National Health Committee

Age-Related Macular Degeneration
National Health Committee (NHC)

The National Health Committee (NHC) is an independent statutory body charged with prioritising new and existing health technologies and making recommendations to the Minister of Health.

It was reformed in 2011 to establish evaluation systems that would provide the New Zealand people and the health sector with greater value for money invested in health.

The NHC Executive is the secretariat that supports the Committee. The NHC Executive’s primary objective is to provide the Committee with sufficient information for it to make decisions regarding prioritisation and reprioritisation of interventions and services. They do this through a range of evidence-based products chosen according to the nature of the decision required and timeframe within which decisions need to be made.

The New Zealand Government has asked that all new diagnostic and treatment (non-pharmaceutical) services, and significant expansions of existing services, are to be referred to the NHC.

In August 2011 the NHC was appointed with new Terms of Reference and a mandate to establish the capacity to assess new and existing health technologies. Its objectives (under Section 4.2 of its Terms of Reference – www.nhc.health.govt.nz) include contributing to improved value for money and fiscal sustainability in the health and disability sector by:

- providing timely advice and recommendations about relative cost-effectiveness based on the best available evidence;
- providing advice and recommendations which influence the behaviour of decision makers including clinicians and other health professionals;
- providing advice and recommendations which are reflected in resource allocation at national, regional and local levels; and
- contributing to tangible reductions in the use of ineffective interventions and improved targeting to those most likely to benefit.

In order to achieve its objectives under Section 4.2 and to achieve ‘Value for Money’, the NHC has adopted a framework of four assessment domains – Clinical Safety & Effectiveness; Economic; Societal & Ethical; and Feasibility of Adoption – in order that assessments cover the range of potential considerations and that the recommendations made are reasonable.

It is intended that the research questions asked will fall across these domains to ensure that when the Committee comes to apply its decision-making criteria, it has a balanced range of information available to it. When the NHC is setting those questions they will have the decision-making criteria in mind.

The 11 decision-making criteria will assist in the determination of the NHC work programme and in the appraisal and prioritisation of assessments.
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National Health Committee (NHC) and Executive  
Disclaimer
Executive Summary

This report explores the model of care for patients with age-related macular degeneration (AMD) and identifies interventions where the National Health Committee (NHC) could conduct further assessment to support improvements in health outcomes and efficiency.

A referral for assessment of bevacizumab was put forward by Waitemata and Auckland District Health Boards (DHBs) as part of the NHC 2013/14 referral round. To determine the appropriateness of the NHC carrying out further work on bevacizumab, AMD as a whole was first assessed.

AMD is the leading cause of blindness in New Zealand in those aged over 50, accounting for half of all cases. It is estimated that 15,000–30,000 people in New Zealand are affected by late (advanced) AMD, with 10,000–20,000 affected by the more severe and rapidly progressive wet form. The prevalence is expected to increase by 20–40% in the 10 years as a result of population ageing.

First-line treatment of wet AMD is with intravitreal injection of vascular endothelial growth factor inhibitor (anti-VEGF) agents, which not only slow loss of vision but can improve vision for a substantial proportion of patients. The agents bevacizumab (Avastin) and ranibizumab (Lucentis) have similar effectiveness, but PHARMAC has restricted ranibizumab use to cases where bevacizumab is not appropriate because of its higher cost. There has been a three to five-fold increase in the volume of bevacizumab procedures in New Zealand in the last five years, and growth in demand for anti-VEGFs can be expected to continue. There is also significant variance between DHBs in the rate of procedures being performed, and how the treatment is delivered.

In New Zealand, current annual costs of AMD are estimated at between $19.5–$31.4 million across the public and private systems, including inpatient and outpatient care, primary care optometry and rehabilitation services. A large proportion of care provision is paid for privately, but the proportion differs across DHBs. Of this cost, $4 million–$8 million is incurred for wet AMD. True current costs of anti-VEGF treatments are estimated at between $3 million and over $6 million, but this cost is probably offset by reductions in other costs of care (such as result from increased risk of hip fracture and earlier admission to aged residential care facilities). The number of people aged 45–85 years with AMD is estimated to increase by 13% by 2026, and those with late AMD by more than 40%, with a resulting increase in costs of treatment of AMD.

An assessment by the NHC of the use of anti-VEGF treatments in AMD could support appropriate planning to ensure that there is equitable access across the country, and by defining the most efficient means of delivery, ensure that patient outcomes are optimised while costs are controlled.

NHC’s role would be to support other players in achieving appropriate prioritisation to meet demand for anti-VEGF agents within other competing priorities for ophthalmological budgets.
1 Purpose

The purpose of this report is to explore the model of care for patients with age-related macular degeneration (AMD) and identify interventions where the National Health Committee (NHC) could conduct further assessment in order to improve health outcomes and efficiency.
2 Introduction

The NHC is tasked with improving health outcomes while maintaining or reducing costs by prioritising the most cost-effective new and existing health technologies. ‘Value for money’ is assessed in terms of health outcomes and cost to the health and disability sector. The NHC’s goal is to improve health outcomes and health sector sustainability through better investment and targeting of technologies and service reconfiguration. The NHC operates within the clinical model of care.

The majority of NHC assessments come through a proactive work programme based on a tiered identification of specific disease and service areas; using programme budget, burden of disease and horizon scanning information. The NHC also undertakes an annual referral round for sector referrals for assessments.

A referral for assessment of bevacizumab (Avastin) was put forward by Waitemata and Auckland District Health Boards (DHBs) as part of the 2013/14 referral round. To meet the remit of the NHC, the wider model of care for all of AMD needs to be considered to identify those points of care where further assessment is justified.

Methods used in this report are provided in Appendix 1.
3 Background

3.1 Age-related macular degeneration (AMD) description

AMD is the leading cause of blindness in New Zealand.\(^1\) However, while vision loss associated with advanced forms of AMD can be so severe that it is legally classified as blindness, it does not normally cause total loss of sight and some side vision is maintained in almost all cases.

AMD is characterised by age-related changes to the macula without any other obvious precipitating cause in people aged 50 years and older.\(^2\) The macula is the central region of the retina, which is the light sensitive tissue at the back of the eye that focuses images and relays them to the brain. It is involved in the detailed central vision important for many daily activities, such as reading, driving and recognising faces. In AMD, the deterioration of the macula causes progressive vision loss in the centre of the field of vision. One or both eyes can be affected.

AMD has two pathologically distinct stages: dry (non-exudative) and wet (exudative or neovascular) AMD.\(^3\) However, it may be more clinically useful to classify AMD as early and late AMD, with late AMD including advanced dry AMD (geographic atrophy; GA AMD) and wet AMD.\(^2\) Usually, only late AMD is associated with significant vision loss.

