

Concomitant Medical Conditions and Total Cost of Care in Patients With Migraine: A Real-World Claims Analysis

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Migraine is a complex disorder that is characterized by moderate to severe unilateral or bilateral head pain that presents suddenly and may be accompanied by visual or sensory symptoms—also known as an aura.¹ To diagnose migraine, the International Headache Society requires that patients must have experienced at least 5 headache attacks, each lasting 4 to 72 hours, and the headache must have had at least 2 of the following characteristics: (a) unilateral location; (b) pulsating quality; (c) moderate or severe pain intensity; and/or (d) aggravation by or causing avoidance of routine physical activity. Additionally, during the headache, the patient must have had at least 1 of the following symptoms: (a) nausea and/or vomiting, and/or (b) photophobia and phonophobia. Lastly, these features must not have been attributable to another disorder.²

In the United States, 39 million patients are affected by migraine, with more than 28 million of them being adult women.³ Migraine attacks can be extremely disabling; in fact, more than 90% of migraine sufferers experience an inability to work or function normally while experiencing migraine.³

According to a recent analysis, the annual economic burden of migraine in the United States is approximately \$78 billion.⁴ Further, it is estimated that the annual total direct and indirect costs of all migraine-related health services are between \$8500 and \$9500 for an individual patient with chronic migraine. Although estimates vary, researchers report that the annual cost for patients with episodic migraine is significantly greater than the cost of care in individuals who do not have migraines. Indirect costs represent a significant portion of the total economic burden of the disease, but the precise percentage of total burden has varied across different studies, with some studies estimating the burden at 40% and others ranging upward to 90%.^{5,6} A recent analysis has suggested that indirect costs may account for 70% of the total costs.⁴ Through a survey conducted by the International Burden of Migraine Study (IBMS), the mean headache-related direct costs over a 3-month period for Americans with chronic migraine and with episodic migraine were calculated at \$1036 and \$383 per person, respectively.⁷

ABSTRACT

This study evaluates the impact of concomitant medical conditions on patients with and without migraine, assessing healthcare utilization, and total cost of care. Medical and pharmacy claims from multiple health plans, both nationally and internationally, were examined to evaluate overall real-world trends in commercially insured patients diagnosed with migraine. A total of 53,608 patients with diagnosis codes for migraine met the study criteria and were matched 1:1 with controls (81.8% female; mean age, 42 years; mean Charlson Comorbidity Index score, 0.34). During the 3-year measurement period, mean medical costs per patient in the migraine cohort were about 1.7 times that of the control group (\$22,429 vs \$13,166). Unique encounters and cost per patient by medical service type for the migraine cohort compared with the control group were as follows: emergency department, 4.13 (\$4000) versus 2.94 (\$2639); hospital inpatient, 3.15 (\$17,748) versus 2.67 (\$16,010); hospital outpatient, 5.14 (\$365) versus 4.85 (\$396); physician office, 36.78 (\$6803) versus 21.39 (\$4069); laboratory, 10.12 (\$1433) versus 7.71 (\$1057); radiology, 7.64 (\$2609) versus 5.94 (\$1733). Mean pharmacy costs per patient were approximately 1.8 times higher in the migraine cohort compared with the control cohort (\$8441 vs \$4588, respectively; $P < .0001$). These results suggest that patients with migraine have more comorbidities compared with those without migraine. These patients also utilize healthcare resources at a significantly higher rate compared with similar patients without a migraine diagnosis. An unmet need exists for new treatment modalities in this patient population. More effective interventions and proper management may lead to improved patient outcomes and healthcare costs for patients with migraine.

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Still, despite the huge population of patients who suffer from migraine and the tremendous economic burden the condition imposes on society, funding for migraine research is lacking. The National Institutes of Health has estimated the funding of research for migraines to be \$31 million in 2019; this is dramatically less than the expected \$6.6 billion investment in cancer research and \$1.4 billion for heart disease research.⁸ Migraine remains a frequently underdiagnosed and misdiagnosed condition, highlighting the need for more efficient diagnosis and for effective acute and preventive treatment options.

For patients with a migraine diagnosis, healthcare payers spend disproportionately more compared with healthy controls; this is primarily attributed to multiple comorbid conditions, resulting in higher healthcare utilization. This study aims to characterize and estimate healthcare utilization and the total cost of care in patients with migraine, compared with patients who have no primary headaches.

