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Research Submission

United States Patients' Perspective of Living With Migraine: Country-Specific Results From the Global "My Migraine Voice" Survey

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Background.—Migraine is associated with debilitating symptoms that can affect daily functioning. "My Migraine Voice" was a large, cross-sectional, multi-country online survey aimed at understanding disease burden directly from people with migraine.

Objective.—This study reports on the social and economic impacts of migraine, specifically the impact on activities of daily living and the costs of migraine, from the point of view of people with migraine in the United States.

Methods.—The online survey was administered to adults with a self-reported diagnosis of migraine who experienced 4 or more monthly migraine days each month for the previous 3 months. Prespecified screening quotas were used so that 90% of respondents reported current or past use of preventive migraine medication, 80% of whom switched treatment (ie, changed their prescribed preventive medication at least once). The remaining 10% were preventive treatment naïve (ie, never used any prescribed preventive medication). Burden of migraine on activities of daily living and caregivers (eg, functional limitations, fear of next migraine attack, sleep problems) and economic burden (eg, out-of-pocket costs, impact on work productivity using the validated work productivity and activity impairment questionnaire) reported by respondents from the United States are presented. Results are stratified by employment status, migraine frequency (chronic vs episodic migraine), and history of preventive treatment.

Results.—Thousand hundred and one individuals with migraine from the United States responded to the survey. Respondents reported limitations completing daily activities during all migraine phases, including during the premonitory/aura and postdrome phases. Most (761/1101 (69%)) relied on family, friends, or others for help with daily tasks and reported being helped a median of 9 days (25th percentile 5 days, 75th percentile 15 days) within the last 3 months. Respondents with chronic migraine reported being helped for more days (median 10 days, 25th percentile 5 days, 75th percentile 23 days) in the last 3 months. Almost all (962/1101 (87%)) experienced sleep difficulties and 41% (448/1101) (48% (336/697) of those with 2 or more preventive treatment failures) were very or extremely fearful of a next migraine attack. Median (25th percentile, 75th percentile) monthly out-of-pocket costs of $90.00 ($30.00, $144.00) in doctor's fees (n = 504), $124.00 ($60.00, $234.00) in health insurance (n = 450), $40.00 ($20.00, $100.00) for prescriptions (n = 630), and $50.00 ($0.00, $100.00) for complementary therapies (n = 255) were reported. Those with 2 or more preventive treatment failures reported higher monthly out-of-pocket doctor fees (median $99.00 ($30.00, $150.00), n = 388). Among employed respondents (n = 661), migraine resulted in 22% absenteeism, 60% presenteeism, 65% work productivity loss, and 64% activity impairment.

Conclusions.—Migraine impacts individuals' activities of daily living, work-life, and financial status, especially individuals with high needs, namely those with 4 or more monthly migraine days and prior treatment failures. People with migraine are

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impaired during all migraine phases, experience fear of their next migraine attack and sleep difficulties, and pay substantial monthly out-of-pocket costs for migraine. Burden is even greater among those who have had 2 or more preventive treatment failures. Impacts of migraine extend beyond probands to caregivers who help people with migraine with daily tasks, employers who are affected by employee absenteeism, presenteeism, and reduced productivity, and society which is burdened by lost and reduced economic productivity and healthcare costs.

Key words: migraine, burden, survey, work productivity, migraine experience, costs

Abbreviations: AMPP American Migraine Prevalence and Prevention, CaMEO Chronic Migraine Epidemiology and Outcomes, IBMS International Burden of Migraine Study, QoL quality of life, US United States, WPAI workplace productivity and activity impairment

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BACKGROUND

Migraine affects 1.04 billion people globally and results in 45.1 million years lived with disability;[1] it is the second leading cause of years lived with disability after low back pain[1] and the first among individuals under 50 years old.[2] In the United States (U.S.), 15.5% of adults reported having migraine or severe headache in the previous 3 months.[3] Migraine disproportionately affects females (21% of females vs 10% of males) and people 18-44 years old (19%).[3]

Migraine impacts all domains of life. Large surveys, such as The International Burden of Migraine Study (IBMS), the American Migraine Prevalence and Prevention (AMPP) Study, and the Chronic Migraine Epidemiology and Outcomes (CaMEO) study, were conducted to capture the disease's wide-ranging burden. The surveys demonstrated that migraine affects the activities of daily living. The majority of those with chronic or episodic migraine reported at least mild associated disability and more than half screened positive for mild, moderate, or severe depression and/or anxiety.[4,5] Approximately half (54%) reported severe migraine-related disability.[6] Recent systematic reviews also showed the psychosocial difficulties associated with migraine[7] and consistently worse health-related quality of life (QoL) of people with migraine.[8,9]

Not only does migraine impact all domains of life, it is also costly to the individual, family unit, employers, insurers, and society. In U.S. surveys, respondents reported the mean cost of chronic migraine in the preceding 3 months to be $1036 and episodic migraine to be $383.[10] Individuals with migraine reported $2916 greater annual total direct healthcare expenditures compared to those without migraine ($8033 vs $5118).[11] Migraine is also associated with significant occupational and academic burden, reducing work and school productivity. Surveys and systematic reviews consistently show that the worker productivity loss due