About 75–80% of AMD patients have early AMD, the most common and less severe form.\(^4\) In early AMD, abnormalities develop in the retinal pigment epithelium (RPE) and lipid deposits (drusen) form underneath the RPE (see Figure 1). When eyes are affected only by drusen and early RPE irregularities, people do not usually suffer noticeable vision loss, although some may have subtle distortions in vision.\(^2\) As the disease progresses, the macula becomes thin and can start to break down. About 4% of patients with early AMD progress to late AMD each year.\(^5\)

Ten to fifteen percent of cases are late-stage dry AMD, characterised by geographic atrophy, focal areas of atrophy of the RPE and degeneration of the light-sensitive photoreceptor cells. There is usually a slow but marked progressive decline in central vision over several years in this stage;\(^2\) and roughly a quarter of patients with atrophic AMD experience severe vision loss or blindness.\(^1\)\(^5\)

Most cases start as dry AMD, and about 10–15% progress to wet AMD.\(^4\) Wet AMD is caused by abnormal growth of new choroidal blood vessels (choroidal neovascularisation; CNV) under the retina, which leak blood and proteins into the macular region. This leakage causes thickening of the retina and fibrosis, resulting in scarring and permanent damage to the photoreceptor retinal cells. CNV includes classic or occult forms; the classic form is associated with more rapid progression. Wet AMD progresses rapidly with acute central visual disturbance followed by unremitting vision loss.

\(^1\) Blindness is defined for this estimate as visual acuity worse than 6/60 (i.e. what the vision-impaired person can see clearly at 6 metres can be clearly seen by an unimpaired person at 60 metres); and/or a visual field of less than 10°.
Without treatment, 40–50% of patients with wet AMD experience severe vision loss\(^2\) in at least one eye within 1 to 3 years,\(^2\) and as many as three-quarters will eventually experience severe vision loss or blindness.\(^5\)

**Figure 1: Pathological processes of age-related macular degeneration**

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No specific cause for AMD other than age-related change has been identified, but risk is increased by smoking, family history and genetic factors.\(^2\) Genetic factors may explain as much as 80% of AMD, with a mutation in the gene for Complement Factor H (a key regulator of the complement pathway) being important in at least half of cases. Various other risk factors have also been proposed, including lifestyle and nutritional factors, and possibly cardiovascular disease.

### 3.2 Prevalence and incidence

Prevalence of AMD tends to be higher among populations of European ancestry than other ethnicities such as Asian people.\(^6\) Particularly relevant to New Zealand, prevalence of AMD among Māori and Pacific peoples is thought to be very low, and more likely to be the polypoidal choroidal vasculopathy variant.

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\(^2\) Loss of at least 6 lines of distance vision.
As there are no recent comprehensive prevalence studies of AMD in New Zealand, estimates are based on extrapolation from international data. However, it should be noted that reported rates vary depending on AMD definition criteria, diagnostic accuracy, and the ethnicities and age ranges studied. In two major Australian studies involving more than 8,000 people, the prevalence of early “age-related maculopathy” was 7–15% depending on the grading criteria and age range (over 40 or 49 years).\(^7,^8\) The prevalence of late AMD ranged from 0.68% to 1.9%, with wet AMD accounting for half to two-thirds of late AMD and the remainder being late dry (GA) AMD.

Wong et al, in a meta-analysis that included only high quality studies that used retinal photographs and standardised grading systems (total \(n = 129,664\)), estimated the global prevalence of any AMD in people aged 45 to 85 to be 8.7%.\(^6\) The rate of AMD was higher among those of European ancestry (12.3%) than those of Asian ancestry (7.4%). Prevalence of late AMD was 0.37% overall and 0.5% in European populations. However, this is likely to be a significant underestimate because those aged over 85 years were excluded. In another meta-analysis of predominantly White populations aged over 50 years (\(n = 57,173\)), the rate of late AMD was estimated to be 2.4%, with approximately half being wet AMD (1.2%) and half being GA AMD (1.3%).\(^9\) All the studies consistently found an exponential increase in the rate of late AMD in those aged over 70 years (example shown in Figure 2).\(^6,^9\)

International estimates of the 5-year incidence of AMD are approximately 8% for early disease, and 1% for late AMD for middle-aged and older populations, again increasing markedly with age.\(^10,^11\) Ten-year incidence is 10–15% for early AMD and 2–4% for late AMD.\(^11\)

**Figure 2: Blue Mountains Eye Study (Australia) prevalence of late AMD (wet or GA) by age 85**

![Graph showing prevalence of late AMD (wet or GA) by age 85](source)

Prevalence rates from the Wong et al. international meta-analysis, stratified by ethnicity, were recently applied to the New Zealand population aged 45–85 years (prevalence in Māori and Pacific peoples was assumed to be zero).\(^12\) This analysis estimated that 184,400 people (10%) aged 45–85...
years had AMD in New Zealand in 2014, with 7,600 people (0.42%) having late AMD. However, the analysis did not apply age-specific prevalence rates. Other data suggest that when those aged over 85 are included, the total prevalence of late AMD for those aged over 45 is approximately double the prevalence for 45–85 year olds. If this is correct, then the estimate of late AMD in New Zealand may be closer to 1% when those aged over 85 are included and the aging of the New Zealand population is considered. The lower age limit for our estimates is 50 years because of the low incidence of AMD in those under 50.

Based on the New Zealand and other analyses, we estimate that 150,000 to 200,000 New Zealanders aged over 50 have AMD. Our estimates use the prevalence rate of 1% of late AMD from the New Zealand analysis to represent a lower limit that may apply in New Zealand for those aged over 50. From the international data, we estimate that in New Zealand:

- between 15,000 and 30,000 people aged over 50 with late AMD, based on an upper limit of 2% for late AMD
- 5,000 to 10,000 people have late dry AMD
- 10,000 to 20,000 people have wet AMD, because wet AMD is between half and two-thirds of late AMD
- approximately 3000–4000 people are newly diagnosed with late AMD each year.

New Zealand has an aging population, so the future prevalence of late AMD can be expected to increase significantly. The New Zealand analysis estimated that the number of people aged 45–85 years with both any AMD and late AMD would increase by 13% between 2014 and 2026. However, the analysis used an average prevalence for 45–85 year olds and doesn’t account for the ageing of the population. Age-specific prevalence estimates for Europeans from the Wong et al meta-analysis, applied to New Zealand population projections by age group, and extrapolated to include those aged over 85, suggests an increase of more than 40% in the number of people in New Zealand with late AMD by 2026; and that the number may double in the next 25 years (see Figure 3). This is consistent with Wong et al’s estimated predicted increases for many other regions: increases in late AMD of 30–50% predicted globally and for Oceania, North America and Asia by 2026, and increases of 80–120% by 2040; although lower rates at 15% and 44% respectively are predicted for Europe. For this analysis, we estimate that prevalence will increase by 10–20% over the next 10 years.
In New Zealand, about half of all cases of blindness in those aged over 50 result from AMD, currently reported as 6000–7000 people.\(^1\) However, evidence that some of these patients have other macular conditions rather than AMD suggests that this may be an overestimate. There is also a group of patients who do not qualify as legally blind but have such severely low vision that they are not able to carry out many of the activities of daily living or hobbies.

The incidence of low vision and blindness among those with AMD may be reducing as a result of better treatments. A Danish study found that the incidence of legal blindness due to AMD halved between 2000 and 2010. As Figure 4 shows, most of the decrease was from 2006 onwards. This coincided with the introduction of the vascular endothelial growth factor inhibitors (anti-VEGF agents; see section 0).\(^1\) In contrast, while the incidence of other non-AMD forms of blindness also decreased by one-third, this occurred almost entirely before 2006.

