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ORIGINAL RESEARCH

# A Comparison of Conventional Intravitreal Injection Method vs InVitria Intravitreal Injection Method

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**Purpose:** To compare use of the conventional intravitreal injection method to the InVitria intravitreal injection device. Three outcome measures were studied: patient comfort, speed of injection and cost-effectiveness.

**Patients and Methods:** A prospective review of 58 patients was undertaken. Patients scored their perceived pain for each part of the conventional injection method using visual analogue scales (VAS), which allows pain to be scored from 0 (no pain) to 100. The same 58 patients scored their perceived pain for each part of the injection process with the InVitria on their follow-up visit. The procedure was timed in both settings and cost to the Trust was analysed.

**Results:** Pain scores when the InVitria was used were lower than when the conventional method was used for all aspects of the intravitreal injection procedure, in particular, when comparing insertion of drape/speculum (mean score 57.56) to insertion the InVitria (mean score 16.50), needle entry (mean score 37.76 to 27.86) and removal of the drape/speculum (mean score 38.72) to removal of the InVitria (11.07). The reduction in pain scores was statistically significant for all aspects of the procedure, except the initial instillation of drops. The InVitria was an average of 1 minute and 32 seconds faster than the conventional method. Use of the InVitria in place of the conventional method provides an annual saving of £24,300 to the Trust based on the number of injections currently performed.

**Conclusion:** The introduction of the InVitria in the Newcastle Eye Centre has had a positive impact on patient comfort, time and cost to the Trust.

**Keywords:** InVitria, drape, speculum, visual analogue scale, pain scores

## Introduction

Intravitreal administration of anti-vascular endothelial growth factor (anti-VEGF) drugs has now become routine practice in the management of macular conditions, the most common of which is neovascular age-related macular degeneration (nAMD); the biggest cause of visual loss and blind registration in patients over the age of 50 years in the developed world.[1–3] Approximately 600,000 people in the UK currently have sight loss caused by AMD, with around 70,000 new cases being diagnosed each year.[4] The increasing ageing population is placing a huge demand on the macular service, which creates a significant capacity challenge. It is vital that regular treatment is delivered to these patients in a timely manner to help maintain visual acuity and few patients are discharged from follow-up due to risk of disease reactivation. In the Newcastle Eye Centre (NEC), the overall amount of attendances

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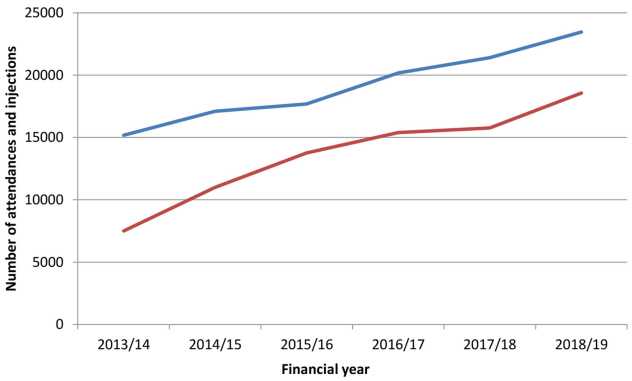


**Figure 1** Number of attendances (blue) and intravitreal injections (red) for all macular conditions increasing yearly in the NEC from 2013/14 to 2018/19.

and injections has increased by 47% and 63%, respectively, over the past 5 years (Figure 1).

The introduction of extended roles for allied health professionals (AHPs) has had a positive impact on capacity issues faced by macular services nationally and AHPs are now performing some roles traditionally carried out by doctors. Consultant-led multidisciplinary teams now assess patients in the macular clinics and deliver intravitreal injection treatment, supported by the Royal College of Ophthalmologists (RCO), the National Institute for Health and Care Excellence (NICE) and the British and Irish Orthoptic Society (BIOS). This change has been found to be beneficial for the service and patients.[5,6] However, despite these ongoing efforts to cope with the ageing population and increasing life expectancy, considerable capacity problems remain.

