

Improving Patient Access to Intravitreal Anti-Vascular Endothelial Growth Factor Treatment through an Integrated Collaborative Team Care Approach

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Abstract

Aim: Intravitreal anti-vascular endothelial growth factor (Anti-VEGF) has become a mainstream treatment for many ophthalmic conditions. Consequently, the demand for the treatment has significantly increased. The significant resource constrained environment necessitated the Palmerston North Hospital Eye Department (PNHED) to introduce solutions to address this increased demand. The two main initiatives adopted were: senior nurse-led macular review clinic (MRC) and nurse-led intravitreal injection clinic. This article will review our current service accessibility and to directly compare it to the results shown in the previous two audits.

Method: The data were collected on an updated macular review clinic patient prospective database and Zeiss optical coherence topography (OCT) forum viewer. The study population was determined by those who have received the intravitreal injection treatment (IVT) between January 2015 and November 2017.

Results: The average waiting times between IVT and subsequent review clinic as well as review clinic and subsequent IVT have been reduced when compared to the previous audit findings. The average period for the unintended delay between the IVT sessions is 6.07 days. The number of IVT given per year has also increased dramatically every year.

Conclusion: PNHED has successfully incorporated both nurses-led MRC clinics and nurse-led IVT clinics. They resulted in a reduction in unintended delays for both reviews and treatment. A secondary benefit of this resource re-allocation has been to improve the accessibility of senior medical officer (SMO) clinic appointments. This has reduced the wait time for new patients requiring initial SMO assessment before starting on IVT.

Keywords: Age-related macular degeneration; Retina; Intravitreal treatment; Anti-VEGF; Anti-vascular endothelial growth factor; bevacizumab; Avastin

Introduction

It has been hypothesised that multiple ocular pathologies are under the direct influence of an angiogenic agent in response to retinal anoxia. This was later identified as the vascular endothelial growth factor (VEGF) [1]. Bevacizumab was originally designed to treat patients with colorectal cancer, especially those with metastatic disease [2]. Shortly after it had been approved for cancer treatment, systemic intravenous bevacizumab was used off-label on patients with wet age-related macular degeneration (AMD). Once the successful outcome was noted, it started to be injected directly into the vitreous cavity, again this was an off-label use. This has resulted in effective treatment for many ocular pathologies while having minimal systemic adverse effects [1]. The main conditions being wet AMD, retinal vascular occlusion, proliferative diabetic retinopathy and diabetic maculopathy. The discovery of intravitreal anti-VEGF treatment has resulted in a paradigm shift, altering our perception towards these chronic ophthalmic pathologies and their prognosis. However, it has not come without a cost. Bevacizumab agent has an approximate half-life of 20 days [3], this treatment often needs to be repeated at a certain interval

in order to maintain the treatment effect. For example AMD, New Zealand's leading cause of blindness, which is estimated to affect about 150,000 to 200,000 people above the age of 50.8 Given that about 10-15% progresses on to wet-AMD, it is currently estimated that about 10,000-20,000 people are affected by wet-AMD, potentially requiring intravitreal anti-VEGF treatment. Unfortunately, with an ageing population, this number is expected to increase by 20-40% in the 10 years [4].

Currently, there are two main challenges when attempting to address this ever increasing demand for the treatment: resources to provide regular review clinic appointments and resources to deliver intravitreal treatment (IVT) to patients in a timely manner. Palmerston North Hospital Eye Department (PNHED), a provincial centre, has introduced two strategies to address these challenges. The main two key initiatives adopted were senior nurse-led macular review clinic (MRC) and a nurse-led intravitreal injection clinic. Botha et al. [5] has already reviewed and discussed how adopting MRC have improved the service accessibility for those who require IVT in PNHED. MRC has now become one of our regular clinics. This has helped in addressing the previously reported bottleneck issue and resulted in shorter follow-up delays. In September 2016, PNHED also introduced nurse-led intravitreal injection clinics to keep up with the increased volume of

intravitreal treatment delivery. Two senior registered ophthalmic nurses have been specially trained and certified to give IVT to patients.

