Geographic Variation in the Use of Triptans and Opioids for the Acute Treatment of Migraine Attacks

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Abstract

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BACKGROUND: Clinical guidelines and published literature suggest that opioids should be used sparingly or avoided in patients with acute migraine due to a lack of evidence of their effectiveness, association with disease progression, and risk of dependence. Triptans are the first line option for the acute treatment of moderate to severe migraine attacks. Despite recommendations, published research suggests that opioids are prescribed more frequently than triptans (53% vs 48%) among patients with migraine. Previous studies have been published for other chronic disease states showing that geographic variation plays a role in prescribing patterns in the United States (US). Moreover, 26 states have passed legislation that limit the prescribing or dispensing of opioids for acute pain. Every state in the Northeast has currently implemented these laws. In addition, the Northeast has the greatest number of headache subspecialists and

primary care physicians per capita Yet, the level geographic differences in prescribing patterns, among triptan and opioid users for patients with migraine, has not been elucidated.

OBJECTIVE: To assess the geographic variations in triptan and opioid prescribing patterns for patients with migraine.

METHODS: We conducted a retrospective cohort analysis using claims data from the IBM® MarketScan® Commercial and Medicare Supplemental databases from January 1, 2016 to December 31, 2018. The target population was adults with migraine who had a migraine-related medical encounter in 2017 with a confirmatory encounter taking place between 31 to 365 days after the initial claim. Baseline characteristics were assessed during the 12-month pre-index period. The 12-month follow-up period was used to assess the outcomes of interest, triptan and opioid utilization, stratified by the four Census-Bureau designated regions: Northeast, Midwest, South, and West. State-level descriptive geographic heat maps were created to depict the patterns of triptan and opioid use in the US. Logistic regression models were used to estimate the binary outcomes of any triptan or opioid use in the follow-up period. Zero-truncated Negative binomial regression models were used to estimate the rate of triptan and opioid use among users in the form of incidence rate ratios (IRR). These analyses were adjusted for age, sex, health plan, presence of chronic migraine, and Elixhauser comorbidity scores.

RESULTS: A total of 147,700 patients met the study inclusion criteria. The mean age was 45 and 84% of the patients were female. The prevalence of chronic migraine in the study population was 13% and the mean (SD) comorbidity score was 1.5 (1.7). In the follow-up period, the mean (SD) number of triptan claims for the Northeast, Midwest, South, and West regions were 2.36 (4.05), 2.50 (4.15), 2.60 (4.27), and 2.66 (4.32) respectively. The mean (SD) number of opioid

claims for the same regions were 1.50 (4.34), 2.20 (5.00), 2.33 (5.13), and 2.35 (5.45), respectively.

Compared to the Northeast, a patient with migraine was more likely to be a triptan user in the Midwest (OR: 1.16; 95% CI: 1.12, 1.20), South (OR: 1.17; 95% CI: 1.14, 1.21), and West (OR: 1.21; 95% CI: 1.16, 1.25). However, among triptan users, there were no significant differences in triptan use when compared to the Northeast for the Midwest (IRR: 0.99; 95% CI: 0.96, 1.02), South (IRR: 1.01; 95% CI: 0.98, 1.04), and West (IRR: 0.99; 95% CI: 0.96, 1.02). Compared to the Northeast, a patient with migraine was more likely to be an opioid user in the Midwest (OR: 1.71; 95% CI: 1.65, 1.78), South (OR: 1.91; 95% CI: 1.85, 1.97), and West (OR: 1.71; 95% CI: 1.64, 1.78). Among opioid users, there was also an increase in opioid use when compared to the Northeast for the Midwest (IRR: 1.21; 95% CI: 1.14, 1.29), South (IRR: 1.17; 95% CI: 1.11, 1.24), and West (IRR: 1.41; 95% CI: 1.32, 1.50).

CONCLUSION: Results of our study suggest that compared to patients in the Northeast, patients from the other regions of the US were more likely to use triptans and opioids. Among triptan users, the rates of use were similar across all regions. However, among opioid users, the rates of use were lowest in the Northeast, followed by the South, Midwest, and West. Future work should formally evaluate the impact of headache subspecialists and opioid use policies on opioid use across regions.

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1. Background

Migraines are a debilitating, neurological disorder that manifest as a headache with associated symptoms such as photophobia, phonophobia and nausea.[1] The prevalence of self-reported migraines in the US population is high, with roughly one out of six Americans affected over a 3-month period.[2]

The American Headache Society (AHS) 2018 clinical guideline for the treatment of acute migraines provides recommendations for treatment based on the strength of evidence available.[3,4] The level of evidence is classified as follows: Level A – effective, Level B – probably effective, Level C – possibly effective, Level U – conflicting/inadequate evidence. All triptans are designated with a Level A recommendation. For the opioids specified in the guidelines, recommendations are as follows: butorphanol nasal spray (Level A), codeine/acetaminophen, tramadol/acetaminophen (Level B), butorphanol intramuscular, codeine, meperidine, methadone, tramadol intravenous, butalbital/acetaminophen/caffeine/codeine (Level C). The guidelines acknowledge that while opioids are possibly effective, they are not recommended for regular use.

Treating migraines with opioids has been associated with greater headache-related disability, healthcare resource utilization, risk of dependence and risk of medication overuse headache.[5-7] Furthermore, opioid use in episodic migraine (EM) has been linked to an increased risk for progression to chronic migraine (CM).[8] However, contrary to the guideline recommendations and available evidence, published research suggests that opioids are prescribed more frequently than triptans (53% vs 48%) among adults with migraine in the United States.[9]

The American Migraine Prevalence and Prevention (AMPP) was a survey based study showing that 35% of triptan users and 59% of opioid users discontinued treatment in the following year; the most common reasons for discontinuation among all patients were failure to relieve pain

(30%), reoccurrence of pain (24%), specific stomach related concerns (21%), and side effects (19%).[10] In a retrospective claims analysis, among incident triptan users, only 41% continued to use triptans as monotherapy, 30% were potential insufficient responders, and 29% did not refill their index triptan over a 24 month follow-up period. Among the triptan insufficient responders, opioids were the most commonly prescribed acute medication.[7]

Published studies of variation in prescribing patterns for other chronic disease states in the US suggest that geography may be a factor.[11-13] Additional evidence reveals that there are large variations in opioid prescribing practices when stratified by states.[14] In the US, 26 states have laws that limit the prescribing or dispensing of opioids for acute pain, with 17 states passing the law in 2017.[15] Every state in the Northeast has currently implemented these laws. Despite the overutilization of opioids and evidence of geographic differences in prescribing patterns, there is no published research that elucidates the geographic variation in triptan and opioid prescribing practices for patients with migraine.