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to episodic migraine is about 4 workdays per year and is about 7 workdays per year due to chronic migraine.[6,12,13]

The IBMS, AMPP, and CaMEO studies contributed significantly to the literature and demonstrated the impact of migraine. However, none reported data on burden among people on preventive migraine treatment. Although those studies did report on burden among people with chronic migraine, and the AMPP and CaMEO studies reported burden of migraine in some domains by low, moderate, and high-frequency episodic migraine, less is known on the impact of migraine among those with 4 or more monthly migraine days and among those with prior preventive treatment failures. The results presented here aim to fill this gap by providing a descriptive overview of the impact of migraine among this group of high-needs patients – namely those with 4 or more monthly migraine days who are on or have used preventive migraine treatments and have needed to change their preventive treatment at least once. This study gathered data directly from people with migraine and reports on the social and economic impacts of migraine, specifically the impact on activities of daily living and the societal and individual costs of migraine for patients in the U.S.

METHODS

Study Design and Participants.—We conducted a large, cross-sectional, multi-country online survey of adult participants (18 years or older) with a self-reported diagnosis of migraine (named the "My Migraine Voice" survey) from September 2017 to February 2018. Results from the U.S. are reported here to present evidence relevant to a U.S. audience; full survey methods are reported elsewhere.[14] In brief, a convenience sample of participants was recruited via patient/consumer online panels and internet support groups for people with migraine. No statistical power calculation was conducted prior to the study. The goal was to include as many people with migraine as possible with 4 or more monthly migraine days; the resulting sample size was based on available respondents.

To be eligible, people with migraine had to have a self-reported diagnosis of migraine, have experienced 4 or more monthly migraine days each month for the previous 3 months, and have not participated in another survey of migraine in the previous 2 months. Prespecified screening quotas were used so that 90% of respondents reported current or past use of preventive migraine medication (responded "Yes" to "Have you ever used any medication prescribed by your doctor to prevent your migraine attacks from happening?"). Among these respondents, 80% switched treatment at least once (responded "Yes" to "Have you ever needed to change the medication prescribed by your doctor to prevent your migraine attacks?"). The remaining 10% of the sample were preventive treatment naïve (responded "No" to "Have you ever used any medication prescribed by your doctor to prevent your migraine attacks from happening?"). These quotas were used to ensure a large number of patients with a history of preventive treatment failures were included in the study.

A pilot study was conducted in 2017 to inform the survey questions.[15,16] Using online bulletin boards, qualitative data from people with migraine and caregivers were collected on the impact of migraine on daily life. In addition, internal pilot tests were conducted to assess the length of the questionnaire.

Participant consent was obtained prior to completing the voluntary survey. Specifically, participants were given an estimate of survey duration (30 minutes), informed their data would remain anonymous, and asked to check a box whether they were willing to participate (Yes/No). Data were collected via an online platform and internet surveys were completed independently by respondents via a website. Machine identification methodologies were used to track unique respondents, but view, participation, and completion rates were not collected. Respondents who completed the survey were compensated in the form of a voucher. This research involved only survey procedures and the subjects could not be subsequently identified (data remained anonymous throughout the study, handled confidentially, and were analyzed and reported in aggregate only). Therefore, it was deemed exempt from the requirement to be reviewed by a human subjects protection committee by the Ethical & Independent Review Services Institutional Review Board under 45 CFR 46.101(b)(2).[17]

Study Variables.—The full questionnaire included 88 questions on sociodemographic characteristics, health/medical history, QoL, healthcare utilization due to migraine, migraine impact on daily life, and migraine treatment patterns. The validated work

productivity and activity impairment (WPAI) questionnaire[18] was imbedded into the survey and asked of currently employed respondents (full and part-time employed). Questions were tailored to specific countries to reflect differences in healthcare systems and the availability of treatments but were not randomized. No statistical correction methods (eg, weighting of items or propensity scores) were used.

In this study, we report on questions related to the social and economic burden of living with migraine among U.S. respondents, including functional burden (length of migraine attack, limitations to activities of daily living), emotional burden (reliance on others, fear of next migraine attack, sleeping difficulties due to migraine), and direct and indirect costs (patient-reported monthly out-of-pocket costs and impact on work productivity).

Functional burden (limitations completing daily activities) was assessed on a 1 to 5 scale (where 1 = not limited at all and 5 = extremely limited) for each migraine phase: Premonitory (warning)/aura, the headache (the attack phase), and postdrome (resolution and recovery). Fear of next migraine attack was assessed on a 1 to 5 scale (where 1 = not fearful at all and 5 = extremely fearful). Out-of-pocket costs for migraine care and treatment were based on self-reported monthly out-of-pocket costs; median (25th percentile, 75th percentile) costs were calculated among those who responded to the survey question on out-of-pocket costs. Impact on work productivity was assessed using the WPAI questionnaire which measures absenteeism (work time missed, calculated as the number of hours missed over the total number of hours worked plus missed); presenteeism (calculated as impairment at work over reduced on the job effectiveness); work productivity loss (calculated as impairment at work over absenteeism plus presenteeism); and activity impairment (calculated as the effect of migraine on the ability to do regular daily activities).[17]

