

# Hospital Burden of Migraine in United States Adults: A 15-year National Inpatient Sample Analysis

Huay-Zong Law, MD\*  
 Michael H. Chung, MD\*  
 George Nissan, MD†‡  
 Jeffrey E. Janis, MD, FACS§  
 Bardia Amirlak, MD, FACS\*

**Background:** Migraine headache is associated with high costs, but changes over time of inpatient burden in the United States are unknown. Understanding longitudinal trends is necessary to determine the costs of evolving inpatient treatments that target biological factors in the generation of pain such as vasodilation and aberrant activity of trigeminal neurotransmitters. We report the migraine hospital burden trend in the United States over 15 years.

**Methods:** Data from the Nationwide Inpatient Sample of the Hospitalization Cost and Utilization Project databases were analyzed from 1997 to 2012. Inpatient costs were reported in dollars for the cost to the institution, whereas charges reflect the amount billed. These parameters were trended and the average annual percent change was calculated to illustrate year-to-year changes.

**Results:** Overall discharges for migraine headache reached a low of 30,761 discharges in 1999, and peaked in 2012 with 54,510 discharges. Average length of stay decreased from 3.5 days in 1997 to 2.8 days in 2012. Total inpatient charges increased from \$176 million in 1999 to \$1.2 billion in 2012. Inpatient costs totaled \$322 million in 2012, with an average daily cost of \$2,111.

**Conclusions:** Inpatient burden rapidly increased over the analyzed period, with hospital charges increasing from \$5,939 per admission and \$176 million nationwide in 1997, to \$21,576 per admission and \$1.2 billion nationwide in 2012. This trend provides context for research examining cost-effectiveness and quality of life benefits for current treatments. The study of these parameters together with better prevention and improved outpatient treatment may help alleviate the inpatient burden of migraine. (*Plast Reconstr Surg Glob Open* 2020;8:e2790; doi: [10.1097/GOX.0000000000002790](https://doi.org/10.1097/GOX.0000000000002790); Published online 23 April 2020.)

## INTRODUCTION

Migraine headache is a common, debilitating disease that causes significant disability.<sup>1-3</sup> It affects nearly 1 in 7 Americans each year, with an estimated 40 million people suffering from migraine headaches.<sup>4-6</sup> Its prevalence is as high as 19% for females and 9% for males.<sup>6</sup> Despite the high prevalence, migraine headache is often not diagnosed correctly and many patients do not undergo appropriate treatment.<sup>7</sup> The age at which patients most

commonly develop migraine headaches is between 25 and 55 years of age, corresponding to their peak earning potential.<sup>8</sup> Thus, high direct medical costs are suffered by individuals and hospitals in addition to the indirect costs of occupational disability and loss of productivity. From a population healthcare perspective, severe headache and migraine disproportionately affect historically disadvantaged populations and can become most burdensome in women during their childbearing age.<sup>9</sup> This inequality in prevalence is important to recognize when understanding the trend of economic burden, particularly considering the recent changes in the climate of insurance coverage in the United States. Previous data have shown direct costs exceeding \$2,500 per migraine patient.<sup>10</sup> However, many indirect financial burdens exist. The most studied aspect is represented by lost work time and productivity, costing up to \$13,000 per year for each migraine sufferer and total cost to employers of \$12 billion.<sup>11,12</sup> In total, the economic impact of migraine headache in the United States is estimated to be between \$13 and \$17 billion annually.<sup>8</sup> In addition to financial factors, the biological and functional effect of migraine can be illustrated by the

From the \*Department of Plastic Surgery, University of Texas Southwestern Medical Center, Dallas, Tex.; †Neurology, Scott and White Health, Baylor University Medical Center, Dallas, Tex.; ‡Neurology, Texas A&M College of Medicine, Bryan, Tex.; and §Department of Plastic Surgery, Ohio State University Wexner Medical Center, Columbus, Ohio.

Received for publication November 22, 2019; accepted February 26, 2020.

Copyright © 2020 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of The American Society of Plastic Surgeons. This is an open-access article distributed under the terms of the [Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 \(CCBY-NC-ND\)](https://creativecommons.org/licenses/by-nc-nd/4.0/), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: [10.1097/GOX.0000000000002790](https://doi.org/10.1097/GOX.0000000000002790)

**Disclosure:** The authors have no financial interest to declare in relation to the content of this article.

higher prevalence of psychiatric comorbidities, including depression, anxiety, and posttraumatic stress disorder in patients with chronic migraines compared with the general population.<sup>13</sup>

Treatment options have traditionally consisted of medical interventions categorized as acute abortive and prophylactic medications. Common prophylactic medications used are  $\beta$ -blockers, antiepileptic medications (topiramate and divalproex sodium), and tricyclic antidepressants. Common acute abortive and analgesic medications include triptans, ergotamines, antiemetics, nonsteroidal anti-inflammatory drugs, and combination opioids, which have a wide array of mechanisms that target different pathways and biological factors in headache generation including such neurotransmitter pathways as serotonin, dopamine, norepinephrine, cyclooxygenase, opioid pain receptors, and calcitonin gene-related peptide (CGRP).<sup>14,15</sup>

