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Patient versus neurologist preferences: A discrete choice experiment for antiepileptic drug therapies

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ABSTRACT

Objective: This assessment was conducted to quantify and compare patient and neurologist preferences regarding antiepileptic drug (AED) attributes for treating epilepsy.

Methods: Patients with epilepsy (≥ 18 years, treated with AEDs) and neurologists were recruited from nationally representative US panels to complete an online survey that included a discrete choice experiment (DCE). Participants chose between two hypothetical AEDs, characterized by six attributes in the DCE, which included 1) level of seizure control/reduction; 2) dosing frequency, 3) diminished coordination and balance, 4) psychiatric issues, 5) diminished energy level, and 6) dietary restrictions. The Sawtooth Software Choice-Based Conjoint (CBC) System for CBC Analysis was used to estimate treatment attribute ranking and weighting.

Results: Of the 720 respondents (518 patients and 202 neurologists), both patients and neurologists ranked seizure control as the most important attribute (rank 1) and dietary restrictions as the least important attribute (rank 6). However, seizure control had a significantly greater weighting in neurologists' decision-making than among patients (45% vs 32%, $p < 0.005$). On the other hand, patients considered the risks of psychiatric adverse effects (19% vs 15%), diminished coordination and balance (16% vs 10%), and fatigue or diminished energy (13% vs 11%) as significantly more important ($p < 0.05$) than did neurologists.

Conclusion: Patients and neurologists had similar preference ranking order, with seizure reduction being ranked the most important attribute. However, neurologist treatment preferences were significantly more influenced by seizure reduction while patient preferences were significantly more influenced by adverse effects that may impact their quality of life. Understanding how patient and neurologist perspectives differ should encourage dialog to communicate the potential risks and benefits of AED therapy and assist in the shared decision-making process.

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1. Introduction

Epilepsy is a chronic neurological condition impacting 3.4 million people in the United States characterized by recurring seizures [1,2]. Patients with epilepsy may require long-term, continuous antiepileptic drug (AED) therapy to achieve adequate and sustained seizure reduction. Despite the availability of many efficacious AED treatment options, one-third of patients with epilepsy remain inadequately controlled [3,4]. Research suggests that patients with epilepsy who are nonadherent to treatment are twice as likely to have inadequate seizure control and significantly poorer health-related quality of life (HRQoL) compared

with patients who are adherent [5,6]. Research suggests that patient adherence to medication is often influenced by the magnitude of treatment effect and other treatment-related factors such as side effects (motor coordination, cognition, and functioning), dosing (treatment complexity and frequency, titration, and convenience), and costs [6–8]. Additionally, patient-related factors such as beliefs about their AED and concerns about side effects may adversely impact treatment adherence [9,10].

While neurologists may presume their own selection of an AED in clinical decision-making reflects patients' treatment preferences and concerns, little is known about the concordance between patient and neurologist preference or nonpreference for specific drug attributes during treatment selection. While evidence suggests that patients and neurologists may both prioritize seizure reduction, patients may have more severe concerns regarding adverse effects and treatment impacts on lifestyle or social factors [11]. Thus, the perceived relative value of potential treatment efficacy and other treatment attributes (such as risks for adverse effects, lifestyle and relationship impacts, convenience

Abbreviations: AED, antiepileptic drug; CBC, choice-based conjoint; DCE, discrete choice experiment; EQ-5D-5L, EuroQol 5 Dimensions 5 Levels questionnaire; HRQoL, health-related quality of life; IES, impact of epilepsy scale.

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factors, and costs) among both patients and neurologists should be mutually understood in order to select a treatment option that may promote patient adherence [12–14].

Additionally, identification of concordance or discordance between patients and neurologists would be helpful in developing AEDs with attributes that are meaningful and have the highest potential to deliver desired outcomes to both groups. However, few studies have assessed AED treatment attribute preferences individually among patients and neurologists, let alone have conducted simultaneous assessments across these groups to assess concordance and/or discordance in relative treatment attribute preferences between neurologists and patients [11]. While studies ranking treatment attributes may provide insight into the importance of individual attributes, they may also provide inaccurate estimates of relative importance due to the inherent assumption that (i) all attributes are weighted as equally important, not requiring trade-offs between their relative weighting, and (ii) the intervals or distances between ranks are equal [15,16]. A more precise approach is to use discrete choice methods that assess trade-offs between attributes. This enables detection of subtle differences in preferences as reflected in weight allocated to each attribute [17,18]. One discrete choice study of patient AED preferences in the United Kingdom revealed that patients highly favored seizure reduction with no adverse effects, but were willing to forego some control in favor of reducing adverse effects [19].