Data Analysis.—Descriptive results are stratified by employment status, chronic vs episodic migraine (defined as ≥15/<15 headache or migraine days per month in the previous 3 months), and history of preventive migraine treatment use. The latter was defined as 4 groups: Preventive treatment naïve, no preventive treatment failures (never changed preventive treatment), 1 preventive treatment failure (changed preventive treatment once), and 2 or more preventive treatment failures (changed preventive treatment 2 or more times). Demographics are shown among all 3 subgroups (employment status, migraine frequency, and preventive treatment history); functional and economic burdens and WPAI results are shown by migraine frequency and history of preventive treatment. For the variables presented in this study, missing/non-response data did not vary by subgroup. Descriptive analyses only (proportions, medians, and interquartile ranges) were conducted using SAS® version 9.4 (SAS Institute, Cary, NC). Because many variables were highly skewed, we presented medians with 25th and 75th percentiles, instead of means and standard deviations. No formal statistical inferences were made. Unless otherwise noted, missing data were excluded from analyses; percentages are calculated from non-missing responses.

RESULTS

Eleven thousand two hundred sixty six individuals with migraine from 31 countries, including 1101 individuals from the U.S., responded to the "My Migraine Voice" survey (overall response rate is not available). Results from all respondents are reported elsewhere;[14] here, we report on the respondents from the U.S.

Survey Sample.—Among the 1101 U.S. respondents, 70% were female and the average age was 41 years old (Table 1). Twenty-nine percent reported having chronic migraine. Sixty percent were employed (of which 77% were full-time employed, 13% were part-time employed, and 9% were self-employed). Of the 40% not employed, 16% were unemployed, 24% were retired, 7% were students, and 40% were homemakers (the remaining were classified as "other"). A little less than half (43%) reported an annual household income of less than $50,000; while 5% reported an annual household income of $150,000 or more. As determined by the screening quota, 10% were preventive treatment naïve; of the remaining on preventive treatment, 18% had no preventive treatment failures, 9% had 1 preventive treatment failure, and 63% had 2 or more preventive treatment failures. One-third of respondents with chronic migraine and one-third of respondents with 2 or more preventive treatment failures indicated that they receive a "disability related allowance"

Table 1.—U.S. Survey Sample

		Currently Employed		Migraine Frequency		Preventive Treatment History			
	All	Yes	No	Chronic	Episodic	No Preventive Treatment	No Preventive Treatment Failures	1 Preventive Treatment Failure	2 or More Preventive Treatment Failures
% (N)	100% (1101)	60.0% (661)	40.0% (440)	29.0% (319)	71.0% (782)	10.1% (111)	18.1% (199)	8.5% (94)	63.3% (697)
Female (% (n))	70.1% (772)	56.7% (375)	90.2% (397)	67.1% (214)	71.4% (558)	78.4% (87)	74.9% (149)	85.1% (80)	65.4% (456)
Age (mean, median [25th percentile, 75th percentile])	41, 38 [31, 51]	38, 35 [30, 45]	45, 45 [34, 55]	40, 37 [32, 49]	41, 38 [31, 51]	44, 44 [33, 55]	42, 39 [31, 55]	45, 48 [33, 56]	39, 37 [30, 48]
Average number of monthly headache or migraine days in last 3 months (median [25th percentile, 75th percentile])	12.3 [8.3, 16.7]	13.0 [8.3, 16.3]	11.7 [8.3, 17.0]	18.7 [16.7, 23.3]	10.0 [7.3, 13.0]	10.0 [7.3, 15.0]	10.0 [7.3, 14.7]	10.0 [6.7, 15.0]	14.0 [9.7, 17.0]
Receive disability related allowance (% yes (n))	22.8% (251)	24.4% (161)	20.5% (90)	30.7% (98)	19.6% (153)	5.4% (6)	8.5% (17)	13.8% (13)	30.8% (215)
Family history of migraine in immediate family (parents, siblings, children) (% yes (n))	60.9% (671)	61.4% (406)	60.2% (265)	65.2% (208)	59.2% (463)	47.7% (53)	50.3% (100)	57.4% (54)	66.6% (464)
Type of treatments used† (% yes (n))									
Over the counter/ bought in pharmacy or other shop without a prescription	63.2% (513)	68.2% (339)	55.2% (174)	64.6% (164)	62.5% (349)	82.1% (55)	61.3% (76)	60.0% (36)	61.7% (346)
Prescribed by your doctor	81.3% (660)	82.3% (409)	79.7% (251)	87.4% (222)	78.5% (438)	28.4% (19)	83.1% (103)	88.3% (53)	86.5% (485)
Complementary therapies (eg, homeopathy, massage, Ayurveda)	33.1% (269)	36.6% (182)	27.6% (87)	34.3% (87)	32.6% (182)	32.8% (22)	31.5% (39)	26.7% (16)	34.2% (192)
Self-reported other chronic conditions									
Anxiety (% yes (n))	37.5% (413)	26.0% (172)	54.8% (241)	35.7% (114)	38.2% (299)	43.2% (48)	36.7% (73)	43.6% (41)	36.0% (251)
Depression (% yes (n))	36.6% (403)	25.9% (171)	52.7% (232)	35.7% (114)	37.0% (289)	38.7% (43)	37.7% (75)	42.6% (40)	35.2% (245)

†Out of 805 respondents who answered this question.

