# Supporting Information

## Supplementary Methods

### Selection of treatment attributes

The selection of the attributes was informed by an expert meeting involving five experts—four physicians and one patient ambassador. The meeting included in-depth discussion of potential attributes and a ranking exercise. Before the meeting with the experts, RTI Health Solutions and UCB Pharma staff met to develop a list of 15 potential attributes to be considered for inclusion in the discrete choice experiments (DCE), selected from a comprehensive list of 67 attributes. The list of 15 potential attributes was presented for discussion during the expert meeting. These attributes were reduction in the frequency of focal (partial-onset) seizures; independence; cognitive problems; clinical depression; other psychiatric adverse events; aggressive behavior; drug-drug interactions; somnolence; fatigue; change in body weight; dizziness; other neurologic adverse events; nausea/vomiting; dosing/pill burden; and cardiovascular adverse events. A ranking exercise was then performed to determine the most and least important attributes, resulting in selection of the final seven attributes.

### Patient satisfaction with the treatment consultation

Patients were asked which treatment aspects were most important to them from the following list:

* Reduction of seizures
* Independence
* Cognitive problems
* Changes in personality
* Fatigue and somnolence
* Other neurologic side effects
* Interactions of the new medication with other medications
* Change in body weight
* Issues with digestion
* Dermatologic issues
* Cardiovascular side effects
* Reproduction/fertility
* None

### Statistical analysis

The random parameters logit (RPL) model related patients’ treatment choices to the attribute levels of each treatment profile in the choice questions. The RPL model mitigated potential estimation bias in the mean preference weight estimates due to unobserved preference heterogeneity among patients by estimating a distribution around each mean preference parameter, and accounted for the fact that each patient made multiple treatment choices over a series (panel) of choice questions.

Based on the specification assumed for each attribute, the following utility model was estimated:

Eq (1) V = βEFF1 × EFF1 + βEFF2 × EFF2

+ βDEP1 × DEP1 + βDEP2 × DEP2

+ βPER1 × PER1 + βPER2 × PER2

+ βTHINK1 × THINK1 + βTHINK2 × THINK2

+ βDIZZ1 × DIZZ1 + βDIZZ2 × DIZZ2

+ βWHT1 × WHT1 + βWHT2 × WHT2

+ βTRD1 × TRD1 + βTRD2 × TRD2 + βTRD3 × TRD3,

where V is the systematic indirect utility for a particular treatment profile, β is a parameter estimate for each attribute level, and variables are as follows:

* EFF1-3: Effects-coded variable indicating the chance of becoming seizure-free (EFF1=60% chance; EFF2=45% chance; EFF3=25% chance). EFF3 was omitted for model identification.
* DEP1-3: Effects-coded variable indicating the chance of developing clinical depression (DEP1=none; DEP2=4% chance; DEP3=10% chance). DEP3 was omitted for model identification.
* PER1-3: Effects-coded variable indicating personality changes (PER1=none; PER2=mild; PER3=moderate-to-severe). PER3 was omitted for model identification.
* THINK1-3: Effects-coded variable indicating trouble thinking clearly (THINK1=none; THINK2=mild; THINK3=moderate-to-severe). THINK3 was omitted for model identification.
* DIZZ1-3: Effects-coded variable indicating dizziness (DIZZ1=none; DIZZ2=mild; DIZZ3=moderate-to-severe). DIZZ3 was omitted for model identification.
* WHT1-3: Effects-coded variable indicating change in body weight in 6 months (WHT1=5% weight loss; WHT2=no change; WHT3=5% weight gain). WHT3 was omitted for model identification.
* TRD1-4: Effects-coded variable indicating feeling sleepy or tired (TRD1=none; TRD2=sleepiness; TRD3=mild-to-moderate tiredness; TRD4=severe tiredness). TRD4 was omitted for model identification.

The preference weights were statistically significantly different from 0 at the 5% level if the confidence interval (CI) did not include 0. The significance of each preference weight indicated the significance of each attribute level relative to the mean effect of that attribute (normalized to be 0).

If the CIs for any pair of levels of the same attribute did not overlap, the mean estimates for those attribute levels were statistically significantly different from each other at the 5% level of significance.