This article is aimed to review how these two strategies have influenced service accessibility and timely delivery of care. It will also directly compare results with the two previous audits, allowing us to reassess the impact of MRC as well as evaluating the newly incorporated nurse-led IVT clinic.

Nurse-led injection clinic

The bottleneck in service delivery was identified to be clinical review follow-up appointments and therefore the MRC was introduced. Following this initiative it became readily apparent the next major issue was the delay in injection appointments, the bottleneck has shifted.¹ The number of intravitreal injections performed in PNHED had increased by 67% from 2012 to 2014 [5]. Unfortunately this trend of an increased need for IVT treatment is expected to continue. Given ophthalmic medical personnel are a limited and expensive resource the strategy of nurse-led IVT clinic was suggested. Nurse-led IVT clinics have been successfully incorporated in many countries and also some regions in New Zealand [6-9].

Two registered nurses were selected and trained for intravitreal injection technique under close SMO supervision. Once they had completed the training, they became credentialed to administer intravitreal injections. These clinics are solely focused on treatment delivery, and therefore very efficient, with short turnaround time. This enables approximately 16-18 treatments to be delivered in a 3-4 h session. We run two nurse-led IVT clinics per week. This means that we have increased our treatment delivery capacity by about 32-36 intravitreal injections per week and thus reducing treatment waiting time.

Aim

This audit was undertaken to review how the MRC and newly introduced nurse-led injection clinic have impacted on waiting times between: IVT and the subsequent follow-up review appointment, decision to treat or re-treat and the subsequent IVT, each IVT when given in a series of two or three consecutive injections, and the total number of IVT that we have given in PNHED between 2015 to 2017.

Method

In order to enable the outcome to be comparable to the previous audits [5], similar inclusion and exclusion criteria were applied to the study population. The study group comprised those patients who met the following criteria;

- Newly started on IVT between January 2015 and November 2017.
- Received the complete induction treatment during the study period.
- Attended their first review appointment post IVT during the study period.
- Minimum of 6 months follow-up during the study period.

The principal data source was the prospective patient database of all patients undergoing treatment for AMD at PNHED. However, the database information was supplemented through a notes review as some information required for this study was not available from the AMD audit database.

After applying these criteria, 249 patients (293 eyes) were recruited.

Data Collection and Analysis

Broadly, the following areas were collected;

- Patient demographics
- The assessment of the eye
- A description of the pathologies present
- The treatment process including timing
- Follow-up

By design the inclusion and exclusion criteria for the study population and the aim were similar to the previous two audits, we were able to compare the outcomes.

The analysis was completed using the R statistical language [10].

Results

Demographics

Total of 249 patients (with 293 eyes) were included in this study. The mean age of the study sample was 73.18 years (SD 12.56) (Figure 1). Further, there was no significant change in the variance or mean of the age of the patients over the three years of this audit (Levene's test for homogeneity of variance $p=0.1179$, and ANOVA $p=0.361$, Df 2).

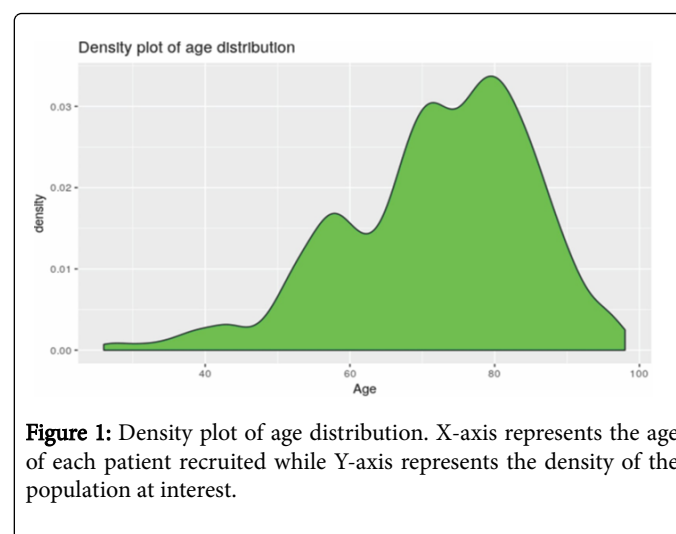


Figure 1: Density plot of age distribution. X-axis represents the age of each patient recruited while Y-axis represents the density of the population at interest.

