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Migraine Prevalence and its Differences among Races and Ethnicities in the United States (2010-2015)

THESIS

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ABSTRACT

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in the United States (2010-2015)

By

Feiyang Tao

Master of Science in Biomedical and Translational Science

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Professor Sheldon Greenfield, Chair

Objective: The purpose of this study is to analyze the trend of migraine prevalence in the United States (US) adult population in 2010-2015 and possible causes of the racial/ethnic differences.

Methods: Data from the 2010-2015 National Health Interview Survey (NHIS) were analyzed. The yearly trend of age and sex adjusted migraine prevalence was estimated by a linear regression. Chi-squared tests were performed to examine the racial/ethnic differences in migraine prevalence. Multivariable logistic regression models were built to evaluate the associations between candidate variables and racial/ethnic migraine prevalence, as well as to explore the interactions between races/ethnicities and migraine contributing factors.

Results: In 2015, migraine prevalences in non-Hispanic Whites, Hispanic Whites, Blacks, Asians, bi-/multi-racial people, and American Indians and Alaska Natives were 15.38%, 14.36%, 15.67%, 10.68%, 20.91%, and 17.36%, respectively. The overall prevalence dropped from 16.28% to 14.95% during 2010-2015, but no significance was detected. Migraine prevalence was significantly lower in Asians and higher in bi-/multi-racial people. No significant difference was seen among other populations. Strong correlations with racial/ethnic migraine prevalence were found in age, sex, poverty status, problems in paying medical bills, depression/anxiety problems, hypertension, current smoking, pain, and sleep disturbances. Higher education, poverty, depression/anxiety problems, hypertension, smoking, and pain had interactions with certain racial/ethnic subgroups.

Conclusion: Migraine prevalence in the US adults was relatively stable during 2010-2015. A lower proportion of contributing factors in Asians and a higher proportion in bi-/multi-racial people may partly explain the racial differences. Interactions between contributing factors and races/ethnicities indicate race/ethnicity-specific associations with migraines.

CHAPTER 1: INTRODUCTION

1. Migraine and its burdens

Migraine is a common syndrome manifesting in recurrent moderate to severe headaches, which is usually unilateral (affecting only one side) and pulsatile (or throbbing), and often associated with muscle pain, nausea, vomiting, photophobia (extreme sensitivity to light), phonophobia (a fear of loud sounds), and lassitude (lack of energy). [1] It can occur in people of all ages, most often in those aged 35 to 55; women are more likely to suffer from migraines than men (2:1 to 3:1). [2][3][4] This type of neurological disease can be disabling due to the exacerbated headaches during daily activities. Considerable personal suffering, impaired quality of life, and high financial cost are caused by migraines throughout the world. [5]- [12]

2. Racial and ethnic differences in migraine prevalence

Some previous studies disclosed differences of migraine prevalence among races and/or ethnicities. The American Migraine Study suggested that migraine prevalence was higher in Caucasians than in African Americans. [13] Steiner et al. and Scher et al. reported that Caucasians had higher migraine prevalence compared to non-White races. [10] [14] Loder and Sheikh extracted data from the 2005 to 2012 National Health Interview Survey, and calculated that the average prevalence of severe headache or migraine was 17.7% for American Indians and Alaska Natives (AIANs), 14.5% for Hispanics, 14.3% for Whites, 14.0% for Blacks, and 9.2% for Asians; female to male prevalence ratios were 2.1 for Whites, 2.5 for Hispanics, 2.1 for Blacks, and 2.0 for Asians. [15] The American Migraine Prevalence and Prevention study, which included White, Black and Hispanic subgroups, revealed that Hispanic women were suffering the most from

chronic migraines (2.26% compared with 1.26% for White women), whereas White men had the lowest prevalence at 0.46%. [16]

3. Gaps in knowledge

Although the prevalence of migraine differs among races and ethnicities, few researchers have looked into the underlying causes of the phenomenon. Identifying the factors influencing the racial/ethnic prevalence would improve the diagnosis and treatment of migraines, especially for minority populations. Further comprehensive studies are required to draw a more accurate conclusion.

4. Research questions and hypotheses

The aim of this research is to analyze the trend of migraine prevalence in the US adult population in 2010-2015 and possible causes of the racial/ethnic differences.

4.1. Question 1: How has the prevalence of migraine in the US changed during 2010-2015?

Hypothesis 1: The migraine prevalence has been steadily increasing during the six years, both in the overall population and individual races/ethnicities.

4.2. Question 2: Did the migraine prevalence differ among races and ethnicities?

Hypothesis 2: There were racial/ethnic differences in migraine prevalence.

4.3. Question 3: What could be the causes of the racial/ethnic differences in migraine?

Hypothesis 3: Possible causes of the differences may be found from sociodemographic characteristics, medical care quality, comorbidities and precipitating factors of migraine.

The following chapters will provide background information on migraine, methods used in this study, results obtained from the analyses, and lastly, discussion of the outcomes.

CHAPTER 2: BACKGROUND

This chapter includes sections of global burden, clinical manifestations, pathogenesis, diagnosis, treatment, and contributing factors of migraine, as well as gaps in knowledge and objectives of this study.

1. Global burden of migraine

Repeated headaches, and often the fear of the next attack, can affect patients' life quality and job performance. This section reviews the burden of migraine from recent reports worldwide.

Migraine was the seventh leading cause of global Years Lived with Disability (YLDs) in 2015, with its worldwide prevalence increasing from 14.0% to 16.6% during the decade 2005-2015; it also ranked eighth among the top causes of YLDs in the United States. [5] From 2007 to 2015, reported migraine prevalence ranged from 11.7% to 22.7% in the US. [2][4][6][7] The American Migraine Prevalence and Prevention study published in 2009 calculated the average per-person annual total costs of migraine (including indirect costs such as lost productivity) to be $7750 for chronic migraine sufferers, and $1757 for episodic migraineurs (those people who experience migraines) in the US. [8] These costs amounted to a total loss of $78 billion in 2014. [9] In addition, migraine was related to 5.4-5.7 excess sickness absence days per person-year among working or student migraineurs, [10] [11] and it increased the excess risk when co-occurring with depression or respiratory disorders. [11] Another study involving eight European countries estimated that the mean annual cost of migraine was €1222 per person, equivalent to a loss of

€111 billion each year for the whole adult population of the European Union (64% of the total annual economic burden of headache disorders). [12]

In short, the burden of migraine is noteworthy worldwide, and cannot be ignored.

2. Clinical manifestations of migraine

This section describes clinical classification and presentation of migraine.

2.1. Migraine with aura (MA, Classic migraine)

In 15-20% of patients, migraine is preceded by visual (most common), sensory, or other neurologic symptoms, called aura. [1] The headache is often but not always unilateral, and tends to have a pulsatile or throbbing quality. In most patients, the frequency of headache is no more than once a week, and the duration varies from 2 hours to 1 day. [1] Recent prospective data suggested that migraine headache could also happen during the aura phase. [17] When the headache occurs, it is often accompanied by nausea, vomiting, photophobia, phonophobia, and/or lassitude. [1]

2.2. Migraine without aura (MO, Common migraine)

Migraine without aura is much more common than migraine with aura, and the headache is most often on both sides of the head or prominent around the eye. Nausea, vomiting, photophobia and

muscle contraction in the neck are commonly seen. If untreated, the headache usually lasts for 4-72 hours and is occasionally terminated by vomiting. [1] Resting in a dark, quiet room during the headache is preferred, and many attacks are resolved in sleep.

2.3. Chronic (Transformed) migraine

In fewer cases, episodic migraine with or without aura can transform over months to years into a chronic migraine.[1] Chronic migraine is defined as headaches occurring 15 or more days a month for more than three months, with the features of migraine on at least eight days a month.[18]

In summary, the classic manifestation of migraine with aura is easily identified, but is less common than migraine without aura; both can transform into chronic migraine, which is infrequently seen but causing more suffering and burden.

3. Pathogenesis

This section provides an overview of the mechanism of migraine development.

Contraction of blood vessels within the skull (intracranial vasoconstriction) and dilation of blood vessels outside the skull (extracranial vasodilation) were once believed to be the respective causes of the aura and the headache phases of migraine, [19] [20] but this theory is no longer

considered viable. [21] [22] [23] [24] Recent studies suggest that a primary disturbance of central neuronal activity may be responsible for both aura and headache. [21]

Cortical spreading depression is a slow wave of neuronal and glial depolarization (a dramatic electrical change) that spreads across the cerebral cortex. [25] [26] It is hypothesized to cause the aura of migraine [27] and activate the sensory part of the trigeminal nerve. [28] [29] The activation of trigeminal nerve in turn results in release of vasoactive neuropeptides, including substance P, calcitonin gene-related peptide, and neurokinin A, [30] which causes sterile inflammation in the pain-sensitive meninges that produce the headache of migraine. [31] Serotonin may also play a role in migraine pathophysiology, but the mechanism is still unclear. [32]

Overall, more and more research is revealing the central neuronal activity itself and the resulting neurogenic inflammation as a possible pathogenesis of migraine.

4. Diagnosis of migraine

This section describes the diagnostic criteria for migraine specified by the International Classification of Headache Disorders, 3rd edition (ICHD-3). [18]

4.1. Migraine without aura (MO)

ICHD-3 diagnostic criteria for migraine without aura (MO) [18] are as follows:

A) At least five attacks fulfilling criteria B through D.

B) Headache attacks lasting 4 to 72 hours (untreated or unsuccessfully treated).

C) Headache has at least two of the following characteristics: (1) Unilateral location; (2) Pulsating quality; (3) Moderate or severe pain intensity; or (4) Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs).

D) During headache at least one of the following: (1) Nausea, vomiting, or both; (2) Photophobia and phonophobia.

E) Not better accounted for by another ICHD-3 diagnosis.

4.2. Migraine with aura (MA)

ICHD-3 diagnostic criteria for migraine with aura (MA) [18] are as follows:

A) At least two attacks fulfilling criterion B and C.

B) One or more of the following fully reversible aura symptoms: Visual, Sensory, Speech and/or language, Motor, Brainstem, or Retinal.

C) At least two of the following four characteristics: (1) At least one aura symptom spreads gradually over ≥5 minutes, and/or two or more symptoms occur in succession; (2) Each individual aura symptom lasts 5 to 60 minutes; (3) At least one aura symptom is unilateral; (4) The aura is accompanied, or followed within 60 minutes, by headache.

D) Not better explained by another ICHD-3 diagnosis, and transient ischemic attack is excluded.

Therefore, physicians should take multiple criteria into consideration when diagnosing migraine.

5. Treatment

Currently, two approaches to migraine treatment are used: prevent the attacks, or relieve the symptoms during the attacks.

5.1. Preventive treatment

Migraine prevention, aimed to reduce frequency, duration, and/or intensity of the headache, is considered more favorable because it results in less dysfunction and improves quality of patients' life. According to the latest guideline from the American Academy of Neurology and the American Headache Society (AAN/AHS), the following medications are proved to be effective for migraine prevention: divalproex sodium, sodium valproate, topiramate, metoprolol, propranolol, and timolol (Level A). [33]

5.2. Acute treatment

Acute treatment is most likely to benefit patients at the first sign of a migraine attack (e.g., when aura or pain begins). Analgesics (such as nonsteroidal anti-inflammatory drugs and acetaminophen) are first choice drugs for mild to moderate migraines, because they are cost-effective and less likely to cause adverse effects than migraine-specific agents. For moderate to severe attacks, migraine-specific agents are first-line, including triptans and ergots. An antiemetic drug (anti-nausea medication) can be used in combination with the above treatment for those patients with nausea or vomiting. [34] [35]

Although there are some anti-migraine medications available, it is essential to use them according to clinicians' instructions. People should avoid overusing the drugs, especially acute

medications, since they have the potential for causing medication overuse headaches (MOH), also called rebound headaches. [18] [36]

6. Contributing factors

Contributing factors are those that may influence occurrence of migraine and that may be responsible for racial/ethnic differences in migraine prevalence. This section reviews these factors in terms of genetics, sociodemographic characteristics, comorbidities of migraine, and precipitating factors of migraine.

