Improving accessibility to intravitreal anti-vascular endothelial growth factor treatment for ophthalmic patients in a peripheral centre

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ABSTRACT

AIM: An exponential rise in patients requiring intravitreal anti-vascular endothelial growth factor (anti-VEGF) treatment has occurred over recent years. We addressed this in Palmerston North by establishing a senior nurse-led macular review clinic. We aimed to determine the current intravitreal service accessibility and compared it to results from 2012.

METHODS: Chart analysis.

RESULTS: Planned follow-up was aimed for 42 days, near the end of the anti-VEGF therapeutic effect. It occurred on average at 45.05 (12 to 127) days after initial treatment induction and 40.7 (14 to 77) days for subsequent follow-ups. Treatment was started on average 29.8 (0 to 139) days after the decision was made. Further injections occurred on average 25.7 (0 to 104) days after the retreatment decision. These findings were similar to 2012 where initial follow-up occurred on average 42 (29 to 89) days following treatment, initial treatment 30 (0 to 78) days after treatment decision and retreatment at 34 (6 to 89) days.

CONCLUSION: Instituting the senior nurse-led macular review clinic has enabled timely review of patients despite significant increases in those requiring treatment and surveillance. The average follow-up appointment delay is within the four week guideline set by NICE.

The introduction of intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents heralded an exciting new era in Ophthalmology, thanks to its improved visual outcomes in conditions where there were previously limited treatment options available.1 Bevacizumab (Avastin) is the agent most commonly used in the New Zealand public health sector due to its cost efficacy.2 There has been a reported three to five-fold increase in the number of intravitreal Bevacizumab procedures performed in New Zealand over the last five years.2 This is attributable to increasing treatment indications, the ongoing need for injections by current patients and the constant addition of treatment naive patients.

Unfortunately, the follow-up appointments associated with these procedures have quickly outstripped budgeted outpatient targets, reduced an already fragile capacity, and created a significant impact on an already overburdened public ophthalmic service.3 With an ageing population, increasing options to manage ophthalmic chronic disease and ophthalmology workforce shortages,4 the current ophthalmic strategies and resourcing is failing to adequately meet this need. Innovative and creative changes in service design and delivery are essential to provide timely access and optimal care in the management of sight-threatening conditions such as exudative age-related macular degeneration (AMD).3

The prevalence of AMD affected patients are forecast to continue to rise due to the ageing population and the chronic nature
of the disease.\textsuperscript{3,5,6} Worsley et al suggests that the prevalence of late AMD in New Zealand is likely to increase by 13.6\% by 2026.\textsuperscript{6} Exudative AMD, which requires intravitreal anti-VEGF treatment to prevent devastating visual outcomes, represents a small, but significant proportion of patients with late AMD.\textsuperscript{6} Once started on treatment, patients require ongoing monitoring and treatment for years and possibly the rest of their lives to maintain good visual outcomes.\textsuperscript{6,7}

Frequent monitoring and prompt treatment are essential, as studies have shown that significant losses in visual acuity occur while awaiting intravitreal anti-VEGF treatment, especially in exudative AMD.\textsuperscript{8–10} Furthermore, the expansion of indications for intravitreal treatment, including diabetic macular oedema, retinal vein occlusions and many others,\textsuperscript{3,11–14} has reduced accessibility, timely surveillance and re-treatment. In the resource limited environment we must be faithful stewards of the resources entrusted to us and develop innovative and creative service provision models to address this crisis. The senior nurse-led Macular Review Clinic supervised, credentialed and audited by consultant ophthalmologists is the model adopted here.

### The macular review clinic (MRC)

Consistent with international experience, Palmerston North Eye clinic has felt the impact of the vanguard of the chronic ophthalmic disease, where the increasing demand for initial assessments and subsequent follow-ups vastly exceeded the department's clinical capacity to meet this demand. This resulted in unacceptable delays to both existing follow-ups and urgent first specialist assessments (FSA).

The intravitreal service was identified as a key area that needed to be addressed to ensure ongoing service accessibility while expanding to meet the increasing clinical need. The number of intravitreal injections performed at the Palmerston North Eye Clinic has increased by more than 67\% between 2012 and 2014 and this dramatic rise is expected to continue.

Modelling exercises have shown that the bottleneck in service delivery for patients requiring intravitreal injections is the provision of clinical review follow-up appointments, where clinical details are reviewed and the treatment plan refined, rather than the injection appointments only.\textsuperscript{7} In response, a senior nurse-led macular review clinic (MRC) was established in an attempt to manage the growing “follow-up” waiting list and free up FSAs with consultants for more complex cases and new referrals.

