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Undertreatment of Migraine in the United States – A Population Based Study

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ABSTRACT

Migraine is a debilitating chronic disease that affects approximately 36 million of the United States population. The objective of the study is to investigate the prevalence and patient's socio demographic characteristics associated with under treatment of migraine in the US. ambulatory care settings. A retrospective population-based study was conducted by analyzing a national database from 2010 National Ambulatory Medical Care Survey (NAMCS). The NAMCS is a national probability sample survey conducted annually by the National Center for Health Statistics. All patient visits coded with a diagnosis of migraine were included in the study. A series of weighted descriptive analyses were used to estimate the prevalence of prescription medications recommended in the American Neurology Association latest practice guidelines on migraine. A multivariate logistic regression was conducted to predict the maximum likelihood of migraine pharmacotherapy associated with patient's socio demographic characteristics. An estimated total of 5.45 million outpatient visits related to migraines occurred in the US. Only 3.08 million visits (56.48%) received at least one migraine prescription. Abortive drugs were prescribed much more than prophylaxis drugs (68.8% vs 31.2%). The results from logistic regression identified patient's gender (OR=0.164, 95%CI: 0.034 – 0.790), race (OR=0.123, 95%CI: 0.029 – 0.520), and ethnicity (OR=0.075, 95%CI: 0.006 – 0.927) contribute significant impacts on the migraine treatment. The study revealed that under treatment of migraine is a significant problem in the US. Future studies are recommended to explore intervention and educational strategies to ensure physicians are well-informed evidence-based practice guidelines and provide timely and appropriate treatment for people with Migraine.

Keywords: Migraine, Population-Based, Undertreatment, NAMCS.

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INTRODUCTION

Migraine is a debilitating chronic disease that affects approximately 36 million of the United States population. Evidence shows that migraine imposes a significant burden on our society. Estimated eighteen-percent of American women and six- percent of men suffer from a form of migraine with female to male ratios ranging from 2:1 to 3:1 and peaking in midlife[1]. The actual cause of migraines is not well understood however; researchers believed that it is the results of neurological abnormalities caused by brain genetic mutations and environmental factors such as bright lights, smoke, odors, etc.[2]. Migraines are believed to arise from changes in the brainstem and its interactions with the trigeminal nerve, a major pain pathway. Migraines is generally divided into two categories (with auras) and (without auras). Migraneurs who suffer from auras are differentiated from those that do not because they usually experience visual, sensory, verbal, or motor disturbances a few minutes before the migraine onset. Migraines can be further categorized into episodic or chronic. Episodic migraines are defined by headaches that occur on less than 15 days out of the month, on the other hand chronic migraines are classified as headaches that occur on 15 or more days out of the month for a period of at least 3 months[3]. During migraine attacks it has been noted that serotonin levels decrease causing the trigeminal system to release neuropeptides, which travel to the meanings and induce headache pain[2]. There is no absolute cure for migraine since its pathophysiology has not been completely revealed. Strategies for migraine management include two options: nonpharmacologic and pharmacologic treatments. Nonpharmacologic treatments include behavioral and lifestyle changes to avoid migraine triggers. Pharmacologic treatments are typically divided into acute or abortive treatment; and preventive or prophylactic treatment. There are various advanced medications from different classes are available to treat migraine. Unfortunately, migraine continues to be under diagnosed and undertreated. When left untreated, Migraineurs typically report feeling sleepier, tired, and with less energy compared to non-migraine sufferers[4]. Migraineurs also experienced a significant deterioration in their quality of life and work productivity. A study conducted by Hawkins et.al found that Migraineurs have a higher average healthcare expenditure than non-migraineurs[5]. Migraine has been linked to higher unemployment rate, early retirement and poor education. Piette and his colleagues also found that in general participants with incomes below $20,000 a year had higher relative odds of non-adherence than those earning at least $60,000 a year. This study concluded that individuals with higher out-of-pocket costs had a greater risk of medication underuse[6]. Researchers believe that a relationship may exist between

patient's demographic and socioeconomic status in migraine diagnosis and medication use. The objective of the study is to investigate the prevalence and patient's sociodemographic characteristics associated with under treatment of migraine in the US. ambulatory care settings.

