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RESEARCH SUBMISSIONS

Real-world assessment of the relationship between migraine-related disability and healthcare costs in the United States

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Abstract

Objective: The objective of this study was to determine the associations among migraine disability assessment scores, healthcare resource utilization (HCRU; medical visits and pharmacy use) and direct medical costs among people with episodic migraine in a real-world setting.

Background: Migraine is a public health concern associated with a substantial economic burden in the United States. However, the association between migraine disability and direct medical costs among people with migraine is unknown.

Method: This retrospective, cohort study used claims and electronic health record data from the Decision Resources Group database. Adults with migraine with or without aura, defined by International Classification of Disease Revision 9 (ICD-9) or ICD Revision 10 (ICD-10) codes, and a completed Migraine Disability Assessment Scale (MIDAS) questionnaire from January 2016 to December 2018 were included (chronic migraine codes not included). The associations of MIDAS score with the cost of HCRU for the 6 months after MIDAS assessment were explored. Results were stratified by treatment setting.

Results: Among 7662 included patients, MIDAS scores were distributed as: 3348 (43.7%; I, little/none), 1107 (14.4%; II, mild), 1225 (16.0%; III, moderate), 893 (11.7%; IVa, severe), and 1089 (14.2%; IVb, very severe). Worsening disability was associated with higher medical costs (adjusted from a multivariable model). In the primary care setting, healthcare visit costs were $206 (95% confidence interval: $144–294) for grade I and $631 ($384–1036) for grade IVb patients; corresponding pharmacy costs were $203 (grade I; $136–301) and $719 (grade IVb; $410–1259). For specialty care (e.g., neurologist), healthcare visits cost $509 ($411–629) for grade I and $885 ($634–1236) for grade IVb patients; corresponding pharmacy costs were $494 (grade I; $378–645) and $1020 (grade IVb; $643–1620).

Abbreviations: CI, confidence interval; DRG, Decision Resources Group; ED, emergency department; EHR, electronic health record; GLM, generalized linear model; HCRU, healthcare resource utilization; HIPAA, Health Insurance Portability and Accountability Act; MIDAS, migraine disability assessment; SD, standard deviation; US, United States; YLD, year lost due to disability.

Conclusion: Higher levels of migraine-related disability (MIDAS assessed) are associated with increased HCRU costs among Americans with episodic migraine. Migraine disability assessment could be useful in the development, testing, and prescription of cost-effective treatments for people with high migraine-related disability.

KEYWORDS
healthcare utilization, medical costs, migraine disability assessment

INTRODUCTION

Migraine is a common, disabling, and recurrent type of neurovascular headache disorder.[1,2] It poses a serious concern to public health in the United States, affecting approximately one in six adults over a 3-month period.[3] According to 2019 data from the Global Burden of Disease study, migraine ranks second among the world's most disabling disorders, as measured by years lost due to disability (YLD), and is the leading cause of YLD in those aged 15 to 49 years.[4,5] Migraine-related disability in the US population is associated with a substantial economic burden.[6] In a retrospective observational analysis, annualized direct medical costs, due to outpatient pharmacy, inpatient stays, and outpatient visits, were significantly higher among patients with migraine compared with those without ($13,032 vs. $3234, respectively [2016 US dollars]; $p < 0.0001$).[7]

A shared goal of acute and preventive migraine treatments is the reduction in the duration of headache/migraine attacks, thereby restoring the ability to function and eliminating the disability associated with the attacks.[8] However, despite numerous pharmacological treatment options in the United States, there are several areas of unmet need among people who experience the pain and disability of migraine disease.[9] In a 2017 survey of participants using oral, acute prescription migraine medications, 95.8% had at least one unmet acute treatment need, most commonly headache-related disability, inadequate 2-h pain freedom, and recurrence within 24 h of initial relief.[9] Ineffective acute migraine treatment is a major risk factor for the progression from episodic migraine, characterized by fewer than 15 headache days per month, to chronic migraine, characterized by 15 or more headache days per month.[8,10,11] The simultaneous use of multiple medications is prevalent among people with headache disorders as they seek to manage their headaches; 40.7% of a study cohort reported taking five or more medications per day.[12] Paradoxically, the regular use or overuse of acute medications can lead to increased headache frequency and progression from episodic to chronic migraine.[8,10,11]

