Migraine Frequency and Health Utilities: Findings from a Multisite Survey

Jeffrey S. Brown, PhD,[1] Peter J. Neumann, ScD,[2] George Papadopoulos, BSc (Hons),[3] Gary Ruoff, MD,[4] Merle Diamond, MD,[5] Joseph Menzin, PhD[6]

[1]Department of Ambulatory Care and Prevention, Harvard Medical School/Harvard Pilgrim Health Care, Boston, MA, USA; [2]Tufts-New England Medical Center Institute for Clinical Research and Health Policy, Boston, MA, USA; [3]Schering-Plough Corporation, Kenilworth, NJ, USA; [4]Westside Family Medical Center, Kalamazoo, MI, USA; [5]Diamond Headache Clinic, Chicago, IL, USA; [6]Boston Health Economics, Inc., Waltham, MA, USA

ABSTRACT

Objectives: Assess the relationship between migraine frequency and health utility.

Methods: Patients aged ≥18 years diagnosed with episodic migraine were enrolled at three US sites representing varied models of health-care delivery. All subjects completed a questionnaire that included demographic and clinical information, a migraine-specific disability questionnaire, and the Health Utilities Index Mark 3 (HUI3). The HUI3 is a generic health status and health-related quality-of-life measure. HUI3 health status data are translated into utility scores anchored by 0 (dead) and 1 (perfect health).

Results: The study enrolled 150 patients. The mean age was 44 years and 87% were female. Mean (±SD) monthly migraine frequency was 4.4 ± 3.6, with 34% reporting ≤2 migraines per month and 20% reporting >6 migraines per month. The mean (±SD) HUI3 score was 0.62 ± 0.26. After controlling for study center, demographics, comorbidities, migraine characteristics, and level of migraine disruptiveness, migraine frequency was found to be significantly ($P < 0.05$) and negatively associated with HUI3 scores. Subjects with >6 migraines per month had an adjusted mean HUI3 score of 0.41; the corresponding mean for those reporting ≤2 migraines per month was 0.67. Migraine frequency was positively associated with higher levels of disability for the emotion, cognition, and pain components of the HUI3.

Conclusions: Among this group of care-seeking patients, migraineurs' health utilities were inversely related to headache frequency. Although these data may not be generalizable to the entire migraine population, they may be useful in assessing the comparative cost-effectiveness of preventive migraine therapies.

Keywords: health utility, HUI, migraine, quality of life.

Introduction

Migraine is a common neurological disorder characterized by severe, disabling headaches usually accompanied by nausea or vomiting, photophobia, and phonophobia [1]. Approximately 6% of men and 18% of women in the United States have experienced migraine, with peak prevalence occurring during prime working years (aged 25 to 55 years) [2–4]. About 50% of migraineurs experience an estimated 1.5 attacks per month, and up to one-quarter experience one or more attacks weekly [3]. The most recent national epidemiological survey of migraine found that 23% of migraineurs had less than one attack per month, and 63% had one to four attacks per month [4]. Despite its prevalence, and the emergence of effective treatment options, many migraine sufferers remain undiagnosed or receive inadequate clinical management [5,6]. Diagnosis and management of migraine are complicated by broad and varied clinical characteristics and frequent concomitance with other neurological conditions such as depression, panic disorder, general anxiety, and epilepsy [7–9].

The economic burden of migraine is substantial because migraine predominately affects young and otherwise productive individuals [10,11]. The majority of this economic burden is related to indirect costs such as absenteeism or reduced/lost workplace productivity (i.e., "presenteeism") borne by employers [11,12]. Direct health-care costs, including those related to drug treatment, physician services, diagnostic testing, hospitalization, and emergency room treatment, are also substantial—potentially exceeding $1 billion annually [12,13]. Direct health costs for migraineurs have been estimated to be at least $50 more per month as compared to a cohort of nonmigraineurs [14].