MATERIALS AND METHOD

Data Source

Data was extracted from the National Ambulatory Medical Care Survey (NAMCS). The NAMCS is a national probability sample survey conducted annually by the Division of Health Care Statistics, National Center for Health Statistics (NCHS) within Centers for Disease Control and Prevention (CDC). The NAMCS samples data are collected from non-federal office-based clinical practice. The basic sampling unit for the NAMCS is the physician-patient encounter or outpatient visit. For each selected visit, physicians completed an encounter form listing diagnoses, medication, and clinical services that they provided. All records contain patient demographic information, including age, sex, race, ethnicity and source of payment. The details of NAMCS sampling design is available to public online[7]. To extrapolate to national estimates, each visit record is assigned an inflation factor called the patient visit weight, which is then used to predict the total number of office visits made in the US. All estimates from the NAMCS are related to the number of patient visits and subject to sampling variability. An estimate is considered reliable if it has a relative sampling errors (SE) of $\leq 30\%$ of the estimate, per NCHS standards. Our study used the 2010 NAMCS data for its timeliness and availability while the project was approved by the institution review board. All data management and analyses described were performed using SAS software (Statistical Analysis System; SAS Institute; Cary, NC, USA).

Data Extraction and Methods

All patient visits to ambulatory physician office with a diagnosis of migraine were included in the study. We comprised all adult patients' visits with ICD-9-CM codes between 340.00 and 346.93 as Migraine diagnosis according to the center for Medicare and Medicaid services. The prescription medications were chosen in the study for migraine treatment were partially adapted from the American Academy of Neurology (AAN) latest practice guideline[8] of group 1 and 2 drugs which represent the medications with evidence-based proven clinical and statistical benefits, then categorized into two groups: abortive and prophylactic medication for migraine. In NAMCS database, up to 8 medications can be recorded for each visit. Each drug code was assigned a unique "generic drug code" by Multum's Lexicon Plus system, which was used to

classified drug entries in the NAMCS. The structure of Multum database allows multiple ingredients drugs being assigned a single generic drug code according to their generic components and therapeutic classifications. Using Eisenberg's sociologic theory, we also identified the following physician and patient characteristics as variables for further analyses: patient's age, gender, ethnicity, insurance type, physician's specialty, office setting, and office ownership.

Statistical Analysis

Each record on the NAMCS data file represents one patient visit. In order to obtain national estimates, the sample weight adjustments and standard error corrections were incorporated in all descriptive and inferential statistical analyses. We first performed a series of descriptive analyses to estimate the national weighted frequency of each drug. Second, a weighted multivariate logistic regression with SAS PROC SURVEYLOGISTICS application was conducted to predict the maximum likelihood of migraine pharmacotherapy (with treatment vs. without treatment) associated with patient's sociodemographic characteristics. Both standard sample design variables (CSTRATM and CPSUM) were included in SAS PROC SURVEY program to adjust for the complex sampling design employed by NAMCS. Two-tailed statistic with p-value less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

An estimated total of 5.45 million outpatient visits related to migraines occurred in the US in 2010.

Table 1: Demographic Characteristics of the Study Population

Patient Visit Characteristics	Weighted Frequency (%)
Gender	
Female	4,345,490 (79.8%)
Male	1,100,447 (20.2%)
Age	
<15	314,781 (7.3%)
15-24	559,458 (13.1%)
25-44	1,666,747 (38.9%)
45-63	1,492,566 (34.8%)
65-74	205,916 (4.8%)
>75	46,977 (1.1%)
Race	
White	3,405,512 (79.4%)
Non-White	880,933 (20.6%)
Ethnicity	
Hispanic	329,446 (7.7%)
Non-Hispanic	3,956,999 (92.3%)

As shown from the study demographics in Table 1, the majority of the patient visit records were from female (79.8%), white (79.4%) and Non-Hispanics (92.3%). Female accounted for nearly four times of migraine visits than male. Of these visits, only 3.08 million (56.5%) received at least one abortive or prophylactic medications used in the treatment of migraine (Figure 1). Figure 2 illustrates the prevalence of FDA-approved abortive and prophylactic medications used in the treatment of migraine in US 2010 outpatient visits. Abortive drugs were prescribed much more than prophylaxis drugs (68.8% vs 31.2%). The most frequently prescribed drug in the abortive group is Sumatriptan, which accounted for 40.3% of total prescriptions. This is followed by Diclofenac (24.7%), Butalbital, Aspirin, Caffeine, plus Codeine (22.1%), Ketorolac (15.4%), etc. (Figure 3). The most frequently prescribed medication in the prophylactic group was Propanolol, which accounted for (26.3%). This is followed by Atenolol (22.7%), Amitriptyline (13.2%), Fluoxetine (10.0%), Divalproex Sodium (9.5%), etc.(Figure 4).