(definition not provided). Twenty-three percent were affected by migraine for 1-5 years, 26% for 6-10 years, and 50% were affected for 11 or more years.

More than half (60%) of respondents had a history of migraine in their immediate family (among parents, siblings, and children), including a high percentage of respondents with chronic migraine (65%) and those with 2 or more treatment failures (67%). Respondents reported many types of comorbid chronic conditions (not shown); the 2 most common were anxiety (38%) and depression (37%). Medications prescribed by a doctor were the most common type of treatment used among all respondents (81%), followed by over the counter medication (63%) and complementary therapies (eg, homeopathy, massage, Ayurveda) (33%).

Migraine Phases and Symptoms, Social and Emotional Burden, and Interictal Anxiety.—Most respondents reported experiencing the premonitory/aura phase (95%) and the postdrome (recovery) phase (98%) of migraine. Half of respondents experienced the premonitory/aura phase of migraine for less than 4 hours and 27% experienced it for 4-24 hours; 44% experienced the headache phase (the attack phase) for 4-24 hours and 33% experienced this phase for more than 24 hours; 39% reported being in the postdrome (recovery) phase for 4-24 hours, 33% reported being it for less than 4 hours, and 26% for more than 24 hours. Respondents were somewhat limited completing daily activities during the premonitory/aura and postdrome phases and were very limited during the headache phase (the attack phase) (Table 2). More respondents with chronic migraine reported being limited in the premonitory/aura (58% very/extremely limited) and postdrome phases (63% very/extremely limited) than those with episodic migraine (37%, 43%, respectively).

Most respondents (69%) relied on family, friends, or others for help with daily tasks during migraine attacks and reported being helped for a median of 9 days in the last 3 months (Table 3); respondents with chronic migraine reported being helped during migraine attacks for a median of 10 days in the last 3 months. Forty-one percent of all respondents (and 48% of those with 2 or more preventive treatment failures) were very or extremely fearful of a next migraine attack (interictal anxiety). Almost all respondents (87%) experienced sleeping difficulties due to migraine.

Economic Burden.—Among the 16-59% of respondents who answered the question on how much money they spent each month on their migraine, respondents self-reported median (25th percentile, 75th percentile) monthly out-of-pocket costs of $90.00 ($30.00, $144.00) in doctor's fees, $124.00 ($60.00, $234.00) in health insurance, $40.00 ($20.00, $100.00) for prescriptions, and $50.00 ($0.00, $100.00) for complementary therapies (Table 4). Respondents with episodic migraine reported similar monthly out-of-pocket costs to those with chronic migraine. Respondents who had not used preventive treatment reported lower monthly out-of-pocket costs across all types of costs (median $50.00 in doctor's fees, $100.00 in health insurance, and $24.00 for prescriptions). Total costs are not reported.

Employed respondents worked 26.7 hours and missed 6.0 hours from work on average in the past 7 days due to problems associated with migraine. Among full- and part-time employed respondents, 22% of work time was missed (absenteeism), 60% of work time was impaired (presenteeism), for a total of 65% work productivity loss due to migraine. In addition, 64% of other activity time was impaired (Table 5). Respondents with chronic migraine had 73% work productivity loss and respondents with 2 or more treatment failures had 71% work productivity loss. Respondents who had not used preventive treatment were less likely to miss work or have reduced on-the-job effectiveness.

DISCUSSION

People with migraine are limited during all phases of migraine, experience fear of a next migraine attack and sleep difficulties due to migraine, and pay substantial monthly out-of-pocket costs for migraine care and treatment. The impact of migraine extends to caregivers who help people with migraine with daily tasks, employers who are affected by employee absenteeism, presenteeism, and reduced productivity, and society which is burdened by reduced economic productivity. Burdens are even greater among those with chronic migraine and those who have had 2 or more preventive treatment failures.

Overall, our findings on the emotional burden of migraine are consistent with other large migraine surveys, including that the daily lives of those with chronic migraine are more severely impacted than those with

Table 2.—Functional Burden by the Migraine Phase

		Migraine Frequency		Preventive Treatment History			
	All	Chronic	Episodic	No Preventive Treatment	No Preventive Treatment Failures	1 Preventive Treatment Failure	2 or More Preventive Treatment Failures
Limitations completing daily activities in the premonitory/aura phase† (median [25th percentile, 75th percentile] (N))	3.0 [3.0, 4.0] (1041)	4.0 [3.0, 4.0] (299)	3.0 [3.0, 4.0] (742)	3.0 [2.0, 3.0] (101)	3.0 [3.0, 4.0] (189)	3.0 [2.0, 4.0] (89)	3.0 [3.0, 4.0] (662)
Very or extremely limited completing daily activities (% (n))	42.7% (445)	58.2% (174)	36.5% (271)	24.8% (25)	36.5% (69)	27.0% (24)	49.4% (327)
Limitations completing daily activities during the headache phase (the attack phase)† (median [25th percentile, 75th percentile] (N))	5.0 [4.0, 5.0] (1094)	5.0 [4.0, 5.0] (316)	4.0 [4.0, 5.0] (778)	4.0 [4.0, 5.0] (110)	4.0 [4.0, 5.0] (197)	4.5 [4.0, 5.0] (94)	5.0 [4.0, 5.0] (693)
Very or extremely limited completing daily activities (% (n))	84.6% (925)	87.0% (275)	83.5% (650)	79.1% (87)	78.2% (154)	86.2% (81)	87.0% (603)
Limitations completing daily activities in the postdrome phase† (median [25th percentile, 75th percentile] (N))	3.0 [3.0, 4.0] (1076)	4.0 [3.0, 5.0] (310)	3.0 [3.0, 4.0] (766)	3.0 [3.0, 4.0] (107)	3.0 [3.0, 4.0] (195)	3.0 [3.0, 4.0] (89)	4.0 [3.0, 4.0] (685)
Very or extremely limited completing daily activities (% (n))	48.6% (523)	62.6% (194)	43.0% (329)	32.7% (35)	36.9% (72)	42.7% (38)	55.2% (378)