All patients referred to the macular service at Palmerston North Hospital are initially assessed in a senior medical officer (SMO) clinic where the decision to start intravitreal treatment is made and discussed with the patient. In our current service it is not possible to perform injections on the day the decision to treat is made, due to time, space and staffing constraints. Instead patients are placed on a waiting list and receive injections at the next available date. Most commonly, patients receive an induction series of three injections, with further treatment on an as needed (prn) basis as determined at the MRC appointments.

During visits to the MRC, best-corrected visual acuity (BCVA) is assessed, macular photographs, autofluorescence and optical coherence tomography (OCT) scans are taken. Such visits also provide opportunity for patient education on diet, dietary supplementation, smoking cessation and Amsler grid monitoring. Clinical oversight in the form of regular meetings between the nurses involved in the clinic and the patient’s consultant ophthalmologist occur, during which the clinical notes, photos and OCT images of patients that may require intervention are reviewed.

### Aims

This retrospective analysis identified patients that were started on intravitreal treatment in 2013 and 2014 at the Palmerston North Eye Clinic. The primary aim was to determine the length of time between receiving intravitreal injections and patient follow-up appointments. These results were compared to a previous audit performed in 2012 in order to assess the impact of the introduction of the Macular Review Clinic. Secondary aims were to determine the length of time between the decision to treat and the initial intravitreal injection, the delay between later decisions to retreat and receiving treatment as well as the percentage of patients that had a stabili-
sation or improvement of their vision while undergoing intravitreal treatment.

Methods

Study population
A retrospective analysis of the clinical records of patients that were treated with intravitreal injections was undertaken. Patients newly started on intravitreal treatment between January 2013 and December 2014 were identified. We excluded all patients that commenced treatment in other centres, received intravitreal injections in combination with other surgical procedures and those that had not yet completed their induction series or had their first follow-up appointment following their induction series at the time of study completion. Eighty-five patients met the inclusion criteria for this study.

Data collection
Data was collected from the clinical records and entered into an Excel spreadsheet. For the initial appointment the following data was entered:
- Date of birth
- Overseeing consultant
- Diagnosis
- Ocular co-morbidities
- Date of diagnosis
- Best-corrected visual acuity (BCVA)
- Central retinal thickness determined on optical coherence tomography (OCT)
- Phakic/pseudophakic
- Intraocular pressures

For each follow-up appointment the following data was entered:
- Date
- Whether they were seen by a consultant, registrar or senior nurse
- BCVA
- Central retinal thickness on OCT

Following each appointment the treatment (if any), as well as date of intravitreal injection was included. Any complications that occurred as a result of the treatment were also recorded.

Data analysis
We determined the initial follow-up delay, as measured from the final injection of the induction series to the first clinic

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**Figure 1:** Patient flow to and through the Macular Review Clinic (MRC). FSA—first specialist appointment. SMO—senior medical officer.
follow-up appointment. We also looked at subsequent clinic delays, as measured from subsequent intravitreal injections to follow-up clinic appointments. To assess the treatment delay we assessed the time between the initial listing date and first intravitreal injection as well as the delay between listing for further injections and the treatment date. Further analysis was also done to compare these results with a previous audit performed in 2012.

The change in BCVA was determined after the initial injection of intravitreal bevacizumab, after three injections (typically an induction series), as well as one year and at final follow-up appointment at the time of conclusion of this study. The number of intravitreal injections required were also determined. A further analysis was done to determine the percentage of patients that had a stabilisation or improvement of vision.

**Results**

Patients ranged in age between 43 and 94 years, with a mean age of 77.32 years, and 50.6% were male. Figure 2 illustrates the conditions treated with intravitreal injections. 48.24% of patients included were receiving intravitreal treatment for exudative AMD, 29.41% for macular oedema due to retinal vein occlusions (RVO), 20% for diabetic macular oedema (DME) and 2.35% for macular oedema due to other causes.

**Follow-up delay**

After the initial injection or induction series of intravitreal bevacizumab the aim was to see patients in 42 days (six weeks), towards the end of the anti-VEGF therapeutic effect. We found that patients were seen on average 45.05 (range 12–127) days after the final injection of the induction series. Almost half of patients were seen in the aimed 42 days (49.4%). 77.1% of patients

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**Figure 2:** Conditions treated with intravitreal injections. 48% of patients were treated for exudative AMD, 30% for macular oedema due to RVO, 20% for diabetic macular oedema and 2% for other conditions.
were seen in 50 days or less. Of those patients that were delayed, 47.6% were seen within a week (seven days) of the aimed follow-up date, 61.9% within two weeks (14 days) and more than 80% within four weeks (28 days).

