Relevant factors for neurologists to define effectiveness of migraine preventive drugs and take decisions on treatment: My-LIFE European Delphi survey

Pozo-Rosich, P.; Gil-Gouveia, R.; Donnet, A.; Poole, A.C.; Gendolla, A.; Afridi, S.; ... ; Tassorelli, C.

Received: 15 March 2021 | Accepted: 24 June 2021

DOI: 10.1002/ejp.1831

ORIGINAL ARTICLE

EJP European Journal of Pain

Relevant factors for neurologists to define effectiveness of migraine preventive drugs and take decisions on treatment. My-LIFE European Delphi survey

Patricia Pozo-Rosich[1,2] | **Raquel Gil-Gouveia**[3] | **Anne Donnet**[4] | **Anne-Christine Poole**[5] | **Astrid Gendolla**[6] | **Shazia Afridi**[7] | **Rainel Sanchez-De la Rosa**[8] | **Gisela M. Terwindt**[9] | **Cristina Tassorelli**[10,11]

[1]Headache Unit, Neurology Department, Hospital Universitari Vall d'Hebron, Barcelona, Spain

[2]Headache Research Group, Vall d'Hebron Research Institute, Universitat Autònoma de Barcelona, Barcelona, Spain

[3]Headache Center, Neurology Department, Hospital da Luz, Lisboa, Portugal

[4]Pain Department, Timone Hospital, Marseille, France

[5]Private Practice: Oslo Headache Centre, Oslo, Norway

[6]Private Practice: Essen, Germany

[7]Headache Service, Department of Neurology, Guy's and St Thomas' NHS Trust, London, UK

[8]Region Europe Medical Department, Novartis Pharma AG, Basel, Switzerland

[9]Department of Neurology, Leiden University Medical Center, Leiden, The Netherlands

[10]Headache Science Center, IRCCS Mondino Foundation, Pavia, Italy

[11]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy

Correspondence
Patricia Pozo-Rosich, Hospital Universitari Vall d'Hebron, Passeig de la Vall d'Hebron, 119, 08035 Barcelona, Spain.
Email: ppozo@vhebron.net

Funding information
Novartis Pharma AG financially supported the development of this project, the medical

Abstract

Background: Clinical guidelines agree that preventive treatment should be considered in patients with uncontrolled migraine despite acute medications or patients with ≥4 migraine days per month. However, the criteria to define the effectiveness of treatment and the factors that inform the decision to (dis)continue it are not clearly defined in clinical practice.

Methods: Overall, 148 healthcare practitioners from five European countries completed a two-wave questionnaire. The Steering Committee defined a simulated set of 108 migraine patient profiles based on the combination of five factors (frequency of the attacks, intensity of the attacks, use of acute migraine medications, patient perception and presence/absence of tolerable side effects). These profiles were used in a Delphi survey among European neurologists to identify the criteria that should be used to decide treatment response and continuation using a conjoint analysis approach.

Results: Consensus was reached for 82/108 (76%) of profiles regarding treatment response, and for 86/108 (80%) regarding treatment continuation. Multivariable logistic regression analysis showed that a ≥50% reduction in the use of acute migraine medications and positive patient's perception of treatment were the most important factors that lead to the decision of continuing (combined factors, OR = 18.3, 95% CI 13.4–25.05).

Conclusions: This survey identifies two relevant outcome measures: one objective (use of acute migraine treatment medications) and one subjective (positive patient perception) that guide the clinician decision to continue preventive treatment in migraine patients.

Significance: In clinical practice, criteria to define the effectiveness of migraine preventive treatment and factors that guide treatment stop or continuation are not clearly defined. In this simulated clinical setting study, a reduction in the use of acute

writing assistance and the page processing charges for this article. The authors have received no payment to write this article.

migraine medications was the factor associated with preventive treatment effectiveness definition. This study also revealed that factors strongly associated with the decision of treatment continuation in real life are the acute migraine medications use and a positive patient's perception of treatment effectiveness.

1 | INTRODUCTION

Migraine affects 80.8 million individuals in Western Europe and more than 1.04 billion all over the world (Stovner et al., 2018), being the first cause of disability in people 15–49 years old worldwide (Steiner et al., 2018). In Europe, 33.8% of migraine patients reported >5 headache days/month (Katsarava et al., 2018). The intensity, duration and frequency of migraine attacks, as well as the overall impact on patient's life, can be significantly reduced with the appropriate use of acute and preventive treatments. However, migraine treatment is not straightforward, since it has to be patient-tailored and the response to preventive treatment is difficult to evaluate and not always complete and clear (American Headache Society (AHS), 2019; Serrano et al., 2017). To further complicate the situation, many of the available preventive treatments show limited tolerability, entailing long-term adherence issues (American Headache Society (AHS), 2019).

Addition of preventive treatment should be considered in all patients with uncontrolled migraine despite acute treatment, and in patients with frequent headaches, i.e., with 4 or more headache days per month (American Headache Society (AHS), 2019). Patients suffering ≥4 headache days per month have poorer health-related quality of life (HRQOL); greater impairment in work productivity and daily activities, as well as higher healthcare resource utilization (Doane et al., 2020). Given the high prevalence and burden of migraine, preventive treatment is of the outmost importance.

Although frequency and severity of the attacks are the two most objective reasons to start on preventive medication in migraine patients, most guidelines suggest to monitor not only migraine frequency, but also impact and associated disability and/or (disease-specific) HRQOL through migraine validated calendar tools and disability instruments (American Headache Society (AHS), 2019; Ahmed et al., 2019; Lanteri-Minet et al., 2014; Steiner et al., 2019). There seems to be, however, no consensus on objective goals to determine therapeutic success. Most of the available instruments are Patient's reported outcome measures (PROMs; Ahmed et al., 2019; Steiner et al., 2019; Tassorelli et al., 2018), that have been used and validated in clinical trials (CTs), but do not necessarily reflect patients' priorities in real life (Haywood et al., 2018; Mannix et al., 2016; Smelt et al., 2014). In some cases, the decision to continue or discontinue with the prophylactic treatment is driven by the burden of the side effects.

In recent years, new preventive treatments have shown to be effective and decrease the intensity of migraine episodes, together with a good tolerability and adhesion profile, in patients with episodic or chronic migraine (Sacco et al., 2019). However, standards for evaluating the effectiveness of preventive treatment exists in daily clinical practice are lacking as are the criteria for treatment discontinuation. The aim of the My-LIFE Response criteria project was to identify factors involved in the definition of preventive treatment response and in the decision of treatment continuation in daily clinical practice through a Delphi survey conducted among European healthcare practitioners (HCP) with experience in migraine.

