Figure 3 Anti-VEGF visit frequency over 7 years (2009–2016).

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Sir,
Reply to: ‘Comment on: ‘One-year real-world outcomes in patients receiving fixed-dosing aflibercept for neovascular age-related macular degeneration’

Thank you for your interest in our article published in *Eye*.¹

The aim of our work¹ was to report real-world outcomes using Aflibercept in treatment-naïve eyes with nAMD per the available evidence (VIEW 1&2).

In your response, you did not determine whether your cohort was composed of only treatment-naïve eyes or it was a mixed group of switched and treatment-naïve ones.

We believe that visual outcomes of our work are satisfactory; in the integrated analysis of the VIEW 1&2 RCTs,² the proportion maintaining vision (losing <15 ETDRS L) was 95% (94% in our cohort), whereas the proportion gaining >15 ETDRS L was 31% (24% in our cohort of the published work).

In our research work, classifying lesions as active/inactive (wet/dry) post loading has been of great benefit; at end of year 1, 136 eyes (53%) were inactive, whereas 119 eyes (47%) remained active. Both groups showed VA gains irrespective of the presence/absence of fluid. In both groups, the proportion maintaining vision (losing <15 ETDRS letters) was 94%. The macular status post loading was a reliable indicator of the macular status at end of year 1. Both groups received the same treatment post loading (Aflibercept Q8W).

We would be interested in knowing the proportion of eyes in your cohort that did not require further injections post loading and what re-injection criteria were used in your centre.

In the modified IVAN protocol you implemented, it is not clear whether post-loading Aflibercept was used monthly (Q4W) or bi-monthly (Q8W). In case you used it monthly (Q4W), what would be the benefit of using Aflibercept every month if the current evidence suggested that its use bi-monthly (Q8W) was not inferior to monthly ranibizumab?²

Once a patient commences anti-VEG therapy, maintaining post-loading gain is a clinical challenge. In your protocol, a REACTIVE regimen was adopted in inactive eyes post loading. We carried on with a PROACTIVE protocol; bi-monthly (Q8W). It might have over-treated a proportion of eyes, but on the other hand, it did not leave the macula under the mercy of the CNV activity as you adopted post loading in inactive eyes.

When monthly treatment was discontinued and a more reactive clinician-guided approach using ranibizumab as required was used, over the subsequent 2 years

Table 1 Southampton *vs* modified IVAN protocol

Dosing protocol	Southampton	Modified IVAN
Drug	Aflibercept	Aflibercept
Cost of drug per intravitreal injection (£)	816.00	816.00
Mean number of doses per year	7	5
Mean number of outpatient visits with OCT, VA, and IVI (£245)	3	5
Mean number of outpatient visits with OCT and VA (£127)	0	7
Mean number of outpatient visits with VA (£118)	4	0
Total mean cost of treatment (£)	6919.00	6194.00

(HORIZON study) there was a gradual reduction in mean vision gain. This trend continued in the further long-term follow-up (SEVEN-UP) study.³

The landmark (VIEW) studies⁴ also showed good results adopting a proactive regimen in year 1 as well as year 2 maintaining the gains achieved in year 1; Q8W in year 1 and a PRN approach being used but capped in year 2, so that treatment was given Q12W even if VA and OCT were stable and not strictly needing a treatment according to the PRN approach.

The CATT study⁵ showed that it was possible to achieve good visual acuity results implementing a PRN protocol, but this was achieved through very strict monthly monitoring, a very low retreatment threshold, and a relatively high number of treatments in the PRN arms; features not easily adopted in a real-world clinical setting as they generate more cost and capacity problems.

The PRN approach does not maintain post-loading gain. The UK EMR study⁶ of 12 951 eyes receiving 92 976 injections showed a gradual reduction (post loading) of visual acuity to below baseline over the course of three years (PRN implemented).

On the other hand, a proactive approach using Aflibercept as per VIEW showed good results in routine clinical practice across the UK⁷ in addition to results comparable to VIEW as achieved in our cohort.¹

This trend of losing vision post loading when PRN regimen is applied can be observed in Figure 1 of your response; your VA results at M12 (3–4 ETDRS L gain) were inferior to both MARINA and ANCHOR, and inferior to what had already been achieved in the major VIEW 1&2 RCTs using Eylea² and inferior to what's been achieved in our cohort.¹

In our research, a total number of seven injections were given; a total of only three follow-up visits were booked per patient per year. In your cohort, Figure 2 shows an average number of five injections/eye/year 1, and an average number of 12 follow-up visits (four times the number of follow-ups in our cohort)/eye/ year were implemented (Figure 3). It is obvious that, in terms of capacity, our model does solve many of the issues (capacity, booking, and so on) from which most of the MR departments in the UK suffer.