2. Objective

The primary objective of this study was to assess the geographic variations in triptan and opioid prescribing patterns for patients with migraine.

3. Methods

3.1 Data Source

Data for the study were gathered from the IBM® MarketScan® Commercial, Medicare Supplemental and Medicaid Multi-State databases from January 1, 2016 to December 31, 2018.[16] Subjects in the Medicaid database were excluded from the study due to the lack of regional identifiers, which was the primary focus of this study. The commercial database consists of

medical and drug data from employers and health plans. The Medicare supplemental database includes the Medicare-covered portion of payment (represented as the Coordination of Benefits Amount or COB), the employer-paid portion and out-of-pocket expenses. For most of the individuals in the database, the medical claims are linked to outpatient drug claims through the use of unique enrollee identifiers. In the most recent year, the MarketScan® databases contained healthcare data for more than 41.2 million covered individuals. The inpatient and outpatient service databases contain claims information including the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) diagnosis codes, Current Procedural Terminology (CPT) codes, and dates of service. The outpatient drug claims database contains prescription details including, National Drug Codes (NDCs), generic identifiers, dispensing date, and quantity.

The MarketScan® databases are designed to address the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA); all data are deidentified. The University of Washington Human Subjects Division Institutional Review Board (IRB) determined that the study did not meet the definition of human subjects research and therefore did not require IRB review.

3.2 Sample Selection

We performed a retrospective cohort study among adults with migraine who were identified between January 1, 2017 to December 31, 2017 (Figure 1). All patients were required to be ≥18 years old on their index date and have ≥2 migraine-related medical encounters in order to establish the index date (Figure 2). The first migraine claim in 2017 was set as the index date with the requirement of having an additional, confirmatory migraine-related medical encounter 31 – 365 days after the index date. Patients were required to have 12 months of continuous

medical and prescription enrollment, before and after the index date. Patients missing the Census Bureau-designated region were excluded from the study. Patients were categorized into four separate cohorts based on their Census Bureau-designated region: Northeast, Midwest, West and South.

3.3 Baseline Characteristics

We assessed baseline demographic and clinical characteristics during the 12-month pre-index period. Baseline demographic characteristics of interest were age, sex, health plan type, Census Bureau-designated region, and metropolitan statistical area (MSA). Baseline clinical characteristics assessed were the Elixhauser comorbidity score along with selected comorbidities: allergic rhinitis, anxiety, bipolar disorder, depression, epilepsy, non-migraine headache, and sleep disorder.[17,18] We selected associated comorbidities based on their significance as an indicator of migraine severity or impact on medication use.[19,20]

3.4 Geographic Definitions and Variables of Interest

The main exposure of interest was the four Census Bureau-designated regions: Northeast, Midwest, South, and West. For the geographic heat maps (Figures 3 & 4), after measuring the total number of triptan and opioid claims at the individual level, we aggregated the data by state.

3.5 Study Outcomes

Our primary study outcomes of interest were the total number of triptan and opioid claims per region. The number of claims was calculated during the 12-month follow-up period after the patient's index date. For our secondary objective, we conducted an opioid scenario analysis with any opioid claims within 15 days of a migraine-related medical encounter being classified as migraine-related opioid use. Previous research has used a similar 15 day criteria to identify non-migraine specific medications that were being used for the treatment of migraines.[7,22]

3.6 Statistical Analysis

3.6.1 Baseline Demographic and Clinical Characteristics

We used descriptive statistics to characterize baseline demographic and clinical characteristics among the study cohorts (Northeast, Midwest, South, West). Continuous variables were presented using means and standard deviations, and categorical variables were presented using frequencies and percentages. Differences in baseline characteristics and unadjusted counts were calculated using t-tests for continuous data and chi-squared tests for categorical data.

3.6.2 Triptans

To examine the factors that affect triptan use among patients with migraine, we conducted two multivariable analyses. We used logistic regression to examine the probability of a patient being a triptan user in the past year.

$$logit(p) = B0 + B1\,x_{region} + B2\,x_{age} + B3\,x_{age^2} + B4\,x_{sex} + B5\,x_{health\ plan} + B6\,x_{chronic\ migraine} + B7\,x_{comorbidity\ score}$$

After the logistic regression was performed, we used a zero-truncated negative binomial regression among triptan users to estimate incidence rate ratios (IRR). The IRR was a ratio of the annual number of triptan claims compared between the Northeast and another region of interest.

$$\log(\lambda) = B0 + B1\,x_{region} + B2\,x_{age} + B3\,x_{age^2} + B4\,x_{sex} + B5\,x_{health\ plan} + B6\,x_{chronic\ migraine} + B7\,x_{comorbidity\ score}$$

Furthermore, we conducted a separate negative binomial regression to compute the marginal effects at the mean (MEM). The MEM was computed by holding all other covariates in the model at the study population means to predict the expected number of triptan claims for an average patient in all four regions. This prediction was conducted using the full study population.

