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Research Submission

Evaluating Migraineurs' Preferences for Migraine Treatment Outcomes Using a Choice Experiment

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Objective.—The impact of migraines on patients is commonly divided between the level of impairment associated with headache symptoms (headache phase) and the quality-of-life effects immediately following the headache (post-headache phase). Evaluations of migraineurs' productivity losses and health-related quality of life have provided an understanding of the burden associated with the headache and post-headache symptoms, but do not quantify the relative importance of each phase from a patient perspective. In this study, we evaluated migraineurs' willingness to accept trade-offs among symptom severity in the headache and post-headache phases, symptom duration in the headache and post-headache phases, and symptom-free time within a general-preference theoretic framework.

Methods.—We administered a choice-format, conjoint-analysis survey, also called a discrete-choice experiment, to a sample of migraineurs from a nationally representative online consumer panel. After inclusion and exclusion criteria were applied, 510 eligible subjects completed the survey. The survey elicited choices between pairs of migraine profiles describing symptom durations and symptom-free time for the headache and post-headache phase.

Results.—Migraineurs in our study were strongly affected by the pain associated with the headache phase. However, experiencing difficulty with daily social and family activities in the post-headache phase also had a statistically significant impact on migraineurs' perceived level of well-being. Migraineurs reported that hypothetical treatments that limited the duration of headache symptoms without allowing them to resume their daily activities for 16 hours after a headache, on average, were less than half as good as treatments that limited both headache and post-headache symptoms.

Conclusion.—Our results suggest that treatments that relieve and shorten symptoms during the post-headache phase can offer significant benefits to migraineurs.

Key words: patient preferences, migraine, conjoint analysis, ictal burden, interictal burden, productivity

Abbreviation: GED general equivalency diploma

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Clinical management of migraine often focuses primarily on headache symptoms, which include acute headache pain, and other symptoms experienced with headache pain. Although headache symptoms are an obvious source of impairment for migraineurs, recent evidence suggests that they only partly predict the migraineur's quality of life in the period following the resolution of acute symptoms.[1-3] Post-headache symptoms limit everyday activities as a consequence of incomplete recovery from migraine symptoms and

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anxiety about migraine headaches returning after the headache symptoms have subsided.[4,5]

Medical costs associated with treating migraines,[6,7] and the economic impact of headache and post-headache symptoms on labor productivity losses, have been widely studied.[8-13] Further, questionnaires that capture patient-reported outcomes have also been used to understand the impact of migraines as they shed light on migraineurs' quality of life related to work, normal family life and relationships, and the emotional consequences of living with the unpredictability of migraines.[1,14-17]

Although evaluations of productivity losses and health-related quality-of-life impacts have proven useful in understanding the burden associated with headache and post-headache symptoms, they do not quantify the relative importance of the 2 types of symptoms from a patient perspective. That is, which migraine symptoms are considered more damaging, and which migraine treatment features would be considered more highly valued by migraineurs themselves? In this study, we did not focus on evaluations of productivity losses or health-related quality-of-life impacts based on patient-reported outcomes. Instead, we quantified migraineurs' perceived value of reducing the severity and duration of headache and post-headache symptoms.

To evaluate and compare migraineurs' assessment of the impact of headache and post-headache symptoms within a general preference-theoretic framework, we conducted a discrete-choice experiment (DCE), also known as a choice-format, conjoint-analysis survey, in which subjects indicated their preferred alternative in a series of pairs of hypothetical migraine treatments. Each migraine treatment affected the amount of time a patient would experience specific headache and post-headache symptoms within a clinically relevant 24-hour period.

METHODS

DCEs increasingly are being used to quantify preferences for outcomes associated with medical treatments.[18] The principle behind DCEs is that treatments can be thought of as combinations of outcomes accepted by patients when they agree to or choose a medical intervention. Thus, patients' choices for constructed treatments indicate the extent to which treatment outcomes satisfy patients' needs or wants.[19,20]

The outcomes used to characterize medical treatments in DCEs are commonly known as attributes. Attributes can include treatment-related clinical and patient-reported outcomes.[21-25] Each attribute is assigned multiple levels that define the severity or the likelihood of an outcome. For example, pain severity could be classified as mild, moderate, or severe, or indicated by the effect of pain on restrictions of daily activities. Different treatment profiles are characterized by varying outcome levels for a common set of treatment attributes.

Better efficacy obviously is more desirable than poorer side effects. However, people often are willing to accept some level of a less desirable outcome in return for a higher level of a more desirable outcome. The pattern of such choices under appropriate experimental controls can reveal the relative importance of treatment attribute levels. In determining the relative impact of headache and post-headache symptoms for migraineurs, this study evaluated migraineurs' willingness to accept trade-offs among symptom severity, symptom duration, and symptom-free time.

Data.—The sample frame consisted of a nationally representative online consumer panel (GfK Knowledge Networks, Inc., Palo Alto, CA, USA). Eligible respondents were US residents with a self-reported physician diagnosis of migraine and who were at least 18 years of age. Of the 1067 individuals invited to participate, 698 (65%) responded to the invitation. Of those who responded, 539 (50.5%) were eligible and consented to take the survey. All of the 539 eligible subjects completed the survey.

While all eligible subjects indicated having a physician diagnosis of migraine, 48 (9%) also reported experiencing cluster headaches. However, only 29 (5.4%) reported symptoms consistent with cluster headaches. We omitted these 29 subjects from the dataset. All other subjects who reported having a physician diagnosis of migraines and were at least 18 years of age were kept in the final sample, leaving a final sample size of 510 for estimation purposes. Figure 1 presents the proportion of respondents included in each part of the recruitment process and the final sample used in this study.