## Supplementary Tables

**TABLE S1** Initial list of antiseizure medication treatment attributes

|  |  |  |
| --- | --- | --- |
| **Benefit or risk** | **Attribute** | **Levels experienced (some, most, all) of the time** |
| **Benefit** | Reduce my number of seizures | Some reduction in frequency and severity/significant reduction for the patient in frequency and severity/seizure-free |
| **Benefit** | Able to live independently: driving, bathing/dressing/cooking/walking/climbing stairs/doing light household | With no, little, or some assistance (add driving as highest level). To add quality of life: "need to have" (=basic needs such as ability for dressing) to live independently a normal life to what is "nice to have" (eg, specific leisure activities) for a normal life |
| **Benefit** | Able to combine with future therapies if needed to obtain better seizure control (and treat other ailments) | Able with (1) all other therapies, (2) some other therapies, (3) no other therapies |
| **Benefit** | Able to maintain work and school schedule without physical limitations | Always, most of the time, none of the time |
| **Benefit** | Able to socialize with my family and friends due to my epilepsy | Always, most of the time, none of the time |
| **Benefit** | Feeling positive and cheerful (some, most, all) of the time (reword mood stabilization, having a normal mood) | Always, most of the time, none of the time (or better, stable, worse mood) |
| **Benefit** | Able to keep up with daily dose schedule/easy to follow doctor's orders/important to have a choice of syrup, pills, or infusion | (Some, most, all) of the time (or number of pills per day 1, 2, 3) |
| **Benefit** | Important for new drug to work quickly/easy to find the right dose | Not, somewhat, very important |
| **Benefit** | Able to avoid falling and hurting myself/worry less about falling | Always, most of the time, none of the time |
| **Benefit** | % chance of being seizure-free over the next 2 years | 1 in 5, 3 in 5, or 5 in 5 chance |
| **Benefit** | Able to participate in sports and exercise without physical limitations | Always, most of the time, none of the time |
| **Benefit** | Able to participate in leisure time activities and hobbies | Always, most of the time, none of the time |
| **Benefit** | Ability to drive a car | Always, most of the time, none of the time/never, only during the day, or any time of day |
| **Benefit** | Able to live independently: bathing/dressing/cooking/walking/driving | With no, little or some assistance |
| **Benefit** | Able to do light household chores/climb stairs | Always, most of the time, none of the time |
| **Benefit** | Able to maintain work schedule without emotional limitations | Always, most of the time, none of the time |
| **Benefit** | Able to maintain work schedule without experiencing pain or discomfort | Levels neither discussed nor proposed |
| **Benefit** | Dose adjustments for renal or hepatic impairment | Levels neither discussed nor proposed |
| **Risk** | Decreased memory and attention (as a result of drug) | Levels neither discussed nor proposed |
| **Risk** | Drug-drug interactions | (Some, most, all) of the time |
| **Risk** | Worrying about the disease, quality of life (social, insecurity) – reduce worry about: having a seizure in the next year, hurting yourself while having a seizure, embarrassing yourself while having a seizure | Slightly, moderately, significantly |
| **Risk** | % chance of feeling dizzy or having blurred vision for a short period | Levels neither discussed nor proposed |
| **Risk** | Gastrointestinal adverse event (nausea, vomiting) – feeling sick | Always, most of the time, none of the time |
| **Risk** | Increase in weight | Minus 15, 0, plus 15 lbs |
| **Risk** | Arrhythmias, QTc, PR, lipid abnormalities | Levels neither discussed nor proposed |
| **Risk** | Reproductive, pregnancy, malformations, contraceptives, developmental | Levels neither discussed nor proposed |
| **Risk** | Willing to pay out of pocket | $0, 25, 75, 150, 300/month |
| **Risk** | Benefit: reducing the chance of death from prolonged seizures or SUDEP/Risks: shortness of breath and swelling or skin diseases | Levels neither discussed nor proposed |
| **Risk** | Blood disorders, bone marrow depression | Levels neither discussed nor proposed |
| **Risk** | Hair loss | None, some, a lot |
| **Risk** | Experience temporary loss of consciousness caused by a fall in blood pressure | (Some, most, all) of the time |
| **Risk** | Feel short of breath | (Some, most, all) of the time |
| **Risk** | Having difficulty learning and remembering new things | (Some, most, all) of the time |
| **Risk** | Fear or worry about having a seizure – reduce worry about: having a seizure in the next year, hurting yourself while having a seizure, embarrassing yourself while having a seizure | Levels neither discussed nor proposed |
| **Risk** | Causes difficulty with daily activities | Levels neither discussed nor proposed |
| **Risk** | Short-term side effects <select one> – Lasts for \_\_\_ | A day, week, month |
| **Risk** | Nausea/vomiting symptoms – feeling sick | (Some, most, all) of the time |
| **Risk** | Risk or chance of death from prolonged seizures | 0, 1, or 2% chance |
| **Risk** | Able to control movement, speech, eye movement, and swallowing | (Some, most, all) of the time |
| **Risk** | Feel heart is racing | (Some, most, all) of the time |
| **Risk** | Difficulty urinating | No, ½ time, always |
| **Risk** | Difficult going to the bathroom | (Some, most, all) of the time |
| **Risk** | Need for counseling for depression | Weekly, monthly, yearly |
| **Risk** | Decreasing dose due to breastfeeding | By 25, 50, or 75% |
| **Risk** | Feeling dizzy/feeling like you are spinning or swaying/feel like I am going to faint | (Some, most, all) of the time |
| **Risk** | Feel drowsy, tired, or pepless | (Some, most, all) of the time |
| **Risk** | Short-term non-psychotic symptoms (irritability, anxiety, nervousness, anger, aggression, apathy, hostility, panic attack, insomnia, belligerence, anger, agitation, restlessness, tearfulness, apathy, altered mood, mood swings, affect lability, psychomotor hyperactivity) – feeling <select from the above>/feel downhearted and blue/thinking about suicide/feeling my epilepsy is hopeless/unable to sleep/experiencing mood changes | (Some, most, all) of the time |
| **Risk** | Long-term non-psychotic symptoms (depression, depressed mood lability, psychomotor hyperactivity, abnormal behavior, adjustment disorder) – feeling <select from the above>/feel downhearted and blue/thinking about suicide/feeling my epilepsy is hopeless/unable to sleep/experiencing mood changes | (Some, most, all) of the time |
| **Risk** | Risk or chance of bruising or bleeding | 0, 5, 10% chance |
| **Risk** | Risk or chance of infection | 0, 5, 10% chance |
| **Risk** | Shortness of breath and swelling | Once a month, once a week, most nights |
| **Risk** | Risk or chance of severe skin disease | 0, 10, 20% chance |
| **Risk** | Risk or chance of headache and fever | 0, 5, 10% chance |
| **Risk** | Experience double vision | Once a month, once a week, most nights |
| **Risk** | Cardiac rhythm | Levels neither discussed nor proposed |
| **Risk** | Short-term cardiovascular: edema, aggravation of hypertension, hypotension, syncope and collapse, aggravation of coronary artery disease | Levels neither discussed nor proposed |
| **Risk** | Long-term cardiovascular: congestive heart failure, arrhythmias, and atrioventricular block, thrombophlebitis, thromboembolism, and adenopathy or lymphadenopathy | Levels neither discussed nor proposed |
| **Risk** | Blood dyscrasias (eg, neutropenia, thrombocytopenia, pancytopenia) | Levels neither discussed nor proposed |
| **Risk** | Aplastic anemia, agranulocytosis, pancytopenia, bone marrow depression,  thrombocytopenia, leukopenia, leukocytosis, eosinophilia, acute intermittent porphyria | Levels neither discussed nor proposed |
| **Risk** | Transient diplopia, oculomotor disturbances, nystagmus, peripheral neuritis, paresthesias, tinnitus, and hyperacusis | Levels neither discussed nor proposed |
| **Risk** | Psychotic symptoms (psychotic disorder  along with hallucination, paranoia, acute psychosis, and psychotic behavior) | Levels neither discussed nor proposed |
| **Risk** | Drug reaction with eosinophilia and systemic symptoms (DRESS), also known as multiorgan hypersensitivity | Levels neither discussed nor proposed |
| **Risk** | Polypharmacy drug interactions | Levels neither discussed nor proposed |
| **Risk** | Risk of liver or kidney damage | Levels neither discussed nor proposed |
| **Risk** | Multiorgan hypersensitivity | Levels neither discussed nor proposed |
| **Risk** | % chance of osteoporosis | Levels neither discussed nor proposed |
| **Risk** | % chance of reproductive disorders, such as mental growth retardation during pregnancy | Levels neither discussed nor proposed |

**TABLE S2** Post hoc subgroup analysis of patient preference weights based on a discrete choice experiment survey before treatment consultation (Enrolled Set [ES], *n* = 305a)

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Subgroup comparison** | ***n*** | ***p* value** |
| **Countryb** | Germany | 134 | .0626 |
| Italy | 76 | .2304 |
| Other countries (Denmark, France, Ireland, the Netherlands, Spain, the UK) | 95 | Reference group |
| **Age** | <65 years | 246 |  |
|  | ≥65 years | 59 | .0408 |
|  | ≤45 years | 147 | .0564 |
| >45 years | 158 |
| **Sex** | Female | 159 | .3396 |
| Male | 146 |
| **Education levelc** | Secondary school or less | 197 | .5891 |
| More than secondary school | 106 |
| **Employmentc** | Employed full-time or part-time | 131 | .2560 |
| Not employed full-time or  part-time | 172 |
| **Time since diagnosisc** | Diagnosed 6.33 or fewer years ago | 153 | .3554 |
| Diagnosed more than 6.34 years ago | 151 |
| **Failed ASMsd** | No failed ASMs or missing values | 166 | .7413 |
| One or more failed ASMs | 139 |
| **Reason for discontinuation of ASM planning to be stoppedc** | Due to lack of efficacy | 148 | .8144 |
| Not due to lack efficacy | 87 |
| **Seizure typec** | With FBTCS | 97 | .3601 |
| Without FBTCS | 88 |
| **Levetiracetam experiencec** | With prior levetiracetam | 180 | .9609 |
| Without prior levetiracetam | 122 |
| **Patient experiencec** | More experienced (diagnosed more than 6.33 years ago and has prior failure with an ASM) | 92 | .3645 |
| Less experienced | 212 |

aAlthough the ES included 310 patients, five did not complete the survey before the consultation. bSystematic differences in preferences were tested between two subgroups at a time using the Wald test. Therefore, the table presents the *P* values for the difference between Germany compared with all other countries and Italy compared with all other countries. The *p* value for the difference between Germany and Italy was *p* = .0325. cThe total subgroup sample size is <305 due to missing data. dPrevious ASMs with a documented reason for discontinuation. Abbreviations: ASM, antiseizure medication; FBTCS, focal to bilateral tonic-clonic seizures.

