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RETINAL DISORDERS

Macula service evaluation and assessing priorities for anti-VEGF treatment in the light of COVID-19

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Abstract

Purpose To assess the treatment position of all patients who have had an anti-VEGF injection in 2020, prior to the UK lockdown on 23 March. To assess methods of service quality evaluation in setting benchmarks for comparison after the situation stabilized. To consider what proportion could be delayed based on national guidelines and varying vision parameters. Finally, to measure how many patients actually attended.

Method A retrospective analysis of data collected from our electronic medical record was performed. Age, sex, reason for injection, visual acuity (VA) for both treated and untreated eyes and number of injections were recorded. The proportion of patients and eyes with ≥ 70 letters were calculated as an assessment of quality of service provision. The proportion of patients that could be delayed was estimated based on published guidelines and varying the parameters of difference between treated and untreated eyes. Finally, the number of patients who actually attended was recorded.

Results About 3364 eyes (2229 neovascular age-related macular degeneration (nAMD), 427 diabetic macular oedema (DMO), 599 retinal vein occlusion (RVO) and 109 other) from 2924 patients were analysed. At the last appointment with injection, 64.4% of patients achieved ≥ 70 letters in their better-seeing eye. Mean VA of the treated eye was 61.5 letters, and 36.9% achieved ≥ 70. The mean number of injections was 16, 90% with aflibercept. Of the patients receiving treatment to one eye, 57.6% was receiving treatment to their worse seeing eye. In 18.2% this eye was > 20 letters worse and in 5.07% > 40 letters worse than the untreated eye. Using Royal College of Ophthalmologists (RCOphth) guidelines, (treat nAMD 8 weekly, delay majority of RVO and DMO) 24.8% would be delayed. From 2738 appointments during the first 4 weeks of lockdown (booked prior to lockdown), doctors rescheduled 1025 and patients did not attend 820, leaving 893 who were seen (33%).

Conclusions Assessing the treatment position of patients prior to COVID-19 lockdown enables objective stratification for prioritization for continued treatment. If RCOphth guidelines were followed 24.8% could be delayed and if treating the worse seeing eye up to 57.6%. Many scheduled patients elected not to attend, with 67% not seen in the first 4 weeks. The impact of non-attendance and delays may be evaluated later.

Keywords Macular · Anti-VEGF · Aflibercept · COVID-19

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Introduction

Retinal disease, due to neovascular age-related macular degeneration (nAMD), diabetic macular oedema (DMO) or retinal vein occlusion (RVO), will lead to loss of vision without treatment. Clinical trials in these conditions have shown that anti-VEGF treatment may preserve or improve vision and they have been widely introduced into the National Health Service (NHS) in the UK since 2008 after approval by NICE (National Institute for Health and Care Excellence) [1]. Most outcome results for anti-VEGF treatment report changes in visual acuity (VA) per eye of a series of patients being treated over time. This can demonstrate the efficacy of a treatment in

the context of a randomized controlled clinical trial. A similar approach with real-world data can demonstrate the effectiveness of a treatment in clinical practice where the effects of facilities, capacity, varying clinical decision making and increased diversity of the patient group treated may be demonstrated [2]. However, loss to follow-up makes these comparisons difficult [3]. As anti-VEGF treatment has been available for over 10 years, another approach to assess the effectiveness of anti-VEGF treatment could be to look at a cross section of patients being treated. Such a snapshot assessment would give a measure of the overall VA being obtained and could potentially be used as a quality assessment measure of a service [4].

Whilst treating one eye of a patient, when the other is normal, does have a benefit on a patient's quality of life, the benefits are larger when both eyes have a visual problem. As VA in both eyes is important to a patient's quality of life it is important to record the best vision from both eyes, whether treated or not [5]. These data may be important if doctors are having to make difficult choices about prioritizing treatment; for example if there is a disruption to treatment provision, such as is happening with the COVID-19 outbreak.

The purpose of this study was to assess the clinical status of all our patients who had had an anti-VEGF injection in the first 3 months of 2020, prior to the UK lockdown on 23 March. Using data on VA and diagnosis, we aimed to assess what proportion of patients could have their treatment delayed, with reference to published guidelines, such as that of the Royal College of Ophthalmologists (RCOphth), which advised delaying the majority of DMO and RVO patients (with a few exceptions) and maintaining nAMD patients on 8-weekly injections unless they reported a drop in vision [6]. Alternative methods include considering the VA difference between treated and untreated eyes. In addition, we wanted to assess VA outcomes as a snap-shot audit compared with other published outcome results, to consider this method's utility as a way of measuring outcomes.