A similar trend has been reported in New Zealand based on the incidence of membership with the New Zealand Blind Foundation.\(^3\) Membership for blindness related to AMD increased by about 10% per year, from approximately nine memberships per 100,000 population in 1995 to 19 in 2005. After 2005, coinciding with the introduction of anti-VEGF treatment, the incidence declined by a similar rate (from approximately 19 memberships per 100,000 population in 2005 to 14 in 2010).\(^1\)

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\(^3\) Criteria for adult membership is visual acuity not exceeding 6/24 in the better eye with corrective lenses, or serious limitations in the field of vision, generally not greater than 20 degrees in the widest diameter in the better eye.
3.3 Health outcomes

A US study, in a 10-year follow-up after first diagnosis of any form of AMD in 32,207 people aged over 68, found the incidence of blindness was 3.2% and the incidences of severe and moderate vision loss were 5.4% and 6% respectively. Rates in those without AMD were 1.2%, 1.3% and 3.6% respectively.\[17\]

AMD is not a primary cause of death. However, it is associated with a greater mortality: people with severe AMD are twice as likely to die from a circulatory disorder.\[18\] AMD is also associated with a health burden that can be quantified as disability-adjusted life-years (DALYs). DALYs are a measure of health burden, and combine the loss of quality and quantity of life. The New Zealand Burden of Disease study estimated that, in New Zealand in 2006, AMD was associated with loss of 1118 disability-adjusted life-years\[4\] (DALYs).\[19\] The study assumed that there were no deaths attributable to AMD, and averaged the effect on quality of life across all people with AMD. This produced a relatively low approximate estimate of an 11% loss of quality of life (disability weight 0.111). It should be noted that people with significant vision loss from AMD would individually have a much greater loss of quality of life.

Even when AMD is relatively mild, it adversely affects quality of life and interferes with activities of daily living, social interaction and participation in leisure or work activities.\[20, 21\] Patients with AMD often experience depression. It is also associated with an increased risk of injury, falls and hip fractures; and with loss of independence needing aged residential care. This loss of independence, particularly, creates a significant health and cost burden. The risk of admission to an aged residential

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\[4\] Disability-adjusted life-years (DALYs) are a measure of health burden, and combine the loss of quality and quantity of life. One DALY is equivalent to loss of a year of life in perfect health.
care facility in patients with AMD has been shown to be 6% higher than for age-matched controls.\[^{17}\]
However, when there is AMD-related severe vision loss or blindness, it is likely that the risk of admission to an aged residential care facility is doubled, as it is in other visually impaired populations.\[^{1,17}\]

### 3.4 Health utilisation and cost

There are no New Zealand studies specifically of the cost of AMD. A 2010 Australian report\[^{5}\] estimated that total direct health care cost for vision loss associated with AMD was AU$359 million per year, and AU$3,350 (NZ$4,300) per year per person with severe vision loss/blindness from AMD.

However, this cost included AU$270 million (an average of $2,500 per patient) spent on the anti-VEGF agent ranibizumab. The pharmaceutical costs for treatment of AMD in New Zealand are likely to be around one-tenth of that, because the much cheaper bevacizumab rather than ranibizumab is used in more than 90% of cases (see section 0). When the direct health costs of ranibizumab are excluded, the cost per patient with severe vision loss/blindness due to AMD was AU $832 per person (around NZ$1,000) per person. Applied to New Zealand, this would suggest direct health costs of over NZ$17 million (excluding pharmaceutical costs) for patients with severe vision loss/blindness due to AMD.

A 2009 New Zealand report on vision loss from any cause (by the New Zealand branch of the same consultancy) estimated direct health costs, including both public and private inpatient, day patient and outpatient, pharmaceuticals, general practitioner (GP), optometry, and aged care costs. They found that:\[^{1}\]

- the costs for severe vision loss/blindness in those aged over 40 were $1,583 per person per year
- an estimated 13,000 people in New Zealand have significant vision loss due to AMD, producing a total cost of $20.5 million per year
- this cost doubles when productivity, carer opportunity and other indirect costs are included and
- costs are increased 10-fold if the loss of wellbeing associated with significant vision loss and blindness is included.

These estimates do not include costs for the much bigger group of patients with early AMD or late AMD with no significant vision loss, although these will incur some health costs from diagnostic testing and follow-up. Both the Australian and New Zealand analyses have some limitations.
4 Model of care for AMD

An overview of the model of care for AMD including patient flows and annual costs is shown in Figure 5. This represents a snapshot in time, with the number of patients in each stage represented in mutually exclusive categories – that is, each patient with AMD is allocated to only one stage of disease. In reality, AMD is a progressive disease, and while some patients have stable disease that progresses only slowly, many patients will move through the stages shown in Figure 5 over periods ranging from months to a number of years. Most patients will be diagnosed with dry AMD before progression to wet AMD. However, a significant number of patients present with wet AMD at first diagnosis. Some patients progress to advanced dry AMD with significant loss of vision without progressing to wet AMD.

The model applies to AMD affecting either one or both eyes. The stage is that for the worse eye, except where a patient’s AMD in the worse eye is too advanced to benefit from treatment, but the patient’s other eye is still being treated.
Figure 5: Model of care for AMD including patient flows and annual costs for New Zealand

Stable early to intermediate dry AMD
**Setting:** Community optometry

- **Diagnosis of early AMD**
  - Presents to optometrist (may be by GP referral).
  - Assessment: patient history, VA, fundus (SBM)
- **Asymptomatic, stable**
  - 2-yearly VA & fundus assessment by optometrist

Progressive dry AMD or suspicion of wet AMD
**Setting:** Outpatient ophthalmology

- **Symptoms or progression necessitating referral to an ophthalmologist**
  - Referral from optometrist/directly from GP from other health service if sudden loss of vision/distortion or other symptoms
  - Assessment: VA and fundus (OCT, fundus photos or AF +/- FFA +/- ICG)

Late dry AMD (GA)
**Setting:** Outpatient ophthalmology

- **Diagnosis of intermediate to late dry AMD**
  - AREDS treatment
  - VA and fundus assessment +/- AF

Wet AMD
**Setting:** Outpatient ophthalmology

- **Diagnosis of wet AMD**
  - Assessment for treatment (VA, OCT, fundus photos +/- FFA +/- ICG)
  - Treatment options
    - Anti-VEGF
    - Photodynamic therapy
    - Laser photocoagulation
    - Treatment failure

Setting: Inpatient treatment

- **N = 4500**
- **Costs = $4.5M**

Population: Low vision
**Setting:** Outpatient and community

- **N = 6000**
- **Costs = $3.7M**
  - Low vision or blindness not amenable to treatment (advanced wet or dry AMD)
  - Low vision rehabilitation
  - Blindness equipment and support

AF = autofluorescence imaging; AREDS = Age-Related Eye Disease Study regimen of high-dose vitamins C and E and zinc with either beta carotene or lutein and zeaxanthin; FFA = fundus fluorescein angiography; GA = geographic atrophy; ICG = indocyanine green angiography; OCT = optical coherence tomography; VA = visual acuity assessment; SBM = stereo biomicroscope.

Source: International clinical guidelines [2, 22, 23] adjusted to New Zealand treatment patterns through consultation with a range of ophthalmologists.
4.1 Methods

The model in Figure 5 was developed using international clinical guidelines,\textsuperscript{[2, 22, 23]} adjusted for New Zealand treatment patterns through consultation with a range of ophthalmologists. The number of patients within each category is based on our estimates of prevalence by stage of disease (see section 3.2).

There are limitations to estimating the costs associated with AMD in New Zealand. The estimates of both prevalence and costs are given in ranges to capture the uncertainty, but should still be interpreted cautiously.