6.1. Genetics

Susceptibility to migraine is strongly influenced by genetics. A family history of migraine in at least one first-degree relative is present in most cases, [37] [38] [39] and twin studies demonstrate the involvement of both genetic and environmental factors. Autosomal dominant inheritance of migraine occurs in several rare but well-recognized syndromes, including familial hemiplegic migraine (mutations identified in three FHM genes: *CACNA1A*, [40] *ATP1A2* [41] and *SCN1A* [42]) and cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL, by mutation in *Notch 3* gene). [43]

6.2. Sociodemographic characteristics

6.2.1. Age and sex

According to clinical observations, people of all age groups can suffer from migraine, but its onset is usually early in life: approximately 25% of cases begin during the first decade, 55% by 20 years of age, and more than 90% before age 40. [1] The prevalence peaks in middle life and is

lower in adolescents as well as those older than 60 years. [2] Two-thirds to three-fourths of cases of migraine occur in women. [1] [2] [3]

6.2.2. Marital status

Results in relation to marital status and migraine have been various and even contradictory. Scher et al. proposed that chronic migraine cases were more likely to be previously married (divorced, widowed, or separated) than married individuals, but no difference was found between married and never married.[14] Wöber et al. also found the divorced population to have a positive association with migraine prevalence compared to those who never experienced divorce.[44] Similarly, Adoukonou et al. divided subjects into single and married/widowed status, and concluded the latter was correlated with higher migraine prevalence.[45] Some other studies observed the hierarchy of migraine prevalence over marital status, in which divorced or widowed individuals had the greatest association with migraine, followed by married people, and single persons came in last.[46] [47] In addition, a population-based door-to-door survey in Turkey found that housewives accounted for the highest proportion of migraine sufferers.[48]

However, marital status was not associated with migraine according to population-based studies in Sweden [49] and in Denmark. [50]

6.2.3. Education level

Stang and Osterhaus reported a higher prevalence of migraine in highly educated subjects. [51] However, Scher et al. concluded that chronic migraine was more common in those with less

education, and remission was positively associated with increased educational levels. [14] Such results were also seen in Spain and Germany. [47] [52] In Sweden, Bingefors and Isacson found that low educational level was associated with headaches in men only. [53] On the contrary, the Turkish survey discovered that migraine was more prevalent in men with higher education. [48] Another study in Sweden showed that there was only a modest association between educational level and headache disorders. [49]

Studies in Brazil and Iran did not find the association between education and migraine significant. [46] [54] Education was not associated with MA in discordant twin-pairs. [50]

6.2.4. Income and poverty

Many studies showed that migraine prevalence was inversely related to household income: people with lower income are more likely to suffer from migraine. [13] [46] [47] [55] [56] Bingefors and Isacson noticed that economic difficulties were associated with headache only in women. [53] Still, some research found no association between income level and migraine prevalence. [54] [57]

Some other researchers noted no correlation between migraine and sociodemographic factors other than age and gender. The cross-sectional study conducted by Rasmussen did not find that any of the sociodemographic variables, namely marital status, educational level, occupational category or employment status, were significantly associated with migraine. [58]

In summary, age and sex have strong correlations with migraine, but there is no concrete association for other sociodemographic factors. These contradictory findings may be affected by sample representability and heterogeneity across different countries and regions worldwide.

6.3. Medical care quality factors

3 steps are necessary to achieve adequate medical care for migraine: (1) appropriate medical consultation; (2) an accurate diagnosis of migraine; and (3) an effective treatment regimen. [59]

Any factors affecting this multi-step process can become barriers to high-quality migraine care and prevention. These factors may include: understanding of the health care process, trust in the medical community, willingness to seek treatment, language barriers, lack of insurance, affordable coverage, care visit rate, diagnostic accuracy, and types of prescribed drugs.

For example, Dodick et al. identified 4 predictors of whether a migraine patient will consult a healthcare professional: age, having health insurance, greater migraine-related disability, and more severe migraine symptoms. [60] Lipton et al. also found that among those consulters, women were far more likely to be diagnosed with migraine than men, suggesting that gender bias in diagnosis may be an important barrier for men. [59] In addition, both overuse of acute migraine medication and ineffective acute treatment of episodic migraine were associated with an increased risk of new-onset chronic migraine. [52] [61]

6.4. Comorbidities of migraine

Comorbidity refers to the greater than coincidental association of separate conditions in the same individuals. [58] Depression and anxiety, obesity, hypertension and dyslipidemia are frequently seen as comorbidities of migraine according to previous data.

6.4.1. Depression and anxiety

Breslau et al. observed significant bidirectional relationships between major depression and migraine. [63] [64] That is, migraine predicts first-onset depression and depression also predicts first-onset migraine. Fernández-de-Las-Peñas et al. also found that depression was positively related to migraine. [47] A large cross-sectional population-based study in Norway revealed that depression and anxiety disorders were both significantly associated with migraine. [65] The association was stronger for anxiety disorders than for depression, [65] [66] and the odds ratios both increased as the headache frequency increased. [65]

6.4.2. Obesity

Body Mass Index (BMI) is defined as the body mass divided by the square of the body height (kg/m^2). BMI under 18.5 is considered underweight, 25.0-29.9 suggests overweight, and obesity is defined by BMI of 30.0 or over. [67] A positive correlation between obesity and migraine has been noted. [14] [47] [49] [68] [69] Bigal et al. concluded that BMI category was not associated with migraine prevalence, but was associated with the frequency of headache attacks: as the degree of obesity went up, it was more likely for the individual to have more headache days per month as the normal weight group. Also, the proportion of subjects with severe headache pain increased

with BMI. [70] In addition, May and Schulte suggested that obesity along with depression was one of the most important modifiable risk factors for chronic migraine. [52]

6.4.3. Hypertension and dyslipidemia

In the multivariable-adjusted regression analyses performed by Goulart et al., an inverse association between hypertension and migraine was confirmed for men, but not for women. By contrast, a positive association between migraine and dyslipidemia was observed only in women, but not in men. [71]

6.5. Precipitating and exacerbating factors of migraine

A precipitating and exacerbating factor of migraine, also known as a migraine trigger, is defined as any factor that on exposure or withdrawal can lead to the development of an acute migraine headache. [72] Avoidance of such trigger factors within migraine patients may alleviate or prevent their suffering from headaches.

In a retrospective study completed by Kelman, about 75% of the migraine patients reported at least one trigger. [73] In order of descending frequency, these factors included: stress, hormones in women, not eating, weather, sleep disturbances, perfume or odor, [58] neck pain, light(s), alcohol, smoke, sleeping late, heat, food, exercise, and sexual activity. Spierings et al. summarized similar results. [74]

Stress is generally considered to be a trigger of migraine. Stressful life events have been identified as risk factors for developing chronic migraine, too. [52] Adoukonou et al. also mentioned that psychological tiredness was the most frequent triggering factor of migraine. [45] Nevertheless, Nazari et al. failed to demonstrate the relation between stress and migraine headaches. [54]

For women, sex hormones remarkably influence susceptibility to migraine. Menstruation is one of the most significant risk factors, and the majority of female migraineurs experience attacks of menstrual migraine, more frequently without aura. [75] [76] In both forms of migraine with and without aura, pregnancy had a favorable effect, especially for migraine without aura. [76] [77] [78] While the use of oral contraceptives worsened both forms of migraine during the hormone-free interval, migraine with aura was particularly exacerbated. [76] [79] [80] Martin et al. also found that the risk of high frequency headache is increased in women during perimenopause compared to premenopause. [81]

Poor sleep quality is uniquely associated with episodic migraine. [47] [82] Vlajinac et al. reported that irregular eating, sleep hours shorter than usual, and smoking more than 10 cigarettes per day had a significant relation with migraine. [83] The National Sleep Foundation has recommended sleep time duration for different age groups. [84] For young adults aged 18-25 years, 7-9 hours of sleep was recommended; 6 hours or 10-11 hours may be appropriate; less than 6 or more than 11 hours were not recommended. These numbers were similar for adults 26-64 years old, except that more than 10 hours of sleep was not recommended. The expert panel recommended 7-8

hours of sleep for the elderly (≥65 years old), adding that less than 5 or longer than 9 hours of sleep was not recommended.

Alcohol drinking and smoking showed varying correlation with migraine in the previous research. Fernández-de-Las-Peñas et al. noticed that ex-smokers were less likely to suffer from migraine than smokers or non-smokers, and alcohol consumption was negatively associated with migraine. [47] Wöber et al. and Aamodt et al. also revealed the negative association between alcohol use and migraine, but current smokers or even second-hand smokers were found to be more likely to have migraine than non-smokers.[44] [85] Another earlier conducted cross-sectional study showed no associations between headache disorders and smoking or alcohol. [58]

Noise was also noted as another precipitating factor of migraine. [48] In addition, Murdin et al. found that induced vertigo could act as a migraine trigger. [86]

In sum, many factors may be involved in migraine, which render the analysis very complicated.

7. Gaps in knowledge and study objectives

This last section explains the remaining gaps in knowledge and my study goals set accordingly.

Differences in migraine prevalence among races and/or ethnicity are not fully understood. Since evidence exists that Caucasians and African Americans responded equally well to treatment in headache specialty clinics, [87] Loder and Sheikh supposed that Blacks might be less likely to seek medical care for migraine than Whites. [15] Underdiagnoses might have also occurred in Hispanic people. [15] However, the lower migraine prevalence in Asians compared to the other races remained unexplained. Without sufficient information, it is difficult to determine how much of the association is genetic or environmental.

The purpose of this study is to visualize the trend of migraine prevalence in the United States, identify possible racial/ethnic differences in the prevalence of migraines, and explore the causes using the contributing factors discussed above. This unprecedented research will provide some new insights into racial predisposition, personalized prevention and individualized treatment of migraine, eventually contributing to improved health care.

CHAPTER 3: METHODS

This is a longitudinal and cross-sectional study using the data from the National Health Interview Survey. The trend of migraine prevalence from 2010 to 2015 was assessed. Age and sex adjusted racial/ethnic prevalence of migraine was compared with different factors. Interactions between race/ethnicity and individual variables were also analyzed to determine the impacts of these factors specifically on race or ethnicity.

1. Data sources and subjects

The most recently released 2015 National Health Interview Survey (NHIS) was used in this study to analyze the racial differences in migraine prevalence among adults (age ≥ 18 years) in the United States. Data from 2010 to 2014 were also extracted to assess the annual trend of age and sex adjusted prevalence of migraine in the adult population.

The National Health Interview Survey (NHIS) is a large-scale, cross-sectional, personal household interview survey annually conducted by the National Center for Health Statistics (NCHS), a part of the Centers for Disease Control and Prevention (CDC). The survey collects data on a broad range of health topics from a nationally representative sample of the civilian non-institutionalized population residing in the United States. It is widely utilized for diverse purposes such as evaluating current health problems in the US population, monitoring the trend of diseases and disabilities, identifying disparities in health care and their causes, and tracking the progress towards national health objectives. [88]

Six dataset files were included in each of 2010-2015 NHIS data releases: Family, Household, Injury Episode, Person, Sample Adult, and Sample Child. Certain supplementary files were provided for specific year(s). For this study, the 2015 Sample Adult file was the main dataset, with a sample size of 33,672, which approximately represented the US adult population of 242,500,657 in 2015.

2. Sample design and data collection

According to the official website of the NHIS, a multistage area probability design is currently adopted, which is a sample of clusters of addresses located in primary sampling units (PSUs, including single counties, groups of adjacent counties or equivalent areas, and metropolitan cities) from each state and the District of Columbia. [89]

NHIS drew certain numbers of PSUs within geographical and racial/ethnic strata. One civilian adult per family was randomly selected, and asked to self-report his/her responses to questions. Face-to-face interviews were performed in interviewees' houses, with possible telephone follow-ups conducted afterwards. Upon the respondent's request or in case of travel difficulty, telephone interviews could be opted for instead.

There was no oversampling in any racial or ethnic groups at the household level; but within the same household, individuals aged 65 or above who are Black, Hispanic, or Asian had a higher chance of being selected. [89] Base weights for each individual were calculated by multiplying

reciprocals of the probability of being selected at every sampling stage. The base weights were then adjusted for non-response, and ratio-adjusted to create final sampling weights. Final weights were also adjusted according to a quarterly post-stratification by age, sex, race or ethnicity classes based on population estimates provided by the U.S. Census Bureau. [90]

3. Measurements

Variables in 3 datasets from the 2015 NHIS were selected for the analysis in this study (Table 1). Variables for migraine prevalence, race and ethnicity, age and sex from the 2010-2014 NHIS Sample Adult files were also used to obtain the annual trend of age and sex adjusted racial/ethnic prevalence of migraine. Table 2 summarizes the identified variables and their characteristics.

Table 1. Selected datasets and information from 2015 NHIS

Dataset name	Selected variable information
2015 Sample Adult file	Migraine prevalence, Age, Sex, Race, Ethnicity, Marital status, Depression and Anxiety, Obesity, Hypertension, High cholesterol, Sleep hours, Trouble falling asleep, Trouble staying asleep, Taking sleep medications, Neck pain, Low back pain, Pain in jaw/front ear, Alcohol drinking, Smoking
2015 Person file	Education level, Insurance coverage, Medical bill payment problems, English proficiency
2015 Family file	Poverty

3.1. Dependent variable (outcome)

Migraine prevalence was assessed from the self-reported answers to the question "During the past three months, did you have severe headache or migraine?" (Variable AMIGR). Respondents were considered as suffering from migraine if they answered yes to the question. Responses of "refused", "don't know" and "not ascertained" were seen as missing values. This variable was recoded to a new dichotomous variable called "migraine".

3.2. Independent variables (predictors)

Race and ethnicity are the primary independent variables in this study. Other predictors identified from the dataset include sociodemographic characteristics, medical care quality factors, comorbidities and triggers of migraine. Variables are taken into the model according to the order: from the most long-lasting, indirect factors to the most recent, direct contributors.

3.2.1. Primary independent variables

- **Race:** Variable RACERPI2 recorded racial identity. There were 6 answers to choose from: White only, Black/African American only, AIAN (American Indians and Alaska Natives) only, Asian only, Race group not releasable, and Multiple race. Native Hawaiians and other Pacific Islanders, as well as those who did not disclose their racial identity, were defined as "Race group not releasable" in the dataset.
- **Ethnicity:** Variable HISPAN_I asked about the respondent's Hispanic origin.

The above two variables were combined to generate the following new dichotomous variables: Non-Hispanic White, Hispanic White, Black, Asian, Multiracial, and AIAN.

3.2.2. Sociodemographic characteristics

- **Age:** AGE_P was a continuous variable ranging from 18 to 85, which has been classified into 4 age subgroups according to population estimates by the U.S. Census Bureau (18-24; 25-44; 45-64; 65+). [91]
- **Gender:** Variable SEX recoded the gender of the respondent. It was recoded into a dichotomous variable "Female".