These medications are not always completely effective and have multiple potential side effects, leading patients to seek alternative treatments. In October 2010, the Food and Drug Administration approved the injection of onabotulinumtoxinA (specifically Botox; Allergan, Dublin, Ireland) for the treatment of chronic migraine headaches. Since then, it has been used effectively by headache specialists, neurologists, and plastic surgeons as a prophylactic treatment.<sup>16–20</sup> Before the recent introduction of erenumab, a CGRP receptor monoclonal antibody, botulinum toxin A was the only Food and Drug Administration–approved prophylactic treatment for chronic migraine. Carefully selected patient also have seen improvement of their headaches after surgical decompression.<sup>21–28</sup>

When these interventions are insufficient to prevent or treat a headache, patients may be admitted to the hospital for further treatments such as intravenous ergotamines, neuroleptics, and antiemetics, as well as nonpharmacologic treatments including cognitive behavioral therapy.<sup>29</sup> In patients who present to the emergency department (ED) for headache symptoms, migraine headaches have been identified as the leading cause of admission.<sup>30</sup> In addition to admissions at the ED, patients may be sent to specialized tertiary headache centers. Although inpatient treatment of migraine headaches is currently based on observational studies and expert opinion, these specialized centers with both inpatient and outpatient programs for migraine headaches were found to result in reductions in both headache disability and direct healthcare expenditure.<sup>31,32</sup> For example, patients may be discontinued from acute medications causing medication overuse headache, initiated on intravenous dihydroergotamine, and enrolled in services such as therapeutic counseling and physical therapy.<sup>32</sup>

In the United States, the cost of inpatient treatment for a single year has been estimated to be \$375 million.<sup>33</sup> Therefore, understanding longitudinal trends is a necessary step for determining the costs of evolving inpatient treatment patterns and provides context for research examining cost-effectiveness and quality of life benefits. This study reports the national longitudinal changes of

the hospital burden of migraine headache over a 15-year interval.

## METHODS

A retrospective review of a national inpatient database was conducted to analyze longitudinal trends in migraine discharges, resource utilization, and costs. The National Inpatient Sample (NIS) is part of the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality. It is a database of hospital inpatient stays derived from billing data submitted by hospitals to statewide data organizations and weighted annually to represent the national healthcare system as a whole. From 1997 to 2012, the number of unweighted discharges included in the database annually ranged from 7.1 to 8.2 million records. Over this period, the sample of hospitals increased from 22 to 44 states and from 1,012 to 4,378 hospitals. The data form a stratified sample that encompasses all payers and are weighted to provide national estimates.<sup>34</sup> We chose this database as it sampled broadly in the majority of states and included thousands of hospitals. No additional weighting was done by us to the data extracted from the national database.

To capture the focused data on migraines, NIS data from 1997 to 2012 were used to identify hospital inpatients with a principal diagnosis of migraine headaches (International Classification of Diseases, Ninth Revision codes: 346.00–346.93). These data were accessed using HCUP-net,<sup>35</sup> a free online query system. Outcomes included were number of discharges, average length of stay (LOS), average hospital cost, and average inpatient charges to determine which specific parameters of inpatient stays, if any, most heavily influence changes in cost burden. Furthermore, a number of variables were accounted for to provide descriptive analysis of the study population, including age group, sex, payer type, income, region, and hospital status such as public versus private, bedside, and teaching status (Table 1).

Hospital inpatient costs were reported in dollars for the actual cost of each admission to the institution. Inpatient charges reflect the amount billed by the hospitals for the entire LOS. It is important to note the difference between costs and charges, which respectively are the estimated cost to the hospital versus charges billed to the patient. To assess how the longitudinal trend of migraines compared with all other diagnosis, the annual number of discharges with the principal diagnosis of migraine headaches was recorded and compared with overall total discharges of all diagnoses. Data on hospital inpatient costs were available only beginning in 2006 and subsequent years. For annual total charges, this was calculated by multiplying the number of admissions by the average charge of each admission. This was performed separately for each year. The average charge per day was calculated by dividing the average charge for each admission by the average LOS. Finally, the average annual percent change (AAPC) was calculated using the Agency for Healthcare Research and Quality preferred equation:  

$$AAPC = \left[ \frac{\text{Final value}}{\text{Initial value}} \right]^{(1/\text{number of years})} - 1 \times 100\%$$
<sup>36</sup>

**Table 1. Demographic Make-up of Inpatient Discharges for Migraine Headache from 1997 to 2012**

Category	n (%)
All discharges	712,607 (100.0)
Age	
1–17	60,123 (8.4)
18–44	369,792 (51.9)
45–64	229,667 (32.2)
65–84	48,499 (6.8)
85+	3,848 (0.5)
Missing	513 (0.1)
Sex	
Male	147,677 (20.7)
Female	562,984 (79.0)
Missing	1,925 (0.3)
Payer	
Medicare	106,378 (14.9)
Medicaid	96,961 (13.6)
Private insurance	427,336 (60.0)
Uninsured	48,429 (6.8)
Other	31,734 (4.5)
Missing	1,695 (0.2)
Owner	
Government	84,886 (11.9)
Private, not-for-profit	530,001 (74.4)
Private, for-profit	95,043 (13.3)
Missing	2,653 (0.4)
Bed size	
Small	92,522 (13.0)
Medium	165,756 (23.3)
Large	450,996 (63.3)
Missing	3,294 (0.5)
Region	
Northeast	125,139 (17.6)
Midwest	196,992 (27.6)
South	289,630 (40.6)
West	100,846 (14.2)

Number and distribution of hospital inpatient discharges for migraine, Nationwide Inpatient Study, over the period of 1997–2012.