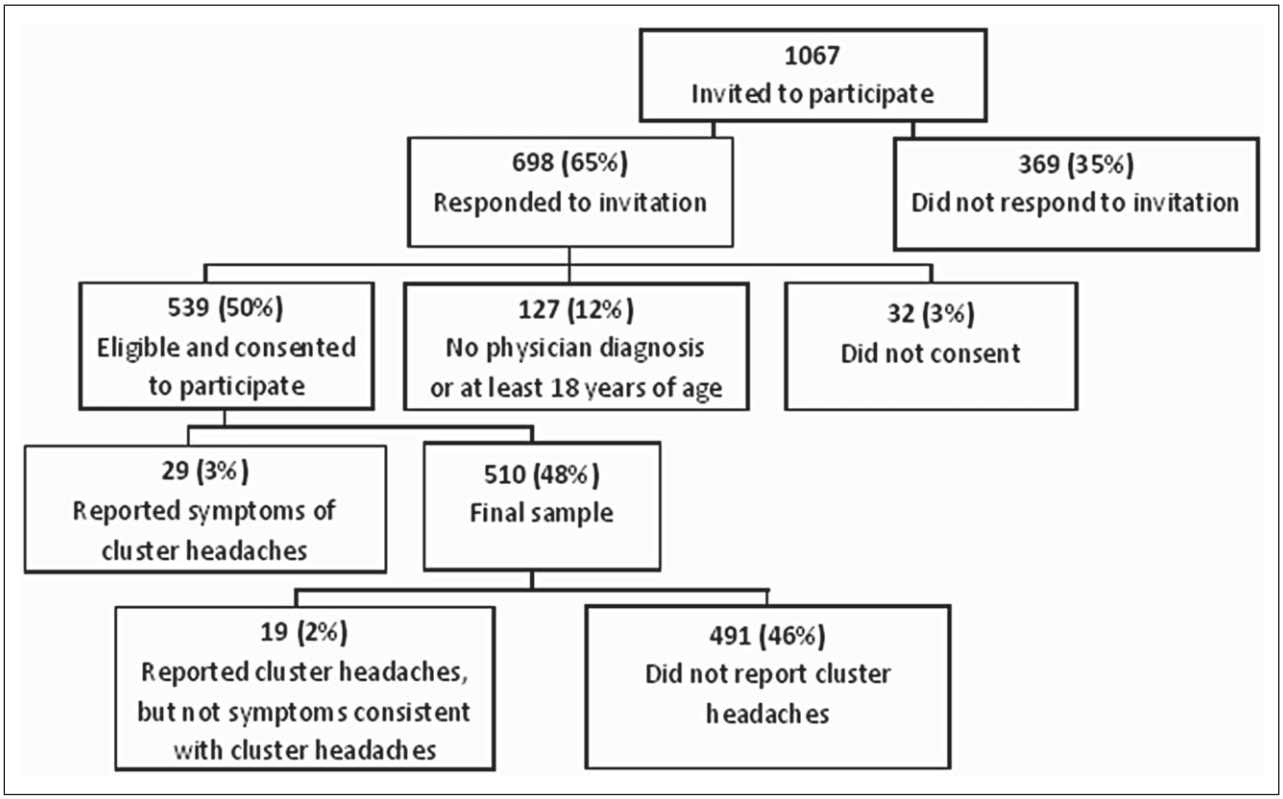

Fig 1.—Proportion of respondents in each stage of data collection and final sample size.

Survey Instrument.—The survey instrument included questions about the subjects' experiences with migraines and the type of treatment they use to manage migraine symptoms. We also included 8 trade-off questions in which respondents were asked to choose between migraine treatments with different attribute levels. Clinical experts were consulted to determine the set of treatment attributes and attribute definitions included in the survey. The levels of the attributes in the survey also were determined in consultation with clinical experts to ensure that the range of the levels for each treatment attribute encompassed the range of duration and severity seen in clinical practice. To evaluate the salience of the attributes and levels, a draft survey instrument was pretested using face-to-face, semi-structured interviews with 20 patients in Philadelphia, Pennsylvania, and in Raleigh, North Carolina. Both the draft and final surveys were approved by RTI International's Office of Research Protection and Ethics (Research Triangle Park, NC, USA).

We described each hypothetical migraine treatment in the trade-off questions as consisting of 3 phases: (1) headache phase, (2) post-headache phase, and (3) symptom-free phase. Treatment profiles specified how long each phase lasted within a 24-hour period and the severity of the symptoms experienced during the phase.

Table 1 summarizes the list of attributes, with the associated phases, that were used to construct the trade-off questions. For the headache phase, we included the duration and severity of the headache symptoms. For the post-headache phase, we included the duration of limitations on activities of daily living related to post-headache symptoms. The duration of the symptom-free phase was simply the difference between the combined headache and post-headache phase durations and 24 hours. The chance that the migraine episode would return in a 24-hour period completed the set of attributes.

Each trade-off question presented a choice between 2 hypothetical migraine treatments with

Table 1.—Attributes and Levels for the Trade-Off Questions

Attributes	Levels	
Headache phase: Migraine headache phase symptoms	Severity: • Throbbing with no sensitivity to light and sound or severe nausea • Throbbing head pain and sensitivity to light and sound, no severe nausea • Throbbing head pain and severe nausea, no sensitivity to light and sound • Throbbing head pain, sensitivities to light and sound, and severe nausea	Duration: • 30 minutes • 1 hour • 3 hours • 8 hours
Post-headache phase: Limitations on ability to work and participate in social activities	Severity: • No limitations (only shown with "0 hour" post-headache duration) • Difficulty doing work and social activities • Cannot work or participate in social activities	Duration: • None (0 hour) • 4 hours • 8 hours • 16 hours
Symptom-free phase	Severity: • No symptoms	Duration: • Difference between 24 hours and the sum of the durations of the headache and post-headache phases
Chance headache returns within 24 hours	Risk level: • No chance • 10% chance • 33% chance • 50% chance	

varying levels of the attributes shown in Table 1. For each question, respondents indicated which medicines they would choose if these were the only treatment options available. Figure 2 presents an example trade-off question (also known as choice question).

