REPORT

# Real-World Health Plan Claims Analysis of Differences in Healthcare Utilization and Total Cost in Patients Suffering From Cluster Headaches and Those Without Headache-Related Conditions

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Cluster headache (CH) is a type of primary headache disorder that is characterized by a group of headaches occurring typically over a period of several weeks (ie, a cluster period).[1] In the United States, about 1 in 1000 adults has experienced CH and the disorder affects men more often than women.[2,3] Clusters are classified as 1 of 2 primary forms: episodic and chronic.[1] Episodic CH is seen in about 80% of patients with CH and presents as at least 2 cluster phases/year, each lasting 7 days to 1 year, that are separated by a cluster-free interval of 1 month or longer.[1,4,5] Chronic CH occurs in about 20% of patients with CH and presents as clusters that occur more than once a year without remission or with a cluster-free interval that is shorter than 1 month.[1,4,5] Three notable features of CH are: excruciating pain, often described as a "red-hot poker in the eye," which typically evokes a reaction such as banging the head against the wall or pacing the room back and forth; pain duration that is shorter than that of a migraine, ranging typically from 15 minutes to 3 hours; and at least 1 accompanying ipsilateral cranial autonomic feature, for example, sweating of the forehead or face, shedding of tears, or blocked nasal passages.[6]



Headache disorders, including CH, cause substantial disability in sufferers.[7] Torkamani et al studied the cognitive and psychosocial function of patients with CH, and the results indicated that such patients often experience poor quality of life and high levels of health-related disability.[7] CH is often debilitating to those afflicted, with almost 20% of patients with CH having lost a job due to the disorder, and 8% being out of work or on disability secondary to headaches.[8] Both Jensen et al and Jürgens et al analyzed impairment in patients with CH, and they found that notable percentages of both patients with chronic and episodic CH were severely impaired, with limited to no ability to work.[9,10] Jensen et al surveyed 85 patients with CH for impairment; 78% of surveyed patients reported daily living restrictions, and the work absentee rate among patients with CH was 30%, significantly higher than that of the general population (12%).[9]

Although CH imposes significant disability in those afflicted, this disorder remains underdiagnosed and undertreated.[6,8] According to the World Health Organization, headache and migraine disorders

## ABSTRACT

**Background:** According to the World Health Organization, headache disorders are underappreciated by many health systems. These disorders have a substantial impact on quality of life, yet the true correlation between headache conditions and increased total healthcare utilization is not well understood. This study further explores the impact of headache conditions on healthcare utilization.

**Objectives:** To assess differences in healthcare utilization and total cost in patients suffering from cluster headaches (CH) compared with patients without headache-related conditions.

**Methods:** Medical and pharmacy claims data from 4 regional health plans were used to evaluate differences in healthcare utilization and cost in patients with a diagnosis code for CH (chronic, episodic, or unspecified) from *International Classification of Diseases, Ninth Revision, Clinical Modification* or *International Classification of Diseases, Tenth Revision, Clinical Modification* compared with a control group of patients without headache-related conditions. Qualifying patients were aged at least 18 years and continuously eligible for their health plan for 3 consecutive years during the study period (January 1, 2009-December 31, 2015). The first date with a diagnosis of CH was considered the index date and the subsequent 3 years of claims data were used for this retrospective analysis. The CH cohort was matched with controls using propensity score matching. Differences between cohorts (CH vs control) were assessed with *t* test or Fisher's exact test as appropriate.

**Results:** A total of 4174 patients with diagnosis codes for CH met the study criteria and were matched 1:1 with controls (gender: 48% male; mean age: 47 years; mean Charlson Comorbidity Index score: 0.30). Mean medical costs per patient in the CH cohort during the 3-year measurement period were 155% higher than those of the control group ($25,805 vs $10,140, respectively). Unique encounters and cost per patient by medical services type for the CH cohort compared with the control group were as follows (encounters [costs]): emergency department: 2151 ($1986) versus 962 ($1268); hospital inpatient: 900 ($7312) versus 253 ($8528); hospital outpatient: 3422 ($12,459) versus 2141 ($7644); physician office: 4113 ($7379) versus 4089 ($3672); home infusion/specialty medications: 817 ($4977) versus 427 ($1720). Visit counts per patient were significantly higher for CH patients in all categories. Mean pharmacy costs per patient for the CH cohort were more than double that of the control group ($9197 vs $4368), with these patients 2.3 times as likely to fill a prescription for an opioid.