Migraine has considerable negative effects on quality of life [9,15–18], with some evidence suggesting that the general well being of migraineurs may be impaired even between attacks [19]. Persons with migraine have difficulty relating to family members [20,21], and regular activities such as housework and social plans are often delayed or canceled because of illness [2,3,15,20]. Studies using the Medical Outcomes Study Short Form-36 (SF-36) (and variations such as the SF-8D and SF-12) have found that migraine sufferers have lower health-related quality of life than nonmigraineurs, with more pain and restriction in their daily activities than patients with many other chronic conditions (e.g., depression, osteoarthritis, and diabetes) [9,15,17,18,22].

Although there is a rich survey-based literature on migraine incidence, treatment, and disease burden [3–5], there are limited data on the frequency of migraine attacks in clinical practice (e.g., average migraines per month for treatment-seeking patients) and on the relationship between frequent migraines and health status, particularly as measured by health utilities [9]. Health utilities, a type of health preference measure used to quantify the preferences of individuals for particular health states, typically vary from 0 (dead) to 1 (perfect health). Distinct from generic health status measures, health utilities also are useful for cost-effectiveness analyses and comparing health state preferences across diseases. Therefore, we set out to measure health utility among a cohort of migraine patients and relate migraine frequency to health utility scores.

Methods

Study Design

A cross-sectional survey was administered to patients aged ≥18 years who were physician-diagnosed with episodic migraine at least 1 year before study enrollment (based on medical chart review at the time of recruitment), and who were not experiencing a migraine at the time of recruitment. Patients were enrolled at three US sites, including a primary care group practice, a specialty headache clinic, and a nonprofit HMO group practice. The sites were selected based on their established experience in conducting clinical research and to provide diversity in geography, patient population, and treatment setting. The principal investigator at each study site was responsible for verification of study inclusion criteria, including migraine diagnosis. A minimum level of monthly migraine frequency was not an inclusion criterion. Each site enrolled consecutive patients until their quota of 50 patients was reached (target enrollment was 150 patients). The surveys were completed between April and September 2004. Before study initiation, a 10-patient pilot study was conducted to

finalize the survey instrument. Patients provided written informed consent. Institutional Review Boards approved the study.

Study Measures

All subjects completed a questionnaire that included items regarding demographic (i.e., age, sex, income, education, race/ethnicity, insurance status, and employment status) and clinical information (monthly migraine frequency, selected comorbidities [yes/no], current use of acute and preventive medications, and overall prescription drug use). To assess comorbidities, we asked patients if they had ever been told by a doctor that they had any of the following conditions: depression, hypertension, arthritis, asthma, epilepsy, diabetes, congestive heart failure, renal disease, heart attack, or stroke. Migraine-specific questions included age at migraine onset, migraine severity (pain on a scale of 1–10), presence of aura, duration of typical migraines (<6 hours, 6–12, 12–24, and >24 hours), disruptiveness of migraines (five-item Likert scale ranging from "not at all" to "somewhat" to "very" disruptive), and migraine-related disability using the Migraine Disability Assessment (MIDAS) questionnaire (3-month recall period). The MIDAS is a brief, widely used questionnaire that captures information on migraine disability over the previous 3 months in terms of missed days of paid work (or school), household work (chores), and nonwork time (family, social, and leisure activities). MIDAS scores are summed and grouped into four disability categories, ranging from "little or none" to "severe" [23].

The primary study outcome—health utilities—was assessed using the Health Utilities Index Mark 3 (HUI3). The HUI3 is a generic and widely used patient-reported measure of health status. It is a 15-item questionnaire focusing on eight health status attributes (vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain), each with five or six levels of disability, for a total of 972,000 different health states [24,25]. A 4-week recall period was used for this study. The attributes are weighted according to preferences obtained from a community sample in Ontario, Canada, and were based on a visual analog scale and standard-gamble assessments [24]. The categorical health status measures are combined into a single global utility score and single attribute scores using a multiplicative multi-attribute utility function. Global and single component scores are interpreted as health utilities, and are anchored by 0 (dead) and 1 (perfect health). The HUI3 has been extensively validated in a variety of settings, conditions, and countries [25–27].