An audit was also carried out of actual attendance at the eye department from 23 March for the first 4 weeks of lockdown to see what effect COVID-19 had on actual patient attendance rates.

Method

Data were collected for all patients who had at least one anti-VEGF injection at Newcastle Eye Department from 1 January until 23 March 2020. Data recorded included age, sex, diagnosis, number of eyes receiving treatment, VA of treated and untreated eyes and total number of injections per eye. Diagnoses were categorized as nAMD, RVO, DMO or 'Other'. 'Other' included choroidal neovascular membranes related to myopia, proliferative diabetic retinopathy (PDR), retinal dystrophies, choroidal rupture, inflammatory lesions, peripapillary and idiopathic. Data were collated into separate datasets by 'eye' and by 'patient'.

Descriptive statistics were calculated for demographic data, VA and injections using Excel 365 for Microsoft Office. The same software was used for production of graphics. Data on age, VA and injections have been summarized using mean, median, SD, IQR and the range to allow for comparison with previously published data, which use a variety of descriptive statistics.

Differences between treated and untreated eyes were calculated such that the number of patients with differing levels of priority could be calculated. For example, the number of patients in whom the treated eye was the better eye or the worse eye. If it was that the treated eye was the worse eye, the number of patients with different levels of difference was calculated to consider priority for treatment such as the number in whom the treated eye was > 20 letters worse or > 40 letters worse. Filtering of data was also used to calculate numbers of patients in different subsets for estimation of proportions of patients that would be appropriate for delay according to RCOphth guidelines.

Clinic attendance data were collected from all macula treatment clinics in the first 4 weeks of lockdown (23 March until 17 April) to assess what proportion of patient appointments was cancelled by clinicians and what proportion of patients attended. Cancellation of patients was based on assessing the medical records, guidelines and after telephone consultations with patients, where possible.

All data were recorded using an electronic medical record (EMR) system (Medisoft Ophthalmology; Medisoft Limited, Leeds, UK), which mandates collection of a standardized data set throughout a patient's care pathway. The lead clinician and Caldicott Guardian (nominee responsible for data protection) at the hospital gave written approval for anonymized data extraction. Anonymized database analyses of this type do not require ethical permission because they are viewed as audit or service evaluations (see http://www.hra.nhs.uk/research-community/ beforeyou-apply/determine-whether-your-study-is-research/). This study was conducted in accordance with the Declaration of Helsinki and the UK's Data Protection Act.

Early Treatment Diabetic Retinopathy Study (ETDRS) VA letter scores at 2 m were recorded. Most VA values were recorded using habitual correction rather than with refraction. Values corresponding to counting fingers, hand movements, light perception and no light perception were substituted with values of 0 letters.

Results

During the study period 2971 patients received injections. Of these, 47 patients with incomplete data were excluded (43

missing VA and 4 missing diagnoses). Of the included 2924 patients, 1672 (57.2%) were women. The mean age at the time of analysis was 77.0 years (median 79, SD 11.6, IQR 71–85, range 20–102). Four hundred and forty patients (15%) received injections to both eyes during the study period, giving a total of 3364 eyes for analysis (2229 nAMD, 427 DMO, 599 RVO and 109 other).

The mean VA for the treated eye was 61.5 letters (median 65, SD 16.0, IQR 53–73, range 0–85). A VA of ≥ 70 letters was measured in 36.9% and < 35 letters in 7.52%. See Table 1 and Figures 1 and 2 for proportions of eyes in VA categories, split by diagnosis.

The mean VA of the better-seeing eye of all patients was 70.8 letters (median 74, SD 12.6, IQR 66–80, range 0–85). A VA of ≥ 70 letters was measured in 1882/2924 (64.4%) patients in their better seeing eye. A VA of < 35 letters was measured in 62/2924 (2.12%) patients in their better seeing eye.

The mean number of injections for a treated eye was 16.2 (median 12, SD 13.7, IQR 6–23, range 1–88). For nAMD, this was 18.6 (median 14, SD 15.1, IQR 7–26.25, range 1–88). For DMO this was 10.1 (median 8, SD 7.96, IQR 4–14, range 1–43). For RVO this was 13.3 (median 6, SD 9.34, IQR 3–19, range 1–56). For 'others' this was 8.03 (median 6, SD 7.19, IQR 3–10, range 1–33). Of the 2484 patients who had received an injection to one eye during the study period, 479 had previously received injections to the other eye prior to the study period (359 for nAMD, 82 for DMO, 21 for RVO and 17 for 'others') and for whom the mean number of injections was 11.8 (median 9, SD 10.2, IQE 6–23, range 1–76) to the previously treated eye.