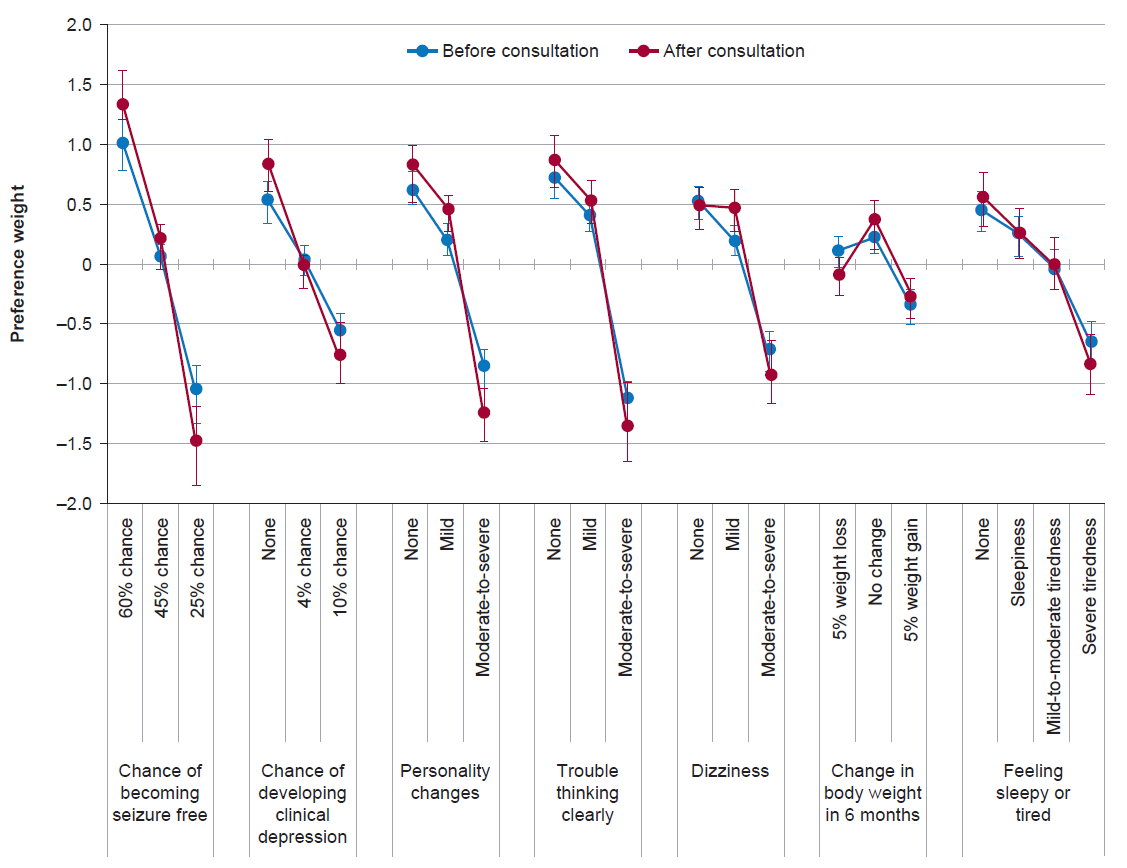
**TABLE S3** Physician conditional relative importance, conditional multinomial logit model (Physician Preference Set, *n* = 94a)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **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  (8.6–11.4) | 6 | 3.1  (1.8–4.4) | 2 | 7.5  (6.2–8.9) | 3 | 6.2  (4.9–7.5) | 5 | 4.4  (3.0–5.7) | 7 | .7  (−.6–1.9) | 4 | 5.4  (3.9–7.0) |

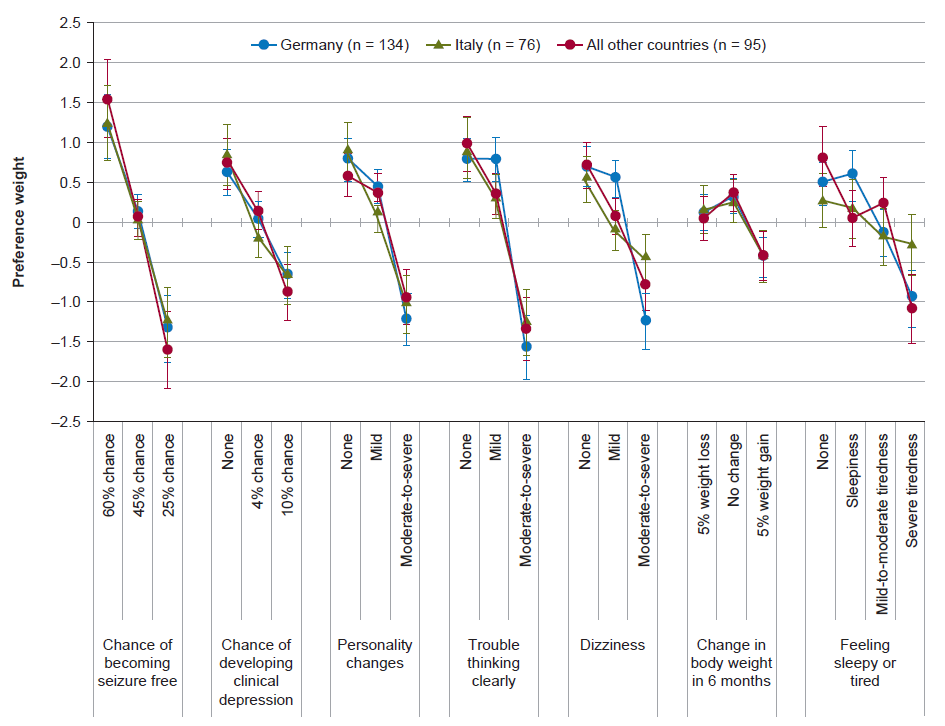
aForty-nine physicians completed a total of 94 surveys (each physician completed the survey for up to three patients).