Publicly-funded inpatient costs for AMD can be approximately captured by ICD-10 codes under the H35.3 code, which includes all degeneration of the macula and posterior pole.\textsuperscript{5} In publicly-funded hospitals in New Zealand in the 2012/13 year, 1,500 people received inpatient or day patient care (3700 discharges) where macular degeneration\textsuperscript{5} was a primary diagnosis. This was at an average cost of $9,100 per person and a total cost of $14 million,\textsuperscript{24} although it should be noted that these sums include all costs associated with the hospitalisation, not just those specifically AMD-related. Other than inpatient intraocular injections ($225), most eye procedures are associated with hospitalisation costs of $2,000 to $4,000.\textsuperscript{25} We estimate that AMD-related inpatient costs are $3,000 on average. However, people admitted as inpatients or day patients to receive anti-VEGF agents would incur only the $225 cost, while other patients could incur significantly higher costs. We have assumed that all AMD patients treated on an inpatient basis have wet AMD because dry AMD generally causes less severe vision loss and fewer complications.

Most care for AMD is outpatient. Outpatient cost data are recorded by the type of service rather than by diagnosis. All of the services relevant to AMD are within broader ophthalmological services and there are no outpatient codes that are specific to AMD (see Table 1).

<p>| Table 1: Ophthalmology outpatient services most commonly relevant to AMD |
|-------------------------------------------------|---------------------------------|------------------|</p>
<table>
<thead>
<tr>
<th>Purchase unit code</th>
<th>Description</th>
<th>2014/15 national price</th>
</tr>
</thead>
<tbody>
<tr>
<td>S40002</td>
<td>First ophthalmological attendance for specialist assessment</td>
<td>$191.07</td>
</tr>
<tr>
<td>S40003</td>
<td>Follow-up ophthalmological attendances for specialist assessment</td>
<td>$158.63</td>
</tr>
<tr>
<td>S40004</td>
<td>Attendance for minor eye procedures (including administration of anti-VEGFs)</td>
<td>$225.29</td>
</tr>
<tr>
<td>S40005</td>
<td>Argon or YAG laser eye procedures</td>
<td>$216.90</td>
</tr>
<tr>
<td>S40006</td>
<td>Additional ophthalmological consults and treatments resulting from increased fundus screening procedures</td>
<td>$327.25</td>
</tr>
<tr>
<td>S40007</td>
<td>From 2014/15 replaces S40004 for intraocular injections of pharmacological agents</td>
<td>Not available</td>
</tr>
<tr>
<td>S40000</td>
<td>From 2014/15 replaces S40004 for outpatient eye procedures not covered under S40005 and S40007</td>
<td>Not available</td>
</tr>
</tbody>
</table>

\textsuperscript{5} ICD-10 code H35.3 includes AMD, angioid streaks, cysts, holes and puckering affecting the macula, toxic maculopathy, Kuhnt-Junius degeneration and degenerative drusen of the macula.
In 2012–13, approximately 280,000 people attended general ophthalmology outpatient or non-admitted emergency department services in publicly-funded hospitals at an average cost of $220 each and total cost of over $60 million.\textsuperscript{[26]} If we estimate that 15% of general ophthalmology attendances are for AMD (with a range of 10 to 25%), our estimated AMD outpatient population is 42,000 (range 28,000 to 70,000), including both dry and wet AMD. The proportions of outpatients that have wet or dry AMD are based on our estimates of prevalence (section 0).

### 4.2 Overall costs

We estimate that AMD is associated with inpatient costs of approximately $4.5 million, and outpatient costs of $7 to $17 million within the publicly funded system. Currently a substantial amount of care for AMD patients is in the private sector; in some regions possibly as many as half of AMD patients are treated privately, including follow-up of all types of AMD and treatment of wet AMD. The upper estimates in this model represent potential costs if all patients were cared for within the public system.

Additionally, we estimate that $4.3 to $6.2 million is spent on optometrist care in the primary care sector, most of which would be paid for privately by the patient. Low vision and blindness services are estimated to cost a further $3.7 million; these costs may fall across various sectors, including publicly-funded outpatient low vision clinics, private low vision services, Blind Foundation services, and other ancillary or allied health professional services.

### 4.3 Dry AMD model

There are very limited options for treatment of dry AMD, with treatment consisting mainly of counselling, smoking cessation, and visual rehabilitation. Preventive treatment with antioxidant vitamins and minerals may be recommended for those with intermediate to advanced dry AMD.\textsuperscript{[2, 22, 27]}

In the current model of care, patients with early and asymptomatic AMD are primarily cared for by optometrists within primary care. We estimate these patients are seen on average once every two years at an average cost of $75 per visit,\textsuperscript{[1]} a total cost of $4.3–$6.2 million. International guidelines indicate that if there are no symptoms, patients with dry AMD should be examined every 6 to 24 months.\textsuperscript{[22]} Measurement of visual acuity and examination of the fundus with stereo biomicroscopy is adequate; more extensive scans such as optical coherence tomography (OCT) are not indicated for asymptomatic early AMD. In New Zealand, there is often not regular follow-up for those with these patients other than the monitoring when patients have their regular optometrist check-up, normally every two years. Based on the prevalence of early AMD, we estimate that 115,000 to 165,000 people may be managed in this way; however, this number is likely to include a proportion of people who do not regularly see an optometrist and remain undiagnosed.
An integral part of the model of care is that patients are advised to self-monitor for significant deterioration of vision (for example, using the Amsler grid test) or new symptoms, which will trigger further investigation and specialist referral to the public or private sector. New Zealand data indicate that somewhere between 28,000 and 70,000 people attend at least one outpatient ophthalmological appointment related to AMD; it was not possible to calculate more precise numbers because publicly-funded ophthalmological consultations are not coded by diagnosis.

We estimate that for 14,000 to 42,000 patients each year the outpatient ophthalmological appointment is a one-off investigative consultation at a cost of $191 per patient (outpatient code S40002) and a total cost of $3–$8 million. The consultation includes measurement of visual acuity and more detailed fundus assessment with scans, as shown in Figure 5. Standard management would include optical coherence tomography (OCT). Fundus fluorescein angiography (FFA) or indocyanine green angiography (ICG) may be used where needed for additional information, to detect polypoidal choroidal vasculopathy or to exclude masquerade conditions; but they are not available in all clinics and additional funding is not provided for their use in the public sector.

Patients with intermediate to late dry AMD may be recommended the AREDS (Age-Related Eye Disease Study) vitamin/mineral regimen to reduce the risk of progression to more advanced stages of dry AMD and to wet AMD. However, this treatment is not funded and must be paid for by the patient at a cost of approximately $400 per year. For those with intermediate to advanced dry AMD,\(^6\) the AREDS combination of high-dose vitamins C and E, zinc and beta carotene or lutein and zeaxanthin was shown to reduce the 5-year risk of further significant progression by about 25%.\(^{28, 29}\)

There is no evidence to support the use of this supplement in those with early AMD.\(^{28}\)

Although regular follow-up of patients with late dry AMD is recommended internationally,\(^{22}\) feedback from New Zealand ophthalmologists indicates that there is no standard in place in public hospitals for follow-up of patients with late dry AMD, largely because of the current lack of effective treatments to offer such patients. Follow-up of late dry AMD is incorporated into our model of care as currently occurring on average only once every two years, costing $191 per visit (outpatient code S40002) and a total of $0.5–$1 million. Internationally the recommended method for assessing progression of late dry AMD (GA) is autofluorescence imaging,\(^{21}\) but this is not yet widely available in New Zealand.