There were 2484 patients receiving treatment to one eye only, and in 969 (39.0%) of these the treated eye was the better eye, and in 1431 (57.6%) it was the worse seeing eye (84 had equal VA in both eyes). Figure 3 shows the VAs of untreated eyes, demonstrating the spike at very low VA, likely representing patients in whom previous treatments have now been stopped. Tables 2 and 3 show the differences between treated and untreated eyes, split by diagnosis into categories of 10. Of note, we can calculate from this data that there are 126 (5.07% of those receiving treatment to one eye) patients in whom the treated eye was > 40 letters worse than the untreated eye and 451 (18.2%) in whom it was > 20 letters worse.

On applying the RCOphth guidelines, 724 patients (24.8%) would be appropriate for deferral.

Appointments had been booked for the first 4 weeks of lockdown for 2738 patients. Doctors rescheduled 1025 after looking at a combination of the above considerations and by speaking to patients by telephone. Patients however also rescheduled or did not attend 820 appointments that had not been planned to be rescheduled, leaving 893 who were seen (33%).

Discussion

Service evaluation

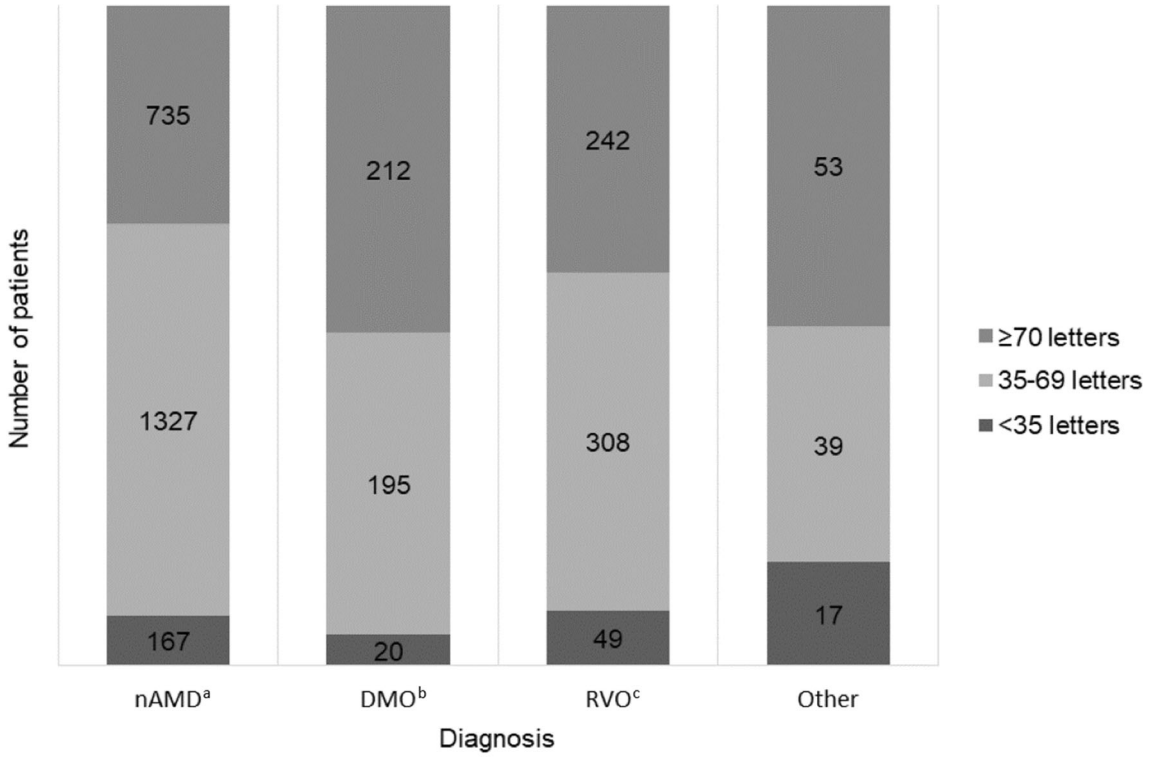
Most results for anti-VEGF treatment report changes in VA per eye over time, but the longer that time the fewer patients will be under follow-up leading to attrition bias. This means comparing the VA at baseline to the VA after a period of time might cause bias due to patients who have not been doing well being discharged or deciding not to attend. In a previous study in our unit, 50% of nAMD patients were no longer under follow-up after 4 years, with death and transfer of care being the most common reasons [3].