Analyses

Bivariate and multivariate (analysis of covariance) analyses were undertaken to assess the relationship

between HUI3 and migraine frequency. The multivariate analyses controlled for study center, demographics (age, sex, and income), presence of depression, presence of any other selected comorbidity (e.g., arthritis, hypertension, asthma), migraine characteristics (migraine severity, presence of aura, and duration), and the level of disruptiveness of migraine to family and friends. We included migraine frequency as a continuous variable in the main model to test the significance of the association between migraine frequency and HUI3 scores. A separate model specified migraine frequency categorically (<2, >2–4, >4–6, >6 migraines per month) to generate adjusted means for each migraine frequency category. Alternative statistical models that included selected interaction terms (e.g., migraine frequency by site and age) and different covariate specifications for migraine pain, duration, and disruptiveness were constructed to assess the robustness of the model estimates. The level of migraine disability was assessed descriptively using MIDAS.

All analyses were performed using SAS Version 9.0 statistical software (SAS Institute, Cary, NC). Data quality procedures were performed on an ongoing basis throughout the data collection period. One study subject provided multiple responses to individual items and therefore was excluded from the HUI3 analysis. The midpoint was used in cases in which a subject provided a range instead of a discrete number for monthly migraine frequency (e.g., 4–5 migraines per month was recorded as 4.5).

Results

Each site enrolled 50 subjects, achieving our target enrollment of 150. The mean (±SD) age was 44 ± 11.6 years, 87% were female, and 87% reported their race as white (Table 1). Subjects had an average of 24 years of migraine history, and 41% reported current use of preventive therapy for migraine. Migraines were described as "moderately" or "very" disruptive to friends and family by 45% of subjects. Subjects reported a mean (±SD) monthly migraine frequency of 4.4 ± 3.6, with 34% reporting ≤2 migraines per month and 20% reporting >6 per month (Table 2). MIDAS Grade IV (severe) disability was reported by 16% of subjects with two or fewer migraines per month, 42% of those with >2–4 migraines per month, 56% of those with >4–6 migraines per month, and 69% of those with more than six migraines per month (Table 3). Interestingly, one-third of those with two or fewer migraines per month reported moderate to severe disability based on MIDAS.

The median (mean ± SD) HUI3 global utility score was 0.66 (0.62 ± 0.26). One in four had HUI3 scores of less than 0.50, and only one in nine had HUI3 scores of at least 0.90. HUI3 global utility scores were lowest in those with frequent migraines and for those who

Table 1 Characteristics of study subjects

Characteristic	Total N	%
Age (years)		
18–34	33	22.0
35–44	41	27.3
45+	76	50.7
Mean age (SD)	44.4 (11.6)	
Sex		
Male	20	13.3
Female	130	86.7
Race/ethnicity		
White	131	87.3
African American	10	6.7
Hispanic	5	3.3
Other	4	2.7
Education		
High school graduate	76	50.7
College graduate	73	48.7
Missing	1	0.7
Annual family income		
Under $40,000	51	34.0
$40,000–$59,000	35	23.3
$60,000+	61	40.7
Missing	3	2.0
Selected comorbidities		
Other pain (neck and back pain)	41	27.3
Depression	38	25.3
Arthritis	26	17.3
Asthma	16	10.7
Hypertension	13	8.7
Diabetes	3	2.0
Epilepsy	1	0.7
Employment status		
Full-time	90	60.0
Part-time	22	14.7
Homemaker	17	11.3
Not employed	11	7.3
Retired	6	4.0
Other	3	2.0
Missing	1	0.7
Insurance		
Private health plan	128	85.3
No insurance (self-pay)	13	8.7
Government health plan	6	4.0
Other	2	1.3
Disability insurance	1	0.7

reported that their migraines were disruptive to family and friends. The mean (±SD) HUI3 global utility score was 0.68 (±0.25) for those reporting ≤2 migraines per month, and 0.55 (±0.22) for those reporting >6 migraines per month. Subjects with self-described "very disruptive" migraines to others had a mean HUI3 global utility score of 0.56.