3.6.3 Opioids

To examine the factors that affect opioid use among patients with migraine, we conducted two multivariable analyses. A logistic regression was used to examine the probability of a patient being an opioid user in the past year.

$$logit(p) = B0 + B1\,x_{region} + B2\,x_{age} + B3\,x_{age^2} + B4\,x_{sex} + B5\,x_{health\ plan} + B6\,x_{chronic\ migraine} + B7\,x_{comorbidity\ score}$$

After the logistic regression, we performed a zero-truncated negative binomial regression among opioid users to estimate incidence rate ratios (IRR). The IRR was a ratio of the annual number of opioid claims compared between the Northeast and another region of interest.

$$\log(\lambda) = B0 + B1\,x_{region} + B2\,x_{age} + B3\,x_{age^2} + B4\,x_{sex} + B5\,x_{health\ plan} + B6\,x_{chronic\ migraine} + B7\,x_{comorbidity\ score}$$

Furthermore, we conducted a separate negative binomial regression to compute the MEM. The MEM was computed by holding all other covariates in the model at the study population means to predict the expected number of opioid claims for an average patient in all four regions. This prediction was conducted using the full study population.

3.6.4 Opioid Scenario Analysis

For our secondary analysis, we conducted a negative binomial regression for our outcome of migraine-related opioid claims to compute the MEM. The MEM was computed by holding all other covariates in the model at the study population means to predict the expected number of migraine-related opioid claims for an average patient in all four regions. This prediction was conducted using the full study population.

$$\log(\lambda) = B0 + B1\, x_{region} + B2\, x_{age} + B3\, x_{age^2} + B4\, x_{sex} + B5\, x_{health\ plan} + B6\, x_{chronic\ migraine} + B7\, x_{comorbidity\ score}$$

4. Results

4.1 Study Characteristics

In total, we identified 655,758 patients with one migraine claim between January 1, 2017 and December 31, 2017 with 147,700 (23%) of them meeting the study inclusion criteria (Figures 1 & 2). The mean age was 45 and 84% of the patients were female (Table 1). A majority of patients (55%) were enrolled in an Exclusive Provider Organization (EPO) or Preferred Provider Organization (PPO). The prevalence of chronic migraine in the study population was 13% and overall, the mean (SD) Elixhauser comorbidity score was 1.5 (1.7). In the follow-up period, 53% of patients used triptans, 41% used opioids, 24% had migraine-related opioid use, 21% used both, and 28% of patients used neither triptans nor opioids. Geographic heat maps detail the variation in unadjusted triptan and opioid counts across the United States (Figures 3 & 4).

4.2 Triptans

The mean number of triptan claims for patients during the one-year follow-up period is shown in Table 2, stratified across the different regions of interest. The Northeast had the lowest unadjusted number of triptan claims followed by the Midwest, South, and West. The results of the adjusted logistic regression suggest that compared to the Northeast, a patient with migraine was more likely to be a triptan user in the Midwest (OR: 1.16; 95% CI: 1.12, 1.20), South (OR: 1.17; 95% CI: 1.14, 1.21), and West (OR: 1.21; 95% CI: 1.16, 1.25) (Table 3). However, among triptan users, there were no significant differences in the number of triptan claims in the Midwest (IRR: 0.99; 95% CI: 0.96, 1.02), South (IRR: 1.01; 95% CI: 0.98, 1.04), and West (IRR: 0.99; 95% CI: 0.96, 1.02) when compared to the Northeast.

Additional results of interest were that the odds of being a triptan user (OR: 1.38; 95% CI: 1.34, 1.43) and triptan use among users (IRR: 1.57; 95% CI: 1.53, 1.61) was higher for patients with chronic versus episodic migraine (Table 3). Men were less likely to become triptan users (OR: 0.75; 95% CI: 0.73, 0.77) and had lower triptan use among users (IRR: 0.94; 95% CI: 0.92, 0.97). Based on the Elixhauser comorbidity score, patients with a greater number of comorbidities were less likely to be triptan users and had lower use.

After adjustment for confounders, the predicted numbers of annual triptan claims for an average patient in the Northeast, Midwest, South, and West were 2.27 (95% CI: 2.22, 2.32), 2.44 (95% CI: 2.39, 2.49), 2.48 (95% CI: 2.45, 2.51), and 2.49 (95% CI: 2.42, 2.54), respectively (Table 5)

4.3 Opioids

The mean number of opioid claims for patients during the one-year follow-up period is shown in Table 2, stratified across the different regions of interest. The unadjusted number of opioid claims was lower in the Northeast, followed by the Midwest, South, and West. The results of the adjusted logistic regression suggest that compared to the Northeast, a patient with migraine was more likely to be an opioid user in the Midwest (OR: 1.71; 95% CI: 1.65, 1.78), South (OR: 1.91; 95% CI: 1.85, 1.97), and West (OR: 1.71; 95% CI: 1.64, 1.78) (Table 4). Among opioid users, there was also an increase in opioid use for the Midwest (IRR: 1.21; 95% CI: 1.14, 1.29), South (IRR: 1.17; 95% CI: 1.11, 1.24), and West (IRR: 1.41; 95% CI: 1.32, 1.50) compared to the Northeast.

Additional results of interest were that the odds of being an opioid user (OR: 1.47; 95% CI: 1.43, 1.52) and opioid use among users (IRR: 1.58; 95% CI: 1.51, 1.66) was higher for patients with chronic versus episodic migraine (Table 3). Men were less likely to become opioid users (OR: 0.94; 95% CI: 0.91, 0.97) but had higher opioid use among users (IRR: 1.28; 95% CI: 1.22,

1.34). Based on the Elixhauser comorbidity score, patients with a greater number of comorbidities were more likely to be opioid users and had higher use.

After adjustment for confounders, the predicted numbers of annual opioid claims for an average patient in the Northeast, Midwest, South, and West were 1.19 (95% CI: 1.15, 1.22), 1.86 (95% CI: 1.81, 1.91), 1.95 (95% CI: 1.91, 1.98), and 2.04 (95% CI: 1.99, 2.10), respectively (Table 5).

4.4 Opioid Scenario Analysis

The mean number of migraine-related opioid claims for patients during the one-year follow-up period is shown in Table 3, stratified across the different regions of interest.

After adjustment for confounders, the predicted numbers of annual opioid claims for an average patient in the Northeast, Midwest, South, and West were 0.35 (95% CI: 0.34, 0.36), 0.55 (95% CI: 0.54, 0.57), 0.59 (95% CI: 0.58, 0.60), and 0.66 (95% CI: 0.64, 0.69), respectively (Table 5).

