Received: 23 July 2021 | Revised: 12 November 2021 | Accepted: 12 November 2021

DOI: 10.1111/epi.17137

Epilepsia®

RESEARCH ARTICLE

Relative importance of clinical outcomes and safety risks of antiseizure medication monotherapy for patients and physicians: Discrete choice experiment eliciting preferences in real-world study "VOTE"

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Abstract

Objective: This study was undertaken to elicit patients' preferences for attributes characterizing antiseizure medication (ASM) monotherapy options before treatment consultation, and to explore the trade-offs patients consider between treatment efficacy and risks of side effects. Further objectives were to explore how treatment consultation may affect patient preferences, to elicit physicians' preferences in selecting treatment, and to compare patient and physician preferences for treatment.

Methods: This prospective, observational study (EP0076; VOTE) included adults with focal seizures requiring a change in their ASM monotherapy. Patients completed a discrete choice experiment (DCE) survey before and after treatment consultation. Physicians completed a similar survey after the consultation. The DCE comprised 12 choices between two hypothetical treatments defined by seven attributes. The conditional relative importance of each attribute was calculated.

Results: Three hundred ten patients (mean [SD] age = 46.8 [18.3] years, 52.3% female) were enrolled from eight European countries, of whom 305 completed the survey before consultation and 273 completed the survey before and after consultation. Overall, this preference study in patients who intended to receive a new ASM monotherapy suggests that patient preferences were ordered as expected, with better outcomes being preferred to worse outcomes; patients preferred a higher chance of seizure freedom, lower risk of developing clinical depression, and fewer severe adverse events; avoiding moderate-to-severe "trouble thinking clearly" was more important than avoiding any other side effect. There were qualitative differences in what patients and physicians considered to be the most important aspects of treatment for patients; compared with patients, physicians had a qualitatively stronger preference for greater chance of seizure freedom and

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avoiding personality changes. Patients' preference weights were qualitatively similar before and after treatment consultation.

Significance: For patients, seizure freedom and avoiding trouble thinking clearly were the most important treatment attributes. Physicians and patients may differ in the emphasis they place on specific attributes.

KEYWORDS
antiepileptic drug, efficacy, patient preferences, shared decision-making, tolerability

1 | INTRODUCTION

It is estimated that almost 70 million people are living with epilepsy worldwide,[1] the majority of whom require treatment with antiseizure medications (ASMs).[2] Although adverse events (AEs) associated with ASMs affect many patients with epilepsy, few studies have evaluated patients' preferences regarding the clinical outcomes and safety risks associated with ASMs.[3–8]

The importance of understanding patient needs and preferences is increasingly recognized.[9–12] There has been a shift toward patient-centered health care, shared decision-making, and involvement of the patient perspective in regulatory decision-making.[13] To provide a more patient-centered treatment framework, it is important to recognize and encourage the integration of medical, behavioral, and social needs for treatment, which can improve patient outcomes, such as quality of life. Explicit consideration of patient preferences could lead to different conclusions relating to the benefit–risk profiles of medicines.[5] By identifying which treatment attributes most influence patient treatment choices and by exploring patient preferences among these attributes, strategies can be developed for groups of patients with similar needs and attitudes, to optimize treatment adherence, effectiveness, and resources, and ultimately provide a more effective approach to care. This could become particularly important in cases in which patients and physicians have different preferences for treatment attributes,[5] because physicians often influence the selection of treatments that patients use.

Preference information can be elicited using qualitative and quantitative methods.[10] Qualitative preference information may be useful in identifying which therapy characteristics are valued most, whereas quantitative preference information can provide estimates of the degree to which different therapy characteristics are valued. Discrete choice experiments (DCEs) are a quantitative method for eliciting preferences, which are increasingly used in health care.[14] In a DCE, patients complete a survey in which they are asked to choose between pairs of hypothetical treatments defined by a set of treatment attributes. Treatment attributes may include efficacy, safety, tolerability, and mode of administration, among others. The attractiveness of each treatment to patients depends on their relative preferences for these attributes. In this regard, DCE surveys are designed specifically to provide information about patients' willingness to accept trade-offs among treatment attributes characterizing different hypothetical treatment profiles.

We conducted a DCE survey as part of a prospective observational study in Europe (EP0076; VOTE) in adult patients with focal seizures who required a change in their ASM monotherapy. The main purpose of this study was to gain insights into patients' preferences for attributes characterizing ASM monotherapy options before treatment consultation (treatment decision), and to explore the trade-offs patients are willing to consider between treatment efficacy and associated risks in terms of side effects. Further objectives were to explore how the treatment consultation may affect patient preferences by comparing patient preferences before and after treatment consultation, to gain insights into

Key Points

- For patients, seizure freedom and avoiding trouble thinking clearly were the most important attributes for an antiseizure medication in monotherapy
- Patient preferences were qualitatively similar before and after treatment consultation
- Physicians placed more weight on efficacy (in terms of seizure freedom) and personality change than did patients
- Exploratory analyses of specific patient subgroups revealed some trends toward heterogeneity in preferences
- Results suggest that discrete choice experiment surveys could be a useful tool for exploring patient preferences as part of real-world evidence studies

physicians' preferences in selecting treatment, and to compare patient and physician preferences for treatment.