Table 2: Likelihood of Receiving Migraine Pharmacotherapy with Significant Variables

Variable	Adjusted odds ratio	95% Wald Confidence Interval
Patient gender		
Female	Ref	
Male (reference)	0.164	0.034 – 0.790 *
Patient race		
White, non-Hispanic (reference)	Ref	-
Black, non-Hispanic	0.123	0.029 – 0.520 *
Hispanic	N/A	N/A
Asian	N/A	N/A
Native Hawaiian, other Pacific Islander	N/A	N/A
American Indian/ Alaska Native	N/A	N/A
Patient Ethnicity		
Hispanic	0.075	0.006 – 0.927 *
Non-Hispanic	Ref	

- Significant with 0.05 ; N/A: insufficient sample size

Table 2 presents the significant patient's characteristics associated with undertreated migraine from multivariate logistic regressions in odds ratio (OR) and 95% Wald confident interval (95%CI). The adjusted odds ratio represents the increased likelihood of receiving migraine prescribing medications based on each socioeconomic characteristic using a reference group in each category. Comparing gender differences, male were less likely to receive migraine drugs than female (OR=0.164, 95%CI: 0.034 – 0.790). Comparing race and ethnicity disparity, Black were less likely to receive migraine drugs than white (OR=0.123, 95%CI: 0.029 – 0.520). Hispanics were less likely to receive migraine pharmacotherapy than non-Hispanics (OR=0.075,

95%CI: 0.006 – 0.927). The present study revealed that the prevalence of migraine under treatment is high in the United States. Only 56.48% of migraineurs received at least one abortive or prophylactic medications in the US. ambulatory settings. Related to prior studies, migraine remains substantial undertreated. A population-based survey study conducted in France found that although 80% of migraineurs was aware that they had migraine, only 18% had medical treatment[9]. Similar, a recent study conducted by Diamond and his colleagues identified that only 12% of migraineurs were taking preventive medication for migraine during the study period. And, majority of subjects discontinued their preventive migraine prescription medications[10]. This study also highlights some interesting patterns of medication utilization among migraineurs, for instance, abortive drugs were prescribed much more than prophylaxis drugs (68.8% and 31.2%, respectively). Our results are consistent with previous national representative study that reported a 47.4 % medication utilization of abortive drugs versus 31% medication utilization of prophylaxis drugs among the non-institutionalized migraineurs in the United States[11]. Our study also showed interesting patterns of migraine medication utilization that came into agreement with previous evidence. In this study, the most frequently prescribed drug in the abortive group is sumatriptan, which accounted for 32.8% of this group. The result is consistent with the report from 2009 National Center for Health Statistics that triptans account for majority of prescriptions issued for specific antimigraine drugs, nearly half of which were for sumatriptan[12]. The reason of this trend in sumatriptan utilization may be due to the availability of generic forms since late 2000s. Among the prophylaxis group our data demonstrates a higher utilization of Propranolol medication. Hence, Propranolol was prescribed in 26.3% of the capture cases followed by Atenolol accounting for 22.7%. In a clinical study, propranolol was found to decrease severity of migraine attacks[13]. Another study evaluated the neurologist and primary care physician's preferences of migraine prophylaxis; found that Propranolol and Amitriptyline are among the most preferred medications[14]. Our study results identified patient's gender, race, and ethnicity contribute significant impacts on the migraine treatment. Evidence of gender disparity is consistent with many national population-based studies that male were less likely to receive prescription medication for the treatment of migraine compared to female[15, 16, 17]. Likewise, despite the lower tolerability of pain reported in black population in previous studies[18, 19]. Blacks were shown to be less likely to report prescription drugs to control migraine than white[16]. That might be explained by the racial disparities in access to health care[20]. The study has some important limitations. First, the study only included the medications with scientific proof in both clinical and statistical benefits according to AAN evidence-based guideline. Therefore, some

commonly off-label medications used from migraine will be excluded in the study such as sertraline. Second, the diagnoses of migraine in NAMCS are based on prescribing physician's individual judgment. Third, information is unavailable concerning duration and dosage of prescribed medications.