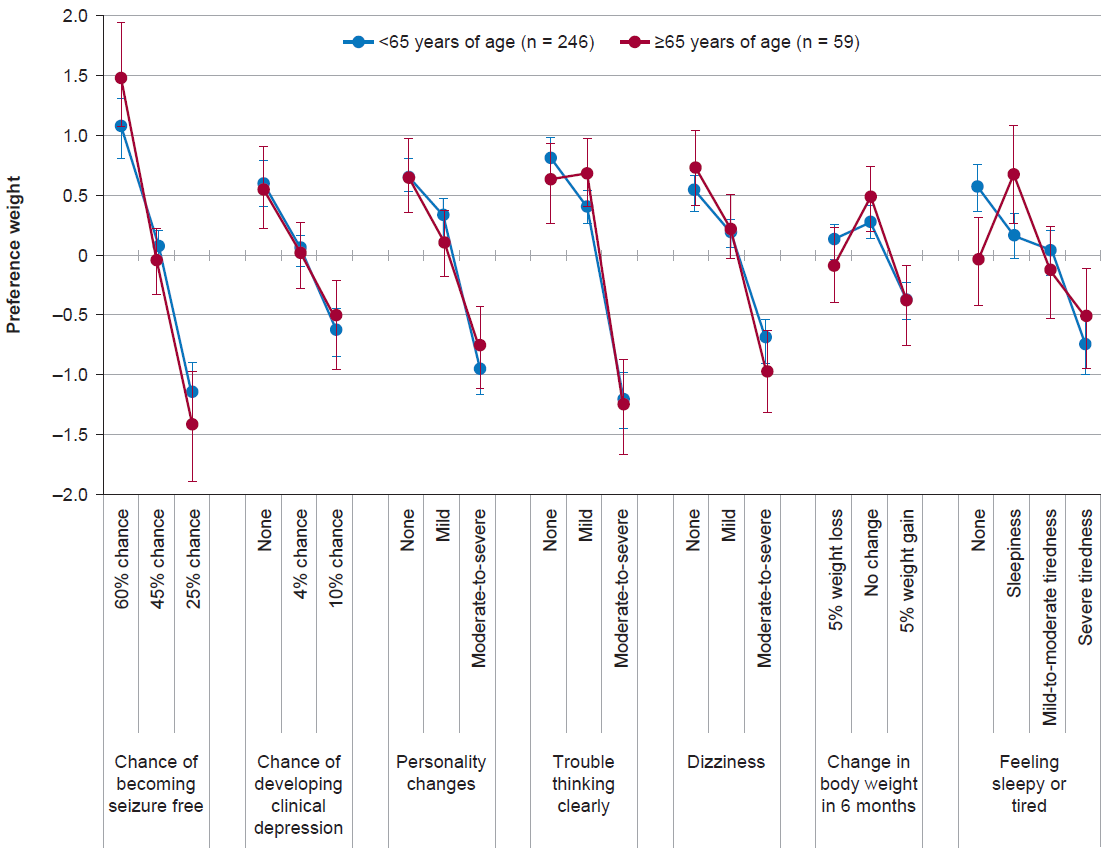
## Supplementary Figures

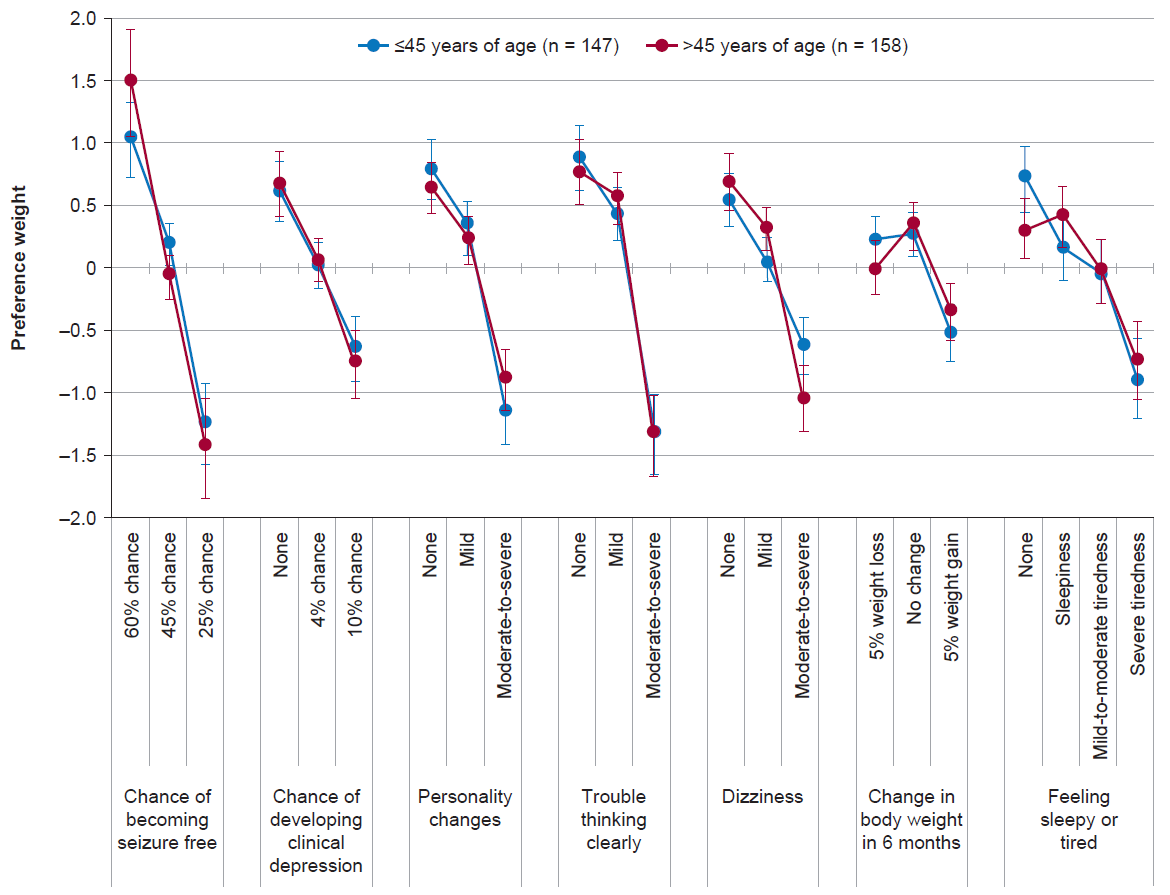
**FIGURE S1** Patient preferences based on a discrete choice experiment survey, before and after treatment consultation, random parameters logit model (Patient Preference Comparison Set, *n* = 273)