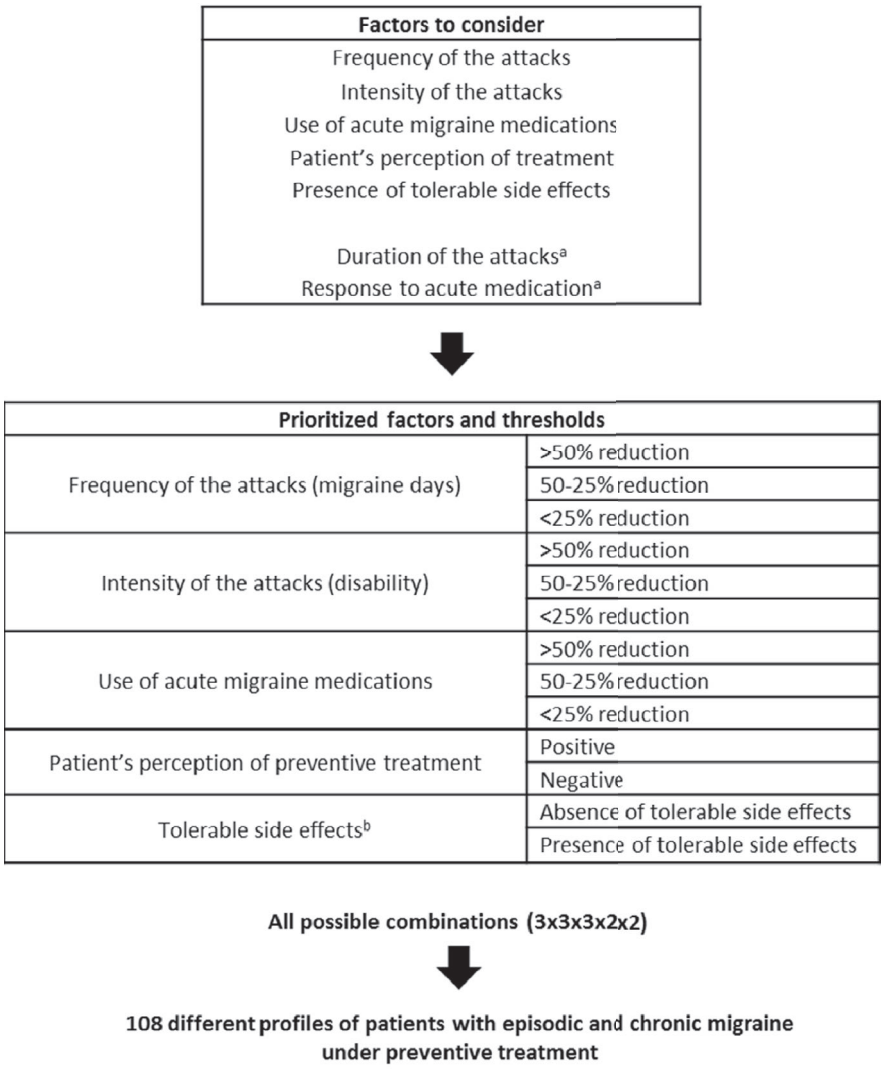
We hypothesized that even though the main endpoint in CTs for migraine preventive treatments is a reduction in the number of days with migraine, in clinical practice other factors are also relevant to assess efficacy.

2 | METHODS

The My-LIFE Response criteria project used a two-round modified Delphi procedure supported by a conjoint analysis approach. The authors met in a Steering Committee (SC) to define the main factors for the evaluation of the efficacy of a preventive treatment and prioritise them. The SC included eight members from France, Germany, Italy, Norway, Portugal, Spain, The Netherlands and United Kingdom.

A non-systematic literature review was conducted to identify the clinical factors that are used to define the response to migraine preventive treatment. On the basis of this literature search and their expertise, the SC agreed on a list of seven factors as the most important criteria to evaluate treatment response and continuation. Of these, the SC prioritized five factors and defined the categories within each of them according to their clinical experience (Figure 1). A set of simulated patient profiles was generated by the combination of two or three categories from each of the agreed factors: frequency of the attacks, intensity of the attacks, use of acute migraine medications, patient's perception of preventive treatment effectiveness and presence/absence of tolerable side effects (Figure 1).

FIGURE 1 Design of patient profiles: factors and thresholds used



[a]These factors were not included in the definition of patient profiles

[b]Tolerable side effects were defined as "side effects where the benefit from the preventive treatment outweighs the inconveniences".

Tolerable side effects were defined as those in which the benefit from the preventive treatment outweighs the inconveniences from the side effects. All possible combinations were made and a total of 108 simulated patient profiles created. For all factors, the term "reduction" was referring to change from baseline. The questionnaire was pre-tested by the SC and the definition of factors and thresholds adjusted to the final version (Figure 1).

2.1 | Design of the Delphi questionnaire

The full set of 108 simulated patient profiles was integrated in a questionnaire that included a section to characterize the participants' profile and another section to collect information regarding their clinical practice (Questionnaire in additional file). The participants were asked to classify the simulated patients according to treatment response as "responder", "partial responder" or "non-responder". They could also select the option "more data needed" whenever they felt that data were insufficient for the classification, and the option "rarely found in clinical practice" if they felt that it was the case. For each profile, participants were asked to decide whether preventive treatment should be continued (Figure 1). The estimated completion time of the questionnaire was 2 hr.

The Checklist for Reporting Results of Internet E-Surveys (CHERRIES) guidelines was followed (Eysenbach, 2004). Completed CHERRIES checklist is included as supplementary material.

2.2 | Panel selection and survey administration

A total of 264 HCP from five European countries (France, Germany, Italy, Spain and the United Kingdom) registered for the study. For participation, panelists had to fulfil the following selection criteria: being either a general practitioner, neurologist, internal medicine or pain specialist; having ≥2 years of experience in migraine treatment, previous experience with the prescription of migraine preventive treatments and prescribing them when deemed necessary, as well as currently having at least one patient under a preventive treatment for chronic migraine. Of the registered panelists, 205 met inclusion criteria, of whom 57 completed the first round of the survey but were lost to follow-up and 148 completed the two rounds of the Delphi questionnaire. The first round was conducted from July 2019 to February 2020; and the second from April to May 2020. Before starting the study, consensus was defined as 70% or more of the panelists agreeing on the classification regarding response to preventive treatment or in the decision for treatment continuation for each patient profile. Only those profiles where no consensus was reached in the first round were held to a second round of voting without changing the questionnaire. The questionnaire was administered through an online platform that ensured data anonymity and confidentiality. As panelists had to give their opinion on their experience without retrieving any patient data or information, no ethics committee approval or informed consent was needed.

2.3 | Statistical analysis

For descriptive analysis, categorical variables were expressed as frequencies and percentages. Bivariate analysis using Pearson's Chi-square was performed to assess the relationship of each factor with response to preventive treatment (responder, partial responder and non-responder) and treatment continuation or not. Stepwise multinomial regression was performed to obtain the factors associated with response to preventive treatment, and stepwise logistic regression to obtain the factors associated with treatment continuation. Multiple correspondence analysis (similar to factor analysis but for categorical variables) was performed. This is a technique used to graphically analyse the dependence/independence relationships of a set of categorical variables, based on the data from contingency tables. For this, it associates to each one of the modalities of the table a point in the space with multiple dimensions, in such a way that the proximity/distance between the calculated points reflects the relationships existing between them. Data were analysed with SPSS version 22, and $p < .05$ was considered statistically significant. No data were missing, lost or excluded of the analysis; therefore, no imputation of missing data was conducted.

3 | RESULTS

3.1 | Participants' profile

All participants who completed both rounds of the survey ($N = 148$) were general neurologists with experience in migraine: 82/148 (55.4%) saw more than 50 patients per week and 101/148 (68.2%) had more than 10 years of experience with migraine. On average, 35.2% (*SD*: 21%, range: 5%–99%) of all the patients seen by participants were suffering from migraine, of whom 26.1% (*SD*: 15%, range: 5%–76%) from chronic migraine (Table S1).