- **Marital status:** Variable R_MARITL gave details of the respondent's marital status, which could be grouped into 3 categories: No marriage (including those who never married and those who are living with partners), Marriage with adverse events (divorce, separation or death of spouse), and Marriage without adverse events.
- **Education level:** The highest level of school completed was documented in the variable EDUC1. It was simplified into 5 levels, and also recoded into a dichotomous variable "H_Edu" which suggested higher education (Bachelor's degree or above).
- **Poverty:** Variable RAT_CAT4 was the ratio of family income to national poverty threshold. The value 1.00 or below was deemed as poverty. It was recoded into a new dichotomous variable "Poverty".

3.2.3. Medical care quality factors

- **Insurance coverage:** Variable NOTCOV was the respondent's self-report of coverage status. It was recoded into a dichotomous variable "NoCoverage"; value of 1 means uninsured, and value of 0 suggests having insurance coverage.
- **Problems in paying medical bills:** Variable MEDBILL was the answer to the question "In the past 12 months did you have problems paying or were unable to pay any medical bills? Include bills for doctors, dentists, hospitals, therapists, medication, equipment, nursing home or home care." It was recoded into a dichotomous variable "Med_bill", with the value of 1 meaning having medical bill payment problems.
- **English proficiency:** Variable ENGLANG was the respondents' self-assessment of how well their English was spoken. There were four types of valid answers: Very well, Well, Not well, and Not at all. English proficiency was identified from the

respondents who answered “Very well” and “Well”. This was recoded into a new dichotomous variable “Eng_prof”.

3.2.4. Comorbidities of migraine

- **Depression/anxiety/emotional problem causes difficulty with activity:** Variable AFLHCA17 was the respondent’s self-report of severe depression, anxiety or emotional problems that caused difficulty with activity. It was recoded into a dichotomous variable “DA_problem”.
- **Obesity:** BMI under 18.5 is considered underweight, 25.0-29.9 suggests overweight, and obesity is defined by BMI of 30.0 or over. [67] Respective dichotomous variables were created according to the above categories.
- **Hypertension:** Variable HYPEV meant having hypertension, as the response to the question “Have you ever been told by a doctor or other health professional that you had hypertension, also called high blood pressure?” It was recoded into a dichotomous variable “HTN”; the value of 1 means yes, and 0 is no hypertension.
- **High cholesterol:** Variable CHLEV recorded the answers to the question “Have you ever been told by a doctor or other health professional that you had high cholesterol?” The recoded variable “HCh” suggests high cholesterol status when the value is 1.

3.2.5. Triggers of migraine

- **Sleep hours:** Variable ASISLEEP was the respondents’ input of average sleep hours they get in a 24-hour period. According to the National Sleep Foundation’s sleep time

duration recommendations, [82] it was classified into 3 categories: Inadequate sleep (<6 hours for age 18-64, and <5 hours for age 65+), Appropriate sleep (6-11 hours for age 18-24, 6-10 hours for age 25-64, and 5-9 hours for age 65+) and Excessive sleep (>11 hours for age 18-24, >10 hours for age 25-64, and >9 hours for age 65+).

- **Trouble in falling asleep:** Respondents were asked "In the past week, how many times did you have trouble falling asleep?" Any specific amounts other than 0 were classified as having trouble in falling asleep.
- **Trouble in staying asleep:** Similar to "Trouble in falling asleep", the variable ASISLPST gave how many times the respondent had trouble staying asleep during the past week. It was recoded into a dichotomous variable "Trouble_staying_asleep".
- **Sleep medication usage:** Variable ASISLPMD was the answer to the question "In the past week, how many times did you take medication to help you fall asleep or stay asleep?" Any number greater than 0 was considered as a positive answer. It was recoded into a dichotomous variable "sleep_medication".
- **Pain:** Variables PAINECK, PAINLB, and PAINFACE recorded that respondents had neck pain, low back pain, or pain in jaw/front of ear in the past 3 months, respectively. Each of them was recoded into corresponding dichotomous variables.
- **Alcohol drinking:** Variable ALCSTAT demonstrated the respondent's alcohol drinking status, which could be classified into three categories: Lifetime abstainer, Former drinker and Current drinker. They were all recoded into dichotomous variables.
- **Smoking:** Similar to drinking status, variable SMKSTAT2 summarizes smoking status, and it could be grouped into Non-smoker, Former smoker and Current smoker.

3.3. Other variables

- Household Number (HHX), Family Number (FMX), and Personal Number (FPX) were uniquely combined for each respondent. These assigned numbers were used to identify individuals and to merge separated datasets from the same year with different aspects of information.
- Pseudo-stratum (STRAT_P) and Pseudo-PSU (PSU_P) were pseudo-levels or simplified versions of the true stratum and Primary Sampling Units variables used in the NHIS sample design. Final annual weight in the Sample Adult file (WTFA_SA) was used as the weight variable.
- A variable for standardized age and sex weight (AS) was created for standardization and adjustment with the corresponding standard weight variable (std_wgt) calculated from the 2015 U.S. Census data.

4. Statistical Analysis

4.1. Statistical software

Stata 14 (StataCorp LP, College Station, TX) was used to perform all statistical analyses.

4.2. Data preparation

4.2.1. Merging datasets

Household Number (HHX), Family Number (FMX), and Personal Number (FPX) were used to identify individuals across the different datasets of the same interview year. These variables were

combined to merge Sample Adult file, Person file and Family file of the 2015 NHIS to incorporate all the variables necessary for analysis.

4.2.2. Variance estimation

Pseudo-stratum (STRAT_P), Pseudo-PSU (PSU_P) and Final annual weight in the Sample Adult file (WTFA_SA) were designed variables required for variance estimation. All the quantitative values including means and proportions, 95% Confidence Intervals (CIs), and adjusted odds ratios (aORs) are adjusted by variance estimation and stratification of age and sex to project the results to the whole US adult population level.

4.3. Statistical tests

The yearly trend of migraine prevalence was analyzed by linear regression. Chi-squared tests were conducted to compare prevalence among different categorical groups. Bonferroni correction was used to calculate the P value for multiple comparisons. Variables significantly associated with migraine in univariate analyses were subjected to multivariate analysis. Multivariable logistic regressions were performed to evaluate the association between migraine prevalence and individual predictors, as well as to explore the interactions between race/ethnicity and associated factors. Associations with P values less than 0.05 were considered statistically significant.

Table 2. Variable summary, 2015 NHIS

Variable	Original name	Variable type	Description	Recoded name(s)
Household number *	HHX	Discrete	Specific number assigned for each household	-
Family number *	FMX	Discrete	Assigned family number within household	-
Person number *	FPX	Discrete	Assigned person number within family	-
Weight φ	WTFA_SA	Continuous	Final annual weight	-
Stratum φ	STRAT_P	Discrete	Pseudo-stratum for file variance estimation	-
Primary sampling units φ	PSU_P	Discrete	Pseudo-PSU for file variance estimation	-
Migraine prevalence	AMIGR	Dichotomous	Had severe headache/migraine in past 3 months	Migraine
Age	AGE_P	Continuous	Age	Age1, Age2, Age3, Age4
Sex	SEX	Dichotomous	Sex	Female
Race	RACERPI2	Categorical	Self-identified race	White, Black, Asian, Multiracial, AIAN
Hispanic ethnicity	HISPAN_I	Categorical	Hispanic subgroup detail	Hispanic
Marital status	R_MARITL	Categorical	Marital status	No_marriage, Marriage_Adverse
Education level	EDUC1	Ordinal	Highest level of school completed	Education, H_Edu
Poverty	RAT_CAT4	Continuous	Ratio of family income to poverty threshold	Poverty
Insurance coverage	NOTCOV	Dichotomous	Medical insurance coverage status	NoCoverage
Medical bill payment	MEDBILL	Dichotomous	Problems paying medical bills	Med_bill
English proficiency	ENGLANG	Ordinal	The extent of speaking English well	Eng_prof
Depression and Anxiety	AFLHCA17	Dichotomous	Depression/anxiety/emotional problem causes difficulty with activity	DA_problem
Obesity	BMI	Continuous	Body Mass Index	BMI_recoded, Underweight, Normal_BMI, Overweight, Obese
Hypertension	HYPEV	Dichotomous	Ever been told you have hypertension	HTN
High cholesterol	CHLEV	Dichotomous	Ever told you had high cholesterol	HCh
Sleep hours	ASISLEEP	Continuous	Average hours of sleep	Sleep_hours, Inadequate_sleep, Excessive_sleep
Trouble falling asleep	ASISLPFL	Discrete	# times having trouble falling asleep, past week	Trouble_falling_asleep
Trouble staying asleep	ASISLPST	Discrete	# times having trouble staying asleep, past week	Trouble_staying_asleep
Sleep medication usage	ASISLPMD	Discrete	# times taking medication for sleep, past week	Sleep_medication
Neck pain	PAINECK	Dichotomous	Had neck pain in the past 3 months	Neck_pain
Lower back pain	PAINLB	Dichotomous	Had low back pain in the past 3 months	Low_back_pain
Pain in jaw/front ear	PAINFACE	Dichotomous	Had pain in jaw/front of ear in the past 3 months	Face_pain
Alcohol drinking	ALCSTAT	Categorical	Alcohol drinking status	Alcohol_recode, Former_drinker, No-alcohol, Current_drinker
Smoking	SMKSTAT2	Categorical	Smoking status	Current_smoker

* Used for merging datasets. φ Used in variance estimation.

CHAPTER 4: RESULTS

This chapter summarizes the results of statistical analyses on the prevalence of migraine among different racial/ethnic groups in the United States. The results are divided into the following 8 sections: sociodemographic characteristics and factors of medical care quality; annual trends in age and sex adjusted migraine prevalence from 2010 to 2015; effects on migraine prevalence of individual sociodemographic or medical care quality factors; multivariable logistic regression models on migraine prevalence with race, ethnicity, sociodemographic characteristics, medical care quality and their interactions; distribution of migraine comorbidities and precipitating factors; single effects and multivariable logistic regressions on migraine of comorbidities; individual correlation of adjusted migraine prevalence and precipitating factors; multivariable logistic regressions on racial/ethnic migraine prevalence with precipitating factors.

1. Sociodemographic characteristics and factors of medical care quality

This section presents the sociodemographic characteristics and medical care quality factors among different races and ethnicities, both in the original sample and the projected population.

1.1. Population composition of the original data

The merged dataset consists of information from 33672 adults in the United States (Table 3a). There are 20855 non-Hispanic whites (61.94%), 4976 Hispanic whites (14.78%), 4673 African Americans (13.88%), 1983 Asians (5.89%), 699 multi-racial people (2.08%), and 392 American Indians and Alaska natives (1.16%). Native Hawaiians and other Pacific Islanders, as well as

those who did not disclose their racial identity, were defined as “race group not releasable” in the original dataset, and therefore not separately described in the table (94, 0.27%).

1.1.1. Age and gender

The average age of the total sample population is 49.94 years, and 44.76% of the respondents are male.

1.1.2. Marital status

29.02% of the population never married or are living with partners; 26.98% have experienced divorce, separation or death of spouse. The rest of the population are married without adverse events.

1.1.3. Education level

13.96% have not completed high school education, 24.93% had high school diploma or equivalent, 31.13% went above high school but less than a bachelor’s degree, 18.57% graduated from college, and 11.41% obtained their master’s or doctorate degrees.

1.1.4. Poverty status

15.86% of the respondents were living below the national poverty threshold.

1.1.5. Medical care quality

10.64% did not have medical insurance coverage, and 13.9% reported having problems in paying their medical bills. English proficiency rate was 93.52%. In the projected population, these proportions remained similar, except that the poverty rate turned out to be lower (12.19%).

1.2. Characteristics of the projected population

1.2.1. Age and gender

When observed among races and ethnicities in the projected population (Table 3b), non-Hispanic Whites were older than other groups (49.39 years), and people with 2 or more races were younger (40.84 years). The female proportion was slightly higher in Blacks (55.48%).

1.2.2. Marital status

Over 40% of bi-/multi-racial people, Blacks, American Indians and Alaska Natives have not experienced marriage (47.23%, 43.67%, and 41.42%, respectively), and Blacks also had the highest proportion of divorced, separated or widowed people; while Asians had the highest rate of marriage without adverse events (65.32%) and the lowest rate of adverse marriage (9.89%).

1.2.3. Education level

The proportion of college graduates was highest among Asian respondents (31.10% Bachelor's, 23.07% Master's or Doctor's degrees), followed by non-Hispanic Whites (22.22% Bachelor's,

13.29% Master's or Doctor's degrees); 31.98% of Hispanic Whites completed less than high school level education, which was higher than any other group.

1.2.4. Poverty status

Poverty rate was the highest among American Indians and Alaska Natives (30.82%), followed by African Americans (21.51%) and Hispanic Whites (21.25%).

1.2.5. Medical care quality

25.88% of Hispanic Whites and 22.55% of AIANs had no insurance coverage. Problems in paying bills were most outstanding for bi-/multi-racial people (23.30%), AIANs (22.33%) and Blacks (21.14%). Hispanic Whites had the lowest proficiency in English (71.36% proficient), followed by Asians (83.77%).

Overall, this sample is reasonably representative of the US adult population. Non-Hispanic White and Asian groups showed preferable socioeconomic status and medical care quality compared to other populations in respect to their marital status, highest education level, poverty rate, insurance coverage, and problems in paying medical bills.