†The survey asked respondents to report limitations completing daily activities on a 1 to 5 scale, where 1 = not limited at all, 2 = a little limited, 3 = somewhat limited, 4 = very limited, and 5 = extremely limited. Excludes those who indicated they do not experience this phase.

Table 3.—Emotional Burden

		Migraine Frequency		Preventive Treatment History			
	All	Chronic	Episodic	No Preventive Treatment	No Preventive Treatment Failures	1 Preventive Treatment Failure	2 or More Preventive Treatment Failures
Rely on family, friends, others for help with everyday tasks during migraine attacks (% yes (n))	69.1% (761)	73.7% (235)	67.3% (526)	57.7% (64)	64.3% (128)	59.6% (56)	73.6% (513)
Time spent being helped (median [25th percentile, 75th percentile] days in the last 3 months)†	9.0 [5.0, 15.0]	10.0 [5.0, 23.0]	8.0 [4.0, 15.0]	6.0 [3.0, 14.5]	8.5 [4.0, 15.0]	7.5 [3.0, 14.0]	10.0 [5.0, 16.0]
Fear of next migraine attack (interictal anxiety)‡ (median [25th percentile, 75th percentile])	3.0 [2.0, 4.0]	4.0 [2.0, 5.0]	3.0 [2.0, 4.0]	3.0 [2.0, 4.0]	3.0 [2.0, 4.0]	3.0 [2.0, 4.0]	3.0 [2.0, 4.0]
Very or extremely fearful of next migraine attack (% (n))	40.7% (448)	54.9% (175)	34.9% (273)	26.1% (29)	28.6% (57)	27.7% (26)	48.2% (336)
Experience sleeping difficulties due to migraine (% yes (n))	87.4% (962)	90.6% (289)	86.1% (673)	82.0% (91)	80.9% (161)	86.2% (81)	90.2% (629)

†Among those who rely on family, friends, others for help with everyday tasks.
‡The survey asked respondents to report fear of next migraine attack on a 1 to 5 scale, where 1 = not fearful at all, 2 = a little fearful, 3 = somewhat fearful, 4 = very fearful, and 5 = extremely fearful.

Table 4.—Self-Reported Monthly Out-of-Pocket Costs for Migraine

	Migraine Frequency			Preventive Treatment History			
Median [25th Percentile, 75th Percentile] US$ (n)†	All	Chronic	Episodic	No Preventive Treatment	No Preventive Treatment Failures	1 Preventive Treatment Failure	2 or More Preventive Treatment Failures
Doctor's fees	$90.00 [$30.00, $144.00] (504)	$100.00 [$50.00, $155.00] (168)	$80.00 [$25.00, $120.00] (336)	$50.00 [$5.00, $100.00] (21)	$50.00 [$20.00, $100.00] (67)	$50.00 [$15.00, $100.00] (28)	$99.00 [$30.00, $150.00] (388)
Prescription fees	$40.00 [$20.00, $100.00] (630)	$77.50 [$20.50, $144.50] (200)	$30.00 [$15.00, $75.00] (430)	$24.00 [$10.00, $50.00] (30)	$25.00 [$10.00, $50.00] (94)	$20.00 [$10.00, $50.00] (53)	$50.00 [$20.00, $100.00] (453)
Co-payment	$30.00 [$15.00, $80.00] (459)	$60.00 [$20.00, $123.00] (155)	$25.00 [$10.00, $50.00] (304)	$20.00 [$7.00, $30.00] (30)	$20.00 [$10.00, $35.00] (69)	$25.00 [$10.00, $50.00] (35)	$48.00 [$20.00, $99.00] (325)
Emergency room visits	$75.00 [$10.00, $150.00] (335)	$99.00 [$50.00, $200.00] (122)	$51.00 [$0, $100.00] (213)	$0 [$0, $55.00] (16)	$64.00 [$0, $241.50] (32)	$5.50 [$0, $75.00] (18)	$80.00 [$40.00, $150.00] (269)
Health insurance	$124.00 [$60.00, $234.00] (450)	$130.00 [$99.00, $233.00] (157)	$120.00 [$50.00, $240.00] (293)	$100.00 [$14.00, $150.00] (29)	$109.50 [$38.00, $255.00] (70)	$117.50 [$80.00, $231.00] (40)	$136.00 [$80.00, $250.00] (311)
Over the counter medication for migraine or related symptoms	$20.00 [$10.00, $50.00] (648)	$30.00 [$15.00, $99.00] (192)	$20.00 [$10.00, $45.00] (456)	$15.00 [$10.00, $20.00] (76)	$15.00 [$10.00, $30.00] (107)	$15.00 [$10.00, $25.00] (61)	$25.00 [$15.00, $70.00] (404)
Transportation to medical appointments	$25.00 [$10.00, $60.00] (388)	$30.00 [$15.00, $99.00] (129)	$20.00 [$10.00, $50.00] (259)	$10.00 [$3.00, $20.00] (29)	$12.00 [$5.00, $30.00] (63)	$20.00 [$10.00, $50.00] (26)	$30.00 [$15.00, $99.00] (270)
Complementary treatment (eg, homeopathy, massage, Ayurveda)	$50.00 [$0, $100.00] (255)	$95.00 [$15.00, $120.00] (93)	$40.00 [$0, $100.00] (162)	$0 [$0, $25.00] (15)	$20.00 [$0, $100.00] (33)	$20.00 [$10.00, $60.00] (17)	$70.00 [$10.00, $100.00] (190)
Childcare	$40.00 [$0, $100.00] (179)	$99.00 [$0, $100.00] (67)	$15.00 [$0, $80.00] (112)	$0 [$0, $0] (9)	$0 [$0, $233.00] (19)	$0 [$0, $50.00] (13)	$50.00 [$0, $100.00] (138)