A widely accepted algorithm was used to generate an experimental design of treatment profile pairs that maximize the amount of statistical information that can be obtained from a given number of questions.[26-30] The experimental design ensured that all severity–duration combinations were statistically identifiable. The resulting design consisted of 64 choice questions divided into 8 survey versions of 8 questions each.

Analysis.—Except for chance of recurrence, all symptom attributes in Table 1 were modeled as categorical variables interacted with outcome durations in 30-minute increments. A random parameters logit (RPL) model provided an estimate of the mean preferences for each outcome in our study design. A latent class logit (LCL) model was used to evaluate variations in the preference for outcomes across respondents, and to estimate the relationships among such variations and observable respondent characteristics.

In the RPL model, treatment choice is explained by the attribute levels for the treatments in the choice questions. The RPL model was used to estimate a parameter for each outcome level, indicating the relative preference for the levels of the outcomes.[31] These parameter estimates can be interpreted as mean preference weights, indicating the preference for each attribute level. Greater preference for an outcome is associated with greater relative preference weights. Relative preference weights can also be related to the marginal impact that each attribute level has on the probability that a treatment is selected by migraineurs. Preference weight estimates are relative to the mean treatment profile in the experimental design.

Unobserved variation in the preference for outcomes across the sample can bias estimates in conventional logit choice models. RPL models avoid this potential bias by estimating additional parameters

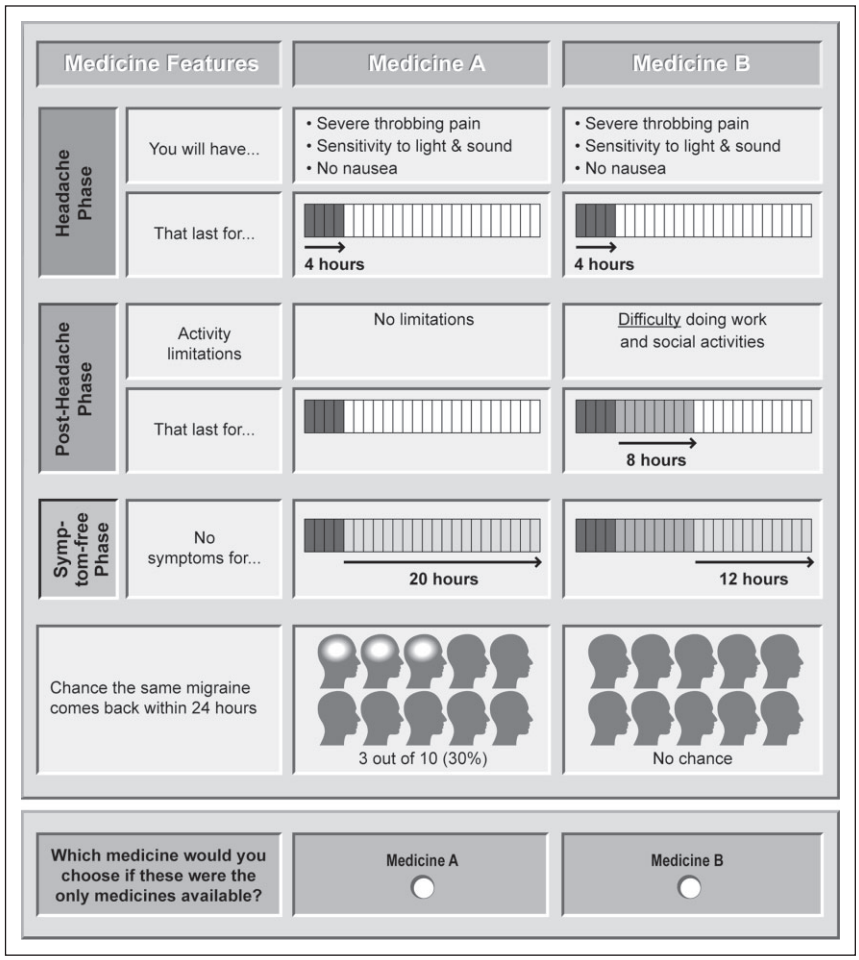

Fig 2.—Example trade-off question.

that characterize the distribution of preferences for attributes and control for its impact on the model estimates.[32]

Although RPL avoids biases from unobserved variation in the preference for attribute levels, it does not explain these variations with observable respondent characteristics. To explain variations in preferences with observable respondent characteristics, we used an LCL model.[33] The LCL model is a logit model that assumes that each respondent belongs to one of several data-defined classes or groups with similar preferences. LCL models stratify choice patterns into these data-defined classes and estimates a set of relative preference weights for each class. Although the probability that a patient belongs to any specific class is not directly observed, once choice patterns have been stratified into classes, it is possible to determine the probability that a patient with given characteristics is a member of each class.

Statistical significance of the differences in relative preference weights and the impact of personal characteristics on class membership was set at a 95% confidence level ($P < .05$). Both the RPL and LCL models were estimated using NLOGIT version 4.0 (Econometric Software, Plainview, NY, USA).

RESULTS

Sample Characteristics.—Table 2 summarizes the demographic characteristics of people who were invited to complete the survey but did not reply to the invitation, people who replied to the invitation to participate but did not complete the survey, and respondents who replied and completed the survey. The mean age of respondents who completed the