2 | MATERIALS AND METHODS

2.1 | Study design and patient characteristics

VOTE (EP0076) was a prospective, observational study conducted in Denmark, France, Germany, Ireland, Italy, the Netherlands, Spain, and the UK. Eligible patients were 18 years and older, with focal seizures (with or without secondary generalization [focal to bilateral tonic–clonic seizures (FBTCS)]), receiving one or more ASMs, who intended to receive a new ASM as monotherapy. Patients who were newly diagnosed and needed first-line treatment, or who intended to taper/stop ASMs (without addition of a new ASM) to achieve monotherapy, were excluded. To be eligible, patients also had to be considered by the treating physician to be reliable and capable of adhering to the study protocol (e.g., able to understand and complete questionnaires).

Eligible patients were followed as per current clinical practices, and the choice of ASM treatment was made independently by the treating physician. Before participating in the study, each patient provided written informed data consent for the use of their medical data. The study was approved by the respective regulatory bodies and ethics committees in accordance with all local requirements and laws of participating countries.

TABLE 1 Treatment attributes and levels in the DCE survey

Attribute	Level
Chance of becoming seizure-free	60% chance
	45% chance
	25% chance
Chance of developing clinical depression	None
	4% chance
	10% chance
Personality changes	None
	Mild
	Moderate-to-severe
Trouble thinking clearly	None
	Mild
	Moderate-to-severe
Dizziness	None
	Mild
	Moderate-to-severe
Change in body weight in 6 months	5% weight loss
	No change
	5% weight gain
Feeling sleepy or tired	None
	Sleepiness
	Mild-to-moderate tiredness
	Severe tiredness

Abbreviation: DCE, discrete choice experiment.

2.2 | DCE survey design

A DCE survey was used in this study as the method for eliciting patients' and physicians' preferences. The DCE design was developed and conducted according to good research practice guidelines published by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR).[15,16] First, a comprehensive review of 67 ASM treatment attributes (Table S1) was conducted to assess suitable attributes to include in the survey (Supplementary Methods). Seven attributes covering effectiveness and AEs were selected for inclusion in the final survey (Table 1). Each attribute was assigned three to four "levels" over which it could vary; for example, the attribute "chance of becoming seizure-free" was assigned levels of 25%, 45%, and 60% (Table 1). Clinically relevant levels were determined using data from clinical trials and refined to encompass the range that was salient to patients.

Based on the selected attributes and levels, 60 choice questions were developed in which patients or physicians needed to choose between two hypothetical treatments (Figure 1). In the descriptions of the attributes and types of treatments, efforts were made to present neutral descriptions that provided an accurate, concise description of the benefits and risks. The combination of attribute levels for each treatment was designed experimentally to allow estimation of preference weight values.[16] The 60 choice questions were divided into five different versions of the survey, comprising 12 questions each, to reduce the burden for respondents. Each respondent (patient or physician) was randomly assigned to one of the five versions. Therefore, the number of choice questions presented to each respondent was limited to 12. The patient and physician versions of the survey were almost identical; the only differences were the description of the treatment scenario and how weight change was presented (Figure 1).

Before survey administration, to confirm that respondents could complete the survey as written and that the content was understood, the survey instruments were pretested in the UK in semistructured qualitative interviews. The patient

Please tick in the box below, the medicine you would choose (Medicine A or Medicine B) if you had to take one of these medicines and these were the only medicines available.

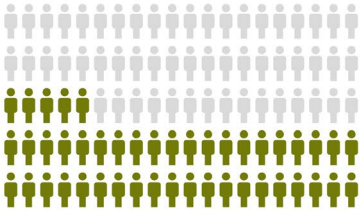
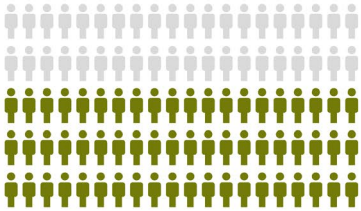
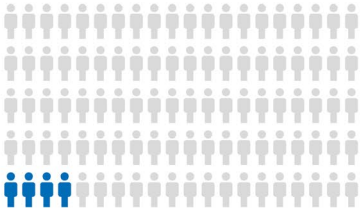
Medicine Feature	Medicine A	Medicine B
Chance of becoming seizure-free	 45% (45 people out of 100)	 60% (60 people out of 100)
Chance of developing clinical depression	 4% (4 people out of 100)	None
Personality changes	Moderate-to-severe	None
Trouble thinking clearly	None	Mild
Dizziness	Moderate-to-severe	None
Change in body weight	No change	Gain___lbs/kg (5% weight gain)
Feeling sleepy or tired	Mild-to-moderate tiredness	Severe tiredness
Which medicine would you choose?	☐	☐