The NEC introduced the use of the InVitria assistant for intravitreal injections in October 2018 (Figure 2). This is a plastic, fully recyclable, disposable device, comprising an angled guide tube to ensure a fixed injection angle (28 degrees), distance from the limbus (3.5mm), and depth (5.6mm). The device holds the eye open and fixes it into place by the application of a gentle downward pressure, also adding an anaesthetic effect. A slight rotation of the device displaces the conjunctiva thereby preventing any vitreous leakage and providing protection of the site once the procedure is complete. Each device comes packaged individually in a box of 25. The InVitria device negates the need for the drape, calliper and speculum used in the conventional intravitreal injection method and thus allows the use of a new injection pack without these additional components.

The InVitria was launched in 2011 and has already received some positive feedback from other units in the

**Figure 2** The InVitria (image courtesy of Veni Vidi).

UK. Ninety-one units are currently using it as the standard technique for intravitreal injections (Veni Vidi, 2019). It has been described as easy to handle and get used to, useful in stabilising the eye to ensure the correct location and position of injection, quick, safe and more cost-effective than the conventional method, with no issues or problems reported in brief feedback from patients.[7] Another study looking into the tolerability of repeated injections concludes that the implementation of steps to improve unpleasant aspects, such as sensation of needle entry and the draping and speculum, should improve patients' experiences considerably.[8]

The aim of this service review was to determine whether the introduction of the InVitria in the NEC has had a positive impact. Three outcome measures were studied: patient comfort, speed of injection and cost-effectiveness compared to the conventional drape and speculum method.

## Methods

Two clinicians prospectively collected data from patients attending a macular clinic provided by the NEC between January and March 2019.

### Inclusion Criteria

Patients were included if they were not receiving their first intravitreal injection and were deemed competent by the clinician to understand and complete the questionnaire used for the review.

## Exclusion Criteria

Patients were excluded if they had undergone a trabeculectomy procedure or a corneal graft, both of which are unsuitable for use of the InVitria.

Patients were administered an intravitreal injection using the conventional drape and speculum method and the same patients received an intravitreal injection with the InVitria on their follow-up visit. Following the injection, the patient completed a questionnaire to grade their discomfort scores for each part of the procedure according to the visual analogue scale (VAS). The questionnaire divided the injection procedure into 6 separate steps: (1) instillation of initial anaesthetic and povidone-iodine (2) insertion of drape/speculum or InVitria (3) needle entry (4) removal of drape/speculum or InVitria (5) discomfort level once procedure complete (6) overall discomfort level of procedure. There was a comments section at the end if patients wished to leave any other feedback.

The VAS is a psychometric response scale, used to determine subjective characteristics or attitudes that cannot be directly measured (Figure 3). The VAS uses a straight 100mm line with verbal and numerical descriptors of each extreme of the symptom to be evaluated at each end, from 0 (no discomfort) to 100 (the most discomfort). The patient is asked to mark a perpendicular line at a position between the extremes, which represents their level of discomfort. It is useful in this type of research as it measures pain that ranges across a continuum of values rather than discrete jumps, such as mild, moderate, severe.[9] This type of qualitative data is useful in enabling the clinician to get an insight into the respondents' world from their point of view. It has previously been successfully used in ophthalmologic studies evaluating pain associated with intravitreal injections.[10–15]

The review did not involve any deviation from injection protocols set out by the RCO, who changed their guidance in 2018 to state that the routine use of a drape, speculum and calliper are no longer considered a requirement due to the introduction of disposable devices.[17]

The procedure was timed for both injection methods using a stopwatch (from immediately before surgical disinfection of hands to immediately following the removal of sterile gloves). The two clinicians involved had decided upon specific injection routine and took approximately the same amount of time for a straight forward injection procedure. This included allowing the recommended three minutes of contact time for the povidone-iodine on the periorbital skin and the lower fornix cul-de-sac prior to injecting, to reduce the risk of endophthalmitis.[17]

Cost-effectiveness was calculated by contacting the Newcastle upon Tyne Hospitals NHS Foundation Trust Supplies and Procurement team and by analysing departmental figures to determine annual expenditure for both injection methods.

Ethical review and approval were not required for this observational study.