Evaluating the effectiveness of migraine treatments is challenging, in part because most outcomes are self-reported.[13] The Migraine Disability Assessment Scale (MIDAS) questionnaire, commonly used to assess treatments in clinical trials, comprises five questions that aim to assess lost time due to headache in the preceding 3-month period (see Supplementary Information for the MIDAS questionnaire).[14,15] It has been shown to be reliable and valid for the assessment of headache-related disability among people who experience migraine[14,15] and is the only instrument shown to correlate with both physicians' assessments of treatment needs and outcomes of treatment.[16] MIDAS scores provide a continuous measure of headache-related disability.[17] These scores can be used to categorize individuals based on headache-related disability grades ranging from I (little or no disability) to IVb (very severe disability).[18] In a randomized controlled trial, patients who received stratified care (choice of migraine treatment determined by MIDAS grade) had significantly better clinical outcomes than those managed with step care strategies.[19] However, the association between MIDAS score and direct medical costs among people with migraine has not been established. The objective of this study was to determine the association between MIDAS grade and healthcare utilization and costs among people with episodic migraine in a real-world setting; we hypothesized that higher MIDAS grade would be associated with increased direct medical costs.

METHODS

Study design and data sources

This retrospective, real-world, cohort study used data obtained from the Decision Resources Group (DRG) database, which includes longitudinal, participant-level medical claims, prescription claims, and electronic health record (EHR) data sourced from transactional clearing houses and EHR providers, respectively. The repository includes data for approximately 300 million people and 90% of health plans in the United States and provides a set of individual health records (tests ordered, test results, diagnoses, comorbidities, medications, therapies, and participant demographics). Ethics committee/institutional review board approval and informed consent were not sought for this study due to the use of de-identified data. According to the US Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, there are no restrictions on the use or disclosure of de-identified health information by covered entities. Claims and EHR data were linked by a HIPAA-compliant encrypted participant key generated by a third party. MIDAS data were made available through the EHR in a limited set of health plans and were available to a limited group of healthcare professionals.

Adults (aged ≥18 years) were included if they had a migraine diagnosis based on claims data and a complete and valid MIDAS questionnaire record in the EHR data between January 1, 2016, and December 31, 2018. Migraine diagnosis codes from the International Classification of Diseases (ICD), Ninth Revision,

Clinical Modification (ICD-9 CM) (346.0 to 346.93) and ICD Tenth Revision, Clinical Modification (ICD-10 CM) (G43.0 to G43.919) were used. Full details of migraine diagnosis codes used in the analysis are provided in the Supplementary Information. People with an invalid MIDAS questionnaire score and those with chronic migraine diagnosis codes were not included, as these codes are largely underutilized.[20,21] Individual medical claims were facility stabilized by choosing only those who had at least one medical event within 1 year preceding the index date (the date on which the first diagnosis of migraine was identified within the study period) and within 1 year following the index date. No statistical power calculation was conducted prior to the study, and sample size was based on data availability (i.e., using all patients that met the study criteria).

Analyses were conducted to determine the association between MIDAS scores of participants with episodic migraine and healthcare resource utilization and total healthcare costs. For participants with more than one completed MIDAS questionnaire, the first available MIDAS score was included, and the completion date of the first questionnaire was taken as the index date.

Statistical analysis

Cohort demographics, comorbidities, and MIDAS scores were summarized using descriptive statistics. Mean and standard deviation (SD) were calculated for continuous variables, and number of participants (%) was calculated for categorical variables. The assumptions required to interpret parametric statistics, that is normal distribution of the dataset, were visualized using a histogram and a five-point summary.