FIGURE 1 Sample choice question from the discrete choice experiment survey (patient version). In the physician version, the text at the top was as follows: *Please tick in the box below, the medicine you would choose for your patient (Medicine A or Medicine B) if these were the only options available*. Change in body weight in the patient version was shown as a 5% gain or loss in pounds (UK and Ireland) or kilograms (other countries) as calculated from the patient's self-reported body weight, whereas in the physician version, this was presented only as 5% weight gain/loss with no calculation

version was pretested with 10 adults with a self-reported diagnosis of epilepsy; the physician version was pretested with nine practicing physicians specializing in neurology or epileptology who treat patients with focal seizures.

2.3 | DCE survey administration

The survey was programmed online and administered electronically to patients and physicians at sites participating in EP0076, which included epilepsy centers and neurology departments in hospitals. Patients completed the DCE survey in the clinic on dedicated tablets, once before ASM treatment consultation with a physician and a second time up to 14 days after treatment consultation.

Each physician completed the DCE survey up to three times for three different patients up to 7 days after the treatment consultation. Physicians were asked to consider a specific patient after consultation with that patient

when answering the 12 hypothetical prescribing decisions (choice questions).

2.4 | Additional assessment of patients' satisfaction with the treatment consultation

For the second time taking the survey, patients were also asked to rate their satisfaction with certain aspects of the treatment consultation process using visual analog scales (VASs; scored 0–100), and to indicate from a list which aspects of treatment were most important to them (Supplementary Methods).

2.5 | Outcome measures

The main outcome was patient preferences for different features characterizing an ASM in monotherapy, and was measured by patients' relative preference weights and the conditional relative importance for each attribute in the DCE survey, before treatment consultation. Further outcomes were the difference in patients' relative preference weights for each attribute before and after treatment consultation, physicians' relative preference weights and conditional relative importance for each attribute, and the difference in these measures between physicians and patients. In addition, patients' satisfaction with the treatment consultation was analyzed.

2.6 | Statistical analyses

Statistical analyses were conducted according to good research practice guidelines published by ISPOR.[17] DCE patient data were analyzed using a random parameters logit (RPL) model, whereas the physician data were analyzed using a conditional multinomial logit (MNL) model because of the small sample size and limited preference heterogeneity in the sample.

Coefficient estimates from the RPL and MNL models were estimated for each treatment attribute level included in the survey and were interpreted as relative preference weights. All estimates are reported with 95% confidence intervals (CIs; see Supplementary Methods). The conditional relative importance of each attribute was calculated as the difference between the preference weights for the most and least preferred level of that attribute. The conditional relative importance was scaled such that the attribute with the highest conditional relative importance was set to 10.

All analyses were performed in the Enrolled Set (ES; all patients with signed data consent and available baseline characteristics), Patient Preference Comparison Set (PPC; all patients in the ES who had completed at least one DCE question in the survey before the treatment consultation and at least one DCE question within 14 days after consultation), and the Physician Preference Set (PPS; all physicians who completed at least one DCE question [within 7 days after treatment consultation]).

Descriptive statistics for baseline patient characteristics and responses to the patient treatment satisfaction questions are provided for the ES.

2.7 | Post hoc patient subgroup analyses

To explore preference heterogeneity, post hoc subgroup analyses were conducted. Subgroups were analyzed by country (Germany vs. other countries [Denmark, France, Ireland, the Netherlands, Spain, the UK], Italy vs. other countries, and Germany vs. Italy), age (≥65 years vs. <65 years, >45 years vs. ≤45 years), sex (male vs. female), education level (secondary school or less vs. more than secondary school), employment (full/part time vs. unemployed/missing), time since epilepsy diagnosis (>6.33 years vs. ≤6.33 years), number of failed ASMs (previous ASMs with a documented reason for discontinuation; none/missing vs. ≥1), reason for discontinuation of previous ASM (due to lack of efficacy vs. not due to lack of efficacy), seizure type (with FBTCS vs. without), levetiracetam experience (with prior levetiracetam vs. without), and patient experience (experienced [diagnosed >6.33 years ago and ≥1 failed ASM] vs. less experienced).