3.2 | Current clinical practice for episodic and chronic migraine treatment

The use of migraine evaluation tools for diagnosis was similar across countries. During the first visit of a migraine patient, 147/148 (99.3%) of participants assessed the diagnosis and the severity of migraine on the basis of a clinical interview and 61/148 (41.2%) also used a patient diary. During follow-up, 131/148 (88.5%) of participants assessed the clinical situation with a clinical interview, 127/148 (85.8%) also used a patient diary, 54/148 (36.5%) used a validated tool to assess chronic migraine (Table S2). The most used tools to assess the impact of migraine were Migraine Disability Assessment (MIDAS; 83/148 (56.1%), ranging from 3/10 (30.0%) in Germany to 23/31 (74.2%) in Italy, $p = .023$) and Headache Impact Test 6-item (HIT-6; 33.8%, similar across countries). Some differences between countries were observed in the use of a patient diary during follow-up (ranging from 22/33 (66.7%) in the United Kingdom to 30/31 (96.8%) in Italy, $p = .005$) and of validated scales (2/10 (20.0%) in Germany to 17/31 (54.8%) in Italy, $p = .009$; Table S2).

Overall, 138/148 (93.3%) of participants had more than 25% of their patients with migraine currently on preventive treatment (from 5/10 (50%) in Germany to 37/37 (100%) in France and Spain, without any statistical difference observed among countries). When asked directly about the criteria that they used to assess the effectiveness of a preventive treatment, participants rated frequency of attacks (132/148 (89.2%) of participants reported to always use it), intensity of the attacks (108/148 (73.0%)) and occurrence of side effects (treatment tolerability, 107/148 (72.3%)) as the most frequently used (Figure 2). Some differences between countries were observed in the frequency of use of the following criteria: treatment tolerability ($p = .002$, ranging from 18/33 (54.6%) in the United Kingdom to 9/10 (90.0%) in Germany), frequency of attacks ($p = .027$, from 25/33 (75.8%) in the United Kingdom to 37/37 (100%) in France and 10/10 (100%) in Germany), patient's perception of treatment ($p = .022$, from 8/31 (25.8%) in Italy to 26/37 (70.3%) in France and

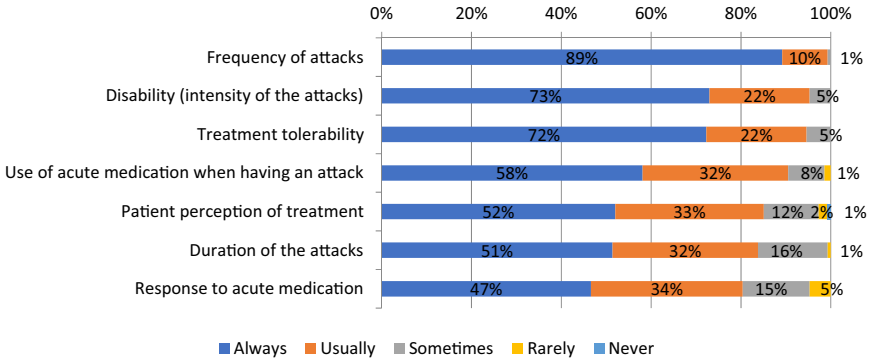


FIGURE 2 Criteria used to assess the effectiveness of preventive treatment in patients with episodic or chronic migraine

TABLE 1 Definition of response to a preventive treatment according to the factors used to define patient profiles

	Consensus reached ($n = 82$)				
	Responder ($n = 9$)	**Partial Responder ($n = 49$)**	**Non-responder ($n = 24$)**	**Consensus not reached ($n = 26$)**	***p* value**
Frequency of the attacks					.001*
>50% reduction	7 (77.8%)	14 (28.6%)	2 (8.3%)	13 (50.0%)	
49%–25% reduction	2 (22.2%)	20 (40.8%)	7 (29.2%)	7 (26.9%)	
<25% reduction	—	15 (30.6%)	15 (62.5%)	6 (23.1%)	
Intensity of the attacks					.530
>50% reduction	4 (44.5%)	14 (28.6%)	6 (25.0%)	12 (46.2%)	
49%–25% reduction	3 (33.3%)	19 (38.8%)	7 (29.2%)	7 (26.9%)	
<25% reduction	2 (22.2%)	16 (32.6%)	11 (45.8%)	7 (26.9%)	
Use of acute migraine medications					<.001*
>50% reduction	9 (100%)	14 (28.6%)	—	13 (50.0%)	
49%–25% reduction	—	29 (59.2%)	3 (12.5%)	4 (15.4%)	
<25% reduction	—	6 (12.2%)	21 (87.5%)	9 (34.6%)	
Patient's perception of treatment					.038*
Positive	8 (88.9%)	26 (53.1%)	8 (33.3%)	12 (46.2%)	
Negative	1 (11.1%)	23 (46.9%)	16 (66.7%)	14 (53.8%)	
Tolerable side effects					.930
Absence	4 (44.4%)	25 (51.0%)	11 (45.8%)	14 (53.8%)	
Presence	5 (55.6%)	24 (49.0%)	13 (54.2%)	12 (46.2%)	

*$p < .05$.

7/10 (70.0%) in Germany) and use of acute migraine medications ($p = .030$, from 16/33 (48.5%) in the United Kingdom to 28/37 (75.7%) in France; Table S3).

3.3 | Conjoint evaluation of the set of patient profiles

Overall, 148 participants evaluated 108 different simulated profiles of patients with episodic or chronic migraine requiring preventive treatment. Overall, no differences were observed between countries in terms on preventive treatment response or continuation.

3.3.1 | Factors used to classify patients' response to preventive treatment

Consensus in the classification of response to treatment was reached for 82 of the 108 profiles (75.9%), with nine profiles considered responders, 49 partial responders and 24 non-responders (Table S4). None of the profiles reached consensus in being classified as "rarely found in clinical practice" or considered to lack data for the classification.

Univariate analysis showed that three factors were significantly associated with response to preventive treatment: reduction in the use of acute migraine medications ($p < .001$), reduction in the frequency of attacks ($p = .001$) and patient's

perception of treatment ($p = .038$; Table 1). Intensity of the attacks was not significantly associated with treatment response classification ($p = .530$), nor was the presence of tolerable side effects ($p = .930$; Table 1).

The relative weight of each factor was analysed with a logistic multinomial regression, a classification method used to predict the relation between a set of nominal independent variables. The association of each factor with treatment response was depicted in a multiple correspondence analysis, a data analysis technique used to detect and represent underlying associations between nominal categorical data (Figure 3). The model explained 51.0% of variability.

3.3.2 | Factors used to decide continuation with preventive treatment

For each patient profile, participants evaluated whether the preventive treatment should be continued or withdrawn. Consensus was reached for 86 of the 108 profiles (79.6%): 44 (40.7%) for treatment continuation and 42 (38.9%) for treatment withdrawal. Treatment continuation was agreed for all profiles classified as responders, and treatment withdrawal for all non-responders (Table 2; Table S4). Regarding partial responders, consensus was reached for 29 of the 49 partial responder profiles (59.2%). Panelists were in favour of continuing treatment in 75.9% of the partial responder profiles for which agreement had been reached (22 of 29, Table 2). Lastly, for those profiles for which no consensus on response to a preventive treatment had been previously reached, treatment continuation was agreed for 13 of the 26 (55.5% of the profiles for which agreement on treatment continuation had been reached; Table 2).

Univariate analysis showed that reduction in the use of acute migraine medications ($p < .001$), patient's perception of treatment ($p < .001$) and reduction in the frequency of attacks ($p = .039$) were associated with the decision to continue or withdraw preventive treatment (Table 3).