†Costs are calculated among only respondents who answered this question. Number of respondents (n) are shown for each cost.

Table 5.—Work Productivity and Activity Impairment Among Employed U.S. Respondents (n = 661)

		Migraine Frequency		Preventive Treatment History			
	All	Chronic	Episodic	No Preventive Treatment	No Preventive Treatment Failures	1 Preventive Treatment Failure	2 or More Preventive Treatment Failures
Absenteeism (work time missed) (mean % (n))	21.5 (610)†	25.9 (185)	19.5 (425)	4.4 (53)	12.5 (96)	11.8 (45)	26.8 (416)
Presenteeism (reduced on-the-job effectiveness) (mean % (n))	60.0 (608)	67.3 (184)	56.8 (424)	35.5 (53)	54.0 (95)	51.8 (45)	65.4 (415)
Work productivity loss (mean % (n))	64.7 (608)	72.7 (184)	61.3 (424)	37.6 (53)	56.9 (95)	53.8 (45)	71.1 (415)
Activity impairment (activity time missed) (mean % (n))	63.5 (661)	69.9 (194)	60.8 (467)	44.7 (57)	57.3 (112)	56.1 (49)	68.2 (443)

†The sample size (n) listed represent the number of respondents available to calculate the variable listed in the row.

episodic migraine,[19] and that people with migraine worry about a next migraine attack,[20] experience low sleep quality,[21,22] and rely on family for help.[23,24] Our study is unique in that it also provides this data by respondents' preventive treatment history. We show that respondents with highest needs (those with 2 or more preventive treatment failures) are severely impacted by migraine. For example, large proportions have interictal anxiety as evidenced by the fear of a next migraine attack (48%), experience sleep difficulties due to migraine (90%), and rely on family, friends, and others for help with everyday tasks during migraine attacks (74%). This group might experience greater emotional burden because of their history of treatment failures, resulting in a feeling of helplessness.

While our findings on the functional burden of migraine are similar to those found in the AMPP Study, which reported that approximately half (54%) of respondents had severe headache-related disability and 30% reported 1-2 days of activity restriction per attack,[6] we also add important detail that this impairment occurs during all migraine phases, extending from the premonitory/aura phase through the postdrome phase.

Our study also adds important data on monthly out-of-pocket costs. Overall, our study shows people with migraine pay substantial out-of-pocket costs, higher than the U.S. average of $92 per month reported in 2016 among people who are privately insured, Medicare and Medicaid beneficiaries, and people who are uninsured,[25] but closer to the $511 per month spent among Medicare beneficiaries in fair/poor health.[26] While the National Health Interview survey provides data on the estimated monthly cost of complementary treatment ($47),[27] our study provides more granularity on specific types of costs. Further, our survey respondents reported higher costs than those reported in the National Health Interview survey (median $20-$124 across all types of costs, including $50 for complementary treatment). In particular, respondents with a history of 2 or more preventive treatment failures pay higher out-of-pocket costs across all types of costs. The higher costs seen in our study could be due to our high-needs sample, namely who experience 4 or more monthly migraine days and have a history of preventive treatment failures. In addition, out-of-pocket costs

were self-reported and unverified, which may have resulted in imprecise data. During our analysis, the difference in mean vs median costs illustrated substantial skewness in the data. Further, these questions received lower response rates than others in the survey. Thus, more research into whether these differences exist in other studies, and if so, why these differences are seen, is needed.