5. Discussion

5.1 Results Summary and References to Previous Research

In this retrospective claims analysis, we assessed the geographic variations in triptan and opioid prescribing patterns for patients with migraine. The results of our unadjusted analysis showed that patients in the Northeast used the fewest triptan, opioid, and migraine-related opioid claims. Although our study is the first to assess geographic variation to describe prescribing patterns for acute migraine medications, some results can be compared to published studies.

Woolley et al. conducted a retrospective cohort study of patients initiating preventive therapy and reported similar numbers of triptan and opioid claims among users.[9] However, they conducted a sensitivity analysis by excluding patients with chronic pain conditions to assess migraine-related opioid use and reported higher migraine-related opioid claims. The results of

our adjusted analysis indicate that while there was less triptan use overall in the Northeast, among triptan users, the number of triptan claims did not vary significantly across regions. However, compared to the Northeast, patients in the other three regions were more likely to be opioid users and had a greater rate of opioid utilization among users. There are numerous factors that could have contributed to these differences in prescribing patterns. Among the four regions of interest, the Northeast has the greatest number of headache subspecialists and primary care physicians per capita.[23,24] Additionally, every state in the Northeast has laws to limit the prescribing or dispensing of opioids for acute pain.[15]

Other findings of note were that men with migraines were less likely to be triptan users and used triptans less frequently than women. Men were also less likely to be opioid users, but among users, the rate of opioid use was greater than in females. These results are corroborated by the findings from Lipton et al., which show that women were more likely than men to take triptans (17% vs 14%).[25] According to the AMPP survey, 13% of men and 11% of women could not take triptans based on their cardiovascular risk and prior medical history.[26]

In our study, based on their Elixhauser comorbidity score, patients with a greater number of comorbidities were less likely to be triptan users and had less triptan use. However, patients with a greater number of comorbidities were more likely to be opioid users and had more opioid use. This relationship may be based on the fact that the Elixhauser comorbidity score is a composite summary of a patient's comorbidities, including cardiovascular disease and risk factors.[17,18] Since triptans are contraindicated in cardiovascular disease, evidence from our study and the body of literature suggests these patients may have been prescribed opioids as an alternative option. There are additional findings from Li et al. that patients with migraine who had more cardiovascular risk factors were more likely to be prescribed opiates over triptans.[27] However,

opioid use in patients with migraines has been associated with disease progression and a decreased response to triptans. It is evident that there is an unmet need in available treatment alternatives for patients with migraine who have cardiovascular disease or risk factors.

5.2 Strengths

To our knowledge, this study is the first to assess geographic variations in treatment patterns for patients with migraine. Additionally, this is the first study to address opioid use in patients with migraine since the US started taking more deliberate actions against the growing opioid epidemic. The requirement of having an additional migraine-related medical encounter 31 to 365 days after the initial claim strengthens our study because migraines are commonly misdiagnosed. In a patient interview study among incident sumatriptan users, 39% of patients discontinued their treatment due to uncertainty about their diagnoses.[28]

5.3 Limitations

Our study has several limitations. The MarketScan® dataset did not contain information about some key potential confounders identified in the literature such as race, income, and occupation. We also excluded the Medicaid population due to their lack of geographic identifiers in the dataset, which limits generalizability. The most specific geographic identifier that was available for our study was MSA. Additionally, our outcome of interest was the number of medications claims and did not provide more detailed information such as dose and day supply. However, other claims-based analyses for patients with migraine have used similar outcome measures.[9,29] This study did not evaluate other treatment options commonly used by patients such as nonsteroidal anti-inflammatory drugs, acetaminophen, and ergot alkaloids. We excluded medications that could be purchased over-the-counter due to the inability to capture meaningful data. Moreover, studies have shown that ergot alkaloids have fallen out of favor in migraine

treatment.[9] Cardiovascular risk factors and disease were not assessed directly, but our study included the Elixhauser comorbidity score.

5.4 Future Directions

We plan to remove all patients who are missing either the MSA or state variable in order to proceed with further analyses. We have a large study population and removing these patients will still result in a study population of 120,000. This is a necessary step in order to improve our primary analysis, as MSA will be included in our adjusted analysis as either a covariate or interaction term. Since our primary analysis uses the four Census Bureau-designated regions, we will conduct a secondary analysis using additional stratification into nine Census Bureau-designated divisions. Our current regions of interest may be too large to reflect the true geographic variation observed in prescribing patterns and our geographic heat map suggests that further stratification should be tested. Another secondary analysis will be conducted by separating states into those with and without opioid dispensing and prescribing laws. It is important to note that since 17 out of 26 states passed legislation during 2017 and our data may not reflect the total impact of these laws.

6. Conclusion

This retrospective claims analysis found that compared to the Northeast, patients in the Midwest, South, and West were more likely to use triptans. However, there were no significant differences in the rates of triptan use among all regions. Patients in the Midwest, South, and West were more likely to use opioids and had higher rates of opioid use compared to the Northeast. Future studies in this field may be warranted with the recent approvals of medications indicated for the acute treatment of migraine attacks.