Again, the relative weight of each factor was analysed with a multivariable logistic regression, and association of each factor with treatment continuation was depicted in a multiple correspondence analysis (Figure 4). The model explained 44.8% of variability and showed that the use of acute migraine medications and the patient's perception of treatment were the most important factors for panelists to decide treatment continuation. Participants were in favour of treatment continuation in patients who had a >50% reduction in the use of acute migraine medications (versus. patients with <25% reduction: OR = 34.7, 95% CI 30.80–39.05), and positive perception of treatment effectiveness (versus. negative perception; OR = 8.1, 95% CI 7.36–8.83). When combining both factors, patients with both a >50% reduction in the use of acute migraine medications and positive perception of

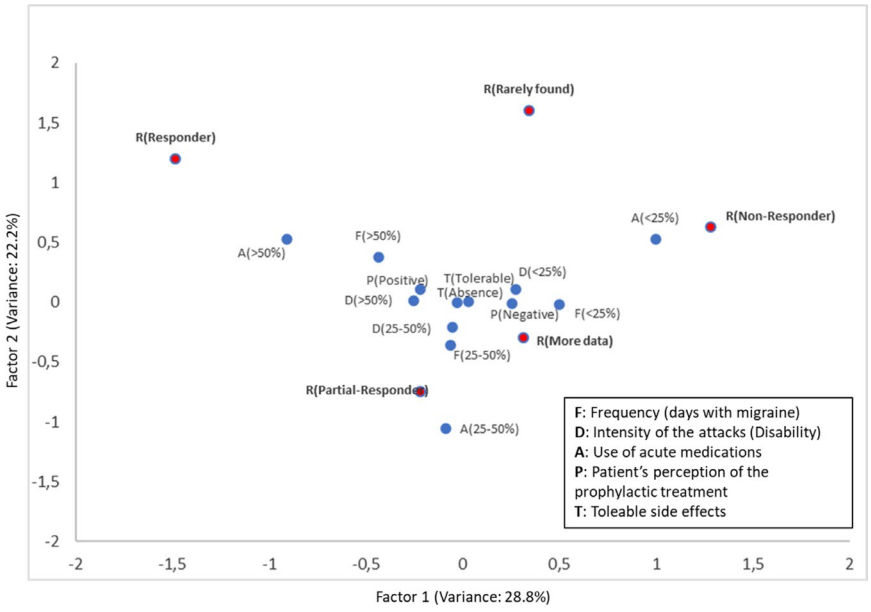


FIGURE 3 Relationship between the factors defined to assess response to a preventive treatment and type of response to this preventive migraine treatment. Multiple correspondence plot. Total variance: 51.0%. Multiple correspondence plot representing the relationship between the factors defined to assess response to a preventive migraine treatment (frequency of attacks, intensity of the attacks, use of acute medications, patient perception with the preventive treatment and tolerable side effects) (blue dots) and the treatment response (red dots). Distance between a blue and a red dot represents their degree of relationship, the shorter the distance, the higher the relationship. Factor 1 accounts for the 28.8% of the variance and appears to be mainly capturing the variability observed regarding the treatment response (note that red dots R(responder) vs R(non-responder) are shown as lowest and highest value across this axis. Factor 2 accounts for the 22.2% of the variance and seems to represent the variability among doubtful cases (in this case we see the red dots R(partial-responder) vs R(rarely found) along this axis.

TABLE 2 Distribution of patient profiles according to treatment response and decision to continue with preventive treatment

Decision to continue	Consensus reached for treatment continuation ($n = 86$)		Consensus not reached for treatment continuation ($n = 22$)
	Continuation ($n = 44$)	Withdrawal ($n = 42$)	
Treatment response			
Responders, *n* (%) ($n = 9$)	9 (100%)	—	—
Partial responders, *n* (%) ($n = 49$)	22 (44.9%)	7 (14.3%)	20 (40.8%)
Non-responders, *n* (%) ($n = 24$)	—	24 (100%)	—
Consensus not reached for treatment response, *n* (%) ($n = 26$)	13 (50.0%)	11 (42.3%)	2 (7.7%)

TABLE 3 Factors used to decide continuation of preventive treatment in patients with episodic or chronic migraine, univariate analysis

	Consensus reached ($n = 86$)			
	Continuation ($n = 44$)	Withdrawal ($n = 42$)	Consensus not reached ($n = 22$)	*p* value
Frequency of the attacks				.039*
>50% reduction	19 (43.2%)	8 (19.0%)	9 (40.9%)	
49%–25% reduction	15 (34.1%)	13 (31.0%)	8 (36.4%)	
<25% reduction	10 (22.7%)	21 (50.0%)	5 (22.7%)	
Intensity of the attacks				.073
>50% reduction	18 (41.0%)	12 (28.6%)	6 (27.3%)	
49%–25% reduction	13 (29.5%)	11 (26.2%)	12 (54.5%)	
<25% reduction	13 (29.5%)	19 (45.2%)	4 (18.2%)	
Use of acute migraine medications				<.001*
>50% reduction	29 (65.9%)	2 (4.8%)	5 (22.7%)	
49%–25% reduction	15 (34.1%)	12 (28.6%)	9 (40.9%)	
<25% reduction	0 (0%)	28 (66.6%)	8 (36.4%)	
Patient's perception of treatment				<.001*
Positive	32 (72.7%)	12 (28.6%)	10 (45.5%)	
Negative	12 (27.3%)	30 (71.4%)	12 (54.5%)	
Tolerable side effects				.430
Absence	25 (56.8%)	18 (42.9%)	11 (50.0%)	
Presence	19 (43.2%)	24 (57.1%)	11 (50.0%)	

*$p < .05$.

treatment had the highest likelihood of treatment continuation (OR = 18.3, 95% CI 13.41–25.05; Table 4).

3.3.3 | Factors used to decide continuation with preventive treatment in partial responders

In order to better understand the factors associated with the decision to continue treatment in partial responders, we specifically analysed this subset of profiles. As seen in all-patient population, both patient's perception of effectiveness of preventive treatment and reduction in the use of acute migraine medications were significantly associated with the decision of continuing with treatment; however, positive patient's perception had a higher relative effect on the decision to continue treatment in partial responders than in all-patient population. When panelists assessed partial responders, positive perception (OR = 9.8, 95% CI 8.64–11.02) and >50% reduction in the use of acute migraine medications (OR = 8.8, 95% CI 7.48–10.40) had similar weight (Table 4).