Respondents in our survey reported more hours missed from work due to migraine (6 hours missed in the past 7 days) than respondents to the AMPP Study (1 day missed in the previous 3 months (N = 162,576)[6]) and the IBMS (1.8 days missed in the previous 3 months (N = 1205)[12]). Unlike these studies, our respondents were required to report 4 or more monthly migraine days to be eligible to participate, which is more than what was required in the AMPP and IBMS samples. Our respondents also reported greater workplace productivity and activity impairment than other international studies of migraine. In a 2018 European survey, 218 respondents with 4 or more monthly migraine days reported 14% of work time was missed (absenteeism) and 36% of work time was impaired (presenteeism), for a total of 39% work productivity loss.[28] This is lower than the 22% absenteeism, 60% presenteeism, and 65% work productivity loss found in our sample and is more similar to the global results of the "My Migraine Voice" survey (13% absenteeism, 48% presenteeism, 52% work productivity loss).[14] Other than being more anxious (38% vs 27%) and being more likely to report a family history of migraine (61% vs 54%), U.S. respondents were similar to all "My Migraine Voice" survey respondents.[14] Thus, it is possible that there is a structural difference in the U.S. workplace, such as fewer guaranteed paid vacation days or sick leave that results in greater workplace productivity loss in the U.S. compared to Europe or globally. Further research on this finding is warranted.

Although we used a convenience sample, you can calculate an estimate of work time missed due to migraine in the U.S. population. Assuming 2% of the U.S. population has chronic migraine[29] and assuming there are 251 million U.S. adults,[30] we can estimate 5 million U.S. adults meet criteria for chronic migraine. In our sample, 61% of those with chronic migraine were currently employed, translating to approximately 3 million employed U.S. adults with chronic migraine. Using our findings (6 hours of work missed due to migraine in the last 7 days), at least 18 million hours of work were missed due to migraine in the last 7 days among employed U.S. adults with chronic migraine. Using an average hourly wage of $27.66,[31] this translates to $498 million in lost productivity per week. There are limitations with this calculation which could result in an overestimate or underestimate. As noted above, our findings showed respondents reported more hours missed than other studies, resulting in a higher cost estimate of lost productivity. Moreover, this calculation could be a conservative estimate as it uses the prevalence of only those with chronic migraine; the actual prevalence of our sample of people with migraine is likely higher. In addition, it does not account for the productivity losses of unemployed adults, including those who are unemployed or underemployed due to migraine. Further research is needed to explore this estimate using a more representative survey sample.

Study Strengths and Limitations.—This study has several limitations. First, we used a convenience sample of online survey respondents who self-selected to participate and have 4 or more monthly migraine days and are on preventive treatment. In particular, the response rate to questions on out-of-pocket costs was self-reported and low (16-59%), likely leading to selection bias. Respondents may not be representative of all people with migraine. In addition, only those with internet access were able to respond to the survey, likely inadvertently excluding respondents of lower socioeconomic status. Second, all data were self-reported, unverified, and may be subject to self-report and recall bias, especially migraine attack information and impact (eg, frequency, severity, and duration) and out-of-pocket costs. Respondents who pay very high out-of-pocket costs might be subject to recall bias and studies show that families can incorrectly estimate out-of-pocket costs vs what is eventually covered by their insurance.[32] Third, while the WPAI is a validated and widely used instrument, and survey questions were informed by a qualitative pilot study, unvalidated survey questions were also used.

Moreover, the online method allowed a wealth of data to be collected from a large sample of individuals with migraine around the world. In addition, this

survey is unique in that it sampled patients with more severe migraine who are less often studied in other large surveys (ie, with a self-reported diagnosis of migraine with 4 or more migraine days per month using or previously used preventive migraine treatment). It also included novel questions, developed based on patient input, not typically included in large migraine surveys, including the length of and functional limitations experienced during each migraine phase and estimated monthly out-of-pocket costs. As a result, this study collected important information on the impact of migraine from patients experiencing frequent migraine attacks and adds comprehensive and recent data to the literature on migraine.

CONCLUSION

Migraine is a worldwide problem, affecting people of all ages, races, income levels, and geographical areas. In this U.S. sample among those with more severe migraine (4 or more monthly migraine days) and especially among those with 2 or more preventive treatment failures, migraine severely impacts daily life and is costly. People with migraine are limited during all phases of migraine, experience fear of a next migraine attack and sleep difficulties due to migraine, rely on family and friends for support, and report productivity losses. Future research should explore the burden of migraine among other subgroups disproportionately affected by migraine (such as females or younger adults) and reexamine workplace productivity loss and out-of-pocket costs to better understand the unique needs of people with migraine living in the U.S.

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REFERENCES

1. Vos T, Abajobir AA, Abate KH, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017;390:1211-1259.
2. Steiner TJ, Stovner LJ, Vos T, Jensen R, Katsarava Z. Migraine is first cause of disability in under 50s: Will health politicians now take notice? *J Headache Pain*. 2018;19:17.
3. *NHIS - Tables of Summary Health Statistics* [Internet]. 2018 [cited 2019 Mar 15]. Available from: https://www.cdc.gov/nchs/nhis/shs/tables.htm
4. Blumenfeld A, Varon S, Wilcox T, et al. Disability, HRQoL and resource use among chronic and episodic migraineurs: Results from the International Burden of Migraine Study (IBMS). *Cephalalgia*. 2011;31:301-315.
5. Adams AM, Serrano D, Buse DC, et al. The impact of chronic migraine: The Chronic Migraine Epidemiology and Outcomes (CaMEO) Study methods and baseline results. *Cephalalgia*. 2015;35:563-578.
6. Lipton RB, Bigal ME, Diamond M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. 2007;68:343-349.

