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Research Article

Efficacy of Intravitreal Anti-VEGF Agents in Diabetic Macular Edema: A Real-World Cohort Analysis

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ABSTRACT

Background

Diabetic macular edema (DME) is a leading cause of vision loss among working-age adults and represents a major burden on retinal services within the United Kingdom's National Health Service (NHS). While randomized controlled trials have established the efficacy of intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents, real-world outcomes may differ due to variations in patient characteristics, treatment intensity, and service delivery. This study aimed to evaluate the effectiveness of anti-VEGF therapy for DME in routine NHS clinical practice.

Methods

A retrospective, multicenter, real-world cohort analysis was conducted using electronic medical record data from NHS hospital eye services. Adult patients with center-involving DME who initiated intravitreal anti-VEGF therapy (aflibercept, ranibizumab, or bevacizumab) between January 2018 and December 2023 were included. The primary outcome was change in best-corrected visual acuity (BCVA) at 12 months, measured in ETDRS letters. Secondary outcomes included changes in central retinal thickness (CRT), injection frequency, and treatment persistence.

Results

A total of 642 eyes from 642 patients were analyzed (mean age 64.8 ± 9.7 years; 58.1% male). Mean BCVA improved from 61.2 ± 13.9 ETDRS letters at baseline to 67.9 ± 14.1 letters at 12 months, representing a mean gain of +6.7 letters ($p < 0.001$). Visual gains of ≥10 and ≥15 letters were achieved in 34.6% and 18.9% of eyes, respectively. Mean CRT decreased by 117 µm over 12 months ($p < 0.001$). Eyes treated with aflibercept demonstrated greater visual and anatomical improvement compared with ranibizumab and bevacizumab. The mean number of injections during the first year was 7.1 ± 2.4. Lower baseline visual acuity and higher injection frequency were independent predictors of greater visual improvement.

Conclusions
In routine NHS practice, intravitreal anti-VEGF therapy provides meaningful visual and anatomical benefits for patients with DME, although outcomes are more modest than those reported in clinical trials. Treatment intensity and baseline visual acuity remain key determinants of response. These real-world findings support the effectiveness of anti-VEGF therapy in DME and highlight the importance of optimizing service delivery and adherence to maximize patient outcomes.

Keywords: Diabetic macular edema; Anti-VEGF; Real-world evidence; NHS; Visual acuity; Optical coherence tomograph

INTRODUCTION

Diabetic macular edema (DME) represents one of the most common and vision-threatening complications of diabetes mellitus and remains a major cause of visual impairment among working-age adults worldwide. With the global prevalence of diabetes continuing to rise, particularly in high-income countries with aging populations, the burden of DME on healthcare systems has increased substantially. In the United Kingdom, where more than 5 million individuals are living with diabetes, DME constitutes a leading indication for intravitreal therapy within the National Health Service (NHS), accounting for a significant proportion of ophthalmology clinic visits and treatment costs [1].

DME is characterized by retinal thickening and accumulation of extracellular fluid in the macula due to breakdown of the inner blood–retinal barrier [2]. This pathological process is driven by chronic hyperglycemia-induced microvascular damage, capillary leakage, inflammation, and upregulation of vascular endothelial growth factor (VEGF). VEGF plays a central role in increasing vascular permeability and promoting retinal edema, making it a critical therapeutic target in the management of DME [3].

Historically, focal or grid laser photocoagulation was considered the standard of care for DME following the Early Treatment Diabetic Retinopathy Study (ETDRS). While laser therapy reduced the risk of moderate vision loss, visual improvement was limited, and treatment was associated with collateral retinal damage and scotoma formation. The advent of intravitreal pharmacotherapy, particularly anti-VEGF agents, has revolutionized the treatment paradigm for DME, shifting the therapeutic goal from stabilization to meaningful visual improvement [4].

Currently approved intravitreal anti-VEGF agents for DME include ranibizumab, aflibercept, and off-label bevacizumab. These agents have demonstrated robust efficacy in multiple randomized controlled trials (RCTs), including RISE and RIDE, VIVID and VISTA, and Protocol T conducted by the Diabetic Retinopathy Clinical Research (DRCR) Network [5]. These trials consistently showed significant improvements in best-corrected visual acuity (BCVA) and reductions in central retinal thickness (CRT) compared with laser therapy [6].