# Results

A consecutive series of the first 58 patients requiring an injection were included. They were being treated for nAMD (n=43), retinal vein occlusions (RVO) (n=10) and diabetic macular oedema (DMO) (n=5). The mean age of the cohort was 79 years, ranging from 55 years to 94 years.

## Discomfort Scores

Seventy-Four patients were initially given a questionnaire following a timed injection using the conventional method. Fifty-eight of these returned to this clinic on their next visit and received an injection using the InVitria and were included in this review. The graph shows the mean scores (and standard error) for the InVitria method and the conventional method for each of the questions (Figure 4).

Patients injected using the InVitria scored lower than those injected with the conventional method for all six questions, which was particularly evident for questions 2, 3 and 4, which also show no overlap of standard error in Figure 4. Question 2 related to the insertion of the drape/speculum (mean score 57.56) and insertion of the InVitria (mean score 16.50). Question 3 related to needle entry for the conventional method (mean score 37.76) and the InVitria (mean score 27.86). Question 4 related to the removal of the drape/speculum (mean score 38.72) and removal of the InVitria (11.07). Paired T-tests (with 90% confidence interval) for each question show there was a statistically significant improvement in mean pain scores


**Figure 3** The Visual Analogue Scale.[16]

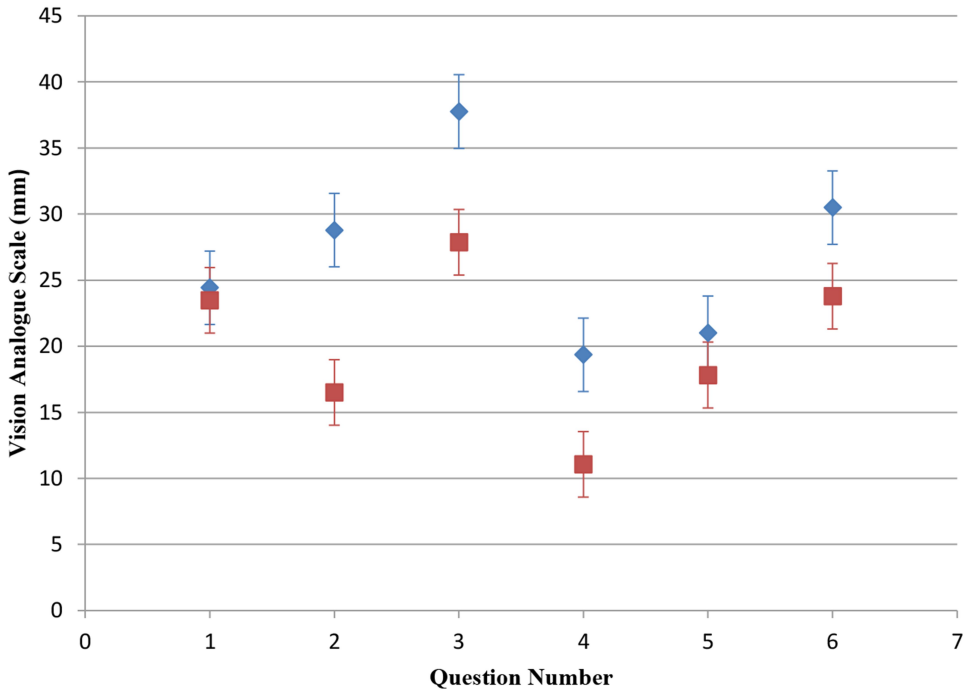


**Figure 4** VAS scores (with standard error) for each question for conventional method (blue) vs InVitria method (red).

when the InVitria was used compared to the conventional method for questions 2 to 6 (p=0.000, p=0.005, p=0.001, p=0.070, p=0.005). The only question where a statistically significant improvement in mean pain score was not shown was question 1 (p=0.167), which related to the instillation of drops at the very start of the procedure.

## Time

Time taken to perform intravitreal injection using the InVitria and the conventional method was recorded using a stopwatch in the 58 patients. All injections were straightforward, with no adverse events occurring during the injection process. The mean time taken to inject using the InVitria was 8 minutes 41 seconds and with the conventional method was 7 minutes 9 seconds. The InVitria was on average 1 minute and 32 seconds faster than the conventional method.