A series of generalized linear models (GLMs) was used to describe the association between MIDAS score and healthcare resource utilization (number of inpatient, outpatient, and emergency department [ED] visits related to migraine), as well as the association between MIDAS score and healthcare costs (total healthcare and pharmacy costs associated with migraine). Total healthcare costs included costs due to inpatient, outpatient, and ED visits; pharmacy costs included acute and preventive migraine treatments for the 6-month period following the MIDAS assessment, which was considered appropriate to ensure that participants could be followed up effectively, while allowing for short-term variability in individual participants.[22] The selected confounders were factors that were potentially associated with the exposure; economic outcomes were not considered to be part of the causal pathway linking exposure and confounders. The GLMs included MIDAS grade as the primary exposure of interest, with adjustment for gender, Charlson comorbidity score, migraine diagnosis (i.e., adjustment for the different migraine diagnosis codes), payer channel, and use of preventive/relief medication; no interactions or nonlinearities were examined. The cohort was divided into two groups, which were assigned based on the primary specialty presented on the index claim: participants treated by primary care physicians and nurse practitioners and those treated by specialists (neurologists, pain and headache specialists, etc.). Classification of physicians as specialists or primary care physicians and nurse practitioners is provided in the Supplementary Information. Negative binomial regression models with a log link function were used to estimate adjusted healthcare resource utilization, and gamma regression models with a log link function were used to estimate adjusted costs. All analyses were performed using R statistical software.

RESULTS

MIDAS score and migraine diagnosis were linked using two separate data sources. Among the 6.5 million people with episodic migraine identified in the medical claims, only a minority (652,428) had overlapping EHR data available. Not all identified EHR claims could be linked to a valid MIDAS score: 11,638 participants had an available MIDAS survey response and 9717 had a complete five-item MIDAS survey. Of these, 7662 participants satisfied the stability criteria and were aged 18 years and above between January 1, 2016, and December, 31, 2018, and were included. Missing cost data were imputed based on average costs values in the dataset.

Participant characteristics

Participant demographics and comorbidities are shown in Tables 1 and 2, respectively. The mean (SD) age of the cohort was 50 (16) years; 78.8% of participants identified as female (gender) and 63.2% were commercially insured. Of the 7662 participants, 2568 (33.5%) had at least one Charlson comorbidity and 3801 (49.6%) had at least one other comorbidity. Among the participants, 3348 (44%) had a MIDAS disability grade of I (little or none), 1107 (14.4%) had a MIDAS grade of II (mild), 1225 (16.0%) had a MIDAS grade of III (moderate), 893 (11.7%) had a MIDAS grade of IVa (severe), and 1089 (14.2%) had a MIDAS grade of IVb (very severe).

Healthcare resource utilization by MIDAS grade

Healthcare resource utilization (captured by number of healthcare visits only) among participants treated in specialty practice and primary care by MIDAS grade is presented in Table 3. Results show similar healthcare resource utilization for participants with MIDAS grades I–IVa, with slightly increased healthcare resource utilization for participants with MIDAS grade IVb.

Direct medical costs due to healthcare visits and pharmacy use by MIDAS grade

Based on adjusted cost estimates from the multivariable GLMs, overall, worsening migraine disability is associated with both increased

TABLE 1 Participant demographics

	MIDAS grade					
	Overall	I	II	III	IVa	IVb
	N = 7662	*n* = 3348	*n* = 1107	*n* = 1225	*n* = 893	*n* = 1089
Age group, years, *n* (%)						
18–24	443 (5.8)	173 (5.2)	78 (7.0)	76 (6.2)	65 (7.3)	51 (4.7)
25–34	1089 (14.2)	374 (11.2)	159 (14.4)	207 (16.9)	147 (16.5)	202 (18.5)
35–44	1410 (18.4)	512 (15.3)	208 (18.8)	241 (19.7)	205 (23.0)	244 (22.4)
45–54	1616 (21.1)	638 (19.1)	255 (23.0)	265 (21.6)	206 (23.1)	252 (23.1)
55–64	1550 (20.2)	739 (22.1)	206 (18.6)	224 (18.3)	169 (18.9)	212 (19.5)
≥65	1554 (20.3)	912 (27.2)	201 (18.2)	212 (17.3)	101 (11.3)	128 (11.8)
Gender, *n* (%)						
Male	1621 (21.2)	855 (25.5)	200 (18.1)	229 (18.7)	154 (17.2)	183 (16.8)
Female	6041 (78.8)	2493 (74.5)	907 (81.9)	996 (81.3)	739 (82.8)	906 (83.2)
Region, *n* (%)						
Midwest	1181 (15.4)	567 (16.9)	166 (15.0)	172 (14.0)	118 (13.2)	158 (14.5)
Northeast	1357 (17.7)	558 (16.7)	244 (22.0)	213 (17.4)	154 (17.2)	188 (17.3)
South	3872 (50.5)	1733 (51.8)	493 (44.5)	664 (54.2)	471 (52.7)	511 (46.9)
West	1233 (16.1)	482 (14.4)	200 (18.1)	174 (14.2)	146 (16.3)	231 (21.2)
Other[a]	19 (0.2)	8 (0.2)	4 (0.4)	2 (0.2)	4 (0.4)	1 (0.1)
Payer[b], *n* (%)						
Commercial	4844 (63.2)	1997 (59.6)	706 (63.8)	798 (65.1)	612 (68.5)	731 (67.1)
Medicare	1334 (17.4)	724 (21.6)	179 (16.2)	163 (13.3)	111 (12.4)	157 (14.4)
Medicare advantage	98 (1.3)	46 (1.4)	16 (1.4)	21 (1.7)	6 (0.7)	9 (0.8)
Medicaid	613 (8.0)	230 (6.8)	90 (8.1)	114 (9.3)	80 (9.0)	99 (9.1)
Other[c]	773 (10.1)	351 (10.5)	116 (10.5)	129 (10.5)	84 (9.4)	93 (8.5)

