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ORIGINAL RESEARCH

Discordance Among Patients and Ophthalmologists Regarding the Burden of Intravitreal Injections

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Purpose: To determine how patients with neovascular age-related macular degeneration (nAMD) or diabetic macular edema (DME) perceive their disease and its treatment and to assess the degree of alignment between patient and clinician perceptions.

Patients and Methods: In June 2024 a survey of 101 patients (50 with DME and 51 with nAMD) and 100 ophthalmologists who treat these conditions completed surveys.

Results: Sixty-six percent and 86% of patients with DME and nAMD, respectively, reported receiving intravitreal injections at least once every 8 weeks. Eighty-two percent required a caregiver and/or public transportation to get to their appointments. The most significant symptoms for patients with DME were vision loss over time (2.89 out of 4.0) and blurred or double vision (2.76), and for those with nAMD were poor night vision (3.43), seeing in low-light conditions (3.27), and blurred vision (2.96). The proportion of patients who were dissatisfied with the education and counseling they received about their disease was greater for nAMD (31%) compared with DME (11%; $P < 0.01$). Ophthalmologists overestimated the extent to which patients perceived that injections were necessary (mean Likert scale score 3.41 vs 3.00; $P < 0.01$) and that patients experienced insurance barriers to receiving treatment (3.00 vs 2.46; $P < 0.01$). They overestimated the extent to which patients became less nervous with subsequent injections after the first (3.40 vs 2.94; $P < 0.01$) and underestimated their difficulty of getting to appointments (2.30 vs 2.64; $P < 0.01$).

Conclusion: This study highlights the significant burden experienced by patients undergoing intravitreal injections and identifies key areas of discordance between patient and clinician perceptions. Targeted education and counseling focused on these differences is indicated to improve patient satisfaction and outcomes.

Keywords: nAMD, DME, anti-VEGF, patient experience, retina

Introduction

From the patient perspective, the burden of anti-vascular endothelial growth factor (VEGF) treatment extends beyond the clinical setting. Patients often face logistical challenges due to the requirement of regular visits to specialized clinics, including transportation barriers, work absenteeism, and the need for a caregiver.[1–3] Intravitreal injections are associated with side effects and can require time off from daily activities and work to recover. In a survey, approximately 50% of patients with retinal vascular diseases reported experiencing side effects after more than half of their treatment visits.[2] In another study, nearly half of patients experienced impairment in activities of daily living after receiving an injection, and 60% reported missing work due to treatments.[1] Patients may also experience significant fear and anxiety related to the injection procedure.[3] Additional emotional and psychological factors include fear of vision loss, depression, and anxiety about long-term disease management.[2,3] Patients may require additional support from psychotherapy, support groups, and services for those with low vision.[4,5] Patients also frequently experience a financial strain associated with the direct and indirect costs of care.[2]

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Accordingly, patient-reported outcomes often reveal dissatisfaction with the frequency of injections and the cumulative toll of ongoing treatment for diabetic macular edema (DME) and neovascular age-related macular degeneration (nAMD).[6] These factors, combined with the physical discomfort and anxiety around the injection procedure itself, contribute to a multidimensional disease burden.[1] Furthermore, clinicians may underestimate the effects of these conditions on patient quality of life.[7,8] These barriers can lead to nonadherence and undertreatment, contributing to suboptimal patient outcomes that are observed in real-world studies compared with clinical trials.[2,9,10]

The primary goal of this study was to characterize the subjective experiences of patients undergoing treatment for DME and nAMD, which is critical to designing patient-centered care models that improve treatment adherence while maintaining therapeutic efficacy. Additionally, we sought to assess the degree of alignment between patient and clinician perceptions. To accomplish this, we developed three separate surveys: one tailored for patients with DME, one for patients with nAMD, and one for clinicians who injected anti-VEGF agents. A mixed methods design was used to capture insights into the burden of disease and treatment challenges as experienced by patients and perceived by clinicians.