No statistical inferences were made or conducted in this study.

## RESULTS

The annual number of discharges for migraine increased at a rate of 3.2% AAPC compared with the trend of all diagnoses which had an AAPC of 0.62% (Fig. 1). Specifically, discharges for migraine headaches reached a low of 30,761 discharges in 1999, and increased to 54,510 in 2012, a rise of 61%. In contrast, the overall number of discharges for all diagnoses increased to a peak in 2008, at which point the trend has proceeded downward, with an overall rise of 9.8% from 1997 to 2012.

Accordingly, the total annual inpatient charges for migraines increased at a higher rate than the average of all other diagnoses (Fig. 2). Annual charges for migraine headache increased 484% from \$201 million to \$1.18 billion dollars per year, with an AAPC of 12.5%. Annual charges for all diagnoses increased 257% from \$375 billion to \$1.34 trillion dollars per year, with an AAPC of 9.0%.

When analyzing the subtle difference in economic burden of costs to the institution versus charges to the patient, the individually measured average cost per admission of migraine increased by an AAPC of 4.5% while charges increased more dramatically at an AAPC of 9.1% (Fig. 3). It is worth noting that cost data became available in 2006.

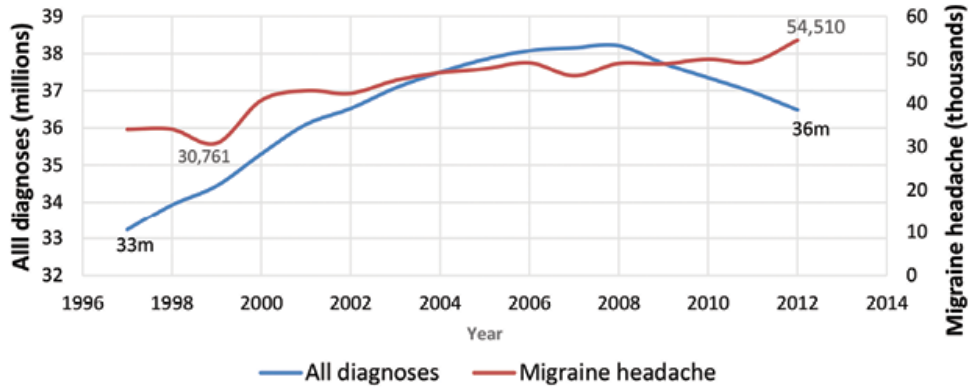
In this interval 2006 through 2012, the costs per admission increased 31% from \$4,505 per admission to \$5,911. The charges for this interval increased 69% from \$12,760 to \$21,576 per admission. The discrepancy between charges and costs per admission increased from \$8,254 to \$15,664, with an AAPC of 11.2%.

From 1997 to 2012, the average LOS for migraine headaches has decreased from 3.5 to 2.8 days. The charges per day for migraine headache increased from \$1,701 in 1997, to \$4,566 in 2006, and \$7,706 in 2012. This is an increase of 353% from 1997 to 2012, and 69% from 2006 to 2012, an AAPC of 9.1%. The costs per day increased 31% from \$1,612 to \$2,111 from 2006 to 2012, with an AAPC of 4.6%.

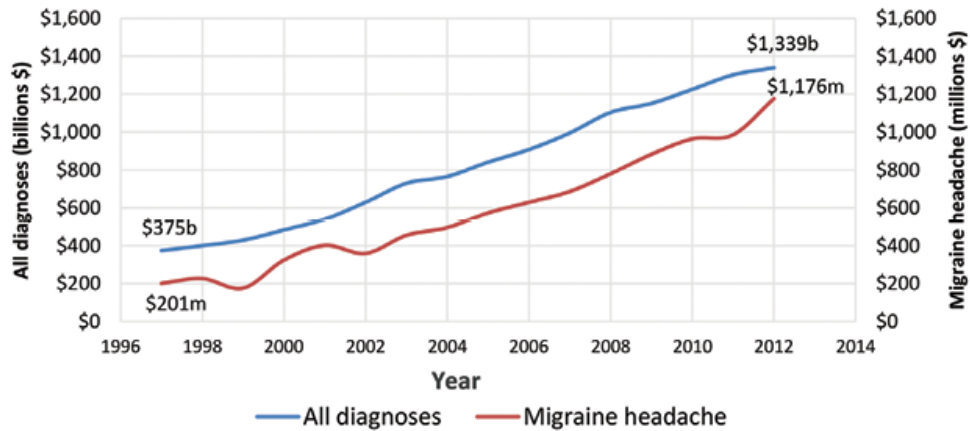
Finally, Figure 4 illustrates the total annual inpatient charges compared with costs for migraine headache. The annual charges for migraine headache increased 568% (AAPC, 13.5%) from a nadir of \$176 million per year in 1999 to \$1.18 billion per year in 2012. The increase in total charges from 2006 to 2012 was 87% (AAPC, 11.0%). For total costs, the increase was 45% (AAPC, 6.4%) from \$222 million in 2006 to \$322 million in 2012, a less dramatic increase than the charges. The discrepancy between total charges and costs from 2006 to 2012 increased 110% (AAPC, 13.1%) from \$407 million to \$854 million per year.