116 (46.6%) of them were female and 132 (53.4%) of them were male patients. The patients in the audit population were predominantly European.

The number of external referrals that had been received during the study period was 125 and the average time between the referral date and specialist consultation was 29.2 days. The other 124 patients were either already enrolled in the same condition but had not yet required any treatment or enrolled with another ocular condition prior to the study period.

The conditions treated with IVT were age-related macular degeneration, retinal vein occlusion, diabetic macular oedema and other macular pathologies such as proliferative diabetes retinopathy.

IVT to IVT

Ophthalmologists prescribe a 'loading dose' for IVT where a series of three consecutive IVT is given [11]. In the majority of cases, the intended interval period between each anti-VEGF injections is about 4 to 6 weeks [11]. However some patients require more frequent IVT due to the speed of disease recurrence (i.e. every 3 weeks). We found that in PNHD the average waiting time between the IVT is about 33 days. When we reviewed the difference between the intended follow-up periods to the actual interval period, the unintended delay (the difference between the two) was 6.07 days.

IVT to Review Appointment

The average period between the IVT appointment and review clinic (either SMO clinic or MRC) was calculated to be 35.21 days. In the previous audit, the intended period between the IVT and the review appointment was decided to be 6 weeks (42 days) so the patients can

be assessed when the anti-VEGF medication's effect is near its end. However, since then, we have reduced the intended period between the two appointments to 4 weeks (28 days) in many patients. After taking this into account, the average of the unintended delay was 4.45 days.

Review Appointment to IVT

Once patients had been reviewed and decided to either treat or re-treat with IVT, the ideal waiting time is 0 day [12]. However many medical guideline organisations such as NICE generally accepts to have a delay period up to 14 days [5,12,13] In PNHD, the average waiting time between when a decision to treat or re-treat was made and to subsequent IVT was 18.5 days.

Follow-up overall

Overall there was no significant difference between the intended follow-up and the actual follow-up periods ($p < 0.001$).

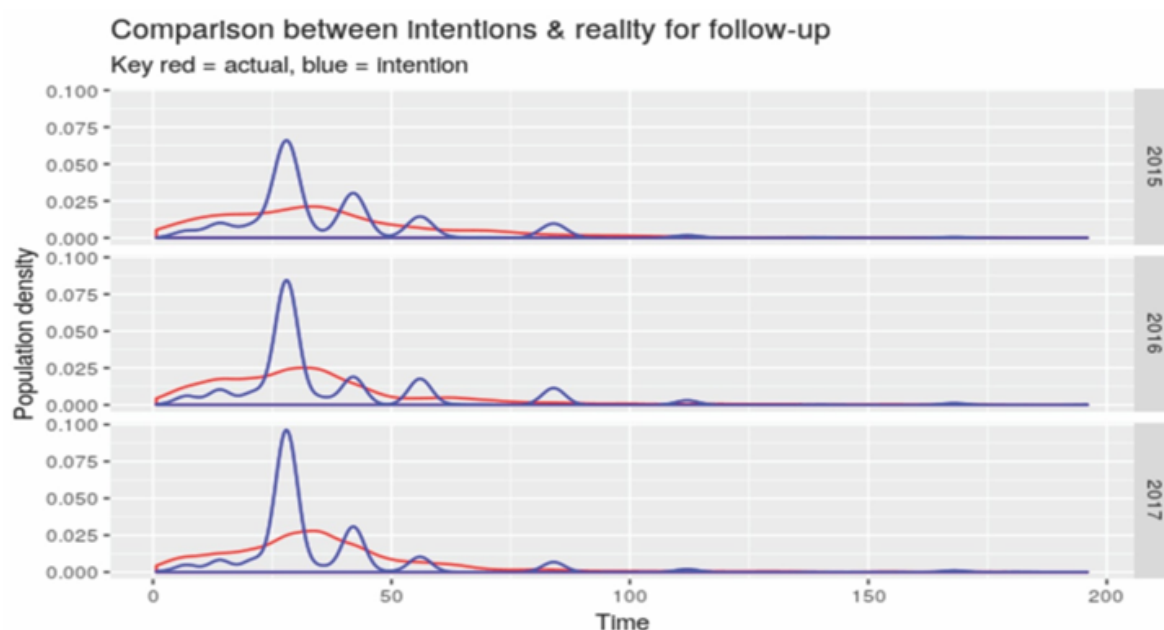


Figure 2: Comparison between the intended follow-up period and the actual follow-up period each year. Red line represents the density plot for actual follow-up period and Blue line represents the density plot for intended follow-up period. X-axis represents time period in days while Y-axis represents population density.