Materials and Methods

Survey Design and Implementation

This study was conducted in accordance with the principles of the Declaration of Helsinki, and all participants provided informed consent. Ethical approval was not required for the present study because it was a quality improvement initiative, utilized survey data that was deidentified, no sensitive information was collected, the study was non-interventional, and participants acted voluntarily.

Two retrospective, web-based patient surveys were distributed to an existing network of patients with DME or nAMD who opted to participate in the study. The network consisted of patients previously enrolled to participate in upcoming clinical trials. The DME and nAMD surveys included 20 and 19 questions, respectively. They were tailored to each disease and consisted of items related to demographics, symptoms, current and past treatments (including medications and frequency), perceptions of care, logistical factors (such as transportation), treatment satisfaction, quality of life, and adherence. See Supplementary Table 1 for the complete list of survey questions. Potential participants received an invitation via Email to complete the online survey. The survey was administered between June 19, 2024, and July 29, 2024. Caregivers could complete the survey on the patient's behalf, if necessary. The survey was available only in English, was non-interventional, participation was voluntary, and only unidentifiable patient data was collected. Patients were included the analysis if they completed the full survey.

For clinicians, a retrospective 20-question survey that addressed demographics, practice patterns, perceptions, and knowledge was distributed to an existing database of ophthalmologists registered with Healio.com (Supplementary Table 1). Potential participants received an Email with an invitation to complete the web-based survey, which was available only in English. Participation was voluntary, and respondents were required to currently administering patient anti-VEGF injections at least weekly. Responses were collected between June 15, 2024, and June 30, 2024.

Data Analysis

Data were entered into Statistical Package for the Social Sciences (SPSS) version 27 (IBM, Chicago, IL, USA) and subject to data cleaning. Data were summarized with statistical parameters of median, mean, range, standard deviation (SD), and percentage of the total, where appropriate. Inferential statistics were used to compare data sets. Significance levels were set at $P < 0.05$. All calculations were reviewed for accuracy.

Results

Study Demographics

A total 101 patients (50 with DME and 51 with nAMD) responded to the survey (Table 1). The mean (SD) age of the DME and nAMD cohorts was 50.9 (10.1) years and 68.9 (7.9) years, respectively. Patients were predominantly White (50% DME, 61% nAMD), Black (22% DME, 24% nAMD) or Asian (14% DME, 6% nAMD). Sixty one-percent and

Table 1 Demographics and Treatment History of Patient Study Population

	DME (n = 50)	nAMD (n = 51)
Time since diagnosis		
<1 year	5 (10%)	7 (14%)
1-5 years	33 (66%)	27 (53%)
6-10 years	10 (20%)	9 (18%)
>10 years	2 (4%)	8 (16%)
Prior treatments		
Bevacizumab	15 (30%)	9 (18%)
Ranibizumab	10 (20%)	7 (14%)
Aflibercept 2 mg	17 (34%)	19 (37%)
Faricimab	4 (8%)	7 (14%)
Aflibercept 8 mg	3 (6%)	4 (8%)
Unsure	7 (14%)	10 (20%)
Other	5 (10%)	9 (18%)
Current treatment		
Bevacizumab	9 (18%)	4 (8%)
Ranibizumab	7 (14%)	4 (8%)
Aflibercept 2 mg	15 (30%)	14 (27%)
Faricimab	5 (10%)	8 (16%)
Aflibercept 8 mg	7 (14%)	3 (6%)
Unsure	5 (10%)	7 (14%)
Not currently being treated	5 (10%)	11 (22%)
Other	6 (12%)	4 (8%)
Age, years	50.9 ± 10.1	68.9 ± 7.9
Ethnicity		
Black	11 (22%)	12 (24%)
Asian	7 (14%)	3 (6%)
White	25 (50%)	31 (61%)
Latino	1 (2%)	1 (2%)
Other	6 (12%)	4 (8%)
Insurance		
Private	19 (38%)	7 (14%)
Public	20 (40%)	31 (61%)
None	11 (22%)	13 (25%)

Abbreviations: DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration.