Methods

This retrospective cohort study examined real-world medical and pharmacy claims from multiple regional and national health plans to evaluate costs and healthcare utilization in commercially insured patients diagnosed with migraine. Qualifying patients were 18 years or older at the index date and were continuously enrolled in the same insurance plan for 3 years during the study period. The study took place from January 1, 2009, to September 30, 2017. Qualifying patients were separated into 2 cohorts. Patients in the migraine cohort had a qualifying diagnosis code of migraine, while patients in the control cohort had no claims of a headache-related or migraine-related diagnosis code. Both populations needed 3 years of available follow-up data and 6 months of baseline data during the claims evaluation window. The index date was defined as the date of the last medical claim, with a diagnosis of migraine with 36 months of subsequent eligibility during the claims evaluation window. The baseline period was defined as 3 months prior to the index date (exclusive of the index date). The follow-up period consisted of 36 months starting on the index date. Patients in the migraine cohort were matched to the control cohort using 1:1 propensity score matching. The sample size of this study was limited to the number of members within the health plan database who met the inclusion criteria. Sample size estimation was not necessary, as the intent was to analyze real-world utilization.

Patient age, gender, and plan type were evaluated. Comorbidities, including number of comorbidities and breakdown by medical characterization were also analyzed. The outcomes of the study relied on healthcare resource utilization by service type (inpatient, outpatient, emergency department [ED], home care, etc) and total all-cause and migraine-related costs. These results were organized from patient count by service type, visit count per patient by service type, cost per patient by service type, and patient count by procedure code of interest. Pharmacy utilization costs included all-cause, migraine-related pharmacy costs, and utilization by drug class.

Patient characteristics were logged into a nonparsimonious logistic regression model to generate propensity scores for the population. Further analysis was performed on the propensity-matched study sample to reduce the effect of confounding variables. Descriptive statistics, such as the mean, median, standard deviation, minimum, and maximum, were generated to characterize the distributions for continuous variables. For categorical variables, cross-tabulation in frequency and percentage were used to report results. Cohort differences in baseline characteristics and utilization were assessed using Student's *t* test or χ^2 test with the Fisher's exact test. A multivariate logistic regression model was performed to estimate the effects of age, gender, and comorbidity index scores on all-cause expenditures for patients with migraine. All statistical analyses were performed using SAS version 9.4 (SAS Institute; Cary, North Carolina).

Results

Demographics

Of the 53,608 patients who qualified for the migraine cohort, 43,834 (81.8%) were female, with a mean age of 42 years and a mean Charlson Comorbidity Index (CCI) score of 0.34 (Table 1). These numbers were the same in the control cohort. In the migraine cohort, 46,721 patients (85.6%) had PPO coverage, 5808 (10.6%) had HMO coverage, and 2051 (3.8%) had other coverage. Regarding comorbidities in the migraine cohort, 6.8% of patients experienced anxiety, 8.9% of patients experienced depression, and 0.7% of patients experienced dyspepsia; in the control cohort, 2.1% of patients experienced anxiety, 3.1% of patients experienced depression, and 0.4% experienced dyspepsia (all *P* values <.0001).

Medical Utilization and Costs

Throughout the 3-year measurement period, overall costs per patient in the migraine cohort were about 1.9 times that of the control group (\$28,209 vs \$15,068, respectively; *P* <.0001). The mean medical costs per patient with migraine, during the same period, were about 1.7 times that of the control group (\$22,429 vs \$13,166, respectively; *P* <.0001) (Table 2). Unique encounters and cost per patient by medical service type for the migraine cohort compared with the control group were as follows: ED, 4.13 encounters (\$4000 cost) versus 2.94 (\$2639); hospital inpatient, 3.15 (\$17,748) versus 2.67 (\$16,010); hospital outpatient, 5.14 (\$365) versus 4.85 (\$396); physician office, 36.78 (\$6803) versus 21.39 (\$4069); laboratory, 10.12 (\$1433) versus 7.71 (\$1057); and radiology, 7.64 (\$2609) versus 5.94 (\$1733). Compared with the control group, patients with migraine had 52.91% more physician office visits (*P* <.0001).