Figure 2 illustrates the distribution and relationship between the intended follow-up and the actual follow-up periods. The increase peak of the blue and red lines reflects the increasing volume of patients being followed up in PNHD. With a static medical workforce one would expect an overall increase in the actual follow-up period. This will likely result in an adjustment to longer intended follow-up periods. However the graph below demonstrates that both intended and actual follow-up periods maintained their distribution position without being moved further along the time axis ($p = 0.28$ and $p = 0.49$ respectively).

The overall patient noncompliance rate was analysed by looking at Did Not Attend (DNA) encounters each year. This rate had dropped by 3.6% over the study period.

Number of IVTs given

With the established MRC and nurse-led injection clinics, the overall turn-over rate for each patient who requires IVT has increased significantly. The total number of IVT that has been delivered to patients has increased dramatically over the past three years. Overall we have administered 555 injections in 2015, 623 injections in 2016, and 791 injections in 2017. If we only include the ones given to the study sample then the numbers are 209, 261, and 300 in 2015, 2016 and 2017 respectively. It is important to note that we have only included IVTs given in the first 11 months for 2017. As might be expected this result is highly statistically significant ($\chi^2 = 42.42$, $df = 2$, $p < 0.001$). Key to delivering this result was the use of nurse injectors (Figure 3).

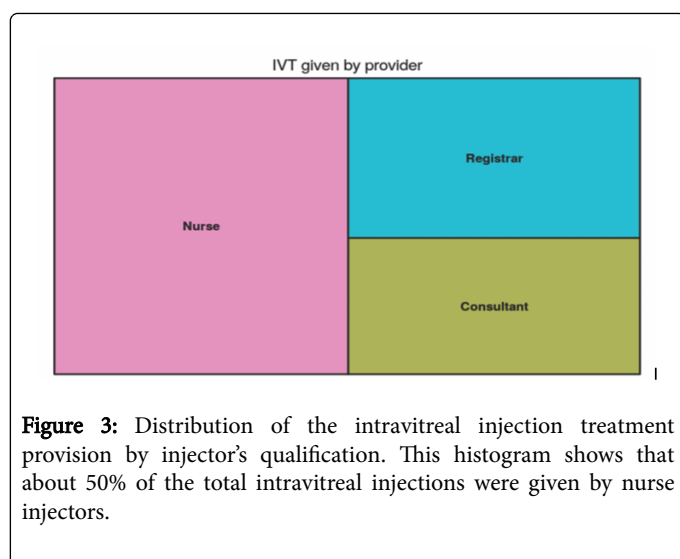


Figure 3: Distribution of the intravitreal injection treatment provision by injector's qualification. This histogram shows that about 50% of the total intravitreal injections were given by nurse injectors.

With the 166% increase in demand coupled with a static service workforce the expectation would be that the intended follow-up periods increase. PNHED have not just maintained intended follow-up periods but actually reduced them by 14% over the past 2 years ($p=0.0002$ F value 8.655, df 2) (Figure 4).