It has previously been suggested that a change in the mean VA should not be used as the only indicator of quality of care and that a good measure of the benefit of a treatment and the quality of the service provision could be defined as the proportion of patients who achieve ≥ 70 letters at any measured time point. This VA outcome is equivalent to driving standard in the UK [4]. Most published data look at the mean VA and proportions of patients achieving this target at yearly timepoints. In the VIEW study, this number changed from 23 to 45% [7], and in the HARBOR study, 46% achieved 70 letters or more at 1 year [8]. In the UK aflibercept users group

Table 1 Visual acuity (VA) of all treated eyes, split by diagnosis

Diagnosis	Total			ETDRS Letter score < 35		ETDRS Letter score 35–69		ETDRS Letter score ≥ 70	
	N	Mean	Median	*N*	%	*N*	%	*N*	%
nAMD	2229	60.8	64	167	7.49	1327	59.53	735	32.97
DMO	427	65.2	69	20	4.68	195	45.67	212	49.65
RVO	599	61.8	66	49	8.18	308	51.42	242	40.40
Others	109	60.4	69	17	15.60	39	35.78	53	48.62
Total	3364	61.5	65	253	7.52	1869	55.56	1242	36.92

ETDRS Early Treatment Diabetic Retinopathy Study, *nAMD* neovascular age-related macular degeneration, *DMO* diabetic macular oedema, *RVO* retinal vein occlusion



a. nAMD Neovascular Age-Related Macular Degeneration
b. DMO Diabetic Macular Oedema
c. RVO Retinal Vein Occlusion

Fig. 1 Visual acuity (VA) of treated eyes (categories)

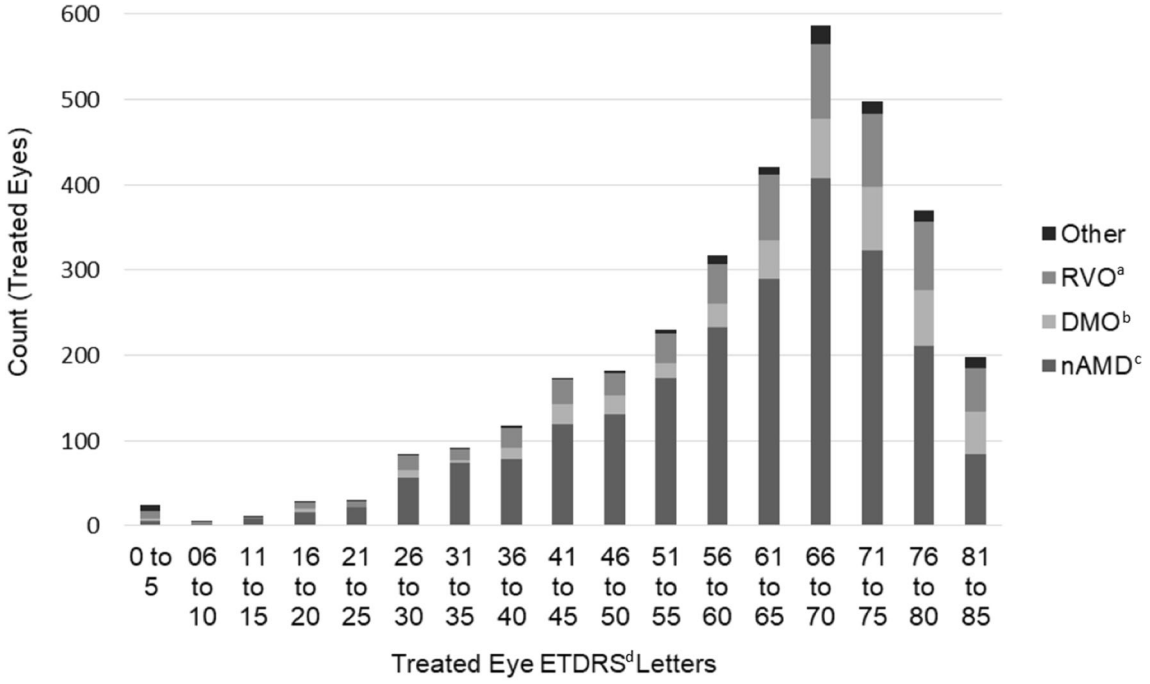
publication on 1-year outcomes from using aflibercept for nAMD, the number with 70 letters or more increased from 16.4% at baseline to 33.7% at 1 year [9]. In a study comparing outcomes of providing aflibercept for nAMD between centres, Talks et al. found that there was significant variation in VA measures between sites after 1 year of treatment, with the percentage of eyes achieving ≥ 70 letters at 52 weeks varying between 20.2% and 42.8%, with an overall percentage of 33.4% [4]. In our centre in the aforementioned study the figures were 37.2% ≥ 70 letters and 9% < 35 letters at 1 year. In the results reported in this current paper the mean VA was 60.8 letters with 37% ≥ 70 letters and 8% < 35 letters, with a follow-up range of < 1 year to > 10, comparable to previous research in the unit.

