separate contracts with Baxter, so prices may vary from DHB to DHB based on e.g. volumes.
[32] Reformulation of medicines requires strict sterile conditions and must be on a named patient basis. It is not something that is likely to be feasible at all DHBs. The exemption under the Medicines Act 1981 to allow hospital pharmacists to reformulate medicines would appear to preclude one DHB supplying reformulated bevacizumab to another

- **Ranibizumab** (Lucentis) – this is funded by PHARMAC as the second-line agent – after non-response to at least three injections of bevacizumab. Even at ~$1250 per dose it is significantly more expensive than bevacizumab, so although comprising only 5-10% of the medication mix, the total cost is higher than for all use of bevacizumab.[33] Ranibizumab is a humanized recombinant monoclonal antibody fragment created from the same parent mouse antibody as bevacizumab, preventing VEGF-A from binding to its receptors. It is the only anti-VEGF antibody medicine approved and funded for the treatment of AMD in New Zealand (approved by Medsafe in 2007). It was developed specifically for intravitreal injections – otherwise has largely the same mechanism of action as bevacizumab.
- **Aflibercept** (Eylea) – this was approved by Medsafe for the treatment of wet AMD in 2013, but is not specifically funded in New Zealand as yet, costing ~$1650 per dose.[33] PHARMAC is considering funding aflibercept as a second-line agent. This was discussed at the May 2017 meeting of PHARMAC's PTAC, with the Committee recommending that aflibercept be funded as second line anti-VEGF treatment for wet AMD after bevacizumab, with a medium priority.[34] The Committee also recommended against funding a third line anti-VEGF agent for wet AMD, and that the proposed access criteria for second line aflibercept be referred to the Ophthalmology Subcommittee for further development, including objective entry and exit criteria.

With aflibercept having a different mechanism of action to bevacizumab and ranibizumab, and a longer half-life it has potential to achieve similar visual acuity outcomes, while being more likely to turn a non-response to a response, and needing fewer injections overall.[35,36] If aflibercept is set as the second-line treatment, and the results of these studies hold, modelling by EY suggests that even without price changes it would be likely to reduce costs by $8.5m over the next 10 years for essentially the same QALY gain that ranibizumab gives, thereby dropping the cost per QALY. Aflibercept may also have a role in the treatment of polypoidal choroidal vasculopathy, a sub-type of AMD more common in those of Asian or Polynesian descent.

[33] ~$1250 for ranibizumab and $1650 for aflibercept is an estimate of the cost based on PHARMAC's request for proposal to make ranibizumab the sole second-line agent. See www.pharmac.govt.nz/news/consultation-2016-09-05-antivascular-endothelial-growth-factor/ There is not a set price for ranibizumab currently; DHBs are required to negotiate their own prices, meaning that the price paid may vary across different DHBs. The $1250 price used in the modelling here is likely the 'best case' for ranibizumab

[34] PTAC minutes May 2017. www.pharmac.govt.nz/assets/ptac-minutes-2017-6.pdf [Accessed 11 August 2017]

[35] Squirrell D, Samalia P, Sheck L, Barnes R, Sharp D. Aflibercept for the treatment of recalcitrant macular degeneration: results from a one year prospective cohort study. The Auckland experience. *Int J Ophthalmol Clin Res* 2016; 53(5)

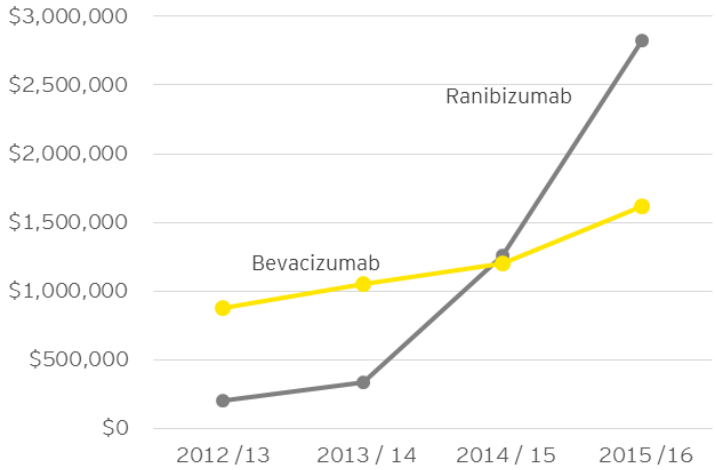
[36] Balaratnasingam C, Dhrami-Gavazi E, McCann JT, Ghadiali Q, Freund KB. Aflibercept: a review of its use in the treatment of choroidal neovascularization due to age-related macular degeneration. *Clinical Ophthalmology* 2015; 9:2355-71

PHARMAC has reported that the first- and second-line anti-VEGF treatments, bevacizumab and ranibizumab, are the 17th and 7th most costly items in New Zealand's public hospitals, respectively. Spending on ranibizumab has increased significantly from $200,000 in 2012/13 to $2.82m in 2015/16 (gross annual cost excluding GST and rebates) as it has become established as a second-line agent for treatment (Figure 5). Spending on bevacizumab has increased from $0.88m in 2012/13 to $1.62m in 2015/16 (Figure 5). While far more bevacizumab is used (estimated at over 90% of treatments), the much higher cost of ranibizumab per dose leads to the higher overall expenditure. It is unclear to us whether the national IDF price for intravitreal injections adequately incorporates the cost of ranibizumab – particularly at the higher usage rates being seen in 2016.

Ziv-aflibercept

A number of clinicians noted this anti-VEGF agent. Ziv-aflibercept, as it is referred to in the US, is a different formulation of the same active ingredient as aflibercept, with the same mechanism of action. Ziv-aflibercept if appropriately re-compounded for use in the eye was suggested to cost in the order of ~$85 per dose compared to ~$1650 for aflibercept (ophthalmologist interview, March 2017). It is not yet used in New Zealand, and treating AMD would be off-label, but there is interest in conducting trials (subject to ethics committee approval). Ziv-aflibercept has been approved in the US under the trade name Zaltrap. In New Zealand Zaltrap has been approved by Medsafe for second-line chemotherapy in combination with other cancer chemotherapy agents for the treatment of metastatic colorectal cancer, with the active ingredient listed as aflibercept (not ziv-aflibercept) on the New Zealand data sheet.

Figure 5: DHB pharmaceutical costs



Source: PHARMAC Annual Report 2015/16. Note that figures include all uses of these medications, not just in AMD.

Anti-VEGF medications have been relatively recently developed, and their long-term outcomes are still being assessed. While short-term risks are well-known and serious adverse events rare, long term risk of side-effects (e.g. stroke risk) are

currently uncertain, and will need to be monitored.[37] It appears that the treatment does not arrest the slow visual acuity deterioration of the underlying dry AMDS disease.[38] The modelling work assumes a continuing general decline in VA, even if a responder, at the same pace as the underlying dry AMD process.

4.2.4 Treatment numbers

Treatment numbers for the 2016 calendar year were compiled for this report, with the treated wet AMD population estimated as 5,490 people – an increase of 12% on 2015 (*see: Appendix C* for details on the data compilation and estimates made).

Intravitreal use of anti-VEGFs can be for different conditions, including wet AMD, diabetic macular oedema (DMO) and retinal vein occlusion (RVO) among others. Estimates for total injections in the publicly-funded system by DHB of treatment are shown in Figure 6 – note that Waitemata DHB patients are managed by Auckland DHB, and Hutt Valley DHB patients are managed by Capital and Coast DHB. AMD proportions were then estimated, and a DHB of domicile analysis performed to estimate age-standardised treatment rates of wet AMD per 1000 people by DHB (Figure 7).

Figure 6: Intravitreal injections by DHB of service in 2016

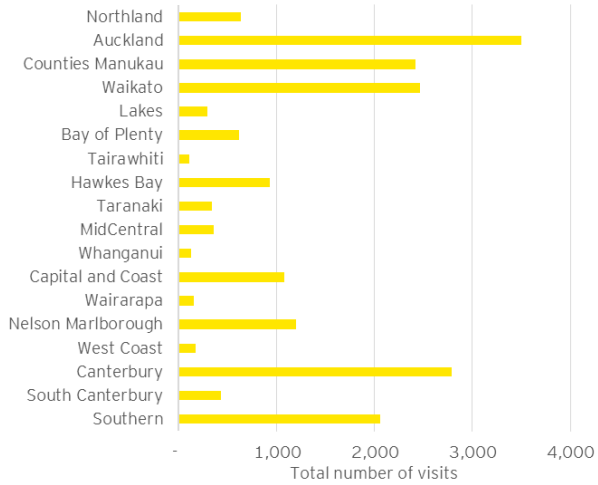
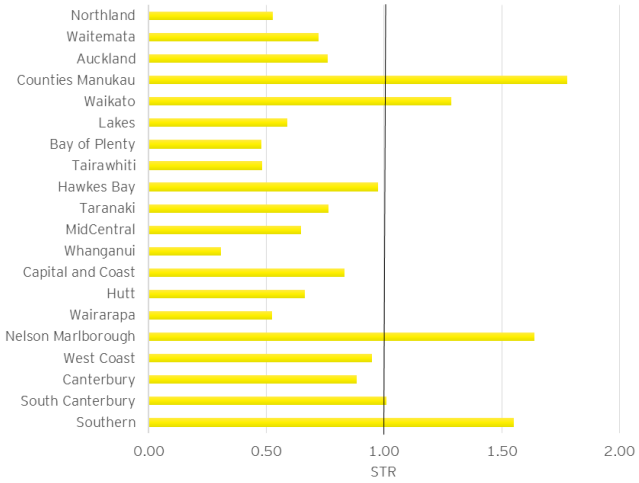


Figure 7: Estimated AMD standardised treatment rate by DHB of domicile in 2016



Source: National Collections, DHB returns. See Appendix C for the details of the data derivation

Age-standardised treatment rates vary significantly across the country, with Counties Manukau, Nelson Marlborough and Southern DHBs showing higher rates of people being injected than other DHBs (Figure 7; *Appendix C*). [39] Year-on-year treatment rates rose significantly between 2015 and 2016 (12%) likely due to changes in treatment models and/or treatment capacity (e.g., Waikato DHB increased AMD treatment by 33% from 2015 to 2016). The median age of the treatment population for wet AMD is 79 years, with an inter-quartile range of 73-

[37] Schmidt-Erfurth U, Chong V, Loewenstein A et al. Guidelines for the management of neovascular age-related macular degeneration by the European Society of Retina Specialists (EURETINA). *Br J Ophth* 2014; 98(9):1144-67

[38] Fighting Retinal Blindness audit results, personal communication.

[39] Counties Manukau DHB estimated rates for AMD may be inflated however, due to a higher prevalence of diabetes in the population which may not have been adequately adjusted for (*see: Appendix C).*

85 years (Figure 8). Pacific and Asian populations have relatively higher presentation rates than the total population at younger ages, potentially reflecting residual confounding by the high prevalence of diabetes in those populations. Treatments for 'European and Other' patients account for 91% of all visits for those aged over 64 years, and from age 80 are at twice the rate of other ethnicities (Figure 9).

Figure 8: Age distribution of the AMD treatment population

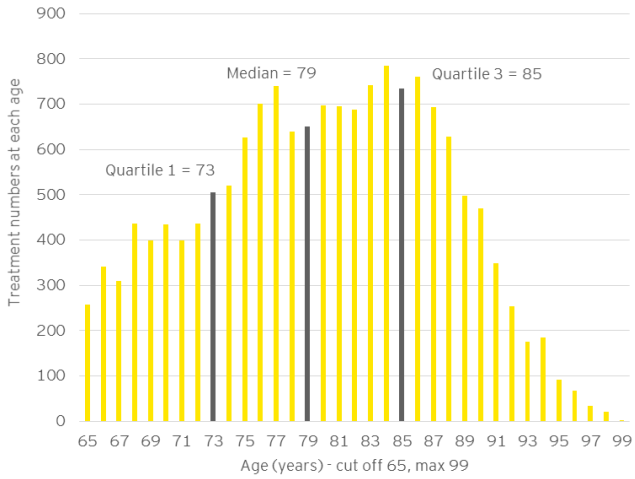
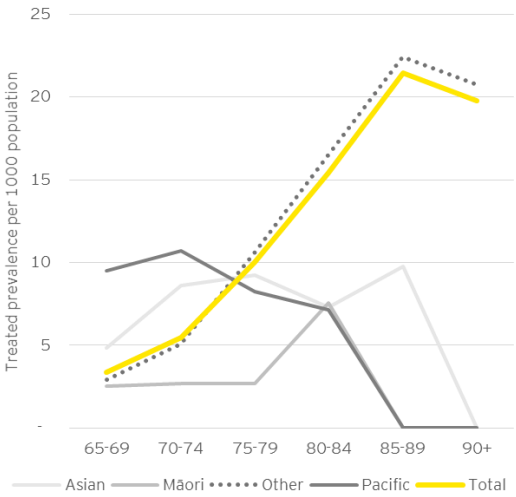


Figure 9: Estimated treatment prevalence for AMD by ethnicity



4.2.5 Treatment workforce

The workforce mix used in AMD treatment varies significantly across the country, from treatment planning and injecting done solely by ophthalmologists, to the use of nurse injectors and other clinicians (e.g., GPs, trainee doctors) in other areas, typically where the model of care is more mature. Some districts see benefit from using health care assistants or other nurses to support injectors, improving the efficiency of administering injections while maintaining cost-effectiveness. Based on DHB returns, ophthalmologists as primary injectors carried out ~33% of injections, with the remainder by appropriately credentialed nurses (~29% of injections), and others (38% of injections) including junior doctors – (both training and non-training), GPs, and MOSS' (Medical Officer Special Scale). The current cost of the injector workforce time in giving intravitreal injections for AMD is estimated at $0.9m per year. EY modelling suggests that if health care assistants were used to support injectors, the total cost would drop to an estimated $0.7m per year (*see: Appendix G*).

The above data relates to the public system. Data are limited regarding the number of AMD patients or treatments in private care, though stakeholder interviews, and data returns from 12 DHBs, suggested that private treatment volumes are lower than public volumes (~10% on average). This is attributed largely to the cost for patients.[40] For example, Nelson Marlborough DHB stated that generally only those

[40] Health insurance coverage falls markedly after age 75, with reimbursement for pharmaceuticals in many policies limited to $100 per treatment.

who are privately insured undergo private treatment (<15%), and in Tairawhiti DHB only two to three private treatments are provided per month (<1%) compared to 288 public treatments (>99%). Some DHBs report a higher rate of private use due to the way that services are configured - for example, approximately a 60:40 split between public and private treatment in Taranaki is estimated.

Overall the system is seeking to maximise the benefit to patients in preserving visual acuity, while minimising the number of visits and injections performed. This latter goal, while maximising cost-effectiveness for DHBs, has the added benefit of reducing visits and unpleasant injections in the eye for patients.

Treatment: why change?

- The population is ageing, placing additional pressure on the already busy ophthalmological workforce. Population and workforce projections indicate that the current model of care in many parts of New Zealand is unsustainable in the medium-term
- Internal DHB reformulation of bevacizumab could save $12 million over 10 years, though appropriate standards must be developed to mitigate the risk of contamination
- Savings as high as 60% of the current workforce cost could be gained in some districts based on a move from ophthalmologist-majority workforces to those with, for example, accredited nurses administering injections
- As the 17th and 7th most expensive public hospital medicines respectively, the costs of bevacimuzab and ranibizumab as first- and second-line agents are already high, and will increase with population growth
- Ophthalmologists consulted, and literature reviewed, suggest that aflibercept would be a more effective second-line agent than ranibimuzab, but access is restricted as it is not currently funded by PHARMAC. If funded as the second-line agent, modelling suggests that $8.5m could be saved over 10 years
- Varied treatment approaches result in apparent inequitable access across the country. Opportunities exist to improve access for patients
- Current treatment intervals vary, but average 13 weeks. A higher level of vision may be retained by patients with a more frequent interval initially, with a potential reduction in injections and a shorter course of treatment overall

4.3 Low vision rehabilitation

Low vision refers to people whose best corrected vision restricts their ability to carry out activities of daily living. This may include people with corrected visual acuity in the better eye of less than 6/12 to light perception and/or significant loss of visual fields and/or contrast sensitivity. For example, vision 6/12 or worse precludes holding a driver's licence, 6/24 or worse is deemed 'clinically blind'.

Low vision rehabilitation services are not part of the service coverage requirements for DHBs, and the number of low vision rehabilitation clinics has decreased over the

years.[41] Stakeholder feedback indicates that most DHBs do not offer adequate services for people with low vision, who the literature states have compared to healthy individuals:

- Twice the rate of social dependence
- Twice the risk of falls
- Three-times the risk of depression
- Four- to eight-times the risk of hip fracture
- Seven times higher health care costs.[42]

There are currently three dedicated DHB low vision clinics:

- Greenlane Low Vision Clinic is open one day per week (Auckland DHB)
- The Burwood Low Vision Clinic operates 2.5 days a week (Canterbury DHB)
- An optometrist at Wellington Hospital works with ophthalmologists to provide a low vision clinic for 0.5 days a week (Capital and Coast DHB).

The clinics provide assessments of vision, including distance and near vision, unaided vision, aided vision, low contrast sensitivity, and field vision. They also have appropriately trained occupational therapists or low vision therapists to consider the functional impact of low vision by assessing how tasks related to daily living are managed, and where appropriate they look at the psychosocial impact of low vision. A few small clinics also operate at the University of Auckland Optometry Clinic and Wanganui Low Vision Trust.

All optometrists receive training in low vision rehabilitation, though some may not choose to offer it in practice. NZAO offers a specific accreditation for low vision rehabilitation, with six optometrists currently so accredited.[43] For private optometrists cost may be a barrier for patient access.

The Ministry's Disability Support Services funds adaptive equipment for people of all ages in situations where this can support them to continue living as safely and independently as possible in their own homes. It also provides equipment for people to work, study or undertake voluntary work, or to support the main carer of a dependent person. For those with vision loss this equipment may include a magnifier to read medicine labels and pantry items, and screen-reader software. However for to people eligible to receive this support they would generally be 6/24 or worse, leaving little external support for those in the 6/12 to 6/24 range. Other supports available include home help and personal care through Needs Assessment and Service Coordination (NASC) organisations for people who have sensory loss.

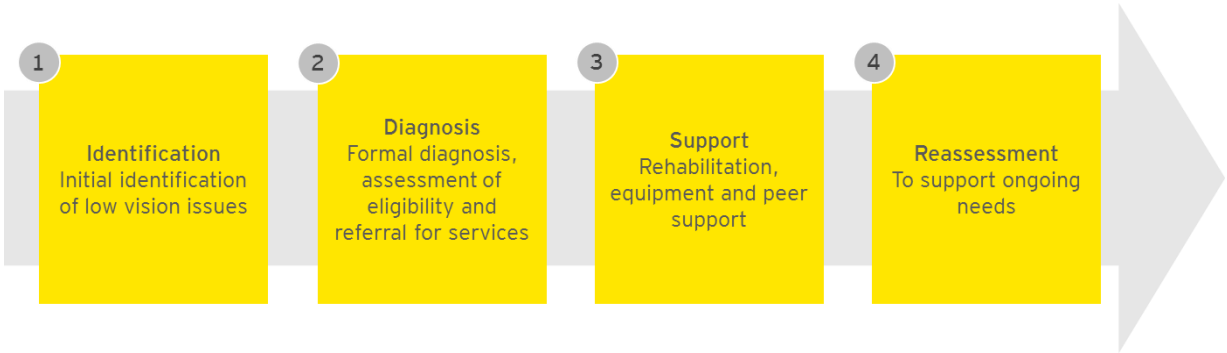
[41] Low vision in this context typically includes those with 6/12 – 6/24 vision. People in this range are unable to drive, yet do not meet eligibility criteria for accessing Ministry-funded Blind Foundation services.
[42] Thompson, A., *Where you live determines how well you can see – access to Avastin for age-related macular degeneration in New Zealand in 2015.*
[43] www.nzao.co.nz/low-vision-guide (accessed 27 July 2017).

The Royal New Zealand Foundation of the Blind (Blind Foundation) provides services for those with 6/24 or worse vision, which includes ~4,000 people with AMD.[44] A few low vision services are offered outside the eligibility criteria, however these are very small in their coverage – for example, one Blind Foundation programme in Northland sees approximately four low vision patients each month. Those who do meet Blind Foundation criteria are required to have a referral letter from an optometrist or GP, creating a cost barrier for some, and many GPs / optometrists are not aware of Blind Foundation services and therefore do not refer eligible patients.

The Ministry is in the process of developing a Low Vision Rehabilitation Services Strategy[45]. Goals under consideration to improve low vision rehabilitation services in New Zealand include:

- People with low vision should have information available in a range of formats (pamphlets, websites, social media) from a range of different sources (health professionals, NGOs)
- National, regional and local pathways to accessing services will be clear. Rehabilitation services will be brought closer to home
- Health professionals will provide integrated services through open and ongoing dialogue across primary care providers, local optometrists and specialists
- People with low vision will have pathways to funded and non-funded equipment, which will help them with daily living. Health professionals will provide information on devices, including low-cost options.

Core functions of low vision rehabilitation services include:[45]



[44] General Stakeholder Workshop, 11 April 2017, Wellington (*see: Appendix B*)
[45] Ministry of Health. *Low Vision Rehabilitation Services Strategy*. In publication [early draft dated Jan 2017 viewed]

Low vision rehabilitation: why change?

- Low vision rehabilitation can improve patient abilities within their sight impairment, decreasing the impact of the vision loss and risk of co-morbidities
- There is limited access to publicly-funded LVR across New Zealand, with those low vision services offered outside of DHB settings not generally publicly covered, resulting in a potential cost barrier
- The Blind Foundation is funded to provide services for those with 6/24 vision or worse, and appears to have good coverage, However those with 6/12 to 6/24 vision (i.e. cannot see well enough to drive) may not have access to publicly-funded low vision rehabilitation services
- People with low vision have twice the rate of social dependence, twice the risk of falls, three times the risk of depression, four to eight-times the risk of hip fracture, and have seven times higher health care costs compared to healthy individuals

4.4 Supporting infrastructure

4.4.1 Workforce

As discussed above, the current AMD workforce comprises a mix of ophthalmologists, optometrists, appropriately credentialed nurses and other injectors, and health care assistants. The ageing population and constrained capacity of ophthalmologists require change to the way that AMD is managed, in order to provide sustainable care into the future.

4.4.1.1 Ophthalmologists

To varying degrees across the country, the current role of ophthalmologists in AMD is to confirm the wet diagnoses, conduct FSAs (where separate from the diagnosis), create and monitor treatment plans and administer injections. There are currently 138 ophthalmologists registered in New Zealand, domiciled in 15 DHBs, and with more than 50% aged over 50 years.[46]

Figure 10: Projected number of ophthalmologists per 100,000 population

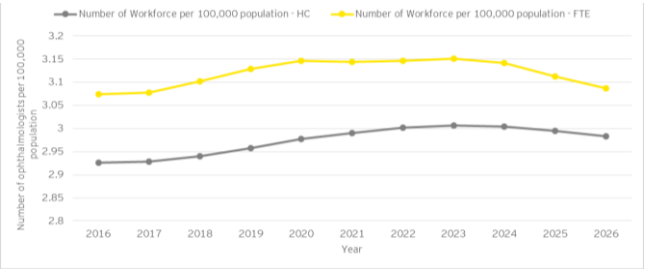
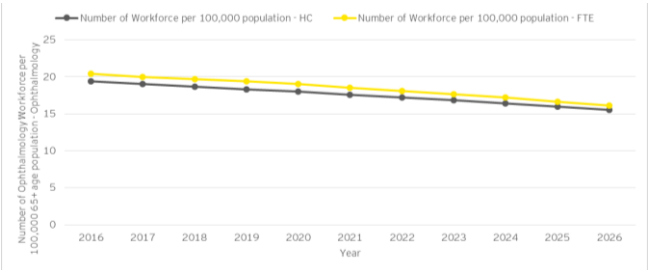


Figure 11: Projected number of ophthalmologists per 100,000 population aged 65+



Source: Health Workforce NZ. Medical Workforce Forecast Model v2.073.xls, 2017.

[46] DHBs without domiciled ophthalmologists are Hutt Valley, South Canterbury, Wairarapa, West Coast, and Whanganui (as per area recorded in the Medical Council figures) – though it should be noted that this does not preclude service provision in these DHBs.

Although the ophthalmology workforce will increase in absolute numbers over the next 10 years, it is likely to decrease by close to 20% relative to the increase in the 65+ population (Figures 10 and 11). In recognition of growing pressure on the available ophthalmologist workforce and as district models of care mature, alternative workforce roles are being introduced, particularly for the administration of injections. These alternative roles (e.g., appropriately credentialed nurses) will be required to enable ophthalmologists to continue providing the diagnosis, treatment planning and oversight needed as demand increases with the ageing population.

4.4.1.2 Injectors

15 of the 18 DHBs of service are currently using clinicians other than the ophthalmologist to some degree to administer injections.[47] Injectors include nurses, registrars (training and non-training), GPs, MOSS, and junior doctors. In all cases injectors remain under the supervision of ophthalmologists. Delivery of the injections requires specific training and rigorous sterile technique. While rare, complications of intravitreal injections are serious and can result in loss of sight.

4.4.1.3 Optometrists

The optometrist workforce is largely community-based in private practice. Optometrists have a key role in AMD care, conducting oculometrics in the community, diagnosing and monitoring dry AMD, and referring suspected wet AMD for a confirmatory diagnosis from an ophthalmologist.

Figure 12: Total optometrist workforce by district and prescribing ability in 2016

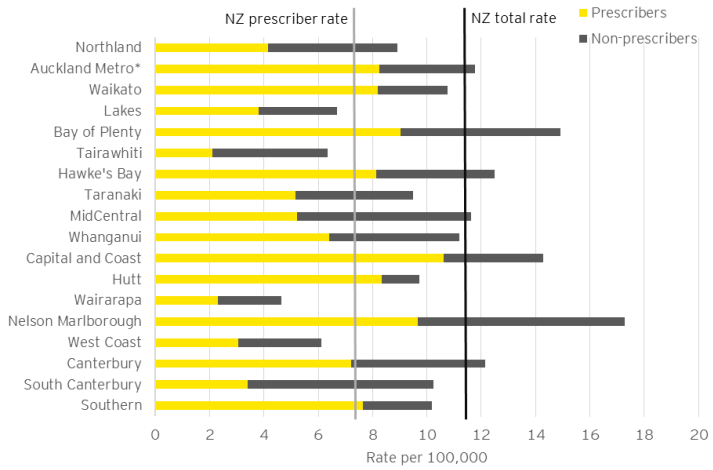
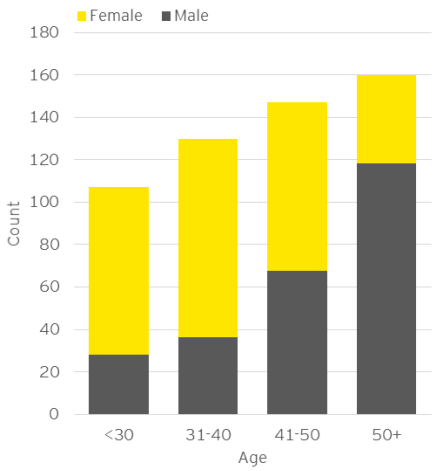


Figure 13: Total optometrist workforce by age and gender in 2016



*Source: NZAO, 2017. *Note: Auckland Metro includes Waitemata, Auckland, and Counties Manukau DHBs, and was aggregated due to lack of within-city specification of location of work*

There are 540 registered optometrists currently practising in New Zealand, spread geographically across all DHBs (Figure 12). The workforce is relatively young, with 43% under the age of 40 (Figure 13). The Auckland University Bachelor of Optometry course is producing 50 graduates per year, of which 20-40% are reported to move overseas, particularly to Australia or the UK. There is an

[47] Out of 18 DHBs as Waitemata and Hutt do not administer intravitreal injections for AMD patients themselves (i.e., as DHB of service)

opportunity for optometrists to provide support in the areas described above, freeing up ophthalmologist time. Additionally, the 43% of optometrists aged under 40 years account for around 60% of those authorised for prescribing presenting an opportunity to extend their involvement in the management of AMD.

In some cases optometrists are assisting with the assessment and progress management of wet AMD patients, and more have expressed an interest in doing this in the future, though this is not currently common practice.[48] Some provide low vision rehabilitation services,[49] and have expressed a willingness to do more, though a lack of public funding for community optometrists can result in a cost barrier for some patients (See: *4.4.2 Funding*).

4.4.1.4 Other workforce

- General practitioners - GPs are often the first port of call for patients with deteriorating vision. GPs do not normally have the appropriate oculometrics to hand, so patients of concern are generally referred to an optometrist, private ophthalmologist or DHB eye department for oculometrics, diagnosis and treatment.[50] The monitoring of dry AMD is more likely to be done by optometrists than GPs
- Clerical staff – in some districts, clerical staff are used to process referrals triaged by clinicians. Clinicians have expressed concern that these are not being accurately processed in a timely fashion, due to limited contextual understanding of eyes and the transient nature of people filling the roles. This can result in delayed intervention for wet AMD patients, leading to visual acuity loss and in some cases the requirement for more extensive treatment
- Orthoptists – in some districts, orthoptists work within multidisciplinary ophthalmology teams in a support function, including providing oculometrics
- Health care assistants – health care assistants are used in some DHBs to support injectors, for example to escort patients from the waiting area to the consulting room, improving session efficiency and reducing costs to treat
- Low vision therapists – a qualification not specifically offered in New Zealand as yet[51], low vision therapists assist people to live safe, productive and independent lives with their vision impairment. The have a focus on the interaction with home and work environmental settings. The role in New Zealand settings is sometimes filled by appropriately experienced occupational therapists (see next)
- Occupational therapists - can undertake a 6-month post-graduate qualification in low vision rehabilitation. The assessment of capability and environmental

[48] For example Waikato DHB has employed three optometrists to work alongside ophthalmologists in a secondary setting.
[49] Six are so accredited through the NZAO.
[50] Referral method varies depending on the district's model of care.
[51] A Diploma Standard exists - www.nzqa.govt.nz/nzqf/search/viewQualification.do?selectedItemKey=2912 but there is no institution currently offering this. A low vision therapist works in the Greenlane Clinic.

impact is an important component of low vision rehabilitation – see low vision therapists above.

Changes in the mix of injectors and the addition of health care assistants to increase the number of injections able to be carried out per session were tested in the modelling (*see: Appendix G*).

Workforce: why change?

- The ophthalmologist workforce is likely to decrease by 20% relative to the 65+ population over the next 10 years, threatening the sustainability of current AMD models of care that rely on the ophthalmologist to administer intravitreal injections
- Optometrist workforce capacity is expanding, a growing number have prescribing rights, and there is willingness to fill extended roles in AMD in New Zealand
- Use of injectors other than ophthalmologists presents an opportunity to better focus ophthalmologist workload
- Inconsistent and inaccurate processing of urgent referrals arising from clerical practice can result in delayed intervention, risking permanent vision loss, and the requirement for more extensive treatment

4.4.2 Funding

- Most AMD treatment occurs in the public system, with an estimated average of 10% occurring privately across the country
  - Overall public expenditure on ophthalmology services in 2016 is estimated at $124m,[52] of which we estimate AMD made up $6.1m or 4.9%. Costs for AMD are projected to more than double to an estimated $12.5m per year by 2036 through population growth and ageing [53]
  - The proportion AMD makes up of ophthalmological outpatient costs for 65+ year olds is expected to increase from 11% in 2016 to 16% by 2036 [53]
  - Contracting for ophthalmology services varies across the country, with a small number of DHBs procuring these services from the private sector. This includes services for patients with AMD. We understand that contracted ophthalmology services are based on price / volume schedules, with the expectation that providers deliver the best mix of these services for their populations. This is also how publicly delivered ophthalmology services operate. However, contracting arrangements with the private

[52] All publicly provided ophthalmology inpatient and outpatient treatments using national IDF prices.
[53] EY analysis, based on population growth and ageing and holding ophthalmological event rates constant at 2016 rates

sector can in effect create caps (or the perception thereof) for the amount of treatment for AMD patients in a given year.

- Private optometrist consultations are not subsidised for AMD. The cost of approximately $100 can result in an access barrier for patients
- GP consultations are subsidised, but still usually require a co-payment which can result in a cost barrier for patients required to access their services[54]
- The Blind Foundation receives Ministry of Health funding to provide services for those with 6/24 visual acuity or worse, but no specific funding for those visually impaired with 6/12 – 6/24 vision
- Funding for vision adaptive equipment is generally only available for adults with 6/24 or worse visual acuity.

4.4.3 Technology

- Optical coherence tomography (OCT) is a key non-invasive imaging test using light waves to take cross-section pictures of the retina. Around 60% of optometrists have OCT machines, though there is variable uptake around the country.[55] However, given the varying levels of sophistication of OCT equipment, and variation in views, scans to show progression need to be taken on the same machine, resulting in duplication of activity between optometrists and eye departments
- No issues were seen with access to fundoscopy. Sometimes high quality cameras are used to capture retinal photos as part of care - stakeholder feedback did not indicate a shortage of these, or any access issues
- There is no uniform process or system for wet AMD referrals around New Zealand. Some have rapid eye assessment pathways, some on-call telephone triage, and others rely on paper referrals. Both GPs and optometrists are able to create referrals for ophthalmologist FSAs in most regions. Content and communication of referrals is varied, through fax, email and electronic systems (optometrists in the South Island do not have the ability to refer through electronic systems yet).[56]

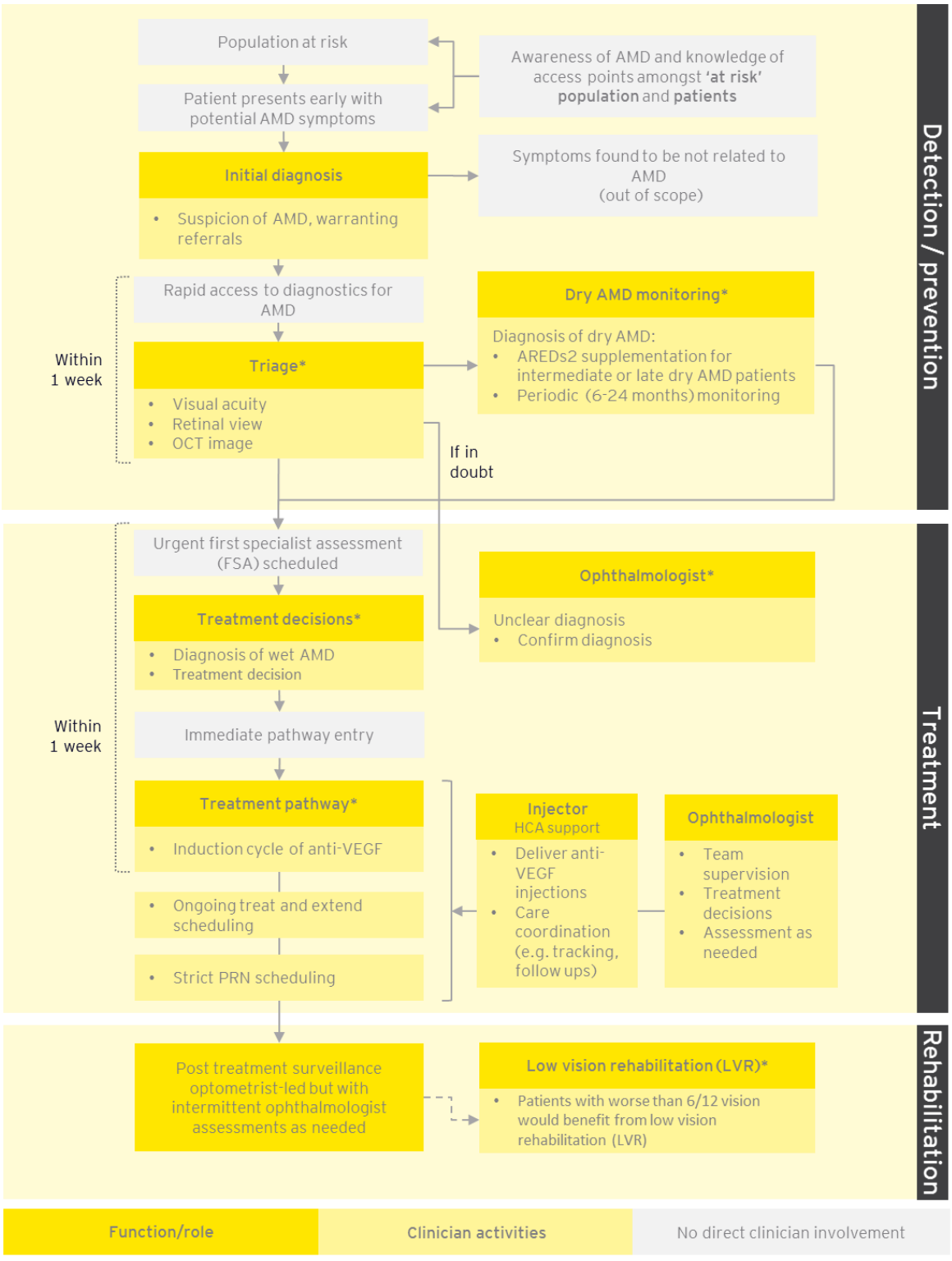
[54] Between 5-10% of 65+ year old New Zealanders did not attend a general practice due to cost at least once in 2015/16. (Ministry of Health. *Annual Update of Key Results 2015/16: New Zealand Health Survey*. 2016, p41

[55] General Stakeholder Workshop, 11 April 2017.

[56] Clinical Director Workshop, 04 April 2017, Wellington; General Stakeholder Workshop, 11 April 2017, Wellington (*see: Appendix B*).

5. Future state

Figure 14: Proposed end to end model of care for AMD



* Entry points for Low Vision Rehabilitation (LVR)

This section outlines the proposed future state for AMD service delivery in New Zealand. Recommended changes and their rationale are given in the text, then summarised as recommendations in the call-out boxes, each with a suggested lead

agency based on the Ministry as the system manager and DHBs as the care deliverer. The recommendations are further described in the Executive Summary section with added notes on organisations to involve, time frames, impact and investment required. The section finishes with suggestions on implementation.

5.1 Proposed end to end model of care

The proposed model of care shown in Figure 14 has been designed to provide maximal patient benefit. It is based on the premise that DHBs should use the most cost-effective resourcing mix, care setting and operating principles available to deliver optimal care for patients who either have or are at risk of having AMD. The model provides a nationally consistent system-level view, with the understanding that detailed planning and design will occur at the district level, considering the following flexible elements:

Recommendation 1 - Encourage national consistency of intervention rates based on determined clinical criteria and patient outcomes, with flexibility in how services are delivered at a district level

Led by: Ministry

- Workforce mix
- Funding arrangements
- Treatment approach.