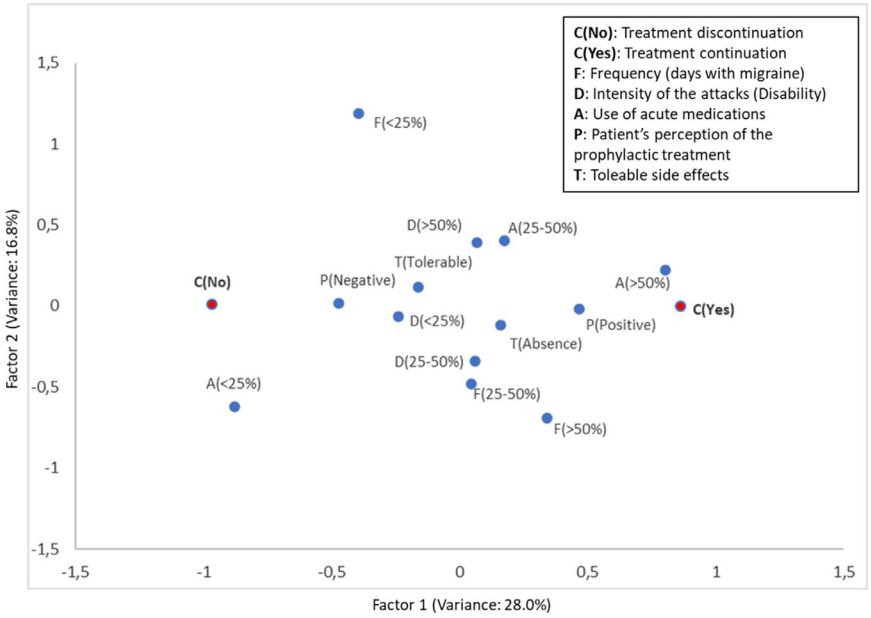


FIGURE 4 Relationship between the factors defined to assess response to a preventive treatment and decision to continue with the preventive migraine treatment. Multiple correspondence plot. Total variance: 44.8%. Multiple correspondence plot representing the relationship between the factors defined to assess response to a preventive migraine treatment (frequency of attacks, intensity of the attacks, use of acute medications, patient perception with the preventive treatment and tolerable side effects) (blue dots) and the decision to continue with the preventive migraine treatment (red dots). Distance between a blue and a red dot represents their degree of relationship, the shorter the distance, the higher the relationship. Factor 1 is mainly capturing the variability regarding treatment continuation (No vs Yes) and gathers a variance of 28.0%, and Factor 2 seems to represent the variability among extreme profiles as far as the Frequency of migraine attacks.

TABLE 4 Decision to continue with the preventive treatment in all patients and in partial responders

	All profiles (n = 108)			Partial responders (n = 49)		
	OR	95% CI	p value	OR	95% CI	p value
Use of acute migraine medications						
50% reduction	34.7	30.8–39.05	<.0001	8.8	7.48–10.4	<.0001
25%–50% reduction	7.0	6.33–7.75	<.0001	3.12	2.71–3.59	<.0001
<25% reduction	—	—	—	—	—	—
Patient's perception of treatment						
Positive	8.1	7.36–8.83	<.0001	9.8	8.64–11.02	<.0001
Negative	—	—	—	—	—	
Use of acute migraine medications/patient's perception of treatment						
>50% reduction/Positive	18.3	13.41–25.05	<.0001	17.4	11.31–26.82	<.0001
>50% reduction/Negative	2.27	1.82–2.84	<.0001	1.79	1.31–2.43	<.0001
25%−50% reduction/Positive	3.70	2.76–4.97	<.0001	6.2	4.1–9.27	<.0001
25%−50% reduction/Negative	0.46	0.37–0.56	<.0001	0.63	0.47–0.84	<.0001
<25% reduction/Positive	0.53	0.44–0.64	<.0001	1.98	1.51–2.58	<.0001
<25% reduction/Negative	0.066	0.06–0.07	<.0001	0.20	0.18–0.23	<.0001

4 | DISCUSSION AND CONCLUSIONS

The results from this Delphi study identify the factors used by neurologists to evaluate the response to preventive treatment and to decide on preventive treatment continuation in a simulated daily practice setting in five European countries.

The main results show that the reduction in the use of acute migraine medications and a positive patient's perception of the preventive treatment are the most strongly associated factors with treatment response definition and treatment continuation.

Current guidelines of the International Headache Society (IHS) for controlled trials of preventive treatment of episodic and chronic migraine recommend as primary endpoints the change in migraine days, change in severe-to-moderate headache days, or responder rate (Diener et al., 2020; Tassorelli et al., 2018). When directly asked, panelists reported the use of frequency and intensity of the attacks as the most used criteria to assess the effectiveness of preventive treatment, confirming that international guidelines are well known among the participants. However, the conjoint analysis of simulated patient profiles allowing to mimic the clinical practice in which the assessment is conducted considering all patient characteristics jointly showed that the reduction in the use of acute migraine medications was deemed more relevant when evaluating treatment response profiles, suggesting that maybe the reduction in the use of acute migraine medications seems to be easier to quantify by clinicians in their daily clinical practice, than frequency or intensity of attacks. On the other hand, a reduction in the use of acute medication could be probably related to frequency and intensity of the attacks. Moreover, intensity of the attacks was not associated with the evaluation of treatment response in this conjoint analysis. This absence is surprising as, in recent years, specifically with onabotulinumtoxinA and in patients who have failed several preventive treatments, severity of pain has been proven to be important for patients, as it translates to a meaningful improvement (Torres-Ferrus et al., 2020).

The use of acute migraine medications was also strongly associated with the decision to continue with preventive treatment. Assessing acute migraine medications use is a recommended secondary endpoint used in CTs of preventive treatments of episodic and chronic migraine (Diener et al., 2020; Tassorelli et al., 2018). In this line, many trials showed a significant reduction in acute migraine medications versus placebo (Andreou et al., 2018; Charles & Pozo-Rosich, 2019; Loder & Rizzoli, 2018). The reduction in medication consumption is likely a surrogate marker of a decrease in migraine frequency and/or intensity of the attacks, which can be quantified in a detailed and objective manner (Aurora et al., 2011). The reduction in acute migraine medications is also important for the well-being of subjects, when considering the risks associated with chronic use of NSAIDs or triptans. Furthermore, use of acute migraine medications >2 days per week is associated with a reduction in the effectiveness of preventive treatment, and it is a risk factor for medication overuse and chronification (Bigal et al., 2008; Buse et al., 2019; Limmroth et al., 2002; Lipton et al., 2015). Since the use of acute migraine medications is a factor associated with preventive treatment response and definition, our results suggest that neurologists are concerned about medication overuse and pay attention to control it. Reduction of acute migraine medications intake also involves a reduced economic burden (triptans are expensive) and reduced acute-medication side effects.

The other factor significantly related to the evaluation of treatment response is patient's perception of treatment and, most importantly, to the decision to continue with the preventive treatment. The patient's impression of change is a recommended secondary endpoint for controlled trials for preventive treatment of episodic and chronic migraine (Diener et al., 2020; Tassorelli et al., 2018), but is rarely used for the evaluation of migraine patients, while it is commonly used for pain patients (Boyd et al., 2019; Derry et al., 2019). Indeed, the patient global impression of change scale (PGIC) has been recently used only in two large controlled CTs to evaluate the effect of migraine therapies (Lipton et al., 2020; Tepper et al., 2019). Another approach is the patient's assessment of the severity of migraine with the Global assessment of migraine severity (GAMS; Sajobi et al., 2019).

Unlike the use of acute migraine medications, patient's perception is a subjective and general measurement based on personal opinion. Although effectiveness was the most used outcome in published studies, the outcomes analysed in CTs and in clinical practice differ. In 2014, a Delphi study conducted among migraine patients on acute migraine medications showed that patients' preferences are focused on fast action and recurrence prevention (Smelt et al., 2014). Failure to understand patient's preferences and perceptions may reduce adherence and compliance, subsequently limiting treatment success (American Headache Society (AHS), 2019). For partial responders this might be even more important, given that those were a frequent scenario in our project (45%), and panelists decided to continue treatment in 76% of them. Therefore, a positive patient's perception had an even higher impact on the decision to continue with the preventive treatment than in all patient profiles population.

