Investigating Patients’ Preferences to Inform Drug Development Decisions: Novel Insights From a Discrete Choice Experiment in Migraine

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Abstract

**Background:** Chronic conditions have important long-term consequences for patients’ personal and social lives and require patient commitment to their management. In this context, the assessment of patients’ preferences for treatment characteristics would increase the current evidence on the impact of diseases to support decision-making processes in the field of public policies and research and development in pharmaceutical industries.

The present study used cases of chronic migraine to assess patients’ preferences, including the analysis of gender differences, for the characteristics of an ideal migraine treatment.

**Methods:** A discrete choice experiment was performed with 466 adults with migraine in Italy who experienced at least 4 attacks per month. We investigated the preferences of patients with respect to five treatment attributes that were identified from a systematic literature review and two focus group elicitations. The heterogeneity of preferences was investigated in a mixed logit model with normally distributed random coefficients.

**Results:** Overall, the respondents considered the presence of adverse events, duration of the treatment effect, reduction of symptom intensity, speed of the effect and the cost born by the patient as the most relevant treatment features. As expected, the patients preferred treatments with lower levels of adverse events and costs and treatments with greater speed, duration of treatment effect and effectiveness in reducing symptom intensity. There was significant preference heterogeneity only for the presence of adverse events. Compared to men, women had significantly higher preferences for quicker treatment effect and limited adverse events and reported higher preferences for costly treatments.

**Conclusions:** The results of our survey help address research and development strategies in the pharmaceutical industry and public policy regarding treatments that are clinically effective and responsive to the needs expressed by patients.

**Background**

Pharmaceutical companies are continuously investing in the research and development of products that are supposed to meet the needs of patients, physicians and payers while adhering to regulatory requirements. The development of a treatment to help improve patients’ lives should be rooted in a solid understanding of the challenges these patients face in their daily activities, their needs and the compromises they are willing to make to obtain relief. To ensure the creation of valuable treatments, all aspects of the healthcare system and treatment decisions need to be aligned with the needs of patients (1). At present, there are limited data describing the scope and overall benefit of existing patient-centred drug development activities (2), and the assessment of patients’ preferences for treatment characteristics in this setting would increase the current evidence on the impact of diseases to support decision-making processes in the field of public policies and research and development in pharmaceutical industries.

Investigating patients’ preferences is essential to inform these decisions for all diseases, but it appears to be particularly important for chronic conditions that require patient commitment to their management, and this
has important long-term consequences for patients’ personal and social lives. Chronic migraine may be considered a paradigmatic example in this respect.

Available data estimate that approximately 12% of adults worldwide develop some form of migraine throughout their lives (3, 4). Migraine is generally classified into episodic migraine (4 to 14 days of migraine a month) and chronic migraine (≥ 15 days of migraine per month). Women are most affected by migraine. In Italy, 6 million people suffer from migraines, and 4 million of the affected are women. Considering the plurality of costs associated with the management of the disease; migraine also has a significant socio-economic weight (5).

The literature includes different studies that evaluated patient preferences for migraine treatment characteristics. A few studies focused on specific treatments such as triptans (6, 7), while other studies focused on preventive treatments only (8, 9). Most studies used ad hoc surveys to investigate patient preferences, but only two implemented discrete choice experiments (9, 10), which allowed the assessment of the relative importance of different attributes. The studies in general were not limited to individuals with migraine but included patients with headache and did not consider gender differences in treatment preferences.

The available evidence highlights that both episodic and chronic migraine present a high social burden and represent an “unmet need” for public health that requires particular attention. Although there is increasing evidence supporting the role of gender in epidemiology and diagnosis, the identification of gender differences in migraine treatment and related efficacy is basically ignored (11). In the presence of a disease that primarily affects women, gaps remain in gender-specific research at preclinical and clinical levels. The same gap occurs in the drug development process, which does not generally consider patient preferences and differences based on gender (12).

The current study expands the existing literature on patient preferences for an ideal treatment for migraine to overcome the identified gaps by considering the specific population of individuals with migraine, applying a solid methodology and investigating gender differences and heterogeneity in these preferences. We employed a discrete choice experiment (DCE) methodology to investigate the preferences of a heterogeneous group of patients for different characteristics of a hypothetical but realistic therapeutic regime for migraine. The ultimate aim is to improve the existing body of knowledge and provide an evidence base to inform patient-centred policies and the research and development decisions made by pharmaceutical industries.