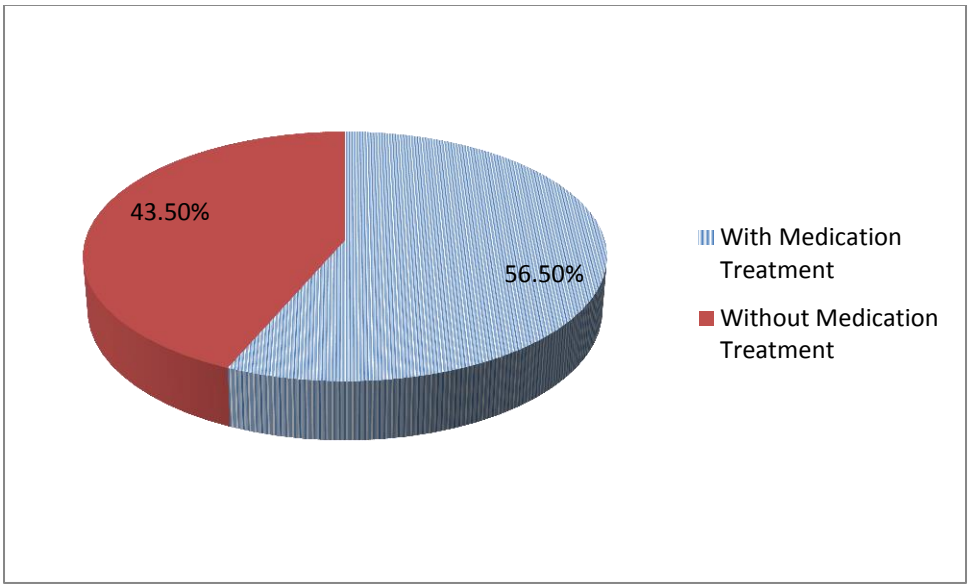

Figure 1: Migraine Medication Treatment in US. Outpatient Settings

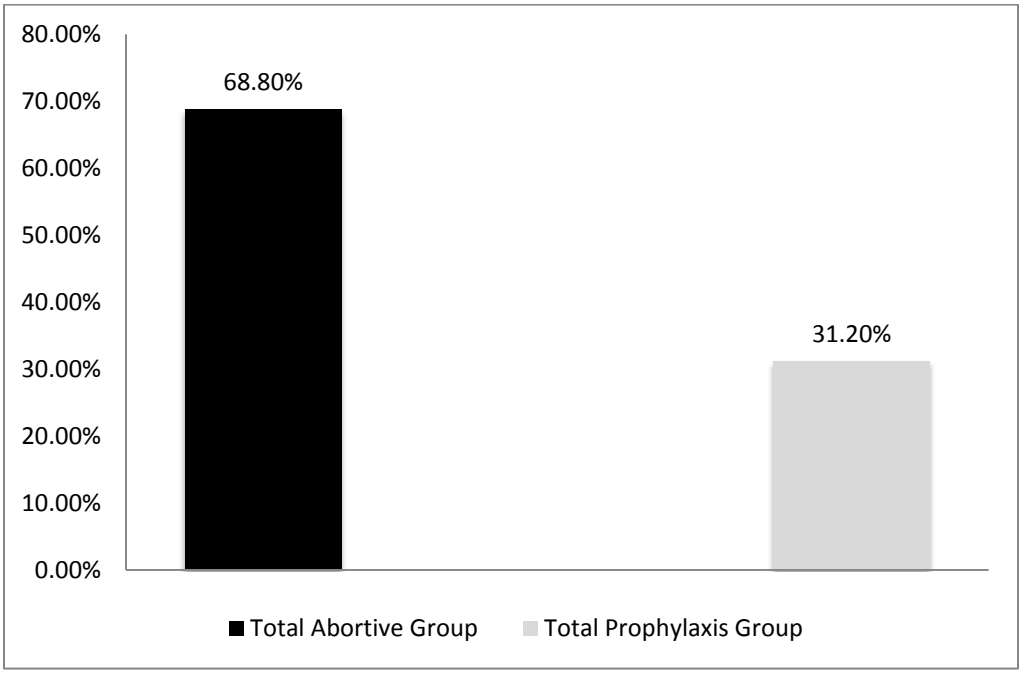

Figure 2: Outpatient Visits with Abortive vs. Prophylaxis Prescription for Migraine Treatment