Despite being a subjective measure, patient's perception can be measured using validated PROMs. According to Haywood et al. (Haywood et al., 2018), three PROMs have acceptable evidence of reliability and validity for headache impact evaluation: HIT-6 (Kosinski et al., 2003), Migraine-Specific Quality-of-Life Questionnaire Version 2.1 (MSQv2.1; Martin et al., 2000) and Patient Perception of Migraine Questionnaire (PPMQ-R; Kimel et al., 2008; Revicki et al., 2006). While HIT-6 and MSQv2.1 assess migraine and headache-specific impact, PPMQ-R assesses the response and satisfaction with migraine-specific treatment. Current guidance recommends HIT-6, HALT-30 (Headache-Attributed Lost Time-30) and HURT (the Headache Under-Response to Treatment) for evaluating quality of life during preventive treatment (Ahmed et al., 2019; Steiner et al., 2019). Besides, MSQ v. 2.1 is also validated for patients undergoing preventive migraine treatment (Cole et al., 2007). However, currently used PROMs may not adequately reflect patients' satisfaction and a broader consensus on the most important outcomes and how to assess them is required (Haywood et al., 2018; Mannix et al., 2016; Smelt et al., 2014). Thus,

extending education on the importance on patient's perception as well as on the use of validated tools may help neurologists and HCP to better assess treatment response and guide decisions on continuation with preventive treatment.

Panelists' clinical practice showed that they commonly follow current recommendations (Ahmed et al., 2019; Steiner et al., 2019) with regard to the use of a patient diary when monitoring preventive treatment, which promotes adherence and provides quantitative data to HCP for the decision on treatment response and continuation. However, most patient diaries are still far from being ideal, and there is an urgent need for newly developed E-health applications including time-locked E-diaries with the incorporation of the Third Edition of the International Classification of Headache Disorders (ICHD-3) criteria. Furthermore, <42% of healthcare providers used a validated scale to assess the impact of preventive treatment on migraine burden. The most used scales to assess patients with migraine in current practice were MIDAS (Stewart et al., 2001) and HIT-6. Both scales are short (MIDAS, five items and HIT-6, six items) and easy to administer, which may increase their use. The use of scales does not necessarily mean that they are valued as decision criteria, but it may warrant that they are probably valued and considered useful.

Lastly, preventive treatments are not devoid of adverse events (American Headache Society (AHS), 2019) and this could partially explain their low use. In our survey, the presence of tolerable side effects did not emerge as a relevant factor in the decision of treatment withdrawal. This suggests that panelists relied more on the patients' perception of treatment effectiveness than on the impact of tolerable side effects, possibly considering the former as the most reliable reflection of the sum of positive and negative effects of treatment on patients' lives. In this frame, it is indeed possible that in the panelists' interpretation, patients are willing to endure tolerable side effects as long as the treatment is taking away a relevant part of their disease burden. This seems an interesting working hypothesis that will need specifically aimed investigations.

4.1 | Strengths and limitations

Even though general practitioners, neurologists, internal medicine and pain specialists were invited to participate, the inclusion criteria regarding experience in migraine and preventive treatments made that only general neurologists were eventually valid for answering the full Delphi survey.

Even if consensus threshold could have been more stringent, when defining it, at the beginning of the project, after a non-systematic literature review, we considered that a 70% of agreement was appropriate. In this regard, it has to be mentioned that all patient profiles were considered for the conjoint analysis, regardless if an agreement was reached on treatment response or treatment continuation or stop.

Since the 108 patient profiles used in the project were artificially created, some profiles may not match the reality. The study design did not consider the classification of the simulated profiles into low-frequency episodic migraine, high-frequency episodic migraine and chronic migraine, and thus the results cannot be grouped into these three clinical scenarios. Moreover, duration of preventive treatment was not included as a factor, and therefore conclusions cannot be drawn on its effect on decision to continue preventive treatment. Other aspects, like patient clinical history and comorbidities, concomitant medications or pregnancy or willingness to become, that can influence treatment decisions, were not considered when defining the patient profiles. Nevertheless, panelists had to take into consideration five different factors simultaneously, and this conjoint analysis approach allowed us to assess the relative weight that each individual factor plays in their treatment decisions.

Even though all participants were general neurologists, 86% of them reported the use of a patient diary indicating a special interest and expertise in headache; subsequently, results reflect real-life clinical practice in Europe. Although the sample size was not very large, we could rely on an enormous data set (108 profiles assessed by 148 panelists) to allow proper and robust multivariable analysis of the simulated profiles. A possible limitation was the questionnaire length (estimated completion time for the questionnaire was 2 hr), which might have caused some bias due to tiredness; in addition, the evaluation order of the simulated profiles was the same for all panelists. In order to minimize the risk of bias, the questionnaire's platform allowed to save the answers, close the platform and continue with the survey later on; however, the platform specifically programmed for this Delphi consensus was not geared to collect who answered the questionnaire at once and how long participants were connected.

It would also have been of interest to evaluate if working in a hospital or in the private setting had an impact on the answers; however, this information was not captured by the questionnaire. Lastly, our project included a limited sample size in some countries that might have influenced the differences observed among countries.

4.2 | Further directions

New preventive treatments for migraine have recently reached the market (e.g.: monoclonal antibodies against calcitonin gene-related peptide [CGRP] or its receptor). These treatments are costly and will translate on higher pressure on clinicians as regards day-to-day decisions about when to continue or not with such expensive treatments, in particular, when dealing with partial responders. Therefore, additional

research on factors that determine the response to preventive treatment, as well as on tools that adequately assess this and consider patients' perception, would help decision making and improve the management of migraine in clinical practice.

As a conclusion, in a simulated clinical setting, a reduction in the use of acute migraine medications is the most strongly associated factor with the preventive treatment effectiveness definition. The reduction in the use of acute migraine medications, followed by a positive patient's perception of treatment effectiveness, is the factor that most strongly associated with the decision of treatment continuation.

ACKNOWLEDGEMENTS

We thank the panelists for their participation in the survey, thanks to Maite Artés, Nathalie Bofarull and Malena Águila (Adelphi Targis S.L.) for the project management and contribution along the project and to Alba Gomez and Alba Llopis for their medical writing assistance with the methods and results sections.

CONFLICT OF INTERESTS

SA has received personal fees from Novartis Pharma AG during the conduct of the project. Outside the submitted work, SA has perceived personal fees from Teva as a speaker and personal fees from Eli Lilly for advisory board participation. AD has received personal fees from Novartis Pharma AG during the conduct of the project. Outside the submitted work, AD has received fees from Allergan, Eli Lilly, Grünenthal, MSD, Novartis, Orkyn, Pfizer, Saint-Jude, Sanofi and Teva. AG has received personal fees from Novartis Pharma AG during the conduct of the project. Outside the submitted work, AG has received fees for advisory boards and lectures from Allergan, Eli Lilly, Grünenthal, Hexal, Novartis, Sanofi and Teva. RG has received personal fees from Novartis Pharma AG during the conduct of the project. Outside the submitted work, RGG has received fees for advisory board's contribution, clinical trials participation or medical education from Allergan, Amgen, Lundbeck, Novartis, Pfizer and Teva. RG has received support for headache research from Sociedade Portuguesa de Cefaleias and Fundação para a Ciência e Tecnologia. AP has received personal fees from Novartis Pharma AG during the conduct of the project. Outside the submitted work she has received fees for advisory board's contribution, clinical trials or medical education from Allergan, Eli Lilly, Lundbeck, Novartis and Teva. PP has received personal fees from Novartis Pharma AG during the conduct of the project. Outside the submitted work, PP-R has received fees for advisory board's contribution, clinical trials participation or medical education from Allergan, Almirall, Amgen, Biohaven, Chiesi, Eli Lilly, Medscape, Novartis and Teva. PP has received support for headache research from La Caixa Foundation, AGAUR, European Commission (ERANet Neuron), Instituto de Salud Carlos III, Migraine Research Foundation, Novartis and PERIS. RS is an employee and stakeholder of Novartis Pharma AG. CT has received personal fees from Novartis Pharma AG during the conduct of the project. Outside the submitted work, CT has received fees for advisory board's contribution, clinical trials participation or medical education from Allergan, Amgen, Eli Lilly, Teva and Medscape. CT has received independent support from the Italian Ministry of Health, European Commission and Migraine Research Foundation. GT has received personal fees from Novartis Pharma AG during the conduct of the project. Outside the submitted work, GT has received grants or consultancy support from Allergan, Eli Lilly, Novartis, Teva, and independent support from Dutch Research Council, NIH, European Community, Dutch Heart Foundation and Dutch Brain Foundation.