**Methods**

To evaluate the preferences of individuals with migraine for treatments characteristics and evaluate how socio-economic characteristics, particularly gender, may influence those preferences, a DCE was implemented (13). The DCE was performed to identify and estimate the relative importance assigned to different characteristics of a hypothetical treatment for migraine.

DCE is a technique to elicit preferences, which is based on the fact that goods or interventions may be described according to their characteristics (or attributes), and each attribute is represented by a defined number of dimensions, called attribute levels, on which the preferences of individuals for these goods depend.
A DCE consists of the presentation of two or more hypothetical scenarios, created by combining attribute levels, to participants who choose among a number of alternative options. Respondents trade-off between the attributes during the decision-making process and select the preferred option. The choices of the respondents indicate the preference or utility attached to a good or intervention and its attributes.

Development of DCE attributes and associated levels

A systematic literature research was performed in March 2018 to retrieve the available evidence on the preferences of patients for the main features of migraine treatments. This preliminary activity allowed the identification of a possible list of treatment characteristics for further investigation via a discussion with a sample of individuals with migraine (see Appendix 1 for details).

The search query led to the selection of 14 studies that contained information about patient preferences that were measured on the basis of more or less structured questionnaires to understand which characteristics of a treatment they considered most important. The population considered was mostly composed of patients with migraine, without distinction based on type (chronic or episodic). The treatment characteristics considered in the various published studies were resolution of symptoms (32%), efficacy (speed of effect, no recurrences, delay in the attack, and persistence of effect) (30%), adverse events (14%), return to daily activities (11%), formulation (11%), and cost (3%). Although these studies investigated both genders, no differences in preferences emerged.

After collecting the available evidence in the international literature, we organized two focus groups to evaluate the characteristics of a hypothetical treatment that the patients considered most relevant in the national context. The focus group was a group interview led by a moderator who followed a structured outline and proposed stimuli to the participants. The idea behind this method is that the considerations or evaluations expressed by each of the participants elicit reactions, comments and reflections from the others, which activates a spontaneous and intense discussion that leads to the sharing of further and more in-depth considerations. Each focus group lasted two hours and involved 8 adult patients who suffered from migraine with an average number of attacks per month greater than or equal to 4 (group 1: mean age 49 years, 37% males; group 2: mean age 45 years, 50% males). The focus group discussion started with the presentation of the participants with their personal characteristics of migraine and with the sharing of treatment features studied in the literature and derived by the literature search. After interactive discussion, each participant rated the treatment features from the most important to the less important. The following five most important characteristics were considered by the participants in the two focus groups:

1. speed of effect (how quickly the treatment relieves the symptoms)
2. reduction in the intensity of symptoms (efficacy-strength)
3. duration of effect (efficacy-duration)
4. adverse events
5. cost born by the patient
Concerning the quantification of the levels of variation of these attributes, the participants reported that the effectiveness, in terms of speed in achieving the effect, should ideally be within 30 minutes of drug administration. Times from 30 to 90 minutes were acceptable, while times over 3 hours were considered excessive. Regarding the efficacy of the treatment in terms of intensity of symptom reduction, acceptable levels were approximately 50%, with ideal values of symptom reduction of at least 90%. Patients believed that the effectiveness of the treatment should ideally last all day, or at least for 8 hours, considering the workday. Furthermore, patients specified the possible side effects (i.e., tachycardia, drowsiness, daze, tingling, gastrointestinal effects) and the preference for treatments with limited adverse events. Regarding the cost born by patients to purchase an ideal treatment, patients found a cost of €50 per month acceptable, but they would be willing to bear a cost of up to €200 per month to have resolution of all symptoms related to migraine. Table 1 reports the summary of attributes and levels discussed during the focus groups. Adverse events severity was classified according to FDA Adverse Event Reporting System (FAERS) (27).

| Attribute / Levels                  | Level 1 | Level 2 | Level 3 | Level 4 |
|------------------------------------|---------|---------|---------|---------|
| Speed of effect (minutes)          | 30      | 80      | 130     | 180     |
| Efficacy-strength                  | 60%     | 70%     | 80%     | 90%     |
| Efficacy-duration (hours)          | 4       | 6       | 8       | 10      |
| Adverse events                     | mild    | moderate| severe  | very severe |
| Monthly cost born by the patient   | €50     | €100    | €150    | €200    |

**Experimental design**

After the elicitation of attributes and associated levels, a DCE with three choice alternatives, (i.e., two alternative choices and an opt-out option) was developed. Inclusion of an opt-out was deemed necessary because forcing respondents to make a choice on a treatment can lead to an over-estimation of the utility for parameters (28). The opt-out option, corresponding to “no treatment” was associated with zero speed of effect, zero percent of symptoms reduction, no duration of effect, no presence of adverse events and no cost born by the patient.