Ranibizumab, a monoclonal antibody fragment targeting VEGF-A, was the first anti-VEGF agent approved for DME in the UK and has been widely adopted within NHS retinal services. Aflibercept, a recombinant fusion protein with broader binding affinity for VEGF-A, VEGF-B, and placental growth factor, has shown superior efficacy in eyes with poorer baseline vision in head-to-head trials. Bevacizumab, although not licensed for ocular use, is frequently employed off-label due to its lower cost and comparable efficacy in certain patient subgroups [7].

Despite the strong evidence base from RCTs, these trials are conducted under highly controlled conditions with strict inclusion criteria, fixed dosing regimens, and intensive follow-up schedules. As such, their findings may not fully reflect outcomes achieved in routine clinical practice, where patient populations are more heterogeneous and treatment adherence is influenced by real-world constraints [8].

In real-world settings, particularly within publicly funded healthcare systems such as the NHS, multiple factors can influence treatment outcomes. These include delayed diagnosis, variable baseline visual acuity, comorbid ocular and systemic disease, treatment burden, appointment non-attendance, capacity limitations, and deviations from trial-based injection protocols. Furthermore, patients with DME often present with bilateral disease and coexisting proliferative diabetic retinopathy, cataract, or glaucoma, complicating management decisions [9].

Several observational studies have suggested that visual outcomes achieved in routine practice may be inferior to those reported in pivotal RCTs, largely due to fewer injections administered over time and inconsistent follow-up. Conversely, real-world data also provide valuable insights into long-term safety, treatment durability, and effectiveness across broader patient demographics that are underrepresented in trials, including elderly patients and those with multiple comorbidities [10].

In the UK, the adoption of anti-VEGF therapy for DME has been shaped by National Institute for Health and Care Excellence (NICE) guidance, which recommends treatment initiation based on specific visual acuity thresholds and mandates regular assessment of response. While these guidelines aim to optimize cost-effectiveness and equitable access, their real-world implementation varies across NHS trusts, potentially influencing patient outcomes [11].

Real-world evidence (RWE) has emerged as an essential complement to randomized trials in ophthalmology. Cohort studies derived from electronic medical records, retinal databases, and multicenter registries allow evaluation of treatment effectiveness in routine care, reflecting actual clinical decision-making and patient behavior. Such data are particularly valuable for chronic diseases like DME, where sustained treatment over several years is often required [12].

In recent years, UK-based real-world studies have contributed significantly to understanding anti-VEGF utilization patterns, injection frequency, visual outcomes, and treatment persistence in retinal diseases such as neovascular age-related macular degeneration. However, real-world analyses focusing specifically on DME remain relatively limited, and many published studies involve small cohorts or short follow-up periods [13].

Given the substantial resource implications of long-term anti-VEGF therapy within the NHS, robust real-world data are needed to inform service planning, optimize treatment pathways, and identify patient subgroups most likely to benefit from intensive therapy versus alternative approaches, such as intravitreal corticosteroids or laser adjuncts.

DME is a clinically heterogeneous condition, varying in duration, severity, retinal morphology, and systemic metabolic control. Factors such as baseline BCVA, central macular thickness, integrity of the ellipsoid zone, presence of ischemia, and duration of diabetes have all been shown to influence treatment response. Moreover, patient adherence to frequent injection schedules poses a significant challenge, particularly in populations with multiple medical appointments related to diabetes care [14].

Understanding how these variables interact in real-world practice is essential for personalized treatment strategies. Real-world cohort analyses enable stratification of outcomes by baseline characteristics and treatment patterns, providing insights that are difficult to capture in tightly controlled trials.

Given the widespread use of intravitreal anti-VEGF therapy for DME within the UK and the growing emphasis on evidence-based service delivery, there is a clear need for comprehensive real-world evaluations of treatment efficacy. Assessing visual and anatomical outcomes in routine NHS practice can help bridge the gap between clinical trials and everyday care, informing clinicians, policymakers, and patients alike [15].