In VIEW, the mean VA at 1 year was 62 letters [7]. A recent 5-year follow-up of 512 eyes had a baseline VA of 57.1 letters, increasing to 63.0 letters at the first year before tailing off, dropping below baseline in year 4 to 55.0 letters at year 5. The proportion of eyes achieving ≥ 70 letters followed a similar pattern, at 32.2% at baseline, 54.4% at 1 year, then gradually dropping to 39.9% at 5 years [10].

In a previous publication by Talks et al. on 1840 treatment-naive eyes on aflibercept therapy for nAMD, it was found that the amount of VA gain depended on the presenting VA and on whether a first or second affected eye was being treated, as second affected eyes are often initiated on treatment with better baseline VA [9].

Mean VA of patients with DMO treated in the VIVID and VISTA randomized trials of aflibercept for DMO was 70 letters at 1 year [11]. A report analysing outcomes in the USA from the Vestrum Health retina database of using anti-VEGF treatment recorded a mean VA at 1 year of 63.5 letters from 1379 eyes treated with aflibercept from an overall database of 15,608 DMO eyes [12], closer to our mean in this snapshot audit. This reflects the expected differences between real-world and trial data as previously discussed.

In a study looking at 5-year outcomes for RVO, the baseline VA was 58 letters from 351 eyes with those in the lowest quartile of baseline VA experiencing increases in VA at 1 and 5 years, and those in the highest quartile of baseline VA experiencing losses. Overall, 79% of patients gained or maintained vision [13]. This is in line with nAMD patients having greatest gains with lower baseline VA, as previously discussed. There are many small-scale real-world studies on RVO, which are difficult to compare with the current dataset due to data reporting and proportions of branch versus central vein occlusions in the sample. However, a recent systematic review and meta-analysis of 2530 eyes with branch retinal vein occlusion (BRVO) from 48 real-world studies found a mixed-effects estimate mean baseline of 54 letters with an



a. RVO Retinal Vein Occlusion
b. DMO Diabetic Macular Oedema
c. nAMD Neovascular Age-Related Macular Degeneration
d. ETDRS Early Treatment Diabetic Retinopathy Study