The choice sets were combined using Ngene software (29). From a full factorial design, an optimal orthogonal in the differences (OOD) design (30) was derived by considering the total number of choices between alternatives equal to 100 (D-optimality = 92.5%). The Ngene software was set to impose design restrictions to ensure that no alternative dominated the other within each choice set. The choice sets were grouped into five blocks. Each block comprised 20 choice sets, ordered differently across blocks. A sample size of minimum of 250 respondents was identified for parameter estimations for the DCE, and the blocks were distributed randomly among them (31). Design blocking, restrictions and creating provisions were done for the estimation of only main effects because all of these factors represent potential threats to statistical efficiency. However, these strategies were used to minimize design complexity, reduce cognitive burden, and enhance response efficiency.
2. Data collection

A questionnaire representing the choice set was administered online in October-November 2018 to a sample of 466 adult patients suffering from migraine with an average number of attacks per month greater than or equal to 4 (see Appendix 2). The web survey was implemented by an external company (Pepe Research https://www.peperesearch.it) which selected respondents from its own database according to the characteristics described above. The survey was pre-tested online on a sample of 27 respondents, who had the chance to report possible comprehension problems and difficulties in the questionnaire completion. This phase did not identify possible comprehension problems or difficulties in executing the tasks.

The following data categories were collected:

- socio-demographic characteristics;
- education level, professional status, net annual income;
- duration of the single migraine attack;
- type of migraine (with or without aura); and
- average number of attacks per month.

The e-survey presented an explanation of the scope of the interview, a description of the different levels and attributes and 20 choices among the three alternatives. Each attribute was carefully explained using patient-friendly language. In order to simulate a clinically relevant decision context we clarified in the questionnaire that patients had to choose only on the basis of the available given information and we explicitly specified an opt-out condition in line with good practice recommendations.

The participants’ task was to evaluate two alternatives (A and B) and the opt-out option (alternative C, no treatment) in each choice set and choose the option that reached the preference from their point of view. An example of a scenario with the choice of three alternatives is reported in Fig. 1.

| Attributes                             | Alternative A | Alternative B | Alternative C (no treatment) |
|----------------------------------------|--------------|--------------|------------------------------|
| Speed of effect (minutes)              | 30           | 80           | 0                            |
| Efficacy-strength (% of symptoms reduction) | 90           | 60           | 0                            |
| Duration of the effect (hours)         | 4            | 6            | 0                            |
| Presence of adverse events             | very severe  | mild         | no adverse events            |
| Monthly cost born by the patient (€)   | 100          | 150          | 0                            |

Figure 1 – Example of choice set

At the end of the survey, 5 questions investigated the importance of the considered attributes (see Table 1) through a Likert scale with 5 levels (not at all important, not very important, quite important, very important, extremely important). One question investigated the difficulties experimented during the choices among the
proposed alternatives, and the possible responses were no difficulties, few difficulties, moderate difficulties, many difficulties and extreme difficulties.

**Data analysis**

Respondent characteristics and responses were summarized using descriptive statistics. The DCE choices were first reviewed to determine whether respondents exhibited dominant preferences (i.e., frequently selected the testing alternative with the best level of a particular attribute) and in which cases the respondents chose the “opt-out” option. For each respondent, dominance scores were calculated for each attribute; a score of 1 was assigned for each question in case the respondent chose an attribute at its best level (e.g., maximum power of the effect, minimum cost, etc.). Therefore, a maximum score equal to 20 for an attribute was assigned to a respondent who showed dominant preferences on this attribute for all 20 questions.

The DCE data were analysed within a random utility maximization framework (32, 33), and a mixed logit regression analysis was used to construct a model of choice behaviour. This approach accommodated the existence of preference heterogeneity—which was anticipated in this sample population—by allowing for variation in the coefficient values across individual respondents. In practical terms, this means that standard deviations were generated to quantify preference heterogeneity for attributes and attribute levels (34).