Subgroup analyses were conducted using RPL models by interacting each attribute level in the model with a dummy-coded variable to identify respondents who were part of one subgroup in a pair and adding all interaction terms to the original RPL model. The estimated parameters on the interaction terms can be interpreted as the difference in preferences between the subgroup of interest (dummy variable = 1) and the reference group (dummy variable = 0). Finally, systematic differences were tested between two subgroups at a time with a Wald test (e.g., by testing the hypothesis that all coefficients on the dummy-variable interactions were zero), with an interaction between each attribute level and a dummy variable equal to one if for one of the subgroups, and zero otherwise. An α level of .05 (or 5%) was used to evaluate statistical significance. A single sample t-test was used to determine the statistical significance of single differences between adjacent attribute levels within each subgroup.

3 | RESULTS

3.1 | Baseline patient characteristics

In total, 310 patients were enrolled (Denmark, 9; France, 23; Germany, 139; Ireland, 3; Italy, 76; the Netherlands, 5; Spain, 33; the UK, 22) between August 2017 and September 2019 (ES), of whom 305 completed the DCE survey before consultation and 273 completed the survey both before and after consultation (PPC). In the ES, 77.4% (240/310) of patients discontinued the previous ASM before starting a new ASM monotherapy. The primary reason for discontinuation of the previous ASM was insufficient efficacy for 48.4% (150/310) of patients and adverse drug reaction for 31.9% (99/310) of patients.

All baseline characteristics are reported for the ES. Patients had a mean (SD) age of 46.8 (18.3) years, and 52.3% were female (Table 2). Among all patients, the majority (64.8%) had secondary school or less than secondary school education as the highest level of education; 80.6% were living with a partner, relative, or friend(s); and 56.1% were not employed, including 24.2% who were retired. Median (range) baseline seizure frequency (standardized number of seizures per 28 days during the 3 months before the first study visit) was .6 (0–112.0). Mean (SD) time since epilepsy diagnosis was 11.2 (12.6) years. Seventy-one (22.9%), 37 (11.9%), and 35 (11.3%) patients had failed one, two, and three or more ASMs, respectively (not including ASMs that patients had started to taper after the first visit). The most common (≥20% of patients) reasons for discontinuing their previous ASM were insufficient efficacy (150 [48.4%] patients) and adverse drug reaction (99 [31.9%] patients). The most common previous ASMs (taken by ≥20% of patients) were levetiracetam (taken by 181 [58.4%] patients) and lamotrigine (taken by 86 [27.7%] patients).

3.2 | Patient preferences

Preferences were ordered as expected, with better outcomes being preferred to worse outcomes (Figure 2); patients preferred a higher chance of seizure freedom, lower risk of developing clinical depression, and fewer severe AEs; avoiding moderate-to-severe "trouble thinking clearly" was more important than avoiding any other side effect, including, for example, a 10% chance of clinical depression.

Calculation of the mean conditional relative importance of each attribute showed that the most important attribute for patients before consultation was the chance of becoming seizure-free (10.0, 95% CI = 7.8–12.2), followed by trouble thinking clearly (8.2, 95% CI = 6.6–9.9),

TABLE 2 Baseline patient characteristics (Enrolled Set, $N = 310$)

Demographics	
Age, mean (SD), years	46.8 (18.3)
Female, *n* (%)	162 (52.3)
Baseline epilepsy characteristics	
Time since first epilepsy diagnosis, mean (SD), years	11.2 (12.6)[a]
Focal seizure frequency/28 days, median (range)	.6 (0–112.0)[b]
ASM treatment history, *n* (%)	
Number of failed ASMs[c,d]	
0	167 (53.9)
1	71 (22.9)
2	37 (11.9)
≥3	35 (11.3)
Primary reason for discontinuation of ASM planning to be stopped[e]	
Insufficient efficacy	150 (48.4)
Adverse drug reaction	99 (31.9)
Remission	13 (4.2)
Unknown	13 (4.2)
Other	42 (13.5)
Socioprofessional status, *n* (%)	
Highest level of education	
Less than secondary school	52 (16.8)
Secondary school	149 (48.1)
Nonuniversity degree	44 (14.2)
University degree	56 (18.1)
Postgraduate degree	7 (2.3)
Missing	2 (.6)
Housing status	
Living with partner, relative, or friend(s)	250 (80.6)
Living alone	52 (16.8)
Living in medical institution	1 (.3)
Other	6 (1.9)
Missing	1 (.3)
Current professional status	
Full-time employed (including self-employed)	107 (34.5)
Part-time employed (including self-employed)	27 (8.7)
Unemployed	174 (56.1)
Retired	75 (24.2)
Unemployed because of epilepsy	35 (11.3)
Student	28 (9.0)
Seeking work (or able to work if a job were available)	15 (4.8)

TABLE 2 (Continued)

Homemaker	8 (2.6)
Other	13 (4.2)
Missing	2 (.6)
Regular assistance because of epilepsy	
No, I do not need any help	270 (87.1)
Yes, a relative/a friend of mine is helping me	34 (11.0)
Yes, I receive help from a paid caregiver	4 (1.3)
Other	1 (.3)
Missing	1 (.3)
Currently unable to drive because of epilepsy	173 (55.8)

Abbreviation: ASM, antiseizure medication.