Pharmacy Utilization and Costs

The average pharmacy costs per patient were approximately 1.8 times higher in the migraine cohort compared with the control cohort (\$8441 vs \$4588, respectively; *P* <.0001) (Table 3). Patients with

migraine were 2.6 times as likely to fill a prescription for a narcotic analgesic compared with control patients (15,277 vs 5932 patients, respectively). Among patients in the migraine cohort, a total of 59.46% of patients had at least 1 narcotic analgesic claim matched to headache (21.41%) or migraine (38.05%) medical claims (Table 4). A greater percentage of patients in the migraine cohort had ED encounters which included administration of narcotic analgesics (1.89%) compared with the control cohort (0.19%; $P < .0001$) (Table 5).

Discussion

Past studies analyzing migraine populations have suggested major economic and noneconomic burdens of migraine. Key findings of this retrospective study indicate that patients with migraine experience costs that are higher than those of patients without these severe headaches and associated symptoms. The higher costs can be attributed to higher numbers of ED visits, physician office appointments, pharmacy costs, and laboratory and imaging costs. Among patients with migraine, a higher proportion of patients utilize all service types. This includes 50% more physician office visits than their control cohort counterparts. Patients with migraine are more likely to visit EDs and to do so more often, possibly for narcotic analgesics. Furthermore, patients with migraine have noticeably higher usage of narcotic analgesics, both in the proportion of patients and the total number of prescriptions. Among patients receiving a narcotic analgesic, those with migraine fill more prescriptions than those without migraine.

Patients with migraine have a higher number of encounters (laboratory, ED, radiology, inpatient hospitalization, outpatient, and physician office) per patient compared with patients without migraine, resulting in higher costs per patient. The diagnoses for these encounters were not evaluated, however, limiting the ability to distinguish the association between encounters that were migraine-related and those that were not.

A possible reason for the much higher use of healthcare resources and costs is the occurrence

TABLE 1. Migraine Demographics

	Migraine (n = 53,608)	Control (n = 53,608)
Female	43,834 (81.8%)	43,834 (81.8%)
Age group		
Mean, years (SD) [median]	42.44 (10.93) [44]	42.44 (10.93) [44]
18-20	1355 (2.5%)	1355 (2.5%)
21-30	7595 (14.2%)	7595 (14.2%)
31-40	14,147 (26.4%)	14,147 (26.4%)
41-50	17,098 (31.9%)	17,098 (31.9%)
51-60	11,871 (22.1%)	11,871 (22.1%)
61-64	1234 (2.3%)	1234 (2.3%)
65+	308 (0.6%)	308 (0.6%)
Charlson Comorbidity index score		
Mean (SD) [median]	0.34 (0.84) [0]	0.34 (0.84) [0]
0	42,380 (79.1%)	42,380 (79.1%)
1	6740 (12.6%)	6740 (12.6%)
2	3119 (5.8%)	3119 (5.8%)
3+	1369 (2.6%)	1369 (2.6%)
Comorbidities		
Anxiety	3633 (6.8%)	1141 (2.1%)
Depression	4779 (8.9%)	1642 (3.1%)
Dyspepsia	385 (0.7%)	191 (0.4%)

TABLE 2. Medical Utilization

	Migraine (n = 53,608)	Control (n = 53,608)	P
Overall cost per patient (\$)	28,209	15,068	<.0001
Medical cost per patient (\$)	22,429	13,166	<.0001
Medical cost-migraine-related (\$)	2023	-	N/A
Patient counts by medical service type			
Laboratory	42,917 (80.1%)	35,223 (65.7%)	<.0001
Emergency department	5138 (9.6%)	1515 (2.8%)	<.0001
Radiology	40,725 (76.0%)	30,174 (56.3%)	<.0001
Inpatient hospitalization	1784 (3.3%)	609 (1.1%)	<.0001
Outpatient	4767 (8.9%)	2772 (5.2%)	<.0001
Physician office	52,703 (98.3%)	46,952 (87.6%)	<.0001

(continued)

TABLE 2. Medical Utilization (Continued)

	Migraine (n = 53,608)	Control (n = 53,608)	P
Encounters per Patient by Service Type			
Laboratory	10.12	7.71	<.0001
Emergency department	4.13	2.94	<.0001
Radiology	7.64	5.94	<.0001
Inpatient hospitalization	3.15	2.67	<.0001
Outpatient	5.14	4.85	--
Physician office	36.78	21.39	<.0001
All-Cause Cost per Patient by Medical Service Type (\$)			
Laboratory	1433	1057	<.0001
Emergency department	4000	2639	<.0001
Radiology	2609	1733	<.0001
Inpatient hospitalization	17,748	16,010	--
Outpatient	365	396	--
Physician office	6803	4069	<.0001