**Table 1** Cost Analysis

| | Conventional Method | InVitria |
|---|---|---|
| Total per injection (including all consumables) | £8.91 | £7.56 |
| Cost per year based on 18,000 injections | £160,380 | £136,080 |
| Total annual saving based on 18,000 injections yearly | | £24,300 |

**Notes:** Courtesy of the Newcastle upon Tyne Hospitals NHS Foundation Trust Supplies and Procurement Department, 2019.

## Cost Analysis

Table 1 shows the break down in the costs of each method. Using the InVitria costs £1.35 less per injection than using the conventional method. Based on the current activity of 18,000 injections per year, the annual saving for the Newcastle Upon Tyne NHS Foundation Trust is £24,300.

# Discussion

Providing a more comfortable procedure is important as in turn it reduces patient anxiety levels and may ultimately lead to better compliance with treatment. The nature of pain means objective measurement is very difficult. We aimed to allow patients to communicate their levels of pain as accurately as possible to achieve an insight into their injection experiences. We opted to use the VAS as it has been described as easy to use, providing reproducible results and applicable to a variety of practice settings.[18] We used a horizontal scale rather than a vertical scale given that there is less chance of perspective error.[19] Numbers or verbal descriptors were not given at intermediate points as this has found to cause clustering of scores around a preferred numeric value.[20,21] There are

conflicting opinions on whether earlier scores should be visible to the patient on succeeding forms.[21–23] Some have found that the respondent may overestimate their score if the previous score is not available[22] but some suggest the respondent may perceive more room to one side of the scale if their previous score is visible[24] and this may influence where they draw the line. We decided to minimise potential bias by concealment of previous responses.

Patients injected using the InVitria reported a more comfortable injection experience for all aspects of the procedure in comparison to the conventional method. All reductions in pain scores were found to be statistically significant, except in relation to the instillation of drops at the very start of the procedure, which is to be expected as it is exactly the same for both methods. The review shows the most uncomfortable part of the procedure for both methods appeared to be needle entry and the least uncomfortable part for both methods was removal of the drape/speculum or InVitria.

Pain is a very subjective and complex characteristic to measure; however, this review most definitely indicates a preference towards the InVitria when considering patient comfort level. This is also supported by feedback from patients in the comments section of the questionnaires, such as:

- The InVitria is quicker with less discomfort
- InVitria felt quicker, did not like drape used previously
- Much preferred new instrument
- New procedure is better, did not like drape or clamp
- 100% better than previous procedure
- I find this method a big improvement, much less uncomfortable and still allows the personal touch

A similar study comparing the InVitria with the conventional method using the VAS found comparable results.[25] The study concluded that lower discomfort scores might be related to the downward pressure applied with the InVitria, which acts as a physical anaesthetic block to the ciliary nerves, and that patients preferred not to have the drape or the speculum.

Another aspect of pain relating to intravitreal injections is when a corneal abrasion occurs. In this service review, we did not come across any cases of corneal abrasion using the InVitria or the conventional method. However, it is thought that the smooth surface of the InVitria device compared to the speculum makes corneal abrasions less likely,[26] which in turn will result in fewer patients returning to the eye emergency department following intravitreal injection.

The average time for an injection with the InVitria was 1 minute and 32 seconds faster than the conventional method. Although a relatively small amount of time, this becomes more significant when considering the number of injections carried out on a day-to-day basis. For a clinic booked with 15 patients per session, assuming 12 of these patients required injecting this would save 18 minutes per session and this time could be utilised to see and treat additional patients. The use of the InVitria in other units has allowed more injections to be performed in a session, providing further financial benefit to hospital Trusts without compromising patient safety.[7] In a similar study of 70 patients, use of the InVitria was also found to be a quicker technique than the conventional method and there was a trend towards patients finding it more comfortable.[26]

Using the InVitria rather than the conventional method currently allows an annual saving of £24,300 for the Newcastle Upon Tyne NHS Foundation Trust, which will increase with the growing numbers of injections. If all ophthalmology units in the UK were to change practice, this could result in extensive savings nationwide. With the current financial pressures faced by NHS Trusts, being pro-active in maximising outcomes while minimising costs where possible is imperative. For a service also under continuous pressure for time and space, this change to practice certainly seems logical.