Table 2.—Sample Demographic Characteristics

Characteristic	Statistic or Category	Completed the Survey n = 539 (Percentage)	Did Not Qualify or Consented		Did Not Respond to Invitation	
			n = 159 (Percentage)	*P* value‡	n = 369 (Percentage)	*P* value‡
Age in years	Mean	43.6 (14.6)†	45.3 (16.8)†	.260	40.7 (14.8)†	.004
	Median	43	46		40	
	Minimum, maximum	18, 104	18, 88		18, 91	
Gender	Male	121 (22.4%)	52 (32.7%)	.008	68 (18.4%)	.143
	Female	418 (77.6%)	107 (67.3)		301 (81.6%)	
Race/ethnicity	White, non-Hispanic	377 (69.9%)	129 (81.1%)	.024	251 (68.0%)	.457
	Black, non-Hispanic	32 (5.9%)	10 (6.3%)		30 (8.1%)	
	Other, non-Hispanic	19 (3.5%)	5 (3.1%)		8 (2.2%)	
	Hispanic	87 (16.1%)	10 (6.3%)		66 (17.9%)	
	2 + races, non-Hispanic	24 (4.5%)	5 (3.1%)		14 (3.8%)	
Education level	Less than high school	41 (7.6%)	9 (5.7%)	.564	31 (8.4%)	.976
	High school diploma or the equivalent (GED)	181 (33.6%)	61(38.4%)		122 (33.1%)	
	Some college	138 (25.6%)	33 (20.8%)		101 (27.4%)	
	Associate degree	54 (10.0%)	18 (11.3%)		37 (10.0%)	
	Bachelor's degree	77 (14.3%)	28 (17.6%)		49 (13.3%)	
	Master's degree	36 (6.7%)	8 (5.0%)		20 (5.4%)	
	Professional or doctorate degree	12 (2.2%)	2 (1.3%)		9 (2.4%)	
Employment status	Working – as a paid employee	241 (44.7%)	76 (47.8%)	.022	198 (53.7%)	.169
	Working – self-employed	37 (6.9%)	9 (5.7%)		19 (5.2%)	
	Not working – on temporary layoff from a job	7 (1.3%)	2 (1.3%)		4 (1.1%)	
	Not working – looking for work	64 (11.9%)	16 (10.1%)		46 (12.5%)	
	Not working – retired	35 (6.5%)	23 (14.5%)		16 (4.3%)	
	Not working – disabled	78 (14.5%)	21 (13.2%)		43 (11.7%)	
	Not working – other	77 (14.3%)	12 (7.6%)		43 (11.7%)	

†Standard deviation.
‡*P* values indicate the statistical significance of differences between people who completed the survey and each non-respondent category. Significance of differences is reported based on chi-square tests for categorical variables and *t*-tests for continuous variables.
GED = general equivalency diploma.

survey was 44 years. Most surveyed subjects were female (78%), white non-Hispanic (70%), and had at least some college education (59%). Fifteen percent of the subjects were disabled or unable to work, and 52% were employed.

People who did not complete the survey (non-respondents) had a mean age of 40 years for those who did not reply to the invitation, and 45 years for those who replied but did not complete the survey. As with respondents, most non-respondents were female and white non-Hispanic. More non-respondents had at least some college education and were employed. Some of these differences were statistically significant. Table 2 also shows information on the significance of the differences that we found between respondents and non-respondents.

Among respondents, the mean age at which subjects were diagnosed with migraine was 25 years. The four most commonly used prescription medicines were sumatriptan (14%), rizatriptan (6%), zolmitriptan (3%), and hydrocodone (3%). Approximately 41% of subjects reported having less than 1 migraine attack per month, while 45% of subjects reported having between 1 and 4 migraine attacks per month, and about 13% reported having 5 or more attacks per month. Fifty-three percent of subjects experienced visual disturbances, and 47% of subjects experienced eye pain during the pre-headache phase. During the headache phase, most subjects experienced throbbing or pounding head pain (86%), pain on one side of the head (69%), pain worsening with activity (76%), nausea (69%), sensitivity to light (90%), neck pain or discomfort (53%), irritability (60%), difficulty thinking or concentrating (82%), or feeling tired and sluggish (52%). The majority of subjects also reported feeling tired and sluggish in the post-headache phase (68%). Most subjects (72%) reported that it took them 1 hour or longer to reach the symptom-free phase after taking a migraine medicine, with the average time being 6.2 hours.

A majority of subjects (52%) reported that a typical migraine would last more than 12 hours if left untreated. Subjects reported that their migraines returned within 24 hours 24% of the time. Among subjects who took both a triptan and a non-steroidal anti-inflammatory drug to treat migraines, 6% used both to treat the same migraine, and 37% reported using the non-steroidal anti-inflammatory drug first. Most subjects (67%) took migraine medicine either before or as soon as they felt pain, and 42% of subjects always took their medicine the same way. The most bothersome symptom reported was throbbing or pounding head pain (85%), and the least bothersome symptom was back pain (16%).

Comparing Headache and Post-Headache Symptoms.—Table 3 shows the parameter estimates from the RPL model and the marginal choice probabilities associated with each attribute level. Results are normalized at zero for the mean effect of all profiles presented to respondents in the survey.

Specification tests indicated that relative preferences for headache phase outcomes were approximately linear in duration. In other words, that relative preferences for a 1-hour change in symptom duration is about the same, regardless of whether the overall duration from which the change occurs was short (eg, 1.5 hours) or long (eg, 8 hours). Functional form tests indicated that the relative preference for the 2 levels of post-headache activity restrictions were quadratic in duration, which means that the effect of an additional hour of activity restriction changed for longer restriction durations.

Figure 3 compares the relative preference weights for migraine headache severities for different durations. The relative preference weights over time are calculated by simply multiplying the parameter estimate obtained from the RPL model for the symptom severity of interest by the number of hours that the symptoms are assumed to last. In Table 3, these parameters were implicitly multiplied by one. Given that units of symptom duration were set to represent 30 minutes, the parameter estimates in Table 3 also represent the relative preference weights for the effect of 30 minutes with each time-dependent outcome. To calculate the effect of 8 hours with any time-dependent outcome, one would have to multiply the parameter estimates in Table 3 by 16 (16 30-minute units equal 8 hours).