A recently published meta-analysis of treatment attribute preference studies for a range of indications found high levels of discordance between patient and health care provider preferences [20]. Published evidence suggests that shared decision-making between physicians and patients often results in higher levels of patient satisfaction, treatment adherence, quality of life, and well-being for patients with chronic diseases or receiving long-term treatment [21]. However, the data on shared decision-making in epilepsy are limited, with one large-scale Australian survey suggesting that nearly one-third of patients felt that their treatment plan did not reflect their views and preferences, suggesting an important treatment gap [22,23].

Given the growing number of potential AED options, each with a varying set of attributes, clarity on the relative valuation of treatment attributes that are important to neurologists as well as patients is vital to increase the preference concordance and facilitate shared decision-making between them [19,24–28].

This study was intended to identify the goals of AED treatment, and the relative importance of each goal, from the perspective of both patients and neurologists, to facilitate discussion and shared decision-making. The present assessment was designed to first determine the relative importance of AED attributes to treatment preference among both patients and neurologists, and then determine the level of concordance and discordance between the two groups of participants.

2. Methods

This cross-sectional web-based survey assessed AED preferences among patients and neurologists. The first step of discrete choice methodology was to determine key treatment attributes, followed by implementation of the discrete choice experiment (DCE).

2.1. Treatment attributes

Candidate attributes and attribute levels were identified through a literature search. Key differentiators such as efficacy, tolerability, and safety profiles of highly prescribed AEDs were reviewed [5,19,29–31]. Identified relevant AED attributes were then rank-ordered and prioritized from high to low preference for both patients and neurologists through pilot testing and consultation with four neurologist key opinion leaders (KOLs) with experience researching and/or treating epilepsy. A qualitative assessment of the expected relative impacts of the candidate attributes on AED treatment decision-making yielded the following six

attributes to be included in this study: (1) seizure control; (2) dosing frequency; adverse effects related to increased risk of (3) diminished coordination and balance, (4) psychiatric issues, and (5) diminished energy level; and (6) AED-associated dietary restrictions.

2.2. Implementation of the DCE

2.2.1. Respondent selection

Participants in this study were provided through the Harris Poll (Harris Insights & Analytics, Rochester, NY), including members of its third-party panel providers. Panel members have previously agreed to participate in surveys on the basis of their pre-registered status as either diagnosed with epilepsy or as neurologists. Invitations describing the rationale, objective, and methods of this study were distributed; members who agreed were eligible if they satisfied the following criteria:

- Patient: ≥ 18 years old, diagnosed with epilepsy by a physician (patient reported), currently undergoing treatment for epilepsy in the US by a physician, and currently residing in the US
- Neurologist: board certified in neurology, actively treating patients with AEDs, currently practicing in the US

Sample sizes of 500 patients and 200 neurologists were considered adequate to draw statistically robust comparisons with similar numbers of attributes and levels [32–35].

The study protocol was exempted from institutional review board approval by the New England Independent Review Board (NEIRB# 15–203) per the rationale that the study involved the use of survey or interview procedures or observation of public behavior from which subjects could not be identified, or that release of the information would not be harmful to the subjects.

2.2.2. Survey design

The survey collected information on patient/neurologist characteristics to provide a description of the population and responses to a choice-based conjoint (CBC) task. Patients were asked to report their demographic characteristics (gender, age, and insurance status), clinical characteristics (treating physician, seizure types, and seizure control), generic quality of life measured by EuroQol 5-dimension and 5-level questionnaire (EQ-5D-5L life), and epilepsy-specific quality of life measured by the Revised Liverpool Impact of Epilepsy Scale (IES). Level of seizure control was measured from patient self-reported assessment on a 4-point scale. Neurologists reported demographics including gender, age, years post-residency, physician type, and practice type.

Respondents completed the CBC tasks from the perspectives of which AED they would rather receive (patients) or prescribe (neurologists). Respondents were presented with 2 hypothetical AEDs, each characterized by various levels of the 6 attributes (4 levels for seizure control; 2 levels for AED-associated dietary restrictions; and 5 levels each for dosing frequency, and adverse effects related to increased risk of diminished coordination and balance, psychiatric issues, and diminished energy level (Table 1/ Fig. 1). This produced 5000 ($4 \times 2 \times 5^4$) possible treatment profiles. The ranges of the various levels for each attribute were chosen to make the tasks cognitively simple for the respondents while eliciting sufficient variability in responses to detect meaningful differences. A Bayesian-optimized orthogonal design was used to generate a statistically efficient pool of candidate AED profiles that was powered per the previously stated sample sizes to elicit accurate preference values. This approach is considered a best practice in discrete choice and conjoint analysis because it minimizes the number of choice profiles that are needed to derive outcomes [36].

2.2.3. Statistical analysis of the DCE

Sociodemographic and patient-reported outcomes were evaluated by descriptive analysis.

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