40% of the patient cohorts with DME and nAMD, respectively, held public insurance (eg, Medicare, Medicaid). Most of the DME (66%) and nAMD (53%) cohorts had been diagnosed 1 to 5 years previously. Four percent and 16%, respectively, had been diagnosed more than 10 years ago. The most common prior treatments were aflibercept 2 mg (34% of patients with DME, 37% of patients with nAMD) and bevacizumab (30% DME, 18% nAMD). Although aflibercept 2 mg remained the most common current treatment (30% DME, 27% nAMD), there were patients who were receiving newer options, such as faricimab (10% DME, 16% nAMD) and aflibercept 8 mg (14% DME, 6% nAMD), compared with older treatments.

The clinician cohort consisted of 100 ophthalmologists who regularly inject patients with anti-VEGF agents (Table 2). Seventy-two percent had been in practice for 1 to 20 years. Most participants worked in multispecialty ophthalmology practices (51%) or retina specialty clinics (41%). On average, clinicians reported seeing a mean (SD) 165.1 (94.0)

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Table 2 Demographics of Study Ophthalmologists Population

	Clinicians (N = 100)
Time in practice	
1-9 years	30 (30%)
10-20 years	42 (42%)
21-30 years	18 (18%)
>30 years	10 (10%)
Practice setting	
Hospital	5 (5%)
Multispecialty ophthalmology	51 (51%)
Retina specialty practice	41 (41%)
Other	3 (3%)
Patients with DME or nAMD seen per week	165.1 ± 94.0 (Range: 25–600)
Anti-VEGF injections administered per week	74.1 ± 50.7 (Range: 4–200)

Abbreviations: DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration; VEGF, vascular epidermal growth factor.

patients with DME or nAMD per week. Additionally, they administered a mean 74.1 (50.7) anti-VEGF injections per week, with a range of 4 to 200 injections per week.

Patient Survey Results

Burden of Disease and Treatment

Figure 1 illustrates survey items addressing the logistical burden of anti-VEGF treatment in terms of both injection frequency and recovery time. Eighty-three percent and 86% of patients with DME and nAMD, respectively, reported receiving injections at least once every 8 weeks. Across both cohorts, 82% noted that they relied on a caregiver and/or public transportation to get to their appointments. Thirty percent of patients with DME and 47% of patients with nAMD reported taking 1 or more days to recover from the injections.

Figure 2 illustrates the symptomatic burden of DME and nAMD rated by patients on a 4-point Likert scale, with a higher number indicating greater perceived burden (a score of 3 indicating *burden* and 4 indicating *major burden*). The mean Likert scores for patients with DME were highest for vision loss over time (2.89) and blurred or double vision (2.76), followed by poor night vision (2.67). The least burdensome symptoms in the DME cohort were distorted objects (2.46), dark spots (2.39), and straight lines appearing curved or distorted (2.28); however, variability was high. Similarly,