After undergoing further intravitreal treatment, beyond the initial induction series, we found that subsequent follow-up appointments occurred on average at 40.7 days with a range of 14 to 77 days. The average was well within the aimed 42 days (six weeks). 56.9% of these follow-up appointments occurred within the aimed 42 days. 87.9% of follow-up appointments occurred in 50 days or less. Of those patients that were delayed 60% were seen within a week (seven days) of the aimed follow-up date, 82% within two weeks (14 days) and more than 98% within four weeks (28 days).

**Treatment delays**

Figure 5 illustrates the initial treatment delay. Patients waited on average 29.78 (range 0 to 139) days for initiation of intravitreal treatment following the decision to treat. This was similar to the results in 2012 where the mean delay was 30 (range 0 to 78) days. 57.6% of patients waited less than
25 days and 84.7% less than 50 days for the initiation of treatment.

Once the decision was made to retreat, patients waited on average 25.72 (range 0 to 104) days for a further intravitreal injection. This was an improvement from 2012 when the mean delay was 34 (six to 80) days. 62% of patients received their injection less than 25 days after listing and 88% in less than 50 days. These findings are illustrated in Figure 6.

**Comparison to previous results**

Table 1 compares the results of this study with an audit performed in 2012.

**Treatment results**

During the course of the study period 48 eyes were started on intravitreal treatment for exudative AMD. The mean age of these
patients was 80.9 (range 59 to 96) years and 47.7% were male. Follow-up duration ranged from six to 28.5 months at the conclusion of this study (with a mean of 15.5 months). The starting BCVA ranged from -0.053 to 2 LogMAR (or 6/5 part to 6/600 Snellen) with a mean of 0.63 LogMAR (or 6/24 Snellen). BCVA was stable, as defined by a loss of visual acuity of less than 0.3 LogMAR (or less than three lines on Snellen testing), in 93.1% after one injection, 90.9% after three injections, 81.5% at one year and 81.3% at final follow-up (mean 15.5 months). An improvement in vision occurred in 51.7% after one injection, 57.6% after three injections, 55.6% at one year and 50% at final follow-up. An improvement of more than -0.3 LogMAR (or more than three lines on Snellen testing) occurred in 13.8% after one injection, 24.2% after three injections, 33.3% at one year and 25% at final follow-up. These results are demonstrated in Figure 8. Patients received one to five injections per year with a mean of 3.7 injections per year.

**Discussion**

There has been a dramatic increase in the number of patients requiring intravitreal treatment over recent years, with a rise of 67% in the number of intravitreal procedures being performed in Palmerston North from 2012 to 2014. This is due to the ongoing treatment needs of the existing patient cohort, continual addition of new patients requiring treatment and the ever expanding indications for intravitreal treatment.14

In order to improve intravitreal service availability and hence efficacy, we need to reduce both the treatment and follow-up delay.

**Table 1:** Comparison of current study results to a similar audit performed in 2012.

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<td>Range (days)</td>
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**Figure 7:** BCVA at the start of treatment, after one injection, after three injections, at one year and at final follow-up.
Follow-up appointment delay
Following intravitreal treatment patients require frequent ongoing clinic follow-up appointments. Access to these follow-up appointments has been shown in modelling exercises to drive the need for increased capacity in an intravitreal service. Previously, all patients receiving intravitreal treatment at the Palmerston North Eye Clinic were seen on a regular basis by a consultant ophthalmologist. However, expanding the roles of non-consultant clinical staff, such as nurses, in a multidisciplinary approach to patient management allows for consultants time to be used more efficiently. Furthermore, advanced nursing has been advocated internationally as a cost-effective service resource to assist in overcoming workforce shortages, with ophthalmic nurses leading AMD triage clinics and wet AMD review clinics in the UK.

In Palmerston North we adopted a similar approach, instituting the senior nurse-led MRC. This has allowed us to increase the number of available follow-up appointments and also freed up consultant appointments in order to see new patients requiring intravitreal treatment in a more timely manner.

We generally aim to see patients within 42 days following an intravitreal injection, towards the end of the anti-VEGF therapeutic effect. We found that the average wait for an initial follow-up appointment during the current study period was 45 days, slightly longer than the 2012 result of 42 days on average. However it is important to note that 77.1% of patients were being seen in 50 days or less with 47.6% of those overdue delayed with less than a week.