The following model of choice behaviour (Model 1) was used to evaluate the impact of different attributes and levels on the preferences for alternative treatment approaches (35):

\[ U_{ij} = \beta_1 \text{ (speed)} + \beta_2 \text{ (efficacy)} + \beta_3 \text{ (duration)} + \beta_4 \text{ (adverse events)} + \beta_5 \text{ (cost)} + \varepsilon_{ij} \]

Where \( U_{ij} \) is the utility individual \( i \) derives from choosing alternative \( j \) in choice situation \( s \), \( \beta_1 - \beta_5 \) are the coefficients of preference weights reflecting the desirability of the attributes, and \( \varepsilon_{ij} \) is the error term assumed independent and identically distributed as an extreme value (random component).

The output of a mixed logit model includes the means and standard deviations (SDs) of random coefficients and their respective confidence intervals (CIs). The mean coefficients represent the relative utility of each attribute conditional on other attributes, and the SDs reflect the degree of heterogeneity among the respondents.

In DCE models, trade-offs between attributes are quantified using marginal rates of substitution (MRS), which measure what amount of an attribute individuals are willing to trade against a decrease in another attribute (36). This measurement provides insight into the relative importance of different treatment attributes for the individual. The inclusion of a cost item among the attributes allows the estimation of MRS in monetary terms, which is known as willingness to pay (WTP). WTP is interpreted as an estimate of the relative values assigned to an attribute included in the choice set, and it is expressed in monetary terms. A WTP analysis was performed starting from the results of the regression analyses for Model 1 and males and females separately. We calculated the WTP for nonmonetary attributes as the ratio of the cost coefficient and mean coefficients for the attributes. The WTP for the treatment attributes was calculated in the overall sample and patient subgroups defined by gender.
We extended the baseline model to examine the drivers of response heterogeneity. More specifically, to investigate the extent to which preferences were driven by a patient’s socio-economic characteristics, gender and age in particular, Model 1 was extended to Model 2, which considered interactions between attributes and respondents’ characteristics. For this model, continuous (i.e., age) and categorical (gender) interaction variables were considered.

The random parameters for all attribute levels were estimated assuming a normal distribution. The Akaike information criterion (AIC) was applied to compare the goodness of fit and to test the extended model against the model with no interactions.

Data analyses were undertaken using Stata (StataCorp. 2019. Stata Statistical Software: Release 15. College Station, TX: StataCorp LP).

Results

All of the 466 participants who enrolled completed the e-survey. The participants had an average age of 43 years (range 18–77), and 66% were women. A statistically significant difference emerged for age between the two genders, with males being older than females (45 years vs. 41 years). Working respondents reported that they had a full-time job in most cases (72%). The annual income ranges were equally distributed over the total number of respondents. Only 7% of respondents preferred to not declare their income. Statistically significant differences emerged between the genders for declared income, with lower incomes for females, who also reported less remunerative working roles.

Considering the characteristics of migraine, females showed a greater and significant duration of attack than males (duration greater than or equal to 4 hours: 70% vs. 49%). Aura affected more females than males (45% vs. 35%).

The socio-demographic characteristics of the sample, including disease characteristics, are summarized in Table 2.
Table 2
– Socio-demographic characteristics of the sample of respondents with the characteristics of migraine