In Table 1, a comparison between Southampton Protocol and the modified IVAN (Your Centre) is made. Our protocol shows better VA outcomes, it is evidence-based, it sorts out capacity issues in addition to the easy implementation. There is definitely a difference in the cost of treatment/eye/year but at the expense of having to fit patients into office visits at an average of 12 follow-ups in your modified IVAN protocol. The IVAN-modified

protocol might comply with being slightly less costly but it is not more cost-effective than Southampton protocol.

A treatment protocol in which the maximum VA gain is achieved with the minimum of clinic visits would not only alleviate capacity issues but also offer a cost-effective option. Our results demonstrate that for treatment-naïve patients with nAMD, treated in a real-world clinical setting, implementing a PROACTIVE fixed-dosing bi-monthly regimen of Aflibercept does offer not only efficacy, safety, and quality, but also cost-effectiveness.

Conflict of interest

HA and AL have received travel support to educational meetings from Bayer Pharmaceuticals.

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Sir, Simple fixation and removal of dacryocystorhinostomy tube

The use of silicone tubes as an adjunct to dacryocystorhinostomy (DCR) surgery is common place although the evidence base for their use remains weak.¹ The tubes are usually fixed intranasally with a variety of techniques, aiming to improve the stability and ocular comfort. It is not known whether different ways of securing the tubes affects the DCR outcome.

Most extubation techniques entail cutting the stents at their inter-punctal portion and any endonasal fixation sutures used, and then pulling the tubes out from the nose, which sometimes requires endoscopic assistance.

We read with great interest the DCR stent fixation and removal technique by Galea *et al*,² which involves insertion of a bicanalicular silicone tube tied with two 6/0 silk sutures, and removal by cutting the loop of the tube close to the lower punctum, followed by pulling the upper cut end of the tube laterally through the upper canaliculus to externalize the rest of the tube and sutures.

Extubation via medial canthus has been documented previously. Crawford³ described removal of silicone tubing (fixed with intraluminal 8/0 silk suture) by grasping the tube below the upper punctum, cutting the loop just above the lower punctum and pulling it out. Dressner⁴ also advocated a relatively similar fixation and removal procedure.

Recently we reported our technique for DCR tube fixation using a short silicone sleeve and external removal via medial canthus.⁵ The fixation is carried out by passing

the bodkins of the O'Donohue tubes through a short (2 mm) silicone (Watzke) sleeve in a crossed manner, followed by partial retrieval of the tubes through the DCR incision. The tightness of the tube is then tested and adjusted by pulling the loop of the tube from the medial canthus (Figure 1a and b).

The tube is simply removed externally by grasping it at the medial canthus with non-toothed forceps and firmly pulling laterally in a single movement (Figure 1c). This obviates the need of any intranasal manipulation or tube cutting. The short sleeve segment rests within the nose before finding its own way out. The patient must be warned to expect a momentary discomfort during removal which quickly passes. In our retrospective analysis of 166 cases of external DCRs using this method, none had retained tube/sleeve material or tube-related canalicular/punctal damage.

A main concern with these extubation techniques via medial canthus is the risk of subtle epithelial injury to the area of the common opening with potential subsequent membrane formation. Although we did not encounter any silicone sleeve related issues, further studies with endoscopic evaluation may unambiguously address this concern. Galea *et al* reported retained tube material in 7.5% of the cases,¹ which may be related to removal of both ends (still joined by sutures) through upper canalicular system.

In conclusion, our very low rate of tubes related complications in terms of both tube stability and patient comfort and the speed and simplicity of adjustment and removal encourages us to promote the use of a 2 mm long silicone sleeve to join the ends of a stent during external DCRs. Its main advantage is the quick and easy removal technique.

Conflict of interest

The authors declare no conflict of interest.

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Figure 1 (a) Partial retrieval of the tube through DCR incision and adjustment of the tension. Note ends already passed through the sleeve in a crossed fashion. (b) Sleeve and stent position post-adjustment (arrow). (c) Removal of the tube via medial canthus by pulling the loop laterally with a Moorefield forceps (without any cutting).