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Patient Preferences in the Treatment of Neovascular Age-Related Macular Degeneration

A Discrete Choice Experiment

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Purpose: The objective of our study was to investigate preferences of patients with neovascular age-related macular degeneration (nAMD) for different anti-vascular endothelial growth factor (VEGF) treatment schemes.

Design: We used a discrete choice experiment (DCE) design as part of a telephone interview.

Participants: Patients with nAMD aged at least 50 years were included in the study.

Methods: Telephone interviews were done between November 2012 and October 2013.

Main Outcome Measures: In our DCE survey, we measured patient preferences toward specific levels of attributes that describe different options in the everyday intravitreal injection treatment setting: (1) treatment scheme; (2) change of visual acuity (VA); and (3) time the patient needs for each visit to the eye specialist.

Results: A total of 284 patients with nAMD with a mean age of 77.4±7.1 years (women: 59.9%) completed the DCE interviews. Of them, 22.9% had poor VA at study inclusion, 54.9% had moderate VA, and 14.1% had good VA; VA was not available for 8.1% of the patients. Generally, patients preferred the attribute levels "improvement in VA" and "short time per specialist visit." The results for the attribute "treatment scheme" were inconclusive because none of the attribute levels (injections every 4 weeks, every 8 weeks, and pro re nata) were associated with statistically significant utility differences. This also mirrors the relative importance of the different attributes in patient decisions: "Change of VA" influenced decision making for a treatment option in 73.6% of cases; "waiting, treatment, and travel time" influenced decision making in 21.0% of cases; and "treatment scheme" influenced decision making for a treatment option in 5.4% of cases. To obtain improved VA instead of a worsening VA, patients in our study stated to be willing to accept a very long time needed per physician visit of 21.2 hours (8.5 hours for improved rather than stable VA and 12.7 hours for stable VA rather than worsening VA).

Conclusions: To prevent deterioration of VA, patients with nAMD seem to be willing to accept a high treatment burden with regular intravitreal injections at short intervals and long periods of waiting, treatment, and traveling for their consultations. *Ophthalmology 2016;■:1–9 © 2016 by the American Academy of Ophthalmology.*

*Supplemental material is available at www.aaojournal.org.

Age-related macular degeneration is a major cause of visual impairment in the developed world.[1] The efficacy and safety of anti-vascular endothelial growth factor (VEGF) therapy in neovascular age-related macular degeneration (nAMD) have been demonstrated in clinical studies.[2] In these studies, bevacizumab, ranibizumab, or aflibercept was injected monthly (Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular AMD, Anti-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in AMD) or every 2 months (VEGF Trap-Eye: Investigation of Efficacy and Safety in Wet AMD 1 and 2), or injections were given on the basis of a pro re nata (PRN) regimen (e.g., Comparison of Age-related Macular Degeneration Treatments Trials, Inhibition of VEGF in Age-related choroidal Neovascularization). Existing studies show that especially the PRN scheme should be accompanied by monthly follow-ups and injections for recurrent or persistent activity given as necessary,[3,4] because the efficacy of a PRN regimen depends on rigorous monthly follow-up.

At present, most evidence from observational studies in routine clinical practice is available for ranibizumab, one of

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the first anti-VEGF drugs approved for the treatment of nAMD that has been available for approximately 10 years. However, recent evidence shows that anti-VEGF treatment is not as effective in the everyday clinical setting as in clinical trials.[5,6] Observational studies have shown that many patients with nAMD do not attend the recommended monthly eye examinations.[4,5,7,8] Also, fewer injections are given in the everyday clinical setting than in clinical studies.[7] It can be assumed that treatment-related causes, such as logistics in terms of monthly follow-ups and regular injections, and healthcare system-related causes, such as reimbursement for injections and co-payments, are underlying factors in this. Long-term courses of injections and regular follow-ups are not easy to adhere to, especially for the elderly,[9] and therefore patient-related causes, such as nonadherence, may also contribute to the lower effectiveness of intravitreal injection therapy in the everyday clinical setting.