| Parameter                                      | Total population | Males  | Females | P-value |
|------------------------------------------------|------------------|--------|---------|---------|
| Gender                                         | 466              | 159 (34%) | 307 (66%) |         |
| Mean age (years)                               | 43 (18–77)       | 45     | 41      | <0.0001 |
| **Education level**                            |                  |        |         |         |
| Primary school                                 | 8%               | 6%     | 9%      | 0.62    |
| High school diploma                            | 52%              | 54%    | 51%     |         |
| Bachelor’s degree                              | 14%              | 12%    | 15%     |         |
| Master’s degree                                | 21%              | 22%    | 20%     |         |
| Doctorate                                      | 6%               | 7%     | 5%      |         |
| **Professional activity**                      |                  |        |         |         |
| White collar                                   | 62.00%           | 78.60% | 53.50%  | <0.0001 |
| Blue collar                                    | 8.80%            | 12.60% | 6.80%   |         |
| Retiree                                        | 2.60%            | 2.50%  | 2.60%   |         |
| Homemaker                                      | 13.50%           | 1.90%  | 19.50%  |         |
| Student                                        | 5.40%            | 0.60%  | 7.80%   |         |
| Unemployed                                     | 7.70%            | 3.80%  | 9.80%   |         |
| **Income ranges declared by the workers (annual net)** |                  |        |         |         |
| Less than €15.000                              | 21%              | 10%    | 29%     | <0.0001 |
| €15.000 - €19.999                              | 21%              | 14%    | 26%     |         |
| €20.000 - €29.999                              | 30%              | 36%    | 26%     |         |
| €30.000 or more                                | 28%              | 40%    | 19%     |         |
| **Duration of migraine attack, frequency and symptoms** |                  |        |         |         |
| Few minutes                                    | 2%               | 4%     | 2%      | <0.0001 |
| Up to 3 hours                                  | 35%              | 47%    | 28%     |         |
| From 4 to 24 hours                             | 43%              | 41%    | 45%     |         |
| 2–3 days                                       | 20%              | 8%     | 25%     |         |
| Average number of attacks per month            | 7.2              | 7.5    | 7.0     | 0.85    |
| Number of attacks per month from 4 to 8        | 76%              | 72%    | 78%     | 0.339   |
| Number of attacks per month from 9 to 15       | 19%              | 23%    | 18%     |         |
| Parameter                                      | Total population | Males | Females | P-value |
|-----------------------------------------------|------------------|-------|---------|---------|
| Number of attacks per month higher than 15    | 5%               | 6%    | 5%      |         |
| Presence of aura                              | 42%              | 35%   | 45%     | 0.037   |

Regarding DCE, the participants reported 9,320 responses (20 questions each), with a significantly high number of cases (38%) in which respondents chose the opt-out option. In addition, 25% of respondents reported having encountered moderate to extreme difficulty in choosing among the alternatives.

The analysis of dominant preferences revealed that only 8 respondents expressed dominant preferences (score = 20) for the presence of adverse events, 7 for speed of effect and 7 for cost. The dominant preferences of other attributes were limited. The overall pattern of results suggests that the presence of side effects, speed of effect and the cost born by the patients were the most important factors for respondents in deciding which treatment they would select.

The full results of mixed logit models are presented in Table 3.

In Model 1, all the attributes significantly impacted the probability of choosing an alternative (p-values < 0.05). The negative sign of the coefficient for speed of effect (-0.00328) indicates that as the time to obtain a treatment effect increased, the patients' likelihood of choosing this scenario decreased. The same results were found for adverse events and cost. In contrast, respondents preferred higher levels for strength of efficacy and duration of effect. Only the presence of adverse events showed a significant preference heterogeneity (standard deviation p-value = 0.003). These results are consistent with the indications received during the focus groups.

In Model 2, all the attributes ($\beta_1 - \beta_5$) significantly impacted the probability of choosing an alternative. The presence of adverse events maintained heterogeneity in the preferences (standard deviation p-value = 0.007).
Table 3
Results of the mixed logit Models 1 and 2