**Conclusions:** The results of this analysis show that CH patients utilize healthcare resources at a significantly higher rate and cost the healthcare system significantly more than similar patients without headache-related conditions. There is an unmet need for new treatment modalities in this patient population to improve outcomes and contain cost.

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For author information and disclosures, see end of text.

are greatly underrated and underreported by health systems and receive too little attention.[11] Because diagnosis and management of CH presents such a challenge for practitioners—particularly those who are not neurologists or headache specialists—effective treatments for the disorder may be underutilized.[12]

Medical management of CH focuses on 1) treatment of acute attacks and 2) preventive treatment that aims to suppress ongoing attacks. According to evidence-based treatment guidelines provided by the American Headache Society (AHS), there is a level A recommendation (established as effective) for acute treatment utilizing subcutaneous sumatriptan, zolmitriptan nasal spray, and high-flow oxygen (12 to 15 L/minute) administered through a nonrebreather face mask over the nose and mouth.[13] Level B recommendations (probably effective) by the AHS for acute treatments include sumatriptan nasal spray, oral zolmitriptan, and sphenopalatine ganglion stimulation.[13] For preventive treatment, these guidelines provide level A recommendation for suboccipital steroid injections and level B recommendation for the use of civamide nasal spray in the prophylactic setting, though work on its development stopped many years ago.[13] The AHS guidelines also include lithium and verapamil as level C recommendations (possibly effective); despite its status as a level C recommendation, verapamil is the most commonly used preventative treatment.[13]

Diagnostic delays can limit the ability to administer appropriate preventative treatment.[5] The time to diagnose CH has improved over the past few decades, dropping from 22 years in the 1960s to 2.6 years in the 1990s.[14] Still, patients see an average of 3 general practitioners prior to receiving a CH diagnosis,[14] and CH remains both poorly managed and underdiagnosed in the afflicted population.[5]

The debilitating impact and underdiagnosis of CH raises questions of the possible correlation between headache conditions, especially CH, and total healthcare utilization. While some international studies have observed a significant impact of CH on direct healthcare costs as well as indirect costs to society, few studies have explored the association of CH and increased healthcare costs and utilization in the United States. This study sought to evaluate the key trends in pharmaceutical utilization, comorbidities, healthcare utilization, and overall costs in patients diagnosed with CH compared with patients without a headache-related diagnosis.

## Methods

This retrospective study examined real-world medical and pharmacy claims from multiple regional health plans with commercially insured and Medicare populations, mainly located in the northeastern United States. Qualifying patients were aged ≥18 years at the index date and continuously enrolled in the same insurance company for 3 years during the study period. The study period spanned from January 1, 2009, to December 31, 2015. Qualifying patients were separated into 2 cohorts: CH and control. The first date with a diagnosis of CH was the index date for the CH population, and study data were the 3 years of claims data incurred following the index date. Patients in the CH cohort had a qualifying diagnosis code of CH (episodic, chronic, or unspecified), while patients in the control cohort had no claims with a headache-related diagnosis code. Patients in the CH cohort were further segmented into those with chronic CH, those with episodic CH, and those whose headache frequency was unclassified (not-defined CH). The control cohort was drawn from qualifying patients with no headache-related diagnosis who had 3 years of available follow-up data from the first date within the study period in which they had eligibility. Patients in the CH cohort were matched to the control cohort using 1:1 propensity score matching.

The sample size for this study was limited to the number of members within the health plan database meeting the inclusion criteria. As the intent was to analyze real-world utilization, sample size estimation was not necessary.