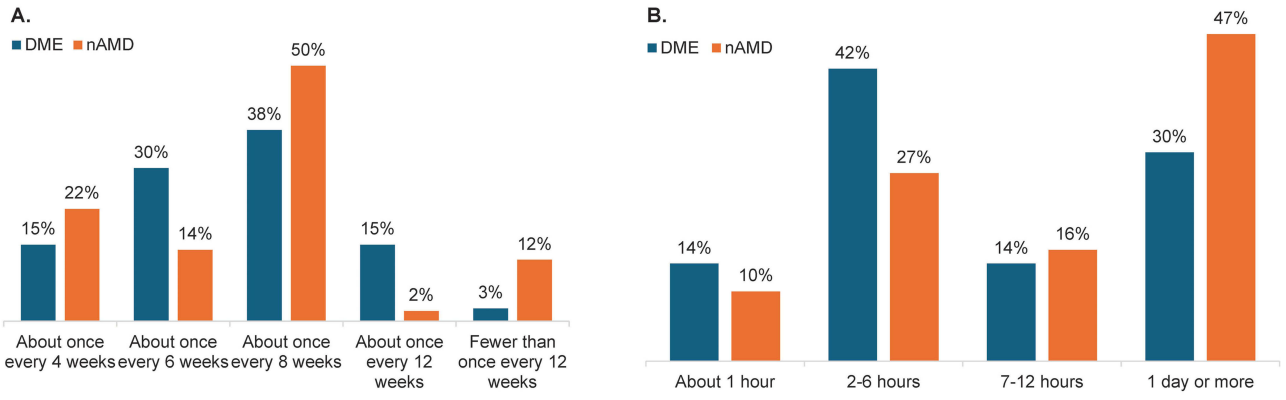

Figure 1 Patient frequency of anti-VEGF injections and time to recover from injections.
Note: Injection frequency (**A**) and recovery time (**B**) of patients receiving anti-VEGF treatments for DME (left blue bars, N=50) or nAMD (right orange bars, N=51).