Tables

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants

	Northeast	Midwest	South	West
N (%)	26475 (17.9)	30378 (20.6)	68448 (46.3)	22399 (15.2)
Demographics				
Age (years), mean ± SD*	46.2 ± 14.2	43.6 ± 12.9	44.24 ± 12.4	44.6 ± 12.7
Female, n (%)*	21854 (82.5)	25344 (83.4)	58598 (85.6)	18445 (82.3)
Metropolitan statistics, n (%)*				
Located in a MSA	16810 (63.5)	23739 (78.1)	48663 (71.1)	19359 (86.4)
Located outside of a MSA	2095 (7.9)	4366 (14.4)	9399 (15.2)	1179 (5.3)
Missing	7570 (28.6)	2273 (7.5)	10386 (13.7)	1861 (8.3)
Health plan type*				
CDHP/HDHP	3824 (14.4)	7459 (24.6)	14890 (21.8)	4673 (20.9)
Comprehensive	506 (1.9)	3130 (10.3)	2164 (3.2)	538 (2.4)
EPO/PPO	18545 (70.0)	13563 (44.6)	36980 (54.0)	12343 (55.1)
HMO	1478 (5.6)	4702 (15.5)	7551 (11.0)	3989 (17.8)
POS	1914 (7.2)	1136 (3.7)	5067 (7.4)	462 (2.1)
Missing	208 (0.8)	388 (1.3)	1796 (2.6)	394 (1.8)
Clinical Characteristics				
ECI, mean ± SD*	1.6 ± 1.7	1.5 ± 1.7	1.6 ± 1.7	1.4 ± 1.6
Chronic migraine, n (%)*	3673 (13.9)	4024 (13.2)	9321 (13.6)	3400 (15.2)
Comorbidities, n (%)				
Allergic rhinitis*	3750 (14.2)	4118 (13.6)	12777 (18.7)	2979 (13.3)
Anxiety*	6201 (23.4)	7306 (24.1)	16952 (24.8)	4878 (21.8)
Bipolar disorder*	591 (2.2)	813 (2.7)	1632 (2.4)	601 (2.7)
Depression*	1946 (7.4)	2898 (9.5)	5087 (7.4)	2111 (9.4)
Epilepsy*	708 (2.7)	734 (2.4)	1861 (2.7)	489 (2.2)
Non-migraine headache*	2675 (10.1)	3420 (11.3)	6782 (9.9)	2364 (10.6)
Sleep disorder*	3788 (14.3)	5194 (17.1)	12713 (18.6)	3974 (17.7)

Sample characteristics of patients with migraine identified in MarketScan® (Commercial and Medicare Supplemental) from 2017 to 2018. All patients were required to have a first migraine claim in 2017 with an additional, confirmatory claim 31 to 365 days afterwards.

Abbreviations: CHDP: consumer-driven health plan; CI: confidence interval; ECI: Elixhauser comorbidity index; EPO: exclusive provider organization; HDHP: high deductible health plan; HMO: health maintenance organization; MSA: metropolitan statistical area; PPO: preferred provider organization; POS: point-of-service

* p-value <0.001

Table 2. Unadjusted Counts of Annual Triptan and Opioid Use

	Northeast	Midwest	South	West	P-value
Number of triptan claims, mean (SD)					
All patients[a]	2.36 (4.05)	2.50 (4.15)	2.60 (4.27)	2.66 (4.32)	<0.001
Patients with ≥1 triptan claim[b]	4.88 (4.65)	4.72 (4.70)	4.88 (4.80)	4.86 (4.83)	0.002
Number of opioid claims, mean (SD)					
All patients[a]	1.50 (4.34)	2.20 (5.00)	2.33 (5.13)	2.35 (5.45)	<0.001
Patients with ≥1 opioid claim[c]	4.94 (6.72)	5.34 (6.62)	5.27 (6.64)	5.80 (7.30)	<0.001
Number of migraine-related opioid claims, mean (SD)					
All patients[a]	0.44 (1.59)	0.65 (1.89)	0.71 (2.03)	0.78 (2.43)	<0.001
Patients with ≥1 opioid claim[c]	1.45 (2.62)	1.57 (2.68)	1.59 (2.81)	1.92 (3.51)	<0.001

Sample of patients with migraine identified in MarketScan® (Commercial and Medicare Supplemental) from 2017 to 2018. All patients were required to have a first migraine claim in 2017 with an additional, confirmatory claim 31 to 365 days afterwards.

Abbreviations: SD: standard deviation

[a] Total study population – 147,700 patients; [b] Triptan users – 77,614 patients; [c] Opioid users 59,926 patients

Table 3. Triptan Use – Multivariable Regression Analyses

Variable	Any Triptan Use in the Past Year Logistic Regression N = 144,914			Annual Number of Triptan Claims Zero-Truncated Negative Binomial Regression N = 76,220		
	Odds Ratio	**95% CI**	**p-value**	**IRR**	**95% CI**	**p-value**
Regions						
Midwest[a]	1.16	1.12 – 1.20	<0.001	0.99	0.96 – 1.02	0.721
South[a]	1.17	1.14 – 1.21	<0.001	1.01	0.98 – 1.04	0.280
West[a]	1.21	1.16 – 1.25	<0.001	0.99	0.96 – 1.02	0.412
Demographics						
Age	1.05	1.04 – 1.06	<0.001	1.06	1.06 – 1.07	<0.001
Age^2	0.99	0.99 – 0.99	<0.001	0.99	0.99 – 0.99	<0.001
Male[b]	0.75	0.73 – 0.77	<0.001	0.94	0.92 – 0.97	<0.001
CDHP/HDHP[c]	0.98	0.95 – 1.01	0.217	1.00	0.98 – 1.03	0.771
Comprehensive[c]	0.84	0.79 – 0.88	<0.001	0.84	0.80 – 0.88	<0.001
HMO[c]	1.05	1.02 – 1.09	<0.001	0.97	0.95 – 1.00	0.067
POS[c]	0.85	0.82 – 0.89	<0.001	0.98	0.94 – 1.02	0.305
Clinical Characteristics						
CM[d]	1.38	1.34 – 1.43	<0.001	1.57	1.53 – 1.61	<0.001
ECI[e]						
1	0.84	0.81 – 0.86	<0.001	0.96	0.94 – 0.98	<0.001
2	0.70	0.68 – 0.72	<0.001	0.93	0.91 – 0.96	<0.001
3+	0.56	0.55 – 0.58	<0.001	0.88	0.86 – 0.90	<0.001

Logistic Regression and Zero-Truncated Negative Binomial Regression results for triptan use in a sample of patients with migraine identified in MarketScan® (Commercial and Medicare Supplemental) from 2017 to 2018. All patients were required to have a first migraine claim in 2017 with an additional, confirmatory claim 31 to 365 days afterwards.