Table 3a. Sociodemographic and medical care quality factors among different races and ethnicities, in 2015 sample population

	Overall [φ]	Non-Hispanic White	Hispanic White	Black	Asian	Multi-race	AIAN [θ]
Valid number of cases (%)	33672 (100%)	20855 (61.94%)	4976 (14.78%)	4673 (13.88%)	1983 (5.89%)	699 (2.08%)	392 (1.16%)
Age (Mean ± Standard Deviation)	49.94±18.38	52.36±18.46	43.79±16.93	49.00±17.72	45.49±17.64	44.77±18.05	44.79±17.18
Male %	44.76%	46.00%	43.95%	38.84%	47.86%	43.63%	45.41%
Marital status							
No marriage [Δ]	29.02%	24.20%	33.98%	41.82%	29.13%	43.23%	42.20%
Married without adverse events[§]	44.00%	47.52%	44.43%	25.60%	55.57%	29.54%	34.53%
Married with adverse events	26.98%	28.28%	21.59%	32.58%	15.30%	27.23%	23.27%
Education (highest completed)							
Less than high school level	13.96%	8.26%	35.62%	17.15%	9.91%	13.47%	25.84%
High school level or equivalent	24.93%	24.86%	26.33%	28.10%	16.17%	19.48%	26.10%
Some college	31.13%	32.54%	24.26%	34.60%	20.64%	42.12%	35.66%
Bachelor	18.57%	21.19%	9.62%	12.46%	30.96%	14.33%	9.56%
Master or Doctor	11.41%	13.15%	4.17%	7.70%	22.32%	10.60%	2.84%
Poverty rate[Ψ]	15.86%	10.52%	27.05%	26.03%	15.09%	20.68%	33.33%
Medical care quality							
No insurance coverage	10.64%	6.67%	26.10%	11.06%	8.22%	12.97%	27.76%
Having problems in paying medical bills	13.90%	12.37%	16.55%	19.91%	5.81%	19.89%	19.64%
Proficient in English[ξ]	93.52%	99.42%	69.01%	97.73%	83.41%	95.85%	88.78%

[φ] Native Hawaiians and other Pacific Islanders are not separately listed.

[θ] AIAN = American Indian and Alaska Native.

[Δ] "No marriage" includes those people who never married and those living with partners.

[§] Adverse events include divorce, separation and death of the spouse.

[Ψ] Family income below national poverty threshold.

[ξ] Identified from the respondents who answered "speak English very well" and "speak English well".

Table 3b. Sociodemographic and medical care quality factors among different races and ethnicities, in projected population

	Overall [φ]	Non-Hispanic White	Hispanic White	Black	Asian	Multi-race	AIAN [θ]
Projected number of cases	242,500,657	157,410,009	33,808,062	29,796,462	14,360,121	4,200,090	2,306,663
(% of overall projected)	(100%)	(64.91%)	(13.94%)	(12.29%)	(5.92%)	(1.73%)	(0.95%)
Average age	47.14	49.39	41.18	44.54	44.70	40.84	43.34
Male %	48.20%	48.59%	50.06%	44.52%	47.60%	46.96%	47.00%
Marital status							
No marriage [Δ]	29.33%	24.98%	35.74%	43.67%	24.79%	47.23%	41.42%
Married without adverse events [§]	53.09%	56.63%	50.70%	34.07%	65.32%	36.29%	44.39%
Married with adverse events	17.58%	18.39%	13.56%	22.26%	9.89%	16.48%	14.19%
Education (highest completed)							
Less than high school level	12.58%	7.96%	31.98%	14.76%	10.31%	16.23%	23.50%
High school level or equivalent	24.79%	24.37%	28.22%	28.58%	14.64%	18.47%	25.68%
Some college	31.13%	32.15%	25.95%	35.00%	20.88%	41.99%	36.46%
Bachelor	19.70%	22.22%	9.96%	13.75%	31.10%	11.45%	10.75%
Master or Doctor	11.80%	13.29%	4.19%	7.90%	23.07%	11.86%	3.61%
Poverty rate [Ψ]	12.19%	8.12%	21.25%	21.51%	11.97%	17.96%	30.82%
Medical care quality							
No insurance coverage	10.44%	6.81%	25.88%	12.18%	7.28%	12.79%	22.55%
Having problems in paying medical bills	14.46%	13.01%	17.22%	21.14%	6.34%	23.30%	22.33%
Proficient in English [ξ]	94.14%	99.30%	71.36%	97.88%	83.77%	95.54%	90.00%

[φ] Native Hawaiians and other Pacific Islanders are not separately listed.

[θ] AIAN = American Indian and Alaska Native.

[Δ] "No marriage" includes those people who never married and those living with partners.

[§] Adverse events include divorce, separation and death of the spouse.

[Ψ] Family income below national poverty threshold.

[ξ] Identified from the respondents who answered "speak English very well" and "speak English well".

2. Annual trends in age and sex adjusted migraine prevalence from 2010 to 2015

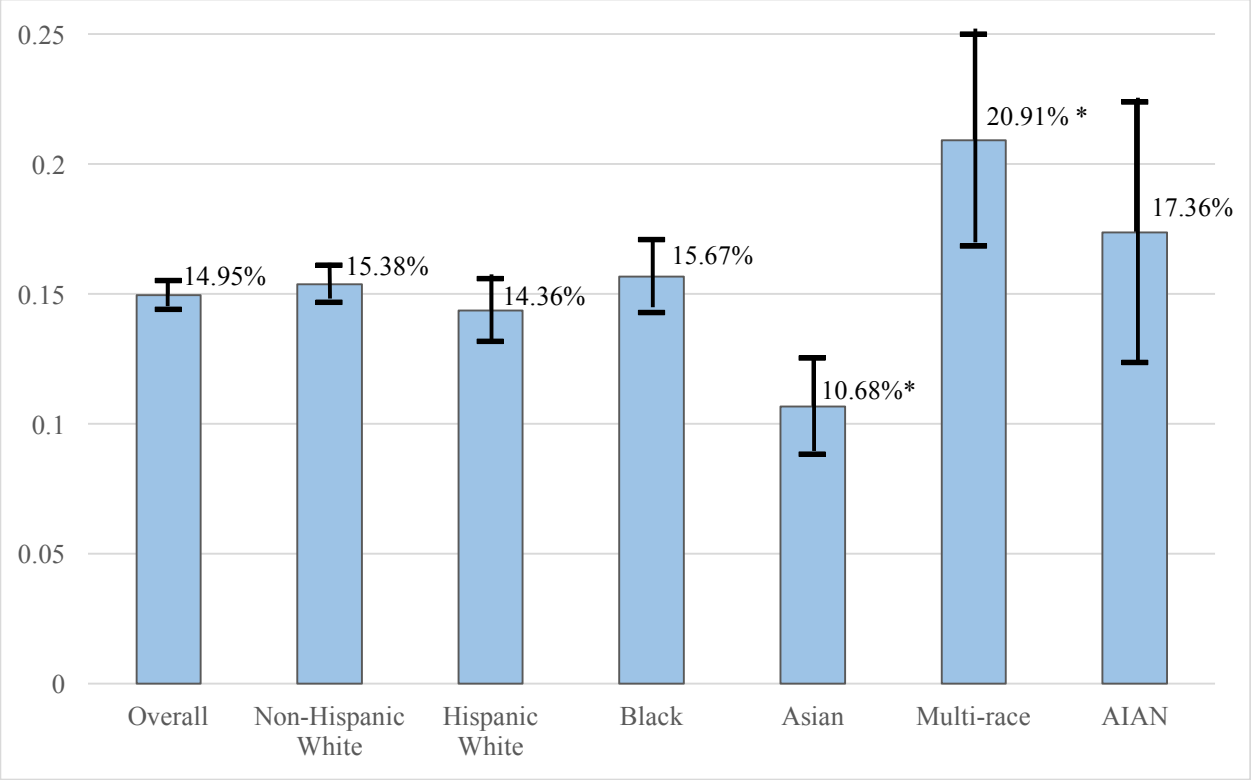
According to the population estimates by the U.S. Census Bureau (Table 4), age and sex adjusted prevalence of migraine by race/ethnicity was calculated (Figure 1).

The overall prevalence in 2015 was 14.95%. 15.38% of non-Hispanic Whites, 14.36% of Hispanic Whites, 15.67% of African Americans, 10.68% of Asians, 20.91% of bi-/multi-racial people, and 17.36% of AIANs reported having migraines. Asians showed the lowest prevalence, and bi-/multi-racial people had higher prevalence compared to non-Hispanic Whites, which is statistically significant. No significant difference was seen among other populations.

Table 4. Population estimates for adult age groups by sex, 2010-2015 US Census Bureau

Year	Age group	Male (% of total)	Female (% of total)	Total
2015	18-24 years	16,008,287 (6.46%)	15,211,605 (6.14%)	31,219,892 (12.60%)
	25-44 years	42,502,715 (17.15%)	42,224,270 (17.04%)	84,726,985 (34.20%)
	45-64 years	41,013,523 (16.55%)	43,052,457 (17.38%)	84,065,980 (33.93%)
	65+ years	21,090,217 (8.51%)	26,670,635 (10.76%)	47,760,852 (19.28%)
	Total	120,614,742 (48.68%)	127,158,967 (51.32%)	247,773,709 (100%)
2014	18-24 years	16,137,577 (6.58%)	15,346,380 (6.26%)	31,483,957 (12.83%)
	25-44 years	42,150,469 (17.18%)	41,931,114 (17.09%)	84,081,583 (34.28%)
	45-64 years	40,743,938 (16.61%)	42,797,012 (17.45%)	83,540,950 (34.06%)
	65+ years	20,331,348 (8.29%)	25,870,382 (10.55%)	46,201,730 (18.83%)
	Total	119,363,332 (48.66%)	125,944,888 (51.34%)	245,308,220 (100%)
2013	18-24 years	16,154,254 (6.65%)	15,373,462 (6.33%)	31,527,716 (12.98%)
	25-44 years	41,805,299 (17.22%)	41,635,722 (17.15%)	83,441,021 (34.36%)
	45-64 years	40,565,830 (16.71%)	42,620,903 (17.55%)	83,186,733 (34.26%)
	65+ years	19,586,266 (8.07%)	25,092,916 (10.33%)	44,679,182 (18.40%)
	Total	118,111,649 (48.64%)	124,723,003 (51.36%)	242,834,652 (100%)
2012	18-24 years	16,072,776 (6.69%)	15,320,887 (6.37%)	31,393,663 (13.06%)
	25-44 years	41,511,694 (17.27%)	41,393,006 (17.22%)	82,904,700 (34.49%)
	45-64 years	40,439,701 (16.82%)	42,493,215 (17.68%)	82,932,916 (34.50%)
	65+ years	18,829,483 (7.83%)	24,331,789 (10.12%)	43,161,272 (17.95%)
	Total	116,853,654 (48.61%)	123,538,897 (51.39%)	240,392,551 (100%)
2011	18-24 years	15,898,872 (6.69%)	15,195,582 (6.39%)	31,094,454 (13.08%)
	25-44 years	41,268,710 (17.35%)	41,222,164 (17.33%)	82,490,874 (34.68%)
	45-64 years	40,401,816 (16.99%)	42,448,658 (17.85%)	82,850,474 (34.84%)
	65+ years	17,933,986 (7.54%)	23,431,979 (9.85%)	41,365,965 (17.39%)
	Total	115,503,384 (48.57%)	122,298,383 (51.43%)	237,801,767 (100%)
2010	18-24 years	15,714,181 (6.68%)	15,052,543 (6.40%)	30,766,724 (13.08%)
	25-44 years	41,108,496 (17.48%)	41,092,731 (17.47%)	82,201,227 (34.95%)
	45-64 years	39,882,964 (16.96%)	41,893,620 (17.81%)	81,776,584 (34.77%)
	65+ years	17,471,973 (7.43%)	23,007,320 (9.78%)	40,479,293 (17.21%)
	Total	114,177,614 (48.54%)	121,046,214 (51.46%)	235,223,828 (100%)

Figure 1. Age and sex adjusted prevalence of migraine by race and ethnicity in 2015



* P<0.05 compared to the migraine prevalence of Non-Hispanic Whites.

Age-adjusted migraine prevalence by sex was also calculated and compared among racial/ethnic subgroups (Figure 2). The highest migraine prevalence was seen in women with 2 or more races (27.91%) and AIAN men (14.82%). Both Asian women and men showed the lowest prevalence of migraines (14.69% and 6.44%, respectively). Female to male ratio of prevalence turned out to be: overall 2.05, non-Hispanic White 2.06, Hispanic White 2.32, Black 1.76, Asian 2.28, bi-/multi-racial 2.06, and AIAN 1.33.