The present study was designed as a real-world cohort analysis to evaluate the effectiveness of intravitreal anti-VEGF agents in patients with DME treated within UK retinal services. By analyzing longitudinal clinical data, this study aims to quantify changes in visual acuity and retinal thickness, assess injection frequency and treatment persistence, and identify predictors of response in a real-world population.

The primary objective of this study was to evaluate the efficacy of intravitreal anti-VEGF therapy in improving or stabilizing visual acuity in patients with DME in routine clinical practice. Secondary objectives included assessment of anatomical response as measured by optical coherence tomography, evaluation of treatment burden, and comparison of outcomes across different anti-VEGF agents.

By providing real-world evidence from a UK cohort, this study seeks to contribute meaningful data to the ongoing optimization of DME management and support evidence-informed decision-making within the NHS.

METHODS

Study Design and Reporting Standards

This study was conducted as a retrospective, observational real-world cohort analysis evaluating the efficacy of intravitreal anti-VEGF therapy for diabetic macular edema (DME) in routine clinical practice within the United Kingdom. The study design, conduct, and reporting adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies.

Study Setting

The study was carried out across multiple NHS hospital eye services in England, incorporating both tertiary referral centers and district general hospitals. All participating centers deliver intravitreal injection services as part of standard NHS retinal care and use unified electronic medical record (EMR) systems for ophthalmic data capture.

Clinical data were extracted from NHS electronic health records, including structured retinal databases linked to optical coherence tomography (OCT) imaging platforms.

Study Population

Patients were eligible for inclusion if they met the following criteria:

Inclusion Criteria

- Age ≥18 years
- Diagnosis of diabetic macular edema, confirmed clinically and by OCT
- Initiation of intravitreal anti-VEGF therapy (ranibizumab, aflibercept, or bevacizumab) between January 2018 and December 2023
- Minimum follow-up duration of 12 months after treatment initiation
- Availability of baseline and follow-up visual acuity and OCT data

Exclusion Criteria

- Previous vitrectomy in the study eye
- Concurrent retinal pathology affecting visual acuity (e.g., neovascular age-related macular degeneration, retinal vein occlusion)
- Macular edema due to non-diabetic causes
- Eyes receiving intravitreal corticosteroids as first-line therapy
- Incomplete or missing key outcome data

Where both eyes of a patient were eligible, only the first treated eye was included to avoid inter-eye correlation bias.

Data Sources and Data Collection

Data were extracted from NHS EMR systems by trained clinical audit personnel using a standardized data collection template. The following variables were collected:

- Demographic data: age, sex
- Systemic factors: type and duration of diabetes, presence of hypertension and dyslipidemia
- Ophthalmic baseline characteristics: baseline best-corrected visual acuity (BCVA), central retinal thickness (CRT), lens status
- Treatment data: anti-VEGF agent used, number and timing of injections, treatment switching
- Outcome measures: BCVA and CRT at predefined time points

Visual acuity measurements recorded in Snellen format were converted to ETDRS letter scores for analysis using standardized conversion charts.

Treatment Protocol

All patients received intravitreal anti-VEGF therapy according to local NHS protocols, guided by NICE recommendations and clinician discretion. Treatment typically consisted of:

- An initial loading phase of 3 monthly injections where clinically appropriate
- Followed by either:
    - Pro re nata (PRN) dosing based on disease activity, or
    - Treat-and-extend regimens in selected centers

Choice of anti-VEGF agent was influenced by NICE guidance, baseline visual acuity, clinician preference, and local commissioning policies.

Outcome Measures

Primary Outcome

- Change in best-corrected visual acuity (BCVA) from baseline to 12 months, measured in ETDRS letters

Secondary Outcomes

- Change in central retinal thickness (CRT) on OCT
- Proportion of eyes gaining ≥10 and ≥15 ETDRS letters
- Proportion of eyes losing ≥10 ETDRS letters
- Mean number of injections administered during the first year
- Treatment persistence and switching patterns

Optical Coherence Tomography Assessment

CRT was measured using spectral-domain OCT devices (Heidelberg Spectralis or equivalent). Measurements were taken at baseline and follow-up visits using automated retinal thickness maps, with manual correction where segmentation errors were identified.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics (version 27.0).