Fig. 2 Visual acuity (VA) of treated eyes

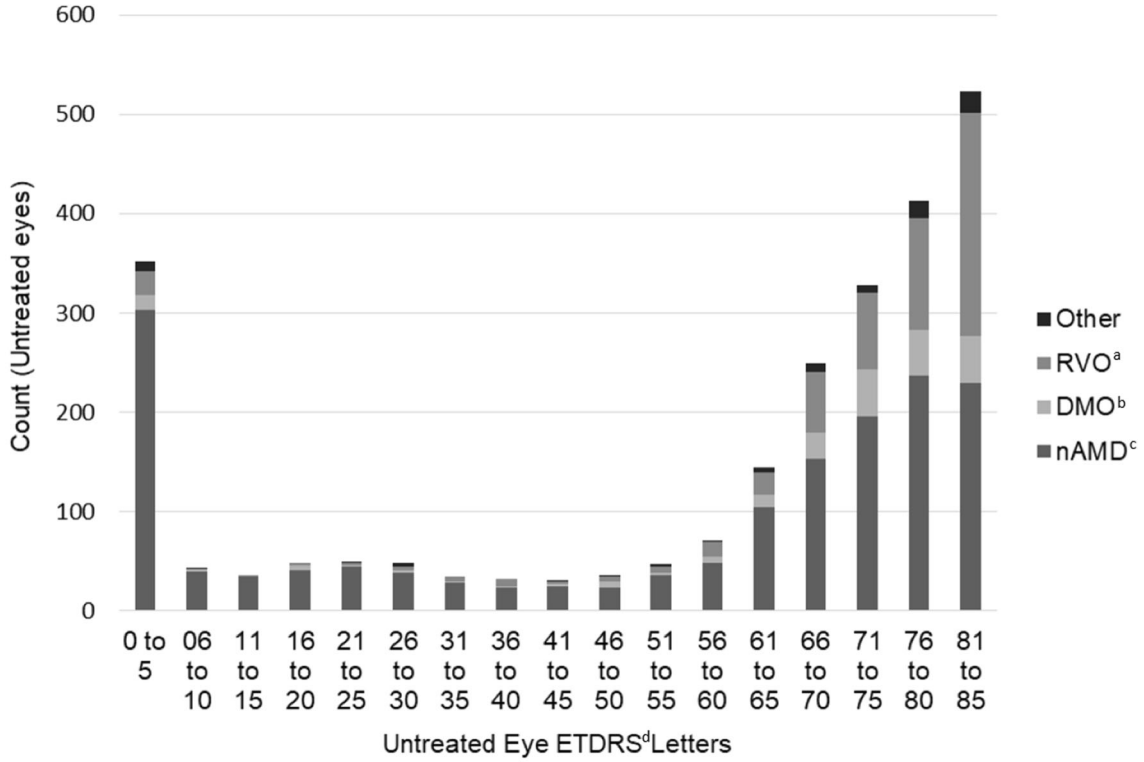
estimated mean change in VA of + 14.6 letters at 12 months and +13.2 letters at 24 months (giving a mean of 67.2 letters) [14]. Gratifyingly, on returning to our data and filtering for BRVO patients only, the mean VA is 66.1 letters.

This snapshot assessment, where there is a mixture of patients with different levels of follow-up, does seem to show that VA levels are in line with previous longitudinal results and does fit with using this method as a quality assessment measure of a service. However, it is difficult to compare studies as practice patterns vary. Its main use may be for repeat assessments of the same service to help monitor over time, such as will be necessary given the change in working practices secondary to COVID-19.

Prioritization

Urgent guidelines to support ophthalmologists managing anti-VEGF patients during the COVID pandemic have been produced. A recent publication in Graefe's recommends prioritizing and maintaining treatment in patients with nAMD (especially those in the first 2 years of treatment), neovascular glaucoma, new cases with significant vision loss, new central retinal vein occlusion cases and monocular or quasi-monocular patients (only one eye > 20/40) [15]. It also suggests that patients with DMO and BRVO are less likely to suffer irreversible vision loss in the short term and postponement of appointments for non-monocular patients may be considered (except for patients with significant vision loss from recent DMO and patients in the acute phase of RVO). These guidelines are relatively comparable with those of the RCOphth in the UK, who recommend injecting nAMD patients 8 weekly and deferring the majority of DMO and RVO patients (with the exception of CRVO with ≥ 6 injections and DMO eyes with severe non-proliferative diabetic retinopathy (NPDR) and active PDR who might require further injection or panretinal photocoagulation) [6]. From our dataset, 724 patients (24.8%) would be appropriate for deferral once these criteria were applied.

A much larger reduction in the need for current appointments would be possible if patients in whom the worst seeing eye was being treated were delayed, at 58%. This could be further adjusted by considering how much difference in VA there is between eyes, for example > 20 or > 40 letter difference. Delaying patients on this basis could be justified due to the larger effect on quality of life of treating the better eye. A study looking at better and worse seeing eyes in patients having anti-VEGF treatment for DMO concluded uniocular VA underestimated the impact of vision loss on quality of life indices compared with binocular VA and suggested that researchers, clinicians and policy planners should consider using the patient's best overall VA in patient-reported outcome evaluation of vision loss [5]. A more recent study found



a. RVO Retinal Vein Occlusion
b. DMO Diabetic Macular Oedema
c. nAMD Neovascular Age-Related Macular Degeneration
d. ETDRS Early Treatment Diabetic Retinopathy Study

Fig. 3 Visual acuity (VA) of untreated eyes

that the level of binocular vision rather than vision from either the better or worse seeing eye had the biggest effect on quality of life measures [16]. We can see that for our cohort the mean VA of the better seeing eye was 70.8 letters, higher than the 61.5 letters for the treated eyes.