Specifically, the proposed model is intended to:

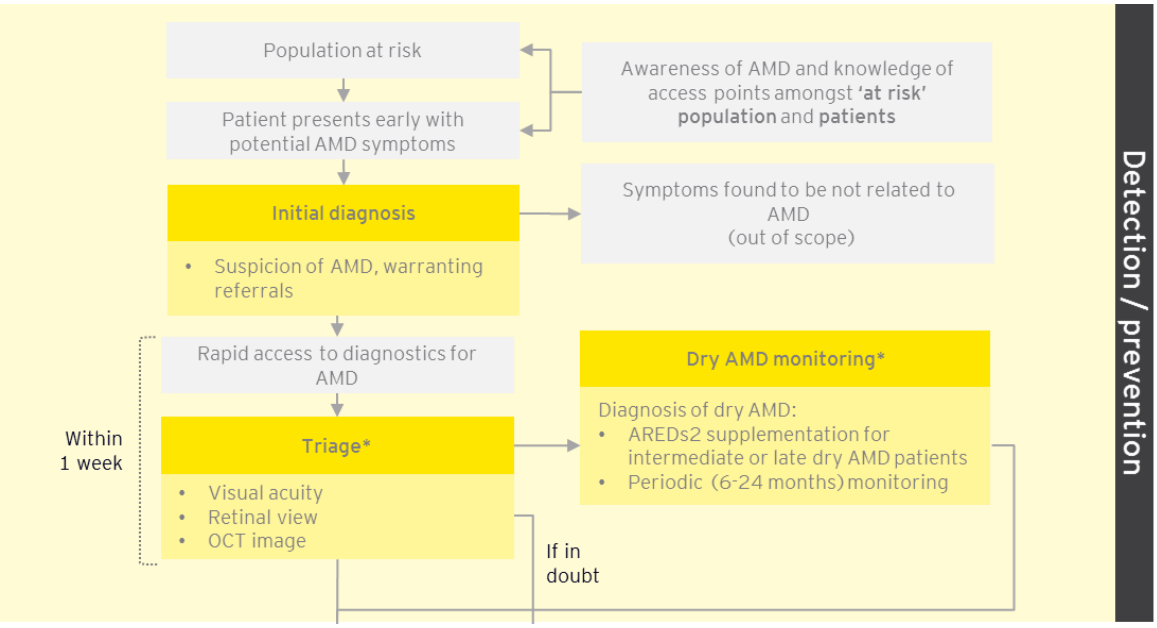
- Enable faster access to diagnosis, treatment and rehabilitation for people most likely to benefit
- Support preventive activities
- Enable care to be delivered closer to home
- Make best use of health professionals' skills and time
- Make best use of technology and other infrastructure within in the New Zealand health system.

Recommendation 2 - Find the most cost-effective resourcing mix and settings of care to maximise patient benefit and efficiency of AMD diagnosis and care

Led by: DHBs

This model of care does not deviate significantly from what is already being done in some districts, while larger adjustments will be required in others (*see: Appendix C*). Overall the model will bring greater national consistency and seek to resolve key issues as identified in the current state section above. To avoid 'reinventing the wheel', we have considered and where appropriate aligned with international best practice models of care (*see: Appendix D*).

5.2 Enhancing prevention and early detection



Prevention and early detection activities will be conducted in the community by GPs and optometrists, with only suspected wet cases reaching ophthalmologists for confirmatory diagnosis and treatment (*see: 5.3 – Enhancing treatment*).

In terms of prevention, retention of the 'better help for smokers to quit' health target is encouraged, along with work targeting good nutrition (clinical guidelines recommend the introduction of a Mediterranean-style diet). The people most at risk are those over 65 years, and those with a family history are 50% more likely to have AMD. To encourage awareness and self-detection in this population, GPs and optometrists should have Amsler grids in clinic rooms,[57] and tutor at-risk patients in their use, including clear communication of key warning signs and when to raise concern with a GP or optometrist.

Recommendation 3 – Encourage AMD community awareness, including Amsler grids visible in GP and optometrist clinic rooms.

Led by: DHBs, Ministry

Community awareness improvement will reduce the time delay between symptom onset and presentation to care, leading to health gain and cost savings.[58]

On early presentation to a GP or optometrist without oculometric training with potential AMD symptoms, a patient should be urgently

Recommendation 4 - Use oculometrics in the community, closer to patients, where possible, with clear referral criteria (i.e., improving consistency)

Led by: DHBs

[57] Amsler grids are not currently on primary care Cornerstone equipment lists

[58] We were unable to directly model the economic and health impact of an awareness campaign. We did examine 'slow access' – simulating delayed access to care, of which this would be a significant part (Section G 5.6) showing increased cost and poorer outcomes. At ~$8m excess cost over 10 years an investment in improving awareness is likely to be cost saving, while generating positive health gain.

referred to a trained provider through a nationally consistent system for referrals for oculometrics as follows:

- OCT scan
- Retinal view/photo
- Visual acuity.

If a patient presents directly to a trained community optometrist, oculometrics must be completed in that or the next available appointment.[59] If the results indicate an inconclusive or wet AMD diagnosis, they should be immediately translated into a referral, the contents of which meet national guidelines, and sent to a district centre for triaging.[60] Time from initial presentation to triage should be no longer than one week (*see: 5.3 – Enhancing treatment*). All DHBs should be clear as to the access to oculometrics in their main geographies (it may be that the DHB may have to provide in some areas) and how urgent referrals are flagged and managed.

Interventions that may further reduce the time delay between the symptoms onset and treatment include electronic referrals and triaging, standardisation of OCT outputs allowing comparisons across machines, and electronic transfers of images to enable more efficient triaging. The pathway for referral for AMD described here should form part of a wider set of guidance and pathways for all acute persistent visual loss ensuring that all causes of visual loss are addressed in a timely manner as appropriate.

Recommendation 5 - Review the evidence for funding of the AREDS2 vitamin regime in the New Zealand context to make preventive treatment easier for patients

Led by: RANZCO

Triaging is to be done by clinicians. Clerical staff processing the triaged referrals are then to be overseen by a clinician to mitigate the risk of unnecessary lag, particularly of urgent referrals. Due to the rapid visual acuity loss associated with wet AMD, all potential wet AMD referrals should be triaged as urgent, and given a same-day or the next available appointment with an ophthalmologist (time from receipt of referral to initial injection should be no longer than one week). The appointment should be funded and timed in a way that allows for an FSA, treatment plan, and first injection if required in the same visit, optimising the patient experience[61].

If oculometrics result in a dry AMD diagnosis, patients will remain in the care of the optometrist, who may recommend the AREDS2 vitamin regime to appropriate patients to slow progression from mid-late dry to wet AMD. Their progression will be periodically monitored every 6-24 months, with the GP kept informed of

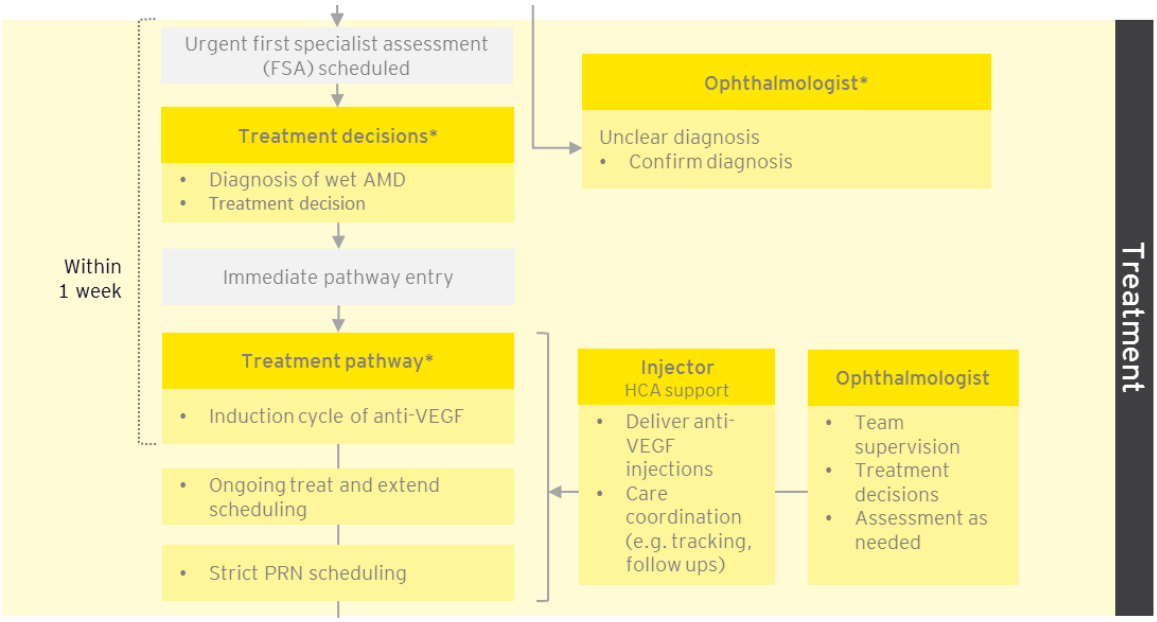
[59] Optometrists may need to go through a training process to ensure that they have the right skills and equipment to conduct oculometrics, support dry AMD monitoring and post-treatment surveillance
[60] If symptoms are found to be unrelated to AMD (e.g., DMO / RVO), they are out of scope of this model of care
[61] It was noted at the General Workshop that some patients need some time to decide whether to go ahead and receive injections, so same day injections may not suit all people

progress.[62] If at any point visual acuity becomes worse than 6/12, the patient should be referred to low vision rehabilitation to support daily living and reduce the risk of co-morbidities (*see: 5.4 – Enhancing rehabilitation*). While evidence for AREDS2 supplements is relatively sparse, based on the main trial it would seem that the AREDS2 regime might be cost effective if centrally purchased by PHARMAC – an application to PHARMAC would be needed, potentially led by RANZCO.

Recommendation 6 - If treatment is indicated, ensure that the first intravitreal injection for wet AMD takes place within one week of a referral for suspected wet AMD

Led by: DHBs

5.3 Enhancing treatment



Following urgent referral and triage, an ophthalmologist should conduct an FSA, design a treatment plan, and ensure the administration of the first injection within the same or closely consecutive appointments. The timeframe from receipt of referral to first injection should be no longer than one week.

Anti-VEGF treatment for wet AMD patients should follow either a **treat and extend** or **strict PRN approach**, depending on DHB eye department capacity. The exact injection schedule will vary depending on the treatment response, but would normally start with the first three injections monthly. A typical pattern[63] might be:

Recommendation 7 - Treatment should follow a treat and extend or strict PRN approach, with timely availability of injections allowing the most cost-effective approach and maximal patient benefit

Led by: DHBs

[62] Monitoring frequency will depend on the patient's stage of dry AMD, with mid-late patients to be monitored more frequently than those with early dry AMD

[63] As used for modelling purposes. Actual schedules will vary, with longer or shorter intervals depending on patient response to anti-VEGF treatment.

- Every month for three months
- Every six weeks for six months
- Every eight weeks for 12 months
- Every quarter for 24 months
- Bi-annually for the remainder of treatment.

Districts will be able to estimate the volumes needed to be delivered for their populations to maximise the benefit to patients, and compare with peers.

While the ophthalmologist will have overall responsibility for the care plan, the eye assessments and decisions to inject will be made by suitably trained nurses or optometrists. At regular intervals, for example after every three injections, an ophthalmologist should assess the patient response and adjust the treatment schedule as necessary. Strict PRN involves active monitoring of the macula, with injections only administered as needed, and an assessment conducted prior to every injection. This reduces the risk of overtreatment, however can be more resource-intensive (ophthalmological / oculometrics workforce, clinic capacity and technology) than the treat and extend approach.

Anti-VEGF medications should be administered as follows:

- Bevacizumab (Avastin) – this should remain the first-line agent, with the process for off-label use standardised to enable ophthalmologists to better use their available consultation time. Medsafe should consider clarifying the Medicines Act with respect to the rules around the reformulation of medicines in hospital pharmacies, including the sterility and training requirements, and the potential to undertake such work for other DHBs. PHARMAC should consider assisting DHBs to have a single contract with the supplier for re-formulated bevacizumab (for those who need it), potentially cutting supply costs.
- Aflibercept (Eylea) – this should be considered for funding by PHARMAC

Recommendation 8 - Given the health benefits able to be gained, and the strong cost-effectiveness of the treatment, consider the adequacy of volumes of treatment delivered based on these protocols

Led by: DHBs

Recommendation 9 - Develop a simpler, nationally consistent approach for ophthalmologists to follow with patients when using bevacizumab and any future off-label treatments

Led by: RANZCO

Recommendation 10 - Clarify the Medicines Act requirements around the reformulation of medicines in hospital pharmacies, including the potential to supply other hospitals

Led by: Medsafe

Recommendation 11 - Explore the potential for DHBs to have a single contract for re-formulated bevacizumab

Led by: PHARMAC, DHBs

Recommendation 12 - Complete the process currently underway to investigate aflibercept as the second line agent for wet AMD treatment

Led by: PHARMAC, DHBs

as the second-line agent after non-response to at least three injections of bevacizumab. A different mechanism of action to bevacizumab gives it the potential to be a more effective second-line agent than ranibizumab (currently the second-line agent). Along with a higher response rate, EY modelling suggests that there would be a 3% drop in the total number of wet AMD injections, and an 8% drop in the total medication cost for wet AMD

- Ranibizumab (Lucentis) – this should be funded as the second or third-line agent – after non-response to at least three monthly injections of bevacizumab, and either as a choice for treatment second-line, or after non-response to aflibercept, third-line

Recommendation 13 - Explore further utility and safety of ziv-aflibercept for ocular use

Led by: RANZCO

- Ziv-aflibercept – as noted above, this is a different formulation of aflibercept not prepared for use in the eye, with the same active ingredient.[64] If able to be safely reformulated and used, EY modelling suggests ziv-aflibercept as a second line agent would be $35 million cheaper than the current ranibizumab over 10 years, and $25 million cheaper than aflibercept. An application to PHARMAC would be needed, potentially led by RANZCO.

Under an ophthalmologist's supervision[65], appropriately credentialed injectors are to administer injections, with the support of an assistant (e.g., health care assistant) as needed. Depending on the available workforce and training available, the injector role could be filled, *inter alia*, from the following professional groups, appropriately credentialed, initially in a secondary care setting[66]:

Recommendation 14 - Use nurse or other trained injectors, with assistants to support efficiency where demand is sufficient, under the supervision of ophthalmologists

Led by: DHBs

- Nurse
- Optometrist[67]
- Medical Officer Special Scale (MOSS), or general practitioner
- Registrar (training or non-training) or Resident Medical Officer (RMO).

If at any point during treatment visual acuity becomes worse than 6/12, the patient should enter low vision rehabilitation to support daily living and reduce the risk of co-morbidities (*see: 5.4 – Enhancing rehabilitation*). Nationally consistent treatment protocols would support services in maintaining quality, and should include criteria for assessing non-response to the current anti-VEGF. Likewise 'starting' and

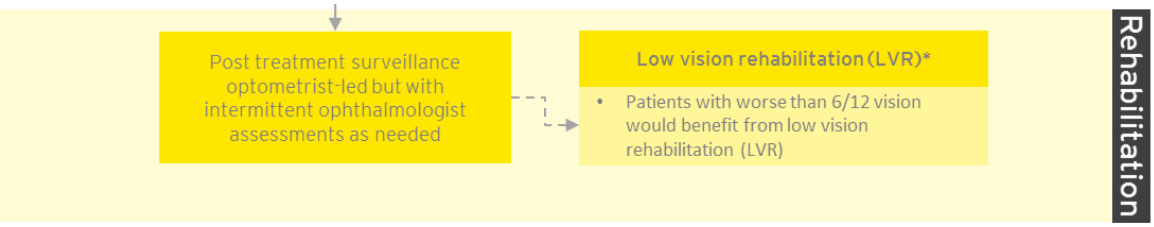
[64] The name 'ziv-aflibercept' is a US term; we have adopted it for this document to be clear where we are referring to formulations of aflibercept not presented for eye treatment
[65] Due to the off-label use of bevacizumab the ophthalmologist must retain overall responsibility for the treatment plan
[66] Intravitreal injections can have rare but dangerous complications. If setting outside secondary care were being considered careful consideration to clinical backup would be needed.
[67] While not currently being used in this role the NZAO believes that with appropriate training optometrists who wished to be involved in this aspect of care could undertake intravitreal injections safely.

'stopping' criteria should be developed, defining when patients are no longer getting a net benefit from treatment and instead enter post treatment surveillance (responded) and / or low vision rehabilitation (did or did not respond) (*see: 5.4 – Enhancing rehabilitation*).

Recommendation 15 - Develop a national AMD treatment protocol, including consistent criteria for starting / stopping / changing anti-VEGF treatment

Led by: RANZCO

5.4 Enhancing rehabilitation



As with prevention and detection, both post-treatment surveillance and low vision rehabilitation (LVR) services should ideally take place in a community setting (though clinicians could be employed by DHBs to offer services in a secondary setting). An exception to this may be intermittent ophthalmologist assessments in a secondary setting for patients who have stopped treatment due to a successful response, to determine whether or not treatment re-entry is required.[68] Regardless of the position in the model of care pathway, patients with worse than 6/12 vision should be eligible for LVR services to support daily living activity and reduce the risk of co-morbidities. Additionally, those with visual acuity worse than 6/24 qualify for Ministry-funded Blind Foundation services.

Low vision rehabilitation for people with 6/12 to 6/24 vision should comprise at minimum a 1-2 hour consultation with a low vision rehabilitation professional (e.g., an optometrist or orthoptist [69]) covering the following elements: [70,71]

Recommendation 16 - Offer a 1-2 hour low vision rehabilitation consultation with appropriate professionals to patients with 6/12 – 6/24 visual acuity

Led by: DHBs

- A low vision clinical evaluation
- Rehabilitation training – techniques for reading, writing, shopping, cooking, lighting and glare control
- Information on obtaining a home assessment if needed
- Information on accessing mobility services

[68] As the care pathway matures in each region it is anticipated that this role will be increasingly managed by optometrists
[69] Orthoptists were not discussed throughout original stakeholder engagement, though if appropriately trained could be a useful workforce to provide LVR support, along with low vision therapists and appropriately trained occupational therapists
[70] Personal communication, stakeholder interviews, Auckland
[71] Funding options must be explored to support the delivery of these consults, and remove the cost barrier for those eligible but not living in a DHB providing such a service

- Assessment of assistive devices (magnifiers, lights, audio devices, etc.)[72]
- Information on resources and support groups.

Often only one session will be needed, though as vision deteriorates some people may benefit from further consultations. A low vision therapist or a trained occupational therapist (OT) can be involved, providing guidance on how to adjust home and work settings to assist that individual to live with low vision. This may include home visits [73].

Services for those with vision 6/24 or worse have not been directly considered by this report, and are expected to continue as per current arrangements.

These and any other low vision rehabilitation services are to align with and follow the structure of the developing Low Vision Rehabilitation Services Strategy (*see: 4.4 – Low vision rehabilitation*).

5.5 Supporting infrastructure

5.5.1 Workforce

The following workforce roles represent varying degrees of change to the current state workforce model, and are intended to support:

- Patient care closer to home
- Better utilisation of existing and potential skillsets, in supporting clinicians to work efficiently and at the top their of scopes
- Existing and projected future workforce capacity
- Funding constraints and opportunities.

These can be compared to the current state workforce roles (*compare: 4.4.1 - Workforce*).

5.5.1.1 Ophthalmologists

The most significant change to the ophthalmologists' role is that they will no longer be required to administer routine injections.[74] A proportion of consultations will remain the same, with capacity released for ophthalmologists to spend more time both conducting FSAs and designing / updating treatment plans, enabling more of a strict PRN approach to be taken for those departments currently with capacity constraints. Ophthalmologists will need to close enough at hand to assist if any complications occur, but will not be expected to be present or to administer

[72] Currently equipment is largely funded by the patient. The Ministry of Health's Disability Support Services does fund some adaptive equipment, though there is no clear application pathway for adult patient vision aids
[73] DHBs could incorporate these consultations and visits into their LVR offering
[74] This is the ideal state, though it is understood that some DHBs will have ophthalmologists administering injections for some time due to resource and other constraints on the training and development of appropriately credentialed nurse or other injectors.

injections routinely (compare: 4.4.1.1 - Ophthalmologists). Even with these changes there is likely to be pressure on ophthalmologist numbers as they reduce proportionate to the number of elderly New Zealanders. The Ministry of Health, HWNZ and RANZCO should undertake workforce planning to consider whether the number of ophthalmology trainee places needs to be expanded, taking into account the increasing role of multi-disciplinary collaborative teams working in eye health departments and projections for future volume of treatment demand.

Recommendation 17 - Design and implement a process for educating and training optometrists to conduct oculometrics, monitor dry AMD, and monitor patients post-treatment

Led by: NZAO

5.5.1.2 Injectors

Under an ophthalmologist's supervision, appropriately credentialed nurses or other injectors are to administer injections. An additional person to assist the injector, for example a health care assistant (HCA) may increase the number of injections possible in a session. Depending on the available workforce, the injector role is most obviously filled by an appropriately credentialed nurse. Other options include an appropriately credentialed:

- Optometrist
- MOSS or GP
- Registrar/RMO (training or non-training).

Investment should be made into developing and facilitating a nationally consistent training scheme for clinicians aspiring to fill the injector role, which could leverage existing injector training schemes. EY modelling suggests that if an injecting workforce of appropriately credentialed nurses was used to administer injections in 2016 rather than the current workforce mix, then $0.4m of resource would have been freed up for other cares *(compare: 4.4.1.3 – Injectors; see Appendix G for details)*. Future work may explore the feasibility of and protocols required for community-based intravitreal injections.

5.5.1.3 Optometrists

The role of optometrists will increase significantly for those appropriately trained and willing to participate more actively in the AMD model of care. This might take the form of an accreditation process, or by other means, ensuring that they have the right training and equipment to conduct oculometrics, support dry AMD monitoring, and carry out post-treatment surveillance. In a community setting, such providers will conduct and refer oculometrics through a nationally consistent electronic system for referrals, monitor the progression of dry AMD, and conduct post-treatment surveillance. All optometrists have training in LVR, and there is an accreditation process established for LVR which could be further promoted.

In a secondary setting, optometrists may be trained as injectors as noted in the section above (*compare: 4.4.1.2 - Optometrists*).

5.5.1.4 Other workforce

- General practitioners – the main change from the current state is increasing the use of Amsler grids during consultations with the 65+ and other at-risk patients to increase public awareness and aid early detection. Improvements in clarity for referral pathways, particularly access to community oculometrics should speed the time from referral to triage
- Clerical staff – the clerical staff role will not change from the current state but referral pathways may require re-design to reduce the risk of inappropriately processing referrals
- Health care assistants – the health care assistant role will be introduced as appropriate at a DHB level to support injectors, delivering cost and efficiency gains, particularly in areas with higher demand and capacity constraints. In modelling, health care assistants appear cost-effective on average in treating more patients at a lower cost – for example increasing the volume of patients seen in a single nurse injector session from 8 unassisted to 12 assisted. However, the margin between using appropriately credentialed nurse injectors alone or with a health care assistant for the 2016 cohort is only $0.1m over a 10-year period (*compare: 4.4.1.4 – Other workforce*).

5.5.2 Funding

Key proposed changes in funding have been noted above, and include:

- PHARMAC to consider funding aflibercept as the second-line agent instead of ranibizumab, due to the different mechanism of action resulting in a higher likelihood of response following non-response to bevacizumab (the first-line agent), resulting in an estimated saving of $8.5m over 10 years
- PHARMAC/DHBs to consider arranging a single contract to get reformulated bevacizumab supplied to those DHBs that need it
- PHARMAC to investigate bulk purchasing of AREDS2 to reduce costs for patients wanting to delay progression from dry to wet AMD. Over 10 years modelling suggests a gain of 400 QALYs at a cost of $4.0m at current retail prices, for a cost per QALY around $9,900. Purchasing in bulk will reduce the cost of AREDS2; if it was by half it would give a cost per QALY of $4,950

DHBs could consider subsidising community-based oculometrics where such services do not exist, or to reduce cost barriers. This could include oculometrics, monitoring, and post treatment monitoring (*compare: 4.5.2 - Funding*).

The Ministry should consider funding options for making low vision rehabilitation more widely available.

There will be significant implementation and change management costs for DHBs to make the changes discussed. The Ministry may wish to provide funding to support and speed up this process. Other funding aspects around implementation are noted in *5.5.5 Making it happen*.

5.5.3 Technology

New technology to support oculometrics will not be introduced, but clear technology specifications will be identified within the training for optometrists to ensure that the technology used reaches an appropriate standard

To enable better communication and information flow through the model of care, structural investment is to be made by the Ministry and DHBs as follows:

- Introduction of a nationally consistent electronic system for referring patients through from early detection to treatment
- Implementation of district triaging centres in areas where these do not already exist.

5.5.4 Performance measurement

To support quality improvement - greater innovation, improved learning and improved performance - across DHB eye health departments, care pathways should be developed for AMD with measurable KPIs at key points. These could include *inter alia:*

Recommendation 18 - To support greater quality improvement for all responsible for delivering the AMD model of care, nationally consistent, measurable performance indicators should be developed and reported on

Led by: Ministry

- Treatment frequency
- Consultation frequency
- Access to LVR services for eligible patient population by domicile

Data should be collected consistently across all DHBs to support measurement of performance against these KPIs, and made available to the Ministry for a system-level view of performance. In addition to the data collected supporting KPIs, a patient-level dataset should be collected and aggregated nationally around:

- Volumes of early dry, mid-late dry and wet AMD patients
- Percentage progression from dry to wet AMD
- Change in VA for patients over time
- Individual medication volumes (e.g., first-, second' and third-line agents; AREDS2) by patient
- Projections in the annual number of injections required for patient cohorts over time.

Recommendation 19 - Improve data collection and analysis according to nationally consistent specifications to allow monitoring of performance and measurement of patient gains made, and to provide a base to continue to improve the management of AMD in New Zealand

Led by: Ministry

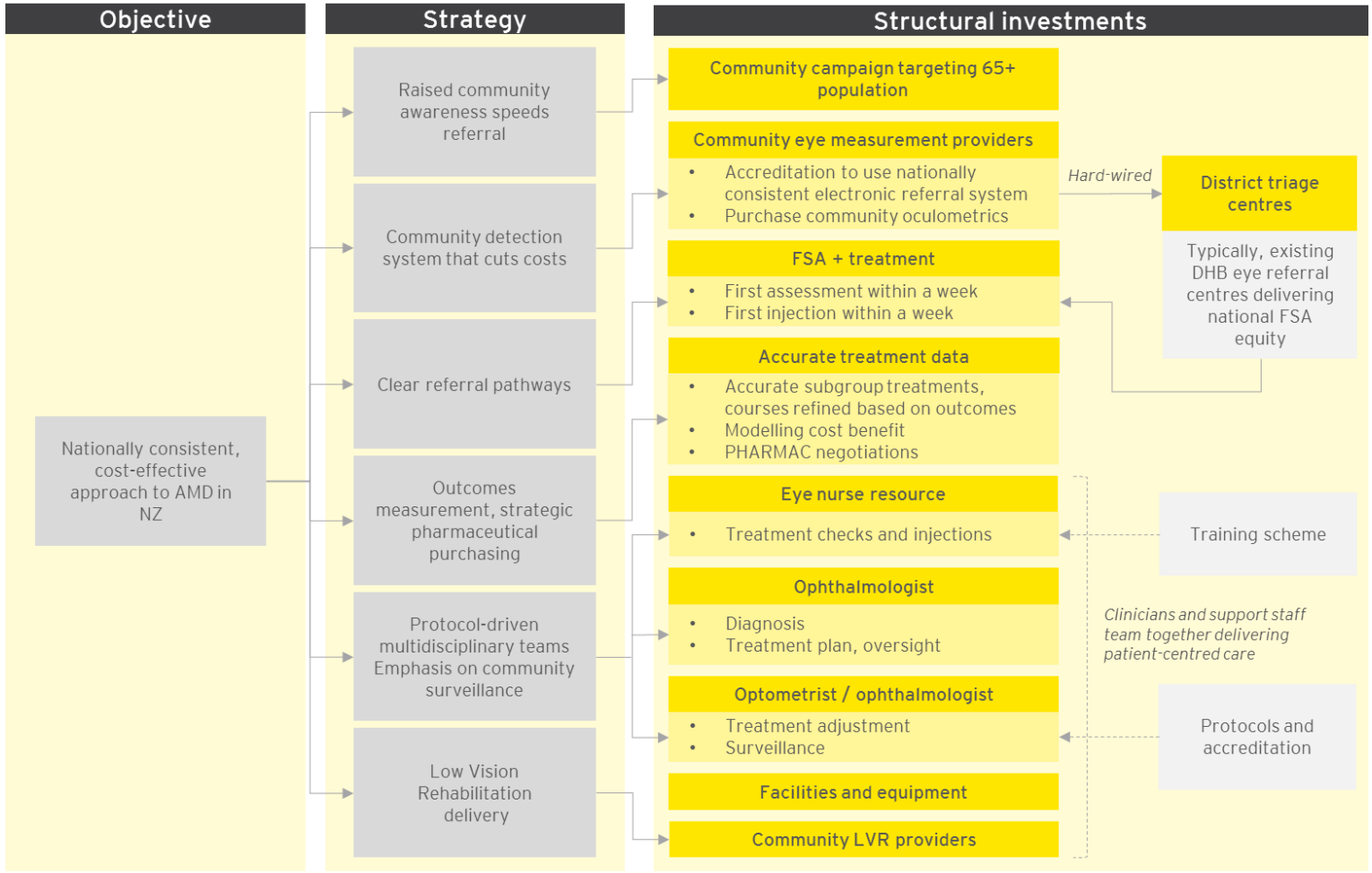
Improved data collection and comparisons with patient outcomes will inform the likely optimal level of interventions. The ideal level of intervention is not necessarily at the current highest DHB level. The aim would be to have the optimal treatment level informed

by linking local structured clinical data to longitudinal outcomes for each DHB. This will require the capture of electronic clinical records as part of workflow in a structured and consistent way. Appropriate alerts can be generated, and complications can be monitored – the consequences of long term use of anti-VEGFs are not well defined.

5.5.5 Making this happen

Drawing the above threads together, a change management programme will be needed to implement these changes to the model of care for AMD, and is further described below. Figure 15 summarises the change areas by strategy.

Figure 15: Areas of change focus by strategy area



5.5.5.1 Implementation steps

As the commissioner of this report, and as the lead agency for the health and disability system, the Ministry of Health has overall responsibility for the management and development of the system. While each recommendation has been given a suggested lead agency, clear governance will be required to provide guidance and oversee progress. We suggest that the Ministry establish a Clinical Working Group, perhaps with an initial two-year mandate, to oversee the changes. It could have representation from the main professions, key agencies and the Ministry itself.[75] A work programme should be developed and appropriate priority given to the changes suggested through the recommendations. While the focus might be on AMD in the first instance, it would be worthwhile considering a group having a wider remit across all eye-related services, with that group then having sub-groups e.g., AMD, glaucoma. Given the cooperation and enthusiasm for involvement that we met during this project we would not expect any difficulty in getting involvement from relevant personnel – indeed there may be difficulty in limiting the size of the group.

Recommendation 20 – A Clinical Working Group will be established with wide sector representation to oversee and guide eye services development

Led by: Ministry

Of particular importance for the Ministry are recommendations 1 and 17. With the aim to have a nationally consistent approach to AMD, a new specification for, and a new approach to data collection is needed to enable accurate and relevant measurement. This new data collection should be straightforward to implement, as all eye services are collecting the relevant data at the moment. It will assess process measures, costs, coverage, and patient outcomes, and allow DHBs to benchmark their services. Next steps would be a matter of determining data fields, data formats and a delivery mechanism to create a clinically meaningful and actionable data resource.[76]

5.5.5.2 DHB Implementation

Each DHB will need to consider the recommendations in this report against their current service models. For some DHBs there may be little change, for others a significant change process may be required. It is likely that DHBs will wish to consider their whole ophthalmology service when making changes – changes to AMD should not decrease access to other urgent eye care – indeed it would be hoped that attention to referral pathways and prioritisation might benefit other eye disease pathways. We anticipate that the changes suggested will be cost-neutral or cost-saving after implementation for the country as a whole, but results within individual DHBs will vary, and there will be implementation costs including staff time required to support the change.

[75] The Radiation Oncology Working Group fulfils a similar role for the Ministry at present, and might provide a model for how such a group would function

[76] The recent development of a radiation oncology minimum data set might provide a model of how to collate data on a specific clinical area.

Given projected increases in demand DHBs will not want to delay making the changes suggested. We particularly note the counter-intuitive 'spend money to save money' aspect of wet AMD care, where earlier initiation of treatment, and timely initial treatment appointments, is likely to lead to less injections required overall – a net cost saving, while delivering better patient care. For most DHBs any 'cost saving' will likely be in the form of the ability to deliver more eye health services within the same budget.

Figure 16: Typical areas to consider for implementation

For DHBs we suggest nine areas for consideration, as shown in Figure 16. These will need to be customised to local circumstances.

1 - Aligned governance and leadership

- Each DHB will be the primary decision-maker and 'owner' of the recommendations, supporting management and clinicians to ensure that their time is focused on delivering on the actions. The DHB will also support further development of organisational partnerships (*see: Effective Partnerships*)
- A unified clinical governance framework will be created, including relevant participants, with district-wide and locality mechanisms to support whole of system professional collegiality and multi-disciplinary teamwork. Membership will include optometrists, nurses, general practitioners, ophthalmologists, and other clinicians as necessary.

2 - Dedicated programme and change management

- The relevant DHB workforce must be well informed on the proposed changes, how they will be achieved in practice, and what is required from them individually. This will require building buy-in to the overall vision and effectively managing change so that the stakeholders become active supporters and change leaders
- A programme management approach is suggested to coordinate and report on progress of the recommendations and achievement of milestones. Other aspects of the eye services may need to be included.

3 - Transparent and systematic prioritisation

- An explicit prioritisation approach is required, to be aligned with what is desirable and affordable, including:
  - Which AMD recommendations required implementation locally
  - How the proposed changes fit with other parts of the eye services
  - A resource allocation framework, with indicative service development / quality improvement plans to support medium-term planning (*see: Funding and Contracting Models*)
  - Data and metrics developed to monitor and test changes (*see: Robust Data & Metrics*).
  - Locality needs assessment / service mapping to identify resource allocation, training and clinical space across the district, informed by powerful analytics (*see: Robust Data & Metrics*).

4 - Effective partnerships

- To support the improvements sought, DHBs should work with:
  - Education providers/other DHBs for training of nurses/other injectors
  - Health of older people services
  - Optometrists/low vision assistance providers.

5 - Robust data and metrics

- Consistent data collected to allow monitoring of performance and measurement of gains made, providing a base to:
  - Benchmark against best practice on relevant metrics to determine appropriate local improvement targets (i.e., what is potentially achievable based on the performance of leading DHBs)
  - Align with regional and national performance, and assess local population needs.

6 - Ongoing communications and engagement

- Early and effective communications and engagement with key stakeholders will be critical during the implementation of the recommendations. The communications and engagement process will celebrate success and accept well-intentioned failure, as well as:
  - Engaging clinical and managerial leaders from the DHBs, general practice, NGOs, and the wider community in implementation
  - Obtain feedback that will inform the ongoing approach to implementation (*see: Feedback & Continuous Improvement*). In general, it will provide stakeholders with timely, relevant and targeted communication throughout implementation, and opportunities to contribute
  - Maintaining engagement with front-line staff to ensure ongoing buy-in from those involved in implementation.

7 - New funding and contracting models

- New approaches to funding and contracting may need to be explored in developing community services to improve patient care and take pressure off hospital services. This may be:
  - As part of design and implementation of new referral and care pathways
  - More broadly to address the best use of community resources to support secondary care services – for example by providing funding to community optometry providers for AMD assessments
  - It may also extend to using contestability to drive innovation and efficiency improvements in district health systems
  - These approaches will be value-based, aimed at achieving Triple Aim objectives, and developed through co-design with partner organisations, providers and communities.

8 - Detailed planning

- Identify dependencies
- Have realistic timeframes
- Mitigation of high risks
- Assessment of costs and savings, performance against budget.

9 - Feedback

- Routinely engage with key stakeholders in relation to all initiatives to understand and report on progress, successes and challenges. This will:
  - Maintain engagement, enable challenges to be overcome, and clarify learnings applicable to future initiatives (*see: Ongoing Communications &* Engagement)
  - Regularly involve stakeholders from across the system, in particular front-line staff, to generate ideas and learnings to support leadership at all levels of the system (*see: Aligned Governance & Leadership*).

5.5.5.3 Other Implementation

Where parties other than the Ministry or DHBs are suggested as leading a recommendation, for example RANZCO for Recommendation 11 or NZAO for Recommendation 15, it is envisaged that this will be coordinated through the Clinical Working Group. Indeed the Clinical Working Group may organise project teams or otherwise determine new leads for these recommendations.

6. Concluding remarks

6.1 Summary

With a prevalence of ~5%, AMD directly and indirectly impacts a large number of New Zealanders. As the New Zealand public system was operating in 2016, we estimate the direct (secondary care) cost of intravitreal injections for wet AMD treatment was $6.1m. Patient sight improvement/maintenance was estimated to generate 2,100 QALYs, at a cost per QALY of $2,900. This does not include the wider social and economic impact of vision loss. While this appears very cost-effective compared to other interventions across the health system, many opportunities for improvement were found.

Assessment of the current state model of care across prevention and detection, treatment and rehabilitation has revealed considerable variation between districts (Figure 7, also *see: Appendix C*). Following the current state assessment and case for change, a future state model of care is proposed - based on the premise that DHBs should use the most cost-effective resourcing mix, care setting and operating principles available to deliver optimal care for patients who either have or are at risk of having AMD. We estimate that the new model could operate on similar funding or less than that used now, and provide better patient care. If the system had operated like this in 2016 we estimate an added 100-200 QALYs would have been gained, at an overall cost per QALY of $2000 – $2500.

The proposed model does not deviate significantly from what is already being done in some districts, though no district is doing all components as yet. The model is intended to deliver greater consistency and to resolve key issues as identified in the current state (*see: Section 1.1 - Recommendations*). The model is intended to operate consistently at the national system level, with flexibility at the district level in relation to workforce mix, funding arrangements, and treatment approach.

Specifically, the proposed model is intended to:

- Enable faster access to diagnosis, treatment and rehabilitation for those people most likely to benefit
- Support preventive activities
- Enable care to be delivered closer to home
- Make best use of health professionals' skills and time
- Support improved data collection and outcomes measurement
- Make best use of the technology and other infrastructure within the New Zealand health system.

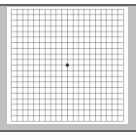
An initial structural investment will be required into systems, training schemes and an accreditation framework to enable delivery of the proposed model of care. As the population ages and creates more demand pressure, this infrastructure will enable the ongoing delivery of optimal AMD care.

6.2 Further investigation

The following are recommendations for further investigation. They relate to areas out of the scope of this report, but will provide valuable direction for ophthalmology services:

- Leverage this model of care for other eye conditions such as diabetic macular oedema, retinal vein occlusion, glaucoma, and diabetic retinal screening
- With the emerging pressures on ophthalmology departments, the Ministry should assist DHBs in assessing the relative value of other ophthalmology interventions, including model of care, workforce and funding impacts
- The exact nature and size of the awareness raising aspects were not determined. It may be worthwhile looking at other eye diseases in addition to AMD in designing the intervention.