TABLE 3. Pharmacy Utilization

	Migraine (n = 53,608)	Control (n = 53,608)	P
Pharmacy Cost (\$)	8441	4588	<.0001
Patient Count by Drug Type			
Overall	36,706 (68.5%)	32,899 (61.4%)	<.0001
Nonnarcotic analgesics	12,439 (23.2%)	4331 (8.1%)	<.0001
Antimigraine	12,918 (24.1%)	138 (0.3%)	<.0001
Migraine prophylaxis	19,201 (35.8%)	6773 (12.6%)	<.0001
Narcotic analgesics	15,277 (28.5%)	5932 (11.1%)	<.0001
Botulinum toxins	2930 (5.33%)	98 (0.18%)	<.0001
Prescription Count by Drug Type			
Nonnarcotic analgesics	8.14	5.24	<.0001
Antimigraine	17.68	11.07	.0007
Migraine prophylaxis	21.66	15.98	<.0001
Narcotic analgesics	14.73	7.45	<.0001
Botulinum toxins	5.90	3.95	<.00001
Prescription Cost by Drug Type (\$)			
Nonnarcotic analgesics	307	208	<.0001
Antimigraine	2217	850	.00012
Migraine prophylaxis	860	445	<.0001
Narcotic analgesics	798	209	<.0001
Botulinum toxins	9,413	8730	<.0001

of multiple symptoms in primary headache patients, including migraine patients, which manifests as multiple comorbidities that do not appear in administrative claims data. In this study, differences in utilization due to multiple comorbidities were mitigated somewhat by propensity matching based on the CCI score. Among patients with migraine, anxiety (6.8%), depression (8.9%), and dyspepsia (0.7%) were more prevalent compared with patients without headaches (2.1%, 3.1%, and 0.4%, respectively).

Limitations

This analysis was based on real-world claims data. Services performed, but not billed, were not captured in the data. This may include physician samples for pharmaceutical products or prescriptions that are typically paid in cash, such as those on special pricing (eg, \$4 generics) lists. Patients were included in the study based on an *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* or *ICD-10-CM* diagnosis code for migraine. There may have been some misdiagnoses, and the presence of a diagnosis code did not necessarily indicate that a headache specialist or neurologist made the diagnosis based on International Classification of Headache Disorders criteria.

Of note, the diagnosis used was "migraine" by the *ICD-9-CM*, which does not distinguish between episodic migraine and chronic migraine, and as noted above, healthcare utilization was different in the 2 groups, with higher utilization found in patients with chronic migraine in the IBMS study. This analysis cannot address this difference. This was a retrospective case-controlled study, not a prospective randomized study.

Conclusions

These study findings indicate that patients with migraine utilize healthcare resources at a significantly higher rate than similar patients without a primary headache-related diagnosis. The higher utilization rates are associated with higher rates of comorbidities, medical symptoms, and use of narcotic analgesics observed in migraine patients. An unmet need exists for new treatment modalities in this patient population.

Treatments that address the underlying pathology may result in the alleviation of most symptoms, reduced utilization of healthcare resources beyond those attributed to migraine, and reduced costs beyond those attributed to migraine. More effective diagnosis, treatment, and prevention of migraine may lead to dramatically improved patient outcomes and the containment of healthcare costs associated with migraine. ■

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TABLE 4. Narcotic Analgesics Associated With Headache or Migraine

	Migraine
Had ≥1 narcotic analgesic claim matched to headache medical claims	4642 (21.41%)
Had ≥1 narcotic analgesic claim matched to migraine medical claims	8251 (38.05%)
Mean per person percentage of narcotic analgesic claims matched to headache medical claims	7.2%
Mean per person percentage of narcotic analgesic claims matched to migraine medical claims	14.4%

TABLE 5. Narcotic Analgesic Use in the Emergency Department

Measure Name	Migraine	Control	P
Had ED encounters which included administration of narcotic analgesic	1040 (1.89%)	105 (0.19%)	<.0001

ED indicates emergency department.

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