After controlling for study site, demographics, comorbidities, migraine characteristics, and level of disruptiveness of migraine to family and friends, as well as the interaction between age and migraine frequency, migraine frequency (specified as a continuous variable) was significantly ($P < 0.025$) and negatively associated with the HUI3 global utility score. Other migraine characteristics (pain severity [$P < 0.77$], presence of aura [$P < 0.07$], and duration [$P < 0.36$]) were not found to be statistically significant predictors of HUI3 scores (Table 4). Findings from the alternative

Table 2 Migraine characteristics of study subjects

Characteristic	Total N	%
Age at onset (years)		
Under 18	69	46.0
18–24	29	19.3
25–34	25	16.7
35+	26	17.3
Missing	1	0.7
Migraine history		
Mean years with migraine (±SD)	24.0 (12.8)	
Migraine type		
Migraine with aura	49	32.7
Migraine without aura	101	67.3
Migraine pain (1 = mild, 10 = severe)		
1 to 4	5	3.3
5 to 7	64	42.7
8 to 10	76	50.7
Missing	5	3.3
Mean migraine pain level (±SD)	7.5 (1.6)	
Migraine duration		
Less than 6 hours	31	20.7
6 to 12 hours	41	27.3
13 to 24 hours	41	27.3
24+ hours	37	24.7
Disruptiveness of migraines		
Not at all	6	4.0
A little	39	26.0
Somewhat	37	24.7
Moderately	51	34.0
Very	17	11.3
Migraine treatments		
Reporting acute medication use	144	96.0
Reporting any current preventive		
Medication use	62	41.3
Monthly migraine frequency		
≤2	51	34.0
>2 to 4	44	29.3
>4 to 6	25	16.7
>6	30	20.0
Mean frequency (±SD)	4.4 (3.6)	

Table 4 Predictors of HUI3 scores according to multivariate analysis of covariance

Characteristic	Parameter estimate	P-value
Age (years)		
<35	Reference category	
35–44	−0.359	<0.001
45+	−0.194	0.026
Sex		
Female	Reference category	
Male	0.041	0.443
Annual family income level		
<$60,000	Reference category	
$60,000+	0.112	0.003
Self-reported depression		
No	Reference category	
Yes	−0.150	<0.001
Any other comorbidities*		
No	Reference category	
Yes	−0.029	0.453
Migraine with aura		
No	Reference category	
Yes	−0.073	0.073
Severe migraine pain†		
No	Reference category	
Yes	0.013	0.768
Migraine duration		
<24 hours	Reference category	
24+ hours	−0.040	0.360
Migraine disruptiveness‡		
No	Reference category	
Yes	−0.092	0.020
Migraines per month§	−0.039	<0.001

*Any comorbidity other than depression.
†Pain of 9 or 10 on a pain scale 1 to 10 (1 = mild, 10 = severe).
‡Migraines rated as "moderately" or "very" disruptive on 5-point Likert scale.
§Specified as a continuous variable.
Note: The model also include site and interaction of age and migraine frequency.
Model R^2 = 0.365, F-value = 4.27, P < 0.001.
HUI3, Health Utilities Index Mark 3.

models with different covariate specifications were consistent with the primary model result that showed migraine frequency was statistically and negatively associated with health utility. The adjusted mean HUI3 global utility score was inversely related to migraine frequency when grouped into four categories, HUI3 global utility score ranged from 0.67 in subjects with ≤2 migraines per month to 0.41 for those experiencing more than six migraines per month and this trend was significant (P = 0.043) (Table 5).

Only 2% of subjects reported no disability on any HUI3 attribute. Nine percent reported disability on only one HUI3 attribute, and 41% reported disability on four or more of the HUI3 attributes. The three HUI3 attributes most impacted by migraine frequency were emotion, cognition, and pain (Fig. 1). The mean single attribute utility scores for emotion (0.89) and cognition (0.88) were significantly lower (P < 0.001) than the mean scores for vision, hearing, speech, ambulation, and dexterity. The mean HUI3 score for pain (0.71) was significantly lower than all other HUI3 components (P < 0.001).