Generally, every treatment should be tailored to the needs of the patient and the disease. Treatments that are effective in clinical trials but have low patient acceptance are likely to be less effective in everyday clinical practice because of inadequate patient adherence.[10,11] Therefore, it is important to collect reliable and valid data on patient preferences when providing therapies, especially for the long-term treatment of chronic diseases such as nAMD.

Little research has been done on the preferences of patients with nAMD with regard to intravitreal injection therapy. One specific unknown factor is the importance patients attach to the change of visual acuity (VA) under anti-VEGF treatment and how they view a higher treatment burden with a higher frequency of injections and monitoring visits to achieve better VA.

Research on the preferences of patients has produced inconclusive results. Patients with nAMD think that the treatment burden is high, but also seem to be willing to accept this to maintain or even improve their VA.[9] Trade-offs between a higher treatment burden and greater effectiveness have not been addressed in previous research. A suitable approach to investigate this are state-of-the-art preference analysis techniques recommended in health-economics guidelines.[12] In accordance with those, we used a discrete choice experiment (DCE) design to assess preferences of patients undergoing intravitreal injections for nAMD.

The DCEs were originally developed for use in the field of economics. They describe and predict choices between 2 or more discrete alternatives, such as choosing between different products (e.g., between different drugs). Specifically, discrete choice analysis examines which alternative product—given existing attributes of the alternatives available—is chosen by a customer, for example, which drug a person would choose given that available drugs differ in route of administration, mode/frequency of administration, side effects, and out-of-pocket costs.[13]

Since the 1990s, DCEs have been increasingly used in healthcare research to address a wide range of health policy issues related to preferences of different stakeholders.[14–16] The main reason for this is that many healthcare decisions or choices that have to be made by stakeholders, specifically patients, show many similarities with choice behavior in consumer markets. In the healthcare sector and consumer markets, more than 1 alternative is usually available, and the alternatives mainly can be described by well-defined attributes. In this study, we used DCE techniques to explore the preferences of patients with nAMD to evaluate the importance of health, nonhealth, and process attributes of a specific healthcare service (intravitreal injections), as well as the relative importance of these different attributes and the trade-offs patients are prepared to make between them.[17] Specifically, we assessed the preferences of patients with nAMD who are faced with the burden of therapy of intravitreal injection therapy and elicited outcomes using a DCE design.

Methods

Study Sample

We conducted this multicenter study in Germany among randomly selected ophthalmologists in office practice and hospital eye clinics offering intravitreal injection therapy. The patients were enrolled consecutively following predefined inclusion and exclusion criteria, and informed consent was obtained. Patients were eligible if they (1) had nAMD; (2) had already received at least 1 intravitreal injection before study inclusion regardless of the drug; (3) were at least 50 years old; (4) would be able to conduct 30-minute telephone interviews in German; and (5) had not participated in another clinical or observational study in the 3 months before inclusion in our study. According to the DCE literature available, we assumed that 250 study participants would be needed for our study.[12] The study was approved by the ethics committees of the Universities of Greifswald, Rostock, and Freiburg (all in Germany). The described research adhered to the tenets of the Declaration of Helsinki.

Data Collection

Basic sociodemographic and clinical characteristics of patients were documented on inclusion in a case report form. Patients were expected to remain in the study for a minimum follow-up observational period of 12 months. The number of injections given and the number of follow-up visits during this period were also documented in the case report form. Preference interviews were conducted by trained interviewers at the end of the observational period in the form of computer-assisted telephone interviews; in preparation of this interview, the choice sets and guidance for the planned experiment were sent to the patients by mail a few days before. In addition to DCE-related questions, patients were asked about their personal living situation and other social circumstances (Supplemental Figure S1, available online at www.aaojournal.org).

Discrete Choice Experiment

We conducted a DCE as part of the phone interview to assess patient preferences. The main reason for using DCE is that simply asking patients to rate treatment-related attributes or choose their preferred item from a scale will generally yield no more information than the fact that patients want all the benefits and none of the indirect or direct costs.[12] Choosing between alternatives forces the patient to make a trade-off between 2 or more options, and choose, as in real life, between treatment options that may increase utility (e.g., improved VA) and decrease utility (e.g., eye examinations every 4 weeks instead of less frequently).