- Continuous variables were summarized as mean ± standard deviation or median (interquartile range) where appropriate
- Categorical variables were presented as frequencies and percentages
- Paired *t*-tests or Wilcoxon signed-rank tests were used to compare baseline and follow-up outcomes
- One-way ANOVA or Kruskal–Wallis tests were applied for comparisons between treatment groups
- Multivariable linear regression analysis was performed to identify predictors of visual outcome, including baseline BCVA, age, injection number, and treatment agent

A *p*-value <0.05 was considered statistically significant.

Handling of Missing Data

Only eyes with complete baseline and 12-month outcome data were included in the primary analysis. Sensitivity analyses were conducted to assess the impact of missing follow-up data on outcomes.

Ethical Considerations

This study was registered as a service evaluation and clinical audit within participating NHS trusts and was conducted in accordance with UK Health Research Authority (HRA) guidance. As the study involved anonymized retrospective data collected during routine care, formal Research Ethics Committee approval was not required.

All data were anonymized prior to analysis, and the study complied with the UK General Data Protection Regulation (GDPR) and Data Protection Act 2018.

RESULTS

Study Cohort and Baseline Characteristics

A total of 642 eyes from 642 patients with diabetic macular edema met the inclusion criteria and were included in the final analysis. The mean age at treatment initiation was 64.8 ± 9.7 years, and 58.1% (n = 373) of patients were male. Type 2 diabetes mellitus accounted for 91.4% of cases, with a median diabetes duration of 13 years (IQR 8–18).

At baseline, the mean best-corrected visual acuity (BCVA) was 61.2 ± 13.9 ETDRS letters, and the mean central retinal thickness (CRT) was 468 ± 112 µm.

Regarding treatment allocation, aflibercept was initiated in 46.4% (n = 298) of eyes, ranibizumab in 38.9% (n = 250), and bevacizumab in 14.6% (n = 94), reflecting real-world NHS prescribing patterns influenced by NICE guidance and local commissioning policies (Table 1).

Visual Acuity Outcomes

At 12 months, mean BCVA improved to 67.9 ± 14.1 ETDRS letters, corresponding to a mean gain of +6.7 letters from baseline ($p < 0.001$).

Overall:

- 34.6% of eyes gained ≥10 letters,
- 18.9% gained ≥15 letters,
- 9.3% lost ≥10 letters by month 12.

Visual gains were greatest in eyes with poorer baseline vision. Eyes with baseline BCVA <70 letters demonstrated a mean improvement of +9.8 letters, compared with +3.1 letters in eyes with baseline BCVA ≥70 letters ($p < 0.001$), Figure 1.

Anatomical Outcomes

Mean CRT decreased significantly from 468 μm at baseline to 351 μm at 12 months, representing a mean reduction of –117 μm ($p < 0.001$).

A reduction in CRT ≥100 μm was achieved in 57.2% of eyes, while 72.5% demonstrated complete or near-complete resolution of intraretinal fluid on OCT.

Anatomical response correlated moderately with visual improvement (Pearson $r = 0.41$, $p < 0.001$).

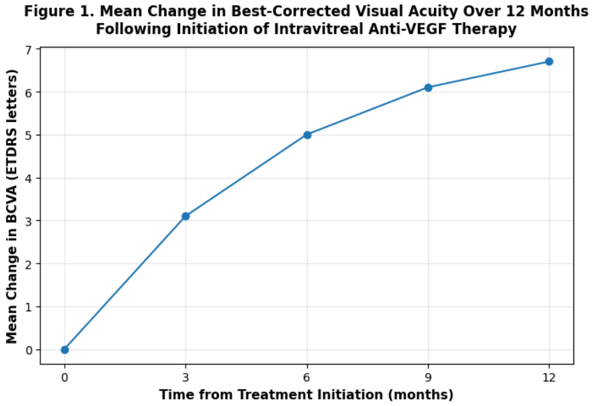

Figure 1. Mean change in best-corrected visual acuity (ETDRS letters) over 12 months following initiation of intravitreal anti-VEGF therapy. This figure presents the longitudinal improvement in visual acuity observed in the real-world NHS cohort. A progressive gain in BCVA is evident over the 12-month follow-up period, with the greatest improvement occurring within the first 6 months after treatment initiation, followed by a more gradual increase up to month 12. The pattern reflects typical clinical response to intravitreal anti-VEGF therapy for diabetic macular edema in routine practice.