However, whichever guideline is followed, the reality might be different as we have found, with just over half of the scheduled patients not attending. Data for planning prioritization might therefore be more useful for rescheduling when services start to return more to normal. Further, it can be used

Table 2 The visual acuity (VA) difference between the treated eye and the untreated eye (treated eye is better eye)

ETDRS Letters	nAMD		DMO		RVO		Other		Total	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%
0–10	151	20.08	42	51.22	61	53.98	5	22.73	259	26.73
11–20	62	8.24	11	13.41	9	7.96	5	22.73	87	8.98
21–30	79	10.51	5	6.10	8	7.08	2	9.09	94	9.70
31–40	91	12.10	4	4.88	8	7.08	2	9.09	105	10.84
41–50	93	12.37	6	7.32	7	6.19	1	4.55	107	11.04
51–60	113	15.03	5	6.10	5	4.42	2	9.09	125	12.90
61–70	104	13.83	5	6.10	8	7.08	3	13.64	120	12.38
71–85	59	7.85	4	4.88	7	6.19	2	9.09	72	7.43
Total	752		82		113		22		969	

ETDRS Early Treatment Diabetic Retinopathy Study, *nAMD* neovascular age-related macular degeneration, *DMO* diabetic macular oedema, *RVO* retinal vein occlusion

Table 3 The visual acuity (VA) difference between the treated eye and the untreated eye (treated eye is worse eye)

ETDRS Letters	nAMD		DMO		RVO		Other		Total	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%
0–10	318	39.45	77	57.89	176	40.00	28	53.85	599	41.86
11–20	238	29.53	28	21.05	107	24.32	8	15.38	381	26.62
21–30	115	14.27	14	10.53	75	17.05	6	11.54	210	14.68
31–40	73	9.06	7	5.26	33	7.50	2	3.85	115	8.04
41–50	40	4.96	3	2.26	27	6.14	4	7.69	74	5.17
51–60	17	2.11	1	0.75	14	3.18	3	5.77	35	2.45
61–70	4	0.50	1	0.75	5	1.14		0.00	10	0.70
71–85	1	0.12	2	1.50	3	0.68	1	1.92	7	0.49
Total	806		133		440		52		1431	

ETDRS Early Treatment Diabetic Retinopathy Study, *nAMD* neovascular age-related macular degeneration, *DMO* diabetic macular oedema, *RVO* retinal vein occlusion

for reassessing the VA of patients after they return to regular treatment, to find out how much vision has been lost and whether it can be recovered. The number of patients who attend a macular service will have been greatly influenced by local circumstance such as government advice on lockdown, how social distancing is applied, the doctor's willingness to see patients and communication with patients. Telephoning patients and providing information on infection prevention measures in a service may have altered the attendance rate in different services. A recently published letter that can be sent to patients helps summarize these issues to provide reassurance to patients and staff [17].

Authors' contributions Conception and design: Talks
Analysis and interpretation: Talks, Stone, Stratton
Data collection: Talks, Stone, Devenport
Overall responsibility: Talks

Data availability Available

Compliance with ethical standards

Conflicts of interest JS Talks: Advisory board; Bayer; Novartis; Allergan; research; Bayer; Novartis; Allergan; Roche; Boehringer Ingelheim
IMS: Research funding Bayer; Boehringer Ingelheim

Ethics approval All data were recorded using an electronic medical record (EMR) system (Medisoft Ophthalmology; Medisoft Limited, Leeds, UK), which mandates collection of a standardized data set throughout a patient's care pathway. The lead clinician and Caldicott Guardian (nominee responsible for data protection) at the hospital gave written approval for anonymized data extraction. Anonymized database analyses of this type do not require ethical permission because they are viewed as audit or service evaluations (see http://www.hra.nhs.uk/research-community/ beforeyou-apply/determine-whether-your-study-is-research/). This study was conducted in accordance with the Declaration of Helsinki and the UK's Data Protection Act.