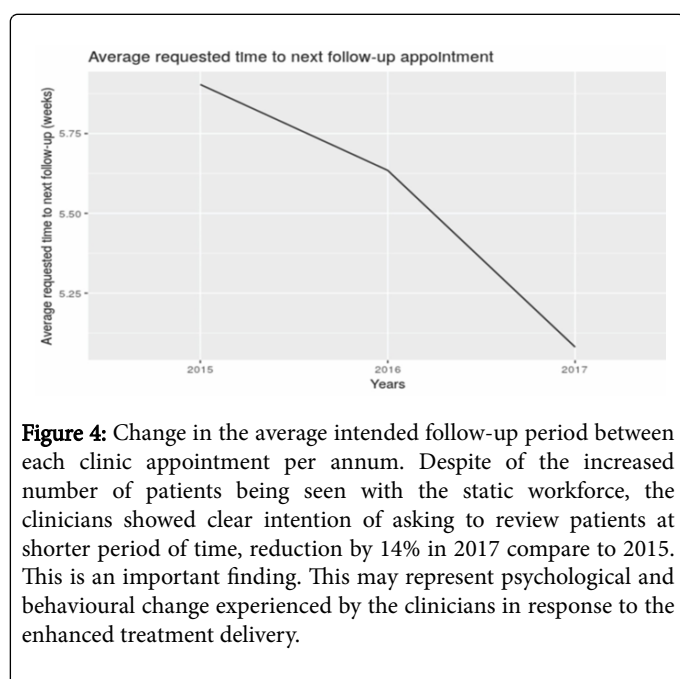


Figure 4: Change in the average intended follow-up period between each clinic appointment per annum. Despite of the increased number of patients being seen with the static workforce, the clinicians showed clear intention of asking to review patients at shorter period of time, reduction by 14% in 2017 compare to 2015. This is an important finding. This may represent psychological and behavioural change experienced by the clinicians in response to the enhanced treatment delivery.

Discussion

The New Zealand healthcare system is facing an important worldwide problem - addressing the increase in healthcare demand that the ageing population requires. Many ophthalmic conditions, such as AMD, are much more prevalent in older people, there is no doubt that the imbalance between the treatment demand and the treatment supply will worsen. Currently, about 3000-4000 New Zealanders are newly diagnosed with AMD each year. At this rate, the number of patients with AMD is expected to increase by 40% by 2026 [4]. One study showed that the burden of these ocular diseases is substantial,

affecting not only patients but also health practitioners, families and caregivers. The most significant of these being the burden of time and finances [14].

PNHED has experienced a similar trend over the past few years. In Botha et al study, the number of IVTs performed in PNHED had risen by 67% from 2012 to 2014 [5]. In this study we have found that when compared to 2015, the number of IVTs performed has increased by 25% and 44% in 2016 and 2017 respectively. Note that in 2017 we only counted the number of IVTs performed in 11 months. When correcting for the reduced period, the estimated increase was 56% in 2017. Although the relative increase in the last two years is less than what was noted in the Botha et al study for the time period 2012 to 2014, it is worth emphasizing that the absolute increase in the number of IVT given.

Currently, in New Zealand, there is a ratio of 1 ophthalmologist to 38,000 people [10] This issue is much more significant in provincial centres. For example, in Palmerston North, the approximate ratio is 1:46,000. Although the Ministry of Health in New Zealand is attempting to address this issue by increasing the number of positions in medical schools, it will take years before the effect materialises. This necessitates prompt action to re-allocate the limited resources to address an immediate concern. Many studies have shown that the utilisation of advanced nursing practice is one successful solution for overcoming the medical workforce shortage [5-9]. A number of studies also showed that appropriate guidance and training, nurse-led intravitreal injection clinic is a cost-effective service that can improve service accessibility while maintaining high quality and safety standards. Many centres, both in New Zealand and overseas, have already demonstrated its success [6-9].

The introduction of nurse-led MRC and nurse-led IVT clinics has resulted in a large number of patients with macular conditions re-distributed away from overburden SMO clinics. This has improved the SMO clinic capacity to see more acute and complicated cases in a more timely manner. In addition, those who require ongoing macular reviews and IVTs have better access to the service due to the increased number of available appointment spaces per given time. This is clearly supported by the reduction in the average time period between IVT and subsequent review clinic, as well as review clinic and IVT compared to the previous two audits (Table 1).