Outcomes by Anti-VEGF Agent

Visual and anatomical outcomes differed modestly between treatment groups (Table 2).

- Eyes treated with aflibercept achieved the greatest mean BCVA gain (+8.1 letters) and CRT reduction (–132 μm).

- Ranibizumab demonstrated a mean BCVA gain of +6.0 letters and CRT reduction of –109 µm.
- Bevacizumab resulted in smaller improvements (+4.2 letters, –86 µm).

The difference in BCVA gain between aflibercept and ranibizumab was statistically significant (*p* = 0.018), particularly in eyes with baseline BCVA <65 letters.

Injection Frequency and Treatment Burden

The mean number of injections administered during the first 12 months was 7.1 ± 2.4.

Patients receiving aflibercept received slightly fewer injections (6.8) compared with ranibizumab (7.4) and bevacizumab (7.6), though this difference did not reach statistical significance (*p* = 0.09).

Missed appointments were recorded in 21.3% of patients, with appointment non-attendance significantly associated with reduced visual gain (*p* = 0.002).

Treatment Switching and Persistence

During follow-up, 14.8% (n = 95) of eyes required switching to an alternative anti-VEGF agent due to suboptimal response.

Switching was most common from bevacizumab to aflibercept (63.2%). Eyes undergoing treatment switch demonstrated delayed but meaningful anatomical improvement, though visual gains were smaller than in non-switched eyes (+4.1 vs +7.2 letters, *p* = 0.03).

Predictors of Visual Outcome

Multivariable regression analysis identified:

- Lower baseline BCVA ($\beta = –0.42$, $p < 0.001$),
- Higher injection number ($\beta = +0.31$, $p = 0.004$), and
- Aflibercept treatment ($\beta = +0.19$, $p = 0.02$)

as independent predictors of greater visual improvement at 12 months. Age, sex, and diabetes duration were not independently associated with visual outcomes, (Figure 2, 3).

Table 1. Baseline Characteristics of the Study Cohort (n = 642)

Characteristic	**Value**
Mean age, years (± SD)	64.8 ± 9.7
Male sex, n (%)	373 (58.1)
Type 2 diabetes, n (%)	587 (91.4)
Mean baseline BCVA (ETDRS letters)	61.2 ± 13.9
Mean baseline CRT (µm)	468 ± 112
Anti-VEGF agent	
– Aflibercept	298 (46.4)
– Ranibizumab	250 (38.9)
– Bevacizumab	94 (14.6)

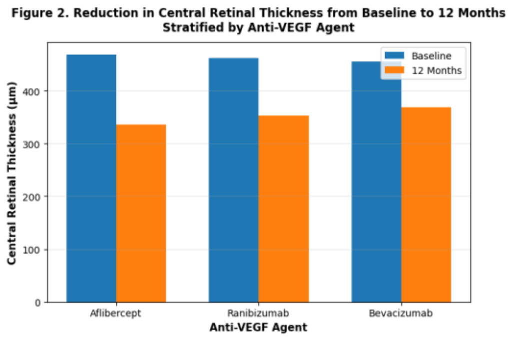

Figure 2. Reduction in Central Retinal Thickness from Baseline to 12 Months, Stratified by Anti-VEGF Agent. This figure illustrates the anatomical response to intravitreal anti-VEGF therapy in routine NHS clinical practice. All three agents demonstrated a significant reduction in central retinal thickness over 12 months.