[a]$n = 309$.

[b]$n = 247$.

[c]Previous ASMs with a documented reason for discontinuation.

[d]ASMs that were not discontinued before first study visit, but started to taper down after first visit, were not counted.

[e]Patients could be counted for more than one discontinuation reason. Patients who discontinued several ASMs for the same reason were counted only once for that reason.

personality changes (6.9, 95% CI = 5.4–8.3), dizziness (5.6, 95% CI = 4.3–6.9), the chance of developing clinical depression (5.2, 95% CI = 3.7–6.7), feeling sleepy or tired (5.0, 95% CI = 3.7–6.3), and change in body weight in 6 months (2.7, 95% CI = 1.8–3.7) (Table 3).

When comparing patient preference before and after treatment consultation (PPC [$n = 273$]; Figure S1), the results showed that preferences were generally qualitatively similar.

3.3 | Patient satisfaction with the treatment consultation

The mean (SD) VAS score for patient satisfaction regarding the way the treatment consultation was taken was 83.2 (20.3; $n = 257$; Table 4), indicating that patients were satisfied with their involvement in the treatment decision. Responses to the patient satisfaction questions (completed after consultation) also indicated that the most important aspects of treatment were reduction of seizures (216 [69.7%] patients), cognitive problems (144 [46.5%]), and personality changes (134 [43.2%]) (ES [$N = 310$]; Table 4).

3.4 | Post hoc subgroup analyses of patient preferences

The post hoc subgroup analyses did not reveal systematically different preferences among most of the patient subgroups (Table S2, Figures S2–S13), with a few minor exceptions.

A small but significant difference in patient preferences was detected between German and Italian patients ($p = .0325$, as assessed using the Wald test; Table S2, Figure S2). Compared with patients living in Italy, those living in Germany placed less importance on avoiding mild trouble thinking clearly, mild dizziness, and sleepiness (t-test). Furthermore, the preferences of patients aged 65 years or older were statistically systematically different compared with those of younger patients ($p = .0408$, Wald test; Table S2, Figure S3). Preferences were not statistically systematically different among other patient subgroups (Table S2, Figures S4–S13).

The attributes were not jointly statistically different between men and women ($p = .3396$, Wald test); however, women placed greater importance on having no change in body weight (t-test on the conditional relative importance of the change in body weight and t-test on the preference weight; Table S2, Figure S5).

3.5 | Physician preferences

As expected, physicians preferred better outcomes for their patients to worse outcomes (PPS, $n = 94$; Figure S14). Compared with patients, physicians had a qualitatively stronger preference for greater chance of seizure freedom and avoiding personality changes, as shown by the most and least preferred levels of those attributes (Figure S14). Mean conditional relative importance calculations showed that the most important attribute for physicians was the chance of becoming seizure-free (10.0, 95% CI = 8.6–11.4), followed by personality changes (7.5, 95% CI = 6.2–8.9), trouble thinking clearly (6.2, 95% CI = 4.9–7.5), feeling sleepy or tired (5.4, 95% CI = 3.9–7.0), dizziness (4.4, 95% CI = 3.0–5.7), the chance of developing clinical depression (3.1, 95% CI = 1.8–4.4), and change in body weight in 6 months (.7, 95% CI = −.6 to 1.9) (Table S3).

4 | DISCUSSION

The results of this European observational study implementing a DCE survey provide further insights into the trade-offs patients are willing to consider between treatment efficacy and side effects when considering a new ASM in monotherapy. The study was designed to observe adults being treated with one or more ASMs who are capable of understanding and completing the questionnaires, and provides data for preferences over two timepoints, which represents a novel approach for epilepsy. Furthermore, a relatively high number of patients were included. Real-world evidence studies do not usually include an analysis of preferences.