Logically, the most preferred outcome in the headache phase was having a migraine headache with no sensitivity to light or sound and no nausea. The

Table 3.—Relative Preference Weights and Marginal Probabilities From Random Parameters Logit Model

Outcome		Parameter Estimates (Standard Error)	Marginal Probability (Standard Error)
Interaction between continuous headache phase duration and headache symptoms†	Throbbing head pain with no sensitivity to light and sound or severe nausea	–0.025 (0.028)	–0.006 (0.003)
	Throbbing head pain and sensitivity to light and sound, no severe nausea	–0.027 (0.031)	–0.007 (0.004)
	Throbbing head pain and severe nausea, no sensitivity to light and sound	–0.033 (0.034)	–0.008 (0.004)
	Throbbing head pain, sensitivities to light and sound, and severe nausea	–0.043 (0.033)	–0.011 (0.004)
Interaction between continuous post-headache phase duration and post-headache symptoms†	Difficulty doing work and social activities	0.004 (0.004)	0.001 (0.001)
	Quadratic term for difficulty doing work and social activities	0.001 (0.000)	0.000 (0.000)
	Cannot work or participate in social activities	–0.004 (0.004)	–0.001 (0.001)
	Quadratic term for not being able to work or participate in social activities	0.001 (0.000)	0.000 (0.000)
Chance the same migraine will return within 24 hours	No chance	0.660 (0.093)	0.159 (0.011)
	10% chance	0.426 (0.076)	0.105 (0.009)
	33% chance	–0.175 (0.058)	–0.044 (0.007)
	50% chance	–0.911 (0.118)	–0.213 (0.014)
Symptom-free time†	Continuous symptom-free phase duration	0.129 (0.025)	0.032 (0.003)

†Assumed change in duration is from no time to 1 hour.

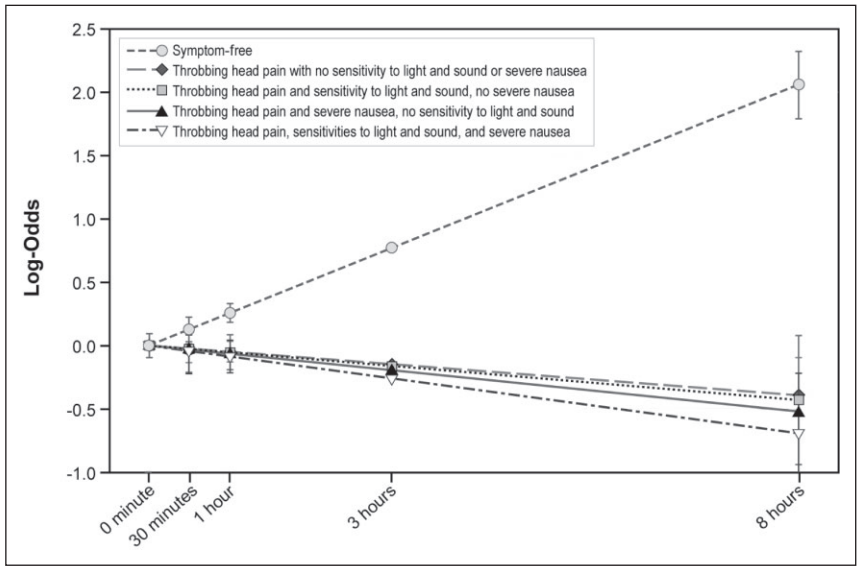

Fig 3.—Preference weights for migraine headache severities over time (n = 510). The parameter estimates from random parameters logit models are log-odds estimates representing the migraine respondents' preferences for attribute level. The vertical bars around each mean preference weight denote the 95% confidence interval for the point estimate. Estimates are most accurate for the average number of hours in the headache phase. Hence, confidence intervals of approximately 2.5 hours are the smallest. In several cases, the confidence interval is smaller than the marker used for the point estimate.

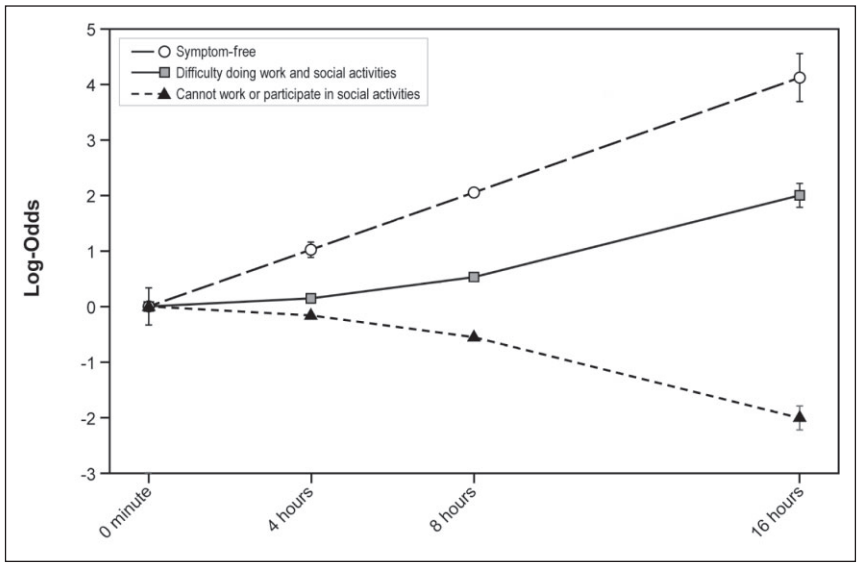

Fig 4.—Preference weights for limitations during post-headache phase over time (n = 510). The parameter estimates from random parameters logit models are log-odds estimates representing the migraine respondents' preferences for attribute level. The vertical bars around each mean preference weight denote the 95% confidence interval for the point estimate. Estimates are most accurate for the average number of hours in the post-headache phase. Hence, confidence intervals of approximately 7 hours are the smallest. In several cases, the confidence interval is smaller than the marker used for the point estimate.

least preferred outcome in the headache phase was experiencing throbbing head pain with sensitivity to light or sound and nausea. As expected, respondents perceived more discomfort from severe nausea than from sensitivity to light or sound.