Focal laser treatment is not recommended. While the treatment can resolve drusen, there is no evidence that this prevents subsequent progression of AMD or visual loss.\(^{21}\) Various surgically implanted intraocular optical aids for end-stage atrophic AMD are under investigation internationally.

Patients with advanced or symptomatic late dry AMD, after exclusion of masquerade conditions, are normally discharged from the hospital clinic and are then managed through low vision or Blind Foundation services (see section 4.5).

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\(^6\) Defined as extensive intermediate drusen, at least one large drusen or non-central GA in one or both eyes, or advanced AMD or visual acuity <20/32 attributable to AMD in one eye.
4.4 Wet AMD

Because wet AMD progresses rapidly, patients presenting to general practitioners or optometrists with symptoms indicative of wet AMD should be referred for an urgent ophthalmology consultation (they should be seen by a specialist within two weeks of development of symptoms or detection of a treatable lesion). The presence of wet AMD is established by fundus assessments including OCT and fundus photographs, with other scans as indicated (e.g. FFA or ICG to detect masquerade conditions or polypoidal choroidal vasculopathy).

Treatment is initiated in wet AMD where there is evidence of CNV activity or progression and the patient is considered likely to benefit. Treatment is likely to be futile when there is permanent structural damage with atrophy to the central macular retinal photoreceptors and/or subretinal scarring where improvement or prevention of further vision loss is unlikely. Assessment for suitability of treatment includes visual acuity and OCT as a minimum.

A possible treatment model for wet AMD is shown in Figure 6; however the service delivery model currently differs between clinics.

Anti-VEGF treatments were introduced to clinical practice for wet AMD in the mid-2000s, and guidelines now recommend intravitreal administration of these agents as first-line treatment of wet AMD. As well as reducing the risk of progression of vision loss, these agents can improve vision for a substantial proportion of patients. Previously available treatments only halted or slowed the progression of vision loss and rarely improved vision. Vertepofin-photodynamic therapy (vPDT) and laser photocoagulation are no longer part of the standard model of care, and are used only in specific cases. Vertepofin-photodynamic therapy may be used for the polypoidal choroidal vasculopathy variant of AMD. Laser may be occasionally used where there is a small well defined lesion well away from the fovea.

In the current model of care, we estimate that 9000–18,000 patients with wet AMD receive outpatient care at a total cost of $4 million–$8 million, with an additional 1500 patients treated as inpatients at an estimated cost of $4.5 million. Anti-VEGF treatment may be given on an inpatient or outpatient basis at a cost of $225 per administration (outpatient code S40004). Based on current evidence that the supply of anti-VEGF treatment is not meeting the potential demand (see section 6.5), we assume that currently half of patients with wet AMD receive an average of four treatments in a year, and the remainder of patients are not treated or are treated privately. However, the number of anti-VEGF treatments and the frequency of assessments and ophthalmological consults, and therefore the costs, will depend on the service model. This currently varies between different centres and is discussed in greater detail in later sections.

Anti-VEGF treatments are used only for as long as a response is maintained. If there is no useful response after the induction period of three anti-VEGF treatments (that is, if vision doesn’t improve beyond 6/60), treatment may be discontinued if the patient is considered unlikely to benefit. If the patient is responding, regular treatment is continued until the eye becomes dry; most ophthalmologists in New Zealand now use the treat and extend regimen, where the interval between treatments is slowly extended as long as response is maintained. If disease activity returns, the
interval between treatments is reduced. Anti-VEGF treatment is discontinued once there is evidence of persistent deterioration in visual acuity and/or identification of anatomical changes in the retina that indicate inadequate response to therapy.\textsuperscript{[30]} About 5–10% of patients don’t respond to the first anti-VEGF agent trialled, but may respond to an alternative anti-VEGF.

Those patients who are unlikely to benefit from initiation or continuation of treatment are assumed to be discharged from the hospital clinic and receive low vision or Blind Foundation services (see section 4.5).

Figure 6: Possible treatment model for wet AMD

<table>
<thead>
<tr>
<th>Assessment of eligibility for treatment (VA, OCT, fundus photos +/- FFA or ICG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wet AMD suitable for anti-VEGF treatment</td>
</tr>
<tr>
<td>Treatment administered and patient monitored by nurse specialist, GP specialist or ophthalmologist</td>
</tr>
<tr>
<td>Initial induction treatment (monthly x 3 treatments)</td>
</tr>
<tr>
<td>Ophthalmologist assessment of response after 3 treatments: OCT, fundus photos +/- FFA</td>
</tr>
<tr>
<td>Inadequate response</td>
</tr>
<tr>
<td>Stabilisation or improvement of AMD</td>
</tr>
<tr>
<td>Trial of alternative anti-VEGF</td>
</tr>
<tr>
<td>Disease progression despite treatment or treatment not tolerated</td>
</tr>
<tr>
<td>Treat until dry: continuation with treat and extend; assessment by ophthalmologist every 1–2 treatments</td>
</tr>
<tr>
<td>Discontinuation of treatment</td>
</tr>
</tbody>
</table>

FFA = fundus fluorescein angiography; GA = geographic atrophy; ICG = indocyanine green angiography; OCT = optical coherence tomography; VA = visual acuity assessment; SBM = stereo biomicroscope; tx = treatments.

4.5 Low vision/blindness

For patients who have significant vision loss or blindness due to either late dry AMD or wet AMD that is not amenable to anti-VEGF treatment, low vision or blindness services are the only management option.
Low vision rehabilitation aims to improve the use of available and functional vision, and can cover a broad range of disciplines and services. Low vision rehabilitation can include psychosocial support; training in use of low vision aids and adaptive techniques for household tasks, orientation and mobility; and development of visual techniques such as eccentric viewing to optimise utility of peripheral vision. Blindness services can similarly include aids, training in adaptive techniques and support.

The Blind Foundation is New Zealand’s main provider of sight loss rehabilitation and services for low vision and blindness. Only two hospitals now provide low vision clinics for those patients who do not meet the Blind Foundation’s membership criteria but have vision impairment that reduces their ability to carry out important activities of daily living (e.g. reading, travel, employment, household tasks and leisure activities). Some low vision services are available privately.

The cost of low vision and blindness services is included in the model of care at an estimated average cost of $620 per person and total costs of $3.7 million. This is based on an average cost of $500 per person for low vision aids and equipment, and an average of two low vision or blindness consultations at $60 per appointment.
5  Intervention points

The following section identifies the points on the model of care for AMD where additional work by the NHC would be valuable to ensure a nationally consistent approach to treatment and optimal use of resources (see Error! Reference source not found.).