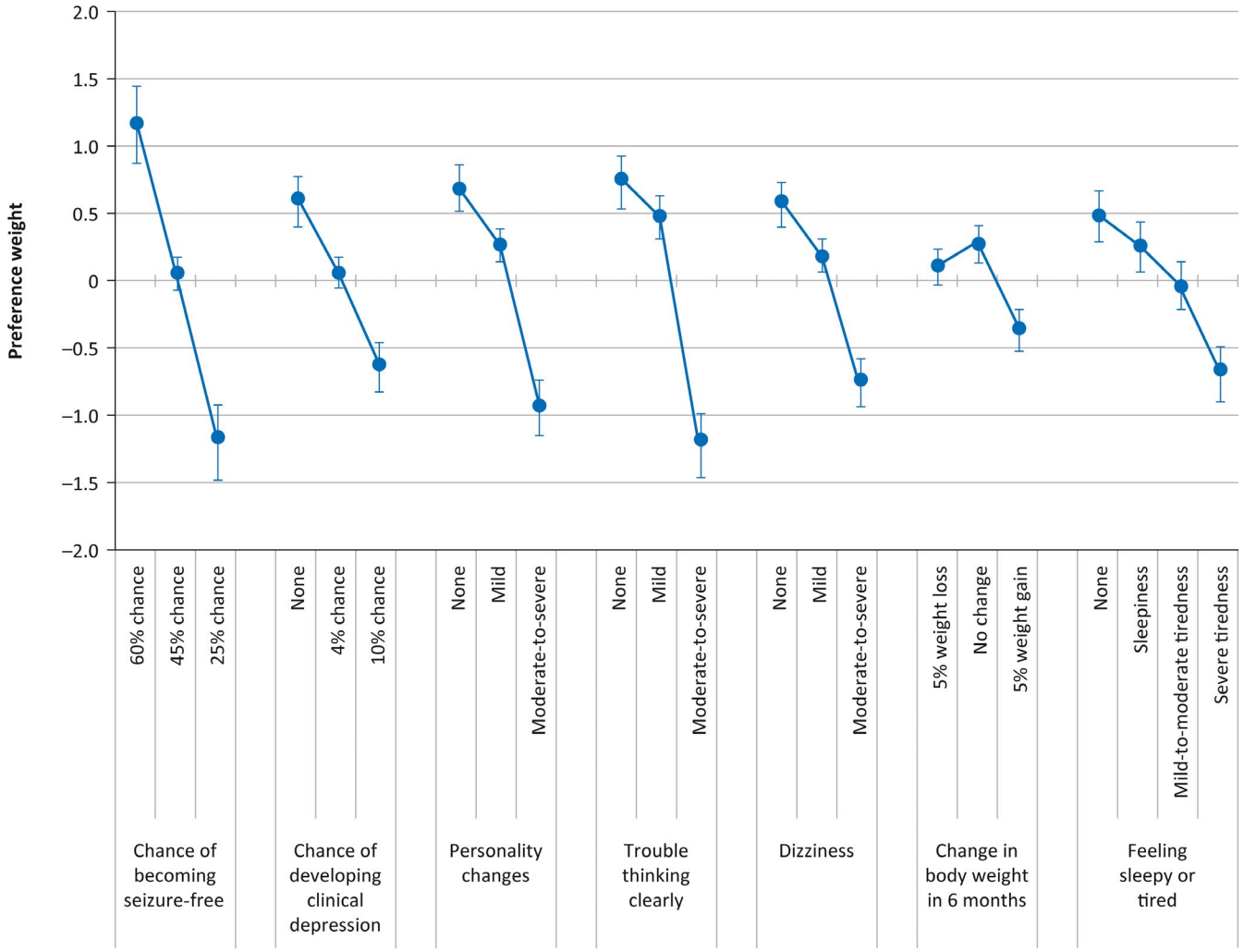


FIGURE 2 Patient preferences based on a discrete choice experiment survey before treatment consultation, random parameters logit model (Enrolled Set [ES], $n = 305$ [although the ES included 310 patients, five did not complete the survey before the consultation]). Error bars represent 95% confidence intervals. The change in utility associated with a change in the levels of each attribute is represented by the difference between those levels of that attribute. Larger differences between preference weights indicate that patients viewed the change as having a relatively greater effect on overall utility. For example, decreasing the chance of developing clinical depression from 4% to no chance yields a change in utility of approximately .5. Likewise, an improvement in trouble thinking clearly from moderate-to-severe to mild yields a change in utility of approximately 1.7. Therefore, moving from moderate-to-severe to mild trouble thinking clearly is preferable to decreasing the chance of clinical depression from 4% to none, because it has approximately three (1.7/.5) times more effect on utility. Another example is comparing preference weights for levels of the chance of becoming seizure-free with preference weights for levels of avoiding feeling sleepy or tired. Increasing the chance of becoming seizure-free from 25% to 45% yields a change in utility of approximately 1.3. Likewise, an improvement in feeling sleepy or tired from severe tiredness to none yields a change in utility of approximately 1.2. Therefore, an increase in efficacy from a 25% to 45% chance of becoming seizure-free is approximately equivalent to eliminating severe tiredness. However, improving the chance of becoming seizure-free from 25% to 60%, a change in utility of approximately 2.4, yields double the effect on utility than does eliminating severe tiredness

In addition, few studies have assessed preferences for diagnostics in epilepsy,[18] and previous studies of preferences for ASM treatment are relatively rare.[3–8]

Efficacy (chance of becoming seizure-free) was considered the most important treatment attribute by these patients. The second most important attribute was avoiding negative effect on cognition in terms of trouble thinking clearly. Preference weights were qualitatively similar before and after treatment consultation, suggesting that patient preferences were not influenced by the treatment consultation.