Appendix A Glossary

Term	Definition
aflibercept	Trade name Eylea, aflibercept is an anti-VEGF with a different mode of action to bevacizumab/ranibizumab, specifically formulated for intravitreal injection
AMD	Age-related macular degeneration. Can be 'dry', or 'wet' aka CNV (choroidal neovascularisation)
Amsler grid	Grid of lines assisting detection of damage to the macula or the optic nerve, can be self-administered 
anti-VEGF	Anti-vascular endothelial growth factor (often pronounced 'anti-v-geff') – term used for a class of drugs that reduce new blood vessel growth – e.g. bevacizumab
AREDs	Age-related Eye Disease Study – a key study identifying vitamin regimes that may delay wet AMD progression. AREDS2 is the recommended regime
bevacizumab	Bevacizumab is an anti-VEGF approved by Medsafe for the treatment of certain types of cancer. It is also commonly re-formulated and used 'off-label' as the first-line treatment for AMD
Blind Foundation	Royal New Zealand Foundation of the Blind; has a specific interest in people with VA of 6/24 or worse
choroid	The vascular layer of the eye, lying between the retina and the sclera
CNV	Choroidal neovascularisation is the creation of new blood vessels in the choroid layer of the eye – the 'wet' part of 'wet' AMD
DALY	Disability-adjusted life year – a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death
DHB	District Health Board
DMO	Diabetic macular oedema
FSA	First specialist assessment – the first contact of a patient with a specialist, e.g. ophthalmologist
GP	General practitioner
HCA	Health care assistant
intravitreal injection	An injection into the vitreous. It is performed to place medicines like anti-VEGFs inside the eye, near the retina
Low vision therapist	Allied health professional assisting patients with visual impairments to improve their functioning in daily life activities
LVR	Low vision rehabilitation – assistance to make the best use of a person's vision – including light, magnification and contrast enhancement, as well as the individual's requirements in daily activities to keep them independent at home, work and within their community

Term	Definition
macula	The central part of the retina, responsible for what we see straight in front of us, at the centre of our field of vision
Ministry	Ministry of Health (MOH)
MOSS	Medical Officer Special Scale
NHC	National Health Committee (functions now merged with the MOH)
NMDS	National Minimum Dataset – the national repository for inpatient data. Some DHBs record their intravitreal injection attendances here. Includes diagnosis information.
NNPAC	National Non-admitted Patient Collection - the national repository for outpatient data. FSAs and intravitreal injection attendances are expected to be recorded here. No diagnosis information is captured
OCT	Optical coherence tomography – key non-invasive imaging test using light waves to take cross-section pictures of the retina
ophthalmologist	Medically-trained specialist in surgical and medical treatment of eye disease
optometrist	Allied health professional trained to provide all aspects of primary eye health care
orthoptist	Allied health professional who specialises in disorders of eye movements and diagnostic procedures related to disorders of the eye and visual system
QALY	Quality adjusted life year - a measure of disease burden, including both the quality and the quantity of life lived
ranibizumab	Trade name Lucentis, ranibizumab is from the same parent antibody as bevacizumab, specifically formulated for intravitreal injection
retina	The light-sensing layer of the eye, bathed in the vitreous
RMO	Resident Medical Officer – registrars and house surgeons
RVO	Retinal vein occlusion
STR	Standardised treatment ratio – adjusts treatment volumes based on the age structure of the population allowing the actual volumes to be compared against that expected from the national rate.
VA	Visual acuity – standard measure of how well a person can see, using e.g. Snellen letter charts: 6/6 – 'standard' vision 6/12 – reduced vision, boundary for driver licensing 6/24 – 'clinically blind' – boundary for Blind Foundation enrolment
vitreous	The jelly-like substance inside the eye
wet AMD	See CNV
ziv-aflibercept	Trade name Zaltrap , ziv-aflibercept is the US term for a cancer treatment formulation of aflibercept (in a similar way as bevacizumab is to ranibizumab), which has the potential to be re-formulated for intravitreal injection

Appendix B Stakeholder engagement

Interviews

No	Name	Organisation
1	Derek Sherwood	Ophthalmologist, Nelson Marlborough DHB
2	Phillipa Pitcher Dianne Sharp	Macular Degeneration New Zealand
3	Emmanuel Jo	Ministry of Health – workforce
4	Lesley Fredrickson	Association of Optometrists
5	Naomi Meltzer	Optometrist, low vision specialist
6	Simon Duff	Ministry of Health – Manager of Elective and National services
7	Stephen Ng	Ophthalmologist Waikato, chair of the New Zealand Branch RANZCO
8	Sarah Welch	Ophthalmologist, Auckland DHB
9	David Squirrell	Ophthalmologist, Retinal specialist, Auckland/Milford
10	Bronwyn Ward	Charge Nurse, Greenlane Eye Clinic
11	James Borthwick	Ophthalmologist, Christchurch, past chair of the New Zealand Branch RANZCO
12	Claire Fitzgerald Catherine Rae	Blind Foundation
13	Tony Wang	PHARMAC

Workshop 11 April 2017

Organisation	Name
Royal Australian and New Zealand College of Ophthalmologists, NZ Branch	Stephen Ng, Helen Hunter
NZ Association of Optometrists Inc.	Lesley Frederikson, Callum Milburn, Rochelle van Eysden, Wilson Sue

Organisation	Name	
District Health Boards (DHBs)	Waikato: Southern: Canterbury: Counties Manukau: Whangarei:	Lyn Scott Nic Johnston Ralph La Salle, Marilyn Ollett Keming Wang, Terri England Krishnee Naidoo, Tracy Wong, Marc Mclean Fiona Bamforth, Brian Kent-Smith
PHARMAC	Tony Wang, Harpreet Singh	
Macular Degeneration New Zealand	Dianne Sharp	
Ministry of Health	Sue Morgan, Chris McEwan, Wikke Bargh-Koopmans, Marianne Linton	
Health Workforce New Zealand (HWNZ)	Emmanuel Jo, Sandra Cumming	
NZ Retinal Specialist	Andrew Thompson, Tauranga	

Others Consulted	
South Island Eye Group	Organised through Janice Donaldson, South Island Alliance, 28 Feb 2017
Ophthalmologists	Ophthalmology National Clinical Directors Workshop 4 April 2017

EY would like to thank all participants in the workshops and interviews for their time and willingness to participate. All findings and conclusions in this report are EY's own: no endorsement is intended or implied from inclusion above.

Appendix C DHB impact analysis

Introduction and purpose

This appendix of the report outlines the DHB impact analysis and methodologies used to estimate the AMD population which then informed some recommendations in the proposed model of care.

Although the majority of the report is focused towards a more nationally consistent model of care, it is important to understand the treatment aspect, as well as what the future may look like in a DHB-specific manner.

The purpose of this Appendix is to:

- Set out the methodology which shows the approach undertaken in estimating the AMD population
- Estimate the current treatment state of AMD in New Zealand at a DHB level and the treatment costs to the health system
    - As a result of these injection volumes and treatment costs, determine why there is a 'case for change' for the level of treatment administered across different DHBs
- Estimate demand impacts of population increase and ageing on the current and proposed levels of treatment.

Methodology

This section details the approach to assess impact and all assumptions made.

Intravitreal injection population

- The estimated publicly-funded treatment population was developed through 2016 inpatient data from NMDS using those with ICD10-AM diagnosis code 'H353 – Macular degeneration', and 2016 outpatient data from NNPAC using those with a purchase unit code 'S40007 – Intravitreal injection'. Note that this includes all injections, not just ones for AMD
- A DRG code 'C03Z – retinal procedures' and an op code '4274003' from NMDS were also used as a cross-reference to ensure that AMD cases had been identified correctly
    - Further information was sought from DHBs, as it became apparent that not all treatments were being captured in the NMDS and NNPAC datasets. Inpatient and outpatient volumes were adjusted by DHB-specific information received from questionnaires that were completed
    - Two methods were used to estimate the AMD proportion of NNPAC-recorded intravitreal injections from those who are receiving intravitreal injections for other reasons such as diabetic macular oedema (DMO) and retinal vein occlusion (RVO).
- DHBs were asked to identify their proportion of AMD patients

- An age-function was created by disease type for the DHBs recording intravitreal injections in the NMDS (using the principal diagnosis codes)

- From the DHB returns, an estimated proportion of outpatient injections attributable to AMD are then applied to those outpatients, and this is added to the confirmed inpatients to give an estimated treatment population by DHB.

Standardised treatment ratio (STR)

- To make more statistically robust comparisons across treatment rates by DHB, an approach similar to that of a standardised mortality ratio (SMR) to age-standardise treatment rates

- The expected number of cases are derived by multiplying the relevant population by an age-specific rate for expected counts by age then summing those over each DHB. The observed counts are then divided by the expected to give the STR. A rate of 1 equates to the New Zealand average.

Treatment costs

- The treatment cost was estimated for 2016 using national IDF prices - 2016 inpatient data from NMDS in the form of the WIES, and 2016 outpatient data from NNPAC for those with a purchase unit code 'S40007 – Intravitreal injection'

- Summing the inpatient and outpatient results gives an estimate for the total cost, which can be examined by age and DHB, adjusting for the proportion of outpatients estimated to have AMD

- These costs were then presented as proportions of total ophthalmology outpatient spend as well as projected purely by the increasing population and age-specific rates to 2036

- Note that these costs are likely to underestimate the true baseline cost over that time due to increasing year-on-year coverage, 2016 costs were 12% higher than 2015.

Current state

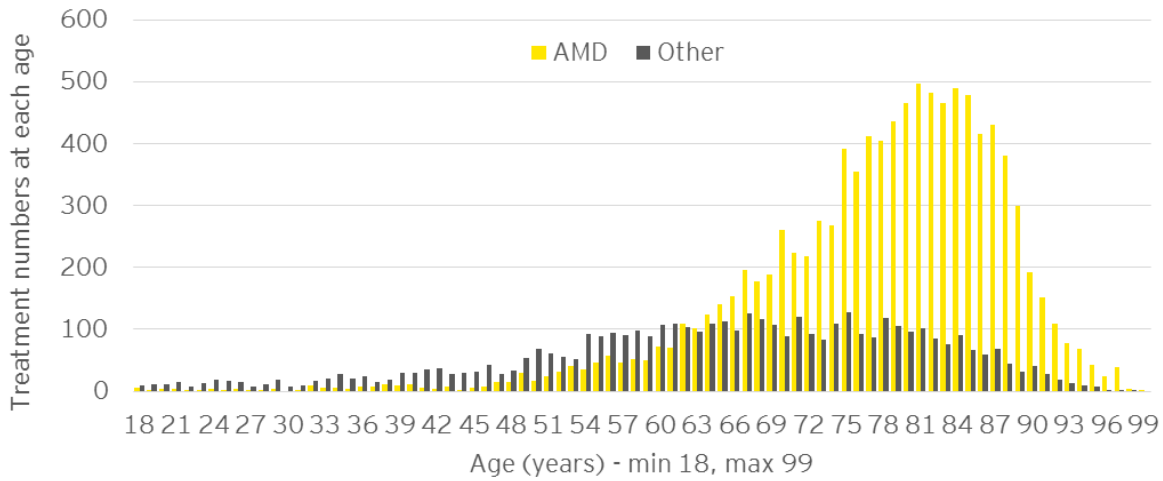
AMD population

Using inpatient data from three DHBs[77] who process intravitreal injections as inpatient procedures in the NMDS, one can measure their distribution of AMD versus non-AMD intravitreal injections. Previous reports have often stated a common minimum AMD age at 50 to inform their estimation[78], though in Figure C1 below, the age at which AMD occurrence is more reliably incident lies around 65. As most DHBs throughout the country do not process intravitreal injections as inpatient procedures, age 65 was used as marker, and injection proportion estimated for older ages. Only publicly-funded intravitreal injections are included.

[77] Bay of Plenty, MidCentral, and Waikato

[78] E.g., The Royal College of Ophthalmologists. *Age-related macular degeneration: guidelines for management*. 2013, The Royal College of Ophthalmologists: London.

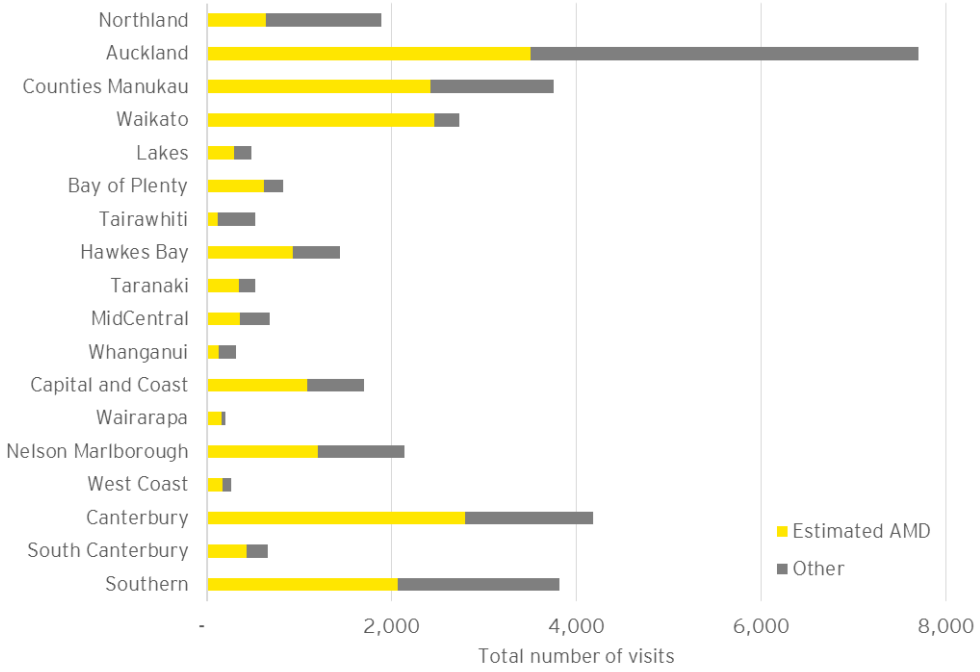
Figure C1: Age distribution of intravitreal injections recorded in the NMDS, AMD compared with other diagnoses, 2016



Treatment rates by DHB

The estimated total intravitreal injection numbers are shown by DHB of treatment in Figure C2, split to show our estimate of the number related to AMD compared with other conditions (e.g. DMO and RVO).[79]

Figure C2: Estimated intravitreal injections by DHB of treatment, 2016



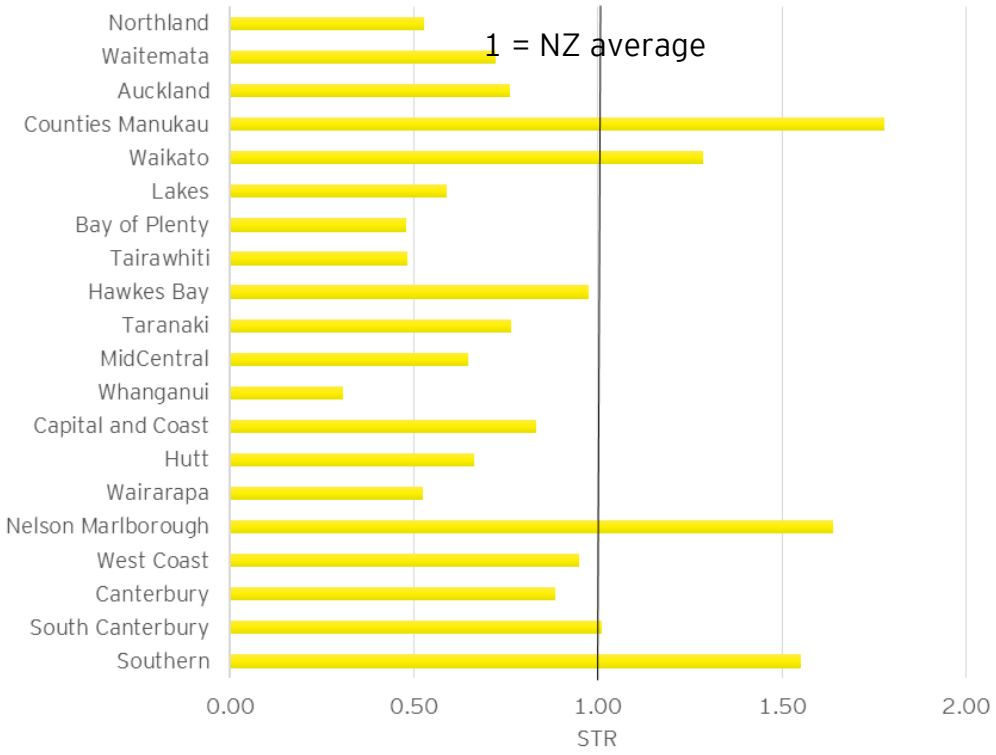
The graph in Figure C3 shows the resultant STR, where age-specific rates are calculated over the population and compared to expected cases by DHB of residence of the patient.[80] The line on the graph indicates the New Zealand average

[79] Note that Figure 6 in the main document is based on this graph, but showing only the estimated AMD-related intravitreal injections

[80] As the NNPAC and NMDS collect data by patient it was possible to count the number of people receiving at least one injection, by age sex and ethnicity and domicile. It is this 'treated' population that is used to derive case numbers, population rates and for population growth projections.

set to one, highlighting the differences seen between DHBs. Counties Manukau, Nelson Marlborough, and Southern have treatment rates that are well over the New Zealand average, while Lakes, Whanganui, Tairawhiti, Bay of Plenty and Wairarapa are near half the average. Some of the differences seen may be due to varying private treatment rates, and there may be some remaining confounding with other eye diseases being treated with intravitreal injections.

Figure C3: Estimated AMD standardised treatment ratios per person by DHB of domicile, 2016



Cost of injections and workforce by DHB

From the data collections, the estimated public expenditure on AMD injections (using national IDF prices) directly calculates at $4.8m in 2016.[81] However this price calculated off NMDS and NNPAC does not include the additional cases identified in DHB returns, which added would give a full price of injecting at $5.2m in 2016. EY modelling suggest that this is less that the current costs of delivery. Based on the analysis in *Appendix G* we believe the cost of delivery of intravitreal injections was closer to $6.1m in 2016.[82] It is this latter figure that has been used in the modelling work.

Estimated AMD treatment costs by DHB (by distributing total costs across treatment populations) are given in Figure C4 and a different view in cost per person 65 years and over given in Figure C5. Figures should be treated as indicative only.

[81] For 2015/16 the purchase unit cost for an intravitreal injection was $235.
[82] This may relate to the rising use of ranibizumab – further investigation of this by the National Pricing Project may be warranted

Figure C4: Estimated AMD injection cost by DHB of domicile

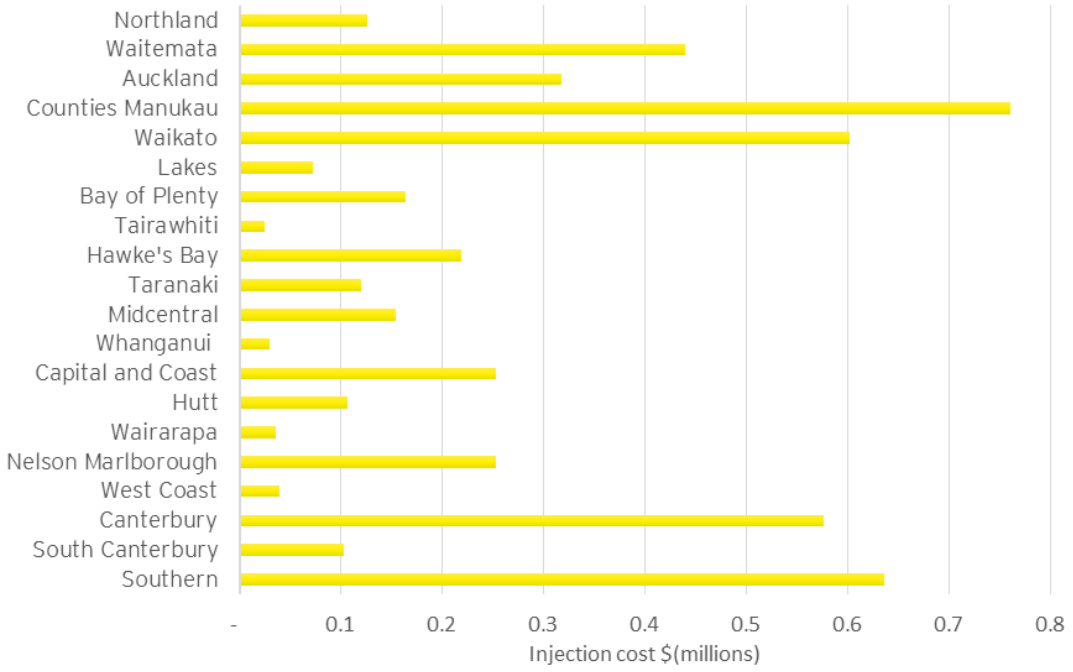
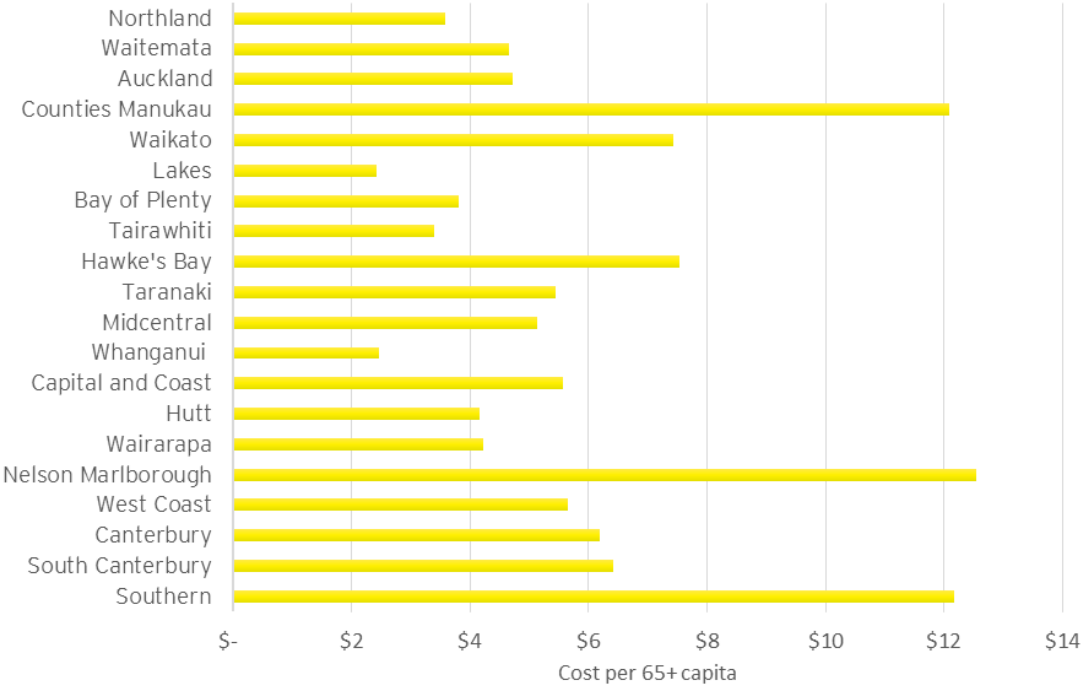


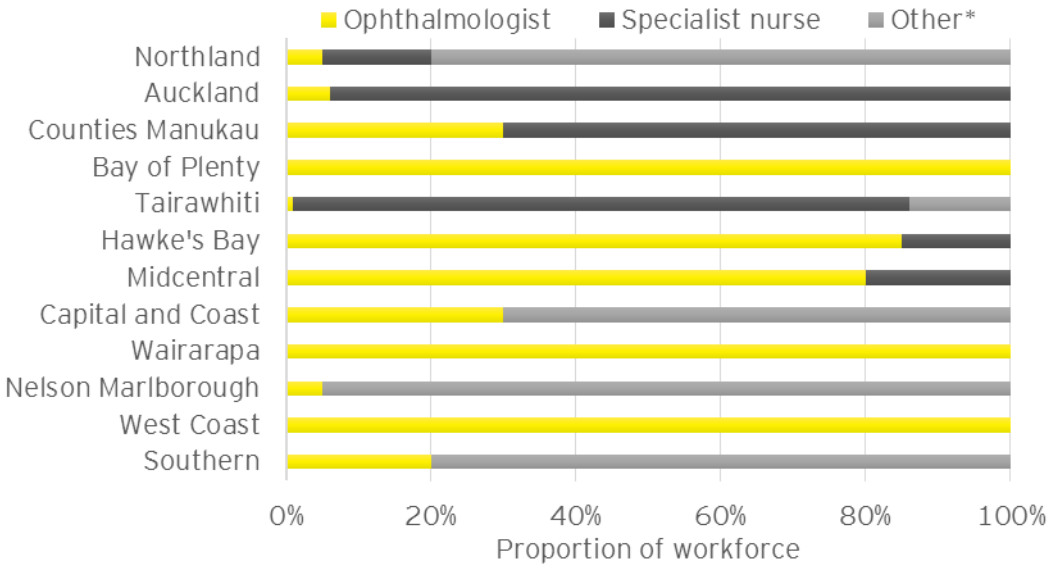
Figure C5: Estimated AMD injection cost by DHB of domicile as a cost per person aged 65+



To further the picture of cost of AMD treatment, current DHB workforces, where available, were assessed (Figure C6). On average, the predominant primary injectors are ophthalmologists (33% of injections), and others (38% of injections) including registrars – both training and non-training, and specialist nurses (29% of injections). For modelling purposes this is converted into a 4-hour-8-injection session, with costs based on PHARMAC average costs. This highlights the likely

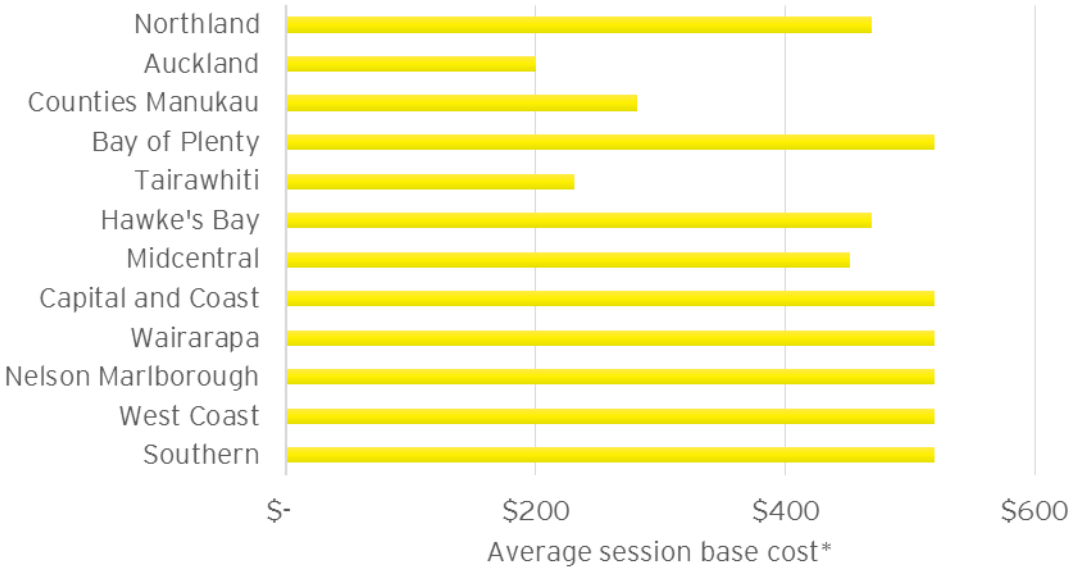
cost-efficiency of DHBs such as Auckland, Counties Manukau, and Tairawhiti due to different workforce utilization (Figure C7).

Figure C6: AMD injector workforce by DHB of treatment



Note: As this is a DHB of service view, Waitemata and Hutt are not included in the workforce graph. A further 6 DHBs did not return a sufficient workforce estimation.
*Other includes registrars, both training and non-training.

Figure C7: AMD injector modelled session cost by DHB of treatment



*Average session base cost only accounts for the clinical staff involved in administering the injections, estimated at a rate of $180 for specialist nurses up to $520 for ophthalmologists (see Appendix G for details). Indicative only.

Future state

The treatment and cost sections of the current state are shown in a potential future state by DHB. For full derivation of the analyses used see *Appendix G*.

Treatment coverage

In terms of treatment coverage, in Figure C3 a large difference in STR was shown especially in comparison to the high treatment rates of Counties Manukau, Nelson Marlborough, and Southern DHBs. As discussed in the stakeholder workshop, this might suggest a lack of treatment in the remaining DHBs, though there will be other effects in play such as the proportion of private provision in that DHB, and potentially increased delivery needed for late presentations in the historical cohort. This leads to the idea of a New Zealand aspirational treatment rate moving others towards these higher treatment DHBs. Feedback in response to this suggested unmet noted correlations between low socio/economic deciles and distance from treatment centres as drivers of non-presenting and untreated cases of eye disease and vision loss.

Table C1: Patient increase required to bridge treatment rate difference

DHB of domicile	2016 Treated AMD rate per 1000 65+	Difference to an aspirational rate of 13	Observed people in 2016	Difference of patients to aspirational rate	Estimated aspiration total 2016	% change in number of patients
Northland	4.2	8.8	134	284	419	211%
Waitemata	5.9	7.1	469	561	1,030	120%
Auckland	6.2	6.8	338	368	707	109%
Counties Manukau	13.7	-0.7	810	-40	770	-5%
Waikato	10.5	2.5	640	153	793	24%
Lakes	4.6	8.4	77	139	216	181%
Bay of Plenty	4.0	9.0	174	385	559	221%
Tairawhiti	3.8	9.2	27	64	91	240%
Hawkes Bay	8.0	5.0	233	145	378	62%
Taranaki	6.5	6.5	128	129	257	100%
MidCentral	5.5	7.5	164	227	391	138%
Whanganui	2.6	10.4	31	125	156	398%
Capital and Coast	6.9	6.1	270	240	510	89%
Hutt	5.5	7.5	114	157	271	138%
Wairarapa	4.3	8.7	38	78	116	204%
Nelson Marlborough	13.4	-0.4	400	-12	389	-3%
West Coast	7.4	5.6	42	32	74	76%
Canterbury	7.4	5.6	614	460	1,074	75%
South Canterbury	8.7	4.3	109	54	164	50%
Southern	13.0	0.0	677	2	680	0%
Total	7.9	5.1	5,491	3,552	9,043	65%

The potential aspirational public treatment rate was discussed in the stakeholder workshop, with 13 per 1,000 people over 65 suggested for use for modelling purposes. This is lower than the average of 13.5 per 1,000 over 65 in the three high treatment DHBs, with potential reasons relating to private treatment capacity and the potential for over-treatment to be occurring. The estimate of 13/1000 is

likely to fall as more patients are treated in a more timely fashion, and as treatment protocols mature. It might be considered the rate needed including private provision. The proposed data collection system will allow the optimal threshold to be informed by outcomes, and processes analysed based on specific sets of clinical criteria.

The aspirational rate is turned into age-specific rates and is used to calculate a rate difference from the current rate for each DHB based on its population structure. This gives an estimate of possible public treatment increases (likely maximum increases – lower ones are expected) in the coming years before population changes are considered. In Table C1 the changes in treatment are shown with the rate difference, its translation to patients, and percentage changes. Note that this assumes private usage differences are removed, and is indicative only. However it appears certain that demand for intravitreal injections will rise in each DHB.

Table C2: Patient increase to bridge aspirational gap by 2020

DHB of domicile	2016 patients	2016 rate/ 1000 65+	2018 est patients	2018 rate/ 1000 65+	2020 est patients	Cost of increase to 2020 ($m)
Northland	134	4.2	277	8.6	419	0.27
Waitemata	469	5.9	749	9.5	1,030	0.53
Auckland	338	6.2	522	9.6	707	0.35
Counties Manukau	810	13.7	790	13.3	770	-0.04
Waikato	640	10.5	717	11.7	793	0.14
Lakes	77	4.6	146	8.8	216	0.13
Bay of Plenty	174	4.0	366	8.5	559	0.36
Tairawhiti	27	3.8	59	8.4	91	0.06
Hawkes Bay	233	8.0	305	10.5	378	0.14
Taranaki	128	6.5	193	9.7	257	0.12
MidCentral	164	5.5	277	9.2	391	0.21
Whanganui	31	2.6	94	7.8	156	0.12
Capital and Coast	270	6.9	390	9.9	510	0.23
Hutt	114	5.5	192	9.2	271	0.15
Wairarapa	38	4.3	77	8.6	116	0.07
Nelson Marlborough	400	13.4	395	13.2	389	-0.01
West Coast	42	7.4	58	10.2	74	0.03
Canterbury	614	7.4	844	10.2	1,074	0.43
South Canterbury	109	8.7	137	10.8	164	0.05
Southern	677	13.0	678	13.0	680	0.00
Total	5,491	7.9	7,267	10.4	9,043	3.34

One approach to managing the expected increased treatment load is to consider efficiencies in the clinics providing injections. For example we modelled the likely impact of the use of additional healthcare assistants or nurses to increase the number patients able to be treated per session. For modelling purposes we assumed an increase of 8 injections to 12 across a 4-hour session (i.e. from 30 minutes per injection to 20 minutes per injection). This would increase the number

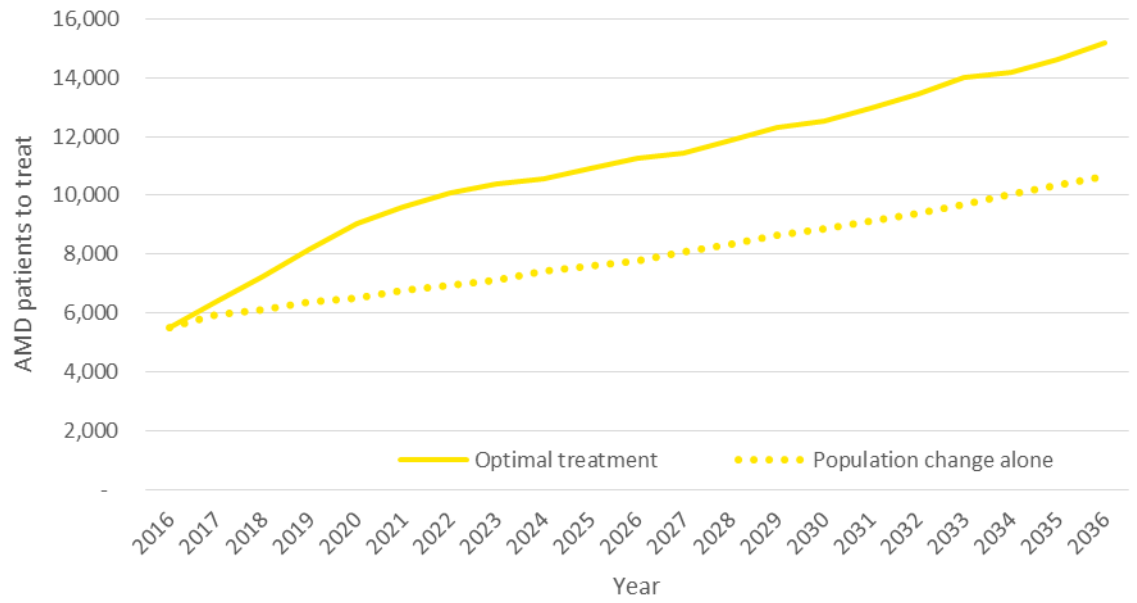
treated while remaining within the same physical and temporal constraints for a slightly greater cost.

Overall a 65% increase in patients is necessary to make up the difference to the aspirational treatment rate. Many DHBs would need increases which are between 2 and 4-fold. If the treatment rate increases at a similar rate as the 12% increase from 2015 to 2016 for another four years, the treatment gap will be bridged, and from there on out the increases will largely be a result of population change alone. Table C2 outlines the changes that could follow in the next four years to reach the aspirational rate, coming in at a total cost increase of an estimated $0.8m per year, or $3.3m over the four years. Note that these are indicative numbers only - actual cost increases will vary by DHB.

If this difference is not addressed in the coming years, it will compound due to the increasing population, so the difference in patient numbers to the aspirational rate in 2036 is estimated at 6,400, compared to the much smaller difference of 3,550 in 2016. These patients will be placed on top of those who are incident as a result of population changes and over the next 20 years a further 4,510 new patients are likely to need treatment for AMD.

Figure C8 shows what the increase may look like over the next 20 years accounting for the increase up to 2020 and comparing it to the population increase alone.

Figure C8: Projected population increase accounting for the treatment increase



Workforce needs

The possible changes in AMD treatment over the coming years will lead to an increase in the number of injections given, which in turn will inform future costs and workforce needs. The population treatment rate increase presented in the previous section can be translated into injection volumes. Table C3, shows this, along with estimated associated costs, and for the effect for the workforce per the number of sessions required. The difference in injections is shown by volume in 2016 and 2036, alongside the session needs.

Table C3: Effect of treatment difference on injections and sessions

DHB of domicile	Observed injections in 2016	Observed sessions in 2016	Difference of injections to aspirational rate 2016	Extra sessions needed for aspirational rate 2016	Difference of injections to aspirational rate 2036	Extra sessions needed for aspirational rate 2036
Northland	636	80	1,137	142	1,973	247
Waitemata	2,203	275	2,244	280	4,379	547
Auckland	1,467	183	1,472	184	2,965	371
Counties Manukau	2,416	302	-160	-20	-326	-41
Waikato	2,464	308	612	76	1,102	138
Lakes	290	36	557	70	961	120
Bay of Plenty	612	77	1,539	192	2,620	328
Tairawhiti	110	14	257	32	435	54
Hawkes Bay	931	116	579	72	975	122
Taranaki	343	43	515	64	858	107
MidCentral	360	45	907	113	1,437	180
Whanganui	126	16	500	62	777	97
Capital and Coast	761	95	960	120	1,791	224
Hutt	342	43	628	78	1,109	139
Wairarapa	153	19	312	39	493	62
Nelson Marlborough	1,785	223	-48	-6	-84	-10
West Coast	168	21	128	16	209	26
Canterbury	2,793	349	1,839	230	3,418	427
South Canterbury	430	54	217	27	339	42
Southern	2,063	258	10	1	16	2
Total	20,453	2,557	14,207	1,776	25,448	3,181

These differences can then be shown in cost format applying the current cost of intravitreal injections as well as DHB specific session costs where available, and if no session costs were available, the average cost of a session across all DHBs was used in its place ($325). Table C4 details the indicative costs associated with the increased injections.

The bulk of increases to the aspirational rate in 2016 are fairly evenly distributed, while the increases in 2036 are far more unbalanced, specifically towards Waitemata, Auckland, and Canterbury DHBs where population increases are likely to have biggest impacts.

Table C4: Effect of treatment difference on injection and session costs ($m)

DHB of domicile	2016 injection cost	2016 session workforce cost	2016 injection cost difference to reach aspirational rate	2016 session workforce cost difference to reach aspirational rate	2036 injection cost difference to reach aspirational rate	2036 session workforce cost difference to reach aspirational rate
Northland	0.15	0.04	0.27	0.07	0.46	0.12
Waitemata	0.52	0.06	0.53	0.06	1.03	0.11
Auckland	0.34	0.04	0.35	0.04	0.70	0.07
Counties Manukau	0.57	0.09	-0.04	-0.01	-0.08	-0.01
Waikato	0.58	0.10	0.14	0.02	0.26	0.04
Lakes	0.07	0.01	0.13	0.02	0.23	0.04
Bay of Plenty	0.14	0.04	0.36	0.10	0.62	0.17
Tairawhiti	0.03	0.00	0.06	0.01	0.10	0.01
Hawkes Bay	0.22	0.05	0.14	0.03	0.23	0.06
Taranaki	0.08	0.01	0.12	0.02	0.20	0.03
MidCentral	0.08	0.02	0.21	0.05	0.34	0.08
Whanganui	0.03	0.01	0.12	0.02	0.18	0.03
Capital and Coast	0.18	0.05	0.23	0.06	0.42	0.12
Hutt	0.08	0.01	0.15	0.03	0.26	0.04
Wairarapa	0.04	0.01	0.07	0.02	0.12	0.03
Nelson Marlborough	0.42	0.12	-0.01	-0.00	-0.02	-0.01
West Coast	0.04	0.01	0.03	0.01	0.05	0.01
Canterbury	0.66	0.11	0.43	0.07	0.80	0.14
South Canterbury	0.10	0.02	0.05	0.01	0.08	0.01
Southern	0.48	0.13	0.00	0.00	0.00	0.00
Total	4.80	0.93	3.34	0.63	5.98	1.11

The potential cost saving due to having only specialist nurses administering injections compared to the current workforce is outlined in Table C5. Again costs are modelled, and indicative only.