Abbreviation: MIDAS, migraine disability assessment.

[a]Other includes the Armed Forces Pacific, Northwest Territories, and Puerto Rico.

[b]Payer channel based on the first claim in the study period with valid payer information.

[c]Other includes payer channels such as Veterans Affairs and other government.

healthcare costs due to medical visits (Figure 1) and pharmacy use (Figure 2).

Among participants treated in specialty practice, increasing total healthcare and pharmacy costs were directly associated with the level of disability, with highest costs among participants with MIDAS grades IVa and IVb. In the analysis of healthcare costs attributable to healthcare visits at 6 months post index (*N* = 1524), costs ranged from $509 (95% confidence interval [CI]: $411–629) for participants with MIDAS grade I to $885 (95% CI: $634–1236) for participants with MIDAS grade IVb. In the analysis of total pharmacy costs at 6 months post index (*N* = 1112), costs ranged from $494 (95% CI: $378–645) for participants with MIDAS grade I to $1020 (95% CI: $643–1620) for participants with MIDAS grade IVb.

A similar result was observed among participants treated in primary care, although mean costs were lower for these participants than for participants treated in specialty practice. In the analysis of healthcare costs attributable to healthcare visits among participants treated in primary care at 6 months post index (*N* = 947), costs ranged from $206 (95% CI: $144–294) for participants with MIDAS grade I to $631 (95% CI: $384–1036) for participants with MIDAS grade IVb. In the analysis of total pharmacy costs at 6 months post index (*N* = 764), costs ranged from $203 (95% CI: $136–301) for participants with MIDAS grade I to $719 (95% CI: $410–1259) for participants with MIDAS grade IVb.

DISCUSSION

Using data from the DRG database, we identified adults with medically diagnosed episodic migraine who completed the MIDAS questionnaire, and then linked their MIDAS grade to healthcare visits and pharmacy use over the subsequent 6 months. Almost three quarters (74.1%) of participants had MIDAS grades of III or lower, indicating that most participants experienced mild to moderate migraine-related disability. Among people treated in primary care, costs associated with office visits and pharmacy use were stable for those with mild to severe migraine-related disability but were slightly increased for those with very severe disability (as indicated by MIDAS