Our results are in line with those of previous studies. A DCE survey in patients showed that seizure reduction was the most important attribute of adjunctive ASM treatment, followed by limitations because of long-term confusion or memory problems.[4] Another DCE survey,

TABLE 3 Patient conditional relative importance, random parameters logit model (Enrolled Set, $n = 305$[a])

Chance of becoming seizure-free	Chance of developing clinical depression	Personality changes	Trouble thinking clearly	Dizziness	Change in body weight in 6 months	Feeling sleepy or tired
Order of importance | mean (95% confidence interval)						
1 | 10.0 (7.8–12.2)	5 | 5.2 (3.7–6.7)	3 | 6.9 (5.4–8.3)	2 | 8.2 (6.6–9.9)	4 | 5.6 (4.3–6.9)	7 | 2.7 (1.8–3.7)	6 | 5.0 (3.7–6.3)

[a]Five patients did not complete the survey before the consultation.

in Chinese patients, found that efficacy was the most important aspect of ASM treatment, although reducing side effects was also a major concern.[6] In addition, a DCE survey that elicited patient preferences toward pharmacogenetic testing before carbamazepine treatment showed that patients were willing to accept a less effective ASM if that treatment had less risk of harm.[7]

The patient population in this study was diverse in terms of demographics, epilepsy characteristics, and treatment history. Exploratory analyses of specific patient subgroups revealed some trends toward heterogeneity in preferences, although given the inherent limitations of post hoc analyses (including reduced statistical power), the subgroup data should be interpreted with caution. The preferences of patients living in Germany statistically systematically differed from those in Italy, as did the preferences of patients ≥65 years of age compared with those of younger patients. Some differences in specific attribute levels were also identified between different patient subpopulations. Patients from Germany placed less importance on avoiding mild trouble thinking clearly, mild dizziness, and sleepiness than patients from Italy. Furthermore, women had a higher preference for no change in body weight than men. This is in line with a previous subgroup analysis of patient preferences in ASM therapy, which found that women had a stronger preference to avoid weight gain.[3] These results, together with previous research,[19] suggest that taking patient characteristics into account may be beneficial when selecting an ASM, supporting the importance of personalized care of patients.

Efficacy (in terms of seizure freedom) was considered by both patients and physicians the most important treatment attribute, and body weight change was the least important. This is consistent with a previous study in which both neurologists and patients ranked seizure reduction as the most important treatment attribute for ASM treatment, with neurologists being even more influenced by seizure reduction than patients were.[8]

However, there were qualitative differences in what patients and physicians considered to be the most important aspects of treatment for patients. Physicians placed more weight on efficacy and personality changes than patients did, as reflected in the conditional relative importance of the treatment attributes. Similarly, the order of importance of the attributes differed between patients and physicians, with personality changes considered second most important by physicians and third by patients, and trouble thinking clearly considered third most important by physicians and second by patients.

Differences between patients and physicians have been found in previous studies. For example, a recent study using DCE data to elicit preferences for ulcerative colitis treatment also identified differences between patients' and physicians' most important treatment attributes; patients

TABLE 4 Patient satisfaction questions after treatment consultation (Enrolled Set, $N = 310$)

Question	VAS score,[a] mean (SD) [n]
When you think back on how the decision for your new treatment was made, how much influence had your doctor and how much influence did you have on that decision?	61.3 (27.0) [$n = 258$]
Now after the decision was made, how would you have preferred the distribution between you and your doctor to have been?	60.2 (21.4) [$n = 255$]
Overall, how satisfied were you with the way the treatment consultation was taken between you and your doctor?	83.2 (20.3) [$n = 257$]
On the scale below please mark how satisfied you were with the information you received from your doctor around the topics that were important for you.	82.2 (21.1) [$n = 260$]
Question and potential answers (multiple answers possible)	**Number of patients (%)**
In your personal opinion, what were the most important aspects in discussing and deciding on the new therapy for you? You can select as many aspects as you like from the list below. If none of the topics listed was of particular importance to you, please select "none."	$N = 310$
Reduction of seizures	216 (69.7)
Independence	121 (39.0)
Cognitive problems	144 (46.5)
Changes in personality	134 (43.2)
Fatigue and somnolence	108 (34.8)
Other neurologic side effects	121 (39.0)
Interactions of the new medication with other medications	65 (21.0)
Change in body weight	62 (20.0)
Issues with digestion	23 (7.4)
Dermatologic issues	39 (12.6)
Cardiovascular side effects	43 (13.9)
Reproduction/fertility	30 (9.7)
None	8 (2.6)

Abbreviation: VAS, visual analog scale.