7. Raggi A, Giovannetti AM, Quintas R, et al. A systematic review of the psychosocial difficulties relevant to patients with migraine. *J Headache Pain*. 2012;13:595-606.
8. Lantéri-Minet M, Duru G, Mudge M, Cottrell S. Quality of life impairment, disability and economic burden associated with chronic daily headache, focusing on chronic migraine with or without medication overuse: A systematic review. *Cephalalgia*. 2011;31:837-850.
9. Abu Bakar N, Tanprawate S, Lambru G, Torkamani M, Jahanshahi M, Matharu M. Quality of life in primary headache disorders: A review. *Cephalalgia*. 2016;36:67-91.
10. Stokes M, Becker WJ, Lipton RB, et al. Cost of health care among patients with chronic and episodic migraine in Canada and the USA: results from the International Burden of Migraine Study (IBMS). *Headache*. 2011;51:1058-1077.
11. Raval AD, Shah A. National trends in direct health care expenditures among US adults with migraine: 2004 to 2013. *J Pain*. 2017;18:96-107.
12. Messali A, Sanderson JC, Blumenfeld AM, et al. Direct and indirect costs of chronic and episodic migraine in the United States: A web-based survey. *Headache*. 2016;56:306-322.
13. Burton WN, Landy SH, Downs KE, Runken MC. The impact of migraine and the effect of migraine treatment on workplace productivity in the United States and suggestions for future research. *Mayo Clin Proc*. 2009;84:436-445.
14. Martelletti P, Schwedt TJ, Lanteri-Minet M, et al. My migraine voice survey: A global study of disease burden among individuals with migraine for whom preventive treatments have failed. *J Headache Pain*. 2018;19:115.
15. Ruiz de la Torre E, Martelletti P, Craven A, et al. Burden and impact of migraine: A caregiver's perspective. *Int Headache Congr*. 2017;37(1S): 319-374.
16. Ruiz de la Torre E, Martelletti P, Craven A, et al. Real-world patient perspective on the burden and impact of migraine. *Int Headache Congr*. 2017;37(1S): 319-374.
17. US Department of Health and Human Services. *Human Subject Regulations Decision Charts* [Internet]. Chart 4. 2016. Available from: https://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html#c4
18. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *PharmacoEconomics*. 1993;4:353-365.
19. Katsarava Z, Buse DC, Manack AN, Lipton RB. Defining the differences between episodic migraine and chronic migraine. *Curr Pain Headache Rep*. 2012;16:86-92.
20. Brandes JL. Migraine and functional impairment. *CNS Drugs*. 2009;23:1039-1045.
21. Yang C-P, Wang S-J. Sleep in patients with chronic migraine. *Curr Pain Headache Rep*. 2017;21:39.
22. Buse DC, Rains JC, Pavlovic JM, et al. Sleep disorders among people with migraine: Results from the Chronic Migraine Epidemiology and Outcomes (CaMEO) study. *Headache*. 2019;59:32-45.
23. Buse DC, Powers SW, Gelfand AA, et al. Adolescent perspectives on the burden of a parent's migraine: Results from the CaMEO study. *Headache*. 2018;58: 512-524.
24. Buse DC, Scher AI, Dodick DW, et al. Impact of migraine on the family: Perspectives of people with migraine and their spouse/domestic partner in the CaMEO study. *Mayo Clinic Proc*. 2016;91:596-611.
25. *Out-of-Pocket Spending* [Internet]. Peterson-Kaiser Health System Tracker. [cited 2019 May 17]. Available from: https://www.healthsystemtracker.org/indicator/access-affordability/out-of-pocket-spending/
26. Cubanski J, Neuman T, Damico A, Smith K. *Medicare Beneficiaries' Out-of-Pocket Health Care Spending as a Share of Income Now and Projections for the Future* [Internet]. Kaiser Family Foundation; 2018 [cited 2020 Jan 2]. Available from: https://www.kff.org/report-section/medicare-beneficiaries-out-of-pocket-health-care-spending-as-a-share-of-income-now-and-projections-for-the-future-tables/
27. Nahin RL, Stussman BJ, Herman PM. Out-of-pocket expenditures on complementary health approaches associated with painful health conditions in a nationally representative adult sample. *J Pain*. 2015;16: 1147-1162.
28. Vo P, Fang J, Bilitou A, Laflamme AK, Gupta S. Patients' perspective on the burden of migraine in Europe: A cross-sectional analysis of survey data in France, Germany, Italy, Spain, and the United Kingdom. *J Headache Pain*. 2018;19:82.
29. Schwedt TJ. Chronic migraine. *BMJ*. 2014;24:g1416.
30. US Census Bureau. *National Population by Characteristics: 2010-2017* [Internet]. 2018. Available from:

https://www.census.gov/data/datasets/2017/demo/popest/nation-detail.html
31. Table B-3. *Average Hourly and Weekly Earnings of All Employees on Private Nonfarm Payrolls by Industry Sector, Seasonally Adjusted* [Internet]. [cited 2019 Mar 28]. Available from: https://www.bls.gov/news.release/empsit.t19.htm
32. Marquis MS. Consumers' knowledge about their health insurance coverage. *Health Care Financ Rev*. 1983;5:65-80.