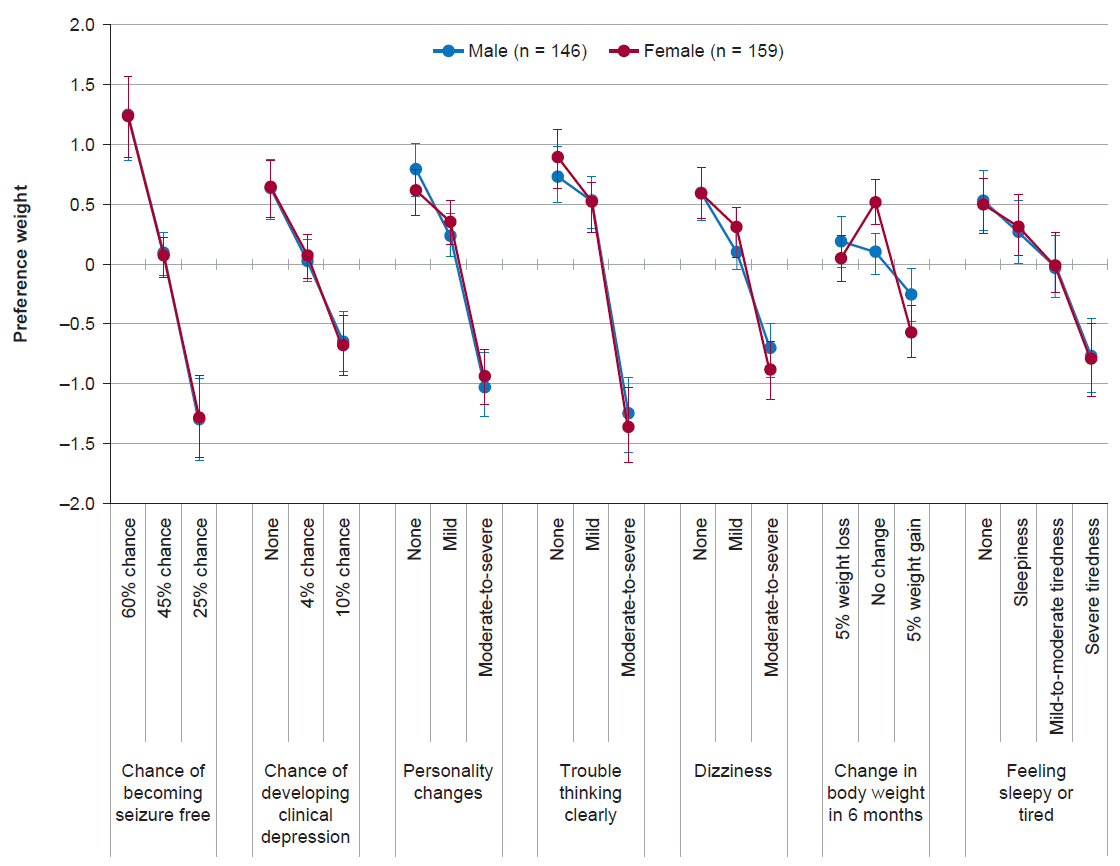


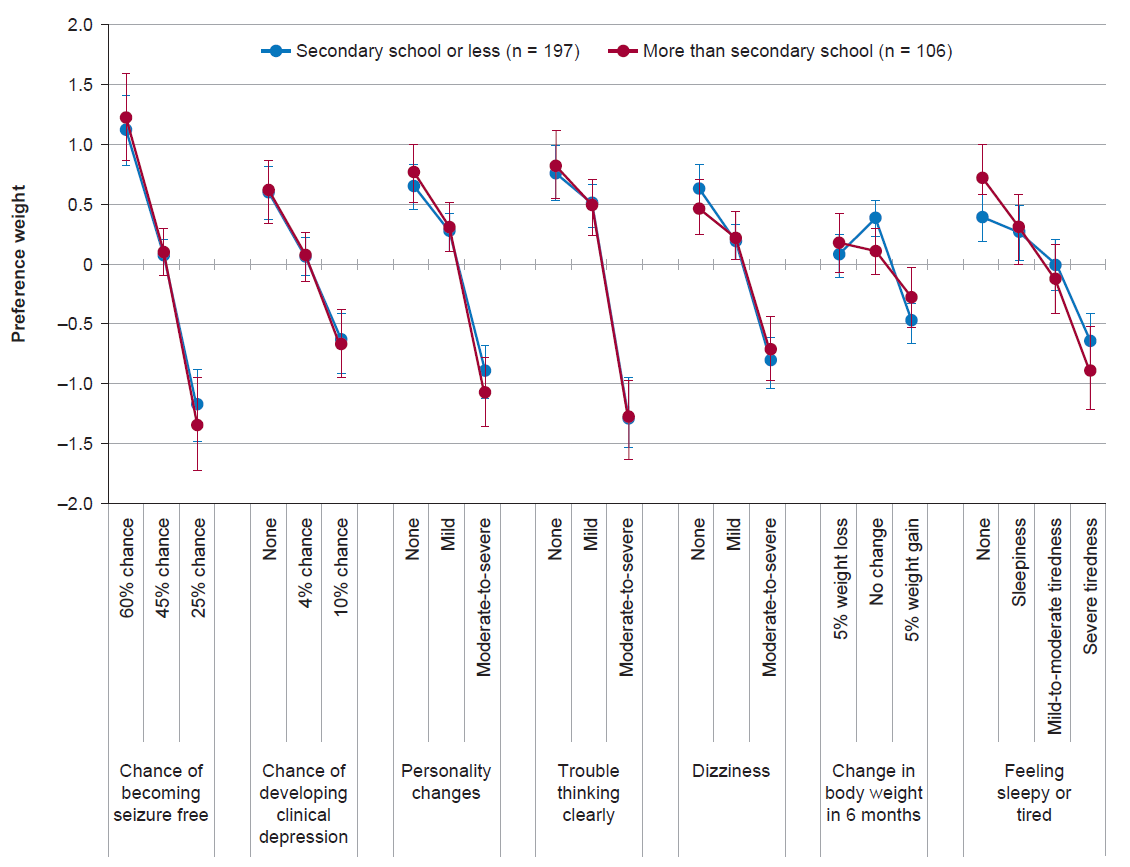
Error bars represent 95% confidence intervals.

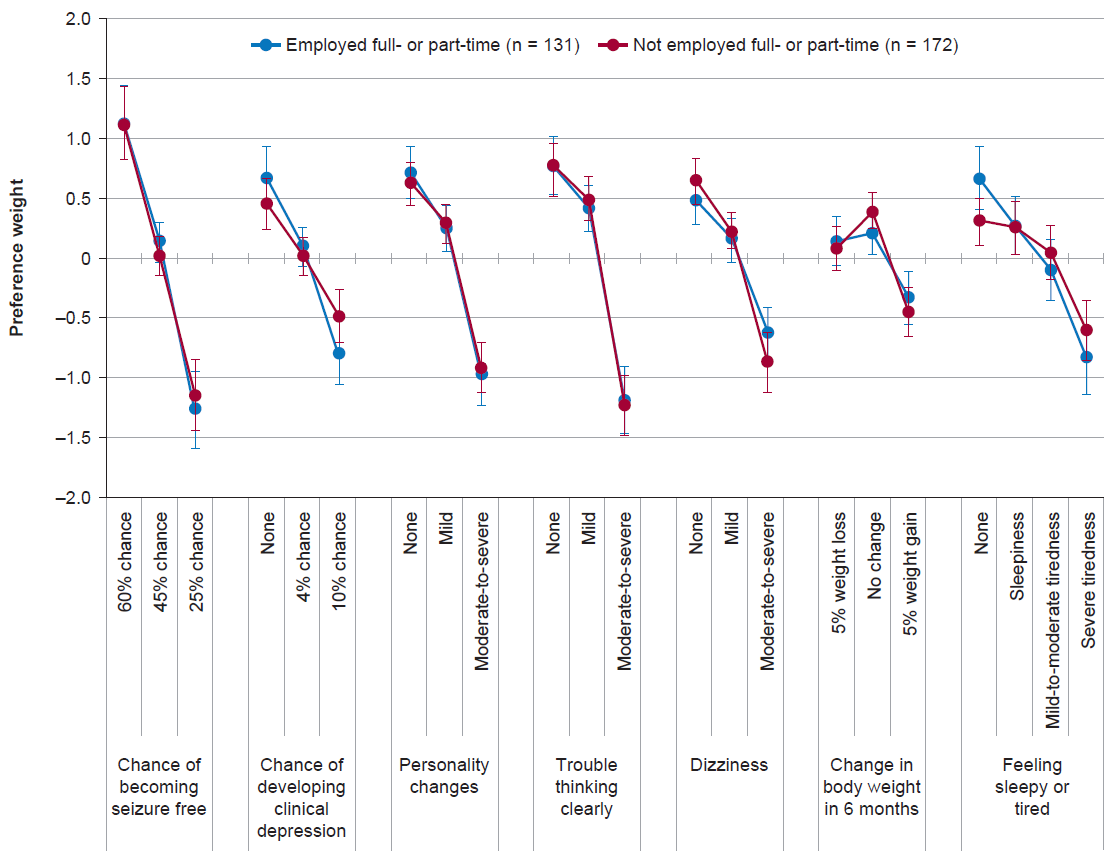
**FIGURE S2** Post hoc subgroup analysis of patient preference weights based on a discrete choice experiment survey before treatment consultation, random parameters logit model (Enrolled Set [ES], *n* = 305a), by country Error bars represent 95% confidence intervals. aAlthough the ES included 310 patients, five patients did not complete the survey before the consultation.

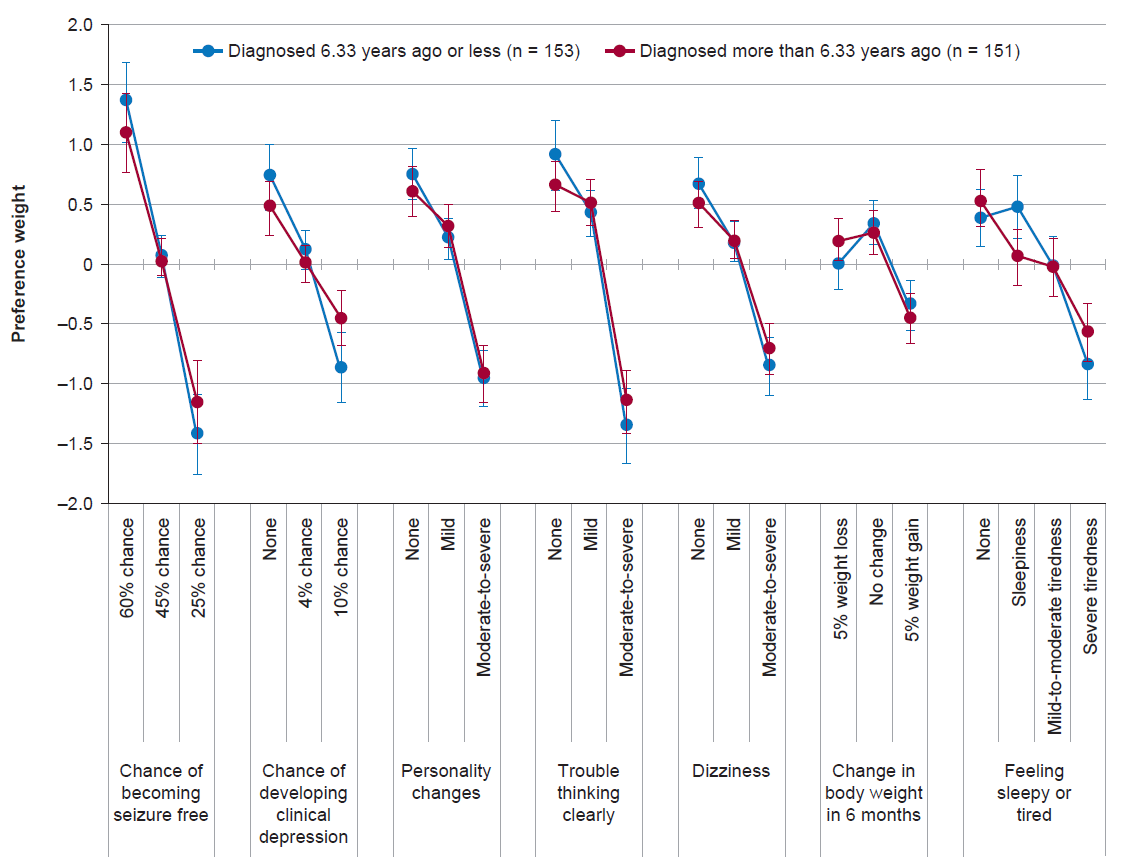
**FIGURE S3** Post hoc subgroup analysis of patient preference weights based on a discrete choice experiment survey before treatment consultation, random parameters logit model (Enrolled Set [ES], *n* = 305a), by age (<65 years vs. ≥65 years) Error bars represent 95% confidence intervals. aAlthough the ES included 310 patients, five patients did not complete the survey before the consultation.