AUTHORS' CONTRIBUTIONS

All authors were involved in the writing of introduction and discussion and the review of all the article and meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE).

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

Given that panelists had to give their opinion based on their own experience without retrieving any patient data or information, and the anonymity of the questionnaire, no ethics committee approval was required. All panelists gave their formal consent to participate in the Delphi survey.

CONSENT FOR PUBLICATION

Not applicable.

DATA AVAILABILITY STATEMENT

The datasets used and/or analysed during this study are available from the corresponding author on reasonable request.

ORCID

Patricia Pozo-Rosich https://orcid.org/0000-0003-0796-4702
Raquel Gil-Gouveia https://orcid.org/0000-0002-4256-4256
Anne Donnet https://orcid.org/0000-0003-0034-5247
Anne-Christine Poole https://orcid.org/0000-0002-2872-4110
Astrid Gendolla https://orcid.org/0000-0002-9884-3158
Shazia Afridi https://orcid.org/0000-0002-8487-5677
Rainel Sanchez-De la Rosa https://orcid.org/0000-0002-7134-1203
Gisela M. Terwindt https://orcid.org/0000-0003-3140-6882
Cristina Tassorelli https://orcid.org/0000-0003-1513-2113

REFERENCES

Ahmed F., Bahra A., Tyagi A., & Weatherby S. (2019). *BASH National headache management system for adults*. British Association for the Study of Headache.

American Headache Society (AHS). (2019). The American headache society position statement on integrating new migraine treatments into clinical practice. *Headache*, *59*, 1–18. https://doi.org/10.1111/head.13456

Andreou, A. P., Trimboli, M., Al-Kaisy, A., Murphy, M., Palmisani, S., Fenech, C., Smith, T., & Lambru, G. (2018). Prospective real-world analysis of OnabotulinumtoxinA in chronic migraine post-National Institute for Health and Care Excellence UK technology appraisal. *European Journal of Neurology*, *25*, 1069–e83. https://doi.org/10.1111/ene.13657

Aurora, S. K., Winner, P., Freeman, M. C., Spierings, E. L., Heiring, J. O., DeGryse, R. E., VanDenburgh, A. M., Nolan, M. E., & Turkel, C. C. (2011). OnabotulinumtoxinA for treatment of chronic migraine: Pooled analyses of the 56-week PREEMPT clinical program. *Headache*, *51*, 1358–1373. https://doi.org/10.1111/j.1526-4610.2011.01990.x

Bigal, M. E., Serrano, D., Buse, D., Scher, A., Stewart, W. F., & Lipton, R. B. (2008). Acute migraine medications and evolution from episodic to chronic migraine: A longitudinal population-based study. *Headache*, *48*, 1157–1168. https://doi.org/10.1111/j.1526-4610.2008.01217.x

Boyd, A., Bleakley, C., Hurley, D. A., Gill, C., Hannon-Fletcher, M., Bell, P., & McDonough, S. (2019). Herbal medicinal products or preparations for neuropathic pain. *Cochrane Database Systematic Review*, *2019*. https://doi.org/10.1002/14651858.CD010528.pub4

Buse, D. C., Greisman, J. D., Baigi, K., & Lipton, R. B. (2019). Migraine progression: A systematic review. *Headache*, *59*, 306–338. https://doi.org/10.1111/head.13459

Charles, A., & Pozo-Rosich, P. (2019). Targeting calcitonin gene-related peptide: A new era in migraine therapy. *Lancet*, *394*, 1765–1774. https://doi.org/10.1016/S0140-6736(19)32504-8

Cole, J. C., Lin, P., & Rupnow, M. F. T. (2007). Validation of the Migraine-Specific Quality of Life Questionnaire version 2.1 (MSQ v. 2.1) for patients undergoing prophylactic migraine treatment. *Quality of Life Research*, *16*, 1231–1237. https://doi.org/10.1007/s11136-007-9217-1

Derry, S., Bell, R. F., Straube, S., Wiffen, P. J., Aldington, D., & Moore, R. A. (2019). Pregabalin for neuropathic pain in adults. *Cochrane Database Systematic Review*, *2019*. https://doi.org/10.1002/14651858.CD007076.pub3

Diener, H.-C., Tassorelli, C., Dodick, D. W., Silberstein, S. D., Lipton, R. B., Ashina, M., Becker, W. J., Ferrari, M. D., Goadsby, P. J., Pozo-Rosich, P., Wang, S.-J., Houle, T. T., van den Hoek, T. C., Martinelli, D., & Terwindt, G. M. (2020). Guidelines of the International Headache Society for controlled trials of preventive treatment of migraine attacks in episodic migraine in adults. *Cephalalgia*, *40*, 1026–1044. https://doi.org/10.1177/0333102420941839

Doane, M. J., Gupta, S., Fang, J., Laflamme, A. K., & Vo, P. (2020). The humanistic and economic burden of migraine in Europe: A cross-sectional survey in five countries. *Neurology and Therapy*, *9*, 535–549. https://doi.org/10.1007/s40120-020-00196-2

Eysenbach, G. (2004). Improving the quality of Web surveys: The Checklist for Reporting Results of Internet E-Surveys (CHERRIES). *Journal of Medical Internet Research*, *6*, e34. https://doi.org/10.2196/jmir.6.3.e34

Haywood, K. L., Mars, T. S., Potter, R., Patel, S., Matharu, M., & Underwood, M. (2018). Assessing the impact of headaches and the outcomes of treatment: A systematic review of patient-reported outcome measures (PROMs). *Cephalalgia*, *38*, 1374–1386. https://doi.org/10.1177/0333102417731348

Katsarava, Z., Mania, M., Lampl, C., Herberhold, J., & Steiner, T. J. (2018). Poor medical care for people with migraine in Europe – Evidence from the Eurolight study. *The Journal of Headache and Pain*, *19*, 1–9. https://doi.org/10.1186/s10194-018-0839-1

Kimel, M., Hsieh, R., McCormack, J., Burch, S. P., & Revicki, D. A. (2008). Validation of the revised Patient Perception of Migraine Questionnaire (PPMQ-R): Measuring satisfaction with acute migraine treatment in clinical trials. *Cephalalgia*, *28*, 510–523. https://doi.org/10.1111/j.1468-2982.2007.01524.x

Kosinski, M., Bayliss, M. S., Bjorner, J. B., Ware, J. E., Garber, W. H., Batenhorst, A., Cady, R., Dahlöf, C. G. H., Dowson, A., & Tepper, S. (2003). A six-item short-form survey for measuring headache impact: The HIT-6^{TM}. *Quality of Life Research*, *12*, 963–974. https://doi.org/10.1023/A:1026119331193