Consent to participate Not applicable

Consent for publication Not applicable

Code availability Not available

References

1. National Institute for Health and Clinical Excellence (2012) Ranibizumab and pegaptanib for the treatment of age-related macular degeneration. https://www.nice.org.uk/guidance/ta155. Accessed 5 May 2020
2. Talks J, Daien V, Finger RP et al (2019) The use of real-world evidence for evaluating anti–vascular endothelial growth factor treatment of neovascular age-related macular degeneration. Surv Ophthalmol 64:707–719. https://doi.org/10.1016/j.survophthal.2019.02.008
3. Pushpoth S, Sykakis E, Merchant K et al (2012) Measuring the benefit of 4 years of intravitreal ranibizumab treatment for neovascular age-related macular degeneration. Br J Ophthalmol 96:1469–1473. https://doi.org/10.1136/bjophthalmol-2012-302167
4. Talks JS, James P, Sivaprasad S et al (2017) Appropriateness of quality standards for meaningful intercentre comparisons of aflibercept service provision for neovascular age-related macular degeneration. Eye 31:1613–1620. https://doi.org/10.1038/eye.2017.86
5. Scanlon PH, Loftus J, Starita C, Stratton IM (2015) The use of weighted health-related quality of life scores in people with diabetic macular oedema at baseline in a randomized clinical trial. Diabet Med 32:97–101. https://doi.org/10.1111/dme.12593
6. The Royal College of Ophthalmologists (2020) Medical retinal management plans during COVID-19. https://www.rcophth.ac.uk/wp-content/uploads/2020/03/Medical-Retinal-Management-Plan-during-COVID-19-UPDATED-300320-1-2.pdf. Accessed 29 Apr 2020
7. Heier JS, Brown DM, Chong V et al (2012) VIEW 1 and VIEW 2 Study Groups. Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. Ophthalmology 119:2437–2448. https://doi.org/10.1016/j.ophtha.2012.09.006
8. Busbee BG, Ho AC, Brown DM et al (2013) HARBOUR study group. Twelve-month efficacy and safety of 0.5 mg or 2.0 mg ranibizumab in patients with subfoveal neovascular age-related macular degeneration. Ophthalmology 120:1046–1056. https://doi.org/10.1016/j.ophtha.2012.10.014
9. Talks JS, Lotery AJ, Ghanchi F et al (2016) First-year visual acuity outcomes of providing aflibercept according to the VIEW study protocol for age-related macular degeneration. Ophthalmology 123:337–343. https://doi.org/10.1016/j.ophtha.2015.09.039
10. Chandra S, Rasheed R, Menon D, et al (2020) Impact of injection frequency on 5-year real-world visual acuity outcomes of aflibercept therapy for neovascular age-related macular degeneration [EPub ahead of print]. Eye 1–9. https://doi.org/10.1038/s41433-020-0851-y
11. Heier JS, Korobelnik JF, Brown DM et al (2016) Intravitreal aflibercept for diabetic macular edema: 148-week results from the VISTA and VIVID studies. Ophthalmology 123:2376–2385. https://doi.org/10.1016/j.ophtha.2016.07.032
12. Ciulla TA, Bracha P, Pollack J, Williams DF (2018) Real-world outcomes of anti–vascular endothelial growth factor therapy in diabetic macular edema in the United States. Ophthalmol Retin 2:1179–1187. https://doi.org/10.1016/j.oret.2018.06.004
13. Wecker T, Ehlken C, Bühler A et al (2017) Five-year visual acuity outcomes and injection patterns in patients with pro-re-nata treatments for AMD, DME, RVO and myopic CNV. Br J Ophthalmol 101:353–359. https://doi.org/10.1136/bjophthalmol-2016-308668
14. Ang JL, Ah-Moye S, Kim LN et al (2020) A systematic review of real-world evidence of the management of macular oedema secondary to branch retinal vein occlusion [EPub ahead of print]. Eye:1–27. https://doi.org/10.1038/s41433-020-0861-9
15. Korobelnik J-F, Loewenstein A, Eldem B et al (2020) Guidance for anti-VEGF intravitreal injections during the COVID-19 pandemic [EPub ahead of print]. Graefe's Arch Clin Exp Ophthalmol:1–8. https://doi.org/10.1007/s00417-020-04703-x
16. Kidd Man RE, Liang Gan AT, Fenwick EK et al (2020) Using uniocular visual acuity substantially underestimates the impact of visual impairment on quality of life compared with binocular visual acuity [Epub ahead of print]. Ophthalmology. https://doi.org/10.1016/j.ophtha.2020.01.056
17. Korobelnik J-F, Loewenstein A (2020) Communicating with patients with nAMD and their families during the COVID-19 pandemic [EPub ahead of print]. Graefe's Arch Clin Exp Ophthalmol:1–3. https://doi.org/10.1007/s00417-020-04697-6