Table 2: Intervention points for AMD: analysis of the value of a National Health Committee assessment

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Description</th>
<th>Status in New Zealand</th>
<th>Population</th>
<th>Effectiveness</th>
<th>Growth</th>
<th>Aspects for consideration</th>
<th>Value of NHC assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-VEGF agents</td>
<td>Pharmaceutical agents</td>
<td>Bevacizumab and ranibizumab funded for use in wet AMD</td>
<td>Wet AMD</td>
<td>Efficacy established in good quality RCTs</td>
<td>High growth</td>
<td>High priority for assessment</td>
<td>High</td>
</tr>
<tr>
<td>Vision rehabilitation programmes</td>
<td>Multifaceted programme including psychosocial approaches, vision aids, and vision training</td>
<td>Two publicly-funded clinics and some privately-funded services</td>
<td>Significant vision loss from dry or wet AMD</td>
<td>Effective if appropriately structured and comprehensive</td>
<td>Current availability may be less than optimal</td>
<td>Lower materiality than anti-VEGF treatment</td>
<td>Moderate</td>
</tr>
<tr>
<td>Prevention of dry AMD progression</td>
<td>AREDS vitamin and mineral regimen</td>
<td>Some but not all vitamins and minerals funded</td>
<td>Intermediate to advanced dry AMD</td>
<td>Supported by RCTs indicating risk of further significant progression is reduced by about 25%, but findings controversial</td>
<td>Not available</td>
<td>Funding of pharmaceuticals is PHARMAC’s remit. Promotion of use may be best achieved through guidelines</td>
<td>Low</td>
</tr>
</tbody>
</table>

AREDS = Age-Related Eye Disease Study

5.1  Dry AMD

This assessment did not identify any interventions within the model of care for dry AMD for which there would be sufficient value in the NHC carrying out further work. Funding of AREDS vitamins/minerals falls within PHARMAC’s remit.

5.2  Wet AMD

As described above, anti-VEGF treatment has superseded both laser photocoagulation and vPDT except in specifically defined situations. As these latter procedures have been largely phased out, further work on these interventions by the NHC would add little value.
5.2.1 Anti-VEGF treatments

Two anti-VEGF agents are funded in New Zealand: ranibizumab (Lucentis) and bevacizumab (Avastin). Pegaptanib, an earlier anti-VEGF, provided less clinical benefit than ranibizumab and was not recommended for use by the UK’s National Institute for Health and Care Excellence (NICE).\[^{33}\] It was never registered for use in New Zealand. A further anti-VEGF agent, aflibercept (Eylea), is authorised for use in AMD and an application for PHARMAC funding in wet AMD will be considered by PTAC in early 2015. However, it may be used in the small proportion of patients who don’t respond to bevacizumab or ranibizumab.

Ranibizumab provides significantly greater clinical benefit than vPDT.\[^{34}\] In clinical trials, 90–95% of patients treated with ranibizumab lost fewer than 15 letters vision over one year, compared with 60–65% in those receiving placebo or vPDT.\[^{34,35}\] Furthermore, visual acuity was improved by 15 or more letters in 30–40% of those treated with ranibizumab, compared with only about 5% of those treated with vPDT or placebo. On average, visual acuity in patients receiving ranibizumab improved (mean gain 7–10 letters), while those in the placebo or vPDT groups lost visual acuity (mean loss 10 letters).\[^{34,35}\] Bevacizumab has similar effectiveness to ranibizumab.\[^{36}\]

While anti-VEGF agents are now clearly established as first-line treatment for wet AMD, there are a number of issues around choice of anti-VEGF. Both bevacizumab and ranibizumab are monoclonal antibodies that bind to and neutralise the biological activity of human VEGF. However, while bevacizumab is the full antibody, ranibizumab is a modified antibody fragment. The two agents originate from the same pharmaceutical company, but in countries outside the United States they are marketed by separate companies. Ranibizumab was developed specifically for the treatment of wet AMD, whereas bevacizumab was developed for use in cancer. It was initially thought that bevacizumab would not be adequately absorbed into intraocular tissues, but this is now known not to be the case, and bevacizumab has been shown to have similar effectiveness to ranibizumab in wet AMD.\[^{36}\] However, marketing approval for the use of bevacizumab in wet AMD has not been sought by the manufacturers, and use for this indication remains off-label.

There are important implications for clinical practice. Ranibizumab is available as a single-use vial for intravitreal administration. Bevacizumab is available only as an intravenous formulation at the dose used in cancer (25 mg per ml in a 4 ml vial), which is more than 50 times greater than the dose required for AMD (1.25 mg). Therefore, bevacizumab must be reformulated under sterile conditions into the correct dose for intravitreal administration prior to use in an AMD patient, and there may be some wastage.

Despite this, bevacizumab has become the treatment of choice in New Zealand because an intravitreal dose costs less than $100, compared with approximately $2,000 for ranibizumab. PHARMAC has restricted use of ranibizumab in AMD 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.

There has been steep growth in use of bevacizumab in the last five years, with the number of procedures having increased three- to five-fold (see section 6.2). As the prevalence of AMD is predicted to increase by 20–40% in the next 10 years, continued growth can be expected. Therefore,
a national planning strategy may be required to ensure equitable access across regions. Efficiency and value for money may also be improved by a consistent approach that optimises delivery of the procedure, including consideration of the issues around as-needed rather than regular treatment, and administration by a nurse rather than a physician. The appropriateness of an assessment by the NHC to address these issues is further discussed in section 6.

5.3 Low vision rehabilitation

Patients with low vision due to late AMD, whether dry or wet, may potentially benefit from low vision rehabilitation.\[^{31}\] There is evidence that it is effective in optimising visual activity, functioning and the ability to cope with low vision.\[^{37, 38}\] However, it is unclear which specific approaches are most effective, what is the optimal level of intensity of intervention, and which is the most appropriate model of delivery.\[^{38-40}\]

Although previously there were 10 low vision clinics in public hospitals around New Zealand, there are only two remaining (Auckland and Christchurch).\[^{32}\] There are also a small number of private low vision clinics around the country.

The appropriateness of an assessment by the NHC to address these issues is further discussed in section 7.
6 Assessment of increased use of anti-VEGF agents

This section assesses issues around the growing use of anti-VEGF agents against the NHC’s key decision making criteria, to determine whether further work by the NHC would be appropriate. The focus is on bevacizumab because it accounts for more than 90% of anti-VEGF use in AMD in New Zealand.

6.1 Clinical safety and effectiveness

The safety and effectiveness of bevacizumab has been established in a number of clinical trials, including the CATT (Comparison of Age-related Macular Degeneration Treatment Trial) study comparing bevacizumab with ranibizumab in 1,185 patients with wet AMD.[36, 41] Bevacizumab had comparable effectiveness with ranibizumab when given monthly, with the mean change in visual acuity score being an increase of eight letters in both groups, and 94% of patients losing fewer than 15 letters vision over a year. Visual acuity was improved by at least 15 letters in more than 30% of patients with regular treatment with either agent.[41]

Currently, there is a lack of consistency between centres about when bevacizumab treatment should be initiated, how often if should be administered, and for how long treatment should continue. The CATT study also 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 (mean increase of 5.9 letters visual acuity with as-needed bevacizumab compared with 8.0 with monthly treatment).[41] Dosing regimens within clinical practice are still evolving, with potentially more effective “treat and extend” regimens being adopted. In this approach, the duration between treatments is slowly extended after an initial intensive monthly treatment phase. Differences in treatment regimens could have important cost implications.