TABLE 2 Participant comorbidities

	MIDAS grade					
	Overall	I	II	III	IVa	IVb
	N = 7662	*n* = 3348	*n* = 1107	*n* = 1225	*n* = 893	*n* = 1089
Charlson comorbidities, *n* (%)						
Chronic pulmonary disease	1054 (13.8)	471 (14.1)	141 (12.7)	175 (14.3)	112 (12.5)	155 (14.2)
Diabetes without complications	925 (12.1)	441 (13.2)	118 (10.7)	142 (11.6)	97 (10.9)	127 (11.7)
Cerebrovascular disease	471 (6.1)	221 (6.6)	66 (6.0)	74 (6.0)	58 (6.5)	52 (4.8)
Diabetes with complications	307 (4.0)	153 (4.6)	32 (2.9)	46 (3.8)	38 (4.3)	38 (3.5)
Peripheral vascular disease	303 (4.0)	149 (4.5)	39 (3.5)	49 (4.0)	31 (3.5)	35 (3.2)
Renal disease	251 (3.3)	144 (4.3)	24 (2.2)	32 (2.6)	26 (2.9)	25 (2.3)
Connective tissue disease-rheumatic disease	237 (3.1)	92 (2.7)	34 (3.1)	41 (3.3)	26 (2.9)	44 (4.0)
Mild liver disease	236 (3.1)	102 (3.0)	22 (2.0)	42 (3.4)	31 (3.5)	39 (3.6)
Congestive heart failure	232 (3.0)	132 (3.9)	32 (2.9)	31 (2.5)	21 (2.4)	16 (1.5)
Cancer	220 (2.9)	115 (3.4)	26 (2.3)	37 (3.0)	17 (1.9)	25 (2.3)
Myocardial infarction	85 (1.1)	35 (1.0)	11 (1.0)	11 (0.9)	13 (1.5)	15 (1.4)
Dementia	82 (1.1)	53 (1.6)	6 (0.5)	6 (0.5)	5 (0.6)	12 (1.1)
Paraplegia and hemiplegia	73 (1.0)	33 (1.0)	11 (1.0)	8 (0.7)	11 (1.2)	10 (0.9)
Peptic ulcer disease	56 (0.7)	21 (0.6)	8 (0.7)	10 (0.8)	10 (1.1)	7 (0.6)
Metastatic carcinoma	22 (0.3)	10 (0.3)	1 (0.1)	4 (0.3)	3 (0.3)	4 (0.4)
AIDS/HIV	22 (0.3)	6 (0.2)	2 (0.2)	4 (0.3)	5 (0.6)	5 (0.5)
Moderate or severe liver disease	4 (0.1)	2 (0.1)	–	1 (0.1)	–	1 (0.1)
Charlson Comorbidity Index score, mean (SD)	2 (2)	2 (2)	2 (2)	2 (2)	2 (2)	2 (2)
Other comorbidities, *n* (%)						
Headache	2097 (27.4)	791 (23.6)	270 (24.4)	358 (29.2)	283 (31.7)	395 (36.3)
Migraine[a]	1349 (17.6)	451 (13.5)	193 (17.4)	254 (20.7)	185 (20.7)	266 (24.4)
Chest pain	946 (12.3)	410 (12.2)	134 (12.1)	142 (11.6)	121 (13.5)	139 (12.8)
Asthma	580 (7.6)	231 (6.9)	82 (7.4)	103 (8.4)	74 (8.3)	90 (8.3)
Musculoskeletal chest pain	461 (6.0)	192 (5.7)	73 (6.6)	65 (5.3)	55 (6.2)	76 (7.0)
Migraine with aura	426 (5.6)	147 (4.4)	46 (4.2)	73 (6.0)	79 (8.8)	81 (7.4)
Osteoarthritis	118 (1.5)	55 (1.6)	13 (1.2)	16 (1.3)	16 (1.8)	18 (1.7)
Uterine leiomyoma	112 (1.5)	41 (1.2)	24 (2.2)	17 (1.4)	10 (1.1)	20 (1.8)
Vascular disorders	100 (1.3)	42 (1.3)	19 (1.7)	18 (1.5)	6 (0.7)	13 (1.2)
Cholecystitis	98 (1.3)	45 (1.3)	9 (0.8)	9 (0.7)	18 (2.0)	19 (1.7)
Hemiplegia	64 (0.8)	28 (0.8)	8 (0.7)	10 (0.8)	8 (0.9)	10 (0.9)
Pulmonary embolism	59 (0.8)	26 (0.8)	6 (0.5)	7 (0.6)	5 (0.6)	15 (1.4)
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	39 (0.5)	20 (0.6)	8 (0.7)	3 (0.2)	2 (0.2)	6 (0.6)
Invasive ductal breast carcinoma	13 (0.2)	9 (0.3)	–	–	2 (0.2)	2 (0.2)
Colon cancer	10 (0.1)	6 (0.2)	–	2 (0.2)	1 (0.1)	1 (0.1)
Arthritis	10 (0.1)	5 (0.1)	1 (0.1)	1 (0.1)	2 (0.2)	1 (0.1)
Cholelithiasis	9 (0.1)	5 (0.1)	1 (0.1)	–	1 (0.1)	2 (0.2)

(Continues)

TABLE 2 (Continued)