Subsequent follow-up appointments occurred more promptly, on average at 40.7 days, within the aimed 42 days. It is encouraging to note that 56.9% of patients were seen in the aimed time frame, with 87.9% of patients following up within a week of their desired appointment.

The institution of the MRC has thus allowed us to keep our follow-up appointment availability stable, despite the exponential increase in patients receiving intravitreal treatment. Increasing the frequency of the MRC in the future will aim to reduce this delay further.

Treatment and re-treatment delay
A significant vision reduction can occur while awaiting intravitreal injections. The longer the delay, the greater the vision loss and the less improvement following treatment in patients requiring treatment for exudative AMD, which includes the majority of our intravitreal treatment patients. We aim for patients to receive intravitreal injections as soon as possible following the decision to treat. Same-day treatment would be the gold standard, unfortunately due to resource constraints, in particular staff and space,
it is seldom possible. Over recent years we have increased the number of intravitreal injection lists in order to improve treatment availability. Unfortunately, the mean waiting time of 29.78 days to initial injection is still longer than the NICE recommended ideal goal of less than two weeks (14 days). However, we have stabilised and reduced the waiting time delay (compared to 2012), despite a dramatic increase in the number of patients requiring intravitreal injections. Furthermore, more than two-thirds of NHS trusts have been unable to comply with the NICE guidelines.\(^1\) Our time to re-treatment has improved with a mean waiting time of 25.72 days, compared to 34 days in 2012.

**Treatment results**

At one year 81.5% of patients in our study started on prn bevacizumab for exudative AMD had a stabilisation of vision, with a mean of 3.7 injections. In the Comparison of Age-Related Macular Degeneration Treatments Trials (CATT)\(^1\) 91.5% of patients that received prn intravitreal bevacizumab had a stabilisation of vision with an average of 7.7 injections. This result demonstrates that Palmerston North is currently under-performing in the number of injections per patient being given over a year and as a result in our intended visual acuity outcomes. However, two important factors should be taken into consideration with regards to these results. Firstly, at the Palmerston North Eye Clinic, visual acuities are taken at the time of patients being listed for intravitreal injections and not on the day of injection. As discussed earlier there is commonly a delay in receiving injections, on average 29.8 days for initial injections and 25.7 days for subsequent injections. Studies have shown that significant losses in visual acuity occur while awaiting intravitreal anti-VEGF treatment, especially in exudative AMD.\(^8\)\(^-\)\(^10\) We can thus assume that visual acuities prior to injections were in fact worse than those recorded and stabilisation and improvement rates are likely higher than found in this analysis. Secondly, patients were not excluded from this study if their BCVAs did not meet a predetermined standard, in a hope to emulate real world clinical situations. In the CATT study\(^1\) only patients with visions between 6/7.5 and 6/96 on Snellen testing were included, however in our study, patients with visual acuities ranging from 6/5 part to 6/600 were included. Patients with very good starting visual acuities are less likely to have an improvement in vision due to the ceiling effect, while patients with very low starting visual acuities are likely to have presented with a degree of scarring and would be less likely to improve also.

**Future directions**

The institution of the senior nurse-led MRC in combination with the expansion of intravitreal injection lists has allowed us to maintain intravitreal service accessibility, despite the ever-increasing intravitreal treatment demand. However, the results do suggest additional innovative solutions need to be sought.

To that end we are currently investigating the adoption of a proactive “Treat and extend regime” to reduce frequency of follow-up visits and improve visual prognosis.\(^1\)\(^9\),\(^2\)\(^0\) We are also evaluating further avenues, including redesigning the eye clinic “space” and addressing staff resourcing to perform immediate same-day intravitreal injections, improving IT audit, tracking and management systems.

We are also currently investigating the feasibility of nurses or other allied personnel performing intravitreal injections in the future. This has been adopted by several institutions in New Zealand and abroad with reports demonstrating this to be a safe and efficient method of improving accessibility in an intravitreal service.\(^2\)\(^1\)\(^-\)\(^2\)\(^3\)

Lastly, the introduction of a fast-track patient referral system from primary health services to allow earlier intervention in conditions requiring intravitreal treatment is also being evaluated for future implementation. However, such a system requires a robust receiving system (of prompt assessment, treatment, monitoring and re-treatment) to manage the additional detected need.

**Limitations**

The patients of three different ophthalmologists were included. Slight variances in treatment decisions naturally occurred.
Competing interests:
Nil.

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