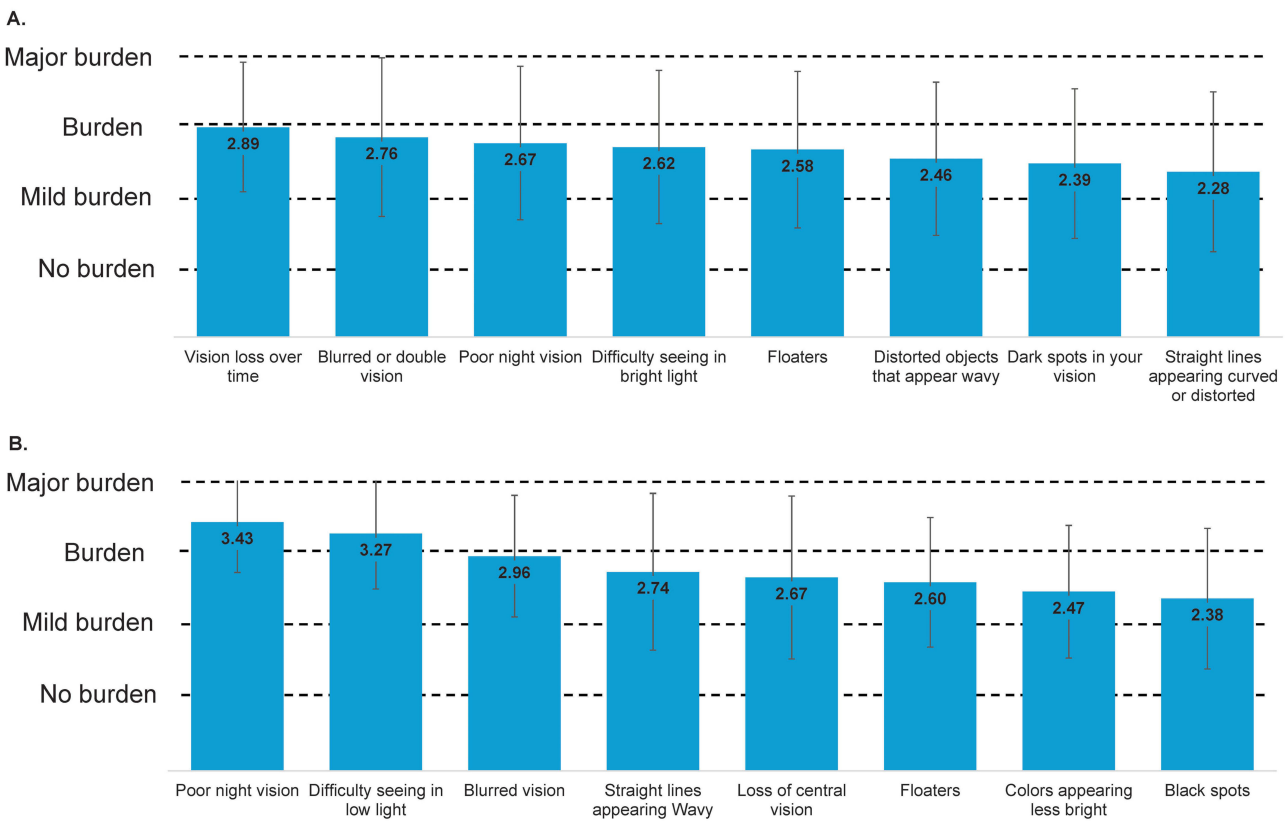

Figure 2 Patient-reported burden of symptoms.
Notes: Burden of symptoms for patients with DME (**A**, N=50) or nAMD (**B**, N=51). Errors bars reflect standard deviation. (4-major burden, 3-burden, 2-mild burden, 1-no burden).

among patients with nAMD, poor night vision (3.43), difficulty seeing in low light (3.27), and blurred vision (2.96) were reported as the most burdensome symptoms. Black spots (2.38) and color perception changes (2.47) were perceived as less impactful, although still rated as a *burden* or *major burden* in at least 40% of patients. While the overall burden across symptoms was slightly greater in the cohort of patients with nAMD compared with DME (mean score across all symptom survey items 2.81 vs 2.58), this finding was not statistically significant ($P = 0.16$).

Patient Perception of Care

Overall, 74% of patients either agreed or strongly agreed that they were satisfied with their current treatment plan. Patient satisfaction with different aspects of their care is shown in Figure 3. Among patients with nAMD, 28% and 27% reported not receiving education about their condition and treatment, respectively, compared with 8% and 10% of patients with DME. When education was provided about DME, approximately 3 times as many patients were satisfied versus unsatisfied with care. Regarding DME treatment, approximately 4 times as many patients were satisfied versus unsatisfied with the education provided. For patients with nAMD, about 3 times as many were satisfied versus unsatisfied with the education provided regarding nAMD and its treatment.

Regarding counseling on disease management, 41% of patients with nAMD and 18% of patients with DME stated they did not receive counseling from the care team. Satisfaction with counseling received was significantly higher for those with DME versus nAMD (60% vs 31%; $P < 0.01$). Similarly, 50% fewer patients with nAMD were very satisfied that their preferences were considered in management decisions versus those patients with DME (40% vs 20%; $P < 0.05$).

Patient and Clinician Perception of Treatment and Burden

Figure 4 summarizes patient and clinician perceptions of the burden of anti-VEGF injections. Patients were asked to what extent they agreed with each statement, whereas clinicians were asked to what extent they believed their patients agreed