Primary outcome variables analyzed were as follows:

- Baseline patient characteristics
  - Age
  - Gender
  - Comorbidities
- Medical utilization and costs
  - Patient count by service type
  - Visit count per patient by service type
  - Cost per patient by service type
  - Patient count by procedure codes of interest
- Pharmacy utilization costs
  - All pharmacy cost and utilization
  - Analgesic cost and utilization
  - Triptan cost and utilization
  - Opiate cost and utilization

Demographic data were entered into a logistic regression model to generate propensity scores for the population. Further analysis was done on the propensity matched population to reduce the effect of confounding variables. Descriptive statistics were generated as a measure of central tendency and variance for continuous variables, including mean, median, standard deviation, minimum, and maximum. For categorical variables, cross-tabulation in count (frequency) and percentage were used to report results. Between-group differences in baseline characteristics and utilization were assessed via *t* test or Fisher's exact test as appropriate. A multivariate model was constructed to examine the effect of age, gender, and comorbidity index score on all-cause expenditures for patients with CH. All calculations were completed using SAS 9.4.

## Results

### Demographics

Of the 4174 patients meeting the CH cohort criteria, 724 (17.3%) were chronic, 751 (18.0%) were episodic, and 2699 (64.7%) were not defined (**Table 1**). The CH cohort was 48% male, with a mean age of 47 years

**TABLE 1.** Demographics

| | Cluster Headaches | | | | |
|---|---|---|---|---|---|
| | Chronic | Episodic | Not Defined | Total | Control |
| Patient Count | 724 | 751 | 2699 | 4174 | 4174 |
| Gender | | | | | |
| F | 368 (50.8%) | 365 (48.6%) | 1427 (52.9%) | 2160 (51.7%) | 2160 (51.7%) |
| M | 356 (49.2%) | 386 (51.4%) | 1272 (47.1%) | 2014 (48.3%) | 2014 (48.3%) |
| Age Group (years) | | | | | |
| 18-29 | 192 (26.5%) | 226 (30.1%) | 818 (30.3%) | 1236 (29.6%) | 1236 (29.6%) |
| 40-54 | 291 (40.2%) | 272 (36.2%) | 1087 (40.3%) | 1650 (39.5%) | 1650 (39.5%) |
| 55-64 | 146 (20.2%) | 151 (20.1%) | 481 (17.8%) | 778 (18.6%) | 778 (18.6%) |
| 65+ | 95 (13.1%) | 102 (13.6%) | 313 (11.6%) | 510 (12.2%) | 510 (12.2%) |
| Charlson Comorbidity Index Score | | | | | |
| Continuous | 0.31 ± 0.83 [0] | 0.30 ± 0.88 [0] | 0.30 ± 0.82 [0] | 0.30 ± 0.83 [0] | 0.30 ± 0.83 [0] |
| 0 | 592 (81.8%) | 626 (83.4%) | 2211 (81.9%) | 3429 (82.2%) | 3429 (82.2%) |
| 1 | 83 (11.5%) | 71 (9.5%) | 311 (11.5%) | 465 (11.1%) | 465 (11.1%) |
| 2+ | 49 (6.8%) | 54 (7.2%) | 177 (6.6%) | 280 (6.7%) | 280 (6.7%) |

**Note:** Continuous data: mean ± standard deviation [median]; discrete data: count (percent).

and a Charlson Comorbidity Index score of 0.30. About 82.2% of patients with CH had a conservative confidence interval (CCI) of 0.

### Medical Costs

Mean medical costs per patient in the CH cohort during the 3-year measurement period were about 2.5 times that of the control group ($25,805 vs $10,140, respectively) (Table 2). Unique encounters and cost per patient by medical service type for the CH cohort compared with the control group were as follows (encounters [costs]): emergency department (ED): 2151 ($1986) versus 962 ($1268); hospital inpatient: 900 ($7312) versus 253 ($8528); hospital outpatient: 3422 ($12,459) versus 2141 ($7644); physician office: 4113 ($7379) versus 4089 ($3672); home infusion/specialty pharmacy: 817 ($4977) versus 427 ($1730). Compared with the control group, patients with CH had over twice as many ED visits, over 1 and a half times as many hospital outpatient visits, and 3 and a half times more hospital inpatient visits.

Mean overall medical costs for chronic CH ($30,502) were about 35% more than those for episodic CH ($22,607) and about 20% more than those for undefined CH ($25,436).