There are potential complications with intravitreal injections, regardless of the substance administered, including periocular infection, endophthalmitis, uveitis, vitreous haemorrhage, retinal detachment and retinal artery occlusion. Risk of these complications requires that any delivery instruments, and the substance to be delivered intravitreally, are sterile; and that appropriate technique is used. Ensuring this may be more important than the reported minor, clinically unimportant differences in safety between ranibizumab and bevacizumab.[42]

6.2 Materiality

Auckland DHB data show that bevacizumab is the anti-VEGF agent of choice in more than 90% of cases, with ranibizumab and aflibercept mainly reserved for those patients who don’t respond to or can’t tolerate bevacizumab.[16]
The national price for intravitreal administration of bevacizumab is $225 (see Appendix 2 for costs). Since the introduction of bevacizumab for wet AMD in 2006, the number of procedures has been growing rapidly (Figure 7). The exact volume of bevacizumab procedures being performed in New Zealand is currently difficult to quantify, because some centres code it as an inpatient/day patient event while others code it under a general minor eye surgery outpatient purchase unit. Also, the diagnosis for which bevacizumab is used is currently not coded when performed on an outpatient basis. These data represent only bevacizumab that is provided publicly; the amount provided privately could be as much again. The numbers represent the number of treatments rather than the number of individuals treated; it can be expected that each patient receiving bevacizumab will have three to eight treatments in a year.

In the 2012/13 year, 5662 intraocular bevacizumab procedures were performed on an inpatient or day patient basis. We estimate that 50–75% were for treatment of AMD, giving a total of approximately 3,000 to 4,000 inpatient bevacizumab procedures for AMD in 2012/13. In the same year, the number of outpatient minor eye procedures coded, which includes bevacizumab and all other types of minor eye procedures, was 17,027. Based on the growth in eye procedures observed since bevacizumab was introduced for use in AMD, we estimate that between 5000 and 10,000 publicly funded outpatient bevacizumab procedures for AMD are currently being performed each year. Thus, total current public spending on bevacizumab (including administration costs) may be in the range of $1.8 to $3.2 million. However, it is unlikely that the full demand for bevacizumab for AMD is currently being met within the public system, and the true costs if all eligible patients were treated could be more than doubled (see section 6.5).

There has been a five-fold increase of inpatient/day patient procedures for intraocular bevacizumab (for any ophthalmological indication) in the last five years, and possibly a three-fold increase in outpatient procedures. Tracking the volume of intraocular bevacizumab use has been identified as a priority by the National Health Board, and a specific outpatient purchase unit code to capture activity will be in place from 2014/15.

Figure 7: Bevacizumab inpatient or day-patient procedures for any ophthalmological indication

![Graph showing the increase in bevacizumab procedures](source: National Minimum Dataset. Extracted by Ministry of Health, 9 July 2014.)
6.3 **Equity and acceptability**

There is variation between DHBs in the number of bevacizumab procedures performed per year, with anecdotal reports that the rate varies from 40–140 procedures per 10,000 population.\(^{16}\) This suggests that there is not geographical equity in access.

Potential ethical and regulatory issues also exist around the use of bevacizumab being off-label when there is an alternative, but much more expensive, agent of similar effectiveness available that has undergone the assessments required for marketing authorisation for AMD. Medsafe has not been asked to approve use of bevacizumab for use in AMD; neither have other international agencies including the US FDA.

Potential safety concerns arise from the need to reformulate the drug because it is only supplied in 25 mg/ml 4 ml vials, and thus must be dispensed into vials of appropriate dosage for intravitreal administration, with an associated risk of contamination.

6.4 **Cost-effectiveness**

Anti-VEGF treatment appears to be cost-effective in the treatment of wet AMD because of the benefits that are achieved compared with usual care.\(^{43}\)

Clinical data have not shown any benefit sufficient to justify the additional cost of ranibizumab ($2,000) over bevacizumab (less than $100) at current prices in New Zealand. This indicates that the latter is currently likely to be highly cost-effective when choosing between the two agents, other than in cases where the patient doesn’t respond to bevacizumab. This is consistent with a number of international cost-effectiveness analyses that have found bevacizumab to be cost-effective over ranibizumab.\(^{44},^{45}\) However, it will be important to understand whether cost savings are achieved with bevacizumab (compared with standard care without anti-VEGF treatment) when all relevant medical costs are considered. The relative cost-effectiveness of ranibizumab may also change in the future if the cost is significantly reduced. Biosimilars of ranibizumab are being developed and can be expected to sell at a significantly lower cost than the current price of ranibizumab. But these agents are not expected be available until at least 2018, and it may be several years after that that the costs reduce to the same as or less than bevacizumab.

Cost of anti-VEGF treatment is likely to be offset by reductions in other costs of care, especially those related to severe vision loss such as increased risk of hip fracture and earlier admission to aged residential care facilities. Anti-VEGF treatment is also likely to provide significant benefits in terms of avoiding (or delaying) the substantial loss in quality of life associated with progression to severe vision loss or blindness.
6.5 Affordability and feasibility of adoption

The rapid growth in use of bevacizumab in recent years is coupled with expected further growth in demand from increased prevalence of AMD in an aging population. A planned approach is needed to ensure equitable access across all DHBs.

The volume of anti-VEGF treatment needed to fully meet demand can be modelled from volumes supplied by Nelson Marlborough DHB (NMDHB). Almost all AMD care is provided publicly in NMDHB, and there are no restrictions on bevacizumab use. There are currently 115 bevacizumab treatments per 10,000 population in NMDHB. With 50–75% of these estimated to be for AMD, this is equivalent to 60–90 treatments per 10,000 population. The volume has almost tripled in the last five years, but growth now appears to have slowed.

Our estimates of bevacizumab volume (see section 6.2) suggest that currently 18–31 anti-VEGF treatments per 10,000 population are being supplied nationally. The Midlands regional service has recently implemented a minimum standard of 40 publicly-funded bevacizumab treatments per 10,000, equivalent to 20–30 treatments for AMD per 10,000 population. Within the DHBs in their region, the rate previously ranged from 20–40 per 10,000 population (estimated 10–30 per 10,000 for AMD). The true demand in this region is thought to be two to three times greater than this, because more than half of AMD care is provided privately.

Thus it can be estimated that to fully meet current demand for anti-VEGF treatment of AMD, the volume supplied by DHBs would need to increase by 40–60 treatments per 10,000 population, representing a two- to three-fold or greater increase for most DHBs. This increase would take volumes from the current estimated 8000–14,000 publicly-funded treatments to 25,000–40,000 per year. In addition, with the population aged over 50 expected to increase by 15–20% over the next 10 years, the number affected by late AMD is expected to increase by 20–40% (see section 3.2).

There are issues around the way that anti-VEGF treatment is currently funded. The current purchase unit is set at $225, regardless of the type or number of investigations performed alongside the bevacizumab administration. The costs of additional scans such as OCT, FFA and ICG are not covered. The purchase unit includes the cost of the pharmaceutical, which currently varies from $20–$80 per dose of bevacizumab depending on the price charged by external pharmaceutical compounding companies if the hospital doesn’t have the specialised facilities to reformulate bevacizumab into intravitreal doses. The purchase unit does not cover the additional cost of ranibizumab (approximately $2,000 per dose) if this is the anti-VEGF of choice. Ways to address this issue include working with the National Health Board on the most appropriate way to fund treatment, which may include funding of courses of treatment rather than individual treatments; and working to get better consistency around the price of intravitreal bevacizumab dosage forms.

Ensuring that patients can gain the best outcomes possible from anti-VEGF treatment without unnecessary costs being incurred may need workforce reconfiguration and a standardised approach to delivery. Issues include the best setting for administering treatment. Currently centres are inconsistent on whether the patient is treated at an outpatient clinic or admitted for a day patient procedure. Some DHBs contract the service out, while others deliver it in-hospital. All of these
factors affect costs, and potentially the ability of each DHB to provide and fund services at an appropriate level to meet demand.