## DISCUSSION

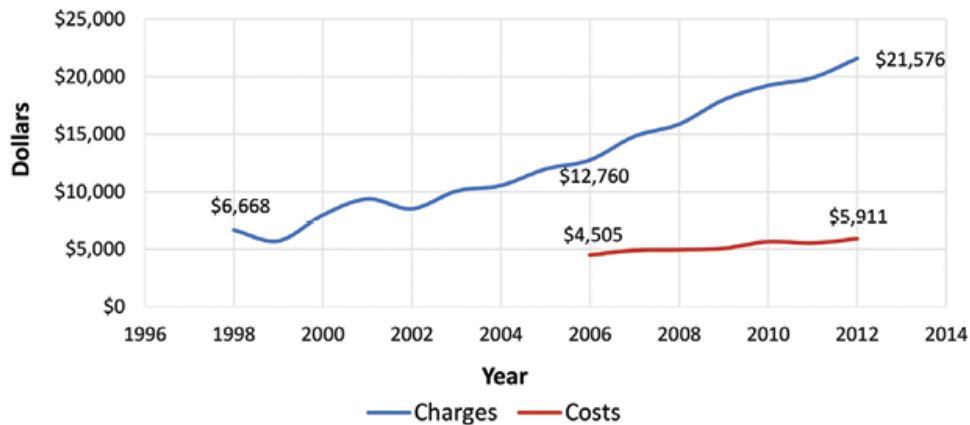
Migraine headaches are responsible for a significant nationwide burden. Our data revealed an annual financial burden totaling \$1.2 billion of inpatient charges and \$322 million of inpatient costs in 2012. A number of previous studies have estimated annual inpatient burden within the time period between 1997 and 2012. One provides a 2008 estimate using the same database, so the estimates are the same.<sup>30</sup> Two previous studies were based on the Thomson Medstat Commercial Claims and Encounters database. An earlier 2004 estimate of \$730 million total inpatient charges billed to patients<sup>10</sup> is 47% higher than our estimate of \$496 million for that year. The discrepancy may be due to an estimation based on the Thomson Medstat Commercial Claims and Encounters database, which is composed of insurance claims from 52 large US employers covered by a variety of health plans. This population excludes the uninsured and those covered by government plans. In 2004, <60% of the population was covered by employer-based health insurance,<sup>37</sup> and those not covered were disproportionately of minority race or foreign-born.<sup>10</sup> Another study used a combination of charge data from the Medstat database, and number of inpatient discharge data from the HCUP database, to estimate the 2010 total inpatient treatment charges at \$375 million, which is significantly less than our estimate of \$960 million for the same year.<sup>33</sup> However, to estimate the mean charges billed for inpatient hospitalization, this study only included claims data that were associated with a primary diagnosis code of migraine headaches or other diagnoses they deemed likely related. In contrast, the data in our study include the entire billed amount for each inpatient



**Fig. 1.** Annual number of discharges for all diagnoses and for migraine headache, NIS 1997–2012. Discharges for migraine headaches increased between 1999 and 2012 at a rate higher than that of all diagnoses. Specifically, migraine discharges rose 61% between 1999 and 2012, with an AAPC of 3.2%, whereas discharges for all diagnoses experienced an overall rise of 9.8% and AAPC of 0.62% from 1997 to 2012.

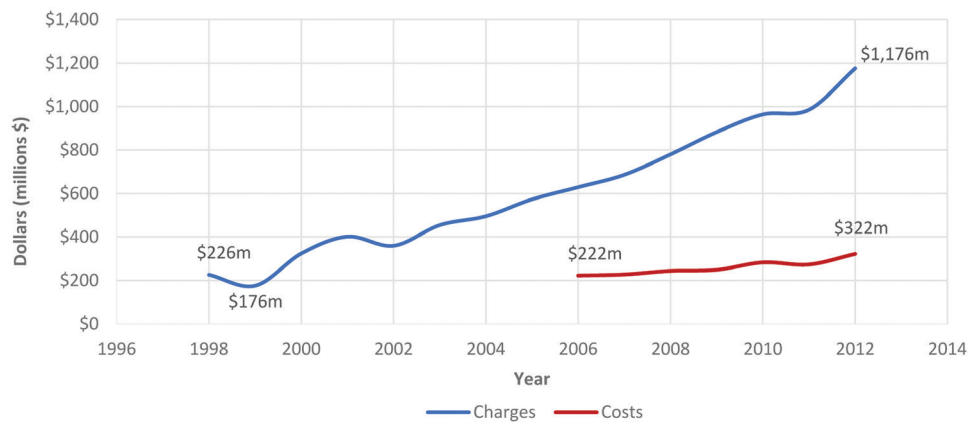


**Fig. 2.** Annual inpatient charges for all diagnoses and for migraine headache, NIS 1997–2012. Annual charges for migraine increased at a higher rate compared with charges for all diagnoses. Migraine charges increased 484% with an AAPC of 12.5%. Annual charges for all diagnoses increased 257%, with an AAPC of 9.0%.