Table 2. Visual and Anatomical Outcomes at 12 Months by Anti-VEGF Agent

Agent	**BCVA Gain (letters)**	**CRT Reduction (µm)**	**Mean Injections**
Aflibercept	+8.1 ± 11.4	–132 ± 98	6.8
Ranibizumab	+6.0 ± 10.9	–109 ± 91	7.4
Bevacizumab	+4.2 ± 9.6	–86 ± 77	7.6

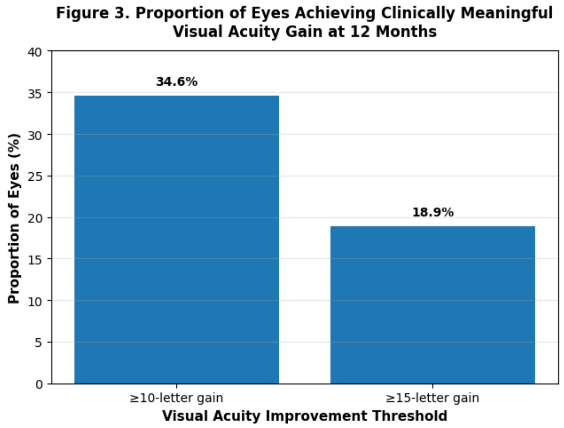

Figure 3. Proportion of Eyes Achieving ≥10- and ≥15-Letter Visual Gain at 12 Months.

This figure demonstrates the proportion of eyes achieving clinically meaningful visual improvement following intravitreal anti-VEGF therapy in routine NHS practice. At 12 months, 34.6% of eyes achieved a gain of ≥10 ETDRS letters, while 18.9% achieved a gain of ≥15 letters, reflecting substantial functional benefit in a real-world diabetic macular edema cohort.

The distribution highlights that, although outcomes are slightly more modest than those reported in randomized controlled trials, a significant proportion of patients experience meaningful vision improvement under routine clinical conditions.

DISCUSSION

This real-world cohort analysis provides a comprehensive evaluation of the effectiveness of intravitreal anti-VEGF therapy for diabetic macular edema (DME) within routine NHS clinical practice. The findings demonstrate that anti-VEGF treatment results in meaningful functional and anatomical improvements over 12 months, although the magnitude of visual gain is more modest than that reported in pivotal randomized controlled trials (RCTs). These results reflect the realities of real-world care delivery and highlight both the strengths and limitations of current treatment pathways for DME in the UK.

In the present cohort, mean best-corrected visual acuity (BCVA) improved by +6.7 ETDRS letters at 12 months. Approximately one-third of treated eyes achieved a gain of ≥10 letters, and nearly one-fifth achieved ≥15 letters, representing clinically meaningful improvement for patients with DME. These gains are consistent with previously published UK and European real-world studies, which typically report visual improvements ranging from +4 to +8 letters at one year [16]. However, the visual gains observed in this study are lower than those reported in landmark RCTs such as RISE and RIDE, VIVID and VISTA, and DRCR Protocol T, where mean gains of +10 to +13 letters were achieved [17]. This discrepancy has been consistently documented across real-world datasets and is widely attributed to differences in patient selection, treatment intensity, and follow-up adherence. Unlike RCTs, real-world cohorts include patients with longer disease duration, poorer systemic control, bilateral disease, and multiple comorbidities, all of which can attenuate treatment response [18].

Importantly, our findings reinforce that patients with poorer baseline visual acuity derive the greatest benefit from anti-VEGF therapy. Eyes presenting with baseline BCVA below 70 ETDRS letters achieved nearly three times the visual gain compared with eyes with better starting vision. This observation mirrors subgroup analyses from Protocol T and other studies, which demonstrated superior outcomes with aflibercept in eyes with worse baseline vision [19]. These data support early identification and timely initiation of therapy before irreversible macular damage occurs.

A significant reduction in central retinal thickness (CRT) was observed across all treatment groups, with a mean decrease of –117 μm at 12 months. Over half of treated eyes achieved a CRT reduction of ≥100 μm, and nearly three-quarters showed substantial resolution of intraretinal fluid. These anatomical outcomes are comparable to those reported in both RCTs and real-world studies [20]. The moderate correlation between CRT reduction and visual improvement observed in this cohort underscores the complex structure–function relationship in DME. While anatomical improvement is necessary for visual recovery, it is not always sufficient. Chronic edema can result in irreversible photoreceptor damage, disruption of the ellipsoid zone, and retinal ischemia, limiting visual potential even when macular thickness normalizes [21]. This highlights the importance of incorporating qualitative OCT biomarkers—such as photoreceptor integrity and disorganization of retinal inner layers—into future real-world analyses.