Figure 2. Age-adjusted migraine prevalence by sex, overall and within subgroups

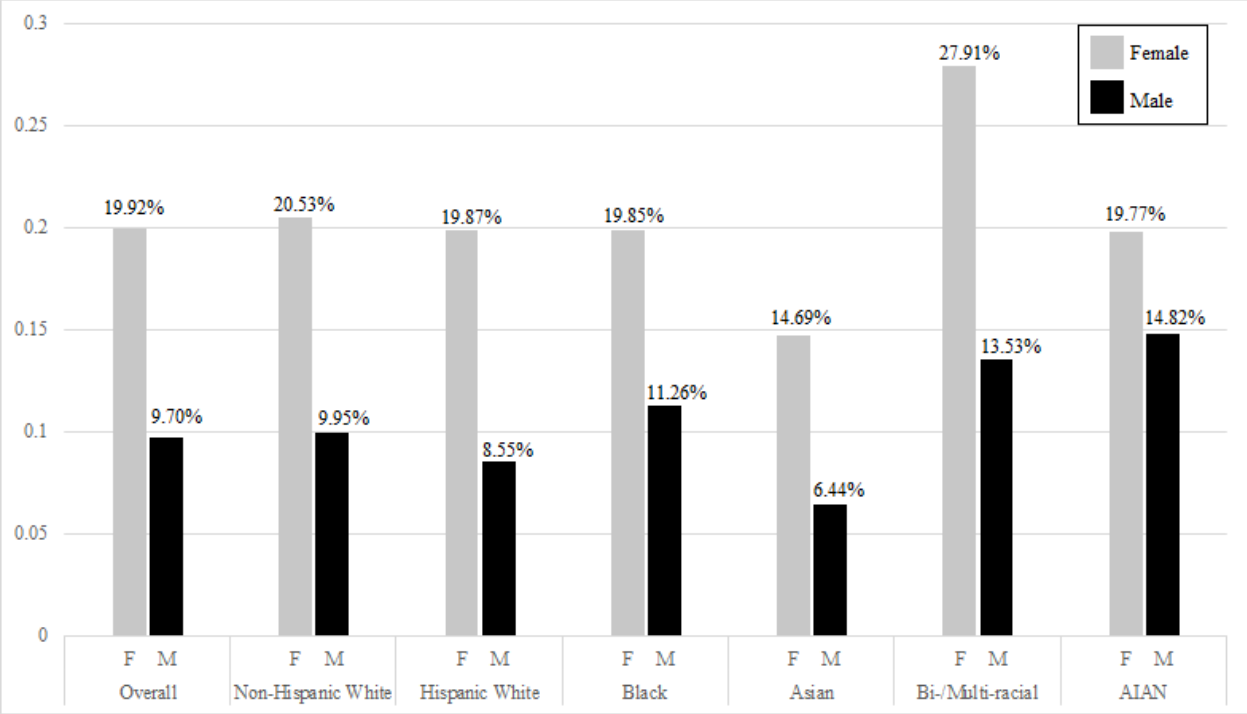


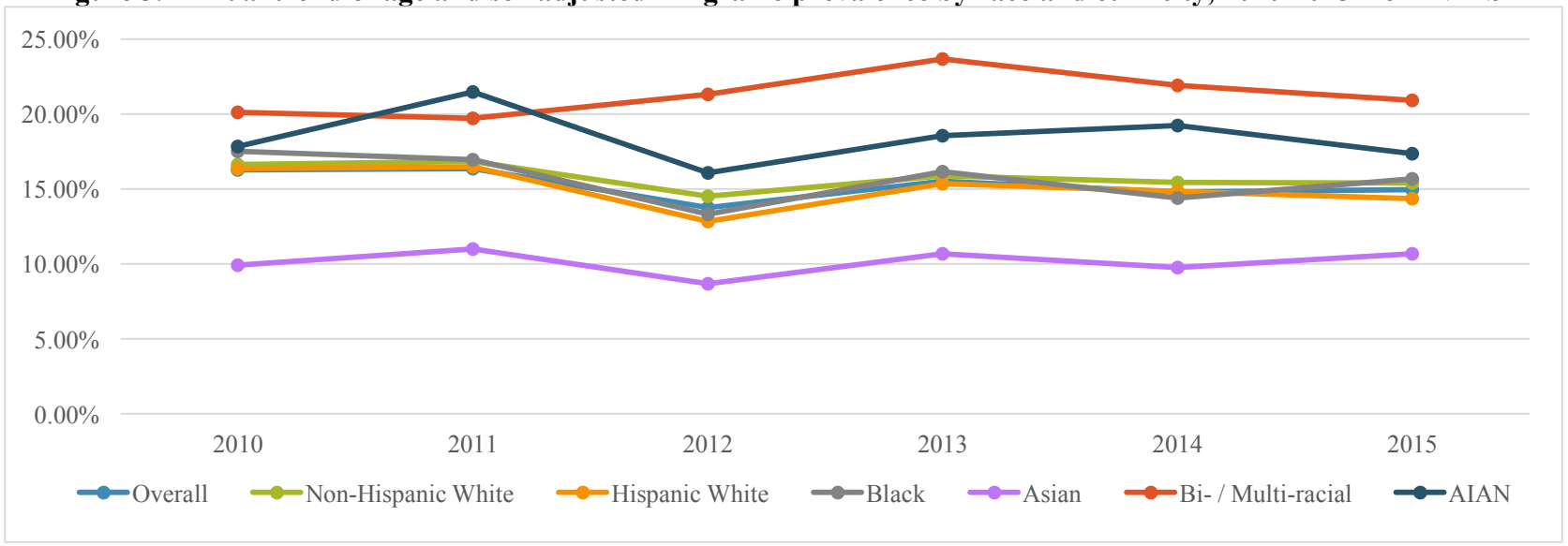
Table 5 and Figure 3 show annual migraine prevalence for overall sample population and each subgroup, between 2010 and 2015. We can see that the numerical values and changing trends of migraine prevalence in Non-Hispanic White, Hispanic White and Black adults were quite similar to each other and very close to the overall prevalence. Multiracial people had the highest prevalence of migraines, and Asians suffered least from migraines in the past 6 years. Although there were some fluctuations, the yearly prevalence of adjusted migraines turned out to be slightly declining, except in multi-racial and Asian populations. However, linear regression revealed no significant changes in any of the subgroups (P=0.292, 0.248, 0.324, 0.340, 0.817, 0.323, and 0.716, respectively). The prevalence line for American Indians and Alaska Natives was seemingly above the non-Hispanic White level every year, but the difference was not statistically significant.

Table 5. Age and sex adjusted migraine prevalence by race and ethnicity, from 2010 to 2015

	2010 % (95% CI*)	2011 % (95% CI)	2012 % (95% CI)	2013 % (95% CI)	2014 % (95% CI)	2015 % (95% CI)
Overall	16.28 (15.76-16.81)	16.34 (15.83-16.84)	13.76 (13.30-14.21)	15.52 (14.98-16.06)	14.79 (14.25-15.33)	14.95 (14.39-15.50)
Non-Hispanic White	16.63 (15.95-17.32)	16.84 (16.17-17.51)	14.51 (13.90-15.12)	15.89 (15.19-16.59)	15.44 (14.71-16.17)	15.38 (14.66-16.10)
Hispanic White	16.36 (15.19-17.53)	16.46 (15.29-17.63)	12.85 (11.70-14.00)	15.34 (14.08-16.61)	14.83 (13.64-16.02)	14.36 (13.15-15.57)
Black	17.50 (16.16-18.83)	16.94 (15.69-18.19)	13.33 (12.23-14.44)	16.14 (14.74-17.55)	14.41 (13.20-15.61)	15.67 (14.26-17.07)
Asian	9.93 (8.28-11.59)	11.01 (9.41-12.62)	8.69 (7.36-10.02)	10.68 (9.04-12.33)	9.75 (8.02-11.48)	10.68 (8.88-12.52)
Bi- or Multi-racial	20.10 (16.60-23.59)	19.70 (15.77-23.63)	21.33 (17.34-25.32)	23.67 (19.78-27.56)	21.93 (17.45-26.40)	20.91 (16.83-24.99)
AIAN [θ]	17.84 (12.59-23.10)	21.48 (16.16-26.79)	16.07 (11.29-20.85)	18.56 (13.60-23.52)	19.24 (13.61-24.87)	17.36 (12.34-22.38)

*CI = Confidence Interval. [θ] AIAN = American Indiahiyou921n and Alaska Native.

Figure 3. Annual trend of age and sex adjusted* migraine prevalence by race and ethnicity, 2010-2015 from NHIS [∂]



*Adjusted according to population estimates from US Census Bureau. [∂] NHIS = National Health Interview Survey.

3. Effects on migraine prevalence of individual sociodemographic or medical care quality factors

The following table shows age and sex adjusted migraine prevalence over each sociodemographic or medical care quality factors, namely age, sex, marital status, education level, poverty, insurance coverage, problems in paying medical bills, and English proficiency. Every odds ratio (OR) was obtained from a logistic regression model adjusted by age and sex.

3.1. **Age**

After adjustment by sex, compared with young adults (18-24 years old), 25-44 year olds had higher migraine prevalence (15.28% vs 18.67%, OR=1.27, P=0.002); the difference between young adults and middle aged people (45-64) was not significant (15.28% vs 15.91%, P=0.747); the elderly (aged 65+) suffered less from migraines (15.28% vs 6.43%, OR=0.35, P<0.001).

3.2. **Gender**

When adjusted by the age group, the odds ratio of having migraines for women is 2.42 against men (19.92% vs 9.70%, P<0.001).

3.3. **Marital status**

In contrast to people with peaceful marriages (14.08%), those without marriage (16.56%, OR=1.24, P<0.001) and with adverse events in marriage (16.77%, OR=1.24, P<0.001) had higher prevalences of migraines.

3.4. **Education level**

When compared to the people with less than high school level education (18.65%), those who held high school diploma or equivalent (14.92%), some college degree (16.46%), bachelor's degree (12.30%) and graduate degree (12.32%) suffered less from migraines (OR=0.74, 0.84, 0.58, and 0.59, respectively; P<0.01).

3.5. **Poverty**

The odds ratio of having migraines for people in poverty is 1.54 (21.61% vs 14.3%, P<0.001).

3.6. **Medical care quality**

Problem in paying medical bills is a positive predictor of migraines (25.74% vs 13.00%, OR=2.37, P<0.001). No statistically significant difference was found in the migraine prevalence between uninsured and insured individuals (16.10% vs 14.83%, P=0.407) and between people who speak English well and those with limited English proficiency (15.01% vs 13.47%, P=0.272).

Overall, migraine prevalence peaks during the ages of 25-44, and then decreases. Female gender, no marriage or adverse marriage, lower education level, poverty, and problems in paying medical bills appear to be positive predictors for migraines.

Table 6. Age and sex adjusted prevalence and odds ratio of migraine over each sociodemographic / medical care quality factors

Factors	Prevalence, % (95% CI)	Odds ratio (95% CI)
Age		
18-24 years	15.28 (13.59-16.98)	1
25-44 years	18.67 (17.65-19.68)	1.27 (1.09-1.47) **
45-64 years	15.91 (14.96-16.85)	1.03 (0.88-1.20)
65 years and above	6.43 (5.77-7.10)	0.35 (0.30-0.42) ***
Sex		
Male	9.70 (8.99-10.40)	1
Female	19.92 (19.08-20.77)	2.42 (2.20-2.67) ***
Marital status		
No marriage[Δ]	16.56 (15.40-17.73)	1.24 (1.12-1.37) ***
Married without adverse events[§]	14.08 (13.17-14.99)	1
Married with adverse events	16.77 (14.84-18.70)	1.24 (1.11-1.38) ***
Education level		
Less than high school	18.65 (17.08-20.22)	1
High school or equivalent	14.92 (13.78-16.05)	0.74 (0.65-0.85) ***
Some college	16.46 (15.54-17.38)	0.84 (0.73-0.95) **
Bachelor	12.30 (11.17-13.44)	0.58 (0.50-0.67) ***
Master or Doctor	12.32 (10.00-14.64)	0.59 (0.51-0.68) ***
Poverty[Ψ]		
No	14.30 (13.64-14.97)	1
Yes	21.61 (20.01-23.20)	1.54 (1.36-1.73) ***
Insurance coverage		
Insured	14.83 (14.23-15.41)	1
Uninsured	16.10 (13.55-18.65)	1.06 (0.92-1.22)
Having problems in paying medical bills		
No	13.00 (12.43-13.57)	1
Yes	25.74 (24.05-27.43)	2.37 (2.14-2.63) ***
Proficient in English[ξ]		
No	13.47 (11.86-15.08)	1
Yes	15.01 (14.43-15.58)	1.09 (0.93-1.27)

** P<0.01; *** P<0.001. CI = Confidence Interval.

[Δ] "No marriage" includes those people who never married and those living with partners.

[§] Adverse events include divorce, separation and death of the spouse.

[Ψ] Family income below national poverty threshold.

[ξ] Identified from the respondents who answered "speak English very well" and "speak English well".

4. Multivariable logistic regression models on migraine prevalence with race, ethnicity, sociodemographic characteristics, medical care quality and their interactions

Step-by-step multivariable logistic regression models were built in order to examine the association of sociodemographic factors on racial/ethnic prevalence of migraines (Tables 7a-7c).

4.1. **Race and ethnicity**

Model 1 started with original comparisons between the non-Hispanic White population and 5 other groups. At first glance Asians had significantly lower migraine prevalence than non-Hispanic Whites (OR=0.72, P<0.01); positive associations with migraines were found in African Americans (OR=1.14, P<0.05) and people with 2 or more races (OR=1.53, P<0.01) compared to non-Hispanic Whites. No significant difference was shown among non-Hispanic Whites, Hispanic Whites and AIANs.

4.2. **Age and gender**

After adjustment by age and sex (Model 2), the difference between African Americans and non-Hispanic Whites was no longer statistically significant.

4.3. **Marital status**

Model 3 included marital status as a new covariate. Both “No marriage” (OR=1.22, P<0.001) and “Adverse marriage” (OR=1.22, P<0.01) showed positive correlation with migraine

prevalence. Model 3a and 3b examined the interaction between marital status and race/ethnicity, with no significance found in each subgroup.

4.4. **Education**

Higher education level (Bachelor's degree or above) was added in Model 4 and showed negative correlation with migraines (OR=0.85, P<0.01). Interestingly, Hispanics and AIANs turned out to have positive interaction with higher education in Model 4a (P<0.001 and P<0.05, respectively). Therefore, for these two populations the odds ratio of having migraines with higher education was 1.19 and 1.73 respectively, as opposed to other racial groups without interactions.

4.5. **Poverty**

Poverty status joined Model 5 and as mentioned above, it had positive association with migraine prevalence (OR=1.49, P<0.001). It also had interactions with Hispanic Whites, Blacks and AIANs (Model 5a). New odds ratios for these groups were 1.31, 1.15 and 0.73, respectively. Previously strong links between migraine prevalence and adverse events in marriage disappeared.