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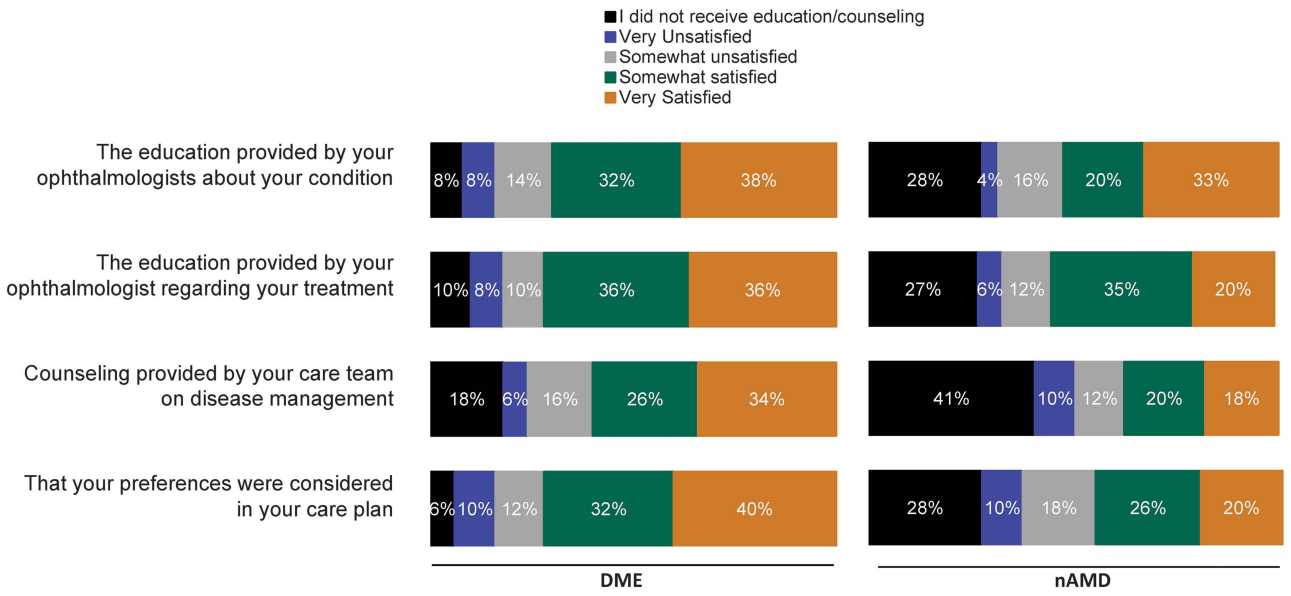

Figure 3 Patient-reported satisfaction with care.
Note: Patient satisfaction with aspects of their care for DME (left, N=50) or nAMD (right, N=51).

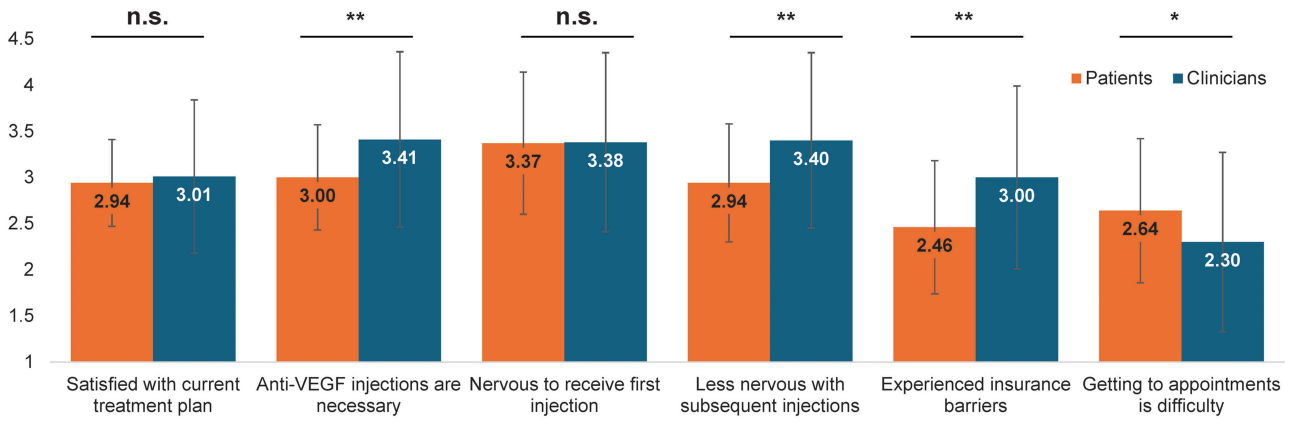

Figure 4 Patient versus clinician perception of care.
Notes: Patient (left, N=101) and clinician (right, N=100) perceptions regarding use of anti-VEGF treatments measured on a Likert scale. (4 agree strongly, 3 agree, 2 disagree, 1 disagree strongly) n.s. = nonsignificant; * = $P < 0.01$; ** = $P < 0.001$. Errors bars reflect standard deviation.

with each. A score of 3 indicated *agree* and a score of 4 indicated *strongly agree*. The patient and clinician cohorts had similar perceptions of the overall satisfaction with the current treatment plan (3.01 for clinicians vs 2.94 for patients; $P < 0.001$). However, clinicians overestimated the extent to which their patients agreed that anti-VEGF injections were necessary (3.41 vs 3.00; $P < 0.001$). Overall, 95% of ophthalmologists agreed or strongly agreed that anti-VEGF injections were necessary to prevent vision decline compared with 63% of patients.