Table C5: Estimated session workforce cost savings ($m)

DHB of domicile	2016 cost saving	2016 cost saving to reach aspirational rate	2036 cost saving to reach aspirational rate
Northland	0.02	0.04	0.07
Waitemata	0.01	0.01	0.01
Auckland	0.00	0.00	0.01
Counties Manukau	0.03	-0.00	-0.00
Waikato	0.04	0.01	0.02
Lakes	0.01	0.01	0.02
Bay of Plenty	0.03	0.07	0.11
Tairawhiti	0.00	0.00	0.00
Hawkes Bay	0.03	0.02	0.04
Taranaki	0.01	0.01	0.02
MidCentral	0.01	0.03	0.05
Whanganui	0.00	0.01	0.01
Capital and Coast	0.03	0.04	0.08
Hutt	0.01	0.01	0.02
Wairarapa	0.01	0.01	0.02
Nelson Marlborough	0.08	-0.00	-0.00
West Coast	0.01	0.01	0.01
Canterbury	0.05	0.03	0.06
South Canterbury	0.01	0.00	0.01
Southern	0.09	0.00	0.00
Total	0.47	0.31	0.54

The final table in this section illustrates what would be possible to build to show the direct effects of each change on any particular DHB. The proposed new data collection would allow the development of such tools to display the relevance and magnitude of each potential change (Table C6). Each DHB would modify the input assumptions to best match their circumstances.

Table C6: Cost-saving potential tool example*

Select number of years to follow cohort from 2016:	10
Select DHB of interest:	Nelson Marlborough

Enter your DHB's number of injections per year:	1,780
Enter your DHB's proportion of patients seen too slow:	5%
Enter your DHB's cost per bevacizumab injection:	$85
Enter your DHB's cost per ranibizumab injection:	$1,250
Enter your DHB's cost per aflibercept injection:	$1,650
Enter your DHB's cost per ziv-aflibercept injection:	$85
Enter your DHB's cost for rehabilitation:	$200
Enter your DHB's proportion of nurse injectors:	0%
Enter your DHB's proportion of ophthalmologist injectors:	5%

	Current state		Slow treatment and detection		AREDs2 uptake 50%		Treat and Extend / As needed		Cheaper bevacizumab		Aflibercept second line		Ziv-aflibercept second line		Rehabilitation		Current workforce	Specialist nurses	Healthcare assistants
DHB	Cost ($m)	Benefit (QALYs)	Cost ($m)	Benefit (QALYs)	Cost ($m)	Benefit (QALYs)	Cost ($m)	Benefit (QALYs)	Cost ($m)	Benefit (QALYs)	Cost ($m)	Benefit (QALYs)	Cost ($m)	Benefit (QALYs)	Cost ($m)	Benefit (QALYs)	Cost ($m)	Cost ($m)	Cost ($m)
Nelson Marlborough	2.8	1,284	4.8	-365	0.2	36	2.2	1,308	2.4	1,284	2.6	1,300	1.9	1,300	1.9	95	0.8	0.3	0.6
Cost-effective (cost per QALY)	2,170		-13,040		6,400		1,700		1,839		1,963		1,438		20,000		-	Y	Y
Cost saving	-		N		Y		Y		Y		Y		Y		Y				

*Note that all DHB costs and QALYs are imputed from Monte Carlo modelling of a 10-year cohort, and if fields were undefined from DHB returns then they were averaged over remaining factors. Also the remaining proportion is imputed and is for other injectors as presented throughout this report. The effect of population change is also factored in based on the DHB selected.

Appendix D International models of care

International models of care for AMD were investigated for relevance to New Zealand. Geographies searched included Australia (Commonwealth, NSW, Qld, Vic, SA, WA); UK (England and Wales, Scotland, Moorfields Eye Hospital London, NICE, Scottish Intercollegiate Guidelines Network); US (Kaiser, InterMountain, Group Health, VA, NIH, US Preventive Services Task Force, American Academy of Ophthalmology); and Canada (any province). European examples (France, Germany, Netherlands, and Scandinavia) were also checked. Sources no older than 2012 were examined, with the more recent ones shown here. Summaries for selected pathways found are given below - abbreviations used are noted in Appendix A.

Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes
Australia & NZ – RANZCO referral guideline	Diagnostic triggers 1. New symptoms suggestive of late AMD of distortion/central blur or loss of vision 2. New symptoms consistent with AMD: ▸ Difficulty reading in dim light ▸ Difficulty in adjusting from different lighting conditions ▸ Brief (<30 min) central blur or dimness on wakening ▸ Reading difficulty 3. History and frequency of symptoms 4. Age 5. Smoking history 6. Family history of AMD Examinations: 1. BCVA (visual acuity) 2. Imaging: OCT+FAF + IR (where available) 3. If <50yo and no FH and no symptoms: Non dilated examination 4. If >50yo or FH or any symptoms: Dilated fundus examination 5. If clinical signs of AMD and no OCT available: refer to an optometry colleague with OCT or to ophthalmologist for a full phenotyping. 6. Diagnosis: use Beckman classification (based upon CFP only) **No new macular symptoms and no signs or imaging changes suggestive of CNV:** 1. Stable vision loss in one eye from AMD and come for monitoring the fellow eye: ▸ Review every 12 months or immediately if any new symptoms ▸ Instruct on Amsler grid, lifestyle advice ▸ Referral to Vision Australia if applicable ▸ Ensure vision meets standards if still driving 2. No macular changes or normal ageing changes (drusen < 63um, or pigment change but no drusen)	*No information*	*No information*	1. RANZCO Referral Pathway for AMD Management by Optometrists (2016).- https://ranzco.edu/ArticleDocuments/514/RANZCO%20Referral%20pathway%20for%20AMD%20management%202016.pdf.aspx?Embed=Y College Guideline

Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes
	▸ Age <50 years - Discharge or per usual follow up for refraction ▸ Age >50 years, no FH - Review every 2 years or as usual practice 3. Early AMD (drusen 63- < 125um, no pigment change) or Intermediate AMD (drusen > 125um, or drusen 63-125um and pigment change) ▸ Age <50 years - Review every 12 months, instruct on Amsler grid, home monitoring lifestyle advice. Consider referral to ophthalmologist for further advice given young onset. ▸ Age >50 years - Review every 12 months instruct on Amsler grid, home monitoring, lifestyle advice. 4. Geographic atrophy (GA): A form of late AMD ▸ Review at 6 months or 12 months depending on vision/ driving status ▸ Inform person of AMD and GA implications ▸ Instruct on Amsler grid, lifestyle advice ▸ Referral to vision Australia if applicable ▸ Ensure vision meets standards if still driving ▸ Consider referral for trial for new intervention for GA 1, 2 ▸ Keep on a data base as GA trials are underway, or refer to an ophthalmologist involved in trials, so that patient can be offered trial participation or could be placed on a registry for future trials. **New macular symptoms, or new macular signs, or new imaging changes where CNV is strongly indicated or cannot be excluded.** 1. Choroidal neovascularization (CNV): A form of late AMD a. Signs suggestive of CNV without symptoms: Sub retinal fluid (SRF) only on OCT without other obvious cause (e.g., central serous choroidopathy), OR: IRC with no other symptoms or signs and no other cause (e.g., diabetic macular oedema) ▸ Refer to ophthalmologist within 2 weeks b. Suspected new onset CNV: Symptoms suggestive of macular disease (distortion, loss of central vision) and no other cause found. OR: No symptoms but unexplained retinal haemorrhage involving the macula. OR: No symptoms but OCT new intra retinal cysts (IRC) + SRF ▸ Refer to ophthalmologist within 1 week:			

Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes
	c. Definite new onset CNV: recent onset symptoms: new onset distortion, loss of central vision, or fresh retinal haemorrhage and OCT intra retinal cysts (IRC) +/- SRF			
US American Academy of Ophthalmology 'Preferred Practice Pattern'	**Diagnosis** An initial history has the following elements - 1. Symptoms ▸ Metamorphopsia (distorted vision) ▸ Decreased vision ▸ Scotoma ▸ Photopsia ▸ Difficulties in dark adaptation 2. Medication and nutritional supplement use 3. Ocular history 4. Medical history (including any hypersensitivity reactions) 5. Family history, especially family history of AMD 6. Social history, especially a quantitative smoking history **Physical examination** ▸ Comprehensive eye examination ▸ Stereoscopic biomicroscopic examination of the macula ▸ Binocular slit-lamp biomicroscopy of the ocular fundus is necessary to detect subtle clinical signs of Choroidal neovascularization (CNV), which includes small areas of hemorrhage, hard exudates, subretinal fluid, macular edema, subretinal fibrosis or pigment epithelial elevation **Diagnostic tests** ▸ Optical Coherence Tomography (OCT) ▸ Fluorescein Angiography ▸ Fundus Photography ▸ Indocyanine Green **Non-neovascular AMD:** **A. Recommended treatment -** Observation with no medical or surgical therapies **1. Diagnosis eligible for treatment -** Early AMD and advanced AMD with bilateral subfoveal geographic atrophy or disciform scars **2. Follow-up recommendations**	**Neovascular AMD:** **A. Recommended treatment** ▸ Aflibercept intravitreal injection 2.0 mg ▸ Bevacizumab intravitreal injection 1.25 mg ("The ophthalmologist should provide appropriate informed consent with respect to the off-label status") ▸ Ranibizumab intravitreal injection 0.5 mg 1. **Diagnosis eligible for treatment -** Macular CNV 2. **Follow-up recommendations** ▸ Patients should be instructed to promptly report symptoms suggestive of endophthalmitis, including eye pain or increased discomfort, worsening eye redness, blurred or decreased vision, increased sensitivity to light or an increased number of floaters ▸ Return examination approximately 4 weeks after treatment initially. Subsequent follow-up and treatment depends on the clinical findings and judgment of the treating ophthalmologist ▸ A maintenance treatment regimen of every 8 weeks has been shown to have results comparable to every 4 weeks in the first year of therapy (in case of Aflibercept intravitreal injection) ▸ Monitoring of monocular near vision (reading/Amsler grid) **Less commonly used treatments for neovascular AMD** ▸ Photodynamic Therapy (PDT) with verteporfin as recommended ▸ Thermal laser photocoagulation surgery as recommended **1. Diagnosis eligible for treatment** **1.1 In case of PDT with verteporfin** ▸ Macular CNV, new or recurrent, where the classic component is >50% of the lesion and the entire lesion is ≤5400 µm in greatest linear diameter ▸ Occult CNV may be considered for PDT with vision <20/50 or if the CNV is <4 MPS disc areas in size when the vision is >20/50 ▸ Juxtafoveal CNV is an off-label indication for PDT but may be considered in select cases	▸ Vision rehabilitation restores functional ability and patients with reduced visual function should be referred for vision rehabilitation and social services. ▸ Educating patients that the visual rehabilitation specialist helps to optimize their existing visual function, rather than "helping them see better" will establish more appropriate expectations around such services. ▸ Special optical or electronic magnifying lenses, bright lights, and electronic reading aids may help patients to read more effectively, but not as well as they did before the onset of AMD. ▸ An Implantable Miniature Telescope (IMT) is an FDA-approved device that may be effective for screened, phakic, motivated patients with end-stage AMD, and it appears to be cost-effective.	American Academy of Ophthalmology- Age-Related Macular Degeneration PPP - Updated 2015 - https://www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp-2015#CAREPROCESS

Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes
	▸ **Intervals -** Return examination at 6-24 months if asymptomatic or prompt examination for new symptoms suggestive of CNV ▸ **Testing -** Fundus photos, fluorescein angiography, or OCT as appropriate **B. Recommended treatment -** Antioxidant vitamin and mineral supplements as recommended in Age-Related Eye Disease Study (AREDs) and AREDS2 reports **1. Diagnosis eligible for treatment -** Intermediate AMD, and advanced AMD in one eye **2. Follow-up recommendations** ▸ **Intervals -** Return examination at 6-18 months if asymptomatic or prompt examination for new symptoms suggestive of CNV ▸ **Testing -** Monitoring of monocular near vision (reading/Amsler grid); fundus photography and/or fundus autofluorescence as appropriate; and fluorescein angiography and/or OCT for suspicion of CNV	**1.2 In case of thermal laser photocoagulation surgery** ▸ May be considered for extrafoveal classic CNV, new or recurrent ▸ May be considered for juxtapapillary CNV **2. Follow-up recommendations** **2.1 In case of PDT with verteporfin** ▸ Return examination approximately every 3 months until stable, with retreatments as indicated ▸ Monitoring of monocular near vision (reading/Amsler grid) **2.2 In case of thermal laser photocoagulation surgery** ▸ Return examination with fluorescein angiography approximately 2–4 weeks after treatment, and then at 4–6 weeks and thereafter depending on the clinical and angiographic findings ▸ Retreatments as indicated ▸ Monitoring of monocular near vision (reading/Amsler grid)		
UK Local Optical Committee Support Unit	**History** ▸ Age (over 55 years) ▸ Family history of maculopathy ▸ Previous ocular history ▸ Systemic disease e.g., hypertension, diabetes ▸ History of ocular surgery- cataract extraction, retinal detachment repair ▸ Myopia ▸ Medication e.g., chloroquine derivatives, tamoxifen ▸ Smoking status (current, ex-smoker or non-smoker) ▸ Excessive exposure to sunlight (UV) **Symptoms** ▸ Any change in vision ▸ Loss of central vision ▸ Spontaneously reported distortion of vision **Questions to be asked:** ▸ When did loss of vision start? ▸ In which eye are symptoms present? ▸ Has the loss of vision occurred suddenly or gradually? **Clinical examination** All patients presenting for a MECS examination with	**Referral letters** Patients requiring referral for macular degeneration must have the following noted on the referral form to the ophthalmologist. ▸ Date ▸ Full name of referring optometrist and practice address ▸ Full details of patient including name, address, telephone number, date of birth ▸ Visual acuities ▸ A clear indication of the reason for referral e.g., macular haemorrhage ▸ A brief description of any relevant history and symptoms including onset ▸ A description of the type of macular degeneration or signs such as drusen, pigment epithelial changes, sub retinal neovascular membrane, haemorrhages, exudates, macular oedema ▸ The urgency of the referral	*No information*	Local Optical Committee Support Unit (supporting opticians and optometrists) Minor Eye Conditions Service (MECS) Pathway (2014) - http://www.locsu.co.uk/uploads/enhanced_pathways_2014/locsu_mecs_pathway_rev_dec_2014_v1.pdf

Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes
	symptoms indicative of a potential macular degeneration should have the following investigations (in addition to such other examinations that the optometrist feels are necessary): ▸ Visual acuity (distance and near) recorded monocularly and compared to previous measures ▸ Refraction as a hyperopic shift can be indicative of macular oedema ▸ Amsler grid or similar assessment of central vision of each eye ▸ Tests of pupillary light reaction including swinging light test for Relative Afferent Pupil Defect (RAPD), prior to pupil dilation ▸ Dilated pupil fundus examination of both eyes with slit lamp binocular indirect ophthalmoscopy using a Volk or similar fundus lens noting: 1. Status of macula 2. Drusen, noting size 3. Haemorrhages, sub-retinal, intra-retinal, pre-retinal 4. Pigment epithelial changes i.e. hyper or hypo pigmentation, 5. Exudates, 6. Oedema i.e. sub-retinal fluid 7. Signs of sub retinal neovascular membrane **Management** If local protocols for the referral of AMD are in place, then these should be followed, otherwise some Hospital Eye Service (HES) ophthalmology departments will not have the facilities to deal with wet age related macular degeneration. In these cases it is best to telephone the department first to find out what procedures to follow. ▸ **Referral ASAP next available clinic appointment** 1. Sudden deterioration in vision + Visual Acuity (VA) better than 3/60 in affected eye 2. Spontaneously reported distortion in vision + VA better than 3/60 3. Sub-retinal neovascular membrane 4. Macular haemorrhage 5. Macular oedema ▸ **Routine referral** 1. Patient eligible and requesting certification of visual impairment 2. Patients requesting a home visit from Social Services			

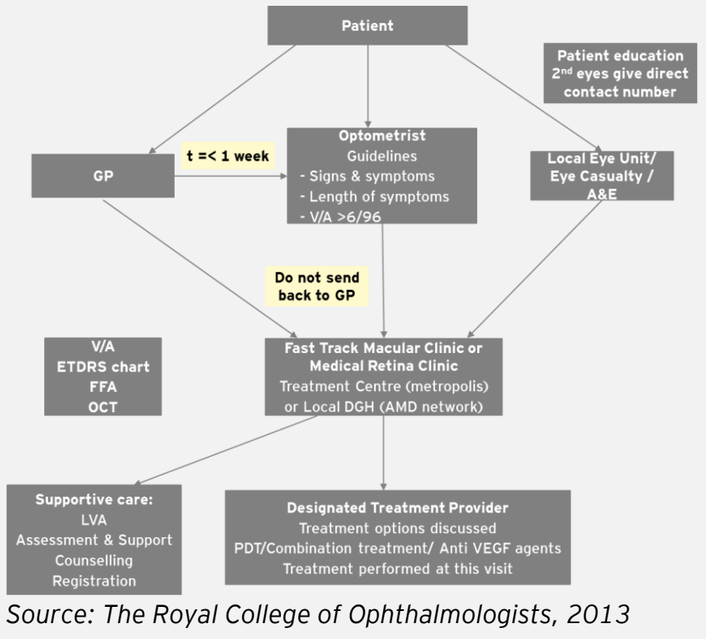
Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes
	to help them manage their visual impairment in their home. 3. Patients requiring a low vision assessment (this may be in the community or the hospital) 4. Patients requiring a routine ophthalmological opinion ▸ **No referral and routine follow-up** 1. Patients with VA 6/96 or worse in the affected eye 2. Patients with dry AMD, drusen and/or pigment epithelial changes ▸ Explain the diagnosis and educate the patient on the early warning signs of wet AMD. ▸ Give stop smoking advice via leaflet if appropriate + advice on healthy diet + protection from blue light ▸ Assess the risk of AMD progression by looking for large drusen (about the size of a vein at the disc margin or larger) and pigmentary changes. If these are both present bilaterally, there is a 50% chance of progressing to advanced AMD within 5 years. Give advice on a healthy diet unless there is moderate loss of vision or significant risk of loss. Provide information on AREDS2 findings & leaflet on AREDS22 supplements ▸ Give information on local services for the visually impaired- public and third sector ▸ Give appropriate information on national voluntary agencies e.g., RNIB, Macular Disease Society ▸ Give advice on driving ▸ Instruct the patient to inform the practice or GP immediately if vision suddenly deteriorates or becomes distorted			
Stockport, UK NHS-led health needs assessment	**Risk factors** ▸ Age ▸ Sex ▸ Smoking ▸ Family history/genetic factors ▸ A few genes have a large effect ▸ A mutation to a single gene is responsible for around half of the risk of AMD in the population ▸ Smoking has a synergistic effect with genetic factors **Referral and diagnosis pathway** **1. Signposting** ▸ GP or Accident and Emergency (A&E) responds to patient's sight concern and signpost patient to	**AMD Clinic Treatment** 1. Discuss choice of treatment 2. If there is treatment consent, then ▸ Determine full treatment plan and follow-up monitoring and treatment appointments ▸ Diagnosis and treatment plan letter to referrer, GP and patient ▸ Proceed with selected treatment in line with CCG agreement list ▸ Release patient with appropriate post-operative care and follow-up information 3. If there is no treatment consent, then discharge to appropriate service or follow-up if appropriate	*No information*	Don't Lose Sight (2014) – a health needs assessment by Stockport – a Joint Strategic Needs' Assessment (JSNA) through the Health and Wellbeing Board (HWB Board http://www.stockportjsna.org.uk/wp-content/uploads/2016/04/Dont-Lose-

Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes
	optometrist. A&E eye unit diagnoses/suspects AMD and refer to AMD clinic ▸ Patient can also self-refer to optometrist **2. Optometrist** ▸ Optometrist diagnoses/suspects AMD, discusses the choice of provider and treatment with patient, and refers patient to AMD clinic **3. AMD clinic - Appointments** ▸ Confirms if patient is registered with a Stockport GP; if not, refers to Host Clinical Commissioning Group (CCG) and informs patient's GP and referrer ▸ If patient is registered with a Stockport GP, then AMD clinic contacts patient to confirm suitable appointment ▸ Appointment letter confirming AMD clinic appointment - Patient and GP **4. AMD clinic - Diagnosis** ▸ AMD testing - visual test, retinal angiopathy and optical coherence test ▸ Diagnosis - Wet AMD ▸ If patient is suitable for treatment, discuss choice of treatment; and if not, then discharge to GP with support from local optometrist ▸ Diagnosis - Dry AMD: Discharge to GP with support from Local Optometrist ▸ Diagnosis - Not AMD: Discharge or refer to appropriate service	**AMD Clinic - Follow-up monitoring and treatment** 1. Patient attends AMD clinic according to treatment plan requirements 2. AMD Testing - Visual Acuity Test, Retina Angiography, and Optical Coherence Test 3. Monitoring Report 4. If patient is not suitable for treatment, then discharge to GP with support from Local Optometrist 5. If patient is suitable for treatment, then confirm treatment plan 6. If treatment plan remains the same, then proceed with selected treatment in line with CCG agreed list and release patient with appropriate post-operative care and follow-up information 7. If the treatment plan is not same and then take the treatment consent 8. If there is no treatment consent, then discharge to appropriate service or follow-up if required 9. If there is treatment consent, then proceed with selected treatment in line with CCG agreed list and release patient with appropriate post-operative care and follow-up information		Sight-Eye-Stockport-HNA.pdf
Oxford University Hospital, UK	Assessment to find the type of AMD (wet or dry) and its response to treatment ▸ Special imaging investigations such as angiography ▸ Optical Coherence Tomography scan of retina ▸ Review by retinal specialist	**Wet AMD Treatment** ▸ Lucentis and Eylea are the most commonly used anti-Vascular Endothelial Growth Factors (VEGFs) at present in the NHS. Anti-VEGFs treatments are only suitable for people with wet AMD if there is not too much pre-existing scarring. ▸ The usual regime when using anti-VEGFs is to start with a course of three injections spaced a month apart; most people need a number of injections over a few years; this will depend on the drug used and patient's response to the treatment. **1. Lucentis (ranibizumab) injections -** The number of injections needed is still not fully known for each individual **2. Eylea (aflibercept) injections -** A patient, if recently diagnosed with wet AMD, will usually be treated with Eylea and will have a course of three injections spaced a month apart, followed by an injection every 2 months for the rest	*No information*	Oxford University Hospitals, Treatment of age-related macular degeneration at Oxford Eye Hospital (2016) - http://www.ouh.nhs.uk/patient-guide/leaflets/files/13840Pmacular.pdf

Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes
		of the first year. After first year of treatment, the patient will be informed about the frequency for further injections. **3. Avastin (bevacizumab) -** Although Avastin is a licensed drug and is available for use in disorders such as wet AMD, it is not currently licensed for treating this specific condition. However, it has been shown in trials to be as clinically effective as Lucentis for the treatment of non-AMD blood vessel growth. **Monitoring of wet AMD and response to treatment** ▸ Retina will be reassessed to check whether the patient needs further treatment ▸ The patient will be informed about the frequency of reassessment of retina at the time of clinic appointment ▸ A retinal imaging assessment involves a colour photograph taken of retina and an OCT scan ▸ The patient will be informed about further treatment either at the appointment or within a week, by telephone or letter; if not received either a phone call or a letter within 10 days of the scan, the patient can contact the AMD Coordinator ▸ Further treatment will only be recommended if wet AMD appears active **Flow within AMD clinic** ▸ The patient's vision will be tested at the time of appointment, with some eye drops put in; and then the patient will be called in to one of the clinic rooms to have an OCT scan. After the OCT scan, the patient will be seen by AMD team for consultation ▸ The patient will be given at least 24 hours to decide to go for anti-VEGF injections, if the injections are beneficial for the patient ▸ If the patient decides to have the anti-VEGF injections on the same day and it is possible to provide them at the clinic, the AMD team will organise the treatment for the patient ▸ If the treatment is not possible on the same day, the patient will be given an appointment, which will be booked by the AMD Coordinator ▸ The patient will be contacted by AMD Coordinator, if booked only to have retinal imaging at the appointment and will be given an appointment for further follow-up and treatment, depending on the results of the retinal imaging		

Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes
		Anti-VEGF injection procedure ▸ At the Oxford Eye Hospital medical, nursing, orthoptic and optometry staff members who are trained to inject will carry out the injections ▸ The actual injection takes only a few seconds, but the whole process might take up to 20 minutes, which includes checks, and cleaning eye and preparing the equipment after the first three injections, the patient's eye will be reassessed to check for a response to the treatment ▸ The AMD team member will decide whether further treatment or monitoring is required ▸ The patient is asked to contact the AMD Coordinator if any sudden deterioration of vision while undergoing treatment or monitoring is noticed ▸ The nursing staff will provide information and counselling regarding expectation from the treatment		
Ontario, Canada Ministry of Health and Long-Term Care	**Risk factors** ▸ Age ▸ Family history ▸ Ethnicity ▸ Smoking ▸ Unhealthy diet ▸ Poor physical health People over the age of 55, whose close relative(s) have been diagnosed with it and who are Caucasian are the most at risk for developing AMD **Screening pathway** A. Education to family practitioners and the public 1. Risk factors for eye disease 2. Need for annual eye exams - consists of the following elements: ▸ Visual Acuity ▸ Intraocular pressure ▸ Anterior segment and lens exam ▸ Dilated fundus exam with slit-lamp biomicroscopy and indirect ophthalmoscopy B. At the completion of the visit, a report should be created and sent to the family practitioner (referring physician or patient-identified primary health care provider) regarding the examination findings and the	**Recommended approach for intraocular injection of VEGF inhibitors for wet AMD** **A. Guidelines for initiating therapy** 1. To receive treatment for wet AMD, patients should be documented to meet the following criteria: ▸ Age >50 ▸ Recent onset of decreased vision or distortion ▸ Presence of drusen ▸ Presence of subretinal haemorrhage associated with retinal thickening ▸ OCT evidence of intraretinal fluid and/or subretinal fluid (but not solely pigment epithelial detachment (PED)) along with subretinal changes consistent with wet-AMD 2. Absence of other pathology to explain visual change 3. Absence of medical or ocular contraindications to intraocular injection 4. Absence of ocular or systemic pathology which would negate the possibility of vision benefit with treatment 5. Patient agrees to return for regular follow-up at intervals as frequently as monthly; potentially for life if treatment is successful In some cases, patients may not meet the criteria listed above for wet-AMD treatment, but may still possibly benefit from treatment. Obtaining an OCT and often an	*No information*	Quality Based Procedures Clinical Handbook for Integrated Retinal Care (2014) – http://www.health.gov.on.ca/en/pro/programs/ecfa/docs/qbp_retinal.pdf "This clinical handbook has been created to serve as a compendium of the evidence-based rationale and clinical consensus driving the development of the policy framework and implementation approach for the Integrated Retinal Quality Based Procedure."

Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes
	suggested interval for re-examination. C. Depending on the findings of the eye exam, a patient may be referred for further assessment and treatment. **Decision to treat pathway** 1. Once referred, all retina patient groups are examined and diagnosed by a treating ophthalmologist. 2. At this point, this individual will conduct a further eye examination which may include specialized testing to achieve a more accurate diagnosis. This specialized testing may include - ▸ Ocular Coherence Tomography (OCT) ▸ Intravenous Fluorescein Angiography (IVFA) ▸ Visual electrophysiologic tests ▸ Ocular ultrasonography ▸ Visual field testing 3. Then, it is determined whether a patient will follow a medical pathway and receive intraocular injection therapy (Anti-VEGF therapy); whether they will receive laser therapy (which is usually, but not always, provided within a hospital, surgery centre or independent health facilities), or if they will be on the surgical pathway and receive surgical treatment at a hospital, surgery centre, or independent health facility.	IVFA is necessary to confirm the diagnosis in this circumstance. Once a firm diagnosis of wet AMD is established, the conduct of therapy will continue as mentioned below. **B. Conduct of therapy** 1. Treatment will normally be initiated with a series of three monthly injections of a VEGF inhibitor with a formal evaluation of treatment effect occurring at the 3rd or 4th month. ▸ To continue in this treatment pathway patients should demonstrate significant reduction (or absence) of intraretinal fluid or significant reduction (or absence) of subretinal fluid, haemorrhage, or retinal thickening. Patients who do not demonstrate these changes should be carefully assessed to determine the reason (incorrect diagnosis, inactive disease with findings mimicking activity, disease unresponsive to treating agent). ▸ If none of these apply, a review by a retinal subspecialist (or a colleague experienced in the management of wet AMD if access to a retinal specialist is limited by geography) should occur and a mutually agreed upon treatment plan established ▸ Where geography limits access to specialist care this review may also be conducted through teleophthalmology if available. 2. Beyond this point continued follow-up and treatment should continue with intervals not usually greater than 3 months; with vision, intraocular pressure, and a fundus examination documented for each visit. 3. In the absence of visible subretinal blood and retinal thickening, an OCT should be obtained at each visit to document the ongoing effectiveness of, and need for, therapy. Increase in intraretinal or subretinal fluid or development of new haemorrhage should prompt a re-evaluation of treatment and frequency. **C. Guidelines for discontinuation of therapy** 1. Loss of useful vision secondary to irreversible structural change 2. Development of ocular or systemic disease precluding intraocular injection		

Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes
		3. Inability to maintain regular follow-up 4. Patient desire to discontinue treatment		
UK Royal College of Ophthalmology Guidelines	**Diagnosis** **1. Clinical** ▸ **Geographic atrophy (GA)** - Fundus autofluorescence along with spectral domain OCT has made it easier to diagnose GA ▸ **Exudative AMD** – Following slit lamp biomicroscopy, the presence or absence of signs including subretinal or sub-RPE neovascularisation, serous detachment of the neurosensory retina, RPE detachment and haemorrhages to be noted ▸ **Idiopathic Polypoidal Choroidopathy (IPC)** **2. Conditions mimicking AMD** ▸ **Exudative macular lesions mimicking AMD** such as diabetic maculopathy, high myopia, inflammatory CNV, central serous chorioretinopathy (CSR) and macular telangiectasia ▸ **Non exudative macular lesions mimicking AMD** such as pattern dystrophy **3. Retinal imaging** – Part of patient management required for diagnosis and monitoring response to therapy. Includes techniques such as colour fundus photography, fluorescein angiography (FA), indocyanine green angiography (ICGA), optical coherence tomography (OCT) and fundus autofluorescence (FAF) **Risk factors** 1. Genetic or nutritional factors – not practical to measure in a clinical setting 2. Factors for advanced AMD ▸ Increasing age ▸ Current smoking ▸ Family history ▸ Cataract surgery, whose effect may at least partly be due to shared risk factors such as age 3. Factors moderately associated with AMD	**Wet AMD Referral Pathway**  *Source: The Royal College of Ophthalmologists, 2013* A&E refers to Accident and Emergency, V/A refers to Visual Acuity, ETDRS refers to Early Treatment Diabetic Retinopathy Study, FFA refers to Fundus Fluorescein Angiography, LVA refers to Low Vision Aid, PDT refers to Photodynamic Therapy, VEGF refers to Vascular Endothelial Growth Factor, and DGH refers to District General Hospital **AMD Referral Pathway** 1. Immediate access to retinal specialists with expertise in the management of exudative AMD for all patients should be available, irrespective of geographic location. 2. Patients should be seen by a specialist with medical retinal expertise within one week of diagnosis and there should be no more than one week between evaluation and treatment.	**Low vision rehabilitation** ▸ In many patients with advanced non-neovascular AMD, reading is difficult despite relatively good distance visual acuity. ▸ Magnifiers and low vision aids are required for these patients. ▸ Using computers in tablet form with inbuilt ability to enhance contrast, change background and zoom for magnification rapidly can be helpful. ▸ For those who have lost the foveal vision, a preferential retinal locus (PRL) will develop over time. There is some evidence that training using biofeedback can help to develop a more stable PRL. **Referral to rehabilitation and low vision services** ▸ If an individual has sight loss, they should be offered access to low vision support and advice at an early stage. Advice and use of task lighting and magnifiers reduce the early impact of sight loss and the risk of falls. ▸ Early advice and support means that an individual can learn how to use their remaining vision more effectively, retaining	Age-Related Macular Degeneration: Guidelines for Management (2013) – https://www.rcophth.ac.uk/wp-content/uploads/2014/12/2013-SCI-318-RCOphth-AMD-Guidelines-Sept-2013-FINAL-2.pdf

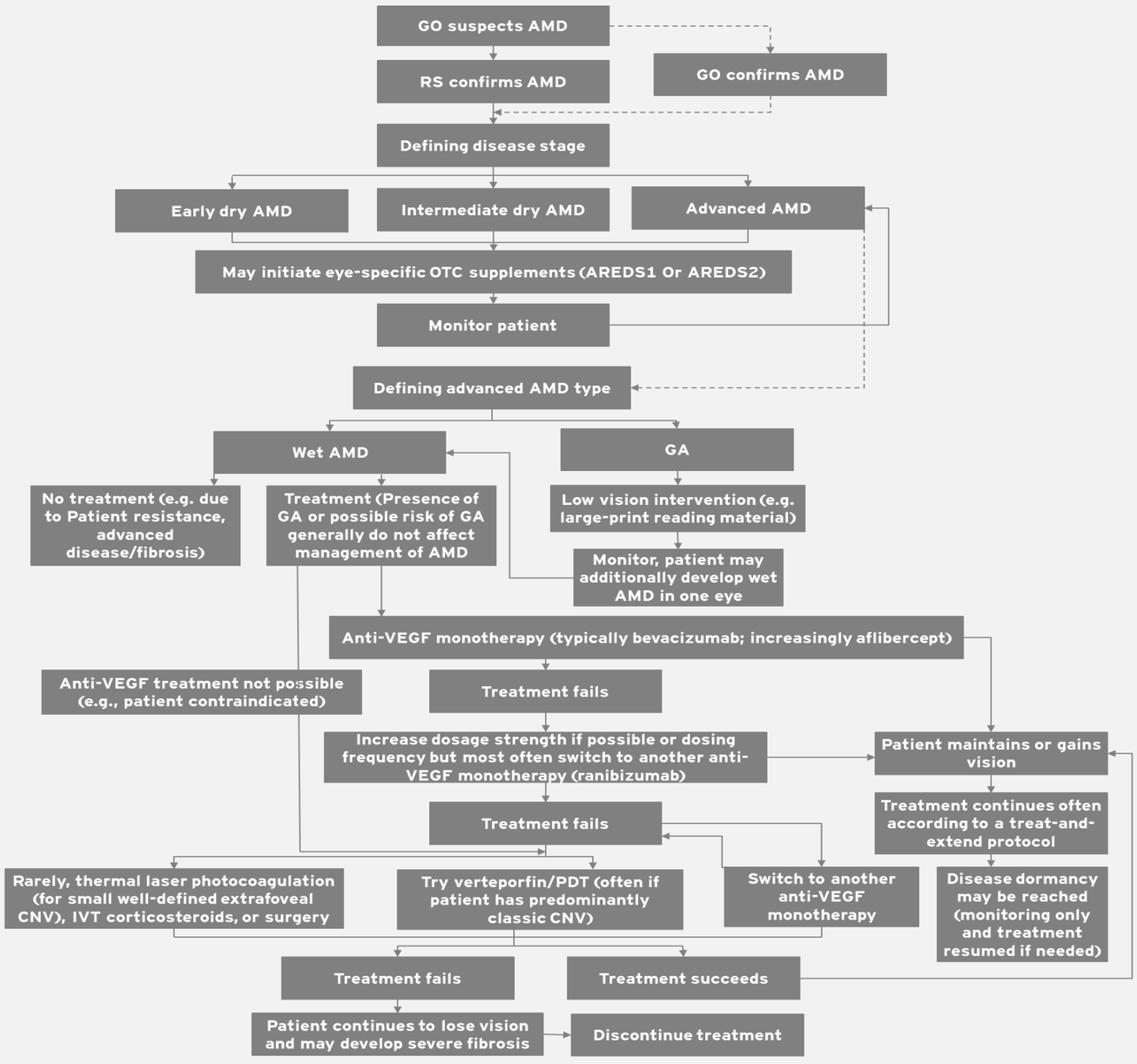
Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes
	▸ Cardiovascular disease ▸ Hypertension ▸ Higher plasma fibrinogen	3. All patients suspected to have exudative AMD by the optometrist, general practitioner, or other health workers should be referred directly to the nearest AMD Centre, Eye Casualty, or Eye Clinic. 4. Optometrists may be used for screening or first examination of patients suspected of having exudative AMD. Referrals from the optometrist should be sent directly to an ophthalmology department, and should not pass through the general practitioner as such a route introduces unnecessary delays. 5. Self referral or presentation to the Eye Casualty/Clinic or AMD Centre of exudative AMD should be encouraged, especially in patients who have second eye involvement. 6. Optometrists with specialist interest (Super Optometrist) are not recommended as such pathways will introduce unnecessary delays, and misdiagnoses. 7. It is assumed that all new patients with choroidal neovascularisation (CNV) secondary to AMD referred to an AMD Centre, will undergo an extended assessment of vision, retinal imaging (FFA and OCT), ophthalmological examination, and then proceed to treatment within one week of diagnosis. 8. Treatment would be expected to follow vision assessment, retinal imaging and ophthalmological assessment if indicated at subsequent follow-up visits. 9. Integrated clinic for AMD patients includes visual assessments and OCT imaging. This may be in the form of virtual clinics where colour and OCT imaging can be reviewed and patients requiring treatment can be identified. Medical assessments and FFA can be triggered from these clinics as appropriate. 10. Treatments such as - intravitreal injections (and/or PDT 3 monthly) can be booked as appropriate subsequent to imaging review. 11. Movement of patients through the AMD clinic depends on whether a one stop or two stop model is adopted. In a one stop model, all examinations, investigations and treatments are undertaken on the same day, while in a two stop model, examinations and investigations take place on one day, followed by treatments during a separate visit. A one stop model is preferable as it minimises patient visits to the clinic, especially as some of them may have to travel significant distances.	independence and confidence. ▸ Find out where and what low vision services are available locally and refer patients with low vision as soon as possible. Some may be hospital based and others may be community based. ▸ It should not be the case that access to a low vision service is certification/ registration led. ▸ The NHS Eyecare Services Programme sets out the expectations from a Low Vision Services and the principles include: 1. Access to rehab and low vision support will vary according to local arrangements. Clinicians should be present or represented on their local low vision committee 2. Low vision services must reflect a multi-disciplinary, multi-agency approach that co-ordinates with other health and social care providers in the area, including services provided at the client's residence at the time. 3. Registration as sight impaired or severely sight impaired should not be a pre-requisite to accessing low vision services. 4. There should be a tailored needs-based assessment for each client following referral to the low vision service. A low vision assessment should always offer:	

Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes
		Ultimately the model adopted by units will depend on staffing and resources.	a. An eye health examination or evidence of recent examination or referral for examination according to local protocols b. A functional visual assessment 5. After assessment, the following should be offered, as appropriate, to the user: a. Prescription/provision of appropriate optical/non-optical aids. The sale of some low vision aids is restricted to certain professionals or requires appropriate supervision, and the supply/loan of aids should be governed by local protocol. b. Advice on lighting, contrast and size, filters, tactile aids, electronic aids and other non-optical aids c. Training and/or therapy to enable optical and non-optical aids and other techniques to be used effectively d. Links to broader rehabilitation services, such as home assessment and mobility as well as possible referral to structured therapy programmes and counselling e. A review of benefits, welfare rights, concessions, support groups, (both local and national)	

Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes
			f. Advice on access to the full range of low vision equipment available for purchase through local society resource centres or the RNIB or direct from retailers	
Queensland, Australia Metro North HHS referral guideline	**Risk factors** ▸ Increasing age ▸ Smoking ▸ Family history of AMD **Detection and diagnosis of AMD** ▸ Amsler Grid ▸ Colour vision test ▸ Viewing the macula with an ophthalmoscope ▸ Fluorescein Angiography ▸ OCT (Optical Coherence Tomography **A. Category 1** 1. Appointment within 30 days is desirable 2. Condition has the potential to require more complex or emergent care if assessment is delayed 3. Condition has the potential to have significant impact on quality of life if care is delayed beyond 30 days **B. Category 2** 1. Appointment within 90 days is desirable 2. Condition is unlikely to require more complex care if assessment is delayed 3. Condition has the potential to have some impact on quality of life if care is delayed beyond 90 days **C. Category 3** 1. Appointment is not required within 90 days 2. Condition is unlikely to deteriorate quickly 3. Condition is unlikely to require more complex care if assessment is delayed beyond 365 days **Out of scope for ophthalmology outpatient services** Dry AMD is not routinely seen unless the practitioner is concerned about progression to wet AMD	*No information*	▸ Low vision optical aids assist in improving vision for people with macular degeneration. ▸ Some of the available resources include spectacles, hand or stand magnifiers, telescopes, computers and closed circuit television. ▸ Brighter illumination is also beneficial besides large print books and newspapers.	1. Adult Referral Evaluation and Management Guidelines (2016) https://www.health.qld.gov.au/__data/assets/pdf_file/0030/612858/mn-cpc-ophthalmology.pdf

Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes

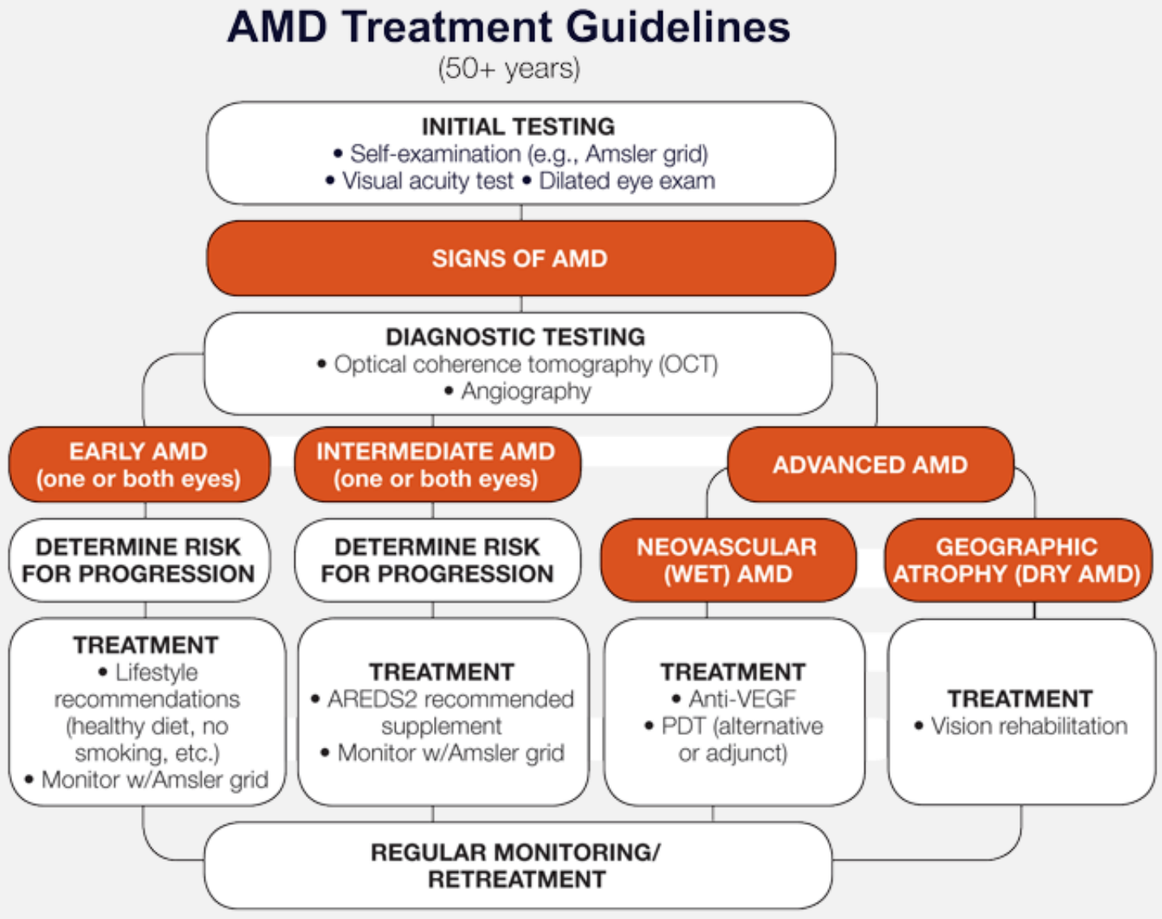
Treatment Decision Flowchart for AMD (US, UK, France, Germany, Japan, Spain and Italy) 2015
https://decisionresourcesgroup.com/report/140902-biopharma-treatment-algorithms-in-wet-age-related-macular/



GO refers to General Ophthalmologist
RS refers to Retinal Specialist;
GA refers to Geographic Atrophy
IVT refers to Intravitreal Pharmacotherapy
CNV refers to Choroidal Neovascularization
PDT refers to Photodynamic Therapy
VEGF refers to Vascular Endothelial Growth Factor

Geography	1. Prevention / detection, dry AMD	2. Treatment of wet AMD	3. Rehabilitation	Source, notes

Harvard University, Boston US
http://eye.hms.harvard.edu/eyeinsights/2015-january/age-related-macular-degeneration-amd



Literature review: Model of care for Age-related Macular Degeneration (AMD)

Building a better working world

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1. Introduction

This literature review has been undertaken to support work on the Assessment of the Model of Care for Age-related Macular Degeneration (AMD). Its purpose is to update the previous literature review (1) for information that has become available since then. This is intended to pragmatically establish the evidence base for assessing three components of the model of care for AMD in New Zealand:

- Component 1: Prevention, early detection and risk stratification
- Component 2: Intravitreal anti-VEGF treatment
- Component 3: Low vision rehabilitation

Economic literature is reviewed separately (see Appendix F).

1.1 Background

1.1.1 Overview

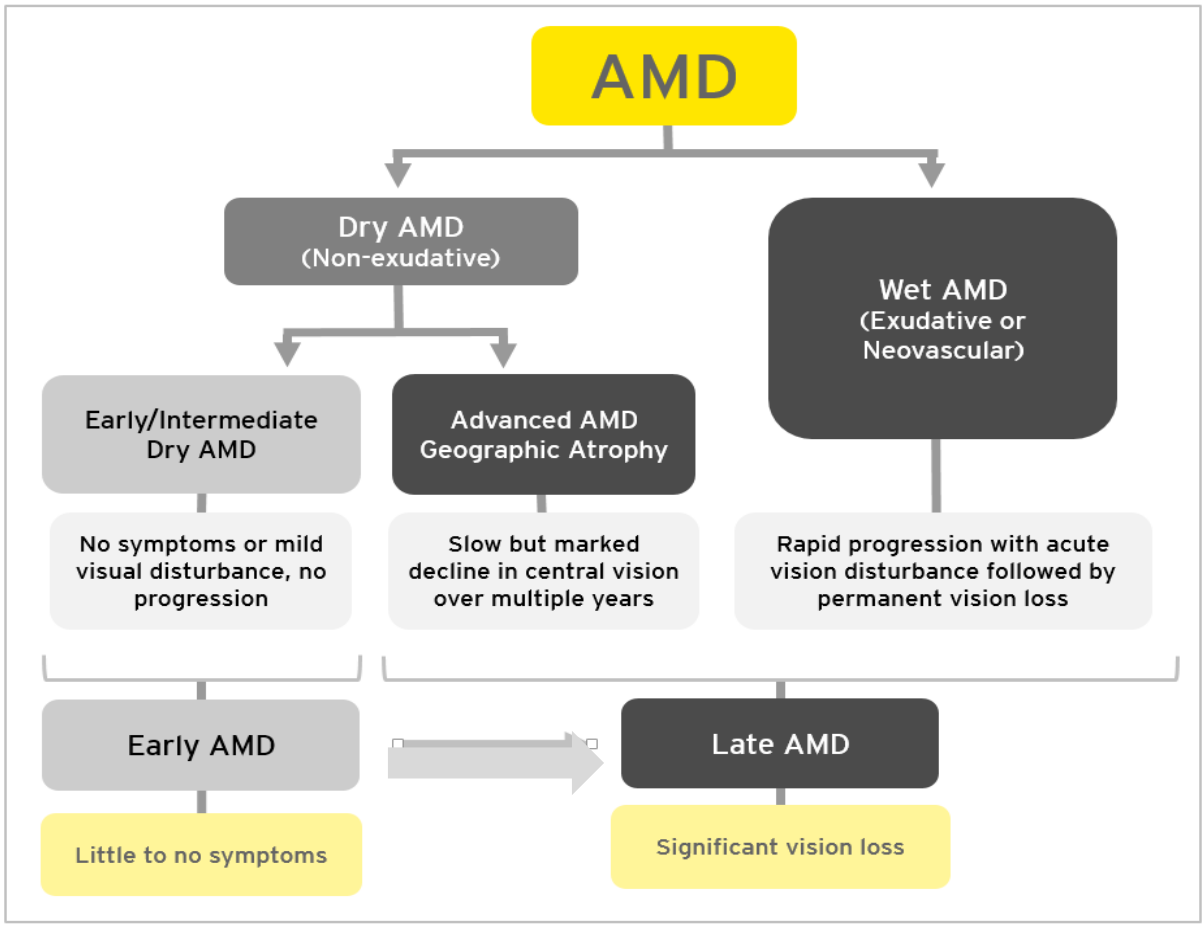
AMD is the leading cause of blindness in New Zealand (1). In AMD, deterioration of the macula causes progressive vision loss in the central field of vision, and can affect one or both eyes. There is no known cause of AMD other than age-related changes, but smoking and family history have been identified as risk factors, as well as genetics, which may explain up to 80% of cases. Other possible risk factors include diet and cardiovascular disease (1).

AMD is characterised by age-related changes to the macula - the central region of the retina which is the light-sensitive tissue at the back of eye involved in detailed central vision. Hence, in AMD, deterioration of the macula causes progressive vision loss in the centre of the field of vision, which can affect one or both eyes (1).

There are two distinct forms of AMD: early and late. Early AMD is the most common and less severe form, and is typically not associated with vision loss or impairment. Early AMD encompasses non-advanced 'dry' AMD, where abnormalities develop in the retinal pigment epithelium (RPE) and lipid deposits (drusen) form underneath the RPE. When dry AMD becomes advanced (geographic atrophy), it is classified as late AMD. Along with advanced dry AMD, late AMD also includes wet AMD (neovascular) (1).

Wet AMD is characterised by abnormalities in new choroidal blood vessel growth (choroidal neovascularization or CNV) under the retina. These leak blood and proteins into the macular regions, causing thickening of the retina, which ultimately results in scarring and permanent damage to the photoreceptor retinal cells. Wet AMD is associated with rapid progression and permanent vision loss. There is currently no specific treatment for dry AMD, but intravitreal anti-VEGF injections are established as an effective treatment for wet AMD (1).

Figure E1: Overview of the various classifications within AMD:



1.2 Incidence and prevalence

There are no recent comprehensive prevalence studies of AMD in New Zealand, therefore, estimates are based on extrapolation from international data. Internationally, reported rates vary depending on AMD definition criteria, diagnostic accuracy, and the ethnicities and age ranges studied. It is estimated that between 150,000 and 200,000 New Zealanders aged 50 years and over have AMD, with 15,000 to 30,000 of those cases being late AMD. Of those late cases, 5,000 to 10,000 are estimated to be late dry AMD and 10,000 to 20,000 are wet AMD. Each year, there are approximately 3,000 to 4,000 new diagnoses of late AMD. The prevalence of late AMD among people aged 45–85 years is expected to increase by 10-20% over the next 10 years through improving survival (1).

The prevalence of AMD tends to be higher among European populations than other ethnicities such as Asian. In New Zealand treated prevalence among Māori, Pacific and Asian people is about half that of the European population (see Figure 5, main report), presumed to be due to genetic factors (1). Approximately 50% of all cases of blindness in New Zealand are attributable to AMD, equating to between 6,000 and 7,000 people. However, the incidence of low vision and blindness among AMD patients has been reducing due to the adoption of anti-VEGF therapy across New Zealand (1). A decline in membership with the New Zealand Blind Foundation for AMD-related vision loss coincided with the introduction of anti-VEGF treatment, decreasing from membership rates from 19 to 14 memberships per 100,000 population from 2005 to 2010) (1).

1.3 Health outcomes and costs

While AMD is not a primary cause of death, it is associated with a higher risk of mortality, and leads to a loss of disability-adjusted life-years (DALYs), which is a measure of health burden, factoring in both quality and quantity of life. AMD through its effect on visual acuity vision field loss at any stage can adversely affect quality of life and interfere with daily activities, which can result in people with AMD requiring formal supports from government such as home-based personal care, household management or support from their families or carers. AMD is associated with an increased risk of depression, injury, falls and hip fractures, as well as an earlier loss of independence and need for aged residential care.

The annual healthcare costs of AMD in New Zealand is estimated to be between $19.5–$31.4 million, across the entire model of care. Of this, $4 million–$8 million is incurred for wet AMD (1).

PHARMAC has reported that the first and second line anti-VEGF treatments, bevacizumab and ranibizumab, are the 17th and 7th most costly items in New Zealand's public hospitals respectively. Spending for ranibizumab has increased significantly from $200,000 in 2012/13 to $2,820,000 in 2015/16 (gross annual cost excluding GST and rebates) as it has become established as a second-line agent for treatment. Spending for bevacizumab has increased from $880,000 in 2012/13 to $1,620,000 in 2015/16 (2). While far more bevacizumab is used (estimated at over 90% of treatments), the much greater cost of ranibizumab per dose leads to the higher expenditure.

2. Methodology

Databases were searched up to 31 January 2017 looking for all publications relating to prevention of AMD, anti-VEGF treatment and low vision rehabilitation for AMD, including systematic reviews, randomised controlled trials, clinical guidelines or other studies. We concentrated on English language papers published between 2014 and 2017, aiming to identify new findings since the previous 2014 review.

2.1 Databases searched

- PubMed
- Google Scholar
- TRIP Database
- Epistemonikos

2.2 Specific websites searched

- World Health Organisation (WHO)
- National Institute for Health and Care Excellence (NICE)

2.3 Search strategy

In addition:

- Citations for 2014-2017 in articles found were checked for relevance
- Key NHC 2015 Report references were checked on PubMed seeking further articles in the 'cited by' section in the PubMed sidebar
- A list of keywords used in the literature search can be found in Section 8.

2.4 Strength of the evidence

The quality of the evidence is determined by the methods used to minimise bias within a study design, and is noted where relevant based on the hierarchy:

1. Best evidence comes from systematic reviews of all the relevant literature, particularly randomised controlled trials, with appropriate weightings
2. Evidence is provided by the randomised controlled trial themselves
3. Non-randomised studies of groups of people where a control group has run concurrently with the group receiving the intervention being assessed – database studies often fall into this category
4. Case series - non-randomised studies where intervention effects are compared with previous or historical information
5. Expert opinion.

2.5 Limitations of the evidence

Interpretation of the AMD literature has to take in to account:

- Weak study designs
- The cumulative effect on outcomes of the learning curve
- Commercial pressures affecting publication

3. Prevention and early detection: Can AMD be prevented?

3.1 Is it possible to slow or stop disease progression?

Key Messages

- Current clinical guidelines outline smoking cessation as a key measure for preventing progression of AMD
- The AREDS2 nutritional supplement regime is currently the most effective treatment available to slow the progression of intermediate and late dry AMD to wet AMD, but was found to have no significant effect on preventing the onset or slowing progression of early AMD
- A particular target might be patients with wet AMD in one eye but not yet the other
- A beta-carotene-free AREDS2 formulation is recommended for AMD patients who are past or current smokers
- Recommendations to adopt a Mediterranean-type diet are sensibly present in guidelines and clinical practice
- Genetic profiles of AMD patients may influence their response to dietary supplements

3.2 Smoking cessation

Smoking is a proven risk factor for AMD (1) and is therefore a viable option for preventing the progression of dry AMD. Recent guidelines, including The American Academy of Ophthalmology's Preferred Practice Guidelines for AMD and that from the European Society of Retina Specialists both strongly recommend smoking cessation when advising AMD patients (3, 39).

3.3 Nutrition

The AREDS2 antioxidant vitamin and mineral regimen, which combines high doses of vitamin C, vitamin E, zinc, copper, and either beta carotene or a combination of lutein and zeaxanthin, has previously been noted as the most viable preventative treatment to slow or stop disease progression. It was shown to significantly reduce the 5-year risk of progression to later stages of dry AMD or to wet AMD, but did not effectively prevent progression of early AMD. It also noted that these findings were controversial. For patients with intermediate to late dry AMD, the International Council of Ophthalmology and Royal College of Ophthalmologists recommend the AREDS2 regimen (1).

3.3.1 Primary prevention - stopping onset or progression at early stages

The literature currently demonstrates a lack of evidence to show that nutritional supplements such as the AREDS2 regimen are effective in preventing the onset of AMD or slowing progression from the early stages of the disease. Multiple systematic reviews note a lack of evidence to support AREDs-based supplementation to prevent the development of AMD or progression of early AMD, and therefore recommend against clinical use of supplements for healthy populations (4-7). This is reinforced by

a meta-analysis by Downie et al which showed that, although it is scientifically plausible, there was no significant effect of nutritional supplements for preventing or delaying the onset of AMD in people who do not exhibit symptoms (8). This review suggested that current evidence-based practice for patients with normal ageing macular changes should therefore not include recommendations for antioxidant nutritional supplements.

3.3.2 Secondary prevention – stopping further progression from intermediate or late

Five papers reviewing the impact of nutritional supplements on AMD concluded that supplementation with the AREDS2-based formula reduces the risk of or slows disease progression among high-risk patients with either intermediate or late AMD (4, 5, 9). This includes patients with one eye with wet AMD to slow progression in the other eye remaining with dry AMD. They suggest that AREDS2-based supplements are currently the most effective treatment available to slow the progression of intermediate to late dry AMD (10), and recommend that nutrient supplementation should remain in the therapeutic spectrum for AMD (5). The carotenoids lutein and zeaxanthin were not found to further reduce the risk of progression from intermediate to late AMD (7, 8). However, higher intakes of these carotenoids have been associated with reduced risk of advanced AMD (10), and may replace beta-carotene in AREDS2 formulations for particular patients, as discussed below.

3.3.3 Beta-carotene-free formulation

A review of two large trials found an increased risk of lung cancer associated with beta-carotene supplementation among smokers (7), therefore recommendations are that current or ex-smokers with moderate or advanced AMD should use the modified, beta-carotene-free AREDS2 formulation (4, 7, 10).

3.3.4 Omega 3 supplementation

While observational studies have shown that consumption of omega 3 long-chain polyunsaturated fatty acids may protect against and reduce the risk of progression to advanced AMD (11), results from randomized control trials (RCTs) fail to support this (7, 11). A review of RCTs found no statistically significant effect on incidence of advanced AMD or progression to advanced AMD. Consequently there does not appear to be high-quality evidence to support inclusion of omega 3 into the supplementation regimen for AMD (7).

3.3.5 Dietary patterns

The literature suggests that it is possible that dietary patterns may prevent AMD and slow its progression, however, the evidence is not strong due to the lack of RCT data (1). RCTs tend not to be a feasible study design for testing dietary patterns, and therefore only evidence from observational studies can be used, which are prone to bias and confounding error (7). Regardless of the lack of high-quality evidence, many papers still recommend particular dietary patterns to patients with AMD on the grounds that they have the potential to both prevent the onset, and slow the progression of AMD. The prevailing dietary advice is adoption of a Mediterranean-type diet, which includes increasing consumption of green leafy vegetables, consuming low-glycaemic index diets, and consuming fish at least twice a week (4, 9). With its clear

benefits for reducing heart disease and diabetes risk it seems a prudent approach to continue this recommendation.

3.3.6 Nutrition and genetic factors

Multiple studies highlight that the efficacy of nutritional supplements is likely to be influenced by patients' genetic profiles. Therefore it is suggested that genetic testing may be beneficial in guiding the use of vitamin supplements for patients with AMD. This approach may avoid use of supplements that could be harmful to some, avoid use where it will have no impact on the disease, and promote use among patients for whom supplements will confer meaningful benefits (5, 8, 9, 12). However, these papers stress the need for further research in order to assess the feasibility of this. No particular testing regime appears ready for implementation at present.

3.4 Is it possible to identify people with potential or early signs of AMD?

Key Messages

- The traditional Amsler grid is a useful patient prompt for testing, but has limited effectiveness as a monitoring tool. It provides a promising basis for future technologies in self-testing
- Optical coherence tomography is a key diagnostic tool but should not be the only tool employed to detect and monitor AMD
- Despite being included in clinical guidelines, the accuracy of autofluorescence imaging is unclear
- While genetic testing has the potential to enhance the precision of diagnosis in the future, it still requires significant further research and refinement

Current diagnostic tests to identify early signs of AMD include visual acuity testing and examination of the interior surface of the back of the eye (fundus), as recommended by international guidelines (1). They recommend that patients with dry AMD and no symptoms be examined every 6-24 months. AMD patients with new symptoms undergo visual acuity tests, retinal exam and examination of the fundus using a non-invasive imaging technique optical coherence tomography (OCT). Sometimes if more information is needed, dye is injected to image blood circulation at the back of the eye (either fundus fluorescein angiography (FFA) or indocyanine green angiography (IGA)). For assessing progression of late dry AMD autofluorescence imaging (a tool which images blood circulation without injecting dye via angiography), may usefully supplement OCT testing, but this is not yet widely available in NZ. Also noted as an additional diagnostic tool is patient self-monitoring via the Amsler Grid Test which is used to detect distortions in vision.

As mentioned earlier, genetic factors may explain as much as 80% of AMD. However genetic testing for risk stratification for use for future diagnostic options remains in the research sphere (1).

3.5 Current diagnosis

3.5.1 Amsler Grid and self-testing

While important as a prompt for patients to get additional testing, a systematic review by Faes et al found that the traditional Amsler grid test is not a sufficiently reliable tool for monitoring vision, with highly variable sensitivity. It did not provide precise, quantifiable measures of visual field defects, and therefore provides limited benefit as a tool for monitoring AMD (13). Additionally, the Amsler grid test is non-interactive, potentially leading to poor compliance for long-term self-testing (14).

However, self-testing and home monitoring have the potential to remove the need for medical professionals to acquire images. New self-testing technologies might approach the sensitivity of OCT examination while optimising speed and convenience. The widespread availability of smartphones today provides an opportunity to harness their capability for self-testing in the future (15). For example, an automated, computerised version of the Amsler test has been developed for use in AMD. It has been found to have high reproducibility for detection of central visual field defects on repeat testing. These central defects have been shown to correspond to anatomical findings on FA imaging (14). This demonstrates the ability of modified Amsler-type tests to improve diagnosis and early monitoring of AMD, however, they require further research and testing to assess their feasibility in the clinical context (15).

3.5.2 Optical coherence tomography (OCT)

Two systematic reviews, Castillo et al and Mowatt et al, looked at the role of OCT in the diagnosis of wet AMD highlighted that only a small number of studies assessed the performance of OCT in the diagnosis of people newly presenting with symptoms of wet AMD. Both found that OCT had relatively high sensitivity for diagnosis but moderate specificity for the monitoring of AMD. They each concluded that while very useful for diagnosis, it should not the only method available for diagnosis and monitoring of AMD, with the more invasive and expensive FFA being the 'gold standard' (16, 17).

3.5.3 Autofluorescence imaging

Recent guidelines describe autofluorescence imaging as having the potential to help identify advanced dry AMD and monitoring its progression, but note that its specific role in practice has not yet been clinically defined (39). A later systematic review by Frampton et al for the NHS found that although autofluorescence imaging is already in use in clinical practice, its accuracy in monitoring or diagnosing AMD is unclear. Evidence from high-quality prospective studies are required to obtain reliable data on its true accuracy and sensitivity (18).

3.5.4 Future diagnosis: Genetic testing

Multiple studies state that 'next-generation' genetic testing for AMD provides an opportunity to enhance diagnosis and monitoring strategies and improve the prospects of preventing vision loss in AMD (14, 19-22). An expert review by Gillespie et al noted that 'next generation' genetic sequencing is on track towards overcoming the current complications of getting a precise diagnosis of genetic ophthalmic conditions like AMD (22).

In its current state, genetic testing does not yet appear suitable for clinical practice, but this may change in the future as more evidence is found (20, 23). One study by

Consugar et al found a particular genetic test to be highly reproducible and accurate, demonstrating its potential benefit as a clinical diagnostic test for AMD (21), while Buitendijk et al found that most current tests are accurate at genotyping, but not at risk prediction (23). Current literature highlights the need for considerable further research to refine this type of diagnostic test and translate new technological findings into current clinical practice (19, 22, 23).

4. Treatment

Key Messages

- Anti-VEGF therapy has been found to significantly improve visual outcomes for patients with wet AMD, and is the best available treatment
- Bevacizumab has comparable effectiveness and safety to ranibizumab while being significantly cheaper
- Anti-VEGF treatment should be initiated as soon as abnormal blood vessel growth under the retina appears (choroidal neovascularization), preferably within a week of referral
- Aflibercept may be a better second-line agent than ranibizumab
- The potential use of ziv-aflibercept warrants further examination

4.1 New Zealand current state and rationale

Clinical guidelines recommend intravitreal anti-VEGF agents as treatment for wet AMD as they reduce the risk of progressive vision loss and improve vision for a large proportion of patients. Ranibizumab (Lucentis) and bevacizumab (Avastin) are the two anti-VEGFs funded in New Zealand. A further anti-VEGF agent, aflibercept (Eylea), is available on a named-patient basis in cases who do not respond to bevacizumab or ranibizumab.

Prior to the introduction of anti-VEGFs in New Zealand, photodynamic therapy was the main treatment for wet AMD. However, photodynamic therapy is no longer part of the standard model of care as anti-VEGFs have been found to provide significantly greater clinical benefit.

The safety and effectiveness of bevacizumab has been established in a number of trials, including the CATT study comparing bevacizumab with ranibizumab. Bevacizumab had comparable effectiveness with ranibizumab when given monthly, showing the same improvements in visual acuity and reductions in vision loss. Due to the large difference in price (Less than $100 for bevacizumab vs over $1000 for ranibizumab), bevacizumab is the first-line treatment and ranibizumab the second-line. Ranibizumab is restricted to cases where the patient does not respond to or has an adverse reaction to bevacizumab, or has had a recent myocardial infarction or stroke (1, 2).

4.2 Effectiveness of anti-VEGF therapy

A Cochrane review of 12 RCTs found that participants treated with three anti-VEGF agents (pegaptanib[83], ranibizumab, or bevacizumab) were more likely to experience improved visual acuity, less likely to lose visual acuity, and were less likely to be legally blind than participants treated with control interventions, after one year of treatment (24). The review did not suggest a significantly higher incidence of adverse events such as endophthalmitis and increased intraocular pressure with intravitreal injections compared with control intervention, highlighting their comparative safety (24).

[83] A less effective anti-angiogenic medication, not licensed in New Zealand as at Jan 2017.

The Cochrane findings are supported by a retrospective, cross sectional study by Park et al which found that three anti-VEGF agents (bevacizumab, ranibizumab and aflibercept) all had a positive impact on patients with AMD, reducing central macular thickness, sub-retinal fluid, and pigment epithelial detachment size, and all improving visual acuity (25).

This evidence is further reinforced by a cohort study by Maguire et al which found that although visual gains during the first 2 years were not always maintained at 5 years, 50% of people had a visual acuity of 20/40 or better and 10% had 20/20 vision. This would not have been attainable in times before anti-VEGFs were available (26). Interestingly, very few patients in the study continued to receive their originally assigned drug or dosing schedule between the end of year 2 and the 5-year follow up, and therefore the study provides limited evidence on the effectiveness of various anti-VEGF treatments and dosing regimens, but rather affirms the efficacy of anti-VEGF therapy overall (26).

4.2.1 Comparable effectiveness between bevacizumab and ranibizumab

Four papers, one multi-centre RCT and three meta-analyses, found bevacizumab and ranibizumab had comparable effectiveness for AMD. All four found bevacizumab and ranibizumab to have equivalent efficacy in improving visual acuity (26-31) and reducing central retinal thickness (27). Chen et al noted that ranibizumab tended to have a better anatomical outcome (28) while Wang et al noted that bevacizumab tended to result in less of a decrease in CRT (30). However, both suggested that these differences were likely to be clinically insignificant (28, 30).

4.2.2 Aflibercept as potential second-line treatment

Aflibercept has a longer half-life in the eye than bevacizumab or ranibizumab (32), and in the VIEW2 trial gave comparable results at 8 weekly dosing to ranibizumab at 4 weeks (33). If costs are similar then aflibercept is likely to be the more cost-effective option through lower numbers of injections being required.

A New Zealand-based study by Squirrel et al investigated the effect of switching wet AMD patients who were nonresponsive to bevacizumab or ranibizumab to aflibercept (29). It concluded that intravitreal aflibercept is a potentially viable treatment strategy for patients with 'uncooperative' AMD, nonresponsive to bevacizumab or ranibizumab, and indeed may be a better second-line agent following bevacizumab than ranibizumab. It demonstrated a trend towards visual improvement and the beneficial effect was maintained at 48 weeks. Furthermore, 62% of patients had resolution of what had previously been recalcitrant subretinal fluid at the end of the study. It also noted no significant adverse events as a result of the treatment. Overall, the study provides longer term outcome data on the effect of switching to aflibercept in patients who have shown an inadequate anatomical response to either bevacizumab or ranibizumab (29).

Early findings from the PLANET study are suggesting that aflibercept is important in the treatment of polypoidal choroidal vasculopathy (33a). This sub-type of AMD is more common in those of Asian or Polynesian descent. If confirmed this would be an important added benefit of having access to aflibercept, particularly for the Auckland and Counties Manukau populations.

4.2.3 Ziv-aflibercept

Ziv-aflibercept[84] is a version of aflibercept formulated for delivery in cancer treatment. In an analogous situation to bevacizumab compared with ranibizumab, ziv-aflibercept has been trialled as an intravitreal treatment, through splitting the larger vials (34, 35). Initial concern around the osmolarity of the formulation do not appear to have been borne out, with small trials of the treatment in the Middle East and Asia being reported with apparently good results (34-38). This is an exciting recent development which might offer significant savings to the New Zealand health system, dropping the cost of aflibercept from ~$1650 to ~ $85 per treatment.

4.3 Cost-effectiveness comparisons

Two cost-effectiveness analyses aimed at determining whether ranibizumab or bevacizumab conferred greater value for patients with AMD. Both concluded that bevacizumab was a more cost-effective option than ranibizumab (39, 40). A separate analysis on the economic literature follows (Appendix F) with more detail on the cost-effectiveness findings.

4.4 Initiation of treatment

There appears to be a lack of consistency regarding when anti-VEGF treatment should be initiated. New Zealand guidelines state that patients with wet AMD should be seen by a specialist within 2 weeks of developing symptoms (1). Although evidence on when anti-VEGF treatment should be initiated is not widely reported in the literature, it is assumed that a regimen should begin as soon as possible after symptoms are detected, because of the substantial vision loss that can occur if treatment is delayed. Recent European and US guidelines state that an anti-VEGF treatment regimen should begin once abnormal blood vessel growth under the retina (choroidal neovascularisation) has been detected via OCT or fundus photographs (3, 41).

4.5 Safety of reformulating bevacizumab

Potential safety concerns regarding the use of bevacizumab in AMD arise because it is only supplied in vials formulated for intravenous cancer treatment, which is over 50 times greater than the required AMD dose. Therefore, bevacizumab must be reformulated under sterile conditions into vials of appropriate dosage for intravitreal administration for AMD patients. Although the differences in safety between ranibizumab and bevacizumab are considered clinically unimportant, bevacizumab has not undergone the assessments required for marketing authorisation for AMD nor been approved for use in AMD in New Zealand (or internationally) (1). Therefore, its use in AMD remains off-label, which is the case in other countries. We note that this off-label situation is due to the manufacturing company's stipulation rather than any particular doubt as to the safety of the product for use in the eye if correctly used.

Two systematic reviews of 13 RCTs in total compared the incidence of serious systemic adverse events between AMD patients who received bevacizumab and those who received ranibizumab (42, 43). Moja et al found a higher risk of gastrointestinal disorders in patients treated with bevacizumab, but noted that the evidence was imprecise, suggesting that if a difference exists, it is likely to be clinically insignificant

[84] Ziv-aflibercept is the name adopted in the US to differentiate formulations for cancer treatment (ziv-aflibercept) from eye treatment (aflibercept). That usage is followed in this report, but note that Medsafe uses the term aflibercept to refer to both formulations.

(42). Both reviews found no clinically significant difference in serious systemic adverse events between the two treatments and therefore concluded that bevacizumab has comparable safety to ranibizumab (42, 43).

4.6 Intensity, duration and time regimen of treatment

Key Messages

- The monthly treatment regime was initially considered the gold standard and is more effective than 'as needed' treatment.
- The 'treat and extend' regime is likely superior to 'as needed' treatment
- The 'treat and extend' regime has comparable results to monthly treatment, whilst reducing the number of injections needed.

There is ongoing discussion around how often anti-VEGF treatment should be administered, and for how long treatment should continue. The CATT study compared monthly treatment with as-needed treatment (average seven doses over 12 months), finding a non-significant trend towards less favourable results with as-needed treatment. The 'treat and extend' regimen is potentially more effective than other clinical regimens. This approach is used by many ophthalmologists in New Zealand and reduces the average number of treatments patients receive compared with monthly treatment. In this regimen, the interval between treatments is slowly extended as long as response is maintained. If disease activity returns, the interval between treatments is reduced (1).

Regarding duration, European guidelines suggest that anti-VEGF treatments be used only for as long as a response is maintained (3). If there is no substantial improvement in vision after the induction period of three anti-VEGF treatments, treatment may be discontinued, or a switch to a second-line anti-VEGF. If the patient is responding, regular treatment is continued until the eye becomes dry, but is stopped once there is evidence of persistent deterioration in visual acuity or identification of anatomical changes in the retina that indicate inadequate response to therapy (1).

Regular monthly administration of anti-VEGFs is an established gold standard approach, but is costly. Consideration of other treatment regimens such as 'treat and extend' or 'as needed' may assist in relieving the current burden of anti-VEGFs on the health system (44, 45).

4.6.1 Fixed interval versus 'as needed'

A systematic review by Schmucker et al investigating the efficacy of 'as needed' versus regular monthly treatment regimens found that, over 2 years, the total number of intravitreal injections required by the patients in the 'as needed' arms were, on average, 8.4 fewer than those having monthly treatment (44). 'As needed' treatment resulted in small decrease in average visual acuity which may not be clinically meaningful, and also a small increase in risk of systemic adverse events for patients treated 'as needed' (44).

This is affirmed by another systematic review by Peden et al and a later retrospective chart review study by Jiang et al which both suggest that a fixed-interval dosing regimen produces better long-term visual acuity outcomes compared to sporadic, as-

needed therapy (46, 48). The systematic review also found that monthly treatment produced better visual acuity outcomes than a less frequent quarterly fixed-interval regimen (46). Recent guidelines also state that while the 'as needed' regimen has comparable safety compared with 'fixed continuous' regimen over one year of treatment, it does not maintain initial visual gains over longer periods of time - and is therefore recommended with caution as it may be slightly less effective than other approaches (41).

4.6.2 'Treat and extend' versus 'as needed'

The systematic review by Chin-Yee et al evaluating the efficacy of 'as needed' versus 'treat and extend' regimens for the treatment of AMD found that while both regimes were beneficial, the treat and extend group showed significantly greater improvements in visual acuity compared to the 'as needed' group. This suggests the superiority of the treat and extend regimen to as needed treatment in a 12-month period (45).

4.6.3 'Treat and extend': Future directions

While current guidelines recommend a fixed-interval, continuous regimen for anti-VEGF therapy (ranging from 4 to 8 weeks), they acknowledge the 'treat and extend' protocol as a potentially successful alternative (3, 41). The 'Fight Retinal Blindness Study' group has demonstrated success with treat and extend regimes (49-50). They also note that earlier treatment leads to quicker control, thus driving better clinical outcomes and fewer overall injections. Similarly, not allowing the duration between injections to get too long drives better control, thus fewer injections overall and better outcomes.

A systematic review by Chin-Yee et al found that treat and extend patients received an average of 8.1 injections over one year (45) compared to monthly treatments at 12 injections over one year. This demonstrates that the treat and extend regimen does reduce the number of injections. An observational study by Arnold et al suggests it to be a good alternative to the monthly approach, with comparable visual outcomes (51), highlighting in a clinical setting it's potential to achieve good visual outcomes while decreasing the burden of treatments and follow-up visits.

Guidelines note that while 'treat and extend' is frequently used in practice, further research is necessary to reach a final consensus on the ideal treatment approach for anti-VEGF therapy (3, 41). Current evidence is limited to smaller, uncontrolled observational studies; therefore larger prospective studies including RCTs to evaluate long-term efficacy of these regimens would be desirable. Some are currently underway in Europe.

4.7 Workforce delivery

Key Messages

- With appropriate training, nurses are a viable and safe option for delivering anti-VEGF injections, and have been used to increase efficiency and capacity of services
- Collaborative, shared care with optometrists in AMD treatment has been raised as an opportunity to improve AMD care – both enthusiasm and concerns exist within the AMD community

Efficiency and cost-containment may be improved by reconfiguring the workforce model for delivery of anti-VEGF therapy. One option is a collaborative model of delivery where the patient remains under the supervision of the ophthalmologist, but injections are delivered by a suitably trained nurse, optometrist, technician or other practitioner (1).

Future models of care for further exploration include these may include collaboration with community optometrists and expanding the nursing role. In particular, experiences from New Zealand suggest that offering collaborative 'one-stop' clinics, where patients are assessed by ophthalmologists and receive injections from nurses is likely to be a safe and effective model of AMD care (47).

4.7.1 Nurse-delivered anti-VEGF treatment

4.7.1.1 Need for training

Three recent studies, including a NZ-based safety audit by Samalia et al at the Greenlane Clinical Centre and a systematic review, looked at the feasibility and impact of nurses delivering anti-VEGF treatment in a clinic environment, in the light of increased demand for treatment. They found that an appropriate training programme, including courses and direct supervision by consultants, is critical to ensuring the success of nurse-led delivery of anti-VEGFs (52, 55, 56).