**Fig. 3.** Hospital charges and costs per admission for migraine headache, NIS 1997–2012. The discrepancy between charges and costs per admission increased from \$8,254 to \$15,664, with an AAPC of 11.2%.





**Fig. 4.** Total annual inpatient charges and costs for migraine headache, NIS 1997–2012. The discrepancy between total charges and costs from 2006 to 2012 increased 110% (AAPC 13.1%) from \$407 to \$854 million per year.

stay. It is unclear which is a more accurate estimation of direct inpatient costs due to migraine headaches because they are known to be associated with an increased risk for comorbidities and may be directly causing other issues that need treatment. However, the longitudinal trend reported in our study should not be affected by this difference and still accurately represents the changing costs over time.

#### Stable Prevalence but Increasing Admissions

The number of discharges for migraine headache increased 61% (AAPC, 3.2%) over our study period, accounting for a significant but secondary share of the 484% (AAPC, 12.5%) overall increase in total charges. Of note, the annual prevalence has remained stable, affecting approximately 1 in 7 Americans.<sup>5</sup> The average LOS decreased 20% from 3.5 to 2.8 days per admission.

#### Disproportional Increases to Daily Inpatient Charges Compared with Inflation

The increase in charges from 1997 to 2012 outpaced the collective rate for all diagnoses together, as well as inflation. For migraine headache, the increase was 484% (AAPC, 12.5%), compared with 257% for all diagnoses (AAPC, 8.9%), and 43% overall for inflation (AAPC, 2.4%) based on the consumer price index.<sup>38</sup> The cause of this increase in charges is likely multifactorial. From our data, we identified inpatient charges per day as the largest contributing factor, with a 353% increase (AAPC, 10.6%) from \$1,701 to \$7,706 in the interval from 1997 to 2012. From the years 2006 to 2012, for which cost data are available, the increase in charges per day increased 69% (AAPC, 9.1%) compared with a cost per day increase of 31% (AAPC, 4.6%). The increasing daily charges for staying in the hospital is likely multifactorial, including possible changes in the cost of medications and pressures on healthcare institutions to increase revenue. A complete discussion on this increase is beyond the scope of this article but should be explored based on the trend found in our data.

#### Factors Contributing to Increasing Costs and the Role of Surgical Decompression

One factor contributing to the increasing hospital charges and costs may be due to more costly inpatient treatment programs for migraine headaches.<sup>39–41</sup> Inpatient treatment methods include intravenous dihydroergotamine, valproic acid, magnesium sulfate, steroids, and sometimes lidocaine infusions. In refractory patients, these treatments are sometimes effective in breaking the headache cycle. However, longer LOS and longer infusions may be necessary for a better outcome.<sup>29,42</sup> As inpatient costs continue to increase at a rapid rate, it is important to determine whether or not tertiary centers are a more cost-effective treatment strategy that decreases overall migraine cost burdens. At one tertiary center, data showed a reduction in ED visits after discharge.<sup>32</sup> More research is required to determine if benefits like this will lead to a reduced overall financial burden and justify migraine inpatient admissions. In addition, surgical decompression has been proven effective for the treatment of chronic migraine headache.<sup>22,25</sup> Research should be done to determine the cost-effectiveness of typical inpatient treatments such as dihydroergotamine, valproic acid, and lidocaine infusions versus the more aggressive and expensive surgical options. To date, there has only been one retrospective study looking at the cost savings of surgical decompression versus traditional outpatient medications.<sup>23</sup>

Another factor is the broader medical system context. Hospitals have used cost shifting in various forms. As Medicare and Medicaid reimbursement transitioned to diagnosis-based reimbursements, charges and reimbursements from third-party payers were increased to maintain the bottom line. In addition, Medicare continued until 2003 to provide additional payments for outlier, high-cost cases based on charges rather than costs, incentivizing hospitals to increase charges to reach the threshold for additional payment.<sup>43</sup>

Reimbursement for charity care continued to be calculated based on charges until 2008, providing another reason for hospitals to continue increasing charges, even though almost all insured payers at this point had negotiated contracts rendering the charges largely irrelevant.

The uninsured and out-of-network patients continued to see the billed charges, so these ever-increasing charges are used to offset losses elsewhere. At the least, these charges are used as starting points for payment negotiations.<sup>43</sup>

### Limitations

One limitation of this study is the high-level view of the national trends. Although the database provides nationwide estimates, this is at the cost of individual patient-level data which would allow for more detailed analysis of individual variables and advanced techniques such as logistic regression. Also unavailable are itemized breakdowns of the components of the charge and cost information. This would allow for a better understanding of the relative contributions of wages, medications, medical supplies, and other overhead costs.