	MIDAS grade					
	Overall	I	II	III	IVa	IVb
	N = 7662	*n* = 3348	*n* = 1107	*n* = 1225	*n* = 893	*n* = 1089
Aortic dissection	9 (0.1)	4 (0.1)	1 (0.1)	2 (0.2)	1 (0.1)	1 (0.1)
Hemiplegic migraine	7 (0.1)	1 (<0.1)	1 (0.1)	1 (0.1)	2 (0.2)	2 (0.2)
Menorrhagia	5 (0.1)	2 (0.1)	–	1 (0.1)	2 (0.2)	–
Nervous system disorders	1 (<0.1)	–	–	–	1 (0.1)	–

Abbreviations: AIDS, acquired immune deficiency syndrome; HIV, human immunodeficiency virus; MIDAS, migraine disability assessment; SD, standard deviation.

[a]Refers to migraine within the 1-year period before the first MIDAS score was given.

TABLE 3 Estimated number of healthcare visits 6 months post index—Multivariable analysis

	Primary care physician or nurse practitioner			Specialist		
	n = 229			*n* = 548		
MIDAS grade	Estimated number of visits[a]	SE	95% CI	Estimated number of visits[a]	SE	95% CI
I	1.5	1.1	1.3–1.8	1.6	1.1	1.3–1.9
II	1.4	1.1	1.2–1.7	1.7	1.2	1.2–2.3
III	1.5	1.1	1.2–1.7	1.8	1.1	1.4–2.3
IVa	1.4	1.1	1.2–1.7	1.7	1.2	1.3–2.3
IVb	1.7	1.1	1.4–2.2	2.2	1.1	1.8–2.8

Abbreviations: CI, confidence interval; GLM, generalized linear model; MIDAS, migraine disability assessment; SE, standard error.

[a]Multivariable GLMs are built for participants with at least one visit within the six-month post index period; control variables that were predominantly common across the models included gender, Charlson score, migraine flag, MIDAS grade, preventive medication, relief medication, age, and payer channel.

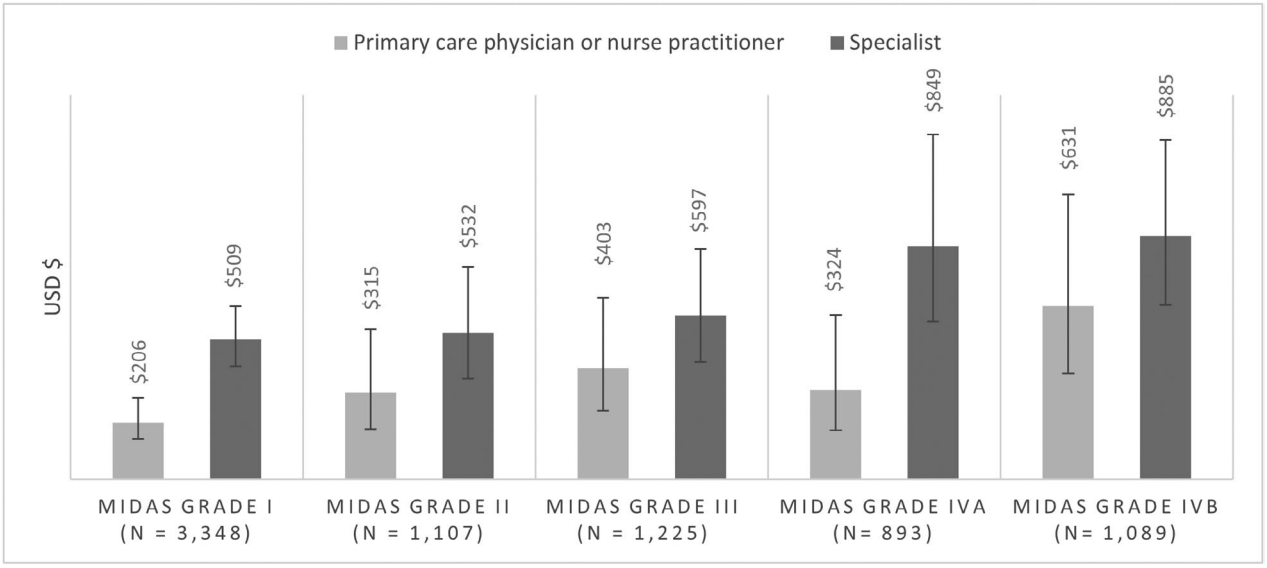

FIGURE 1 Mean (95% CI) costs attributable to healthcare visits, 6 months post index by MIDAS grade (expected costs derived from the multivariable GLM). Control variables that were predominantly common across the GLMs included gender, Charlson score, migraine flag, MIDAS grade, preventive medication, and relief medication. CI, confidence interval; GLM, generalized linear model; MIDAS, migraine disability assessment