4.6. **Medical bill payment problems**

As is seen from Table 5c, when the variable "Having problems in paying medical bills" was introduced into Model 6, higher education no longer showed statistical correlation with migraines (P=0.133). Significant associations with migraines were found in medical bill payment

problems (OR=2.27, P<0.001). There were no apparent interactions between race/ethnicity and medical bill payment problems (Model 6a).

Table 7a. Multivariable logistic regressions on migraine with race, ethnicity, sociodemographic characteristics, medical care quality factors, and their interactions[#]

	OR (95% CI) [ψ]				
	Model 1	**Model 2 (+Age, Sex)**	**Model 3 (+Marital status)**	**Model 3a (+Race x No marriage)**	**Model 3b (+Race x Adverse marriage)**
Non-Hispanic White	1	1	1	1	1
Hispanic White	1.00 (0.89-1.13)	0.89 (0.79-1.01)	0.89 (0.79-1.00)	0.89 (0.77-1.03)	0.87 (0.76-1.00)
African American / Black	1.14 (1.01-1.29) *	1.01 (0.90-1.14)	0.97 (0.85-1.09)	0.96 (0.81-1.14)	0.99 (0.86-1.15)
Asian	0.72 (0.59-0.87) **	0.63 (0.52-0.77) ***	0.65 (0.53-0.79) ***	0.67 (0.54-0.83) ***	0.64 (0.52-0.80) ***
Biracial or Multiracial	1.53 (1.18-1.98) **	1.39 (1.06-1.83) *	1.35 (1.03-1.78) *	1.36 (0.98-1.89)	1.26 (0.92-1.72)
AIAN [θ]	1.36 (0.91-2.02)	1.22 (0.79-1.88)	1.20 (0.77-1.85)	1.06 (0.62-1.80)	1.25 (0.77-2.02)
Age					
18-24	-	1	1	1	1
25-44	-	1.29 (1.11-1.49) **	1.41 (1.20-1.66) ***	1.41 (1.20-1.66) ***	1.41 (1.20-1.65) ***
45-64	-	1.03 (0.88-1.20)	1.14 (0.96-1.36)	1.14 (0.96-1.36)	1.14 (0.96-1.35)
65+	-	0.35 (0.30-0.42) ***	0.38 (0.31-0.46) ***	0.38 (0.31-0.46) ***	0.38 (0.31-0.46) ***
Sex					
Male	-	1	1	1	1
Female	-	2.42 (2.20-2.67) ***	2.42 (2.19-2.67) ***	2.42 (2.19-2.67) ***	2.42 (2.19-2.67) ***
Marital status					
No marriage	-	-	1.22 (1.11-1.35) ***	1.23 (1.09-1.38) **	1.22 (1.10-1.35) ***
Married	-	-	1	1	1
Adverse marriage	-	-	1.22 (1.09-1.36) **	1.22 (1.09-1.37) **	1.22 (1.06-1.35) **
Interaction (Model 3a)					
Hispanic x No marriage	-	-	-	0.99 (0.79-1.23)	-
Black x No marriage	-	-	-	1.01 (0.77-1.33)	-
Asian x No marriage	-	-	-	0.88 (0.57-1.36)	-
Bi/Multiracial x No marriage	-	-	-	0.98 (0.57-1.71)	-
AIAN x No marriage	-	-	-	1.29 (0.60-2.79)	-
Interaction (Model 3b)					
Hispanic x Adverse marriage	-	-	-	-	1.11 (0.83-1.49)
Black x Adverse marriage	-	-	-	-	0.87 (0.67-1.14)
Asian x Adverse marriage	-	-	-	-	1.04 (0.57-1.88)
Bi/Multiracial x Adverse marriage	-	-	-	-	1.53 (0.81-2.93)
AIAN x Adverse marriage	-	-	-	-	0.73 (0.31-1.76)

[#] Interaction terms between race/ethnicity and single variable were included in only one model. [ψ] CI=Confidence Interval.
[θ] AIAN=American Indian and Alaska Natives.
*P<0.05; ** P<0.01; ***P<0.001.

Table 7b. Multivariable logistic regressions on migraine with race, ethnicity, sociodemographic characteristics, medical care quality factors, and their interactions[#] (continued)

	OR (95% CI)			
	Model 4 (+Education)	**Model 4a (+Race x Higher education)**	**Model 5 (+Poverty)**	**Model 5a (+Race x Poverty)**
Non-Hispanic White	1	1	1	1
Hispanic White	0.85 (0.74-0.96) *	0.69 (0.59-0.82) ***	0.78 (0.69-0.89) ***	0.83 (0.71-0.96) *
African American / Black	0.95 (0.84-1.08)	0.86 (0.71-1.05)	0.91 (0.80-1.04)	1.00 (0.86-1.16)
Asian	0.65 (0.53-0.80) ***	0.77 (0.54-1.11)	0.62 (0.51-0.77) ***	0.67 (0.53-0.83) ***
Biracial or Multiracial	1.35 (1.03-1.77) *	1.36 (0.80-2.34)	1.34 (1.01-1.77) *	1.31 (0.94-1.83)
AIAN [θ]	1.08 (0.69-1.67)	0.70 (0.38-1.29)	1.03 (0.65-1.62)	1.36 (0.83-2.25)
18-24 years old	1	1	1	1
25-44 years old	1.42 (1.21-1.66) ***	1.42 (1.21-1.68) ***	1.41 (1.20-1.67) ***	1.42 (1.20-1.68) ***
45-64 years old	1.14 (0.96-1.35)	1.14 (0.96-1.36)	1.18 (0.98-1.41)	1.18 (0.98-1.42)
65+ years old	0.37 (0.30-0.45) ***	0.37 (0.30-0.45) ***	0.38 (0.31-0.47) ***	0.39 (0.31-0.48) ***
Female	2.42 (2.20-2.67) ***	2.43 (2.20-2.68) ***	2.36 (2.13-2.61) ***	2.37 (2.15-2.62) ***
No marriage	1.21 (1.09-1.33) ***	1.20 (1.09-1.33) ***	1.15 (1.03-1.27) *	1.15 (1.03-1.27) *
Adverse marriage	1.19 (1.07-1.33) **	1.19 (1.06-1.32) **	1.12 (1.00-1.25)	1.10 (0.98-1.24)
Education				
Less than Bachelor level	1	1	1	1
Higher education	0.85 (0.77-0.94) **	0.78 (0.70-0.87) ***	0.89 (0.80-0.98) *	0.88 (0.80-0.97) *
Interaction (Model 4a)				
Hispanic x Higher education	-	1.53 (1.22-1.92) ***	-	-
Black x Higher education	-	1.17 (0.91-1.51)	-	-
Asian x Higher education	-	0.80 (0.53-1.20)	-	-
Bi/Multiracial x Higher education	-	0.99 (0.53-1.82)	-	-
AIAN x Higher education	-	2.22 (1.00-4.90) *	-	-
Poverty				
No	-	-	1	1
Yes	-	-	1.49 (1.31-1.70) ***	1.82 (1.53-2.16) ***
Interaction (Model 5a)				
Hispanic x Poverty	-	-	-	0.72 (0.54-0.97) *
Black x Poverty	-	-	-	0.63 (0.47-0.83) **
Asian x Poverty	-	-	-	0.60 (0.33-1.09)
Bi/Multiracial x Poverty	-	-	-	1.00 (0.54-1.85)
AIAN x Poverty	-	-	-	0.40 (0.19-0.85) *

[#] Interaction terms between race/ethnicity and single variable were included in only one model. [Ψ] CI=Confidence Interval.
[θ] AIAN=American Indian and Alaska Natives. *P<0.05; ** P<0.01; ***P<0.001.

Table 7c. Multivariable logistic regressions on migraine with race, ethnicity, sociodemographic characteristics, medical care quality factors, and their interactions[#] (continued)

	OR (95% CI) [Ψ]	
	Model 6 (+Med bill) [§]	**Model 6a (+Race x Med bill)**
Non-Hispanic White	1	1
Hispanic White	0.78 (0.68-0.89) ***	0.82 (0.71-0.94) **
African American / Black	0.87 (0.76-0.99) *	0.91 (0.78-1.07)
Asian	0.68 (0.55-0.83) ***	0.66 (0.52-0.84) **
Biracial or Multiracial	1.26 (0.95-1.67)	1.16 (0.86-1.56)
AIAN [θ]	0.99 (0.64-1.54)	1.01 (0.59-1.71)
18-24 years old	1	1
25-44 years old	1.41 (1.19-1.54) ***	1.41 (1.19-1.67) ***
45-64 years old	1.18 (0.98-1.42)	1.18 (0.98-1.42)
65+ years old	0.42 (0.34-0.52) ***	0.42 (0.34-0.52) ***
Female	2.33 (2.10-2.57) ***	2.33 (2.10-2.57) ***
No marriage	1.13 (1.02-1.26) *	1.13 (1.02-1.26) *
Adverse marriage	1.05 (0.93-1.17)	1.04 (0.93-1.17)
Higher education	0.93 (0.85-1.02)	0.93 (0.85-1.02)
Poverty	1.42 (1.25-1.62) ***	1.42 (1.25-1.62) ***
Problems paying medical bills		
No	1	1
Yes	2.27 (2.04-2.52) ***	2.38 (2.07-2.74) ***
Interaction (Model 6a)		
Hispanic White x Med bill	-	0.81 (0.62-1.07)
Black x Med bill	-	0.84 (0.63-1.11)
Asian x Med bill	-	1.23 (0.57-2.65)
Bi/Multiracial x Med bill	-	1.28 (0.65-2.51)
AIAN x Med bill	-	0.95 (0.41-2.20)

[#] Interaction terms between race/ethnicity and single variable were included in only one model. [Ψ] CI=Confidence Interval.

[§] "Med bill" = Problems in paying medical bills.

[θ] AIAN=American Indian and Alaska Natives.

*P<0.05; ***P<0.001.

5. Distribution of migraine comorbidities and precipitating factors

Table 8a lists the distribution of comorbidities and precipitating factors (triggers) within the whole sample and different racial/ethnic subgroups. Data in Table 8b is for the projected US adult population.

5.1. Overall distribution

5.1.1. Migraine comorbidities

Overall, self-reported difficulties caused by depression, anxiety or emotional problems occurred in merely 2.21% of the whole population, while obesity, hypertension and high cholesterol accompanied 37.99%, 31.16%, and 27.97% of these people, respectively.

5.1.2. Migraine precipitating factors

10.81% of the population did not get the recommended hours of sleep during the past week (8.41% inadequate, 2.40% excessive), 35.72% had troubles in falling asleep, 38.81% had troubles in staying asleep, and 13.57% took medications for their sleep.

Prevalence of pain in neck, lower back or jaw/front ear was 16.09%, 29.83% and 4.15%.

Former drinkers, current drinkers and current smokers accounted for 14.23%, 65.12% and 15.11% of the projected population, respectively.

5.2. Comparison among races and ethnicities

5.2.1. Depression and anxiety problems

Difficulties from depression and anxiety problems were the least self-reported by Asians (0.97%), while the rate was the highest in people with 2 or more races (5.11%).

5.2.2. Obesity

The obesity rate was outstanding in American Indians and Alaska Natives (50.51%), African Americans (48.12%), and bi-/multi-racial people (44.02%) but rather low in the Asian population (15.59%).

5.2.3. Hypertension and high cholesterol

African Americans had the highest rate of hypertension (38.74%), while it was the lowest in Hispanics (22.90%), followed by Asians (23.34%). Non-Hispanic Whites had the greatest proportion of individuals with high cholesterol (30.04%).

5.2.4. Sleep disturbances

American Indians and Alaska Natives seemed to suffer more from sleep disturbances with the highest proportions of inadequate sleep (13.68%), troubles in falling asleep (46.04%) and troubles in staying asleep (46.32%), followed by biracial/multiracial people and non-Hispanic Whites.

5.2.5. Pain

Prevalence of neck pain and lower back pain was higher in AIANs and bi-/multi-racial people, while lowest in the Asian population (neck pain 11.41%, lower back pain 18.93%).

5.2.6. Alcohol consumption and smoking

American Indians and Alaska Natives had the largest proportion of former drinkers (25.41%) and current smokers (19.28%), followed by biracial/multiracial people and non-Hispanic Whites. Non-Hispanic Whites showed the largest number of current drinkers (69.70%). The proportions of former drinkers, current drinkers and current smokers were all the lowest in Asians (10.52%, 49.78%, and 7.18%, respectively).

In summary, migraine comorbidities and triggers were more prevalent in biracial/multiracial people and AIANs, compared to other racial groups. Surprisingly, the Asian population was the least impacted by these factors, especially in the aspects of depression/anxiety problems, obesity, sleep disturbances, pain, alcohol drinking and smoking.