### Future Considerations

Further studies are needed to evaluate for interventions that may improve prevention and others that may improve efficiency in care. Treatment efficacy has been associated with improvement in workplace productivity and lower rates of absenteeism, leading to reduced indirect costs.<sup>44–46</sup> Another recent study demonstrated that tertiary care can reduce disability, healthcare utilization, and costs associated with migraine complications that may arise in patients who do not seek specialized care.<sup>32</sup> More recent interventions such as botulinum toxin injection and surgical decompression in carefully selected patients may reduce the severity and frequency of symptoms, decreasing the long-term inpatient burden.<sup>24</sup> These relatively new treatment modalities are rapidly evolving, and their respective cost-effectiveness are being studied. Recent monoclonal antibody injections targeting CGRP or its respective receptor show promising results as well.<sup>47–49</sup> As efficiency and cost efficacy are improved, we may see further changes in the socioeconomic burden of chronic migraine.

The current NIS data extend to 2017, and our data are collected and analyzed up to 2012. Although the addition of several years would reveal some useful information on the economic cost impact of emerging treatments, the NIS was redesigned starting in data year 2012, changing to sample of discharges from all hospitals participating in the HCUP.

Reanalyzing the trends from 2012 with the new NIS redesigned for a 10- to 15-year period can provide a more accurate insight into these new emerging treatments, which can then be compared with previous decades. We do plan to reanalyze the data from 2012 to 2022 as a follow-up article in several years.

Other studies are needed to determine whether the increased charges and costs may be associated with improved quality of life and decreased indirect costs. The discrepancy between costs and charges is reflective of system-wide issues and trends, and deserves revisiting as the consequences of the Affordable Care Act are borne out.

Finally, it is worthwhile to discuss the differences between chronic and episodic migraine in the context of healthcare burdens. It is estimated that each year, 2.5% of episodic migraine will undergo transformation into chronic migraine.<sup>50</sup> Several studies have shown that

chronic migraine, compared with episodic migraine, incur significantly higher healthcare cost, increased treatment utilization, higher rates of comorbidities, and worse health-related quality of life.<sup>7,51,52</sup> A 2009 study showed that chronic migraine patients required more primary care visits, ED visits, pain clinic visits, and specialist visits compared with their episodic counterparts.<sup>53</sup> Stewart et al<sup>54</sup> reported that chronic migraine patients had higher occupational absenteeism and presentism, with approximately 1 out of 5 patients reported being occupationally disabled, compared with 1 in 10 of episodic migraine patients. Therefore, better treatment methods in earlier states of migraine progression and identification of risk factors for transformation may lead to reduced economic burden at the expense of an increased initial cost.

## CONCLUSIONS

Migraine is oftentimes underdiagnosed and undertreated, leading to self-diagnosis and subsequent self-treatment, and possibly causing medication overuse. These factors lead to increased urgent care and hospitalizations, which adds to its healthcare cost burden. The inpatient burden is increasing rapidly, with hospital charges increasing from \$5,939 per admission and \$176 million nationwide in 1997, to \$21,576 per admission and \$1.2 billion in total charges in 2012. In the 6 years from 2006 to 2012, total annual costs increased from \$222 to \$322 million per year.

These data are collected up to 2012 and do not represent the most recent potential changes in the trend with the latest approval of Botox and CGRP antibodies mentioned in this article. Despite the last datapoint being 7 years ago, it will be very interesting to see how this longitudinal trend over 15 years compares to data from this decade for which the study is undergoing.

The causes of the rise in charges and costs, as well as the discrepancy between hospital charges and cost, should be evaluated alongside actual reimbursement. Finally, better prevention and improved outpatient treatment may help alleviate the inpatient burden of migraine.

**Bardia Amirlak, MD, FACS**

Department of Plastic Surgery  
University of Texas Southwestern Medical Center  
1801 Inwood Road  
Dallas, TX 75390

E-mail: [bardia.amirlak@utsouthwestern.edu](mailto:bardia.amirlak@utsouthwestern.edu)

## REFERENCES

1. Saylor D, Steiner TJ. The global burden of headache. *Semin Neurol*. 2018;38:182–190.
2. Malone CD, Bhowmick A, Wachholtz AB. Migraine: treatments, comorbidities, and quality of life, in the USA. *J Pain Res*. 2015;8:537–547.
3. Taşkapılıoğlu Ö, Karlı N. Assessment of quality of life in migraine. *Noro Psikiyatr Ars*. 2013;50(Suppl 1):S60–S64.
4. Lipton RB, Bigal ME, Diamond M, et al; AMPP Advisory Group. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. 2007;68:343–349.
5. Smitherman TA, Burch R, Sheikh H, et al. The prevalence, impact, and treatment of migraine and severe headaches in the

