INTRODUCTION

Migraine headache is a common, debilitating disease that causes significant disability.1–3 It affects nearly 1 in 7 Americans each year, with an estimated 40 million people suffering from migraine headaches.4–6 Its prevalence is as high as 19% for females and 9% for males.6 Despite the high prevalence, migraine headache is often not diagnosed correctly and many patients do not undergo appropriate treatment.7 The age at which patients most commonly develop migraine headaches is between 25 and 55 years of age, corresponding to their peak earning potential.8 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.9 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.10 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.11,12 In total, the economic impact of migraine headache in the United States is estimated to be between $13 and $17 billion annually.9 In addition to financial factors, the biological and functional effect of migraine can be illustrated by the

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.

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higher prevalence of psychiatric comorbidities, including depression, anxiety, and posttraumatic stress disorder in patients with chronic migraines compared with the general population.\(^{13}\)

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).\(^{14,15}\)

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.\(^{16-20}\) 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 patients also have seen improvement of their headaches after surgical decompression.\(^{21-28}\)

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.\(^{29}\) In patients who present to the emergency department (ED) for headache symptoms, migraine headaches have been identified as the leading cause of admission.\(^{30}\) 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.\(^{31,32}\) 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.\(^{32}\)

In the United States, the cost of inpatient treatment for a single year has been estimated to be $375 million.\(^{33}\) 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.\(^{34}\) 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,\(^{35}\) 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, bed size, 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: \[
AAPC = [(\text{Finalvalue} / \text{Initialvalue})^{(1 / \text{num years})} - 1] \times 100%.\]

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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 13.1%. 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.30 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 patients31 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,7 and those not covered were disproportionately of minority race or foreign-born.56 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.59 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 admission.

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                      | 60,125 (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                     | 51,784 (7.4)  |
| Missing                   | 1,695 (0.2)   |
| Owner                     |               |
| Government                | 84,886 (11.9) |
| Private, not-for-profit   | 530,001 (74.4) |
| Private, for-profit       | 95,043 (13.5) |
| 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.
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 AACP of 3.2%, whereas discharges for all diagnoses experienced an overall rise of 9.8% and AACP 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 AACP of 12.5%. Annual charges for all diagnoses increased 257%, with an AACP 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 AACP of 11.2%.
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. 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. 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. 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. 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. 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. 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.

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.

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.\textsuperscript{43}

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.\textsuperscript{44–46} 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.\textsuperscript{47} 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.\textsuperscript{48} 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.\textsuperscript{49–51}

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.\textsuperscript{50} 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.\textsuperscript{7,51,52} 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.\textsuperscript{53} Stewart et al\textsuperscript{44} 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.

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