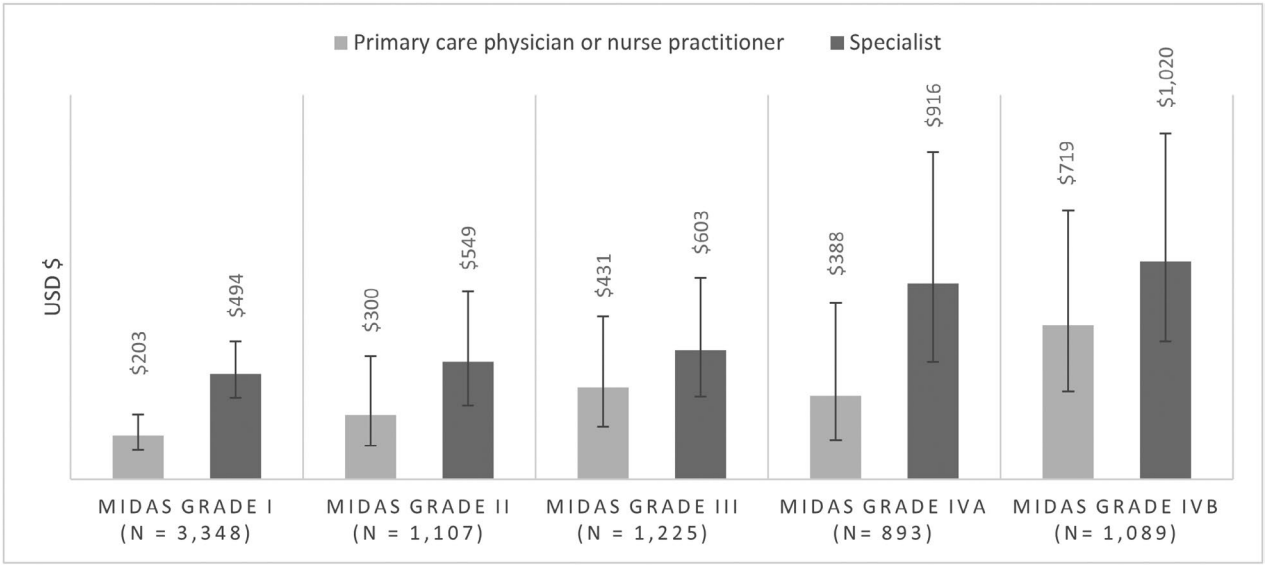

FIGURE 2 Mean (95% CI) pharmacy costs 6 months post index by MIDAS grade (expected costs derived from the multivariable GLM). Control variables that were predominantly common across the GLMs included gender, Charlson score, migraine flag, MIDAS grade, preventive medication, and relief medication. CI, confidence interval; GLM, generalized linear model; MIDAS, migraine disability assessment

grade IVb). Among those treated in specialty care, costs increased with higher MIDAS grades. Although mean costs due to healthcare visits and pharmacy use were higher among participants treated in specialty practice, further analysis is required to determine if this cost difference is of statistical significance.

Previous studies have examined factors associated with healthcare resource utilization among people with migraine. An analysis of costs among commercially-insured individuals in the United States identified specific factors associated with high direct healthcare costs among people with migraine; these include increased acute medication use (opioids and triptans) and more migraine-related ED visits.[23] Another study of US commercial health plan data suggests that triptan-prescribed persons who do not achieve a sufficient treatment response, many of whom resort to potent medications like opioids, have significantly higher all-cause and migraine-related healthcare resource utilization than those who respond and continue on triptans.[24]