Patients and clinicians had similar perceptions of nervousness about the first injection (3.37 for patients vs 3.38 for clinicians; $P = 0.73$). However, clinicians overestimated the extent to which patients became less nervous over time with subsequent injections (3.40 vs 2.94; $P < 0.001$). Disparities were also observed in perceptions of treatment burden. Clinicians overestimated the extent to which patients experienced insurance barriers (3.00 vs 2.46; $P < 0.001$). In addition, 62% of physicians indicated that insurance difficulties were their greatest barrier when treating with anti-VEGF

agents (Supplementary Figure 1). Finally, clinicians underestimated the difficulties experienced by patients in getting to appointments (2.30 vs 2.64, $P < 0.01$).

Discussion

The findings of this survey study highlight how patients experience the burdens associated with nAMD and DME as well as key discrepancies between patient and clinician perceptions. The frequency of anti-VEGF injections needed to maintain efficacy of treatment can disrupt activities of daily living and create logistical challenges for patients.

Our study characterized several potential barriers to optimal care from the patient perspective. Sixty-six percent and 86% of patients with DME and nAMD, respectively, received injections at least every 8 weeks, with more than 80% relying on a caregiver or public transportation to travel to their appointments. This can create disparities in access to care, as some patients may lack transportation options or available caregivers. In addition, one-third to one-half of patients reported taking 1 or more days to recover from injections. Patients may miss work to attend and recover from injection appointments, adding further logistical and financial burdens.[1]

These findings are potentially relevant to improving patient outcomes in the real world, which often fall short of those achieved in clinical trials.[10–15] In observational studies, patients typically receive fewer injections compared with clinical trial regimens. For example, in a retrospective study, patients with DME received a median of 4 injections in the first year after diagnosis, and 60% did not receive any treatment.[14] Another study of patients with DME found that the mean number of injections decreased from years 1 to 6 of treatment.[10] Eyes that received a greater number of injections experienced the largest visual acuity gains.[10] A similar pattern is seen in real-world studies for nAMD. In a retrospective study, patients with nAMD received a mean of 7.3 injections in the first year of treatment.[11] Another study showed that patients with nAMD who received a greater number of injections experienced greater visual acuity gains.[13] Overall, these studies indicate a pattern of undertreatment in DME and nAMD. This may be due to either nonadherence (failure to adhere to the planned treatment regimen) or nonpersistence (treatment discontinuation or loss to follow up).[11,16] In a systematic review, reported rates of nonadherence and nonpersistence in nAMD were up to 60% at 24 months.[17] Associated patient factors included worse presenting visual acuity, greater travel distance for treatment, medical comorbidities, and lack of transportation.[17] A meta-analysis of patients receiving anti-VEGF treatments found a pooled nonpersistence rate of 28% at 12 months.[18] The barriers identified in our survey are possible contributors to treatment nonadherence, nonpersistence, and suboptimal patient outcomes.[2,9]

Our findings are similar to other studies that identified logistical factors as key to patient adherence to anti-VEGF therapy. In a survey of patients with nAMD and DME, clinic-related issues, such as the lack of a caregiver to accompany them to appointments, were among the most frequently identified.[1] Similar to our findings, nearly half of patients in that study had impairment in activities of daily living due to treatment, and almost two-thirds reported missing work.[1] Other survey studies have found similar rates of inability to participate in daily activities due to discomfort from treatment.[6,19] Qualitative studies have also identified the transportation burden placed on family members and caregivers as an important patient concern.[20] Therefore, it is not surprising that patients generally prefer treatment regimens that require fewer clinic visits.[19]