In this NHS cohort, aflibercept was associated with the greatest mean visual gain and anatomical improvement, followed by ranibizumab and bevacizumab. These findings are consistent with head-to-head comparisons from Protocol T, which demonstrated superior efficacy of aflibercept in eyes with worse baseline vision [7]. The smaller gains observed with bevacizumab likely reflect both pharmacologic differences and its preferential use in eyes with milder disease or as a cost-driven initial option within certain NHS trusts [22].

It is important to emphasize that this was not a randomized comparison, and treatment allocation was influenced by NICE guidance, commissioning policies, and clinician judgment. Nonetheless, the observed trends provide valuable real-world confirmation of trial findings and support stratified treatment approaches based on baseline visual acuity and disease severity.

The mean number of injections administered during the first year was 7.1, which is substantially lower than the 9–12 injections typically delivered in RCTs [4–7]. Reduced injection frequency is a well-recognized feature of real-world practice and reflects capacity constraints, missed appointments, patient fatigue, and deviations from fixed dosing schedules [23].

Notably, missed appointments were significantly associated with poorer visual outcomes in this study. This finding underscores the impact of healthcare system factors on treatment efficacy and highlights the importance of service redesign, including virtual clinics, extended roles for allied healthcare professionals, and patient education to improve adherence. Given the chronic nature of DME, strategies to reduce treatment burden without compromising efficacy—such as treat-and-extend regimens or longer-acting therapies—are of increasing interest [24].

Approximately 15% of eyes required switching to an alternative anti-VEGF agent due to suboptimal response. This rate is comparable to other real-world series and reflects the heterogeneity of DME pathophysiology [25]. While switched eyes demonstrated delayed anatomical improvement, visual gains were smaller than in eyes responding to first-line therapy, suggesting that early identification of poor responders is critical.

Emerging evidence supports the use of intravitreal corticosteroids in selected patients with inflammatory-predominant DME or inadequate anti-VEGF response [16]. Real-world datasets such as the present cohort can help identify clinical characteristics predictive of poor anti-VEGF response and inform personalized treatment strategies.

Multivariable analysis identified baseline BCVA, injection frequency, and anti-VEGF agent as independent predictors of visual outcome. Age, sex, and diabetes duration were not independently associated with visual gain, consistent with prior reports [2,17]. These findings reinforce the principle that modifiable treatment factors—particularly timely initiation and adequate treatment intensity—play a central role in determining outcomes.

The lack of association between diabetes duration and visual response may reflect the complex interplay between systemic control, retinal ischemia, and structural damage, variables not fully captured in routine EMR datasets. Integration of systemic biomarkers and retinal imaging metrics into future analyses may enhance predictive modeling.

From a clinical perspective, this study confirms that intravitreal anti-VEGF therapy delivers meaningful benefit for patients with DME in real-world NHS practice, even when treatment intensity is lower than in clinical trials. However, the gap between trial efficacy and real-world effectiveness remains substantial. Addressing this gap requires system-level interventions, including improved clinic capacity, streamlined care pathways, and enhanced patient engagement. From a health-service standpoint, these findings are particularly relevant given the rising prevalence of diabetes and the increasing demand for retinal services in the UK. Anti-VEGF therapy represents a significant cost burden for the NHS, and real-world effectiveness data are essential for informing commissioning decisions and long-term service planning [18].

The strengths of this study include its large sample size, multicenter NHS setting, and use of routinely collected EMR data, enhancing generalizability. The longitudinal design allowed assessment of both functional and anatomical outcomes over 12 months.

Limitations include the retrospective nature of the study, potential variability in OCT devices and visual acuity measurement, and incomplete capture of systemic factors such as glycemic control. Additionally, treatment regimens were not standardized, reflecting real-world practice but limiting causal inference. Despite these limitations, the findings provide an accurate representation of contemporary NHS outcomes. Prospective real-world registries linking ophthalmic and systemic health data would further enhance understanding of DME management.