Table 3 Migraine Disability Assessment (MIDAS) by patient-reported monthly migraine frequency and mean HUI3 score

Number of patient-reported migraines per month	Migraine Disability Assessment grade*							
	I. Little or no disability		II. Mild disability		III. Moderate disability		IV. Severe disability	
	N	%	N	%	N	%	N	%
≤2	12	24.5	20	40.8	9	18.4	8	16.3
>2 to 4	5	11.6	5	11.6	15	34.9	18	41.9
>4 to 6	1	4.0	2	8.0	8	32.0	14	56.0
>6	3	10.3	2	6.9	4	13.8	20	69.0

*MIDAS data were missing for 4 subjects.
HUI3, Health Utilities Index Mark 3.

Table 5 Unadjusted and adjusted mean HUI3 global scores by patient-reported number of migraines per month

Number of patient-reported migraines per month	Mean (SD) HUI3 global utility score	
	Unadjusted	Adjusted*
≤2	0.68 (0.25)	0.67 (0.44)
>2 to 4	0.63 (0.26)	0.57 (0.35)
>4 to 6	0.60 (0.21)	0.52 (0.28)
6+	0.55 (0.22)	0.41 (0.59)

*Based on the analysis of covariance results, adjusted for study site, demographics (age, sex, income), and clinical characteristics (comorbidities, migraine pain severity, presence of aura, migraine duration, and disruptiveness of migraine to family and friends), and the interaction of migraine frequency and age. Trend is significant ($P = 0.043$).
HUI3, Health Utilities Index Mark 3.

Conclusions

To our knowledge, this is the first study of migraine patients to assess health preferences using the HUI. Using a combination of HUI3 utility scores and MIDAS evaluations, we found that migraineurs' level of disability is inversely related to headache frequency. After controlling for study site, sociodemographics, and clinical characteristics, migraine frequency was the only migraine characteristic that was statistically and negatively associated with HUI3 global utility scores. Self-reported migraine pain severity, presence of aura, and migraine duration were not significant predictors of HUI3 scores. The finding that self-reported pain severity was not associated with HUI3 score may be due to the lack of variation in reported pain; one-half of patients rated the pain of a typical migraine as 8 or above on a scale of 1 (no pain) to 10 (severe pain). We tested various alternative models (e.g., multiple interaction terms, including/excluding variables) and variable specifications (e.g., pain specified as greater than or less than 5, 7, and 8, duration specified as greater than or less than 12 hours) and did not observe a difference in the overall findings.

Most disability was found in the emotion, cognition, and pain components of HUI3, indicating the specific pathways by which migraine headaches impact overall health utility. Disability in the pain attribute was expected and helps validate the HUI3 measure in migraine. Disability in the emotion and cognition components may be related to the presence of other neurological conditions (e.g., depression) [7–9] and the high level of disruptiveness to family and friends attributed to migraines and migraine frequency.

Previous health status studies have reported that migraine patients have a lower quality of life, based on various measures, than that of the general population [9,15,16,18,22,28]. This was also seen in our study: subjects had a mean HUI3 global score of 0.62, compared with a mean HUI3 score of 0.86 for a US community sample aged 18 to 44 years of age and 0.78 for those aged 45 to 64 years [29]. Comparing our results with HUI3 studies in other clinical areas can help put our findings for migraineurs in broader perspective. Persons in our study had similar HUI3 global utility scores to a cross-sectional sample of patients with Type 2 diabetes (0.64) [30] and those with intermittent claudication eligible for revascularization (0.66) [31]. The mean HUI3 scores for subjects in our study were lower than those of patients visiting a rheumatology clinic (0.68) [32], but higher than that of patients with difficult-to-control epilepsy (0.56) [33] and mild or moderate Alzheimer's disease (0.39 and 0.19, respectively) [34]. Although each of these studies reported HUI3 scores, the study methodologies are not necessarily consistent, and direct comparisons should be made with caution.