Lanteri-Minet, M., Valade, D., Geraud, G., Lucas, C., & Donnet, A. (2014). Revised French guidelines for the diagnosis and management of migraine in adults and children. *J Headache Pain*, *15*, 2. https://doi.org/10.1186/1129-2377-15-2

Limmroth, V., Katsarava, Z., Fritsche, G., Przywara, S., & Diener, H.-C. (2002). Features of medication overuse headache following overuse of different acute headache drugs. *Neurology*, *59*, 1011–1014. https://doi.org/10.1212/WNL.59.7.1011

Lipton, R. B., Cohen, J. M., Gandhi, S. K., Yang, R., Yeung, P. P., & Buse, D. C. (2020). Effect of fremanezumab on quality of life and productivity in patients with chronic migraine. *Neurology*, *95*, e878–e888. https://doi.org/10.1212/wnl.0000000000010000

Lipton, R. B., Fanning, K. M., Serrano, D., Reed, M. L., Cady, R., & Buse, D. C. (2015). Ineffective acute treatment of episodic migraine is associated with new-onset chronic migraine. *Neurology*, *84*, 688–695. https://doi.org/10.1212/WNL.0000000000001256

Loder, E., & Rizzoli, P. (2018). Pharmacologic prevention of migraine: A narrative review of the state of the art in 2018. *Headache*, *58*(Suppl 3), 218–229. https://doi.org/10.1111/head.13375

Mannix, S., Skalicky, A., Buse, D. C., Desai, P., Sapra, S., Ortmeier, B., Widnell, K., & Hareendran, A. (2016). Measuring the impact of migraine for evaluating outcomes of preventive treatments for migraine headaches. *Health and Quality of Life Outcomes*, *14*, 143. https://doi.org/10.1186/s12955-016-0542-3

Martin, B. C., Pathak, D. S., Sharfman, M. I., Adelman, J. U., Taylor, F., Kwong, W. J., & Jhingran, P. (2000). Validity and reliability of the migraine-specific quality of life questionnaire (MSQ version 2.1). *Headache*, *40*, 204–215. https://doi.org/10.1046/j.1526-4610.2000.00030.x

Revicki, D. A., Kimel, M., Beusterien, K., Kwong, J. W., Varner, J. A., Ames, M. H., Mahajan, S., & Cady, R. K. (2006). Validation of the revised Patient Perception of Migraine Questionnaire: Measuring satisfaction with acute migraine treatment. *Headache*, *46*, 240–252. https://doi.org/10.1111/j.1526-4610.2006.00289.x

Sacco, S., Bendtsen, L., Ashina, M., Reuter, U., Terwindt, G., Mitsikostas, D.-D., & Martelletti, P. (2019). European headache federation guideline on the use of monoclonal antibodies acting on the calcitonin gene related peptide or its receptor for migraine prevention. *The Journal of Headache and Pain*, *20*, 6. https://doi.org/10.1186/s10194-018-0955-y

Sajobi, T. T., Amoozegar, F., Wang, M., Wiebe, N., Fiest, K. M., Patten, S. B., & Jette, N. (2019). Global assessment of migraine severity measure: Preliminary evidence of construct validity. *BMC Neurology*, *19*, 53. https://doi.org/10.1186/s12883-019-1284-8

Serrano, D., Lipton, R. B., Scher, A. I., Reed, M. L., Stewart, W. F., Adams, A. M., & Buse, D. C. (2017). Fluctuations in episodic and chronic migraine status over the course of 1 year: Implications for diagnosis, treatment and clinical trial design. *The Journal of Headache and Pain*, *18*. https://doi.org/10.1186/s10194-017-0787-1

Smelt, A. F. H., Louter, M. A., Kies, D. A., Blom, J. W., Terwindt, G. M., van der Heijden, G. J. M. G., De Gucht, V., Ferrari, M. D., & Assendelft, W. J. J. (2014). What do patients consider to be the most important outcomes for effectiveness studies on migraine treatment? Results of a Delphi study. *PLoS ONE*, *9*, e98933. https://doi.org/10.1371/journal.pone.0098933

Steiner, T. J., Jensen, R., Katsarava, Z., Linde, M., MacGregor, E. A., Osipova, V., Paemeleire, K., Olesen, J., Peters, M., & Martelletti, P. (2019). Aids to management of headache disorders in primary care. *The Journal of Headache and Pain*, *20*, 57. https://doi.org/10.1186/s10194-018-0899-2

Steiner, T. J., Stovner, L. J., Vos, T., Jensen, R., & Katsarava, Z. (2018). Migraine is first cause of disability in under 50 s: Will health politicians now take notice? *The Journal of Headache and Pain*, *19*, 17. https://doi.org/10.1186/s10194-018-0846-2

Stewart, W. F., Lipton, R. B., Dowson, A. J., & Sawyer, J. (2001). Development and testing of the Migraine Disability Assessment (MIDAS) Questionnaire to assess headache-related disability. *Neurology*, *56*, S20–8. https://doi.org/10.1212/wnl.56.suppl_1.s20

Stovner, L. J., Nichols, E., Steiner, T. J., Abd-Allah, F., Abdelalim, A., Al-Raddadi, R. M., Ansha, M. G., Barac, A., Bensenor, I. M., Doan, L. P., Edessa, D., Endres, M., Foreman, K. J., Gankpe, F. G., Gopalkrishna, G., Goulart, A. C., Gupta, R., Hankey, G. J., Hay, S. I., … Murray, C. J. L. (2018). Global, regional, and national burden of migraine and tension-type headache, 1990–2016: A systematic analysis for the Global Burden of Disease Study 2016. *The Lancet Neurology*, *17*, 954–976. https://doi.org/10.1016/S1474-4422(18)30322-3

Tassorelli, C., Diener, H. C., Dodick, D. W., Silberstein, S. D., Lipton, R. B., Ashina, M., Becker, W. J., Ferrari, M. D., Goadsby, P. J., Pozo-Rosich, P., & Wang, S. J. (2018). Guidelines of the International Headache Society for controlled trials of preventive treatment of chronic migraine in adults. *Cephalalgia*, *38*, 815–832. https://doi.org/10.1177/0333102418758283

Tepper, S. J., Krege, J. H., Lombard, L., Asafu-Adjei, J. K., Dowsett, S. A., Raskin, J., Buchanan, A. S., & Friedman, D. I. (2019). Characterization of dizziness after lasmiditan usage: Findings from the SAMURAI and SPARTAN acute migraine treatment randomized trials. *Headache*, *59*, 1052–1062. https://doi.org/10.1111/head.13544

Torres-Ferrus, M., Gallardo, V. J., Alpuente, A., & Pozo-Rosich, P. (2020). Influence of headache pain intensity and frequency on migraine-related disability in chronic migraine patients treated with OnabotulinumtoxinA. *The Journal of Headache and Pain*, *21*, 88. https://doi.org/10.1186/s10194-020-01157-8

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Pozo-Rosich, P., Gil-Gouveia, R., Donnet, A., Poole, A.-C., Gendolla, A., Afridi, S., Sanchez-De la Rosa, R., Terwindt, G. M., & Tassorelli, C. (2021). Relevant factors for neurologists to define effectiveness of migraine preventive drugs and take decisions on treatment. My-LIFE European Delphi survey. *European Journal of Pain*, 25, 2177–2189. https://doi.org/10.1002/ejp.1831