Our study identified a variety of symptoms due to nAMD or DME that created either a burden or major burden for patients. The most significant symptoms of patients with DME were vision loss over time and blurred or double vision. Patients with nAMD identified poor night vision, difficulty seeing in low-light conditions, and blurred vision as having the greatest impact. While our study did not directly address additional symptoms related to treatment, patients also commonly report discomfort secondary to administration of povidone-iodine prior to the anti-VEGF injection, the injection itself, and after the anesthetic wears off.[6] In addition to their physical effects, these symptoms create an emotional and psychosocial burden for patients.[20,21] Patients may experience anxiety and fear related to the possibility of vision loss from the disease as well as to the injections and their associated discomfort.[6,20] Treating ophthalmologists must find a balance minimizing the burdens for patients and maximizing treatment efficacy.[12]

While overall satisfaction with treatment was fairly high in our study, with 74% of patients either agreeing or strongly agreeing that they were satisfied with their care, nonetheless several important areas of dissatisfaction were identified. More than one-quarter of patients with nAMD and DME reported not receiving education about their condition and

treatment. Dissatisfaction with education and counseling was greater for patients with nAMD compared with those with DME. Notably, 41% of patients with nAMD reported not receiving counseling about their disease management from their care team. The reasons for the observed differences between nAMD and DME are unknown, but differences in patient age, education, or sociodemographic factors could be possible contributing factors. These findings highlight areas for potential targeted interventions by clinicians to increase treatment adherence and satisfaction with care.

Finally, our study identified important differences between how patients and clinicians perceived their disease burden and treatment. Involvement of the patient in a shared decision-making process has been shown to improve patient satisfaction and adherence to treatment of chronic conditions that require long-term therapy.[22] This process requires that clinicians understand the patient experience and communicate clearly and effectively. Importantly, clinicians overestimated the extent to which patients agreed that anti-VEGF injections were necessary. This highlights a potential area for patient counseling and education that could have implications for treatment adherence. The treatment burden was also perceived differently. Clinicians also overestimated the degree to which patient nervousness secondary to injections abated over time and underestimated the influence of transportation and logistical difficulties associated with getting to appointments. Although ophthalmologists perceived insurance difficulties as the greatest barrier when implementing anti-VEGF treatments, patients found their experience of insurance barriers to be less important. The identified discrepancies between patient and clinician perceptions indicate areas where communication and education might be improved to better facilitate an individualized and effective treatment approach.

This study's primary strength is that it highlights both the patient point of view and differences in perceptions between patients and clinicians. This information can be valuable for guiding patient education and care as well as future studies. However, this study does have several limitations. Survey studies are inherently influenced by recall errors and subjectivity of responses. They are also limited to participants who choose to respond; therefore, selection bias may be a factor. Furthermore, our patient cohort consisted of those who expressed interest in clinical trials, and our clinician respondents were primarily ophthalmologists working in multispecialty practices or retina subspecialty groups. Thus, these results may not be generalizable to other patient or clinician populations. Finally, while we identified correlation between various factors in our survey, causality is not established, and other confounding factors can be involved in the observed relationships.

Conclusion

The findings of this survey study call attention to key barriers to effective treatment for patients as well as critical areas where patient and clinician perception of disease and treatment burdens are misaligned. Overall, these results underscore the large burden that patients face in undergoing treatment for nAMD and DME. In the future, therapy that provides greater durability, fewer injections, and fewer clinic visits can help reduce the burden for patients, improve adherence, and facilitate better overall patient outcomes. Furthermore, optimal treatment will require greater understanding and communication between patients and clinicians.

Data Sharing Statement

Relevant data are included in the manuscript. A complete dataset can be provided upon request from the corresponding author.

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Disclosure

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