| Attributes                                | Model 1          |                       |                       | Model 2          |                       |                       |
|-------------------------------------------|------------------|-----------------------|-----------------------|------------------|-----------------------|-----------------------|
|                                           | Mean coefficient | Standard              | Mean coefficient     | Standard         | Mean coefficient     | Standard              |
|                                           | values           | deviations            | values               | deviations       | values               | deviations            |
|                                           | β                | p-value               | β                    | p-value          | β                    | p-value               |
| Speed of effect (minutes)                 | -0.0033          | < 0.00001             | 0.0005               | 0.8500           | -0.0018              | 0.1830                |
| Efficacy-strength (% of symptoms reduction) | 0.0242           | < 0.00001             | 0.0002               | 0.9030           | 0.0244               | < 0.00001             |
| Duration of the effect (hours)            | 0.0891           | < 0.00001             | -0.0008              | 0.9680           | 0.0903               | 0.0070                |
| Presence of adverse events                | -0.7580          | < 0.00001             | -0.2012              | 0.0030           | -0.4484              | < 0.00001             |
| Monthly cost born by the patient (€)      | -0.0054          | < 0.00001             | 0.0009               | 0.5220           | -0.0046              | 0.0010                |
| Female*speed of effect                    |                  |                       | -0.0037              | < 0.00001        |                       |                       |
| Female*efficacy-strength                  |                  |                       | 0.0037               | 0.0670           |                       |                       |
| Female*duration of the effect (hours)     |                  |                       | 0.0237               | 0.1280           |                       |                       |
| Female*presence of adverse events         |                  |                       | -0.3346              | < 0.00001        |                       |                       |
| Female*monthly cost born by the patient   |                  |                       | 0.0012               | 0.0690           |                       |                       |
| Age*speed of effect                       |                  |                       | 0.0000               | 0.5960           |                       |                       |
| Age*efficacy-strength                     |                  |                       | 0.0000               | 0.7310           |                       |                       |
| Age*duration of the effect (hours)        |                  |                       | -0.0003              | 0.6850           |                       |                       |
| Age*presence of adverse events            |                  |                       | -0.0031              | 0.0660           |                       |                       |
| Age*monthly cost born by the patient      |                  |                       | 0.0000               | 0.1600           |                       |                       |
| Attributes                              | Model 1                          | Model 2                          |
|----------------------------------------|----------------------------------|----------------------------------|
|                                        | Mean coefficient values          | Mean coefficient values          |
|                                        | Standard deviations              | Standard deviations              |
|                                        | β                                | p-value                          | β                                | p-value                          |
|                                        |                                  |                                  |                                  |                                  |
| N. observations                       | 27,681                           | 27,681                           |
| N. of respondents                     | 466                              | 466                              |
| Log-likelihood                        | -8664                            | -8550                            |
| Akaike information criterion (AIC)    | 17,338                           | 17,114                           |

Gender interactions were statistically significant for speed of effect, presence of adverse events and cost. The results revealed that, compared to men, women had significantly higher preferences for quicker treatment effect and the presence of limited adverse events, and they reported higher preferences for more costly treatments. Age did not seem to influence the preferences of patients.

According to the Akaike information criterion, Model 2 showed a better fit than Model 1.

The WTP analysis performed on the base-case mixed logit model (Model 1) showed that respondents would be willing to pay €0.61 to anticipate the effect of the treatment by one minute, everything else being equal. Patients would be willing to pay €4.52, €16.66 and €141.68 to acquire a one percentage point increase in the strength of symptom reduction, for having an additional hour of effect duration and for de-escalating the adverse events, respectively, with everything else being equal. These results show that the reduction of adverse events is the most important dimension for which patients would be willing to pay the highest amount.

The WTP analysis performed separately on males and females showed a higher willingness to pay for women compared to men for all of the considered attributes (€0.98 vs. €0.18 to anticipate the effect of the treatment by one minute, €5.25 vs. €3.72 to gain a one percentage point increase in the strength of symptom reduction, €19.60 vs. €12.62 for having an additional hour of treatment effect duration, and €172.69 vs. €97.10 for de-escalating the adverse events).

The responses on the Likert scale were consistent with the results obtained in the DCE, and they confirmed the presence of adverse events as the most important treatment feature. The following other attributes, in order of importance, were efficacy-strength, speed of effect, duration of the effect and cost born by the patient (see Table 4).
Table 4
– Assessment of the importance of the considered attributes on the Likert scale

| Grading                  | Speed of effect | Efficacy-strength | Duration of the effect | Presence of adverse events | Monthly cost |
|--------------------------|-----------------|-------------------|------------------------|---------------------------|--------------|
| Extremely important      | 33.9%           | 30.0%             | 26.6%                  | 58.2%                     | 26.0%        |
| Very important           | 33.0%           | 40.6%             | 37.8%                  | 22.3%                     | 30.5%        |
| Quite important          | 28.5%           | 27.5%             | 31.1%                  | 14.6%                     | 32.6%        |
| Not very important       | 4.1%            | 1.7%              | 3.9%                   | 4.3%                      | 8.6%         |
| Not at all important     | 0.4%            | 0.2%              | 0.6%                   | 0.6%                      | 2.4%         |

**Discussion**

For many patients suffering from migraine, finding the right combination of clinical treatment and routine is a lifelong challenge. Where different treatment strategies are available, it is of the utmost importance to support the treatment choices of patients to improve their compliance with therapies.