One of the major limitations to this service review is that all patients received the conventional injection method first and an injection with the InVitria on their follow-up visit. This may give rise to order effect bias in that a pain tolerance may have developed over time or the patients may have felt more comfortable or familiar over successive treatments. It may have also caused a response bias whereby new is often perceived as being better. The InVitria was being introduced as standard practice across all Trust sites at the time of the review so it would have been difficult to avoid this; however, a crossover design would have been more appropriate so that patients were randomised into having each method either on the first or the follow-up visit in the study. The sample size was also relatively small.

As conditions requiring intravitreal injections are typically age-related, the cohort of patients included in the review were elderly. Some previous studies indicate the application of VAS in the elderly patients is difficult due to

cognitive impairments or motor skills,[27] however, we did not encounter any of our patients having difficulties. With increased use of the InVitria in the NEC, data on endophthalmitis rates must of course be analysed to determine if this has been impacted by the change in practice. A limitation of the InVitria device is that it cannot be used in patients following a trabeculectomy or corneal graft.

## Conclusion

This service review provides an evaluation that the introduction of the InVitria has had a positive impact in the NEC, which contributes to the current small pool of evidence regarding the use of the InVitria in real-world practice. Patients appear to find it more comfortable and it speeds up and standardises the procedure, potentially allowing more injections in a clinic. It has also provided a substantial cost saving to the Trust. The NHS must continuously adapt, improve and evolve, delivering health care in a consistent and sustainable way. We must strive to provide better experiences and outcomes for patients with use of the most appropriate resources. This involves exploring alternative ways to deliver care and making informed decisions to do things differently. We look forward to conducting further research into the impact of the InVitria.

## Disclosure

Mr James Talks reports grants, personal fees, non-financial support from Bayer, grants, attended conference and participated in research for Novartis, participated in research for Roche and Allergan, outside the submitted work. The authors report no other conflicts of interest in this work.