Treatment strategies for migraine have primarily targeted management of acute episodes. Preventive therapy is recommended for those with frequent or disabling attacks [35,36], and there is some evidence
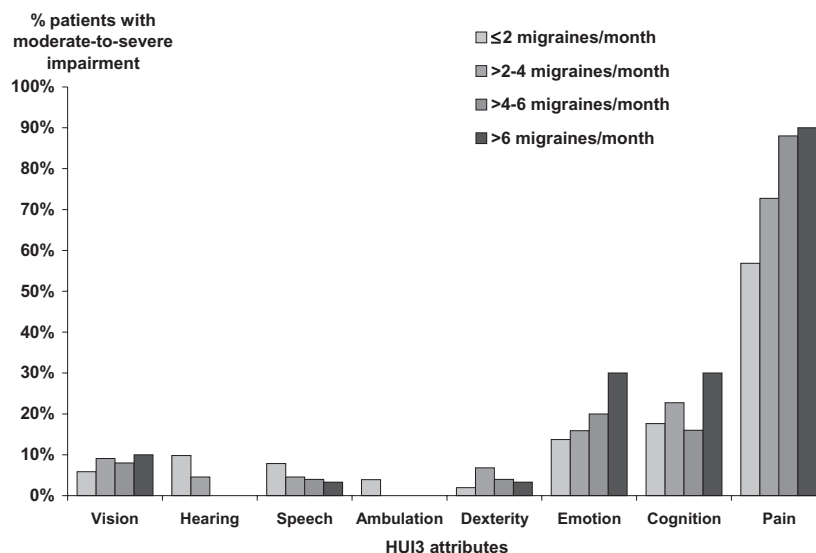

Figure 1 Frequency of HUI3 attributes associated with moderate-to-severe disability by monthly migraine frequency (level 3 or higher severity for all attributes except cognition, which was > level 4 severity). HUI3, Health Utilities Index Mark 3.

that prevention is cost-effective [37–39]. Medications used for migraine prevention include beta-blockers (e.g., propranolol), tricyclic antidepressants (e.g., amitriptyline), serotonin antagonists, and neuromodulators (e.g., topiramate and divalproex sodium) [40–43]. Public and private health-care purchasers in the United States and abroad are increasingly demanding comparative cost-effectiveness evaluations of new therapies such as those for migraine prevention, but those analyses are often limited because relevant health utility data are not available. The health utility data presented here can be used to estimate changes in quality-adjusted life years from preventive migraine treatment and may prove useful in assessing the comparative cost-effectiveness of various preventive migraine therapies [44].

The strengths of our study include a relatively large sample size for a health utility study, inclusion of a disease-specific health status measure (MIDAS), the geographic diversity and variation in the method of health-care delivery of the study sites, and the range of assessments included in the questionnaire. As for limitations, this was a cross-sectional survey of treatment-seeking patients, and as such, our sample is not representative of the overall migraine population. The American Migraine Prevalence and Prevention study—an epidemiological survey of US households to identify of the prevalence of migraine—found that, based on the MIDAS questionnaire, 64% of migraineurs had little to no disability (MIDAS Grade I) and 11% had severe disability (MIDAS Grade IV) [4]. In comparison, 41% of our cohort reported severe disability and only 14% reported little or no disability based on the MIDAS questionnaire. As such, our findings may not apply to persons who are able to manage their condition through self-care or have less frequent migraines; most migraine patients experience far fewer migraines per month than our study cohort [4]. Another limitation of our study is that we were not able to review subjects' medical charts, which might have helped control for other potential confounders in relating migraine frequency to health utilities. We also could not compare our cohort to the underlying populations at the three study centers. In addition, it should be noted that there is some debate over the validity of multiplicative multi-attribute utility functions such as those used in the development of the HUI3 [45]. Finally, we did not assess the relationship between acute and preventive migraine treatments, as the data collected for this utility study were inappropriate to support such an evaluation of the impact of those treatments.

In summary, our study of care-seeking migraineurs suggests that these patients suffer from fairly frequent migraines, and their self-reported health status is inversely related to headache frequency. Moreover, these individuals, on average, had health utility scores in line with other patients who have debilitating chronic illnesses. These findings suggest that reducing migraine frequency may ease the burden of migraine headache and improve the quality of life for migraineurs.

References

1 Headache Classification Subcommittee of the International Headache. The International Classification of Headache Disorders (2nd ed.). Cephalalgia 2004; 24(Suppl. 1):S9–160.