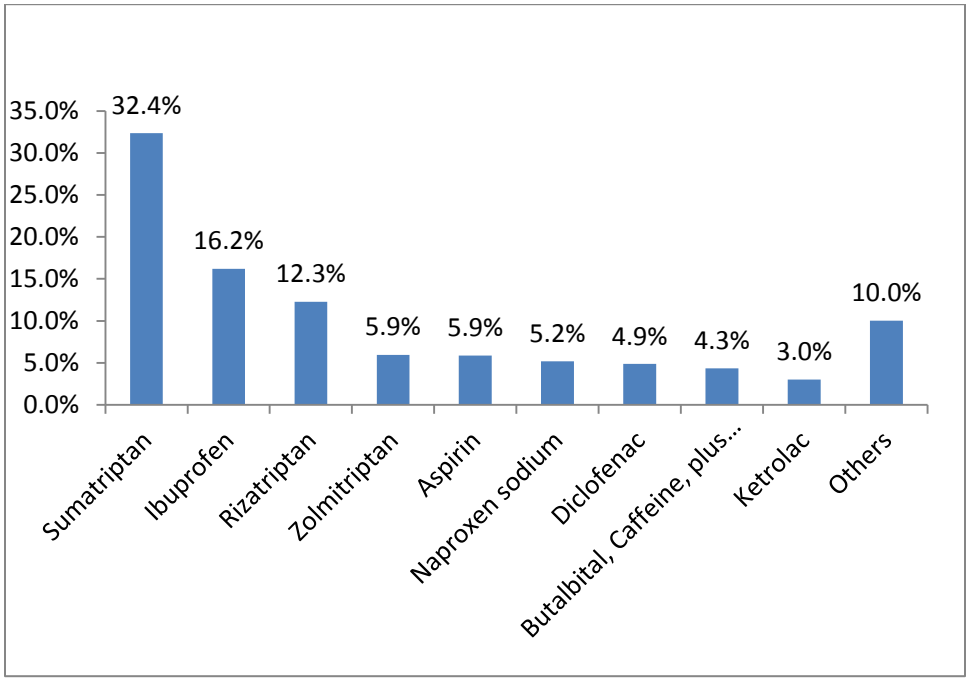

Figure 3: Outpatient Visits with Abortive Prescription for Migraine Treatment

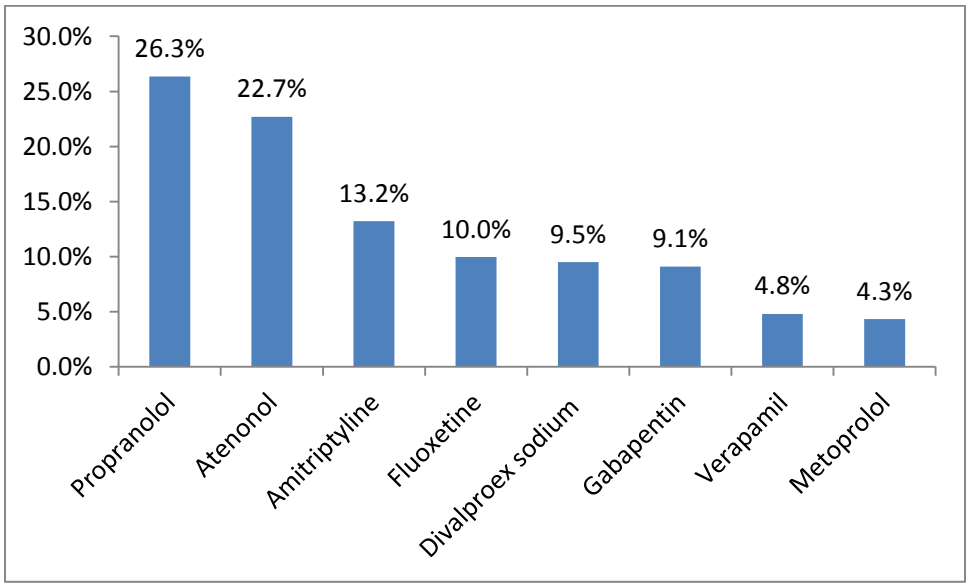

Figure 4: Outpatient Visits with Prophylaxis Prescription for Migraine Treatment

CONCLUSION

This study revealed a substantial under treatment of individuals with migraine in the United States despite evidences show that responsive prevention and treatment of migraine is incredibly important. Knowledge of factors that are associated with under treatment of migraine may help to identify subgroups that need additional care and attention. Future studies are recommended to explore intervention and educational strategies to ensure physicians are well-informed evidence-based practice guidelines and provide timely and appropriate treatment for people with Migraine.

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