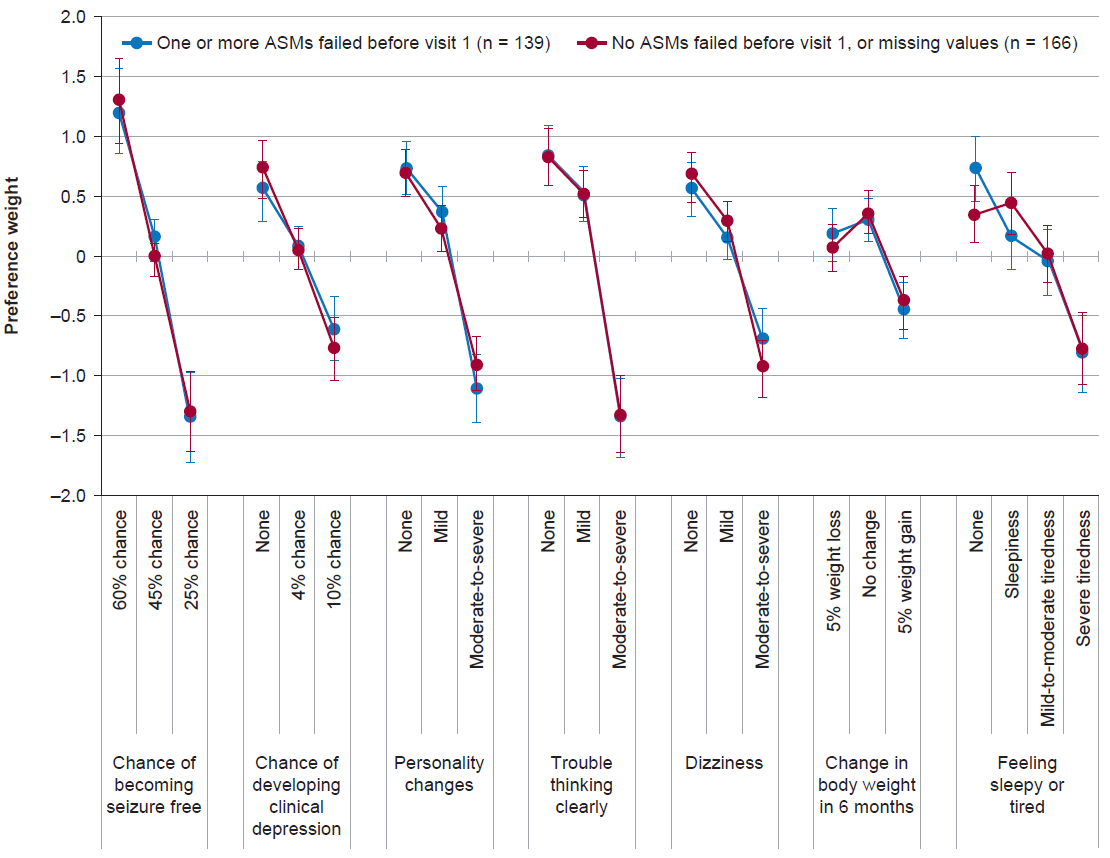
**FIGURE S4** Post hoc subgroup analysis of patient preference weights based on a discrete choice experiment survey before treatment consultation, random parameters logit model (Enrolled Set [ES], *n* = 305a), by age (≤45 years vs >45 years) Error bars represent 95% confidence intervals. aAlthough the ES included 310 patients, five patients did not complete the survey before the consultation.

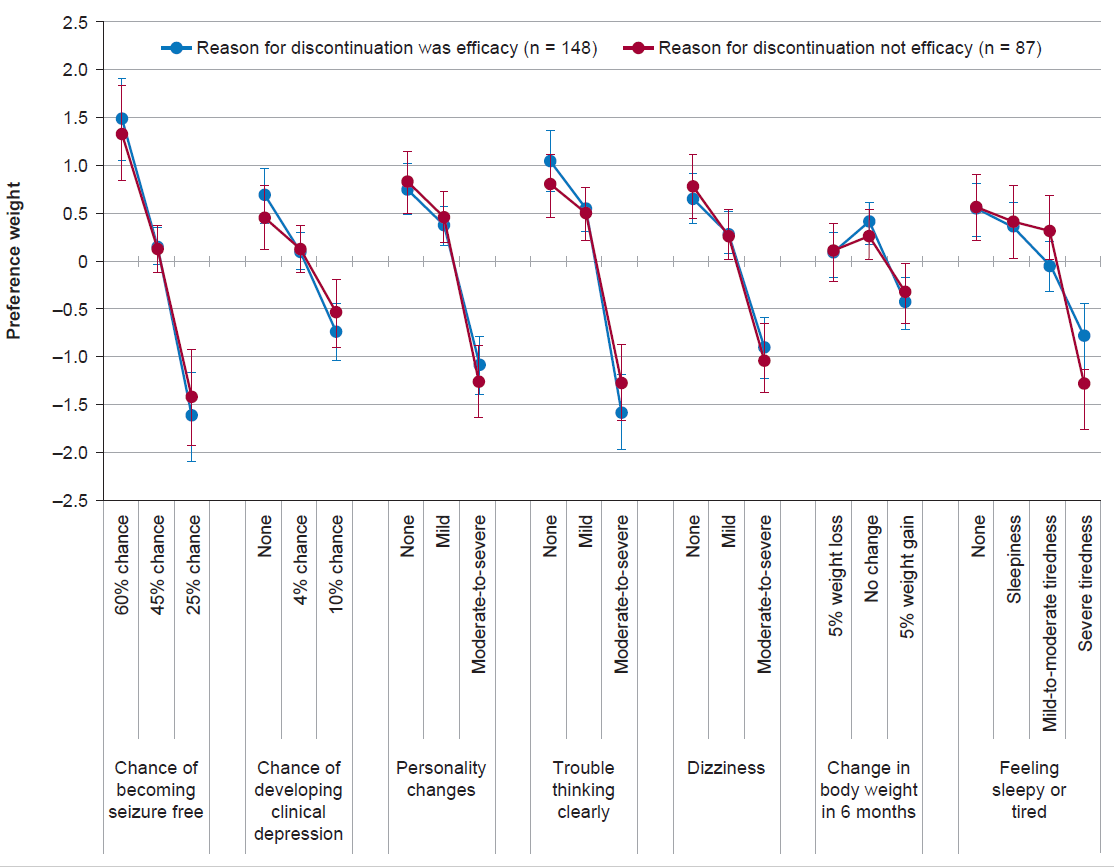
**FIGURE S5** Post hoc subgroup analysis of patient preference weights based on a discrete choice experiment survey before treatment consultation, random parameters logit model (Enrolled Set [ES], *n* = 305a), by sexError bars represent 95% confidence intervals. aAlthough the ES included 310 patients, five patients did not complete the survey before the consultation.