While the demand for anti-VEGF treatment of wet AMD is expected to increase, there is potential for the cost per treatment to decrease. For instance, the treat and extend regimen, which is currently used by the majority of (but not all) ophthalmologists in New Zealand, reduces the average number of treatments patients receive compared with monthly treatment, and has an acceptable level of effectiveness that is superior to as-needed treatment. Models of delivery within a collaborative team where the patient remains under the supervision of the ophthalmologist, but injections are delivered by a specialised general practitioner or nurse, have the potential to save costs, as has been demonstrated at some DHBs. There is also potential for monitoring costs to be reduced if an agreed standard can be achieved for how many scans are needed during a treatment course and follow-up.

### 6.6 Policy congruence

There is good policy congruence with other work around AMD happening in the National Health Board, particularly the Elective Services team. Currently some DHBs deliver bevacizumab as a day patient procedure and count it against their elective targets, while others deliver the treatment on an outpatient basis and can’t count it against their elective targets. A consistent national approach to service delivery could help address this issue.

The National Health Board has also expressed the need for a better understanding of how supplying anti-VEGF treatment to meet demand affects the mix of ophthalmological procedures, and whether funding the increasing volume of anti-VEGF procedures will put other necessary eye interventions at risk.
7 Risks and opportunities

This report has identified that the priority issue in management of AMD is the growing use of anti-VEGF agents, particularly bevacizumab. When considered against the NHC’s decision-making criteria, there are a complex array of issues that may warrant further work in this area.

The risk of not doing an assessment is that growth in the number of anti-VEGF procedures could be inappropriate and that the model of service delivery could be suboptimal, creating unnecessary costs. If growth of anti-VEGF treatments is excessive, other procedures needing funding within DHBs ophthalmological budgets may be at risk. On the other hand, patient outcomes may be compromised if people do not receive timely anti-VEGF treatment. Experience with the use of bevacizumab in the treatment of diabetic macular oedema at Auckland DHB showed that growth in use can be inappropriate when patient selection criteria and defined treatment models are not followed.

An assessment by the NHC could support a rationalised approach to planning, to ensure that anti-VEGF agents can be equitably accessed across the country; and that patient outcomes are optimised while costs are controlled, by defining the most efficient means of delivery. There is potential for DHBs to cost-save and be able to plan more effectively if there is a nationally agreed trajectory of growth and model of care.

NHC’s role would be to support other players in achieving appropriate prioritisation to meet demand for anti-VEGF agents within competing priorities for ophthalmological budgets. For instance, the Royal Australian and New Zealand College of Ophthalmologists and the New Zealand Association of Optometrists have agreed with the Ministry of Health to convene a working group to develop a new ophthalmology prioritisation tool. This tool will encompass bevacizumab so that access decisions can be made based on assessment of need and ability to benefit.

Despite the promise of anti-VEGF treatment for those with wet AMD amenable to treatment, groups of patients remain for whom the options for management are very limited. No specific treatments are yet available for patients in whom advanced geographic atrophy has severely and irreversibly affected vision. Similarly, there are currently no other well established effective treatments for patients with wet AMD that is too advanced to be amenable to anti-VEGF treatment, or those that are no longer responsive to anti-VEGF treatment. Visual rehabilitation may be the only management option for these patients.

Although visual rehabilitation is a lower priority for NHC assessment than anti-VEGF treatment because the potential health gains are much less (i.e. visual rehabilitation supports development of adaptive techniques rather than addressing the disease process), it is a key aspect of the model of care for AMD. An NHC assessment could be appropriate to help to ensure that those patients that are excluded from or exit the anti-VEGF treatment model receive optimal care.

Identifying which visual rehabilitation techniques and models of delivery are most effective and cost-effective is an issue. Further issues have been identified in Australia, about inappropriately low
volumes of referral to visual rehabilitation and barriers to uptake among those who are referred;[40] and may warrant investigation in New Zealand.

Figure 8: Appraisal of different AMD interventions against selected NHC decision-making criteria

<table>
<thead>
<tr>
<th>Disease</th>
<th>Health/independence</th>
<th>Materiality</th>
<th>Policy congruence</th>
<th>Equity</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>AREDS</td>
<td></td>
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<tr>
<td>Vision rehabilitation</td>
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<tr>
<td>Anti-VEGFs</td>
<td></td>
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</table>

Key
- **Very well/Low risk of assessment/High risk of no assessment**
- **Well/Some risk of assessment or no assessment**
- **Somewhat/Some risk of assessment/Low risk of no assessment**
- **Not really/Some risk of assessment/High risk of no assessment**
- **None/High risk of assessment/Low risk of no assessment**

Source: 2014 NHC Executive Appraisal
Appendix 1: Method

Model of care

To inform the model of care, various guidelines were searched, including guidelines from the National Institute for Health and Care Excellence, Royal College of Ophthalmologists and International Council of Ophthalmology. Systematic reviews were used to provide additional information about specific interventions.

Prevalence and health outcomes

There are no good New Zealand data on the prevalence of AMD. Thus, reports that extrapolated data from Australia to New Zealand demographics\(^1\) and international estimates were used.\(^9\) Projected prevalence was calculated by applying international estimates of the prevalence of AMD by five-year age group to the projected New Zealand population by five-year age group from 2011 to 2061.\(^{14}\)

Health outcome data for AMD were obtained from the New Zealand Burden of Diseases, Injuries and Risk factors Study, 2006–2016 (NZBDS).\(^{19}\) The disability-adjusted life year (DALY) figures from the NZBDS in this report are for the New Zealand population in 2006; these are the most recent data available from the NZBDS.

Costs

The cost of AMD was taken from reports by Access Economics that calculated a range of public and private costs.\(^{1,5}\) The cost of ophthalmology visits was the Outpatient Purchase Unit national price.

The volume of bevacizumab procedures was extracted from the Ministry of Health National Minimum Dataset and National Non-Admitted Patients Collection. These datasets include inpatient, day patient outpatient and non-admitted emergency department procedures. However, the outpatient purchase unit under which bevacizumab has been funded until this year is non-specific (“minor eye surgery”), so it was not possible to calculate exact volumes of outpatient procedures.

The cost of a bevacizumab procedure was based on the cost weight that has now been assigned to same day ophthalmological injections of therapeutic agents (cost weight = 0.0478; 2014/15 Inpatient/Day patient Purchase Unit = $4,681.97; cost per procedure = $225).\(^{46}\) This cost includes all activity associated with the inpatient/day patient event: nursing and physician time, tests and procedures, pharmaceuticals “hotel” costs (e.g. laundry, cleaning etc), overheads and capital. Outpatient costs for bevacizumab administration and other interventions such as ophthalmological consultations were based on national prices for Outpatient Purchase Units. The outpatient price of bevacizumab is also currently $225. The Outpatient Purchase Unit cost includes the activities associated with the outpatient event, e.g. nurse and physician time, administration, overheads and capital.
References


National Health Committee (NHC) and Executive

The National Health Committee (NHC) is an independent statutory body which provides advice to the New Zealand Minister of Health. It was reformed in 2011 to establish evaluation systems that would provide the New Zealand people and health sector with greater value for the money invested in health. The NHC Executive are the secretariat that supports the Committee. The NHC Executive’s primary objective is to provide the Committee with sufficient information for them to make recommendations regarding prioritisation and reprioritisation of interventions. They do this through a range of evidence-based reports tailored to the nature of the decision required and timeframe within which decisions need to be made.

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