The present study employed a DCE to investigate gender differences in preferences for a set of attributes of treatment for migraine. The key feature of the study model was the use of a mixed logit model that allowed us to account for heterogeneity in preferences driven by observable characteristics (primarily gender) and test for the existence of residual significant heterogeneity in non-observable characteristics.

The presence of adverse events, duration of the treatment effect, reduction of the intensity of the symptoms, speed of the effect, and cost born by the patient were, in that order, the attributes considered most relevant by the respondents. These data are consistent with our international literature review, which reported these five attributes as the most important in 79% of studies. These results are consistent with another DCE involving 510 patients with migraine in the USA (10), which investigated the severity and duration of symptoms in headache and post-headache phases, the limitation in activity and the chance of migraine attack recurrence. The study showed that hypothetical treatments that relieved and shortened symptoms during the post-headache phase offered significant benefits to individuals with migraine. The same results were found in another DCE study (9) that focused on migraine prevention, in which 72% of respondents rated treatment effectiveness as the most important aspect. The present study revealed that all the attributes significantly impacted the probability of choosing an alternative and that in general, respondents preferred lower levels for speed of effect (quick response), adverse events and cost and higher levels for strength of efficacy and duration of effect.

Only the presence of adverse events was associated with significant heterogeneity with respondents’ preferences. The interaction analysis also highlighted that compared to men, women had significantly higher preferences for quick treatment effect and the presence of limited adverse events and that women reported higher preferences for costly treatments. Women, who in general report a worse quality of life than men,
seemed willing to pay more than males to receive a more effective treatment. Age did not influence patients’ preferences.

As direct beneficiaries of health services, patients have a widespread awareness of the impact and the effects of a treatment on their condition and on different aspects of their life. The incorporation of patient preferences in the drug development process may be of paramount value. Different initiatives have started so far in order to integrate the patient’s voice into therapeutic development and regulatory review. An example is the Patient-Focused Drug Development (PFDD) initiative (37), which includes meetings that aim to help FDA understand the burden of disease from the patient perspective and to gain an appreciation for the factors that are taken into account by patients when a treatment is chosen. Similar developments started also in Europe, with the incorporation of patient preferences into the assessment of oncology treatments by the European Medicines Agency (EMA) (38). Again, the European Patients Academy on Therapeutic Innovation (EUPATI) (39) focused on education and training to increase the capacity and capability of patients to be valuable contributors to medicines research and development. The PREFER initiative, built upon the experiences and outcomes of previous projects and initiatives, aims at establishing recommendations to support development of guidelines for industry, Regulatory Authorities and HTA bodies on how and when to include patient perspectives on benefits and risks of medicinal products (40).

This study provides novel insight into this growing body of literature, but some limitations need to be recognized. First, involved patients were recruited via an online survey, and this population may be biased towards the ability to use a computer or a mobile device; moreover, only respondents with internet access were able to complete the questionnaire (41). Second, in the range of levels presented, a significant portion of the sample did not appear to use a trade-off between the attributes and chose the opt-out option in 38% of cases. Third, as a cross-sectional hypothetical experiment among respondents, the elicited preferences described in this study may change over time, especially once respondents experience different treatment strategies for migraine. Therefore, while the results are internally valid, generalizability beyond the study context cannot be explicitly guaranteed (42). However, these concerns not peculiar to our own study but represent general concerns pertaining to the application of stated preferences techniques (42).

Conclusions

To date, there is no resolutive treatment for migraine. Nausea, visual disturbances, and hypersensitivity to sounds, smells and light make the disorder more complex, and patients may not even be able to get out of bed on the worst days. Although the range of pharmacological opportunities in use today is being enriched, drug development activities are still not patient-centred and do not take into account patients’ preferences. The results of our survey can help address the research and development strategies of the pharmaceutical industry towards treatments that are clinically effective and responsive to the needs expressed by the patients.

Declarations

Ethics approval and consent to participate
The study has been approved by the Ethics Committee of Bocconi University (ref. n. 0068538, 08 May 2018).

Consent for publication

Not applicable.

Availability of data and materials

Data are available from the authors upon reasonable request.

Competing interests

The authors have nothing to disclose.

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Authors' contributions

RT, AT: Conceptualization; CR: Data curation; CR, AT: Formal analysis; RT: Funding acquisition; CR, AT: Investigation; RT, AT: Methodology; RT: Project administration; AT: Supervision; CR, AT, RT: Writing - review & editing.

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