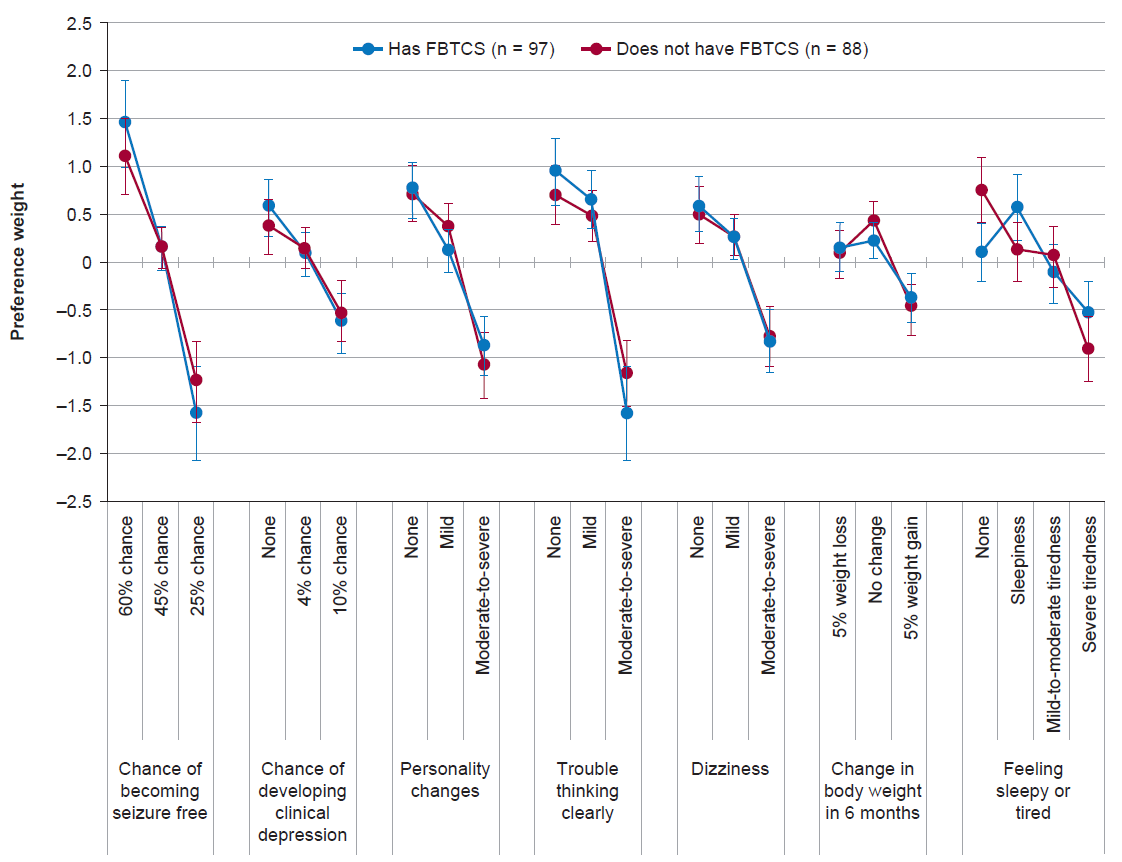
**FIGURE S6** Post hoc subgroup analysis of patient preference weights based on a discrete choice experiment survey before treatment consultation, random parameters logit model (Enrolled Set [ES], *n* = 303a), by education levelError bars represent 95% confidence intervals. aAlthough the ES included 310 patients, five patients did not complete the survey before the consultation, and the total subgroup sample size is <305 due to missing data.

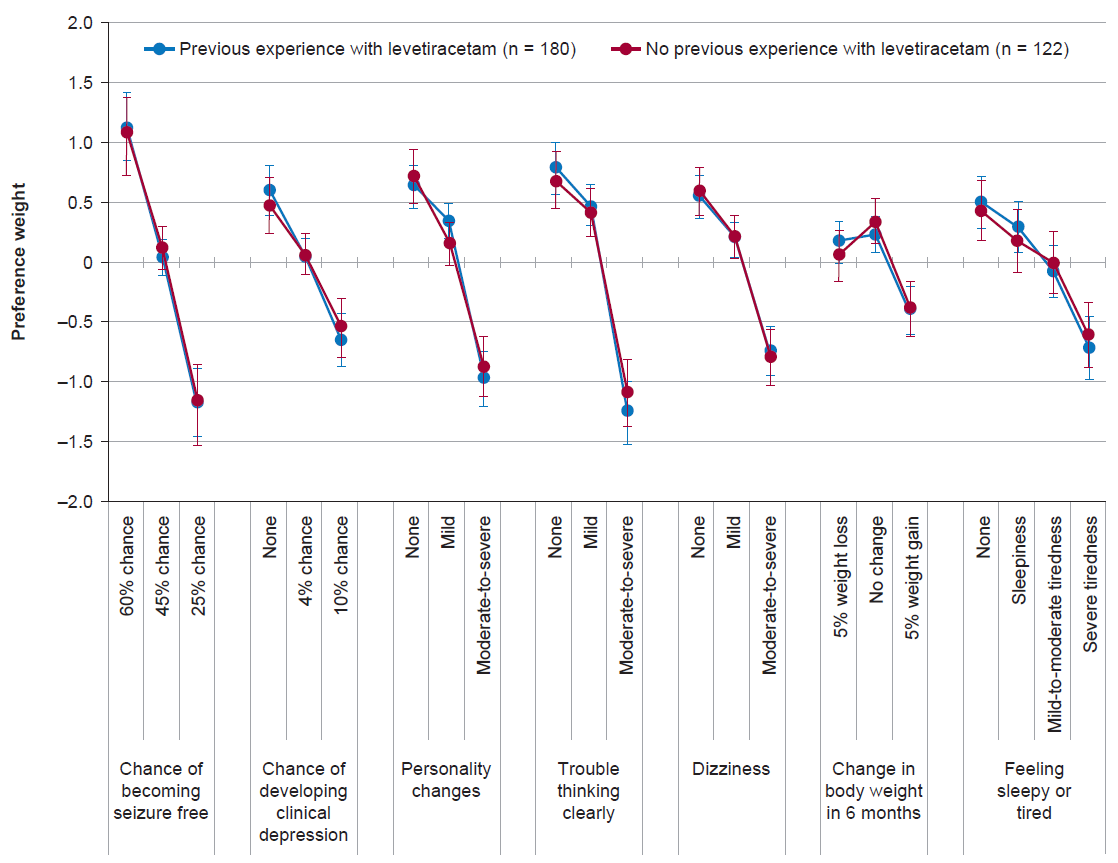
**FIGURE S7** Post hoc subgroup analysis of patient preference weights based on a discrete choice experiment survey before treatment consultation, random parameters logit model (Enrolled Set [ES], *n* = 303a), by employmentError bars represent 95% confidence intervals. aAlthough the ES included 310 patients, five patients did not complete the survey before the consultation, and the total subgroup sample size is <305 due to missing data.