## References


1. Augood CA, Vingerling JR, de Jong PT, et al. Prevalence of age-related maculopathy in older Europeans: the European Eye Study (EUREYE). *Arch Ophthalmol*. 2006;124(4):529–535. doi:10.1001/archopht.124.4.529
2. Bunce C, Wormald R. Leading causes of certification for blindness and partial sight in England and Wales. *BMC Public Health*. 2006;6:58. doi:10.1186/1471-2458-6-58
3. NICE Guidelines (NG82) 2018; 2018 Available from: https://www.nice.org.uk/guidance/ng82/chapter/Context. Accessed July 30, 2020
4. National Eye Research Centre 2019 Available from: https://www.nercuk.org/age-related-macular-degeneration. Accessed 14.October.2019.
5. Varma D, Lunt D, Johnson P, Stanley S. A novel approach to expanding the role of nurses to deliver intravitreal injections for patients with age related macular degeneration. *Int J Ophthalm Pract*. 2013;4((2):68–74). doi:10.12968/ijop.2013.4.2.68
6. DaCosta J, Hamilton R, Nago J, et al. Implementation of a nurse delivered intravitreal injection service. *Eye*. 2014;28(6):734–740. doi:10.1038/eye.2014.69
7. Hasan H. The role of injection assistant devices in establishing a nurse-led AMD service. *Eye News*. 2018;24:6.
8. Tailor R, Beasley R, Yang Y, Narandran N. Evaluation of patients' experiences at different stages of the intravitreal injection procedure – what can be improved? *Clin Ophthalmol*. 2011;5:1499–1502. doi:10.2147/OPTH.S24358
9. Gould D, Kelly D, Goldstone L, et al. Visual Analogue Scale. *J Clin Nurs*. 2001;10(5):697±706. doi:10.1046/j.1365-2702.2001.00525.x
10. Cintra LP, Lucena LR, Da Silva JA, Costa RA, Scott IU, Jorge R. Comparative study of analgesic effectiveness using three different anesthetic techniques for intravitreal injection of bevacizumab. *Ophthalmic Surg Lasers Imaging*. 2009;40(1):13–18. doi:10.3928/15428877-20090101-05
11. Yau GL, Jackman CS, Hooper PL, Sheidow TG. Intravitreal injection anesthesia– comparison of different topical agents: a prospective randomized controlled trial. *Am J Ophthalmol*. 2011;151(2):333–337. doi:10.1016/j.ajo.2010.08.031
12. Moisseiev E, Regenbogen M, Bartfeld Y, Barak A. Evaluation of pain in intravitreal bevacizumab injections. *Curr Eye Res*. 2012;37(9):813–817. doi:10.3109/02713683.2012.681335
13. Rifkin L, Schaal S. Factors affecting patients' pain intensity during in office intravitreal injection procedure. *Retina*. 2012;32(4):696–700. doi:10.1097/IAE.0b013e3182252ad3
14. Güler M, Bilgin B, Capkın M, Simsek A, Bilak S. Assessment of patient pain experience during intravitreal 27-gauge bevacizumab and 30-gauge ranibizumab injection. *Korean J Ophthalmol*. 2015;29(3):190–194. doi:10.3341/kjo.2015.29.3.190
15. Van Asten F, van Middendorp H, Verkerk S. Are intravitreal injections with ultrathin 33-g needles less painful than the commonly used 30-G needles? *Retina*. 2015;35(9):1778–1785. doi:10.1097/IAE.0000000000000550
16. Hayes MHS, Patterson DG. Experimental development of the graphic rating method. *Psychol Bull*. 1921;18:98–99.
17. Royal College of Ophthalmologists Ophthalmic Service Guidance Intravitreal Therapy. 2018. Available from: https://www.rcophth.ac.uk/wp-content/uploads/2018/02/Intravitreal-Injection-Therapy-August-2018-2.pdf. Accessed July 30, 2020.
18. Todd KH. Clinical versus statistical significance in the assessment of pain relief. *Ann Emerg Med*. 1996;27(4):439–441. doi:10.1016/S0196-0644(96)70226-3
19. Dixon JS, Bird HA. Reproducibility along a 10 cm vertical visual analogue scale. *Ann Rheum Dis*. 1981;40:87–89. doi:10.1136/ard.40.1.87
20. Huskisson EC, Wojtulewski JA, Berry H, Scott J, Hart FD, Balme HW. Treatment of rheumatoid arthritis with fenoprofen: comparison with aspirin. *Br Med J*. 1974;1(5900):176–180. doi:10.1136/bmj.1.5900.176
21. Scott J, Huskisson EC. Graphic representation of pain. *Pain*. 1976;2(2):175–184. doi:10.1016/0304-3959(76)90113-5
22. Joyce CR, Zutshi DW, Hrubes V, Mason RM. Comparison of fixed interval and visual analogue scales for rating chronic pain. *Eur J Clin Pharmacol*. 1975;8(6):415–420. doi:10.1007/BF00562315
23. Bodian CA, Freedman G, Hossain S, Eisenkraft JB, Beilin Y. The visual analogue scale for pain: clinical significance in postoperative patients. *Anesthesiology*. 2001;95(6):1356–1361. doi:10.1097/00000542-200112000-00013
24. Kelly AM. The minimum clinically significant difference in visual analogue scale pain score does not differ with severity of pain. *Emerg Med J*. 2001;18(3):205–207. doi:10.1136/emj.18.3.205
25. Ratnarajan G, Nath R, Appaswamy S, et al. Intravitreal injections using a novel conjunctival mould: a comparison with a conventional technique. *Br J Ophthalmol*. 2013;97(4):395–397. doi:10.1136/bjophthalmol-2012-302155
26. Eaton AM. Striving to Improve Intravitreal Injections. *Rev Ophthalmol*. 2013;2:254.
27. Hawker GA, Mian S, French M. Measures of Adult Pain: visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), Mcgill Pain Questionnaire (MPQ), Short-Form Mcgill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Am Coll Rheumatol*. 2011;63(S11):S240–S252.