### Pharmacy Costs

Mean pharmacy costs per patient were about twice as much ($P < .01$) in the CH cohort than in the control cohort ($9197 vs $4368, respectively) (Table 3). Overall prescription costs for chronic patients with CH ($12,534) were approximately 53% more than for episodic patients with CH ($8209) and 46% more than for not-defined patients with CH ($8570). Patients with CH were 2.3 times as likely as control patients to fill a prescription for an opioid. Chronic patients with CH had 28% more prescription fills than episodic patients with CH, and 24% more fills than not-defined patients with CH (30.66 vs 23.90 vs 24.79, respectively). Patients with CH were also 4.7 times more likely to receive a prescription for an opiate during the study period than were control patients (4502 patients vs 968 patients, respectively).

## Discussion

Past studies analyzing CH populations have suggested a major economic and noneconomic burden of CH. Gaul et al analyzed questionnaires distributed to patients with CH, and the results suggested that CH led to a substantial socioeconomic impact on patients due to both direct healthcare costs and indirect costs due to disability.[15] Like Gaul et al, this study found a correlation between CH and increased healthcare costs.[15] The results of this study support the conclusion that the presence of CH and headache-related diagnoses is associated with higher healthcare cost. Not only did patients with CH incur significantly higher overall healthcare costs, but costs for each service type were significantly higher for patients with CH than for control patients.

Underdiagnoses and improper CH management may lead to increased hospital and ED utilization by patients with CH, totaling significantly more ED visits and hospital inpatient and outpatient visits than control patients. Effective preventative treatment of CH may result in decreased visits by patients with CH, ultimately resulting in fewer incurred healthcare costs.

Patients with CH in this study were more likely to be female, which differs from most studies of CH populations, and most

**TABLE 2.** Medical Costs

| | Cluster Headaches | | | | | |
|---|---|---|---|---|---|---|
| | Chronic | Episodic | Not Defined | Total | Control | *P*[a] |
| Overall Medical Cost per Patient | 30,502 ± 50,131 [15,091] | 22,607 ± 39,721 [12,158] | 25,436 ± 45,851 [11,553] | 25,805 ± 45,650 [12,225] | 10,140 ± 39,412 [3383] | <.01 |
| Patient Counts by Medical Service Type | | | | | | |
| Diagnostic Testing | 697 (96.3%) | 715 (95.2%) | 2583 (95.7%) | 3995 (95.7%) | 3231 (77.4%) | <.01 |
| Emergency Department | 361 (49.9%) | 366 (48.7%) | 1424 (52.8%) | 2151 (51.5%) | 962 (23.0%) | <.01 |
| Home Infusion/Specialty Rx | 191 (26.4%) | 148 (19.7%) | 478 (17.7%) | 817 (19.6%) | 427 (10.2%) | <.01 |
| Hospital Inpatient | 175 (24.2%) | 160 (21.3%) | 565 (20.9%) | 900 (21.6%) | 253 (6.1%) | <.01 |
| Hospital Outpatient | 609 (84.1%) | 599 (79.8%) | 2214 (82.0%) | 3422 (82.0%) | 2141 (51.3%) | <.01 |
| Physician Office | 716 (98.9%) | 748 (99.6%) | 2649 (98.1%) | 4113 (98.5%) | 4089 (98.0%) | .79 |
| Cost per Patient by Medical Service Type | | | | | | |
| Diagnostic Testing | 4332 ± 6133 [2446] | 3524 ± 4434 [1973] | 3822 ± 5305 [2065] | 3857 ± 5321 [2015] | 1515 ± 3160 [549] | <.01 |
| Emergency Department | 2106 ± 8091 [853] | 1509 ± 2074 [851] | 2078 ± 4635 [896] | 1986 ± 5095 [870] | 1268 ± 2044 [802] | <.01 |
| Home Infusion/Specialty Rx | 4162 ± 27,345 [700] | 6245 ± 53,046 [495] | 4910 ± 47,087 [545] | 4977 ± 44,470 [557] | 1730 ± 8450 [170] | <.01 |
| Hospital Inpatient | 8105 ± 24,429 [3784] | 6621 ± 9062 [3117] | 7261 ± 15,455 [3431] | 7312 ± 16,736 [3443] | 8528 ± 45,509 [6768] | .68 |
| Hospital Outpatient | 14,965 ± 32,281 [5018] | 10,277 ± 18,780 [3215] | 12,360 ± 24,639 [4339] | 12,459 ± 25,328 [4312] | 7644 ± 45,146 [1506] | <.01 |
| Physician Office | 8740 ± 14,147 [4970] | 6924 ± 10,631 [4077] | 7139 ± 14,527 [4043] | 7379 ± 13,843 [4181] | 3672 ± 9495 [1742] | <.01 |