2 Lipton RB, Stewart WF, Diamond S, et al. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. Headache 2001;41:646–57.

3 Lipton B, Scher AI, Kolodner K, et al. Migraine in the United States: epidemiology and patterns of health care use. Neurology 2002;58:885–94.

4 Lipton RB, Bigal ME, Diamond M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. Neurology 2007;68:343–9.

5 Lipton RB, Diamond S, Reed M, et al. Migraine diagnosis and treatment: results from the American Migraine Study II. Headache 2001;41:638–45.

6 Harpole LH, Samsa GP, Matchar DB, et al. Burden of illness and satisfaction with care among patients with headache seen in a primary care setting. Headache 2005;45:1048–55.

7 Lipton RB, Ottman R, Ehrenberg BL. Comorbidity of migraine: the connection between migraine and epilepsy. Neurology 1994;44(Suppl. 7):S28–32.

8 Breslau N, Schultz LR, Stewart WF, et al. Headache types and panic disorder: directionality and specificity. Neurology 2001;56:350–4.

9 Lipton RB, Hamelsky SW, Kolodner KB, et al. Migraine, quality of life, and depression: a population-based case-control study. Neurology 2000;55:629–35.

10 Solomon GD, Price KL. Burden of migraine. A review of its socioeconomic impact. Pharmacoeconomics 1997;11(Suppl. 1):S1–10.

11 Stang P, Cady R, Batenhorst A, Hoffman L. Workplace productivity. A review of the impact of migraine and its treatment. Pharmacoeconomics 2001;19:231–44.

12 Hu XH, Markson LE, Lipton RB, et al. Burden of migraine in the United States: disability and economic costs. Arch Intern Med 1999;159:813–18.

13 Coukell AJ, Lamb HM. Sumatriptan. A pharmacoeconomic review of its use in migraine. Pharmacoeconomics 1997;11:473–90.

14 Clouse JC, Osterhaus JT. Healthcare resource use and costs associated with migraine in a managed health-care setting. Ann Pharmacother 1994;28:659–64.

15 Essink-Bot ML, Van Royen L, Krabbe P, et al. The impact of migraine on health status. Headache 1995;35:200–6.

16 Terwindt GM, Ferrari MD, Tijhuis M, et al. The impact of migraine on quality of life in the general population. The GEM Study. Neurology 2000;55:624–9.

17 Durham CF, Alden KR, Dalton JA, et al. Quality of life and productivity in nurses reporting migraine. Headache 1998;38:427–35.

18 Lipton RB, Liberman JN, Kolodner KB, et al. Migraine headache disability and health-related quality-of-life: a population-based case-control study from England. Cephalalgia 2003;23:441–50.

19 Dahlof CG, Dimenas E. Migraine patients experience poorer subjective well-being/quality of life even between attacks. Cephalalgia 1995;15:31–6.

20 Smith R. Impact of migraine on the family. Headache 1998;38:423–6.

21 Kryst S, Scherl E. A population-based survey of the social and personal impact of headache. Headache 1994;34:344–50.

22 Osterhaus JT, Townsend RJ, Gandek B, Ware JE. Measuring the functional status and well-being of patients with migraine headache. Headache 1994;34:337–43.

23 Lipton RB, Stewart WF, Sawyer J, Edmeads JG. Clinical utility of an instrument assessing migraine disability: the Migraine Disability Assessment (MIDAS) questionnaire. Headache 2001;41:854–61.

24 Feeny D, Furlong W, Torrance GW, et al. Multiattribute and single-attribute utility functions for the health utilities index mark 3 system. Med Care 2002;40:113–28.

25 Furlong WJ, Feeny DH, Torrance GW, Barr RD. The Health Utilities Index (HUI) system for assessing health-related quality of life in clinical studies. Ann Med 2001;33:375–84.

26 Furlong WJ, Feeny DH, Torrance GW, Barr RD. The Health Utilities Index (HUI®) system for assessing health-related quality of life in clinical studies. McMaster University Centre for Health Economics and Policy Analysis Research Working Paper Series #01-02. March 2001.