Table 8a. Comorbidities and triggers of migraine among different races and ethnicities, in sample population (2015)

	Overall[φ]	Non-Hispanic White	Hispanic White	Black	Asian	Multi-race	AIAN[θ]
Valid number of cases (%)	33672 (100%)	20855 (61.9%)	4976 (14.8%)	4673 (13.9%)	1983 (5.9%)	699 (2.1%)	392 (1.2%)
Depression/Anxiety problems	838 (2.5%)	557 (2.7%)	104 (2.1%)	103 (2.2%)	23 (1.2%)	40 (5.7%)	11 (2.8%)
Obesity	11161 (33.1%)	6701 (32.1%)	1725 (34.7%)	1993 (42.6%)	262 (13.2%)	279 (39.9%)	165 (42.1%)
Hypertension	11745 (34.9%)	7431 (35.6%)	1283 (25.8%)	2144 (45.9%)	489 (24.7%)	233 (33.3%)	143 (36.5%)
High cholesterol	9783 (29.1%)	6625 (31.8%)	1125 (22.6%)	1247 (26.7%)	507 (25.6%)	173 (24.7%)	90 (23.0%)
Sleep disturbance							
Inadequate sleep hours	2772 (8.2%)	1492 (7.2%)	407 (8.2%)	580 (12.4%)	134 (6.8%)	94 (13.4%)	55 (14.0%)
Excessive sleep hours	902 (2.7%)	605 (2.9%)	72 (1.4%)	178 (3.8%)	32 (1.6%)	10 (1.4%)	4 (1.0%)
Troubles in falling asleep	11994 (35.6%)	7769 (37.3%)	1634 (32.8%)	1548 (33.1%)	551 (27.8%)	291 (41.6%)	170 (43.4%)
Troubles in staying asleep	13028 (38.7%)	8929 (42.8%)	1500 (30.1%)	1599 (34.2%)	498 (25.1%)	294 (42.1%)	173 (44.1%)
Usage of sleep medications	4757 (14.1%)	3391 (16.3%)	518 (10.4%)	569 (12.2%)	118 (6.0%)	98 (14.0%)	56 (14.3%)
Neck pain	5704 (16.9%)	3821 (18.3%)	740 (14.9%)	678 (14.5%)	219 (11.0%)	158 (22.6%)	76 (19.4%)
Low back pain	10539 (31.3%)	6916 (33.2%)	1381 (27.8%)	1425 (30.5%)	392 (19.8%)	260 (37.2%)	140 (35.7%)
Pain in jaw/front ear	1492 (4.4%)	1007 (4.8%)	194 (3.9%)	169 (3.6%)	41 (2.1%)	49 (7.0%)	24 (6.1%)
Alcohol drinking							
Former drinker	5252 (15.6%)	3429 (16.4%)	648 (13.0%)	751 (16.1%)	205 (10.3%)	113 (16.2%)	93 (23.7%)
Current drinker	21053 (62.5%)	14078 (67.5%)	2792 (56.1%)	2476 (53.0%)	999 (50.4%)	455 (65.1%)	206 (52.6%)
Current smoker	5415 (16.1%)	3612 (17.3%)	571 (11.5%)	817 (17.5%)	170 (8.6%)	149 (21.3%)	88 (22.4%)

[φ] Native Hawaiians and other Pacific Islanders are not separately listed.

[θ] AIAN = American Indian and Alaska Native.

Table 8b. Comorbidities and triggers of migraine among different races and ethnicities, in projected population (2015)

	Overall[φ]	Non-Hispanic White	Hispanic White	Black	Asian	Multi-race	AIAN[θ]
Projected number of cases	242,500,657	157,410,009	33,808,062	29,796,462	14,360,121	4,200,090	2,306,663
(% of overall projected)	(100%)	(64.91%)	(13.94%)	(12.29%)	(5.92%)	(1.73%)	(0.95%)
Depression/Anxiety problems	2.21%	2.45%)	1.68%	1.69%	0.97%	5.11%	3.58%
Obesity	37.99%	37.25%	40.03%	48.12%	15.59%	44.02%	50.51%
Hypertension	31.16%	32.34%	22.90%	38.74%	23.34%	28.55%	30.37%
High cholesterol	27.47%	30.04%	21.20%	22.87%	25.92%	22.88%	25.90%
Sleep disturbance							
Inadequate sleep hours	8.41%	7.36%	8.30%	13.62%	7.53%	12.6%	13.68%
Excessive sleep hours	2.40%	2.53%	1.39%	3.26%	1.92%	1.36%	1.94%
Troubles in falling asleep	35.72%	37.40%	31.67%	34.62%	26.64%	39.94%	46.04%
Troubles in staying asleep	38.81%	42.57%	29.77%	34.72%	25.14%	42.30%	46.32%
Usage of sleep medications	13.57%	15.50%	9.58%	11.62%	5.62%	14.25%	14.03%
Neck pain	16.09%	17.50%	13.02%	13.94%	11.41%	18.25%	19.48%
Low back pain	29.83%	31.71%	26.43%	28.50%	18.93%	32.83%	33.15%
Pain in jaw/front ear	4.15%	4.49%	3.57%	3.45%	2.17%	7.26%	5.60%
Alcohol drinking							
Former drinker	14.23%	15.04%	11.48%	13.97%	10.52%	14.79%	25.41%
Current drinker	65.12%	69.70%	59.48%	55.71%	49.78%	65.51%	55.32%
Current smoker	15.11%	16.59%	9.87%	16.46%	7.18%	18.3%	19.28%

[φ] Native Hawaiians and other Pacific Islanders are not separately listed.

[θ] AIAN = American Indian and Alaska Native.

6. Single effects and multivariable logistic regressions on migraine of comorbidities

The table below summarizes single effects of 4 suggested migraine comorbidities: depression and anxiety problems, obesity, hypertension and high cholesterol. Each of them were positively associated with migraine prevalence (OR=5.17, 1.26, 1.67, and 1.47, respectively; P<0.001 for each). This association applied to both men and women in hypertension and high cholesterol, in contrast to previous study. [52] Nevertheless, men had a higher odds ratio of having migraines with hypertension, and a lower odds ratio of having migraines with high cholesterol than women.

Table 9. Age and sex adjusted prevalence and odds ratio of migraine over comorbidities

Factors	Prevalence, % (95% CI) [Ψ]	Adjusted odds ratio (95% CI)
Depression and Anxiety problems		
No	14.28 (13.73-14.83)	1
Yes	44.52 (38.48-48.55)	5.17 (4.08-6.56) ***
Conditions according to BMI		
Underweight	15.61 (10.77-20.46)	0.96 (0.67-1.38)
Normal BMI	14.21 (13.17-15.24)	1
Overweight	14.14 (13.09-15.18)	1.01 (0.89-1.14)
Obesity	16.90 (15.89-17.91)	1.26 (1.13-1.41) ***
Hypertension (overall)		
No	13.33 (12.68-13.98)	1
Yes	20.94 (19.15-22.72)	1.67 (1.49-1.87) ***
Hypertension (male)		
No	8.31 (7.51-9.10)	1
Yes	14.53 (12.50-16.56)	1.80 (1.51-2.14) ***
Hypertension (female)		
No	18.10 (17.11-19.09)	1
Yes	27.14 (24.33-29.70)	1.60 (1.41-1.82) ***
High cholesterol (overall)		
No	13.82 (13.17-14.47)	1
Yes	19.60 (17.71-21.50)	1.47 (1.33-1.62) ***
High cholesterol (male)		
No	8.85 (8.02-9.67)	1
Yes	11.51 (9.09-13.92)	1.39 (1.16-1.66) ***
High cholesterol (female)		
No	18.54 (17.58-19.50)	1
Yes	27.29 (24.17-30.40)	1.51 (1.33-1.72) ***

[Ψ] CI=Confidence Interval. ***P<0.001.

Table 10 is the result of multivariable logistic regressions including migraine comorbidities. Obesity did not manifest correlation with migraines in Model 7. In Model 7a, depression/anxiety problems showed interactions with American Indians and Alaska Natives ($P<0.05$). The new odds ratios should be 0.73. Hypertension interacted significantly with Hispanic and Asian subgroups (Model 7c, $P<0.05$), and their odds ratios would increase to 1.89 and 2.28. No racial/ethnic migraine prevalence appeared to be more greatly affected by high cholesterol in Model 7d.

Table 10. Additional multivariable logistic regressions on racial/ethnic prevalence of migraine with its comorbidities

	OR (95% CI) [Ψ]				
	Model 7 (+Comorbidities)	**Model 7a (+Race x Depression/Anxiety)**	**Model 7b (+Race x Obesity)**	**Model 7c (+Race x Hypertension)**	**Model 7d (+Race x High cholesterol)**
Non-Hispanic White	1	1	1	1	1
Hispanic White	0.83 (0.72-0.95) **	0.82 (0.72-0.95) **	0.85 (0.71-1.02)	0.75 (0.63-0.89) **	0.84 (0.72-0.98) *
African American / Black	0.86 (0.74-1.00) *	0.85 (0.73-0.99) *	0.97 (0.79-1.19)	0.83 (0.68-1.02)	0.84 (0.71-1.00)
Asian	0.73 (0.58-0.92) **	0.72 (0.57-0.90) **	0.69 (0.52-0.90) **	0.63 (0.49-0.82) **	0.72 (0.56-0.92) **
Biracial or Multiracial	1.17 (0.88-1.57)	1.10 (0.82 -1.49)	1.02 (0.66-1.58)	1.00 (0.69-1.45)	1.11 (0.78-1.58)
AIAN [θ]	1.17 (0.75-1.82)	1.25 (0.79-1.96)	1.35 (0.70-2.60)	1.25 (0.72-2.15)	1.00 (0.61-1.63)
Age					
18-24	1	1	1	1	1
25-44	1.31 (1.09-1.57) **	1.31 (1.09-1.57) **	1.31 (1.09-1.58) **	1.30 (1.09-1.56) **	1.31 (1.09-1.57) **
45-64	0.94 (0.76-1.16)	0.94 (0.76-1.15)	0.94 (0.76-1.16)	0.93 (0.75-1.14)	0.94 (0.76-1.15)
65+	0.29 (0.23-0.38) ***	0.29 (0.23-0.38) ***	0.29 (0.23-0.38) ***	0.29 (0.23-0.38) ***	0.29 (0.23-0.38) ***
Female	2.52 (2.26-2.81) ***	2.52 (2.26-2.81) ***	2.53 (2.26-2.82) ***	2.51 (2.25-2.80) ***	2.52 (2.26-2.81) ***
No marriage	1.14 (1.02-1.27) *	1.14 (1.02-1.27) *	1.14 (1.02-1.27) *	1.14 (1.02-1.27) *	1.14 (1.02-1.27) *
Poverty	1.31 (1.15-1.50) ***	1.31 (1.15-1.50) ***	1.32 (1.15-1.50) ***	1.31 (1.15-1.50) ***	1.31 (1.15-1.50) ***
Having problems in paying medical bills	2.05 (1.82-2.31) ***	2.06 (1.82-2.32) ***	2.05 (1.82-2.31) ***	2.05 (1.82-2.31) ***	2.05 (1.82-2.31) ***
Comorbidities					
Depression/Anxiety problems	3.60 (2.78-4.67) ***	3.34 (2.41-4.61) ***	3.62 (2.79-4.69) ***	3.61 (2.78-4.68) ***	3.59 (2.77-4.66) ***
Obesity	1.05 (0.94-1.17)	1.05 (0.94-1.17)	1.08 (0.94-1.23)	1.05 (0.95-1.17)	1.05 (0.95-1.17)
Hypertension	1.46 (1.27-1.67) ***	1.46 (1.28-1.67) ***	1.46 (1.28-1.67) ***	1.34 (1.14-1.57) ***	1.46 (1.28-1.67) ***
High cholesterol	1.24 (1.11-1.39) ***	1.24 (1.11-1.39) ***	1.24 (1.11-1.39) ***	1.24 (1.11-1.39) ***	1.22 (1.06-1.41) **
Interactions with each variable [#]					
Hispanic	-	1.18 (0.60-2.33)	0.93 (0.70-1.26)	1.41 (1.05-1.91) *	0.94 (0.71-1.24)
Black	-	1.29 (0.66-2.55)	0.78 (0.59-1.03)	1.10 (0.80-1.52)	1.08 (0.77-1.51)
Asian	-	2.02 (0.45-9.10)	1.42 (0.80-2.55)	1.70 (1.01-2.88) *	1.07 (0.62-1.86)
Bi/Multiracial	-	2.18 (0.71-6.67)	1.34 (0.74-2.42)	1.62 (0.88-2.99)	1.29 (0.66-2.52)
AIAN	-	0.22 (0.05-0.99) *	0.75 (0.30-1.88)	0.82 (0.41-1.62)	1.75 (0.56-5.49)

[#] Interaction terms between race/ethnicity and single variable were included in only one model. [Ψ] CI=Confidence Interval.

[θ] AIAN=American Indian and Alaska Natives. *P<0.05; ** P<0.01; ***P<0.001.

7. Individual correlation of adjusted migraine prevalence and precipitating factors

Table 11 lists selected migraine precipitating factors – sleep disturbance (sleep hours, troubles in falling or staying asleep, and/or usage of sleep medications); pain in neck, lower back, or jaw/front ear; alcohol consumption and smoking – and their individual associations with age and sex adjusted migraine prevalence.

7.1. **Sleep disturbances:** Compared to recommended hours of sleep, both inadequate and excessive sleep hours were significantly associated with migraine occurrence (OR=2.32 and 2.01, respectively; P<0.001 for each). Troubles in falling asleep (OR=2.73), and in staying asleep (OR=2.59), as well as sleep medication usage (OR=2.52) were also positively correlated with migraines (P<0.001 for all).

7.2. **Pain in the past 3 months:** Neck pain, low back pain and pain in jaw/front ear were all positive predictors of migraines, with their odds ratios of 4.73, 3.31 and 6.17, respectively (P<0.001).

7.3. **Alcohol consumption:** Former drinkers (18.27%, OR= 1.55, P<0.001) and current drinkers (14.80%, OR=1.13, P<0.05) had statistically higher migraine prevalence than lifetime alcohol abstainers (13.91%).

7.4. **Smoking:** Many more current smokers were suffering from migraines compared to non-smokers (21.53% vs 13.72%, OR=1.78, P<0.001).