Interestingly, the unintended delay between IVT and review clinic was 4.45 days, which is slightly longer than the 3.05 days that was found in Botha et al study. However, it is crucial to point out that in Botha et al study the intended follow up period was set at 42 days for every patient. During this study period, a significant number of patients were aimed to be followed up in 28 days instead of 42 days. This adjustment has been made due to the recognition of the benefit of more timely treatment. This increased capacity is reflected in the actual average waiting time between IVT and review clinic has reduced from 42 in 2012 and 45.95 in 2013-14 down to 35.21 days in 2015-17. The average waiting time period between the review clinic and subsequent IVT has been calculated to be 18.5 days. This is still longer than NICE guideline's recommendation of fewer than 14 days. However, it is almost 10 days of improvement from our previous audit finding of 28.3 days [5].

Patient noncompliance has always been an important impeding factor to the patient management model. During this study period, there was a 3.6% reduction in patient noncompliance rate. One likely explanation for this is an improvement in patient awareness and

engagement in their condition and treatment plan. This could be a result of having a shorter interval between each appointment. However further auditing and analysis is required in order to accurately assess

what the long-term trend is. It would also be useful to analyse the issue of lost to follow-up in the future study.

	IVT to Review			Review to IVT			IVT to IVT
	2012	2013-14	2015-17	2012	2013-14	2015-17	2015-17
Avg time (days)	42	45.05	35.21	31.2	28.3	18.5	32.96
Unintended delay (days)	0	3.05	4.45	31.2	28.3	18.5	6.07

Table 1: Comparison of current study result to the previous two audits performed in PNHED.

Lastly, it is important to acknowledge that the strategies employed have successfully improved the quality of patient management in the face of increased demand, with the rapidly rising number of patients requiring treatment. We have not only achieved a shorter waiting time between the appointments but also managed to serve higher number of patients compared to the previous two audits. This positive outcome was also noted within the current audit. Between 2015 and 2017 the volume of patients seen in PNHED has increased every year while the service workforce has remained stable. In accordance with the natural relationship between demand and supply, one would expect to see an outcome of increased actual follow-up period. This can subsequently lead to an increase in intended follow-up period as providers become aware of their service limitations. However none of these anticipated outcomes were observed in this audit. This emphasises the success achieved by collaborative integrated team care approach.

References

- Kim LA, D'Amore PA (2012) A Brief History of Anti-VEFG for the Treatment of Ocular Angiogenesis. *Am J Pathol* 181: 376-379.
- Rosen IS, Jacobs IA, Burkes RL (2017) Bevacizumab in Colorectal Cancer: Current Role in Treatment and the Potential of Biosimilars. *Target Oncol* 12: 599-601.
- Kazazi-Hyseni F, Beijnen JH, Schellens JHM (2010) Bevacizumab. *The Oncologist Exp* 15: 819-825.
- National Health Committee (2015) Age-Related Macular Degeneration.
- Botha V, Ah-Chan J, Ramachandran N (2016) Improving accessibility to intravitreal anti-vascular endothelial growth factor treatment for ophthalmic patients in a peripheral centre. *N Z Med J* 129: 56-66.
- McDonald EM, Ram F (2016) seeing into the future: ophthalmologists and specialist nurses working together. *N Z Med J* 129: 1438.
- Gregg E (2017) Nurse-led Ranibizumab intravitreal injections in wet age-related macular degeneration: a literature review. *Nurs Sand* 31: 44-52.
- Gallagher MJ (2017) Introduction of a nurse-led intravitreal injection service in ophthalmology. *Br J Nurs* 26: 800-803.
- MiYeoung V, Patel R, Raynel S (2016) Nurses Step UP to Meet Demand for Specialist Eye Treatment 16: 26-27.
- R Core Team (2018) R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.
- Duodecim (2016) Evidence summaries for the Finnish Current care Guideline Wet-age-related macular degeneration. *Current Care Guidelines*.
- Tuuminen R, Uusitalo-Jarvinen H, Aaltonen V, Hautala N, Kaipainen S, et al. (2017) The Finnish national guideline for diagnosis, treatment and follow-up of patients with wet age-related macular degeneration. 95: 1-9.
- NICE (2018) Age-related Macular Degeneration. NICE guideline.
- Prenner JL, Halperin LS, Rycroft C, Hogue S, Williams Liu Z, et al. (2015) Disease burden in the treatment of age-related macular degeneration: findings from a time-and -motion study. *Am J Ophthalmol* 160: 725-731.