[a]Responses to patient satisfaction questions were recorded on the VAS. Scores range from 0 to 100, with higher scores denoting more doctor influence or higher satisfaction and lower scores denoting more patient influence or less satisfaction.

were considerably more risk-averse than physicians.[20] DCE data have also been used to estimate the utility of alternative ASMs, and it was found that the rank order of ASMs inferred from patient preference data may differ from that inferred from clinical trial results.[5]

This study had a few limitations. All DCE scenarios were hypothetical in nature and may not fully predict decisions made in a clinical setting, where other considerations come into play, such as cost or access to care. The set of treatment attributes was limited to seven to prevent difficulty in completing the tasks; inclusion of additional attributes may have influenced the results, although a comprehensive review was performed to ensure that the most relevant attributes were selected. Furthermore, the order of patient and physician preferences was dependent on the highest and lowest levels of each attribute. Also, the RPL model did not converge with the PPS data, and the data were instead analyzed using an MNL model, which does not mitigate potential bias.

Overall, this preference study conducted as part of an observational study in patients who intended to receive a new ASM monotherapy suggests that for patients, the chance of seizure freedom and avoiding trouble thinking clearly were the most important treatment attributes. The results also showed that patient preferences were similar before and after treatment consultation, that preferences for specific attributes may vary in different patient subpopulations, and that physicians and patients may differ in how much emphasis they place on specific attributes; physicians placed more weight on efficacy and personality

change than did patients, and patients placed more weight on trouble thinking clearly than did physicians. These findings inform physicians about the relative importance to patients of different ASM treatment attributes, including cognitive versus psychobehavioral side effects, and may help in shared decision-making in the clinic when an ASM is chosen. Moreover, the results of this study suggest that DCE surveys could be a useful tool for exploring the relative importance of efficacy and tolerability for patients as part of real-world evidence studies. Future studies could further assess patient preferences over time, and how specific events (such as hospitalization, serious AEs, and lifestyle changes) may affect preferences.

ACKNOWLEDGMENTS

This study was funded by UCB Pharma. The authors thank the patients and their caregivers in addition to the investigators and their teams who contributed to the study (investigators are presented in the appendix). The authors would also like to thank Kimberly Moon, BA, BS, PMP (RTI Health Solutions, Research Triangle Park, NC, USA) for assistance in project management during the study, Marc de Backer, MD (UCB Pharma, Brussels, Belgium) and Michael Colopy, PhD, MPH (UCB Pharma, Raleigh, NC, USA) for their assistance during setup of the study, and Michael Bretschneider, MSc (UCB Pharma, Monheim am Rhein, Germany) for project management during the conduct of the study, as well as Philippe Kahane, MD, PhD (Epilepsie et Malaises Neurologiques, Pavillon de Neurologie, CHU de Grenoble, Grenoble, France), Marc De Backer, MD (UCB Pharma, Brussels, Belgium), and Hina Naz Abbasi, MBBS, SCE, CCT, MRCP (Institute of Neurological Sciences, Queen Elizabeth University Hospital, Glasgow, UK) for their contribution to the selection of treatment attributes. Publication management was provided by Vincent Laporte, PhD (UCB Pharma, Brussels, Belgium). Writing assistance was provided by Jayna Patel, PhD, CMPP (Evidence Scientific Solutions, Horsham, UK) and Emily Chu, PhD (Evidence Scientific Solutions, London, UK), and was funded by UCB Pharma.

CONFLICT OF INTEREST

F.R. has served as a consultant for Arvelle Therapeutics, Eisai, GSK, GW Pharmaceuticals, MediLearn India, and UCB Pharma; has received research grants from the Detlev-Wrobel-Fonds for Epilepsy Research, the Deutsche Forschungsgemeinschaft, the German Ministry for Education and Research, and the State of Hessen; and has received speaker's honoraria from Eisai, GW Pharmaceuticals, and UCB Pharma. Y.W. has received honoraria for lectures and consultations from Bayer, BIAL, Eisai, LivaNova, Novartis, and UCB Pharma. I.L., M.Br., and L.J. are employees of UCB Pharma. J.Su. is a former employee of RTI Health Solutions, which received funding from UCB Pharma to conduct the preference study, but is now an employee of Duke Clinical Research Institute (Duke University, Durham, NC, USA). M.Bo. is an employee of RTI Health Solutions. J.Sm. has received payment from UCB Pharma to participate in this study. F.V. has received speaker's fees from BIAL, Eisai, Sandoz, and UCB Pharma. C.B. has received personal compensation from Arvelle Therapeutics, Desitin, Eisai, GW Pharmaceuticals, Idorsia Pharmaceuticals, UCB Pharma, and Zogenix for consulting services or speaking activities. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Rosenow F, Winter Y, Leunikava I, Brunnert M, Joeres L, Sutphin J, et al. Relative importance of clinical outcomes and safety risks of antiseizure medication monotherapy for patients and physicians: Discrete choice experiment eliciting preferences in real-world study "VOTE". Epilepsia. 2022;63:451–462. doi:10.1111/epi.17137