The vertical bars around each parameter estimate in Figure 3 indicate 95% confidence intervals. Mean estimates are statistically different from each other at the 5% level of significance or better if confidence intervals do not overlap for adjacent levels of a particular attribute. All preference weights for different severities of headache symptoms were statistically different from preference weights for no symptoms. However, differences in respondents' preferences were not statistically significant across headache severities.

Figure 4 shows preference weights for daily activity limitations during the post-headache phase for different durations. To calculate these effects, it is necessary to consider the duration of interest and the squared value of that duration, and multiply them by the parameter on the severity of interest and the parameter on the quadratic term for that severity, respectively. Respondents again logically preferred having difficulty with work and other social activities to not being able to work or participate in social events. Again as expected, time with no symptoms was the most strongly preferred outcome. Contrary to results for outcomes in the headache phase, importance weights for outcomes in the post-headache phase were statistically significantly different among daily activity limitations.

We used the relative preference weights to calculate importance weights for different durations of headache and post-headache symptoms. For a given duration, differences in the preference weights indicate the relative importance of moving from one attribute level to another attribute level. For example, the relative importance of an improvement from 8 hours of throbbing pain with no nausea and sensitivity to light or sound to having no symptoms at all for 8 hours is approximately 2.4 (2.1 minus –0.3). Similarly, in the post-headache phase, an improvement from 16 hours of difficulty doing work or social activities to no post-headache limitations for 16 hours has a relative importance of approximately 2.1 (4.1 minus 2). Therefore, an improvement from 8 hours of throbbing pain with no nausea and sensitivity to light or sound to having no symptoms is about as important to patients as an improvement from 16 hours of diffi-

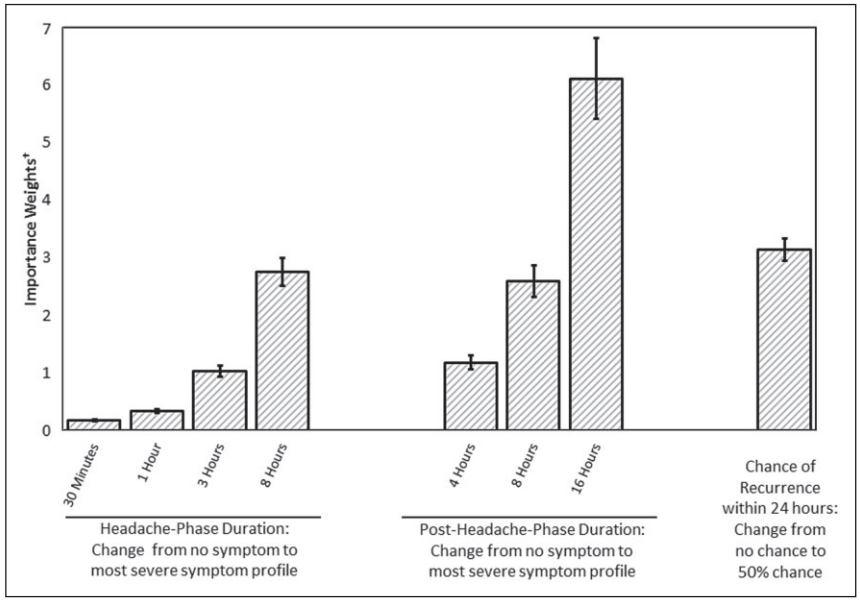

Fig 5.—Importance weights (n = 510). The vertical bars around each mean importance weight denote the 95% confidence interval for the point estimate. †Absolute difference in log odds between the best and worst levels of each attribute.

culty doing work or social activities to 16 hours of no post-headache limitations (2.4 divided by 2.1 = 1.14). We compared the relative importance of migraine symptoms using the relative preference weights derived from the estimates in Table 3. The absolute scale of relative importance scores is arbitrary, and the importance score for each attribute level is meaningful only when compared with other importance scores.

Relative Importance of Treatment Features.—The vertical distance between the preference weight for the best and worst levels of an attribute can be interpreted as the overall relative importance of the attribute over the ranges presented in the survey. Figure 5 compares the mean relative importance scores (and 95% confidence intervals) for the treatment attributes in the study.

Given the range of levels of the attributes in the study, the most important attribute to respondents was not being able to work or participate in social activities for 16 hours. The possibility of recurrence was more important than 3 hours of throbbing head pain with nausea and sensitivity to light or sound ($P > .05$). As duration in a migraine phase decreased, the importance of symptom severity during that phase also decreased.

We can compare relative importance among attributes as we did for changes in attribute levels. For example, an improvement from 16 hours of not being able to work or participate in social activities to no symptoms was more than 5 times as important as an improvement from 4 hours of not being able to work or participate in social activities to no symptoms.

Although mean relative importance differed across attributes, some of these differences were not statistically significant. For example, 8 hours of throbbing head pain with nausea and sensitivity to light or sound was not statistically different from a 50% chance of recurrence at the 5% level of significance ($P > .05$).

Relative Effect of Possible Migraine Medications.—As an example of the type of evaluations that can be made with the preference information collected in this study, we considered 4 outcome profiles that could result from migraine treatments. Figure 6 summarizes the relative effect of each profile on migraineurs' reported level of well-being. To calculate the effect of each profile, we summed preference weights for each migraine symptom in the profiles. For example, 30 minutes of headache symptoms without nausea or sensitivity to light and sound had a preference weight of –0.006. The preference weight