Abbreviations: CHDP: consumer-driven health plan; CI: confidence interval; ECI: Elixhauser comorbidity index; EPO: exclusive provider organization; HDHP: high deductible health plan; HMO: health maintenance organization; IRR: incidence rate ratio; PPO: preferred provider organization; POS: point-of-service
Reference category: [a] Northeast; [b] Female; [c] EPO/PPO; [d] Episodic Migraine; [e] ECI score = 0

Table 4. Opioid Use – Multivariable Regression Analyses

Variable	Any Opioid Use in the Past Year Logistic Regression N = 144,914			Annual Number of Opioid Claims Zero-Truncated Negative Binomial Regression N = 58,729		
	Odds Ratio	**95% CI**	**p-value**	**IRR**	**95% CI**	**p-value**
Regions						
Midwest[a]	1.71	1.65 – 1.78	<0.001	1.21	1.14 – 1.29	<0.001
South[a]	1.91	1.85 – 1.97	<0.001	1.17	1.11 – 1.24	<0.001
West[a]	1.71	1.64 – 1.78	<0.001	1.41	1.32 – 1.50	<0.001
Demographics						
Age	1.05	1.04 – 1.06	<0.001	1.13	1.12 – 1.13	<0.001
Age^2	0.99	0.99 – 0.99	<0.001	0.99	0.99 – 0.99	<0.001
Male[b]	0.94	0.91 – 0.97	<0.001	1.28	1.22 – 1.34	<0.001
CDHP/HDHP[c]	0.95	0.92 – 0.97	<0.001	0.97	0.93 – 1.01	0.190
Comprehensive[c]	1.15	1.08 – 1.21	<0.001	1.15	1.06 – 1.25	<0.001
HMO[c]	0.94	0.91 – 0.97	<0.001	0.87	0.83 – 0.92	<0.001
POS[c]	0.90	0.86 – 0.94	<0.001	0.82	0.76 – 0.89	<0.001
Clinical Characteristics						
CM[d]	1.47	1.43 – 1.52	<0.001	1.58	1.51 – 1.66	<0.001
ECI[e]						
1	1.39	1.35 – 1.43	<0.001	1.40	1.33 – 1.47	<0.001
2	1.81	1.76 – 1.87	<0.001	1.68	1.59 – 1.77	<0.001
3+	2.99	2.90 – 3.08	<0.001	2.42	2.31 – 2.53	<0.001

Logistic Regression and Zero-Truncated Negative Binomial Regression results for opioid use in a sample of patients with migraine identified in MarketScan® (Commercial and Medicare Supplemental) from 2017 to 2018. All patients were required to have a first migraine claim in 2017 with an additional, confirmatory claim 31 to 365 days afterwards.

Abbreviations: CHDP: consumer-driven health plan; CI: confidence interval; ECI: Elixhauser comorbidity index; EPO: exclusive provider organization; HDHP: high deductible health plan; HMO: health maintenance organization; IRR: incidence rate ratio; PPO: preferred provider organization; POS: point-of-service
Reference category: [a] Northeast; [b] Female; [c] EPO/PPO; [d] Episodic Migraine; [e] ECI score = 0

Table 5. Expected Counts of Triptan and Opioid Claims

	Northeast	Midwest	South	West
Predicted # of triptan claims, mean (95% CI)	2.27 (2.22 – 2.32)	2.44 (2.39 – 2.49)	2.48 (2.45 – 2.51)	2.49 (2.42 – 2.54)
Predicted # of opioid claims, mean (95% CI)	1.19 (1.15 – 1.22)	1.86 (1.81 – 1.91)	1.95 (1.91 – 1.98)	2.04 (1.99 – 2.10)
Predicted # of migraine-related opioid claims, mean (95% CI)	0.35 (0.34 – 0.36)	0.55 (0.54 – 0.57)	0.59 (0.58 – 0.60)	0.66 (0.64 – 0.69)

Predicted counts were calculated for each region, for a representative patient, holding all other variables in the negative binomial model at their means. Predictions were conducted in the full sample of patients with migraine identified in MarketScan® (Commercial and Medicare Supplemental) from 2017 to 2018. All patients were required to have a first migraine claim in 2017 with an additional, confirmatory claim 31 to 365 days afterwards.
Abbreviations: CI: confidence interval

Table 6. Geographic Variations in the Number of Triptan and Opioid Claims

Region	Triptan		Opioids	
	Mean (SD)	**CV***	**Mean (SD)**	**CV***
Northeast	2.36 (4.05)	172%	1.18 (3.85)	325%
Midwest	2.50 (4.15)	166%	1.72 (4.31)	251%
South	2.60 (4.27)	164%	1.78 (4.39)	246%
West	2.66 (4.32)	163%	1.95 (4.87)	249%

A coefficient of variation was conducted in the sample of patients with migraine identified in MarketScan® (Commercial and Medicare Supplemental) from 2017 to 2018. All patients were required to have a first migraine claim in 2017 with an additional, confirmatory claim 31 to 365 days afterwards.
Abbreviations: CV: coefficient of variation; SD: standard deviation
*CV = coefficient of variation (= SD/mean*100%)