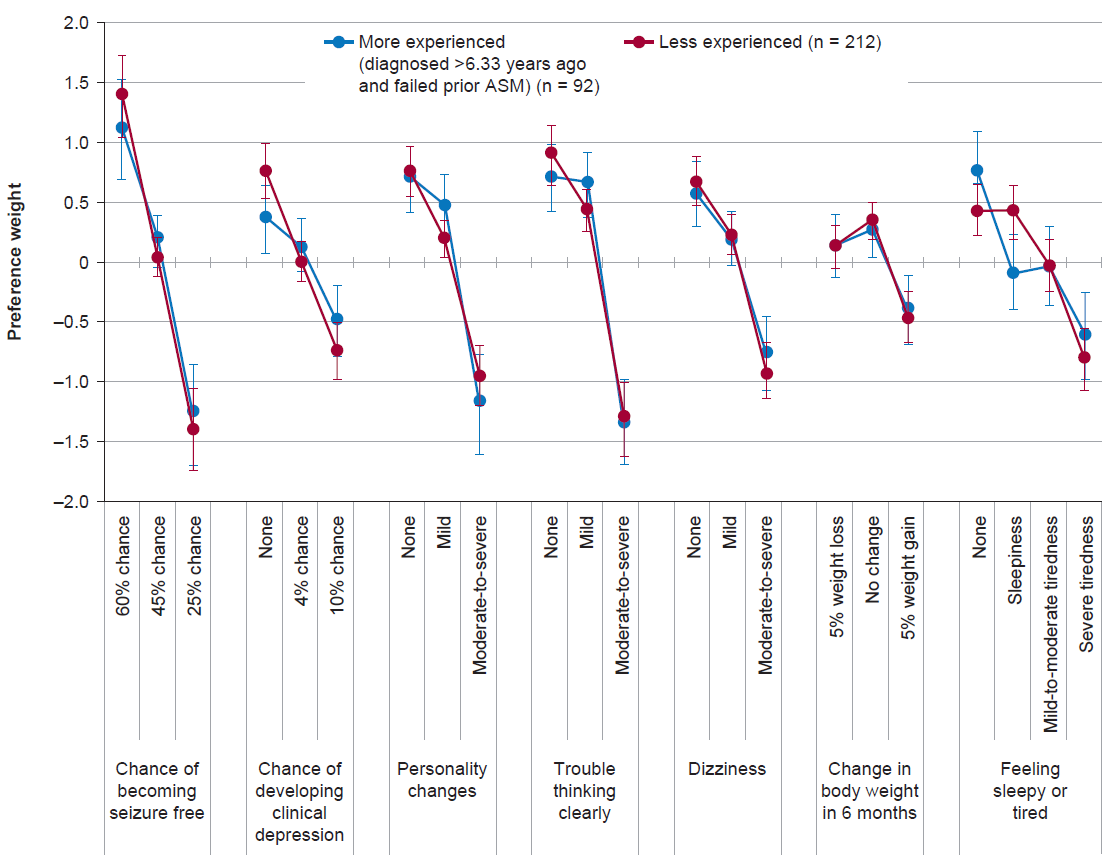
**FIGURE S8** Post hoc subgroup analysis of patient preference weights based on a discrete choice experiment survey before treatment consultation, random parameters logit model (Enrolled Set [ES], *n* = 304a), by time since epilepsy diagnosis Error bars represent 95% confidence intervals. aAlthough the ES included 310 patients, five patients did not complete the survey before the consultation, and the total subgroup sample size is <305 due to missing data.

**FIGURE S9** Post hoc subgroup analysis of patient preference weights based on a discrete choice experiment survey before treatment consultation, random parameters logit model (Enrolled Set [ES], *n* = 305a), by failed ASMsbError bars represent 95% confidence intervals. aAlthough the ES included 310 patients, five patients did not complete the survey before the consultation. bPrevious ASMs with a documented reason for discontinuation. ASM, antiseizure medication.

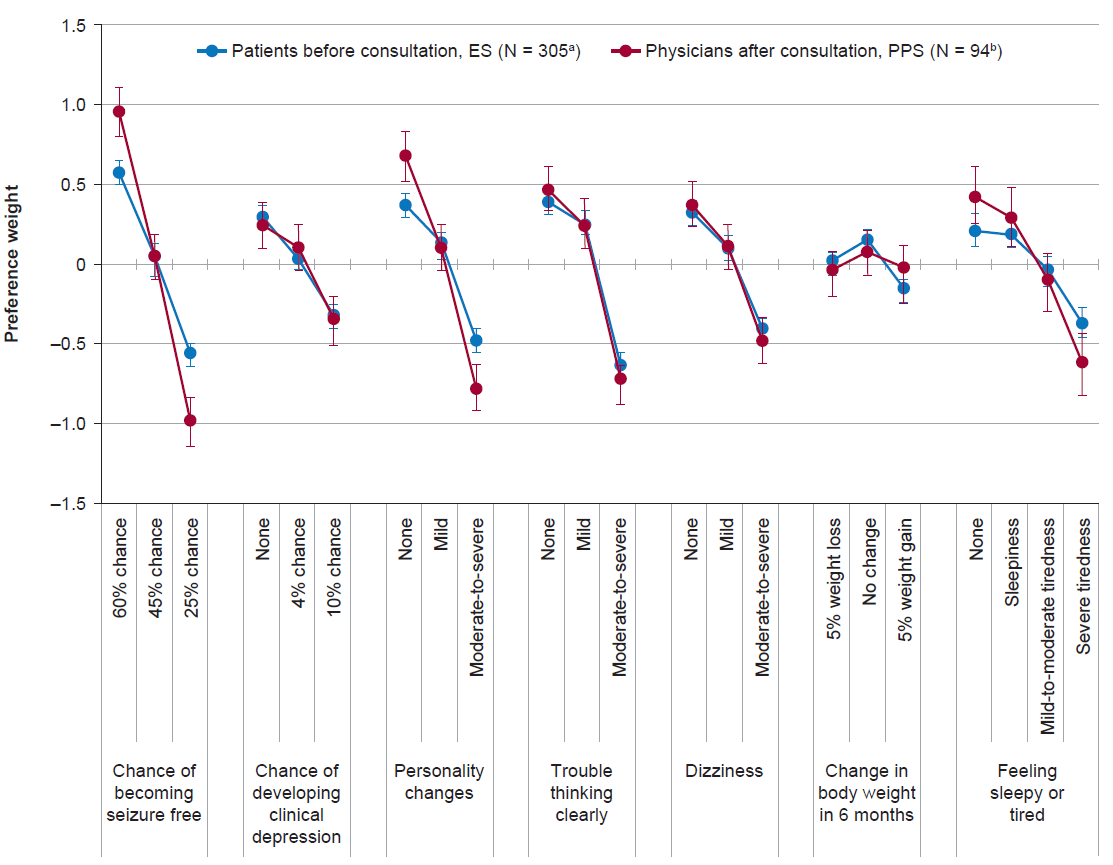
**FIGURE S10** Post hoc subgroup analysis of patient preference weights based on a discrete choice experiment survey before treatment consultation, random parameters logit model (Enrolled Set [ES], *n* = 235a), by reason for discontinuation of previous ASMs Error bars represent 95% confidence intervals. aAlthough the ES included 310 patients, five patients did not complete the survey before the consultation, and the total subgroup sample size is <305 due to missing data. ASM, antiseizure medication.

**FIGURE S11** Post hoc subgroup analysis of patient preference weights based on a discrete choice experiment survey before treatment consultation, random parameters logit model (Enrolled Set [ES], *n* = 185a), by seizure typeError bars represent 95% confidence intervals. aAlthough the ES included 310 patients, five patients did not complete the survey before the consultation, and the total subgroup sample size is <305 due to missing data. FBTCS, focal to bilateral tonic-clonic seizures.

**FIGURE S12** Post hoc subgroup analysis of patient preference weights based on a discrete choice experiment survey before treatment consultation, random parameters logit model (Enrolled Set [ES], *n* = 302a), by levetiracetam experienceError bars represent 95% confidence intervals. aAlthough the ES included 310 patients, five patients did not complete the survey before the consultation, and the total subgroup sample size is <305 due to missing data.

**FIGURE S13** Post hoc subgroup analysis of patient preference weights based on a discrete choice experiment survey before treatment consultation, random parameters logit model (Enrolled Set [ES], *n* = 304a), by patient experience Error bars represent 95% confidence intervals. aAlthough the ES included 310 patients, five patients did not complete the survey before the consultation, and the total subgroup sample size is <305 due to missing data. ASM, antiseizure medication.

**FIGURE S14** Patient and physician preferences based on a discrete choice experiment survey, conditional multinomial logit model



aAlthough the ES included 310 patients, five patients did not complete the survey before the consultation. bForty-nine physicians completed a total of 94 surveys (each physician completed the survey for up to three patients). ES, Enrolled Set; PPS, Physician Preference Set.

## Investigator appendix

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