Given the established association between headache days and headache-related disability,[25] and increased headache days and increased healthcare resource utilization,[26,27] an association between headache-related disability and healthcare resource utilization is expected. Although previous studies have recognized increased levels of headache-related disability as a predictor of consultation with a healthcare professional for headache, to the best of our knowledge, this study is the first to explore the relationships between MIDAS grades and healthcare resource utilization and direct medical costs.[28,29] It demonstrates the potential use of the MIDAS questionnaire in the development, testing, and prescription of treatments for migraine. In addition, MIDAS captures days of missed work or school due to headache (absenteeism), and days during which headaches led to reduced productivity (presenteeism) and thus may be used to estimate indirect costs. Therefore, it could be used as a tool to facilitate the targeting of specific pharmacological treatments to people with high direct and indirect migraine-related costs, thereby alleviating the substantial economic burden associated with the disorder in the United States.

The data used in the current study are taken from a nationally representative repository, which includes people from all geographic regions of the United States and covers ~90% of US health plans. However, a potential limitation of the data is that healthcare services provided by out-of-network providers may not be captured by the databases. Although there are systems in place to ensure data quality within real-world databases, there will be missing and erroneous data, coding imperfections, lack of standardization of clinical measures, variations between clinical testing centers, and measurements that are taken with varying periodicity. Furthermore, certain variables of interest within the database may be recorded inconsistently.

While migraine is most common between the ages of 18 and 44 years,[3] 61.6% of the patients included in the current study were aged 45 years and above, suggesting that older adults may be overrepresented in the databases and the sample may not be fully representative of the population with migraine in the United States. The inability of patients to work due to disability, whether related to migraine or not, could be a potential confounder, impacting their MIDAS score. In addition, only those diagnosed with episodic migraine were included, resulting in the exclusion of both people with chronic migraine and those who fluctuate between episodic and chronic migraine, which is common among individuals who experience the pain and disability of migraine.[22] Participants were also limited to those who had a minimum of one medical event within 1 year preceding the index date and within 1 year following the index date. This could potentially have resulted in selection of people with low MIDAS grades using more care than average, leading to underestimation of the trend between increasing MIDAS grade and increased

healthcare resource utilization. The analysis was also limited to healthcare visits and pharmacy costs over the 6 months post index in order to ensure that participants could be followed up effectively. However, if healthcare resource utilization and costs remained stable among participants from 6 months to 1 year post index, it may be inferred that the annual costs would be approximately double the reported costs. With regard to the increased medical costs accrued by participants treated in specialty practice, compared with those in primary care, there may be hidden costs that are distinct from their headache-related disability, for example, patient comorbidities and additional administrative burden.[30] Although our multivariable analysis normalized potential covariates, a limitation of our findings is the fact that we are unable to quantify how much of the variance in migraine treatment cost is due to MIDAS grade, compared with other factors; this could be the topic of further research.

Finally, although the sampling approach used allowed for analysis of the association between MIDAS grades and healthcare resource utilization or costs, further analyses that allow evaluation of the impact of changes in MIDAS score over time may have greater application in terms of treatment development and testing.

CONCLUSION

Migraine-related disability, as assessed using the MIDAS questionnaire, is associated with increased healthcare resource utilization and costs among people with episodic migraine in the United States. Therefore, the MIDAS questionnaire has the potential to be a useful tool in the development, testing, and prescription of cost-effective interventions for migraine among people for whom the direct and indirect costs of migraine are high.

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CONFLICT OF INTEREST

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AUTHOR CONTRIBUTIONS

Study concept and design: Linda Harris, Gilbert L'Italien, Anil Kumar, Prafullakumar Seelam, Chris LaVallee, Vladimir Coric, Richard B. Lipton. *Acquisition of data*: Linda Harris, Gilbert L'Italien, Anil Kumar, Prafullakumar Seelam. *Analysis and interpretation of data*: Linda Harris, Gilbert L'Italien, Anil Kumar, Prafullakumar Seelam, Chris LaVallee, Richard B. Lipton. *Drafting of the manuscript*: Linda Harris, Anil Kumar, Prafullakumar Seelam, Chris LaVallee. *Revising it for intellectual content*: Linda Harris, Gilbert L'Italien, Vladimir Coric, Richard B. Lipton. *Final approval of the completed manuscript*: Linda Harris, Gilbert L'Italien, Anil Kumar, Prafullakumar Seelam, Chris LaVallee, Vladimir Coric, Richard B. Lipton.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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