- United States: a review of statistics from national surveillance studies. *Headache*. 2013;53:427–436.
6. Burch RC, Loder S, Loder E, et al. The prevalence and burden of migraine and severe headache in the United States: updated statistics from government health surveillance studies. *Headache*. 2015;55:21–34.
  7. Bigal ME, Serrano D, Reed M, et al. Chronic migraine in the population: burden, diagnosis, and satisfaction with treatment. *Neurology*. 2008;71:559–566.
  8. Lipton RB, Bigal ME. Migraine: epidemiology, impact, and risk factors for progression. *Headache*. 2005;45(Suppl 1):S3–S13.
  9. Burch R, Rizzoli P, Loder E. The prevalence and impact of migraine and severe headache in the United States: figures and trends from government health studies. *Headache*. 2018;58:496–505.
  10. Hawkins K, Wang S, Rupnow M. Direct cost burden among insured US employees with migraine. *Headache*. 2008;48:553–563.
  11. Serrano D, Manack AN, Reed ML, et al. Cost and predictors of lost productive time in chronic migraine and episodic migraine: results from the American Migraine Prevalence and Prevention (AMPP) study. *Value Health*. 2013;16:31–38.
  12. Hawkins K, Wang S, Rupnow MF. Indirect cost burden of migraine in the United States. *J Occup Environ Med*. 2007;49:368–374.
  13. Minen MT, Begasse De Dhaem O, Kroon Van Diest A, et al. Migraine and its psychiatric comorbidities. *J Neurol Neurosurg Psychiatry*. 2016;87:741–749.
  14. Cameron C, Kelly S, Hsieh SC, et al. Triptans in the acute treatment of migraine: a systematic review and network meta-analysis. *Headache*. 2015;55(Suppl 4):221–235.
  15. Ong JY, De Felice M. Migraine treatment: current acute medications and their potential mechanisms of action. *Neurotherapeutics*. 2018;15:274–290.
  16. Aurora SK, Dodick DW, Diener HC, et al. Onabotulinumtoxin A for chronic migraine: efficacy, safety, and tolerability in patients who received all five treatment cycles in the PREEMPT clinical program. *Acta Neurol Scand*. 2014;129:61–70.
  17. Silberstein SD, Dodick DW, Aurora SK, et al. Percent of patients with chronic migraine who responded per onabotulinumtoxin A treatment cycle: PREEMPT. *J Neurol Neurosurg Psychiatry*. 2015;86:996–1001.
  18. Lipton RB, Rosen NL, Ailani J, et al. Onabotulinumtoxin A improves quality of life and reduces impact of chronic migraine over one year of treatment: pooled results from the PREEMPT randomized clinical trial program. *Cephalalgia*. 2016;36:899–908.
  19. Amirlak B, Sannic K, Pezeshk R, et al. The Anatomical Regional Targeted (ART) BOTOX injection technique. A new injection paradigm for the treatment of chronic headaches and migraines. *Plast Reconstr Surg Glob Open*. 2016;4:e1194.
  20. Janis JE, Barker JC, Paletas M. Targeted peripheral nerve-directed onabotulinumtoxin A injection for effective long-term therapy for migraine headache. *Plast Reconstr Surg Glob Open*. 2017;5:e1270.
  21. Guyuron B, Reed D, Kriegler JS, et al. A placebo-controlled surgical trial of the treatment of migraine headaches. *Plast Reconstr Surg*. 2009;124:461–468.
  22. Guyuron B, Kriegler JS, Davis J, et al. Five-year outcome of surgical treatment of migraine headaches. *Plast Reconstr Surg*. 2011;127:603–608.
  23. Faber C, Garcia RM, Davis J, et al. A socioeconomic analysis of surgical treatment of migraine headaches. *Plast Reconstr Surg*. 2012;129:871–877.
  24. Ducic I, Felder JM III, Fantus SA. A systematic review of peripheral nerve interventional treatments for chronic headaches. *Ann Plast Surg*. 2014;72:439–445.
  25. Janis JE, Barker JC, Javadi C, et al. A review of current evidence in the surgical treatment of migraine headaches. *Plast Reconstr Surg*. 2014;134:131S–141S.
  26. Gfrerer L, Maman DY, Tessler O, et al. Nonendoscopic deactivation of nerve triggers in migraine headache patients: surgical technique and outcomes. *Plast Reconstr Surg*. 2014;134:771–778.
  27. Gfrerer L, Guyuron B. Surgical treatment of migraine headaches. *Acta Neurol Belg*. 2017;117:27–32.
  28. American Society of Plastic Surgeons. *Policy Statement: Migraine Headache Surgery*. 2018. Available at [https://www.plasticsurgery.org/Documents/Health-Policy/Positions/ASPS-Statement\\_Migraine-Headache-Surgery.pdf](https://www.plasticsurgery.org/Documents/Health-Policy/Positions/ASPS-Statement_Migraine-Headache-Surgery.pdf). Accessed June 1, 2015.
  29. Marmura MJ, Goldberg SW. Inpatient management of migraine. *Curr Neurol Neurosci Rep*. 2015;15:13.