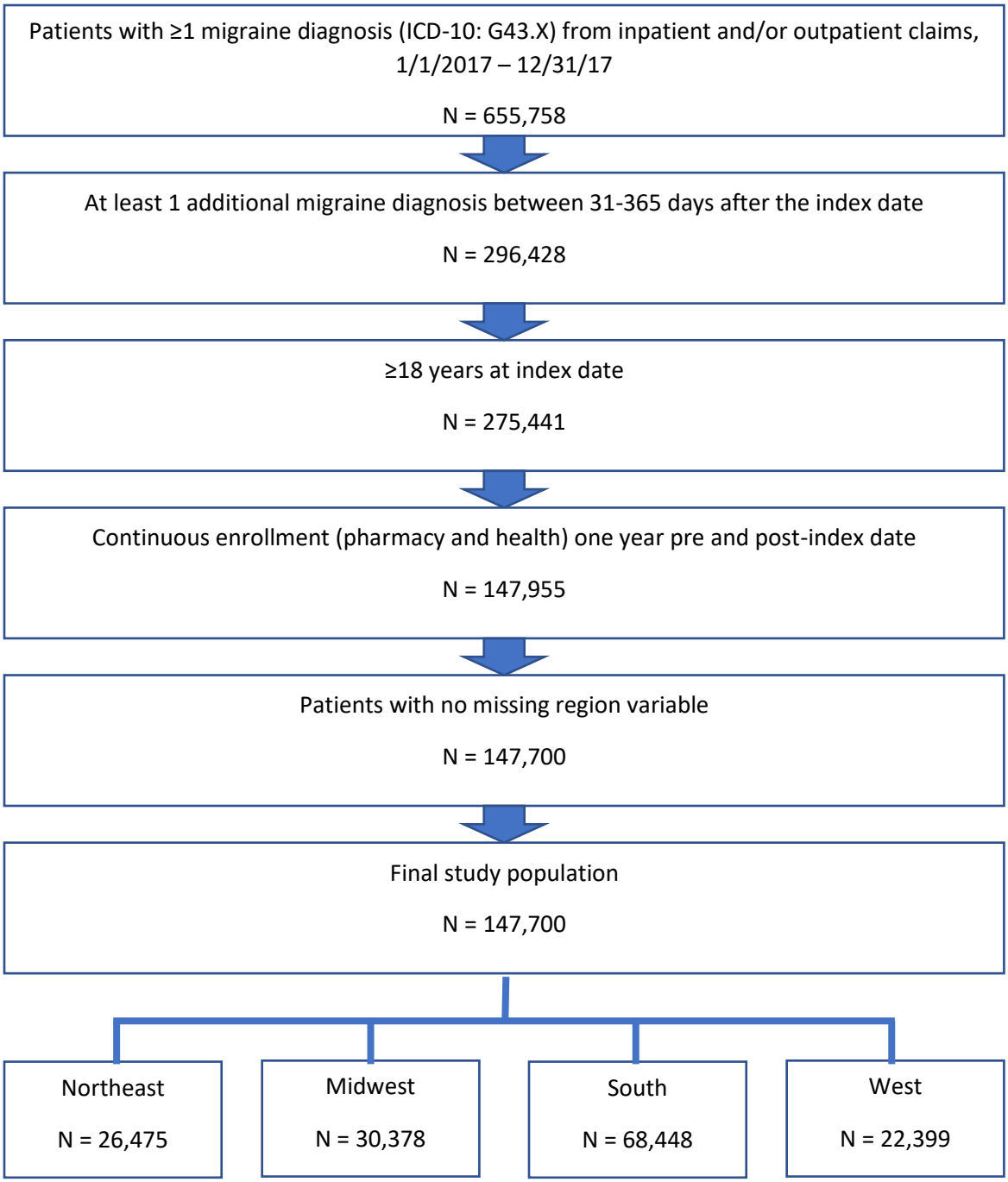
Table 7. Triptan Use by Type of Triptan

	Northeast N = 26,475	**Midwest** N = 30,378	**West** N = 68,448	**South** N = 22,399
Total triptan count, (proportion of total)	62,224 (100)	75,795 (100)	59,406 (100)	178,305 (100)
Almotriptan	503 (1)	4Fi99 (1)	390 (1)	1376 (1)
Eletriptan	7192 (12)	6108 (8)	4152 (7)	17,627 (10)
Frovatriptan	1415 (2)	1041 (1)	1348 (2)	2832 (2)
Naratriptan	2553 (4)	3343 (4)	3055 (5)	6451 (4)
Rizatriptan	14,358 (23)	17,689 (23)	14,477 (24)	47,225 (26)
Sumatriptan	31,771 (51)	42,529 (56)	32,175 (54)	91,505 (51)
Zolmitriptan	4432 (7)	4586 (6)	3809 (6)	11,289 (6)

Triptan use was quantified among the sample of patients with migraine identified in MarketScan® (Commercial and Medicare Supplemental) from 2017 to 2018. All patients were required to have a first migraine claim in 2017 with an additional, confirmatory claim 31 to 365 days afterwards.