4.7.1.2 Improved capacity and efficiency

Delivery of anti-VEGFs by nurses was shown to improve short-term capacity and subsequently ease the burden on the services (45, 52, 56), as well as make better use of medical staff time and release physicians for other clinical work (52, 56). Studies also stated that nurse delivery of anti-VEGF therapy could lower the cost per treatment (52, 55, 56), as long as nurses are sufficiently trained and time spent per patient does not increase (55).

4.7.1.3 Safety

Studies by Asrin-Rasul et al and Michelotti et al deemed nurse delivery of anti-VEGFs safe, citing a very low rate of complications such as endophthalmitis and raised intraocular pressure (55, 56). This rate was comparable to that of physician-delivered anti-VEGF therapy (52, 55). Overall, studies note that nurse-delivered anti-VEGF therapy appears to be a feasible option to meet the increasing demand for anti-VEGFs whilst minimising costs and increasing capacity without compromising safety (52, 55, 56). However, the systematic review by Michelotti et al raised the need for more studies to explore and compare implementation and training strategies (55). The Royal

College of Ophthalmologists recently changed its anti-VEGF delivery policy, now stating that the delivery of anti-VEGF agents by non-physician health care practitioners is reasonable, given that appropriate training and supervision are provided (55).

A NZ-based study by Botha et al in Palmerston North investigated the implementation of a senior nurse-led review clinic to address the significant rise in anti-VEGF treatments (57). The clinic enabled timely review of AMD patients, despite the increase in the number of patients requiring treatments and monitoring (57). Improved timeliness in access for AMD patients is likely to reduce the chance of vision loss that occurs while awaiting anti-VEGF treatment (57). These findings suggest another area where nurses might play a role in the AMD model of care.

4.7.2 Collaboration and shared care with optometrists

A qualitative study by Townsend et al on attitudes towards shared care for AMD found enthusiasm among health professionals and service users for optometrists and ophthalmologists to work collaboratively in monitoring AMD patients. This was seen as having potential to relieve burden on hospital eye services and provide a more patient-centred option (58). Conversely, service users and ophthalmologists raised concerns over variable standards of care related to optometrist competency and the potential for referral delays if stable AMD became active again and required retreatment. However, specialist training for optometrists under ophthalmologist supervision may have the potential to both address competency issues and improve trust and communication necessary for successful collaborative shared care (58). In New Zealand optometrists undergo a five year training programme and 65% are able to prescribe medication, so are relatively advanced compared to optometrists operating elsewhere (see section 4.4.1.3 in the main document).

4.7.3 Genetic treatments

A US review noted that around 5 percent of the human population carries genetic mutations that can cause inherited retinal diseases (53). Gene therapy could possibly be used to replace a deficient gene and restore function. For 'wet' AMD gene therapy has the potential to alter the production or function of existing cell proteins (e.g. vascular endothelial growth factor), which trigger conditions in the eye that can lead to vision loss (54). While exciting possibilities exist, no impact on current treatment modalities are expected over the next ten years.

5. Low vision rehabilitation: What assists people with AMD to live independent lives?

Key messages

- Even a single low vision rehabilitation visit, with clear explanation and demonstration of lighting and vision aids can improve activities of daily living for people with low vision
- Mental health interventions focused on problem solving and adaptive behaviour can improve short-term depression outcomes in patients
- Further research is needed to determine how to maintain these effects over time
- Multidisciplinary interventions show promise for improving visual function among AMD patients

Low vision rehabilitation (LVR) is important for all people losing sight, whether from AMD that is not amenable to anti-VEGF therapy or from any other cause. It is an important component of the overall model of care for AMD. Currently, there is some evidence supporting the effectiveness of low vision rehabilitation for optimising visual activity and improving ability to cope with low vision (1). There is a lack of clarity regarding which approaches are most effective, and a need for further research into the optimal level of intervention intensity, and the most appropriate model of delivery.

The Ministry is developing a Low Vision Rehabilitation Services Strategy aiming to improve low vision rehabilitation services in New Zealand (59). The Strategy supporting documentation (60) notes the relative effectiveness of low vision rehabilitation.

Maculopathy affects central vision, and as the macula is used in light conditions (if there is insufficient light the peripheral retina is used), a combination of light, magnification and contrast enhancement are the most common requirements for assisting a patient to use their remaining vision more efficiently. The role of LVR is to assess the patient's requirements for each of these factors, which can vary from patient to patient. The impact of other co-morbid conditions both optical and medical are also checked, as well as the individual patient's requirements in daily activities to keep them independent at home, work and within their community.

As each patient will have a different set of requirements a range of equipment may need to be demonstrated. Training in the use of the aids as well as in other strategies for overcoming the effects of AMD (and other pathologies) will be carried out. Patient may be linked to other LVR providers such as peer support groups, Low vision therapists or appropriately trained occupational therapists can provide assistance for modifying home and work environments – eg lighting – and can do home assessments and support or Blind Foundation if appropriate. (60)

The technology of low vision aids has advanced hugely in the digital era – with even basic e-readers and IPads able to act in that role. There is already wearable text to speech readers with object and face recognition available and in use. As the research

and development of technology continues, there will be more advancements at a higher cost than traditional magnifiers and lamps.

A brief review of relevant recent papers was carried out to supplement the findings of these reports, though these tend towards the research end of the spectrum, with little available on the effectiveness for the different components of general low vision rehabilitation clinic delivery noted above.

5.1 Viewing training and adaptive strategies

Adaptive strategies and training is an area of low vision rehabilitation identified in the literature as holding potential benefit for AMD patients. A systematic review by Gaffney et al found that eccentric viewing training and steady eye strategies can improve near visual acuity, reading speed, and performance of daily activities for people who have experienced central vision loss, but did not find an influence of training on distance visual acuity or quality of life (61). It highlighted the need for further research to establish the true potential and cost-effectiveness of including adaptive strategies such as eccentric viewing into clinical practice for AMD (61).

A further meta-analysis by Hamade et al of similar low vision rehabilitation strategies including microperimetry training, microscopes teaching program and eccentric viewing training, similarly found an improvement on reading speed, noting that the eccentric viewing training program showed the greatest improvement. It also found no improvement in depression scores as a result of these strategies (62). These technologies are not in general use in practice.

5.1.1 Psychosocial rehabilitation to address depression

Between 10% and 30% of patients with AMD develop depression, which is associated with greater levels of disability, medical costs, and mortality due to factors such as poor adherence to medication (63). A systematic review by Cimarolli et al of clinical trials testing mental health interventions among older AMD patients found them to have positive short-term results, especially those incorporating problem-solving techniques and behavioural activation (structured treatment aiming to increase adaptive behaviour) (62). In particular, one RCT by Rovner et al compared an intervention combining behaviour activation with traditional low vision rehabilitation to one combining supportive therapy (non-directive emotional support) and low vision rehabilitation. It found that the former showed greater potential to prevent depression and enable subjects to remain socially engaged. It was also associated with greater improvements in functional vision compared to the supportive therapy intervention (63).

However, these effects did not appear to be maintained over time and additional studies are needed to determine optimal dosage or additional sessions necessary to prevent depressive symptoms long-term (64). It concluded that screening for depression should be incorporated in regular practice, given the availability of relatively simple and valid tools (64).

5.1.2 An integrated, multidisciplinary approach

Another area of low vision rehabilitation explored in the literature was integrated multidisciplinary interventions aimed at targeting a range of physical and mental health outcomes for AMD patients. The aforementioned systematic review by Cimarolli et al found that integrated mental health and low vision interventions halved the

incidence of depressive disorders compared to standard outpatient low vision rehabilitation in patients with AMD (64). It concluded that promoting interactions between services such as ophthalmology, optometry, rehabilitation, psychiatry, and behavioural psychology may help to improve delivery of care, prevent depression, and achieve better outcomes for AMD patients (64).

This was also outlined in an earlier retrospective study by Amore et al., which investigated a rehabilitative approach that included psychological counselling from psychologists, examination by an ophthalmologist, low vision devices training by an orthoptist, prescription of low vision aids, and orientation and mobility lessons (65). They found that attending a customised low vision intervention based on the multidisciplinary approach seems to be effective for improving visual function in AMD (65).

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6.1 Updated literature review references

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7. Literature search keywords

Prevention	Diagnosis	Treatment	Rehabilitation	AMD
► Nutrition* ► Supplement* ► AREDs ► Vitamin ► Minerals ► Antioxidant ► Diet* ► Primary prevention ► Secondary prevention ► Minerals ► Carotenoid ► Smoking ► Cessation ► Quit*	► Detect* ► Early ► OCT ► Optical coherence tomography ► SBM ► Stereo biomicroscopy ► FFA ► Fundus fluorescein angiography ► IGA ► Indocynine green angiography ► AF ► Autofluorescence imaging ► VA ► Visual acuity test ► Amsler grid test ► Genetic ► Direct to consumer genome ► Risk ► Predict* ► Stratif*	► Anti-VEGF ► Anti Vascular Endothelial Growth Factor ► Treatment ► Therapy ► Injection ► Bevacizumab ► Avastin ► Ranibizumab ► Lucentis ► Pegapanib ► Aflibercept ► Cost effective* ► Effective ► Initiat* ► Dosing ► Regime	► Low vision care ► Low vision rehabilitation ► Workforce ► Nurse delivery ► Nonphysician ► Collaborat* ► Anxiety ► Depression ► Counsel* ► Psychosocial ► Psychologist ► Intervention ► Equipment ► Modification ► Device ► Training ► Exercise ► Eccentric viewing training ► Visual acuity ► Multidisciplinary	► Age related macular degeneration ► Age related macular degeneration ► Macular degeneration ► ARMD ► AMD

Appendix F Economic evaluations

Reference (Author, Year, Setting)	Methodology, Model Type, Perspective	Patient States	Transition Probabilities & Patient Utilities	Costs	Primary Outcomes & Sensitivities	Conclusions
Anti VEGF cost effectiveness						
Elshout et al. 2014 Netherlands The cost-utility of aflibercept for the treatment of age-related macular degeneration compared to bevacizumab and ranibizumab and the influence of model parameters.	▸ Monte Carlo simulation at patient level ▸ 2012 euros using Dutch CPI ▸ Discounting: costs 4%p/a ▸ Outcomes: 1.5% p/a ▸ Timeframes: 2 and 5 year ▸ Societal perspective.	▸ No patient states ▸ Average age 77.7yrs ▸ Baseline Visual Acuity average 58.6.	1. VA in best-seeing eye.	Direct: ▸ Diagnostic, treatment (injection + administer), outpatient visits Indirect: ▸ Transportation, home care, nursing home QOL, utility.	Results were dependent on: ▸ Whether one or two eyes were included ▸ The time horizon of simulation ▸ Whether low vision care costs were included.	▸ Aflibercept is a cost-effective treatment for AMD over ranibizumab ▸ Aflibercept is not a cost effective treatment when compared to bevacizumab.
Hurley et al. 2008 US Cost-effectiveness of ranibizumab for neovascular age-related macular degeneration.	▸ Markov model ▸ 2004 USD ▸ Discounting: costs & QALYS 3%p/a Timeframes: 1 year cycle modelled patients for up to 10 years ▸ Societal perspective (caregiving costs) and health care funder's perspective.	▸ VA based, log-MAR scale, 5 states: ▸ 90 ▸ 75 ▸ 60 ▸ 45 ▸ 30 This corresponded to the number of letters read as >85, 70-80, 55-65, 40-50, <35 ▸ Each year either: ▸ VA gain 15 letters, no change, lose 15, lose 30, death ▸ Age - 67 and 77 year old women and men separated by gender.	▸ VA in best seeing eye ▸ Utilities for 5 states: 0.89, 0.89, 0.81, 0.57, 0.52. (Brown) ▸ Transition probabilities based on MARINA ▸ Patients treated as per MARINA dosing for first 2 years then every 3 months after that.	Direct: ▸ Treatment (drug, dispense, admin), medical care for AMD, medical care for vision loss, cost of caregiving (excludes patient type, travel).	▸ Cost-effectiveness of ranibizumab compared with no ranibizumab over 10 years. Ranging costs of treatment from Drug price ($1950) to cost of Avastin ($50) ▸ Results were dependent on including/excluding caregiver costs Outcomes Measures: ▸ Prob. of blindness, ▸ No. of QALY gained ▸ Direct costs.	▸ Probability of blindness reduced over 10 years when ranibizumab was successful compared to no treatment ▸ From a societal perspective, ranibizumab was cost-saving ▸ From a health care funder's perspective, ranibizumab was an efficient treatment when it cost less than $1000 per dose.

Reference	Study Background & Model Type	Model Parameters: Patient State	Transition Probabilities, Utilities	Costs	Outcomes, Sensitivity, Issues	Conclusions
Patel et al. 2010 US Cost-utility analysis of bevacizumab versus ranibizumab in neovascular age-related macular degeneration using a Markov model.	▸ Markov Model ▸ 2007 USD ▸ Discounting: 3%p/a Timeframes: 3 month ▸ cycles over 20 years ▸ US payer perspective.	4 health states: ▸ Stable vision ▸ Improved vision ▸ Worsening vision ▸ Death.	▸ Utilities: 0.57, 0.81, 0.52, 0 respectively. Adjusted from BROWN ▸ Transition probabilities for ranibizumab taken from MARINA and ANCHOR trials ▸ Probabilities for bevacizumab from four published studies ▸ Patients treated with monthly injections.	Direct: ▸ Treatment (physician visit, drug cost, diagnostic tools) Inputs: ▸ Costs, transition probability, utilities.	Primary outcome measure: ▸ CER - incremental cost to obtain one additional QALY gained Sensitivity analysis: ▸ Drug costs.	▸ Outcome: Based on a WTP defined at $50,000 per QALY gained, bevacizumab was cost-effective versus ranibizumab 95% of the time because of lower acquisition costs and increased efficacy (QALY gained).
Raferty et al. 2007 UK Ranibizumab versus bevacizumab: modelling cost effectiveness.	▸ Markov Model ▸ Discounting: 3.5% p/a costs and utilities ▸ Timeframes: 3 month cycles over 10 years or less depending on life expectancy.	▸ 6 states (not defined) ▸ 5 defined by a range of 3 lines of VA and a death state ▸ Patients started in second less severe state to allow for improvement or worsening ▸ Two groups of patients were modelled, those gaining and those losing VA ▸ Age - 75yrs -85yrs or death.	▸ Utilities: based on BROWN ▸ Transition probabilities based on relevant ranibizumab trial ▸ Patients treated with monthly injections.	Direct: ▸ Treatment (cost per injection, admin costs were estimated).	▸ How much more effective would ranibizumab have to be to justify its higher price?	▸ For ranibizumab to achieve an acceptable cost effectiveness relative to bevacizumab it would have to score 2.5 times better in terms of visual acuity. This seems highly unlikely given the similarity of the molecules and the limited data available.
Stein et al 2013 US Cost-effectiveness of bevacizumab and ranibizumab for newly diagnosed neovascular macular degeneration.	▸ Markov model 2012 USD ▸ Discounting: 3%p/a. ▸ Timeframes: 20 years ▸ Hypothetical cohort of patients over 80 years.	▸ 11 states: 20/12-20/20 20/25-20/40 20/50-20/80 20/100-20/160 ≤20/200 ▸ Endophthalmitis, venous thrombotic event, myocardial infarction, cerebrovascular accident, vascular death, other death.	▸ Utilities: 0.92, 0.84, 0.76, 0.66, 0.61 (BROWN) ▸ Treatment frequency: tested monthly and as needed ▸ VA in best-seeing eye.	Direct: ▸ Eye care provider visits, monitoring, treating side effects, blindness, admin of treatment, drug costs.	▸ Monthly vs as needed bevacizumab and ranibizumab Sensitivity: ▸ Costs, ▸ Utilities ▸ Health state transitions.	▸ In conclusion, bevacizumab administered on an as needed dosing schedule confers the greatest value ▸ Ranibizumab dosed monthly or as needed confers considerably less value than bevacizumab, mainly due to its considerably higher per-injection cost.

Reference	Study Background & Model Type	Model Parameters: Patient State	Transition Probabilities, Utilities	Costs	Outcomes, Sensitivity, Issues	Conclusions
Prevention – Vitamin and Antioxidant Therapy						
Hopley et al 2004 Australia (Great Britain data) Cost utility of screening and treatment for early age related macular degeneration with zinc and antioxidants.	▸ Multi-cohort decision analytic model ▸ PPP to convert AUD to pound ▸ Discounting: QALYS and costs at 6%p/a. Timeframe: 7 years ▸ Third party payer perspective.	Health states: used AREDs categories. ▸ 1: normal macula to a few small drusen ▸ 2: Multiple small drusen, single or non-extensive intermediate size drusen, pigment abnormalities ▸ 3: Absence of advanced AMD in both eyes, with at least one large drusen at macular centre, or extensive intermediate drusen or geographic atrophy (GA) not involving the central macula ▸ 4: No advanced AMD in one eye, with vision impairment from AMD in fellow eye.	▸ VA in best seeing eye ▸ Utility: BROWN. ▸ Model based on data from the AREDs16 and the Blue Mountains Eye Study ▸ Treatment frequency: costs based on 2 and 4 treatments per person, per year.	Direct: ▸ Schedule fees (Aus. Medicare Benefits schedule data), zinc and antioxidant formulations (Aus. market price), repeat population screening was modelled to occur every 5 years.	Aim: ▸ To assess the cost effectiveness of high dose zinc and antioxidants for delaying and reducing the progression of early age related macular degeneration (AMD) Sensitivity ▸ Monthly treatment (zinc and antioxidants) costs ▸ Utility value ▸ QALY discount rate ▸ Real discount rate ▸ Screening costs.	▸ The rates of progression of early to late AMD can be reduced by high dose supplements, but require screening ▸ Targeted screening should arguably be part of routine optometric and ophthalmic practice ▸ Mostly beneficial for 65+ age group.
AREDs 2001 Age-Related Eye Disease Study Research, G, A randomized, placebo-controlled, clinical trial of high dose supplementation with vitamins C and E and beta carotene for age-related cataract and vision loss	▸ Major clinical trial sponsored by the National Eye Institute				▸ AREDs was designed to learn more about the natural history and risk factors of age-related macular degeneration (AMD) and to evaluate the value of supplementation to delay progression to wet AMD.	▸ Results from the AREDs showed that high levels of antioxidants and zinc significantly reduce the risk of advanced AMD and its associated vision loss. ▸ Estimated as many as 300k cases of advanced AMD could be avoided in the U.S. over 5 years if all eligible patients took vitamin supplements containing antioxidants plus zinc.

Reference	Study Background & Model Type	Model Parameters: Patient State	Transition Probabilities, Utilities	Costs	Outcomes, Sensitivity, Issues	Conclusions
Rein et al 2006 U.S Cost-effectiveness of Vitamin Therapy for Age-Related Macular Degeneration.	▸ Computerized, stochastic, agent-based model. 2003 ▸ Discounting: 3%p/a Timeframes: Up to 50 years (50-100 years old or until death). ▸ Costs taken from health care perspective.	Five states: ▸ 0 = No abnormalities 1 = Large drusen or RPE abnormalities in one eye/both. ▸ 2 = Drusen in both, RPE in both, or one eye of each ▸ 3 = At least large drusen in one eye ▸ 4 = Large drusen and RPE abnormalities in both eyes.	▸ Progression probabilities between states 1-4 and from those states to GA and choroidal NV (AREDs). ▸ AMD progression based on a joint assessment of both eyes until the patient's first eye progressed to advanced AMD, after which the model simulated disease progression in each eye independently.	Direct: ▸ Vision related medical care, vision related nursing home placements and total costs. Inputs: ▸ Percentage of patients who enter each state, percentage who progress to GA, percentage who enter low vision services Excluded: ▸ Time of caregivers, lost productivity.	Outcome measures: ▸ Extent of disease progression. ▸ Years and severity of visual impairment. ▸ Cost of ophthalmic care and nursing home services ▸ QALY Sensitivity: ▸ cost of vitamins ▸ discount rate Limitations: ▸ Excludes costs of caregivers, social assistance, rehabilitation, assistance payments, and lost productivity.	▸ Compared with no therapy, vitamin therapy yielded a cost-effectiveness ratio of $21,387 per QALY gained and lowered the percentage of patients with AMD who ever developed visual impairment in the better seeing eye from 7.0% to 5.6%.
Further Economic Evaluations						
Deloitte Access Economics 2016 New Zealand Socioeconomic cost of macular degeneration in New Zealand.	▸ Report on economic cost of vision loss from AMD, so that action can be taken to eliminate blindness and vision loss. ▸ Cost-effectiveness of anti-VEGF treatment	Log MAR scale used in better seeing eye ▸ No AMD and early – 6/3 to 6/9.5 ▸ Mild - <6/12 to 6/18 ▸ Moderate - <6/18 to 6/60 ▸ Severe (blindness) - <6/60.	Disability weights ▸ Mild – 0.011 ▸ Moderate – 0.060 ▸ Severe – 0.225 (table 8.1).	▸ Treatment costs (costs may be underestimated as they exclude administration) ▸ Other financial costs (productivity, caregiver time)	▸ Total cost of vision loss due to AMD. ▸ Total cost of blindness.	▸ The total cost of vision loss due to AMD in New Zealand was estimated to be $391.1 million in 2016, comprising $89.6 million in economic (financial) costs and $301.5 million in loss of wellbeing costs.
Deloitte Access Economics 2011 Australia A clear outlook on Age-related Macular Degeneration.	▸ Data converted to 2009 Prices using historical health inflation.	Mainly used AREDs classification scale ▸ No AMD – AREDs 1 ▸ Early – AREDs 2 ▸ Early (expanded) – AREDs 3 ▸ Late – AREDs 4.	▸ MARINA and ANCHOR studies for changes in VA. ▸ Risk of progressing from early to late was estimated by AREDs group. 1. Association of maximum drusen size and area. 2. Low freq. of RPE	▸ Costs: AIHW 2004-2005 ▸ Health system expenditure - based on health system data from Australia Institute of Health and Welfare. ▸ These include GP appointments, nursing homes, health admin		

Reference	Study Background & Model Type	Model Parameters: Patient State	Transition Probabilities, Utilities	Costs	Outcomes, Sensitivity, Issues	Conclusions
			depigmentation and/or geographic atrophy in the absence of decrease retinal pigment 3. Large drusen in both eyes is a strong risk factor.	costs etc. ▸ Other financial costs: Low vision aids, cost of care, DWL, productivity losses (limited).		
Schmier & Levine 2016 US. Economic Impact of Progression of Age-related Macular Degeneration.	▸ Literature review. ▸ Economic burden of AMD by disease stage.			Costs Considered ▸ **Drusen:** Outpatient monitoring (direct medical cost) ▸ **Dry**: Outpatient monitoring, vitamins are an out of pocket cost for most people (direct medical). Living aids, home modification (limited impact) (direct non-medical). Care-giving and loss of productivity (indirect) ▸ **Wet:** outpatient monitoring, treatment (direct medical) Living aids, home modifications (DN-M). Care-giving and loss of productivity (indirect).	▸ Costs of AMD across VA levels: These increased with deteriorating VA, with the cost of caregiver time increasing the most.	▸ Conclusion: diagnosis of wet AMD rather than deterioration of VA is the primary driver of costs.
Brown et al. 2000 Utility values and age-related macular degeneration.	▸ Cross sectional study. ▸ Utility values for health states of AMD	States: 1. (20/20-20/25) 2. (20/30-20/50) 3. (20/60-20/100) 4. (20/200-20/400) 5. Counting fingers to light perception.	▸ Patients were measured empirically using time trade-off and standard gamble methods. ▸ TTO utility of 5 states: 0.89,0.81,0.57,0.52,0.40 ▸ BROWN have shown that the utilities associated with ophthalmic disease are most highly correlated with visual acuity in the better seeing eye and exhibit good retest reliability.			▸ Establish utility values for patients with AMD. ▸ Those in G1 willing to trade 11% of their remaining life for perfect vision. G5 60% of their lifetime.

Reference	Study Background & Model Type	Model Parameters: Patient State	Transition Probabilities, Utilities	Costs	Outcomes, Sensitivity, Issues	Conclusions
Boyer et al 2007 Subgroup Analysis of the MARINA Study of Ranibizumab in Neovascular Age-Related Macular Degeneration.	▸ MARINA ▸ Ranibizumab v PDT in treating wet AMD ▸ Type of AMD: Minimally classic or occult choroidal neovascularization ▸ Study timeframe: 24 months.		▸ Monthly treatment intervals.		Outcome measures: ▸ Analysing transition probabilities between VA levels ▸ % of people gaining or losing 15 letters over 2 years.	▸ The most important predictors of VA outcomes were, in decreasing order of importance, baseline VA score, CNV lesion size, and age.
Kaiser et al 2007 Ranibizumab for Predominantly Classic Neovascular Age-related Macular Degeneration: Subgroup Analysis of First-year ANCHOR Results	▸ ANCHOR ▸ Type of AMD: classic choroidal neovascularization ▸ Study timeframe: 12 months.	▸ Comparing ranibizumab with verteporfin photodynamic therapy.	▸ Monthly treatment intervals.		Outcome measures: ▸ Analysing transition probabilities between VA levels ▸ % of people gaining or losing 15 letters over 1 year.	▸ As in the MARINA subgroups analysis, the most important predictors of VA outcome are, in descending order of importance, baseline VA score, CNV lesion size, and patient age.
Thompson 2015 New Zealand Where you live determines how well you can see	▸ Report on Avastin funding in New Zealand DHB's and the need for equitable access.		▸ Co-morbidities estimated for anyone with vision loss ▸ 2 x risk of falls ▸ 2x rate of social dependence ▸ 3x risk of depression ▸ 4-8x risk of hip fracture ▸ Significantly reduced employment.		▸ Anti VEGF outcomes of affected persons: 95% achieve stable vision 40% retain driving vision 30% gain 3 lines of vision. ▸ Wet MD if left untreated causes blindness in 75% of patients after 3 years, with 50% blind at 3 months.	▸ Considerable inequity of access to funded Avastin. It would be more equitable if a national planning strategy was developed by the Ministry of Health

Age-related Macular Degeneration

Building a better working world

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1. Introduction

This Appendix outlines the economic analysis and modelling undertaken to inform the recommendations set out in the main body of the report (see: *section 1.1*). In order to assess the potential economic impacts for patients, providers and funders, modelling of key aspects of each of the major components of the overall model of care AMD was undertaken. Modelling included estimating the costs and benefits of current care approaches to AMD in New Zealand as well as the additional potential additional costs and benefits of proposed changes to the model of care. All economic modelling was undertaken from a public payer perspective, with health-related benefits estimated using patient utility values associated with vision loss.

Three inter-connected economic models reflecting the major components of the model of care for AMD were developed:

- Model 1: Prevention, early detection
- Model 2: Intravitreal anti-VEGF treatment
- Model 3: Low vision rehabilitation.

The models were developed in an inter-connected manner to enable estimation of costs and benefits of each major component of the model of care individually, and the overall costs and benefits from the overall, end-to-end model of care.

Two modelling approaches were used in order to show the net costs and benefits for different population cohorts:

- Modelling approach 1: A well-defined, controlled population is considered, wherein a 10-year prospective cohort is simulated using a Monte Carlo approach to show potential costs and benefits arising from adjustments in the model of care. This approach enables understanding of the cost-effectiveness of each component of the model of care for a defined cohort over time
- Modelling approach 2: In order to estimate the total costs and activity load on the system including allowing for ageing population pressures and the effects of mortality, a 20-year time series was modelled.

Assumptions in each model vary based on estimated demand, intervention effectiveness and how interventions are provided (e.g., by what type of workforce). Base case, scenario and sensitivity analysis of each component was undertaken to show potential future states. The assumptions and inputs used in modelling were informed by economic evaluations of AMD, current New Zealand AMD data, stakeholder interview and workshop feedback.

The specific questions guiding the economic modelling undertaken are listed in Table 1 – shown for each of the major components of the overall model of care.

Table 1: Key modelling considerations

Detection/ Prevention	Treatment	Rehabilitation
► Is the use of AREDS2 to treat patients with mid-late dry AMD a cost effective intervention? ► What are the implications of delays in time to first treatment?	► Would a different mix of therapeutic products provide better cost-effectiveness? ► Would a different treatment schedule provide better cost-effectiveness? ► Would a different mix of providers of treatment provide better cost-effectiveness? ► What are the implications (e.g., clinical benefit; workforce; costs) of constrained treatment frequency and access? ► What are the implications (e.g., workforce; costs) of moving to more nationally consistent treatment rates? (See: *Appendix C*)	► What are the costs and benefits of low vision rehabilitation services? ► What are the implications of moving to more nationally consistent access to low vision rehabilitation services?

1.1 Purpose

The purpose of this Appendix is to:

- Set out the methodology used for modelling
- Describe the current state of AMD in New Zealand and the related costs to the health system
- From an economic perspective, determine overview the 'case for change' in certain components of the current model of care (e.g., capacity constraints, technical inefficiencies and/or potential to improve patient outcomes)
- Describe the costs and benefits of different model of care scenarios
- Demonstrate the acknowledged demand impacts of an ageing population on the current model of care and associated resource use, and how demand might be better met as a result of the proposed future model of care.

2. Economic evaluations

A number of AMD economic evaluations have been conducted internationally (see Appendix F). One New Zealand specific evaluation of the economic and societal costs of AMD has been identified (Deloitte, 2016).[85] Deloitte's evaluation focused on the economic impact of AMD in New Zealand and analysed the cost-effectiveness of some areas in the model of care such as anti-VEGF injections and timely/adequate treatment. Some of their key findings included:

- Total cost of vision loss from AMD was estimated at $391.1m in 2016
- Cost-effectiveness of using anti-VEGF treatments (compared to no treatment) was estimated at $5,803 per Disability Adjusted Life Year (DALY) averted
- Cost-effectiveness of timely and adequate treatment was estimated at $8,210 per DALY averted
- Investing $4.9m in awareness and education would lead to a $13.5m benefit in the year modelled: 2016.

The majority of international evaluations of AMD have been cost effectiveness or cost utility studies, and have focused on the relative benefits (e.g., Quality Adjusted Life Years [QALYs] gained) of different therapeutic treatment strategies (e.g., relative cost-effectiveness of different therapeutic products for 'wet' AMD). Key findings across studies include:

- Bevacizumab has been generally found to be cost effective compared to ranibizumab and aflibercept because of lower acquisition costs and comparable treatment efficacy
- Bevacizumab administered on a treat and extend dosing schedule appears to provide the greatest value (e.g., incremental costs and QALYs gained)
- If non-responsive to bevacizumab, aflibercept may have more chance of obtaining a treatment response than ranibizumab
- Wet AMD rather than deterioration of visual acuity is the primary driver of costs. This is driven by anti-VEGF costs, increased outpatient monitoring and caregiver time.
- Vision loss through AMD increases the risk a person will suffer a fall(s), depression, hospitalisations, and will require long-term care either in the home or in institutional facilities (e.g., Age-Related Residential Care).

[85] Note that societal costs are out of scope for this report.

3. Methodology and assumptions

3.1 Data sources

The following data sources have been used in economic modelling:

- The National Minimum Dataset (NMDS) and National Non-Admitted Patient Collection (NNPAC). These datasets were used to estimate the treatment population - NMDS using those with the ICD-10 code 'H353 – Macular degeneration', and NNPAC using those with a purchase unit code 'S40007 – Intravitreal injection'
- DHB questionnaires – each DHB was asked to identify their proportion of AMD outpatients as NNPAC only records the intravitreal injection so it was necessary to estimate those patients who are receiving injections for other reasons such as diabetic macular oedema (DMO) and retinal vein occlusions (RVO)
- PHARMAC Cost Resource Manual version 2.2 was used as a source for various workforce costs
- Brown et al. was used to estimate utility values for varying AMD statuses.[86]
- Pharmaceutical costs were sourced from PTAC estimates and workshop participants as noted in the main report. This are only indicative, and may be further confounded by any confidential rebates, caps and other features of agreements on pharmaceuticals between PHARMAC and drug suppliers.

3.2 Model approach

Two approaches were used for economic modelling of AMD presented in this Appendix. The first approach uses a simulation method to explore what happens over the course of 10 years for a single, well-defined cohort. The second approach uses a time series method to estimate disease burden, treatment sessions, and costs for the total AMD population over the next 20 years.

3.2.1 Model 1: Simulated prospective cohort

This modelling approach simulated a 10-year prospective cohort using Monte Carlo simulation to capture the prognosis of AMD and to assess the impact of different models of care on costs and patient outcomes in a controlled environment.

3.2.1.1 Inputs:

- Cohort initial year (default 2016), runs for 10 years from the chosen year and sets the size of the population according to the estimated population of the year selected

[86] Brown GC, Sharma S, Brown MM, Kistler J. Utility Values and Age-related Macular Degeneration. Arch Ophthalmol. 2000;118(1):47-51.

- 2016 estimated AMD 65+ population (simulated Gaussian value using 71,000 as a starting point[87])
- Standard deviation of AMD 65+ population (default is 1,000 to account for the ranges found in literature)[88,89,90]
- Number of iterations (default is 100 to ensure randomness does not play too large a role in the estimation)
- Short time to treatment (default TRUE, if FALSE it means that there is a higher proportion who have fallen too far in visual acuity (VA) before reaching the treatment stage. It is set at a 5% higher progression to blindness due to slow treatment)
- Treatment schedule:
  - 'Constrained' - this characterises the current system where there are a small number of patients who do not receive successive treatments within a timely follow-up period, leading to need for slightly extended treatment as the time period between their treatments impacts on their clinical outcomes (this is the default or base case scenario)
  - 'Slow access' which means more injections are needed for treatment as clinical benefit is impacted by delays in access to treatment
  - 'Monthly' which is every month similar to Australia
  - 'Treat and extend / strict PRN' which is considered by clinical stakeholders to be the current optimal treatment strategy
- Second line treatment (default is 'ranibizumab' as per current treatment protocols. Scenario testing included setting 'aflibercept' as second line treatment, with the assumption that on average one less injection is needed to be as effective as ranibizumab)[91,92]
- Addition of 'noise' to initial prevalence (default FALSE, if TRUE adds Gaussian variation to initial distribution of AMD status) to provide an indication of uncertainty and the impact of lower or higher prevalence rates on costs and benefits.

[87] National Health Committee. 2015. Age-Related Macular Degeneration, pp 11.
[88] Seddon JM, Chen CA. The epidemiology of age-related macular degeneration. *Int Ophthalmol Clin*, 2004. 44(4): p.17-39., and Deloitte Access Economics and M P, *Eyes on the future: a clear outlook on age-related macular degeneration*. 2011, Macular Degeneration Foundation: Sydney (NSW)
[89] National Health Committee. 2015. *Age-Related Macular Degeneration*, pp 11
[90] Deloitte Access Economics and M P, Eyes on the future: a clear outlook on age-related macular degeneration. 2011, Macular Degeneration Foundation: Sydney (NSW)
[91] Balaratnasingam C, Dhrami-Gavazi E, McCann JT, Ghadiali Q, Freund KB. Aflibercept: a review of its use in the treatment of choroidal neovascularization due to age-related macular degeneration. *Clinical Ophthalmology* 2015; 9:2355-71
[92] Schmidt-Erfurth U, Kaiser PK, Korobelnik JF, et al. Intravitreal aflibercept injection for neovascular age-related macular degeneration: ninety-six-week results of the VIEW studies. *Ophthalmology* 2014; 121(1):193-201

3.2.1.2 Assumptions

Key modelling assumptions are described in Table 2. Further notes regarding specific aspects of each assumption are described at relevant points below.

Table 2: Model assumptions

Assumption	Sub-categories	Values	Source and comments
AMD status distribution at beginning of 10-year period	Early to moderate dry	83.8%	Derived from: ► National Health Committee. 2015. *Age-Related Macular Degeneration*, pp 11. ► Seddon JM, Chen CA. The epidemiology of age-related macular degeneration. *Int Ophthalmol Clin*, 2004. 44(4): p.17-39.
	Late dry	3.5%	*As above*. Assumes only people over 65 years of age fit within this category.
	Wet	7.0%	
	Blind or atrophied	5.7%	
Progression proportions	From early or moderate to wet	2.7%	Derived from: ► National Health Committee. 2015. *Age-Related Macular Degeneration,* pp 11 ► Deloitte Access Economics and M P, *Eyes on the future: a clear outlook on age-related macular degeneration*. 2011, Macular Degeneration Foundation: Sydney (NSW) ► Seddon JM, Chen CA. The epidemiology of age-related macular degeneration. *Int Ophthalmol Clin*, 2004. 44(4): p.17-39.
	From early or moderate to late dry	1.3%	*As above*. Considers recent year-on-year treatment increases.
	From late dry to wet	10%	
	Non-response to anti-VEGF	10%	Derived from: ► Brown DM, et al, Ranibizumab versus verteporfin photodynamic therapy for neovascular age-related macular degeneration: Two-year results of the ANCHOR study. *Ophthalmology*, 2009. 116(1): p.57-65 e5. ► Rosenfeld PJ, et al, Ranibizumab for neovascular age-related macular degeneration. *N Engl J Med*, 2006. 355(14): p.1419-31.

Assumption	Sub-categories	Values	Source and comments
	Treatment to post-treatment	7.5%	5-10% of people are non-responders: ► National Health Committee. 2015. *Age-Related Macular Degeneration*, pp 21, 24. ► Zhang XY, et al, Comparison of bevacizumab and ranibizumab in age-related macular degeneration: a systematic review and meta-analysis. *Int J Ophthalmol*, 2014. 7(2): p.355-64.
AREDS2	Uptake proportion	10%	Derived from: ► National Health Committee. 2015. *Age-Related Macular Degeneration*, pp 19. ► International Council of Ophthalmology, *Age-related macular degeneration (management recommendations)*. 2011, International Council of Ophthalmology: Belgium. ► International Council of Ophthalmology, *Age-related macular degeneration (initial and follow-up evaluation)*. 2011, International Council of Ophthalmology: Belgium. ► 28,000 people per year, translates down due to 65+ age.
	Positive effect proportion	25%	
	Cost per year	$440	
	Length of effectiveness	3 years	
Treatment schedule (decay curves)	'Constrained'	Column 1	Derived from DHB returns based on number of injections and approach by practitioners – see Table 8 for the decay by injection scheme.
	'Treat and extend / strict PRN'	Column 2	
	'Slow access'	Column 3	
	'Monthly'	Column 4	
	Treatment change	5%	Effectiveness of treatments 90-95%. ► Zhang XY, et al, Comparison of bevacizumab and ranibizumab in age-related macular degeneration: a systematic review and meta-analysis. *Int J Ophthalmol*, 2014. 7(2): p.355-64.