  30. Lucado J, Paez K, Elixhauser A. In: Headaches in U.S. hospitals and emergency departments, 2008: statistical brief #111. *Healthcare Cost and Utilization Project (HCUP) Statistical Briefs*. 2006.2006. Available at [https://www.ncbi.nlm.nih.gov/books/NBK56047/pdf/Bookshelf\\_NBK56047.pdf](https://www.ncbi.nlm.nih.gov/books/NBK56047/pdf/Bookshelf_NBK56047.pdf). Accessed June 1, 2015.
  31. Freitag FG, Lake A III, Lipton R, et al; US Headache Guidelines Consortium, Section on Inpatient Treatment Chairpersons. Inpatient treatment of headache: an evidence-based assessment. *Headache*. 2004;44:342–360.
  32. Freitag FG, Lyss H, Nissan GR. Migraine disability, healthcare utilization, and expenditures following treatment in a tertiary headache center. *Proc (Bayl Univ Med Cent)*. 2013;26:363–367.
  33. Insinga RP, Ng-Mak DS, Hanson ME. Costs associated with outpatient, emergency room and inpatient care for migraine in the USA. *Cephalalgia*. 2011;31:1570–1575.
  34. Agency for Healthcare Research and Quality (AHRQ). Healthcare Cost and Utilization Project (HCUP). Available at <http://www.ahrq.gov/data/hcup/#hcup>. Accessed June 1, 2015.
  35. Agency for Healthcare Research and Quality (AHRQ). HCUPnet. Healthcare Cost and Utilization Project. HCUPnet Home. Available at <http://hcupnet.ahrq.gov>. Accessed June 1, 2015.
  36. Brian Moore PD, Katharine Levit BA, Anne Elixhauser PD. Costs for Hospital Stays in the United States, 2012. Available at <https://www.hcup-us.ahrq.gov/reports/statbriefs/sb181-Hospital-Costs-United-States-2012.jsp>. Accessed June 1, 2015.
  37. US Census Bureau. Income, Poverty, and Health Insurance Coverage in the United States: 2004. 2005. Available at <https://www.census.gov/prod/2006pubs/p60-231.pdf>. Accessed June 1, 2015.
  38. US Bureau of Labor Statistics. CPI Inflation Calculator. Available at [http://www.bls.gov/data/inflation\\_calculator.htm](http://www.bls.gov/data/inflation_calculator.htm). Accessed June 1, 2015.
  39. Kelley NE, Tepper DE. Rescue therapy for acute migraine, part 3: opioids, NSAIDs, steroids, and post-discharge medications. *Headache*. 2012;52:467–482.
  40. Kelley NE, Tepper DE. Rescue therapy for acute migraine, part 2: neuroleptics, antihistamines, and others. *Headache*. 2012;52:292–306.
  41. Kelley NE, Tepper DE. Rescue therapy for acute migraine, part 1: triptans, dihydroergotamine, and magnesium. *Headache*. 2012;52:114–128.
  42. Nagy AJ, Gandhi S, Bholra R, et al. Intravenous dihydroergotamine for inpatient management of refractory primary headaches. *Neurology*. 2011;77:1827–1832.
  43. Shannon M, Joynt J. No Method to the Madness: The Divergence Between Hospital Billed Charges and Payments, and What to Do About It. Health Affairs Blog, October 7, 2013.doi: 10.1377/hblog20131007.034767. Available at <https://healthaffairs.org/doi/10.1377/hblog20131007.034767/full/>. Accessed September 1, 2016.
  44. Burton WN, Landy SH, Downs KE, et al. 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.
45. Cady RK, Sheftell F, Lipton RB, et al. Economic implications of early treatment of migraine with sumatriptan tablets. *Clin Ther.* 2001;23:284–291.
  46. Stang P, Cady R, Batenhorst A, et al. Workplace productivity. A review of the impact of migraine and its treatment. *Pharmacoeconomics.* 2001;19:231–244.
  47. Hou M, Xing H, Cai Y, et al. The effect and safety of monoclonal antibodies to calcitonin gene-related peptide and its receptor on migraine: a systematic review and meta-analysis. *J Headache Pain.* 2017;18:42.
  48. Mitsikostas DD, Reuter U. Calcitonin gene-related peptide monoclonal antibodies for migraine prevention: comparisons across randomized controlled studies. *Curr Opin Neurol.* 2017;30:272–280.
  49. Puledda F, Messina R, Goadsby PJ. An update on migraine: current understanding and future directions. *J Neurol.* 2017;264:2031–2039.
  50. 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.
  51. Bigal ME, Rapoport AM, Lipton RB, et al. Assessment of migraine disability using the Migraine Disability Assessment (MIDAS) questionnaire: a comparison of chronic migraine with episodic migraine. *Headache.* 2003;43:336–342.
  52. Meletiche DM, Lofland JH, Young WB. Quality-of-life differences between patients with episodic and transformed migraine. *Headache.* 2001;41:573–578.
  53. Munakata J, Hazard E, Serrano D, et al. Economic burden of transformed migraine: results from the American Migraine Prevalence and Prevention (AMPP) study. *Headache.* 2009;49:498–508.
  54. Stewart WF, Wood GC, Manack A, et al. Employment and work impact of chronic migraine and episodic migraine. *J Occup Environ Med.* 2010;52:8–14.