27 Horsman J, Furlong W, Feeny D, Torrance G. The Health Utilities Index (HUI®): concepts, measurement properties and applications. Health Qual Life Outcomes 2003;1:54.

28 Solomon GD, Skobieranda FG, Gragg LA. Quality of life and well-being of headache patients: measurement by the medical outcomes study instrument. Headache 1993;33:351–8.

29 Luo N, Johnson JA, Shaw JW, et al. Self-reported health status of the general adult U.S. population as assessed by the EQ-5D and Health Utilities Index. Med Care 2005;43:1078–86.

30 Maddigan SL, Majumdar SR, Toth EL, et al. Health-related quality of life deficits associated with varying degrees of disease severity in type 2 diabetes. Health Qual Life Outcomes 2003;1:78.

31 Bosch JL, Halpern EF, Gazelle GS. Comparison of preference-based utilities of the Short-Form 36 Health Survey and Health Utilities Index before and after treatment of patients with intermittent claudication. Med Decis Making 2002;22:403–9.

32 Conner-Spady B, Suarez-Almazor ME. Variation in the estimation of quality-adjusted life-years by different preference-based instruments. Med Care 2003;41:791–801.

33 Wiebe S, Matijevic S, Eliasziw M, Derry PA. Clinically important change in quality of life in epilepsy. J Neurol Neurosurg Psychiatry 2002;73:116–20.

34 Neumann PJ, Sandberg EA, Araki SS, et al. A comparison of HUI2 and HUI3 utility scores in Alzheimer's disease. Med Decis Making 2000;20:413–22.

35 Ramadan NM, Silberstein SD, Freitag FG, et al. Evidence-Based Guidelines for Migraine Headache in the Primary Care Setting: pharmacological Management for Prevention of Migraine. American Academy of Neurology. Available from: http://www.aan.com/professionals/practice/pdfs/gl0090.pdf [Accessed September 15, 2005].

36 Snow V, Weiss K, Wall EM, Mottur-Pilson C, American Academy of Family Physicians American College of Physicians-American Society of Internal Medicine. Pharmacologic management of acute attacks of migraine and prevention of migraine headache. Ann Intern Med 2002;137:840–9.

37 Brown JS, Papadopoulos G, Neumann PJ, et al. Cost-effectiveness of topiramate in migraine prevention: results from a pharmacoeconomic model of topiramate treatment. Headache 2005;45:1012–22.

38 Brown JS, Papadopoulos G, Neumann PJ, et al. Cost-effectiveness of migraine prevention: the case of topiramate in the UK. Cephalalgia 2006;26:1473–82.

39 Brown JS, Rupnow MF, Neumann P, Friedman M, Menzin J. Cost effectiveness of topiramate in the prevention of migraines in the United States: an update. Manag Care Interface 2006;19:31–8.

40 Brandes JL, Saper JR, Diamond M, et al. Topiramate for migraine prevention: a randomized controlled trial. JAMA 2004;291:965–73.

41 Silberstein SD, Neto W, Schmitt J, et al. Topiramate in migraine prevention: results of a large controlled trial. Arch Neurol 2004;61:490–5.

42 Diener HC, Tfelt-Hansen P, Dahlof C, et al. Topiramate in migraine prophylaxis—results from a placebo-controlled trial with propranolol as an active control. J Neurol 2004;251:943–50.

43 Duke University, Center for Clinical Health Policy Research. Drug treatments for the prevention of migraine headache. Prepared for the Agency for Health Care Policy and Research under Contract No. 290-94-2025. Available from the National Technical Information Service; NTIS Accession No. PB99-127953; 1999. Report No.: Technical Review 2.3.

44 Gold MR, Siegel JE, Russell LB, Weinstein MC. Cost-Effectiveness in Health and Medicine. New York: Oxford University Press, 1996.

45 Stevens KJ, McCabe CJ, Brazier JE. Mapping between visual analogue scale and standard gamble data: results from the UK Health Utilities Index 2 valuation survey. Health Econ 2006;15:527–33.