Assumption	Sub-categories	Values	Source and comments
Utility	Early to moderate	0.95	Midpoints from Brown GC, Sharma S, and Brown MM. Utility Values and Age-related Macular Degeneration. *Arch Ophthalmol*. 2000;118(1):47-51.
	Late dry	0.85	
	Wet	0.70	
	Severe wet	0.575	
	Blind or atrophied	0.475	
Rehabilitation	Proportion reached	18%	Derived from: ► Macular Degeneration New Zealand. Macular Degeneration Facts, (n.d.). Accessed from "http://mdnz.org.nz/assets/Files/MDNZ-Macular-Degeneration-Facts-Flyer-LR.pdf" ► Similar to taking half of those treated and late dry AMD from Auckland, Capital and Coast, and Canterbury DHBs.
Discounting	Rate for costs and QALYs	3%	A discounting rate of 3% was chosen in line with economic evaluations from: ► Paulden M, O'Mahony JF, and McCabe C. Discounting the Recommendations of the Second Panel on Cost-Effectiveness in Health and Medicine. 2016, Paceomics working paper.
Current treatment workforce (% of administers, and cost per session)	Ophthalmologist	33%, $520	Derived from: ► PHARMAC Cost Resource Manual version 2.2 ► DHB/NZ Nurses Organisation Collective Agreement 2012 -2015.
	Specialist nurse	29%, $180	
	Other	38%, $260	
	Health care assistant (HCA)	N/A, $85	
Injections per 4-hour session	Without Health Care Assistant (HCA)	12	As advised by stakeholders
	With HCA	8	

- AREDS2 uptake and efficacy was modelled as a perpetual decrease in progression by splitting those who take up AREDS2 into four groups - being each of those in their first, second, and third year of AREDS2 and those post-AREDS2. On average this means an effective base case uptake of around 6%

- Utility was not adjusted for the background disutility from increasing age related to co-morbidities, given the comparisons undertaken are within the same population cohort. QALY estimates may be slightly inflated compared to analyses which did adjust for age-related morbidity
- Reductions in quality of life through the injection process, and side-effects of treatment have not been included (difficult to find any quantification of this)
- Treatment schedules involve a course of treatment with varying numbers of injections based on the regime selected – as shown in Table 3. Note that the first year is the diagnosis year – meaning that on average patients will only require 6 months of treatment. For simplicity, treatment strategy changes in terms of drug administered were only applied at the end of each year (bevacizumab to second line 5%, and second line to third line 5%).

Table 3: Modelled injection schedules

Year of treatment	Constrained	Treat and extend / strict PRN	Slow access	Monthly
One	5	6	7	6
Two	6	5	8	12
Three	4	3	6	12
Four	3	2	6	12
Five	2	1	4	12

3.2.1.3 Algorithm

1. All outputs are cleared and iterations declared are set up in a loop to execute a specified number of times (e.g., 100)
2. Iteration loop:
    a. The estimated prevalence rate is applied across the initial population, with and without noise depending on scenario being tested
    b. This gives an initial treatment population who are distributed across the initial treatment year and by drug type using a time decaying function. AREDS2 patients are distributed at this stage across those likely to progress with a decaying function across pre-AREDS2, the three years of delay (where it is being effective), and post-AREDS2. The injection schemes are then used to estimate clinic sessions for delivering the injections and associated costs in the first year. QALYs gained from interventions are also estimated based on a difference in VA between intervention and no intervention, alongside the rehabilitation population

c. Cohort loop:

   i. The simulation then runs to the next year by multiplying the AMD status groups (e.g., dry, wet) by associated transition probabilities to get the next year's statuses, with costs and QALYs calculated based on transitions between status groups and assumed impact of interventions

   ii. Within each step of the treatment schedule the previous year is moved down one until they are in their fifth year where they on average stop treatment. This balances those patients who leave the treatment schedule earlier in time due to VA dropping too low and mortality with those who receive injections for the rest of their life. Potential transitions from each drug to another drug are modelled each year. This entire step is repeated for the AREDS2 population who will follow a different progression, with costs and QALYs calculated as a difference from the main cohort

   iii. After each annual transition, injections and their costs are calculated. QALYs are also calculated as a gain above the initial state of treatment – so for the first 3 years successful treatment is equivalent to moving up a utility category (i.e., an AMD status group), and the following two years back down to the initial starting point for an individual

   iv. Rehabilitation costs and QALYs gained are calculated using a utility gain of 0.01 (further explanation of this value is given in 'Rehabilitation' below)

   v. The cohort loop is repeated for each year in the 10-year range where people progress from early and late dry to wet AMD and others finish treatment

d. The results from the cohort loop are added on top of the output tables, and then the iteration loop runs the number of times it has been set

3. The results table is then divided by the number of iterations to give an averaged simulation table across all of the iterations.

3.2.1.4 Output

- Status table and graph with total QALYs over time
- Sessions table and graph over time
- Injection cost and QALYs gained over time, and average cost per QALY
- AREDS2 and rehabilitation cost and QALYs gained over time, and average cost per QALY
- Sessions table by type of workforce administering injections and presence of a supporting healthcare assistant or nurse over time
- Sessions cost table by administration team (current state, all medical professionals, all specialist nurses, or all ophthalmologists) and presence of a supporting healthcare assistant or nurse over time.

3.2.2 Model 2: Projected AMD status, sessions, and cost

The second approach uses a 20-year time series model to assess a mixture of projected population estimates and rates and the likely impacts at a total population level resulting from changes in AMD prevalence and models of care.

3.2.2.1 Inputs

- Are the same as the first model except each year a new cohort enters the model as the New Zealand population grows and ages.

3.2.2.2 Assumptions

- Are the same as first model.

3.2.2.3 Algorithm

1. Time series loop
    a. Sets up a population of the current year (2016)
    b. Runs the first model's algorithm for each initial year and extracts the simulation averaged first transition year
    c. Iterates through each year from 2016 to 2036.

3.2.2.4 Outputs

- Projected status table with total QALYs over time
- Projected sessions table over time
- Projected injection cost and QALYs gained over time, and cost per QALY
- AREDS2 and rehabilitation cost and QALYs gained over time, and cost per QALY.

4. Detection and prevention

Economic modelling included estimating the potential impact of:

- Increased uptake of AREDS2
- Earlier detection of AMD.

As described in *Section 4.2* of this report, AREDS2 can slow the progression of AMD providing quality of life benefits for patients, and potentially some cost savings to funders through delayed need for therapeutic interventions. For modelling purposes, AREDS2 were assumed to be taken by a proportion of those who are looking likely to progress from late dry to wet AMD, and was explored in depth in the model through simulating what occurs over time.

Initial engagement with stakeholders suggested that the timeliness of access to diagnostic tests and how that impacts on time to treatment was important with patient outcomes. Further feedback from stakeholders suggests that time to detection and diagnosis is of less concern currently than the time between treatments within the current system. However, delay in detection and diagnosis will have an impact particularly in capacity constrained systems. As such, an assumption around delay in detection and diagnosis was integrated as a loss function over time on the population to estimate the potential impact of delay. Note the treatment schedule was developed into the entire treatment journey by changing injection frequency over an average five year period of treatment to capture the time between treatments more robustly. This is described in below detail under *section Treatment* below.

4.1 Current state

Currently uptake of AREDS2 by people with AMD is estimated to be fairly low. Stakeholders suggest it is likely to be 10% of people with late dry AMD – compared with the previous estimate included in the NHC report ~18%.[93] Evidence from the AREDS2 trial suggests that approximately 25% of users might experience a delayed onset of progression to wet AMD for between two to three years.[94] AREDS2 treatment is estimated to cost approximately $440 per person per year.

Using model approach 1, when the 2016 defined cohort is followed through to 2026, it shows that AREDS2 treatment has a small positive effect on patient outcomes – see Figure 3 and Figure 4. Based on the assumptions used for modelling, approximately 120 cases of wet AMD would be delayed, providing a QALY gain of 100 – since patients that benefit would not experience loss of vision and anxiety associated with wet AMD. Over the ten years, AREDS2 use would incur a total cost of $0.68m for users. Note that this analysis of the current state does not include people ageing into the population or drop off due to successful

[93] National Health Committee. 2015. Age-Related Macular Degeneration.
[94] Note that the AREDS studies were carried out in USA. To the extent that New Zealander's general diet is better than that of the US expected benefits may be somewhat lower than is shown here. We have not attempted to quantify this

treatment, mortality and other health issues - so is likely to overestimate the total benefit for the eligible population.

Figure 1: Cohort modelled current state AREDS2 cost and QALYs gained

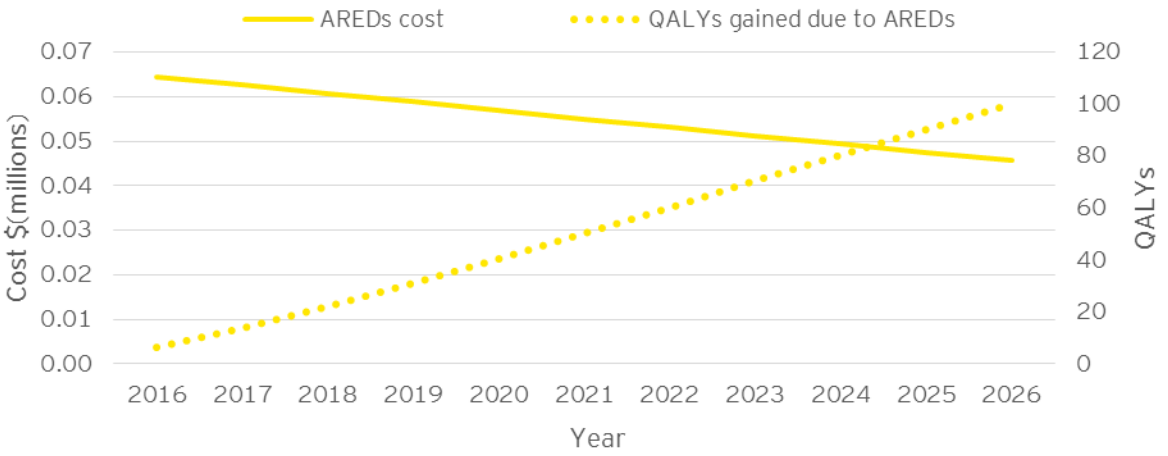
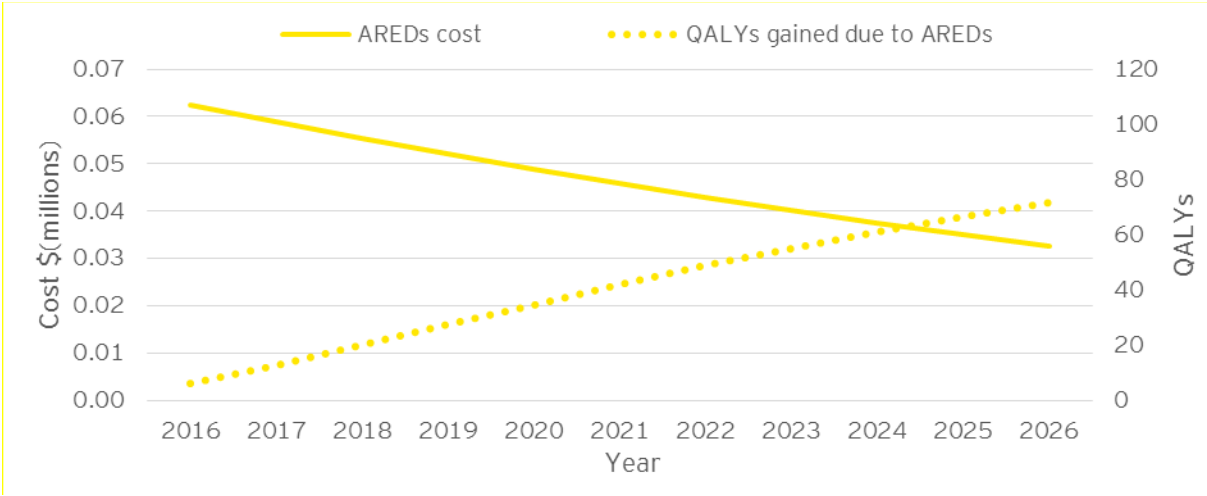


Figure 2: Cohort modelled discounted current state AREDS2 cost and QALYs gained



Timely movement through diagnosis, to the treatment stage is reported by stakeholders as effective. However, workshop feedback indicated that inconsistencies in detection are present in some regions. This is a result of local service constraints and transport issues if the VA of a patient has deteriorated past the driving threshold.

If patients face delays or issues with detection/diagnosis then treatment can be delayed which leads to a need for more intensive treatment over a longer period.[95] Over a 10-year modelled cohort, up to 5,000 QALYs may be lost, compared to if the 10% assumed to have slower access to treatment had received this earlier. For the first year of treatment costs would increase by $1.2m on average to compensate for the need of more frequent treatments to provide clinical benefits.

[95] Gillies MC, Campain A, Walton R, Simpson JM, Arnold JJ, Guymer RH, et al. Time to initial clinician-reported inactivation of neovascular age-related macular degeneration treated primarily with ranibizumab. *Ophthalmology*, 2015 122(3), 589-594

The net cost impact would be an additional $27m over a 10-year modelled cohort. Given this, it appears more beneficial to detect, diagnose and treat patients earlier, and on an appropriate treatment schedule, rather than later.

Why change?

- On average, 1,250 to 1,350 people per year are expected to progress from dry to wet AMD, based on an estimated transition from modelling approach 1 of people in the modelled cohort between 2016 and 2017. This is balanced out somewhat by mortality and those completing their course of treatment and returning to adequate vision.
- Based on the modelled effectiveness of AREDS2 in the current state, if uptake were to increase due to improved awareness or a public subsidy for AREDS2 then benefits could be realised.

4.2 Cost-effectiveness of AREDS2

Using rates from the current state and modelling approach 1 ('10-year cohort'), if the uptake of AREDS2 increased to 50% (via increased awareness or public subsidy) approximately 600 cases of wet AMD could be delayed. This would produce a gain of 500 QALYs – see Figures 3and 4. The total cost over 10 years would be $3.4m, equating to an average cost per QALY of $6,800. Again note that this analysis of a potential future state does not include people ageing into the population or drop off due to successful treatment, mortality and other health issues so is likely to be an optimistic estimate of the outcome in the population, which is explored in the projected time series analysis below.

Figure 3: Cohort modelled future state AREDS2 cost and QALYs gained

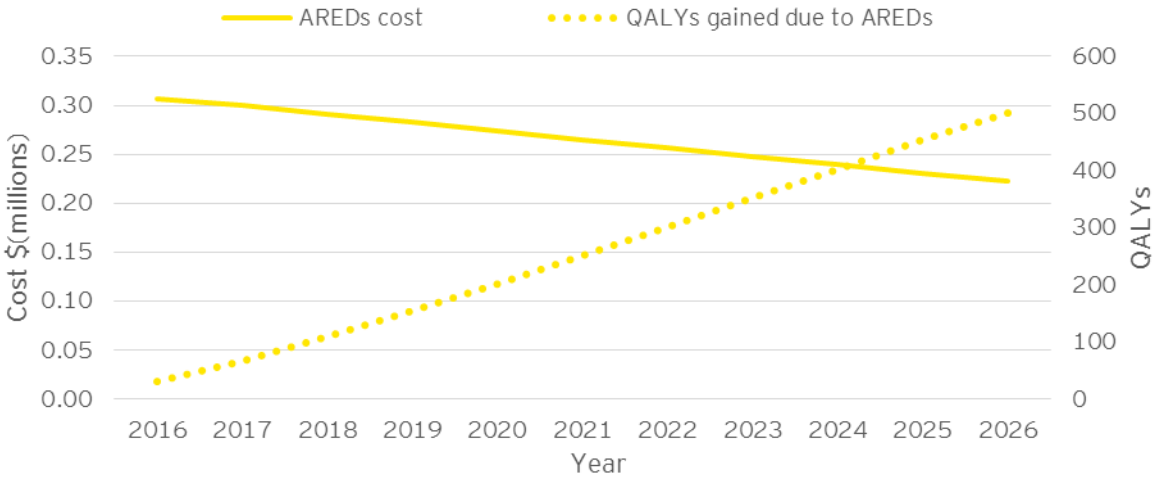
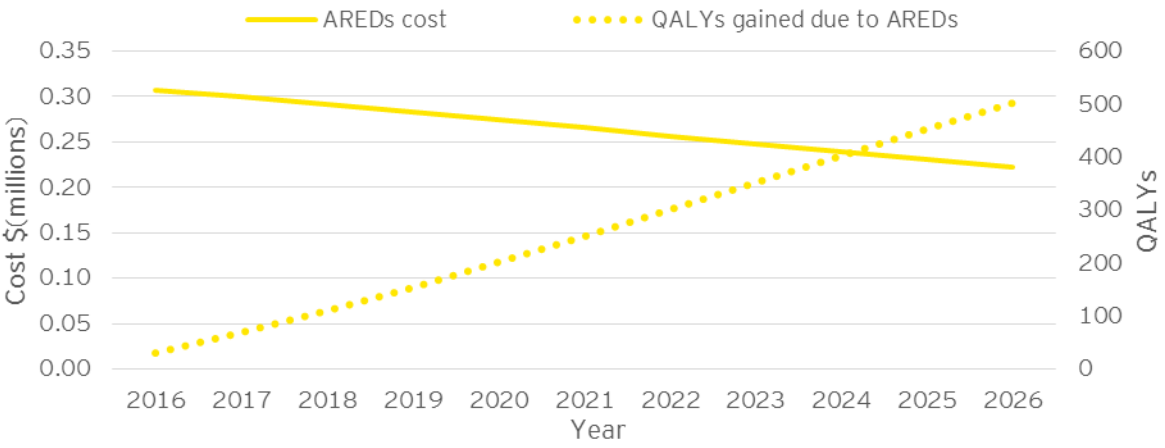


Figure 4: Cohort modelled discounted future state AREDS2 cost and QALYs gained



4.3 Summary and projected time trends

As the population ages, the prevalence of AMD will increase, meaning there will be greater numbers of people who could benefit from AREDS2. If uptake of AREDS2 were to increase then this would reduce the number of cases that progress to wet AMD in a given year. Other things being equal, this would free up capacity in the system to provide care for people with wet AMD.

Given the potential effectiveness of AREDS2, public and clinician awareness of the regime could increase uptake. Alternatively, some form of public subsidy could be introduced. This would shift direct costs to public funders but would provide an opportunity for cost saving by delaying the number of patients needing anti-VEGF injections in a given year. A bulk-purchase arrangement for AREDS2 could defray some of the cost implications for public funders. For example, if such an arrangement cut the cost of AREDS2 by half, this would decrease the average cost per QALY to $3,400 from $6,800 cost per QALY (current state uptake of 10% of people with late dry AMD).

It is important to realise that model approach 1 does not account for mortality and the ageing population and so provides an optimistic picture of the effectiveness of AREDS2. When run through model approach 2, as shown in Figures 5 and 6, which accounts for this, the QALY gain over 20 years is 930 at a total cost of $9.2m for an average cost per QALY of $9,900. When discounted this drops to 440 QALYs at a total cost of $6.7m. Again if purchased in bulk this could drop the cost per QALY by half to $4,950.

Figure 5: Time series modelled future state of AREDS2 cost and QALYs gained

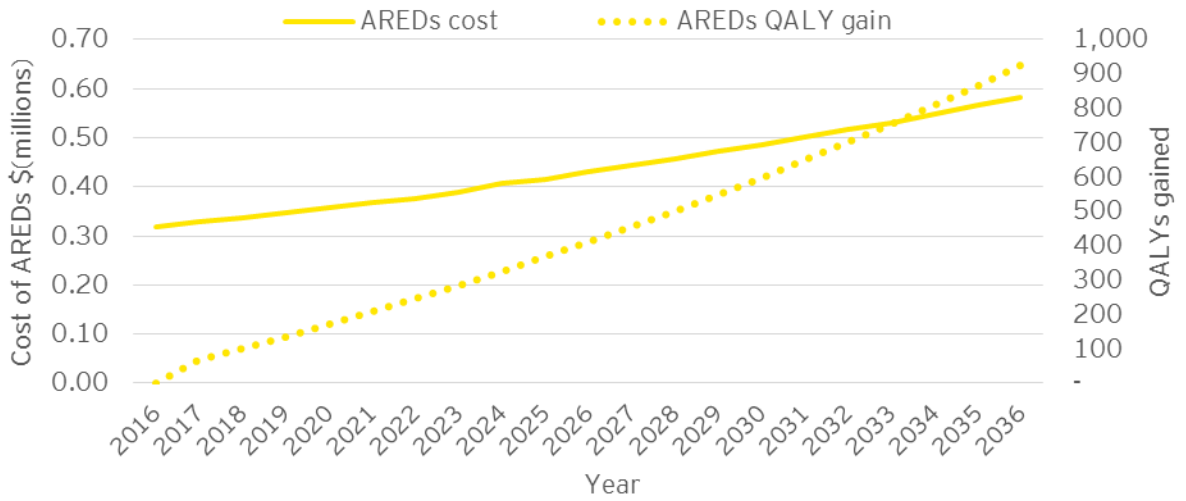
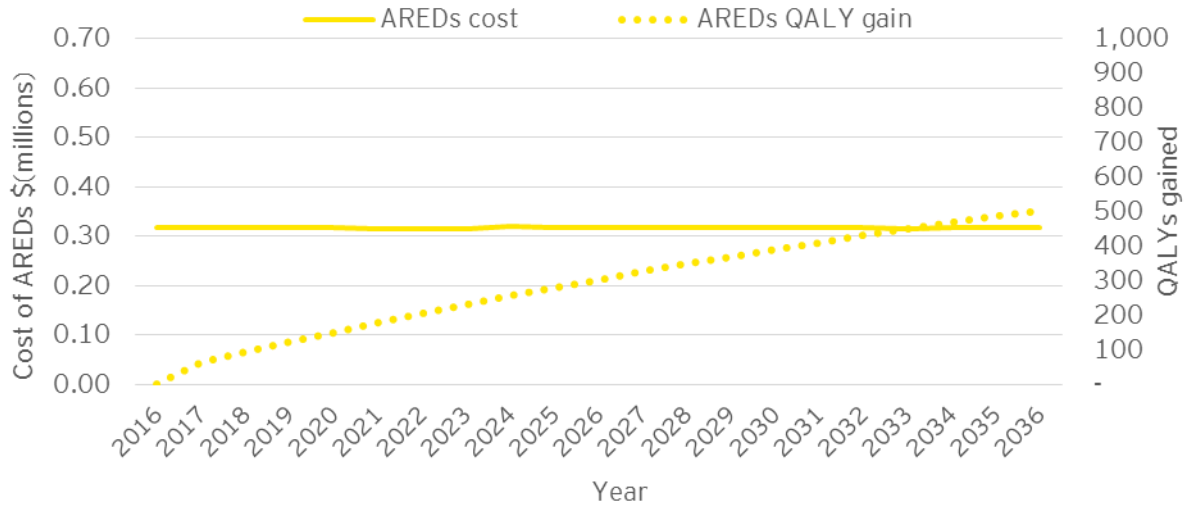


Figure 6: Time series modelled discounted future state of AREDS2 cost and QALYs gained



5. Treatment outline

As discussed in *Section 1.1* of this report, there is a need for change in the current treatment model for AMD.

In order to assess the impacts of potential changes in the treatment model, the following scenarios were assessed:

- A more optimal treatment schedule of 'treat and extend / strict PRN'
- Aflibercept as the 2nd line anti-VEGF agent
- Using specialist nurses, who are less costly, to perform the injections
- Health care assistants aiding medical or nursing professionals in injection delivery
- The impact of patients starting treatment later in the disease state ('slow access').

Anti-VEGF medications used in economic modelling, and their costs are as follows:

- Bevacizumab (Avastin) – first line agent. Off-label use is approved by PHARMAC through the hospital pharmaceutical fund. Needs reformulation for use, a service offered privately (e.g., by Baxter New Zealand, based in Auckland) for ~$85 per dose. Note: some hospital pharmacies have developed this service internally (Auckland, Canterbury and Southern DHBs), at ~$30-40 per dose excluding implementation costs
- Ranibizumab (Lucentis) – this is approved for funding as the second line agent – after non-response to at least three monthly injections of bevacizumab. It is approximately 15 times the cost of bevacizumab (~$1,250)
- Aflibercept (Eylea) – this is not specifically funded in NZ. Currently New Zealand's third line treatment and is approximately 20 times the cost of bevacizumab (~$1,650)
- Ziv-aflibercept – this will likely be able to fill a similar role to aflibercept for ~$85 per injection and has a similar mechanism as aflibercept.

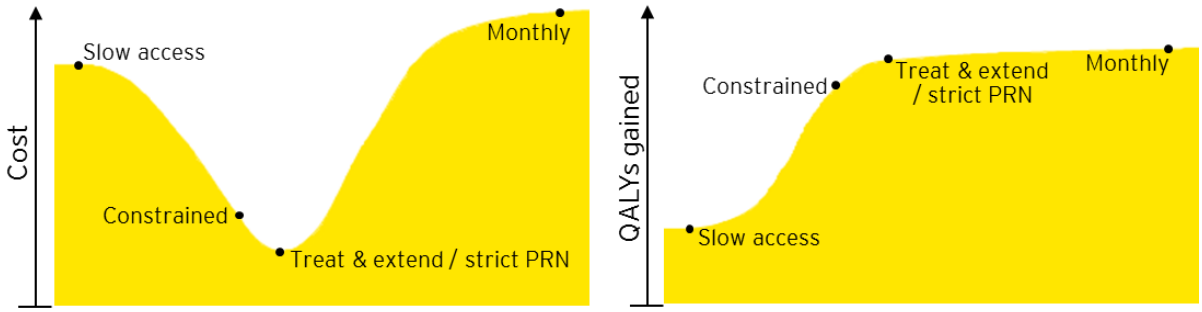
Modelling only considered treatment in a public setting due to a lack of private sector data.

5.1 Treatment schedules

Following the first anti-VEGF injection for wet AMD patients, the current New Zealand treatment approach attempts to follow a 'treat and extend / strict PRN' schedule – subject to capacity constraints, which vary by DHB. Treat and extend follows a set injection schedule (e.g., monthly injections for the first three months, with larger intervals ongoing). Strict PRN involves active monitoring of the macula, with injections only administered as needed. This reduces the risk of overtreatment, however, it is more resource-intensive than the treat and extend approach. Therefore it is only used by DHBs with sufficient capacity (workforce, physical capacity and technology).

Figure 7 shows where the different schedules might fit in relation to each other. The treatment schedule defined as 'constrained' is where New Zealand likely currently sits. Most patients are treated as 'treat and extend / strict PRN' but approximately 10% start treatment too late - so their potential VA gain as a result of treatment is reduced and they need a greater number of treatments.[96] Due to the increasing prevalence of AMD in New Zealand and associated workload, the possibility of delivering an optimum 'treat and extend / strict PRN' schedule as shown in Figure 7 may decrease, resulting in treatment schedules resembling 'slow access' (discussed further below). Note that assumptions underpin this figure at a high-level. Monthly injections were used in initial trials, and are shown for comparator purposes only.

Figure 7: Relative cost and QALY curves for the defined schedules



5.2 Current model of anti-VEGF treatment

Under the current state Figure 8 shows the typical 'averaged' number of injections a patient will receive over five years. Lower injection numbers in the first year reflect the delay some patients face between initial diagnosis and the start of treatment (note that the initial year contains on average 6 months of treatment – people commencing treatment throughout the year). The higher injection number in the second year reflects the fact it includes a full year to treat within. Each year onwards, injection numbers will diminish as the patient's condition stabilises (some exceptions occur where patients worsen and will be moved on to second or third line treatments).

This individual patient decay is applied to the modelled population cohort in Table 4, and then processed into costs in Table 5. It should be noted that an estimated IDF-based price of injections in 2016, $5.2m, was also used to help inform the cost modelling assumptions. It used data from DHB returns which was developed into a New Zealand-wide cost; however, through stakeholder feedback we learned that the IDF price underestimates the significant cost of ranibizumab. This led to model adjustments for the high cost of ranibizumab and so our current best estimate of the cost in 2016 through modelling is $6.1m for the secondary care cost of intravitreal injections as a treatment of wet AMD.

[96] Gillies MC, Campain A, Walton R, et al. Time to initial clinician-reported inactivation of neovascular age-related macular degeneration treated primarily with ranibizumab. *Ophthalmology* 2015;122(3):589-594

Figure 8: 'Constrained' injection decay

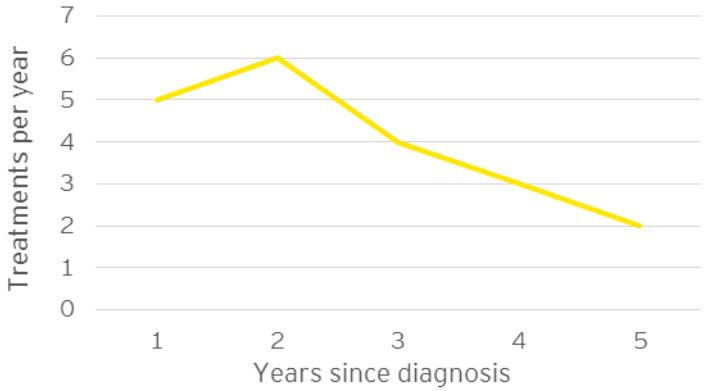


Table 4: Cohort modelled current state injection volumes

Year	Bevacizumab	Ranibizumab	Aflibercept	Total
2016	18,100	2,100	480	20,680
2017	18,000	2,100	470	20,570
2018	17,300	2,100	430	19,830
2019	16,200	1,900	390	18,490
2020	14,800	1,700	350	16,850
2021	13,200	1,500	310	15,010
2022	11,800	1,400	280	13,480
2023	10,400	1,200	240	11,840
2024	9,100	1,100	210	10,410
2025	7,800	900	180	8,880
2026	6,700	800	160	7,660
Total	143,400	16,800	3,500	163,700

Table 5: Cohort modelled current state injection costs ($m)

Year	Bevacizumab	Ranibizumab	Aflibercept	Total
2016	1.5	2.6	0.8	5.0
2017	1.5	2.6	0.8	4.9
2018	1.5	2.6	0.7	4.8
2019	1.4	2.4	0.6	4.4
2020	1.3	2.1	0.6	3.9
2021	1.1	1.9	0.5	3.5
2022	1.0	1.7	0.5	3.1

Year	Bevacizumab	Ranibizumab	Aflibercept	Total
2023	0.9	1.5	0.4	2.8
2024	0.8	1.3	0.4	2.4
2025	0.7	1.1	0.3	2.1
2026	0.6	1.0	0.3	1.8
Total	12.3	20.5	5.9	38.2

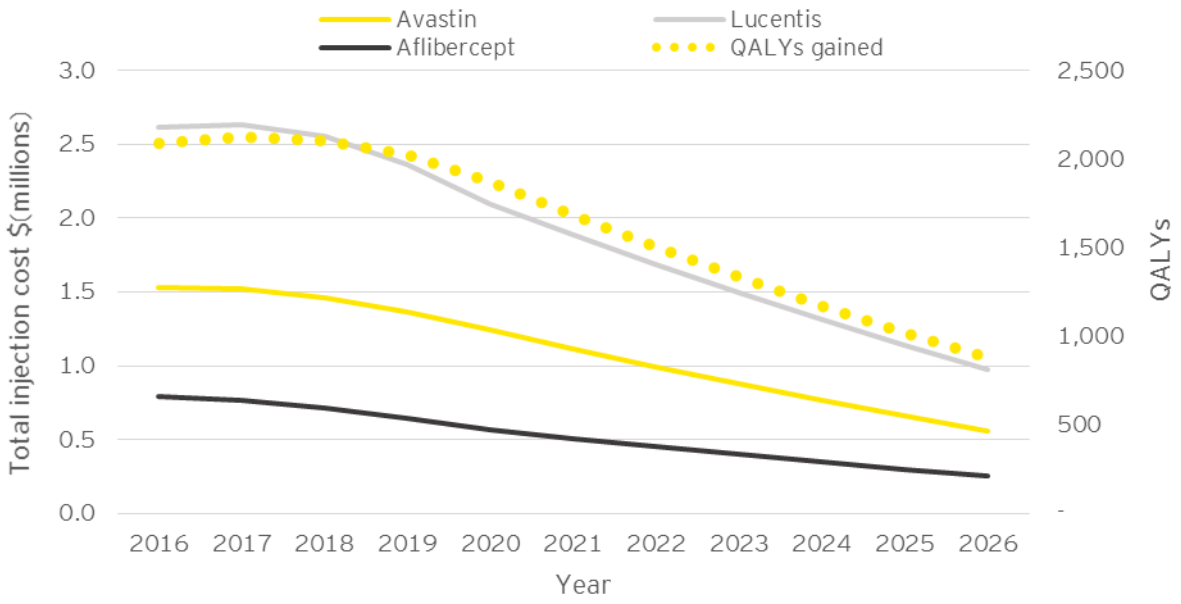
Over the 10-year defined cohort, a total of 163,700 anti-VEGF treatments are performed at a cost of $38.2m to the health sector. 17,600 QALYs are gained over the 10 year period relative to if no treatment for any patients had occurred. This is presented in Figure 9. The average cost per QALY of the current anti-VEGF treatment scheme in this cohort view is $2,170.[97]

The proportion of injections by drug type and their share of costs are estimated to be:

- Bevacizumab injections 88% of total injections, but only 32% of the total costs
- Ranibizumab injections 10% of total injections, but 53% of the total costs
- Aflibercept injections 2% of total injections, but 16% of the total costs.

Note: If bevacizumab can be sourced from local hospital pharmacies for $35 a dose, this would decrease the total cost of anti-VEGF treatment by 18% on average. If ziv-aflibercept was introduced as second line it would decrease the total cost of anti-VEGF treatment by 49% on average. Finally, if both were implemented the total cost would reduce by 71% on average.

Figure 9: Cohort modelled current state injection cost by anti-VEGF and total QALYs gained



[97] Note this cost per QALY is based on the 10-year cohort, without deaths etc.; as such is a theoretical construct. See Section 5.7 for the time series QALY derivation.

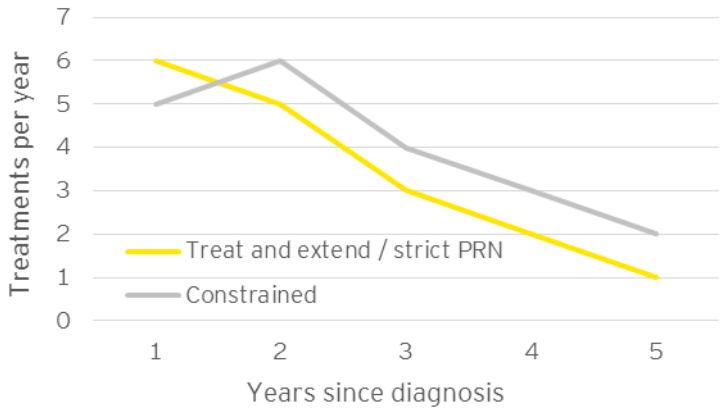
Why change?

- Current state is 'constrained' in treatment delivery, so more optimal treatment schedules could provide large benefits
- Aflibercept is a more cost-effective second line treatment than ranibizumab so should be considered
- Sessions are completed at a high medical labour cost currently which could be substantially reduced by higher use of specialist nurses and HCAs
- As the AMD population increases, the danger of slipping into 'slow access' schedules increases, which would increase costs and reduce potential utility gains.

5.3 Moving to 'treat and extend / strict PRN'

Treatment of AMD remains in a 'constrained' state, wherein the time between treatments is longer than optimum. This results in more VA deterioration leading to longer periods of treatment for people with wet AMD.[98] A more optimal 'treat and extend / strict PRN' schedule is shown in Figure 10.

Figure 10: 'Treat and extend / strict PRN' injection decay



The total injections under this treatment schedule and associated costs are presented in Tables 6 and 7 - along with a percentage change from the current state. These numbers are presented as if the optimal schedule was implemented and running for 2016.

[98] Gillies MC, Campain A, Walton R, et al. Time to initial clinician-reported inactivation of neovascular age-related macular degeneration treated primarily with ranibizumab. *Ophthalmology* 2015;122(3):589-594

Table 6: Cohort modelled injection volumes with 'treat and extend / strict PRN'

Year	Bevacizumab	Ranibizumab	Aflibercept	Total
2016	15,900	1,700	390	17,990
2017	15,600	1,700	360	17,660
2018	14,800	1,600	320	16,720
2019	13,700	1,400	290	15,390
2020	12,400	1,300	260	13,960
2021	11,100	1,100	230	12,430
2022	9,800	1,000	200	11,000
2023	8,700	900	180	9,780
2024	7,500	800	150	8,450
2025	6,500	700	130	7,330
2026	5,500	600	110	6,210
Total	121,500 (18%decrease)	12,800 (31%decrease)	2,620 (34%decrease)	136,920 (20%decrease)

Table 7: Cohort modelled injection costs with 'treat and extend / strict PRN' ($m)

Year	Bevacizumab	Ranibizumab	Aflibercept	Total
2016	1.3	2.1	0.6	4.1
2017	1.3	2.1	0.6	4.0
2018	1.3	2.0	0.5	3.7
2019	1.2	1.8	0.5	3.4
2020	1.1	1.6	0.4	3.1
2021	0.9	1.4	0.4	2.7
2022	0.8	1.3	0.3	2.4
2023	0.7	1.1	0.3	2.2
2024	0.6	1.0	0.3	1.9
2025	0.6	0.9	0.2	1.6
2026	0.5	0.7	0.2	1.4
Total	10.3 (19%decrease)	15.9 (29%decrease)	4.4 (34%decrease)	30.5 (25%decrease)

When a 'treat and extend / strict PRN' treatment schedule is used there is on average 2,700 less injections needed per year, which translates into a saving of an estimated $7.7m as well as a QALY gain of an estimated 17,940. This puts the average cost per QALY in the cohort view at around $1,700.[99] As such, based on the assumptions used for modelling, this approach appears cost saving relative to the status quo.

[99] Note this cost per QALY is based on the 10-year cohort, without deaths etc.; as such is a theoretical construct. See Section 5.7 for the time series QALY derivation.

5.4 Cost-effectiveness of aflibercept as the second line treatment

Currently ranibizumab is the second line treatment for AMD in New Zealand. Workshop feedback and clinical evidence indicates that the treatment pathway could be less costly if aflibercept was the second line treatment because of its increased efficacy at treating wet AMD. Patients receiving aflibercept require one less treatment per year then ranibizumab users on average.[100,101]

The total injections needed and associated costs, when aflibercept is used as the second line treatment are shown in Tables 8 and 9. The percentage change in total injection numbers from the current state is included.

Table 8: Cohort modelled injection volumes with aflibercept as second line agent

Year	Bevacizumab	Aflibercept	Ranibizumab	Total
2016	18,000	1,600	640	20,240
2017	18,000	1,500	620	20,120
2018	17,200	1,500	590	19,290
2019	16,100	1,300	540	17,940
2020	14,700	1,200	470	16,370
2021	13,200	1,100	420	14,720
2022	11,700	1,000	380	13,080
2023	10,300	800	330	11,430
2024	9,000	700	290	9,990
2025	7,800	600	250	8,650
2026	6,600	600	220	7,420
Total	142,600 (1% decrease)	11,900 (29% decrease)	4,750 (36% increase)	159,250 (3% decrease)

Table 9: Cohort modelled injection costs with aflibercept as second line agent ($m)

Year	Bevacizumab	Aflibercept	Ranibizumab	Total
2016	1.5	2.0	1.1	4.6
2017	1.5	1.9	1.0	4.5
2018	1.5	1.8	1.0	4.3
2019	1.4	1.7	0.9	3.9
2020	1.3	1.5	0.8	3.5
2021	1.1	1.3	0.7	3.2
2022	1.0	1.2	0.6	2.8
2023	0.9	1.1	0.6	2.5

[100] Balaratnasingam C, Dhrami-Gavazi E, McCann JT, Ghadiali Q, Freund KB. Aflibercept: a review of its use in the treatment of choroidal neovascularization due to age-related macular degeneration. *Clinical Ophthalmology* 2015; 9:2355-71.