CONCLUSIONS

This UK real-world cohort analysis demonstrates that intravitreal anti-VEGF therapy produces significant visual and anatomical improvements in patients with diabetic macular edema treated within the NHS. Although outcomes are inferior to those reported in randomized trials, they are consistent with other real-world studies and reflect the realities of routine clinical care. Optimizing treatment intensity, improving appointment adherence, and individualizing therapy based on baseline characteristics are essential to maximizing visual outcomes and ensuring sustainable delivery of DME care in the UK healthcare system.

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No external funding was received for this study. The work was conducted as part of routine NHS service evaluation and clinical audit activities. No pharmaceutical company or commercial entity had any role in the study design, data collection, analysis, interpretation, or manuscript preparation.

CONFLICT OF INTEREST

The authors declare that they have no competing financial or non-financial interests that could have influenced the conduct or reporting of this study. The authors have no financial relationships with manufacturers of anti-VEGF agents discussed in this manuscript.

CONSENT FOR PUBLICATION

Not applicable. This study contains no identifiable individual-level data, images, or personal information.

ETHICAL APPROVAL

This study was conducted as a retrospective service evaluation and clinical audit of routine care within participating UK National Health Service (NHS) hospital eye services. In accordance with UK Health Research Authority (HRA) guidance and NHS Research Ethics Committee (REC) regulations, formal ethical approval was not required, as the study involved the secondary use of anonymised data collected during standard clinical care and did not involve any deviation from usual treatment pathways.

All data were handled in compliance with the UK General Data Protection Regulation (GDPR) and the Data Protection Act 2018. Patient identifiers were removed prior to analysis, and no individual patient consent was required for the use of anonymised retrospective data.

AUTHOR CONTRIBUTIONS

- James R. Whitmore, MBBS, FRCOphth:
  Conceptualization; Methodology; Clinical supervision; Data curation; Investigation; Writing – original draft; Writing – review and editing; Project administration; Corresponding author responsibility.
- Sarah L. Thompson, PhD:
  Methodology; Formal analysis; Validation; Writing – review and editing; Visualization; Interpretation of results; Critical intellectual input.
- Daniel P. Harrington, MSc:
  Data curation; Software; Formal analysis; Visualization; Statistical modelling; Data management; Writing – review and editing.

All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work, ensuring accuracy and integrity in accordance with journal and institutional standards.

DATA AVAILABILITY STATEMENT

The datasets generated and/or analysed during the current study are not publicly available due to NHS data governance and patient confidentiality regulations but are available from the corresponding author on reasonable request, subject to institutional approvals and data-sharing agreements in accordance with NHS policies.

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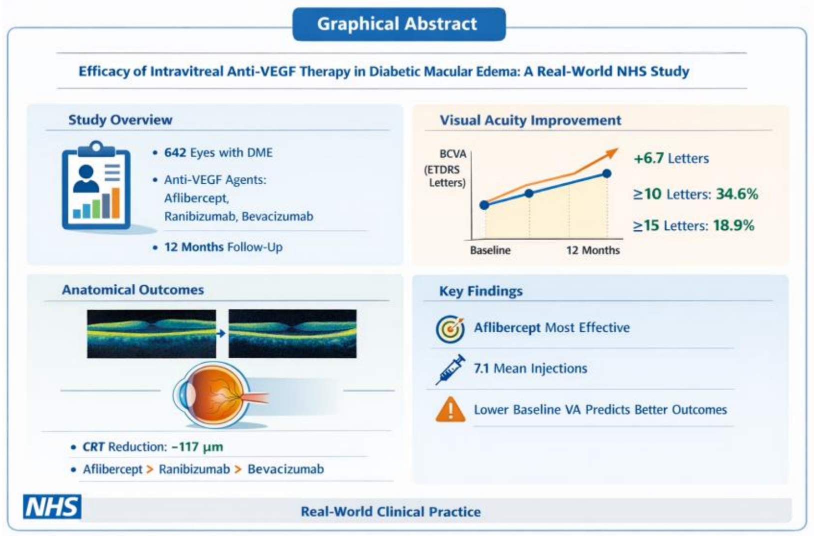

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