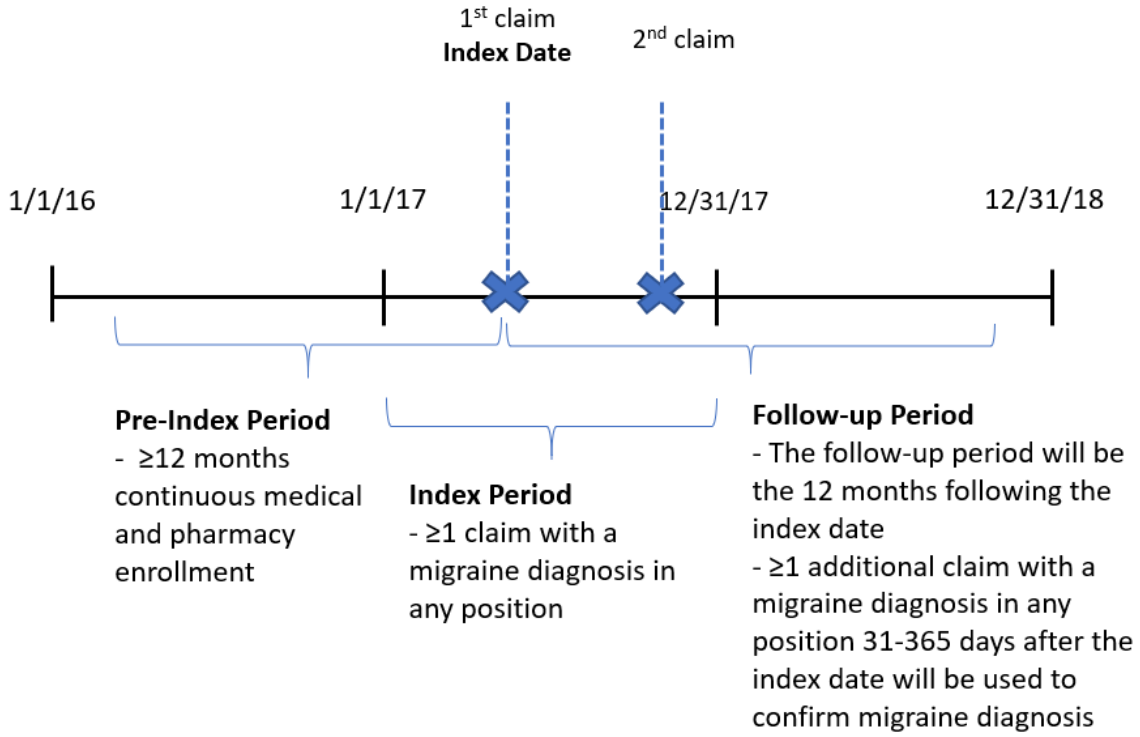
Figures

Figure 1. Study Cohort Selection



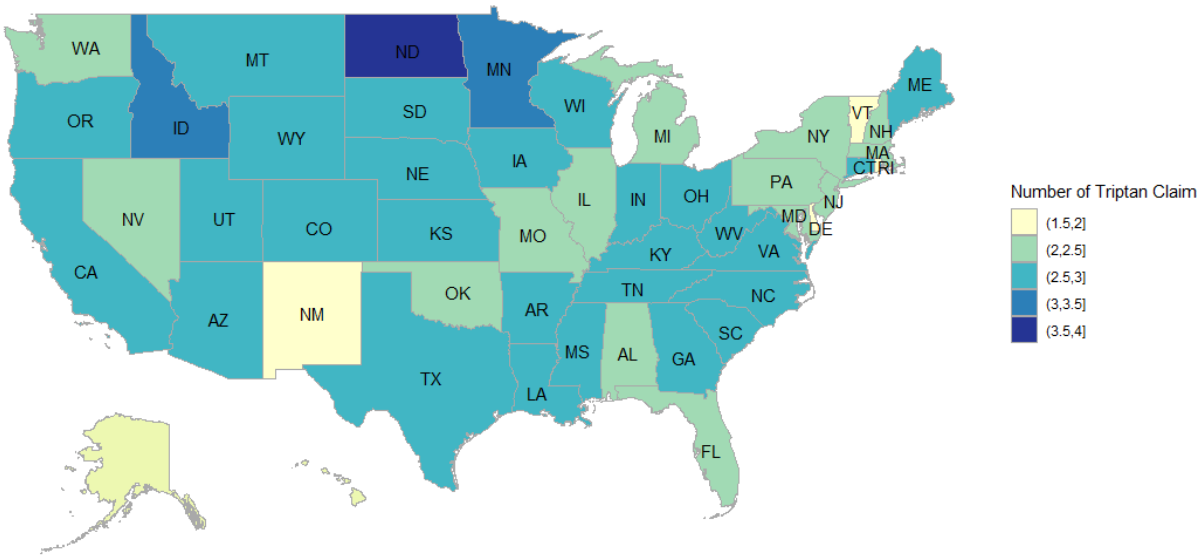
Sample of patients with migraine identified in MarketScan® (Commercial and Medicare Supplemental) from 2017 to 2018. All patients were required to have a first migraine claim in 2017 with an additional, confirmatory claim 31 to 365 days afterwards.

Figure 2. Study Timeline



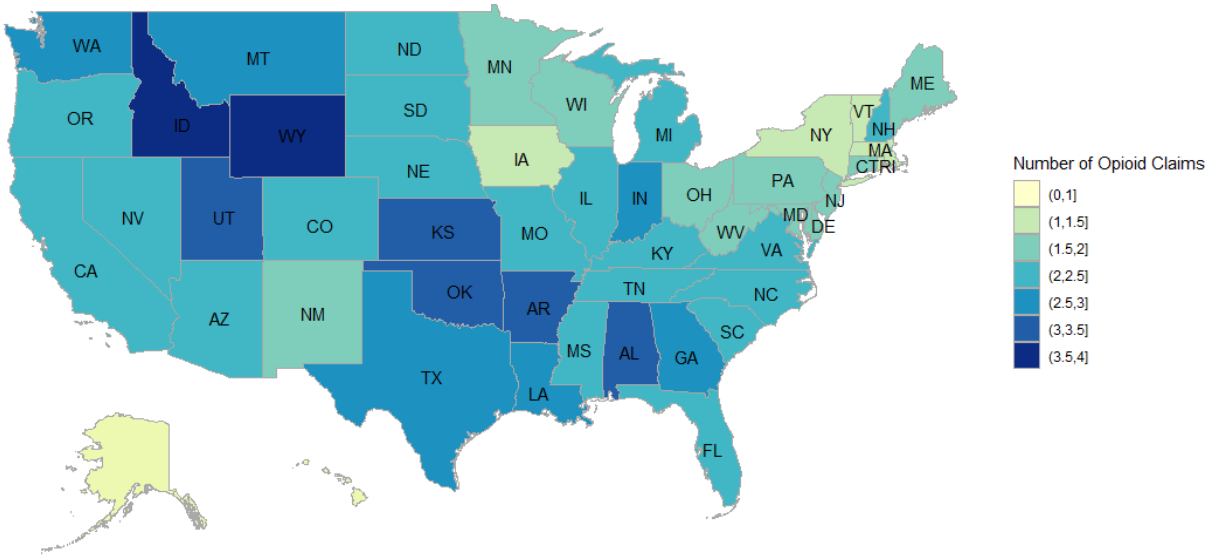
Sample of patients with migraine identified in MarketScan® (Commercial and Medicare Supplemental) from 2017 to 2018. All patients were required to have a first migraine claim in 2017 with an additional, confirmatory claim 31 to 365 days afterwards.

Figure 3. Annual Number of Triptan Claims per Patient with Migraine by State



Sample of patients with migraine identified in MarketScan® (Commercial and Medicare Supplemental) from 2017 to 2018. All patients were required to have a first migraine claim in 2017 with an additional, confirmatory claim 31 to 365 days afterwards.

Figure 4. Annual Number of Opioid Claims per Patient with Migraine by State



Sample of patients with migraine identified in MarketScan® (Commercial and Medicare Supplemental) from 2017 to 2018. All patients were required to have a first migraine claim in 2017 with an additional, confirmatory claim 31 to 365 days afterwards.

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