[101] Schmidt-Erfurth U, Kaiser PK, Korobelnik JF, et al. Intravitreal aflibercept injection for neovascular age-related macular degeneration: ninety-six-week results of the VIEW studies. *Ophthalmology* 2014; 121(1):193-201.

Year	Bevacizumab	Aflibercept	Ranibizumab	Total
2024	0.8	0.9	0.5	2.2
2025	0.7	0.8	0.4	1.9
2026	0.6	0.7	0.4	1.6
Total	12.3	14.9 (27% decrease)	8.0 (36% increase)	35.0 (8% decrease)

When aflibercept is used as the second line treatment over a 10-year modelled cohort, the total cost to the health system falls by 8%. Table 10 explores the cost-effectiveness of aflibercept as second line.

Table 10: Cost-effectiveness of Aflibercept as second line treatment

	Current state		Aflibercept change	
Injections	Anti-VEGF	Volume	Anti-VEGF	Volume
Second line	Ranibizumab	16,800	Aflibercept	11,900
Third line	Aflibercept	3,500	Ranibizumab	4,750
Total		20,300		16,650
Costs	Anti-VEGF	Cost ($m)	Anti-VEGF	Cost ($m)
Second line	Ranibizumab	20.5	Aflibercept	14.9
Third line	Aflibercept	5.9	Ranibizumab	8.0
Total		26.4		22.9
QALYs	Anti-VEGF	QALYs gained	Anti-VEGF	QALYs gained
Second line	Ranibizumab	2,300	Aflibercept	2,490
Third line	Aflibercept	620	Ranibizumab	660
Total		2,920		3,150
Average cost per QALY	Current state	Cost per QALY ($)	Aflibercept change	Cost per QALY ($)
Total		$9,030		$7,270
ICER		N/A		Cost saving

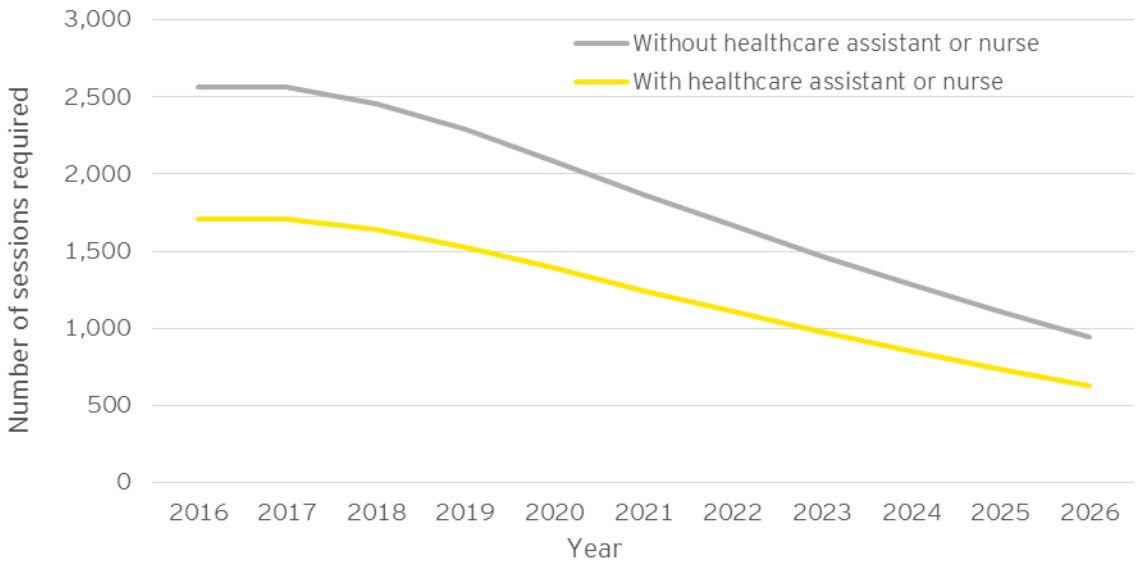
5.5 Anti-VEGF sessions and workforce used

The common practice of delivering anti-VEGF injections in New Zealand is in outpatient clinics, which are grouped into clinical sessions of ~4 hours in lengths. There is wide variation in the workforce delivering injections with DHBs using a mix of medical and nursing professions (see below). Some regions report benefit from using health care assistants to support injectors, which they consider improves the productive efficiency of administering injections. Stakeholders advised that:

- A medical or nursing professional injecting by themselves requires one session to do on average 8 injections
- A medical or nursing professional injecting with the aid of a health care assistant (HCA) requires one session to do on average 12 injections. Therefore, using a HCA assistant means less sessions are required to complete an equal number of treatments.

Total current injection numbers, from Table 4 have been broken into sessions, with and without a HCA, shown in Figure 11. In year one there were an estimated 20,680 anti-VEGF treatments based on DHB questionnaire submissions and national datasets. Based on the assumptions above, this would require 2,590 sessions if a medical or nursing professional were working by themselves or 1,720 if they were aided by a HCA.

Figure 11: Cohort modelled current state session volumes by HCA presence



The workforce approach to treatment varies significantly across the country, from treatment planning and injecting done solely by ophthalmologists, to the use of nurse injectors and other clinicians (e.g., GPs, training doctors) in other areas, typically where the model of care is more mature. The distribution of the workforce is explored further in *Appendix C*.

On average the reported distribution of workforce used for injecting and estimated costs[102] per workforce:

- Ophthalmologists administer 33% of all sessions at a modelled cost of $520 per session
- Medical professionals administer 38% of all sessions at a modelled cost of $260 per session
- Specialist nurses administer 29% of all sessions at a modelled cost of $180 per session.

[102] PHARMAC Cost Resource Manual v2.2.

In 2016, when 2,590 sessions were completed, and the assumption is made that none involving an HCA were completed, the total cost to the health system would be about $0.9m using cost assumptions from the PHARMAC Cost Resource Manual as guide. Whereas if each session had been completed with an HCA then 1,720 sessions would have occurred at a total cost $0.7m - a net fiscal saving of about $0.2m. However, this does not include any cost savings from further substitution of ophthalmologist time to specialist nurses or other trained injectors. Note that:

- Current sessions without HCAs cost on average $325
- Current sessions with HCAs cost on average $410.

Specialist nurses as primary injectors - It has been identified that using appropriately trained specialist nurses as the primary injectors would be less costly to the health system if they could deliver a treatment session at ~$180 which is approximately one third (35%) of the modelled cost of an ophthalmologist ($520). Similar savings would be possible with appropriately trained optometrists.

- In 2016, with the current workforce distribution used to administer treatments, the total cost is $0.9m
- If nurses were to administer 100% of injections in 2016, it would cost the health system $0.4m
- Producing a net saving of $0.5m.

Health care assistants aiding session delivery – This would enable the number of sessions required to decrease by a third. However, when HCAs are used the cost of delivering these sessions goes up. HCAs are cost effective, for aiding in delivery of sessions, by a small margin. To maximize efficiency requires making the best use of HCAs alongside promoting the use of specialist nurse injectors or other medical and allied health professionals trained to deliver the injections. Where patient demand is already being met, consideration should include whether or not adding an HCA would be cost-effective or at least over what time scale cost-effectiveness might be met.

5.6 Effect of 'slow access' on costs

Slow access to treatment has been indicated as a concern for DHBs, especially with ageing population pressures, as it risks poor health outcomes and escalating health system costs. As soon as slow access occurs, potential VA gain is diminished, and therefore the gain in QALY received from treatment is extremely limited.

To try and maintain VA, a greater amount of treatments are required per year when the eye lesions are more advanced – for example if access to treatment is delayed. The modelled number of injections per patient, per year, when slow access occurs is shown in Figure 12. It is expanded, via model approach 1, into a population cohort in Tables 11 and 12.

Figure 12: 'Slow access' injection decay

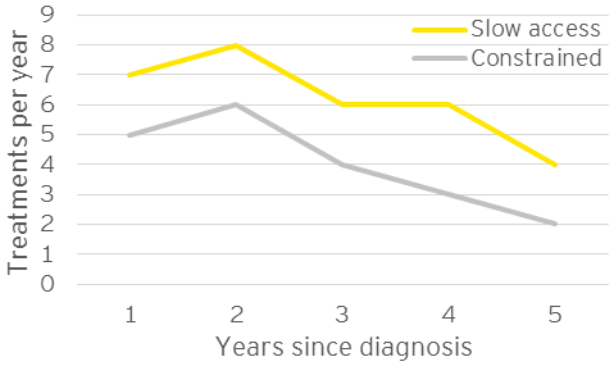


Table 11: Cohort modelled 'Slow access' injection volumes

Year	Bevacizumab	Ranibizumab	Aflibercept	Total
2016	21,000	2,400	590	23,990
2017	20,900	2,500	580	23,980
2018	20,200	2,500	540	23,240
2019	18,900	2,300	490	21,690
2020	17,300	2,000	430	19,730
2021	15,500	1,800	390	17,690
2022	13,800	1,600	350	15,750
2023	12,200	1,400	310	13,910
2024	10,600	1,300	270	12,170
2025	9,200	1,100	230	10,530
2026	7,800	900	200	8,900
Total	167,400 (17% Increase)	19,800 (18% Increase)	4,380 (25% Increase)	191,580 (17% Increase)

Table 12: Cohort modelled 'Slow access' injection costs ($m)

Year	Bevacizumab	Ranibizumab	Aflibercept	Total
2016	1.8	3.0	1.0	5.8
2017	1.8	3.2	1.0	5.9
2018	1.7	3.1	0.9	5.7
2019	1.6	2.8	0.8	5.3
2020	1.5	2.5	0.7	4.7
2021	1.3	2.3	0.6	4.2
2022	1.2	2.0	0.6	3.8
2023	1.0	1.8	0.5	3.3
2024	0.9	1.6	0.4	2.9

Year	Bevacizumab	Ranibizumab	Aflibercept	Total
2025	0.8	1.4	0.4	2.5
2026	0.7	1.2	0.3	2.2
Total	14.3 (16% Increase)	24.9 (21% Increase)	7.2 (22% Increase)	46.3 (21% Increase)

'Slow access' conditions would cause total injection numbers over 10 years to increase by 17%, and session numbers would have to increase by 12%. As a result costs would increase by 21% for a QALY gain of only 10,400, compared to that of 'constrained' at 19,900 QALYs gained. This means this scenario is significantly cost adding ($8m over 10 years), and delivers less quality of life than the current, 'constrained' state.

Ergo avoiding a 'slow access' scenario is critical to avoid inflated health care costs and significant pressure on an already tightly constrained workforce. This scenario could lead to a larger group of AMD patients who are untreated, which would add significant flow on costs to rehabilitation services and co-morbidities (fractures, early aged care admissions) associated with significant loss of vision.

5.7 Summary and projected time trends

In terms of the potential future states over time, it is necessary to estimate what the future state could look like, accounting for factors such as ageing of the population, mortality, and movement towards a more optimal treatment schedule. This section details the effect of cheaper bevacizumab and using aflibercept as second line agent in terms of cost, and shows the effect of workforce model changes on system costs. The potential cost savings of ziv-aflibercept are also discussed. Table 13 below presents the cost-effectiveness of the major treatment schedules considered over the next 10 years as a time series – it has also considered workforce costs.

Table 13: Cost-effectiveness of treatment schedules

	Treat and extend / strict PRN	Constrained	Slow access
Total cost ($m)	59	80	125
Total QALYs	28,500	27,700	14,900
Average cost per QALY ($)	2,070	2,900	8,400
ICER	-	27,500	Cost adding; less effective

The current system, termed 'constrained', is delivering at around $2,900 per QALY, compared to the proposed future state with an estimated $2,070 per QALY.

For the current state, the cost over 20 years is likely to be:

- $148m for all injections, with $46m for bevacizumab, and $78m for ranibizumab (when discounted $107m, $33m, and $57m respectively).

In contrast, in a more optimal future state with cheaper bevacizumab and aflibercept as the second line treatment, the costs over 20 years become $87m for all injections, with $17m for bevacizumab, $44m for aflibercept (when discounted are $63m, $12m, and $32m respectively). This is shown in Figures 13 and 14, and means that:

- A saving of $61m can be made over the next 20 years:
  - $22m of which is due to better treatment scheduling
  - $27m of which is due to an assumed cost reduction of bevacizumab to $35 per injection
  - $12m of which is due to second line aflibercept
- The use of ziv-aflibercept as a second line instead would cost $3m and therefore save an estimated additional $42m on top of the proposed more optimal future state, and when compared to the current state would save $76m. A change such as this could reduce injection costs by 50%.

Figure 13: Time series modelled future state of injection costs over 20 years

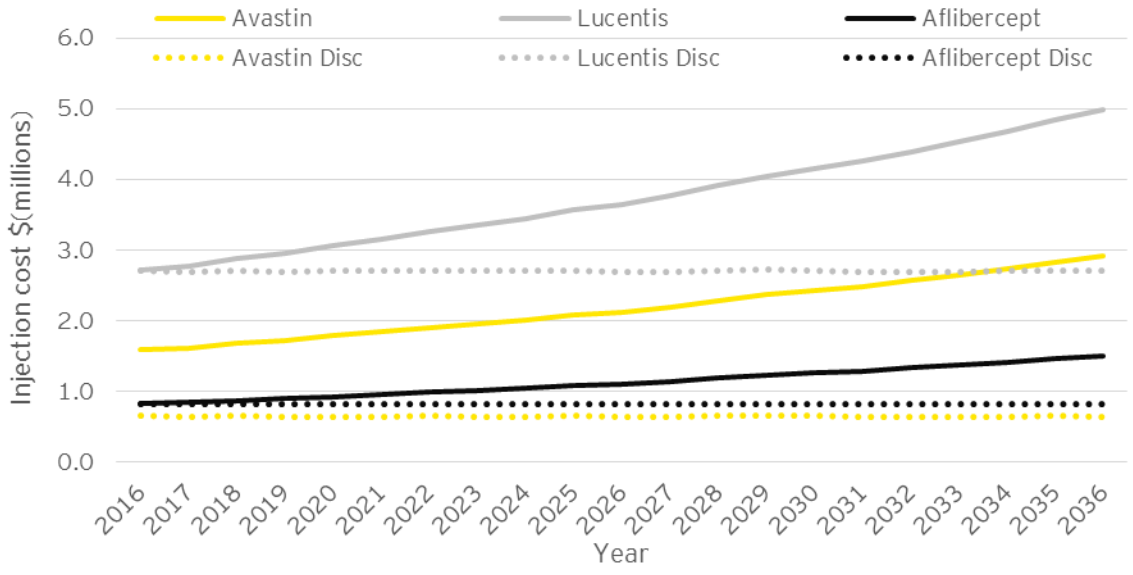
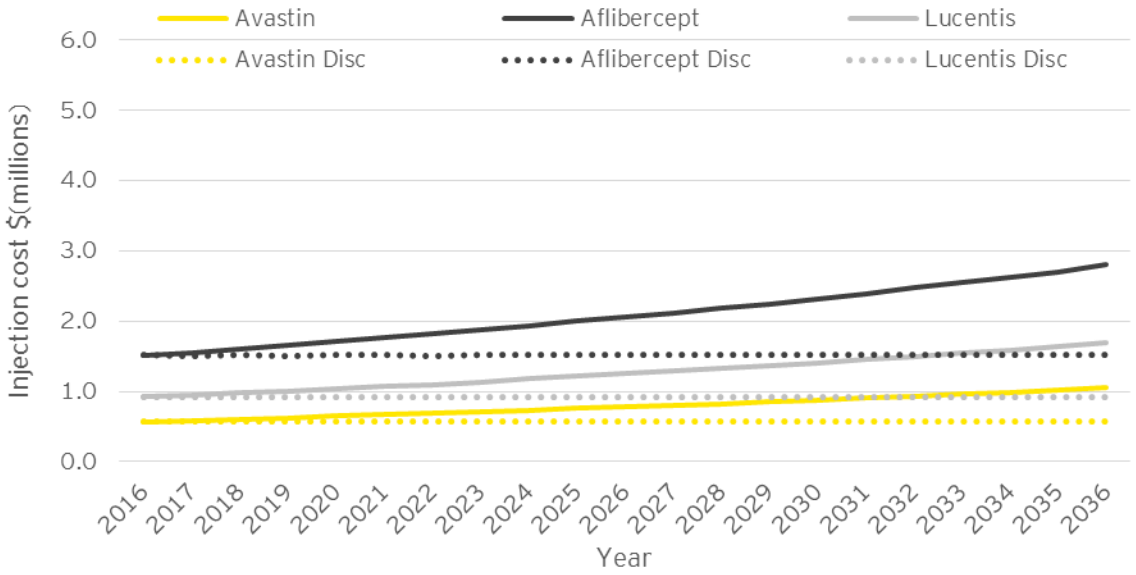


Figure 14: Time series modelled future state of injection costs over 20 years



The effect of changing treatment mix does not largely impact the number of sessions, only a small reduction due to the effectiveness of aflibercept is found. The main point of difference related to workforce is a cost difference due to a change to a systemic specialist nurse-led injection model alongside HCAs, where this makes sense for DHBs.

For the current state, the cost over 20 years is likely to be:

- $33m for all sessions (workforce related costs).

If all sessions were currently completed with a HCA, then the cost over 20 years is:

- $26m, a saving of $7m, and if discounted then $19m in total.

If specialist nurses become the sole injectors, alongside treatment mix changes, then the cost over 20 years is likely to be:

- $11.8m for all sessions, $11.6m if HCAs are used for all sessions, and when discounted give $8.6m and $8.4m respectively. This can be seen in Figures 15 and 16.

This gives a saving over workforce costs estimated at $21.3m over 20 years.

Figure 15: Time series modelled current state of workforce costs over 20 years

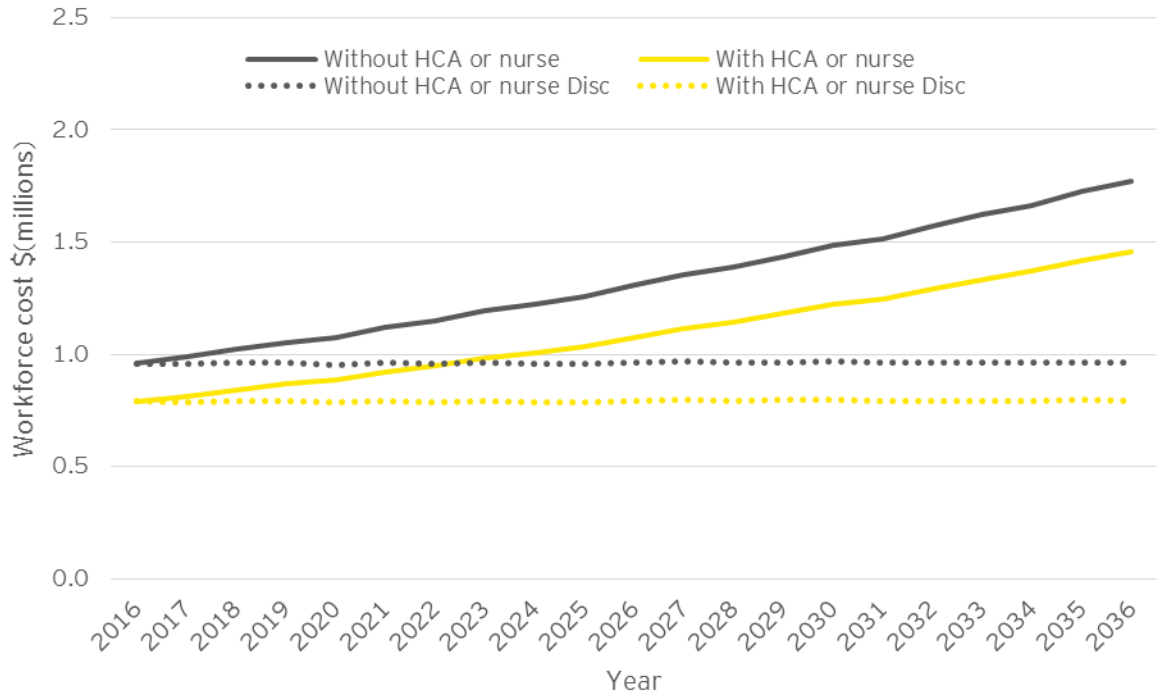
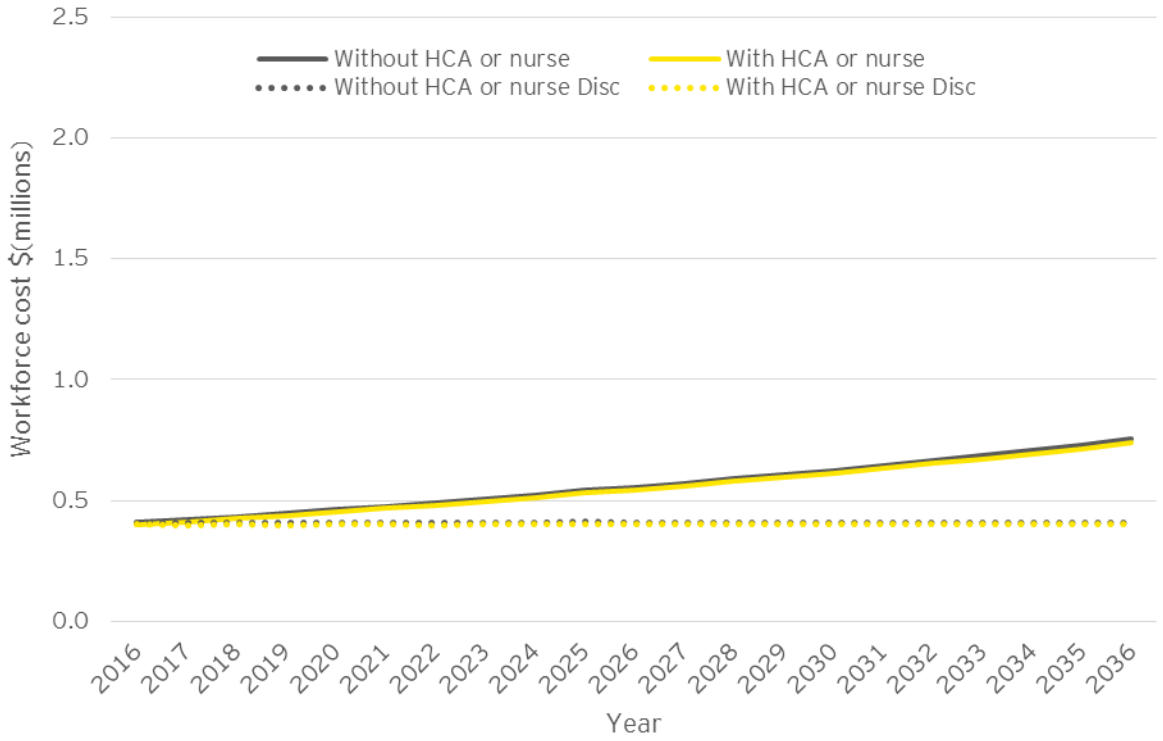


Figure 16: Time series modelled future state of workforce costs over 20 years



In summary multiple scenarios were run in the treatment model in order to establish costs and benefits of changing the model of care. The best case scenarios are as follows.

- 'Treat and extend / strict PRN' is the ideal scenario as it is key to finding the right balance between 'slow access' and 'monthly' treatments and is more optimal than New Zealand's currently 'constrained' schedule
- Economic modelling suggests that aflibercept be used as the second line treatment as it reduces the total cost of anti-VEGF to the health system
- Economic modelling suggests that a higher proportion of specialist nurses be trained and used to reduce injection administration costs
- Careful consideration is needed when choosing the balance between sessions completed with a HCA or medical / nursing professionals by themselves. Using HCAs is cost effective, but DHBs should assess whether local demand warrants the delivery of additional sessions facilitated via an HCA model.

6. Rehabilitation

- As discussed in *Section 4.4*, low vision services are not part of service coverage requirements for DHBs, and the number of low vision rehabilitation clinics has decreased over the years. Access across the country is unequal as most areas do not offer adequate services for people with low vision.
- Low vision services in New Zealand include three dedicated low vision clinics offering consultations in public settings:
- Greenlane Low Vision Clinic is open one day per week (Auckland)
- The Burwood Low Vision Clinic operates two and a half days a week (Christchurch)
- An optometrist at Wellington Hospital works with ophthalmologists to provide a low vision clinic for half a day a week.

6.1 Current state

It has been estimated that out of all AMD patients with some sort of vision loss (those with late dry or wet AMD), only around 18% are accessing rehabilitation services.[103] This is supported by the fact that only Auckland, Capital and Coast, and Canterbury DHBs provide some rehabilitation services, and as they represent 36% of the total late dry and wet AMD population based on 2016 numbers, it means around half of those populations are likely to access rehabilitation services of some form. Due to lack of literature surrounding utility gain of low vision rehabilitation, especially for those between 6/12 and 6/24 (not clinically blind and cannot drive), the utility gain of rehabilitation has been set at 0.01 QALYs. This is an estimate that requires further validation, particularly with the increased risks of among other things falls, other injuries and depression with this low vision group. The cost for the rehabilitation package offered to patients is assumed to be $200.

Over a 10-year, the defined cohort modelled number of people accessing rehabilitation increased from 1,280 to 2,250. The total cost to the health system is currently estimated at $4.7m for a gain of 230 QALYs as shown in Figures 17 and 18. Even though there are only a small amount of QALYs gained, rehabilitation services may substantially reduce co-morbidities from AMD, such as fractures, depression and early aged care admissions. Consequently the total costs of these patients to the health system should reduce, providing for alternative uses of expensive hospital infrastructure.

[103] Macular Degeneration New Zealand. Macular Degeneration Facts, (n.d.). Accessed 20 Jul 2017 from http://mdnz.org.nz/assets/Files/MDNZ-Macular-Degeneration-Facts-Flyer-LR.pdf

Figure 17: Cohort modelled current state rehabilitation cost and QALYs gained

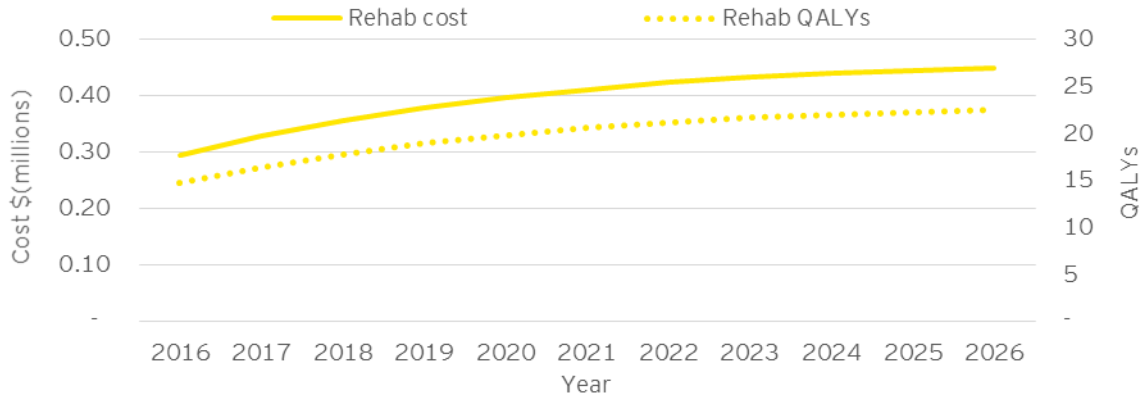
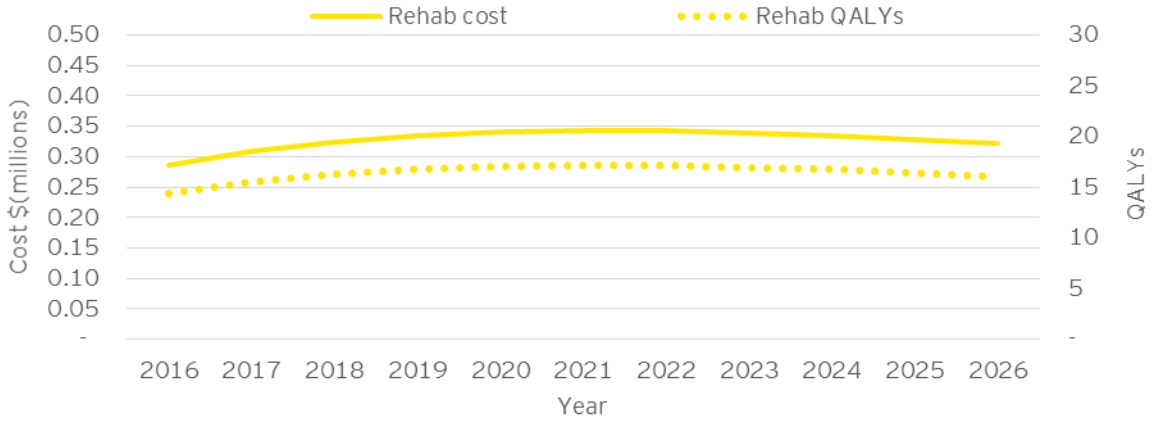


Figure 18: Cohort modelled discounted current state rehabilitation cost and QALYs gained



Why change?

- The Blind Foundation is only funded to provide services for those with 6/24 vision or worse, so although those with 6/12 or worse vision cannot see well enough to drive, they do not have access to funded low vision rehabilitation services
- Private services offered outside of public settings are often not funded, therefore resulting in a cost barrier
- People with low vision have a higher risk of co-morbidity (this has not been modelled due to a lack of sufficient data).

6.2 Increasing rehabilitation coverage

The assumption made is that every person who meets the rehabilitation threshold will have access to low vision services in the future, and this is a focus of the Ministry's low vision rehabilitation services strategic direction. Over 10 years, the total number accessing rehabilitation would increase from 7,200 to 12,600. The total cost of rehabilitation for all late dry and wet AMD patients accessing is estimated at $26m for a gain of 1,300 QALYs as shown in Figures 19 and 20.

Figure 19: Cohort modelled 100% coverage rehabilitation cost and QALYs gained

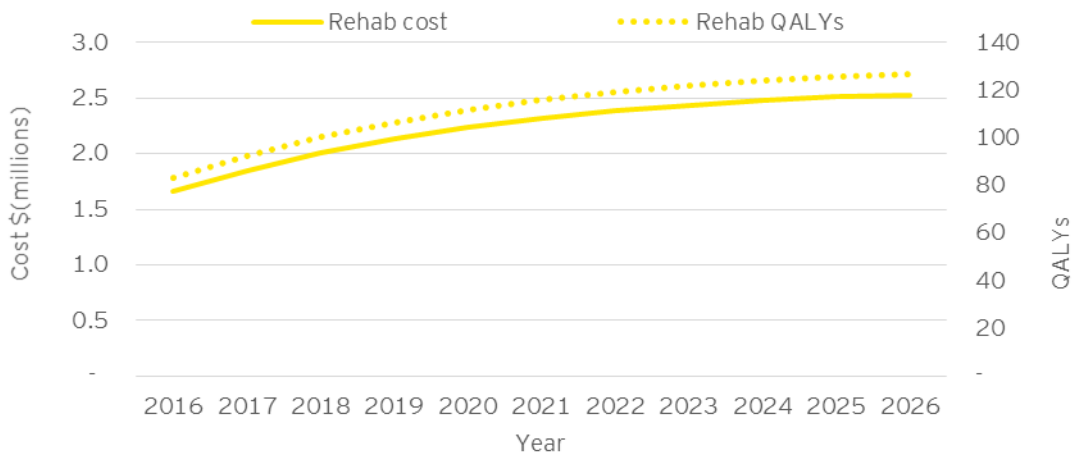
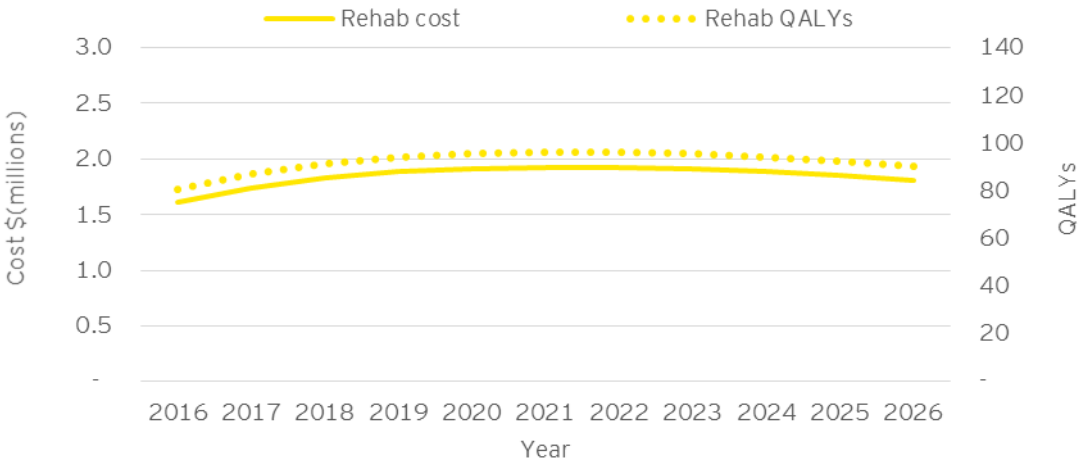


Figure 20: Cohort modelled discounted 100% coverage rehabilitation cost and QALYs gained



6.3 Summary and projected time trends

In accounting for mortality and the ageing population, the number accessing rehabilitation services is likely overestimated in the cohort modelled approach. This section details the change in rehabilitation costs over the next 20 years for the future state of 100% rehabilitation coverage.

For the future state, the cost over 20 years is projected to be $49m for 2,500 QALYs - at around $20,000 per QALY it appears a reasonable investment. If discounted then is $36m for 1,800 QALYs, and the number in rehabilitation would increase from 7,200 to 15,700. This is shown in Figures 21 and 22.

Figure 21: Time series modelled future state of rehabilitation cost and QALYs gained

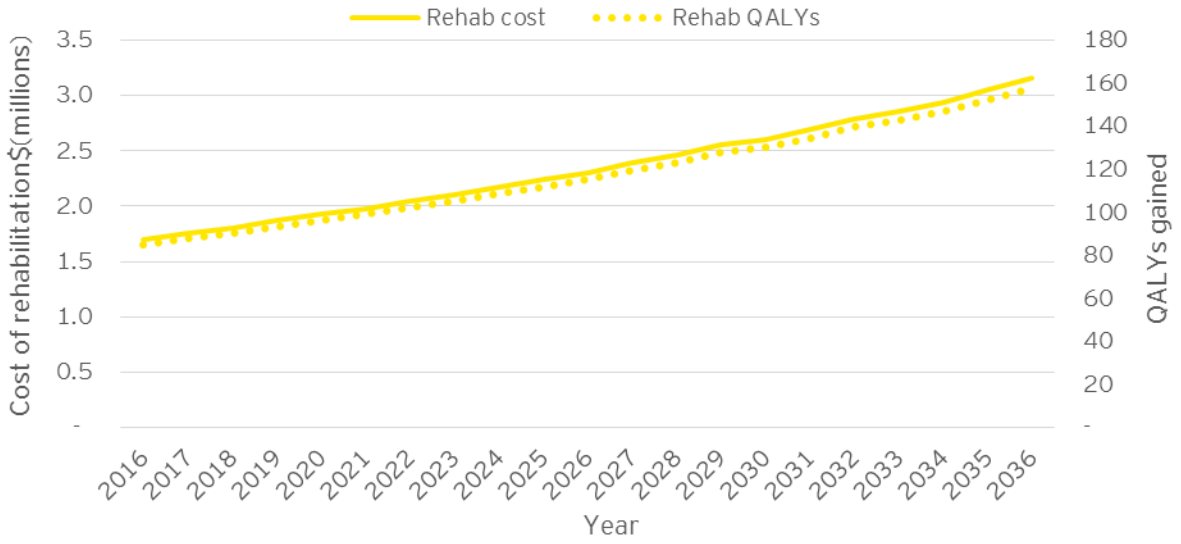
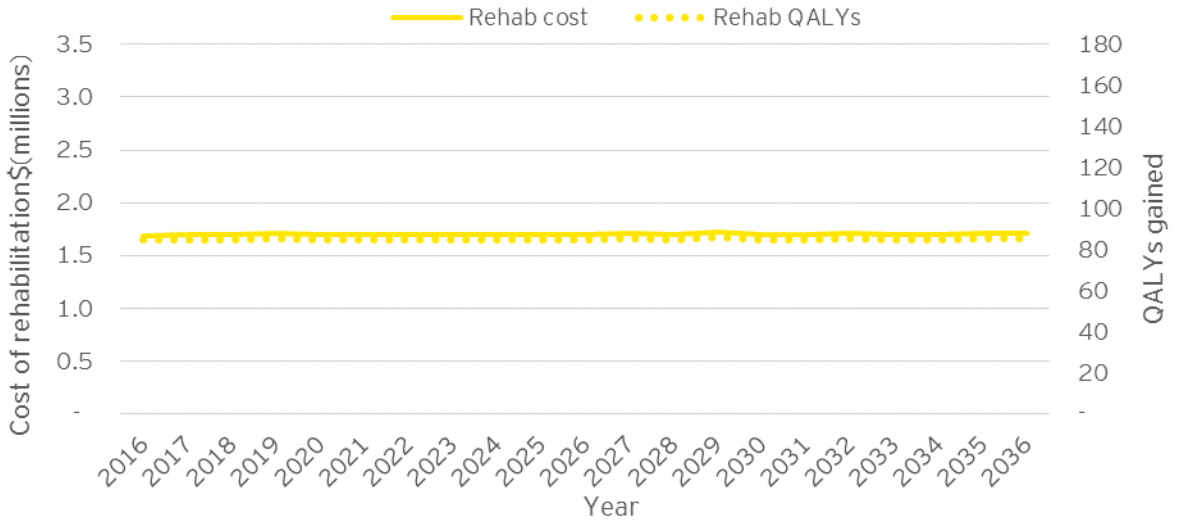


Figure 22: Time series modelled discounted future state of rehabilitation cost and QALYs gained



7. Summary tables

Tables 14 and 15 below summarise the various potential effects changes in the model of care for AMD may have.

Table 14: Summary table of costs and QALYs gained in modelled scenarios

Scenario	Scenario	Model approach used	Cost ($m)	QALY	Cost per QALY
Detection	Slow time to treatment	Cohort	1.2	-5,000	-
AREDS2	Current state 10% uptake	Cohort	0.7	100	*6,600*
AREDS2	Future state 50% uptake	Cohort	3.2	500	*6,500*
AREDS2	Future state projected forward	Time series	9.2	1,200	*9,900*
Treatment	Current state	Cohort	38.2	19,900	2,170
Treatment	Current state projected forward	Time series	148	27,700	2,900-
Treatment	Aflibercept second line	Cohort	30.5	19,900	1,970
Treatment	'Slow access' schedule	Cohort	46.3	10,400	4,960
Treatment	Future state projected forward	Time series	87	28,800	2,070
Rehabilitation	Current state	Cohort	4.7	230	*20,400*
Rehabilitation	Future state	Cohort	26	1,300	*20,000*
Rehabilitation	Future state projected forward	Time series	49	2,500	*19,600*

Note: AREDS2 and Rehabilitation estimates are more speculative

Table 15: Summary table of costs of sessions by HCA presence

Scenario	Model approach used	Sessions without HCA	Cost without HCA ($m)	Sessions with HCA	Cost with HCA ($m)
Current workforce	Cohort	2,590	0.9	1,720	0.7
Current workforce projected forward	Time series	-	33.0	-	26.0
Future workforce	Cohort	2,590	0.4	1,720	0.4
Future workforce projected forward	Time series	-	11.8	-	11.6

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