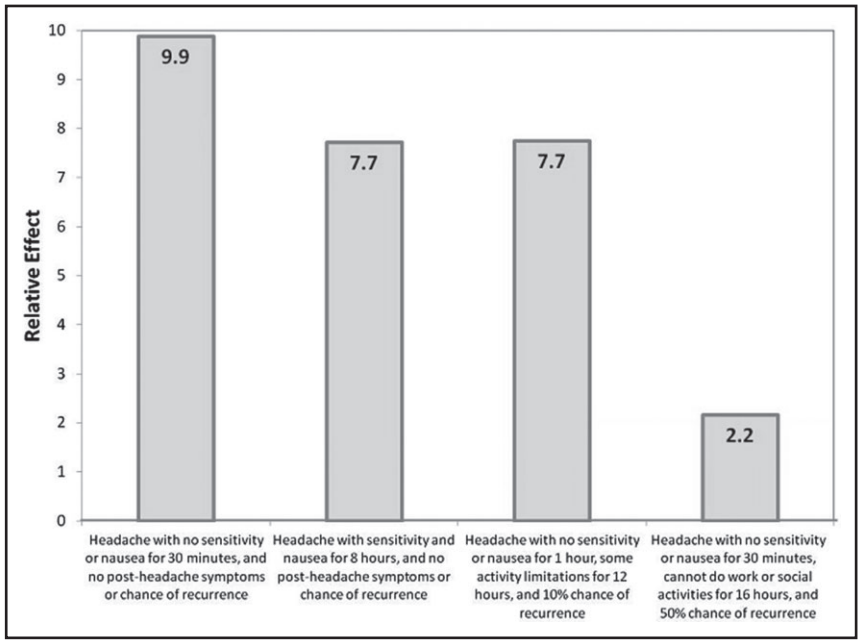

Fig 6.—Relative effect of medications for 4 treatment profiles (n = 510).

for 8 hours of not being able to do work or social activities was –0.5. Adding the two weights (–0.5006), we calculate the effect of having 30 minutes of headache symptoms without nausea or sensitivity to light and sound, followed by 8 hours of not being able to do work or social activities.

In Figure 6, the effect of each profile is scaled relative to the least damaging migraine episode (no symptoms during the headache or post-headache phase), assigned a value of 10, and the worst profile that can be created with the attributes and levels in the study, assigned a value of zero. Although the absolute value of the effects in Figure 6 is arbitrary, the relationships among the values for the profiles reflect their relative importance. For example, having a headache for 30 minutes, followed by no pain or limitations on daily activities, has a relative importance score of approximately 9.9. On the other hand, having the same headache for 30 minutes, but followed by 16 hours of not being able to do any social or family activities, has a relative importance score of approximately 2.2. Thus, a treatment that prevents post-headache symptoms is about 4.5 (9.9 divided by 2.2) times as important as having the same headache followed by 16 hours of not being able to do any work or social activities. On the other hand, 8 hours of the most severe headache symptoms (7.7) were considered equivalent to an hour of headache without light and sound sensitivity or nausea, 12 hours of some activity limitations, and a 10% chance of recurrence (7.7).

Patient Characteristics and Preferences.—The LCL model identified 3 respondent classes. The number of respondent classes was determined using the Bayesian information criterion (BIC).[34] Because LCL estimates a set of preference weights for each respondent class, adding classes increases the number of parameter estimates required, which can result in overfitting the model. The BIC quantifies the model fit but adds a penalty for each additional class requested by the user. Table 4 shows the parameter estimates and standard errors for each of the 3 classes and estimates for the parameters determining class membership.

Although no single respondent characteristic determined the probability of being in a given class, certain respondent characteristics increased the probability of being in a given class. We call these parameters class membership parameters. Estimates on class membership are relative to the effect of each characteristic on the probability of being in class 3. For example, if a class membership parameter for

Table 4.—Parameter Estimates From Latent Class Logit Model

		Parameter (Standard Errors)		
Outcome Parameters		Class 1	Class 2	Class 3
Interaction between continuous headache phase duration and headache symptoms	Throbbing head pain with no sensitivity to light and sound or severe nausea	–0.0610 (0.0199)	0.0936 (0.0141)	–0.0417 (0.0197)
	Throbbing head pain and sensitivity to light and sound, no severe nausea	–0.0767 (0.0207)	0.1172 (0.0163)	–0.0129 (0.0226)
	Throbbing head pain and severe nausea, no sensitivity to light and sound	–0.0502 (0.0235)	0.0675 (0.0165)	–0.0361 (0.0221)
	Throbbing head pain, sensitivities to light and sound, and severe nausea	–0.0719 (0.0236)	0.0859 (0.0162)	–0.0226 (0.0219)
Interaction between continuous post-headache phase duration and post-headache symptoms	Difficulty doing work and social activities	0.0064 (0.0028)	0.0120 (0.0022)	–0.0196 (0.0035)
	Difficulty doing work and social activities squared	0.0014 (0.0004)	0.0014 (0.0003)	0.0017 (0.0005)
	Cannot work or participate in social activities	–0.0064 (0.0028)	–0.0120 (0.0022)	0.0196 (0.0035)
	Cannot work or participate in social activities squared	–0.0014 (0.0004)	–0.0014 (0.0003)	–0.0017 (0.0005)
Chance the same migraine will return within 24 hours	No chance	0.8935 (0.1014)	0.2222 (0.0680)	2.3382 (0.1291)
	10% chance	0.6561 (0.0910)	0.2005 (0.0689)	1.1876 (0.0960)
	33% chance	–0.2649 (0.0765)	–0.1725 (0.0711)	–0.4372 (0.1020)
	50% chance	–1.2847 (0.1134)	–0.2501 (0.0663)	–3.0887 (0.1020)
	Continuous symptom-free phase duration	0.1248 (0.0162)	0.0759 (0.0121)	0.0683 (0.0183)
Class-Membership Parameters		Class 1	Class 2	Class 3
Constant		1.5033 (0.8733)	0.9749 (0.9998)	—
Age (Years)		–0.0084 (0.0104)	–0.0082 (0.0128)	—
Gender (Male = 1, Female =0)		0.3462 (0.3778)	0.4497 (0.4387)	—
Marriage (Married or living with partner =1, Otherwise = 0)		–0.1922 (0.3064)	–0.4414 (0.3639)	—
Education (At least high school =1, Less than high school = 0)		1.1249 (0.5532)	0.1182 (0.5456)	—
OTC medication (Take OTC medications for migraines = 1, Otherwise = 0)		0.5237 (0.3330)	0.1349 (0.3896)	—
Frequency of attacks (Fewer than 3 migraines per month = 1, Otherwise = 0)		–0.4669 (0.3420)	–0.7714 (0.3980)	—
Reported severity of post-headache symptoms 1 (Can do all or many social and family activities with some difficulty =1, Otherwise = 0)		–0.2485 (0.3908)	–0.1638 (0.4673)	—
Reported severity of post-headache symptoms 2 (Can do some or cannot do most social and family activities = 1, Otherwise = 0)		–1.5266 (0.4017)	–1.1651 (0.4929)	—
Prescription drugs (Use both triptans and NSAIDs to treat migraines = 1, Otherwise = 0)		0.0009 (0.0005)	0.0001 (0.0007)	—