Rx indicates prescription.
Notes: Continuous data: mean ± standard deviation [median]; discrete data: count (percent).
[a]*P* value based on testing total cluster versus control.

**TABLE 3.** Pharmacy Costs

| | Cluster Headaches | | | | | |
|---|---|---|---|---|---|---|
| | Chronic | Episodic | Not Defined | Total | Control | *P*[a] |
| Overall Prescription Fills per Patient | 30.66 ± 23.23 [25] | 23.90 ± 19.09 [19] | 24.79 ± 20.74 [19] | 25.66 ± 21.04 [20] | 12.34 ± 11.33 [9] | <.01 |
| Overall Prescription Cost per Patient | 12,534 ± 21,528 [5497] | 8209 ± 17,353 [3095] | 8570 ± 19,913 [2477] | 9197 ± 19,839 [2947] | 4368 ± 13,379 [891] | <.01 |
| Patient Counts by Rx Type | | | | | | |
| Analgesics | 477 (65.9%) | 451 (60.1%) | 1734 (64.2%) | 2662 (63.8%) | 1017 (24.4%) | <.01 |
| Triptans (oral) | 205 (28.3%) | 180 (24.0%) | 667 (24.7%) | 1052 (25.2%) | 35 (0.8%) | <.01 |
| Triptans (subcutaneous) | 92 (12.7%) | 95 (12.6%) | 172 (6.4%) | 359 (8.6%) | 3 (0.1%) | <.01 |
| Opiates (all) | 411 (56.8%) | 369 (49.1%) | 1471 (54.5%) | 2251 (53.9%) | 968 (23.2%) | <.01 |
| Opiates (associated with an ED visit) | 94 (13.0%) | 103 (13.7%) | 382 (14.2%) | 579 (13.9%) | 125 (3.0%) | <.01 |
| Verapamil | 148 (20.4%) | 145 (19.3%) | 324 (12.0%) | 617 (14.8%) | 25 (0.6%) | <.01 |
| Lithium | 31 (0.4%) | 16 (0.2%) | 43 (0.5%) | 90 (1.1%) | 9 (0.1%) | <.01 |
| Valproic Acid | 205 (28.3%) | 180 (24.0%) | 667 (24.7%) | 1052 (25.2%) | 35 (0.8%) | <.01 |

ED indicates emergency department; Rx, prescription.
Note: Continuous data: mean ± standard deviation [median]; discrete data: count (percent).
[a]*P* value based on testing total cluster versus control.

patients with CH had a CCI of 0. Notably, patients with CH were significantly more likely to receive a prescription across all prescription types, and the pharmacy costs for patients with CH were more than double than those for the control group. Most patients with CH can be successfully treated; however, some do not respond to therapy and may have to try alternatives until finding an effective treatment, which can lead to increased pharmacy costs and utilization.[16] Earlier diagnosis and proper management of CH may help to contain pharmacy costs by streamlining the process of CH therapy.

### 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 generic) lists. Patients were included in the study based on an *International Classification of Diseases, Ninth Revision, Clinical Modification* or *International Classification of Diseases, Tenth Revision, Clinical Modification* diagnosis code for cluster headache. There may have been some misdiagnoses, including that of migraine patients, 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. The specific type of cluster headache cannot always be determined with claims data.

## Conclusions

These study results showed that patients identified from the data as patients with CH utilize healthcare resources at a significantly higher rate than do similar patients without a headache-related diagnosis. An unmet need exists for new treatment modalities in this patient population. More effective interventions and proper management, along with earlier diagnosis of CH, may lead to improved patient outcomes and contained CH-associated healthcare costs. ■

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