NSAIDs = non-steroidal anti-inflammatory drugs; OTC = over the counter.

class 2 is positive and significant in a specific characteristic, it means that having that characteristic increases the chance of being in class 2 relative to the chance of being in class 3. Respondents had a greater likelihood of being members of class 1 if they reported having a higher level of education (estimate = 1.12, standard error = 0.5532, $P = .04$). Respondents were less likely in class 1 and class 2 if they reported experiencing moderate or severe post-headache symptoms, as opposed to milder symptoms. Finally, respondents had a greater chance of being members of class 3 if they reported experiencing more debilitating migraine episodes. Although not shown in Table 4, the result for class 3 can be inferred because reports of having debilitating migraine episodes decrease the chance of being in class 1 and class 2.

Respondents who were likely in class 1, approximately 62% of the total sample, were negatively affected by any type of migraine, did not distinguish between sensitivity to light or sound and nausea, but were concerned about experiencing the most severe type of headache. Respondents who were likely in class 2, approximately 20% of the total sample, had little concern about milder headaches. However, these respondents tended to be much more concerned about limitations in daily activities. Respondents who were likely in class 3, approximately 18% of the total sample, were particularly concerned about the chance of recurrence.

DISCUSSION

As one might expect in the real world, migraineurs in our study were strongly affected by the pain associated with headache symptoms. Although, on average, other symptoms such as sensitivity to light and sound plus pain, and nausea plus pain, affected migraineurs more than pain alone, the impacts of these additional symptoms were small and not statistically different from pain alone at the study sample size.

In terms of post-headache symptoms, migraineurs in our study discriminated clearly among levels of limitations on daily activities. Even experiencing only some difficulty in doing daily social and family activities had statistically significant impact on migraineurs' perceived level of well-being. Specifically, our results suggested that, for short periods of post-headache symptoms, the change from no limitations to some limitations on daily activities affects migraineurs more than a change from already having some limitations to not being able to do daily activities altogether. For longer periods of post-headache symptoms, this relative impact of post-headache symptoms is reversed.

With respect to symptom duration, an hour of headache symptoms was perceived to have a greater impact than post-headache symptoms. However, as shown in the scoring of the example treatment profiles, the accumulated effect of post-headache symptoms can affect patient well-being as much as the headache symptoms if the post-headache symptoms last long enough. This result highlights the importance of measuring incidence of post-headache symptoms in the population of migraineurs, and suggests that focusing on the burden associated with the headache phase alone may significantly underestimate the impact of migraines to patients.

Preferences for symptom severity and duration varied across respondents in the sample. Although, on average, respondents in the study were concerned with both headache and post-headache symptoms, a closer look at individual preferences indicated that most respondents appeared to be more concerned with the impact of headache symptoms. A smaller yet significant number of respondents perceived post-headache symptoms as having a more detrimental effect than headache symptoms.

Our results also indicated that reported migraine severity is a strong predictor of treatment outcome preferences. Respondents who reported experiencing more debilitating migraine headaches (ie, class 3 respondents) logically were the most affected by the possibility of recurrence. On the other hand, pain is a subjective experience, and some respondents who reported experiencing milder migraine attacks simply may have a higher pain threshold, and consequently were less concerned by mild headaches and more concerned with the features of migraine headaches that affected their everyday lives (ie, class 2 respondents). Finally, other respondents had milder and less frequent migraine episodes. To respondents in this

category (ie, class 1), any migraine headache was perceived to significantly affect them.

It is important to note that the distribution of the classes we identified and the variations in preferences for migraine symptoms are not intended to characterize the experience of migraineurs in clinical practice. These results are only meant to elicit potential differences in the impact of headache or post-headache symptoms across the migraineurs types that we were able to identify in our sample. To describe clinical practice with our relative preference results, it would be necessary to only consider the importance of current symptom experienced by migraineurs. Furthermore, it would be necessary to determine the distribution of the identified migraineurs types in the general population and weigh our sample accordingly. Both of these steps go beyond the scope of the current study.

While choice-format, conjoint-analysis methods are increasingly used to support regulatory decisions, to identify optimal treatment guidelines, and to promote patient-centered medicine, such methods have limitations. The most important limitation is that respondents evaluate hypothetical treatments. DCE trade-offs are intended to simulate plausible clinical decisions but obviously do not have the clinical or emotional consequences of actual decisions. Thus, differences can arise between stated and actual choices. We attempted to minimize such potential differences by offering treatment alternatives that mimicked real-world trade-offs as closely as possible. Nevertheless, there are many factors that can influence actual treatment decisions that are not accounted for in our study. In particular, simplified hypothetical settings ignore important real-world contexts, including severe headaches that occur at inconvenient times, such as a wedding or job interview, compared with days without important plans or activities. Also, consensus on methodological standards is evolving; thus, our approach is one among several alternative preference elicitation methods available to outcomes researchers.[35] Finally, even though the panel used to recruit subjects for this study is representative of the American population as a whole, and migraine is a highly prevalent condition, the portion of the panel who completed this preference survey might not be strictly representative of the general population of migraineurs.

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