Table 11. Age and sex adjusted prevalence and odds ratio of migraine over triggers

Precipitating factors	Prevalence, % (95% CI) [Ψ]	Adjusted odds ratio (95% CI)
Sleep hours		
Inadequate	26.94 (24.61-29.27)	2.32 (2.04-2.64) ***
Normal	13.60 (13.02-14.19)	1
Excessive	28.88 (21.18-36.59)	2.01 (1.53-2.88) ***
Troubles in falling asleep		
No	10.16 (9.54-10.78)	1
Yes	23.01 (22.08-23.95)	2.73 (2.51-2.97) ***
Troubles in staying asleep		
No	10.27 (9.65-10.90)	1
Yes	22.21 (21.22-23.30)	2.59 (2.38-2.82) ***
Usage of sleep medications		
No	13.12 (12.54-13.71)	1
Yes	27.30 (25.34-29.26)	2.52 (2.26-2.82) ***
Neck pain		
No	11.05 (10.53-11.56)	1
Yes	35.07 (33.11-37.03)	4.73 (4.28-5.23) ***
Low back pain		
No	10.28 (9.71-10.85)	1
Yes	26.48 (25.22-27.74)	3.31 (3.02-3.62) ***
Pain in jaw/front ear		
No	13.47 (12.94-14.00)	1
Yes	46.72 (42.91-50.53)	6.17 (5.31-7.16) ***
Alcohol drinking		
Lifetime alcohol abstainer	13.91 (12.73-15.09)	1
Former drinker	18.27 (16.33-20.22)	1.55 (1.33-1.81) ***
Current drinker	14.80 (14.11-15.48)	1.13 (1.01-1.27) *
Current smoker		
No	13.72 (13.15-14.29)	1
Yes	21.53 (19.96-23.10)	1.78 (1.60-1.97) ***

[Ψ] CI=Confidence Interval. *P<0.05; ***P<0.001.

8. Multivariable logistic regressions on racial/ethnic migraine prevalence with precipitating factors

Precipitating factors discussed above were sequentially added in the previous multivariable logistic regression models on migraines (minus marital status and higher education), in the order of their associations from low to high (Tables 12a-12d).

8.1. **Drinking and smoking:** When adjusted by age, sex, marital and poverty status, medical bill payment problems and comorbidities, the odds ratio of having migraines for former drinkers was 1.28 ($P<0.01$), and 1.13 for current drinkers ($P=0.065$), compared to lifetime alcohol abstainers (Model 8). After smoking was included in Model 9, there was no longer significant correlation between marital status and migraine prevalence. An interaction between African American race and current smoker status was detected ($P<0.01$) with the odds ratio changed to be 0.95. No interactions were found between race/ethnicity and alcohol consumption.

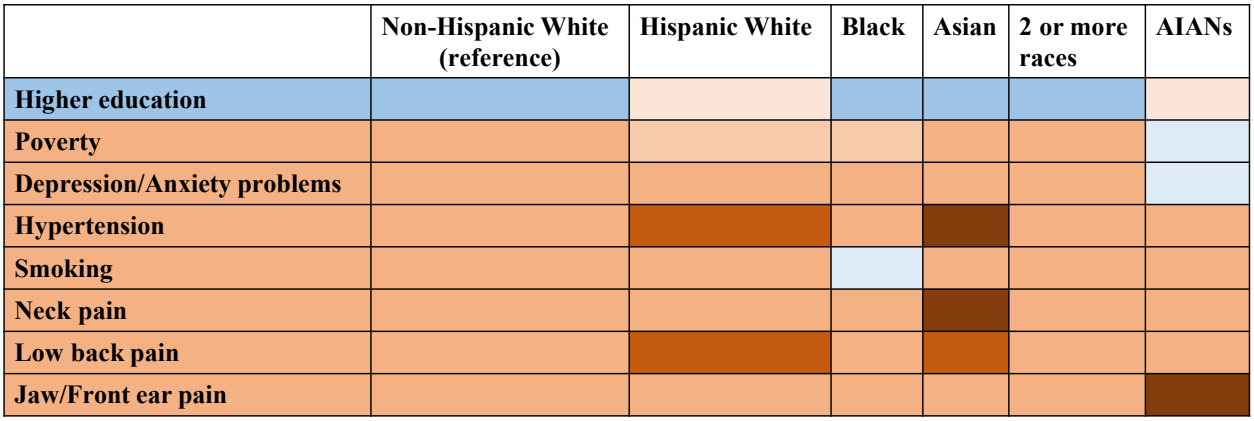
8.2. **Pain in neck, lower back, and jaw/front ear**: After three variables of pain were introduced into Model 10, alcohol consumption and high cholesterol were no longer associated with migraine prevalence. All of the racial/ethnic differences compared to non-Hispanic Whites had been notably reduced. Pain in jaw or front ear produced the largest odds ratio of the three (3.44), followed by neck pain (2.63). Migraine prevalence in the Asian population was influenced more significantly by neck pain ($P<0.05$), with the interacted odds ratio to be 4.08. There was also interaction between Hispanic ethnicity and lower back pain ($P<0.05$, new OR=2.24), between

Asian race and lower back pain (P<0.05, new OR=2.62), and between AIANs and facial pain (P<0.01, new OR=28.61).

8.3. **Sleep disturbances:** 5 variables (inadequate sleep hours, excessive sleep hours, troubles in falling asleep, troubles in staying asleep, and taking sleep medications) were added in Model 11, and they all resulted in significantly positive correlations with migraine prevalence (OR=1.31, 1.48, 1.58, 1.38, and 1.33, respectively). Interactions were not detected in any of the racial/ethnic subgroups.

In summary, strong correlations with racial/ethnic migraine prevalence were found in age, sex, poverty status, problems in paying medical bills, serious depression and anxiety, hypertension, current smoking, pain in neck/lower back/jaw/front ear, inadequate or excessive sleeping hours, troubles in falling or staying asleep, and sleep medication usage. Marital status, higher education, obesity, alcohol drinking and high cholesterol also showed some associations with migraine, but not so significant as other variables. Hispanic populations had positive interactions with higher education, hypertension, and lower back pain, and negative interaction with poverty. African Americans had negative interactions with poverty and smoking. There were positive interactions between Asian races and neck/low back pain. American Indians and Alaska Natives tend to be more greatly affected by higher education and facial pain, and they had a negative interaction with poverty and depression/anxiety problems. Biracial or multiracial people did not show significant interactions with any of the variables (Figure 4).

Figure 4. Interactions between races/ethnicities and contributing factors of migraine*



* Non-Hispanic White population is chosen as the reference group. The bluish color indicates negative correlation, and the orange color means positive association. The cells change into lighter colors when the association becomes weaker, and deeper colors suggest the stronger effect of a certain factor on a specific subgroup.

Table 12a. Additional multivariable logistic regressions on migraine with precipitating factors

	OR (95% CI) [ψ]				
	Model 8 (+Alcohol Drinking)	**Model 8a (+Race x Former drinker)**	**Model 8b (+Race x Current drinker)**	**Model 9 (+Smoking)**	**Model 9a (+Race x Smoking)**
Non-Hispanic White	1	1	1	1	1
Hispanic White	0.83 (0.73-0.95) **	0.83 (0.72-0.95) **	0.79 (0.65-0.96) *	0.87 (0.77-0.99) *	0.89 (0.78-1.03)
African American / Black	0.89 (0.78-1.02)	0.91 (0.79-1.05)	0.79 (0.64-0.97) *	0.91 (0.79-1.04)	0.99 (0.85-1.16)
Asian	0.74 (0.59-0.92) **	0.78 (0.62-0.98) *	0.67 (0.49-0.92) *	0.76 (0.61-0.95) *	0.78 (0.62-0.98) *
Biracial or Multiracial	1.21 (0.93-1.57)	1.21 (0.91-1.60)	0.97 (0.61-1.56)	1.22 (0.94-1.59)	1.14 (0.83-1.55)
AIAN [θ]	1.11 (0.72-1.71)	1.22 (0.77-1.91)	0.87 (0.46-1.64)	1.12 (0.72-1.73)	1.04 (0.67-1.61)
Age					
18-24 years old	1	1	1	1	1
25-44 years old	1.26 (1.06-1.50) *	1.26 (1.06-1.50) *	1.19 (1.05-1.35) **	1.22 (1.02-1.45) *	1.22 (1.02-1.46) *
45-64 years old	0.88 (0.72-1.08)	0.88 (0.73-1.08)	0.79 (0.69-0.90) **	0.86 (0.70-1.04)	0.86 (0.70-1.04)
65+ years old	0.28 (0.23-0.36) ***	0.28 (0.23-0.36) ***	0.28 (0.23-0.36) ***	0.28 (0.23-0.36) ***	0.29 (0.23-0.36) ***
Female	2.47 (2.23-2.74) ***	2.47 (2.23-2.73) ***	2.47 (2.23-2.74) ***	2.50 (2.23-2.36) ***	2.49 (2.25-2.75) ***
No marriage	1.12 (1.01-1.24) *	1.12 (1.01-1.23) *	1.11 (1.01-1.23) *	1.09 (0.98-1.21)	1.09 (0.99-1.21)
Poverty	1.32 (1.16-1.51) ***	1.32 (1.16-1.51) ***	1.33 (1.17-1.51) ***	1.26 (1.10-1.44) **	1.26 (1.11-1.44) **
Problems paying medical bills	2.08 (1.86-2.32) ***	2.08 (1.86-2.32) ***	2.08 (1.86-2.32) ***	2.00 (1.79-2.24) ***	2.00 (1.78-2.23) ***
Comorbidities					
Depression/Anxiety problems	3.93 (3.06-5.05) ***	3.93 (3.06-5.05) ***	3.92 (3.05-5.04) ***	3.79 (2.94-4.88) ***	3.77 (2.93-4.85) ***
Hypertension	1.42 (1.26-1.61) ***	1.42 (1.26-1.60) ***	1.42 (1.26-1.60) ***	1.42 (1.25-1.60) ***	1.42 (1.26-1.60) ***
High cholesterol	1.24 (1.11-1.38) ***	1.24 (1.11-1.38) ***	1.24 (1.12-1.38) ***	1.24 (1.12-1.38) ***	1.24 (1.12-1.38) ***
Alcohol drinking					
Former drinker	1.28 (1.09-1.51) **	1.33 (1.10-1.62) **	1.26 (1.06-1.49) **	1.23 (1.04-1.45) *	1.23 (1.04-1.46) *
Current drinker	1.13 (0.99-1.28)	1.13 (1.00-1.28)	1.05 (0.89-1.24)	1.08 (0.95-1.23)	1.09 (0.96-1.24)
Current smoker					
No	-	-	-	1	1
Yes	-	-	-	1.41 (1.26-1.59) ***	1.50 (1.31-1.73) ***
Interactions with each variable [#]					
Hispanic White	-	1.06 (0.89-1.45)	1.09 (0.85-1.39)	-	0.85 (0.62-1.18)
Black	-	0.86 (0.60-1.25)	1.21 (0.93-1.59)	-	0.63 (0.45-0.88) **
Asian	-	0.55 (0.27-1.12)	1.16 (0.77-1.75)	-	0.86 (0.38-1.93)
Bi/Multiracial	-	1.00 (0.51-1.95)	1.37 (0.77-2.43)	-	1.37 (0.70-2.70)
AIAN	-	0.68 (0.26-1.76)	1.49 (0.66-3.33)	-	1.34 (0.47-3.78)

[#] Interaction terms between race/ethnicity and single variable were included in only one model. [ψ] CI=Confidence Interval.
[θ] AIAN=American Indian and Alaska Natives. *P<0.05; ** P<0.01; ***P<0.001.

Table 12b. Additional multivariable logistic regressions on migraine with precipitating factors (continued)

	OR (95% CI) [ψ]			
	Model 10 (+Pain)	**Model 10a (+Race x Neck pain)**	**Model 10b (+Race x Low back pain)**	**Model 10c (+Race x jaw/front ear)**
Non-Hispanic White	1	1	1	1
Hispanic White	0.93 (0.81-1.07)	0.91 (0.79-1.06)	0.82 (0.70-0.97)**	0.94 (0.81-1.08)
African American / Black	1.03 (0.90-1.18)	1.00 (0.84-1.18)	1.02 (0.83-1.25)	1.00 (0.86-1.16)
Asian	0.87 (0.70-1.07)	0.77 (0.61-0.98) *	0.75 (0.59-0.94) **	0.83 (0.67-1.03)
Biracial or Multiracial	1.18 (0.90-1.56)	1.17 (0.82-1.66)	1.03 (0.70-1.51)	1.22 (0.93-1.61)
AIAN [θ]	1.12 (0.73-1.72)	1.21 (0.71-2.05)	1.14 (0.60-2.15)	0.96 (0.60-1.54)
Age				
18-24 years old	1	1	1	1
25-44 years old	1.03 (0.86-1.22)	1.03 (0.86-1.22)	1.03 (0.86-1.22)	1.03 (0.87-1.22)
45-64 years old	0.66 (0.54-0.80) ***	0.65 (0.54-0.79) ***	0.65 (0.54-0.79) ***	0.66 (0.54-0.80) ***
65+ years old	0.22 (0.18-0.28) ***	0.22 (0.18-0.28) ***	0.22 (0.18-0.28) ***	0.22 (0.18-0.28) ***
Female	2.36 (2.13-2.61) ***	2.36 (2.13-2.61) ***	2.36 (2.13-2.61) ***	2.36 (2.13-2.61) ***
Poverty	1.16 (1.02-1.33) *	1.16 (1.01-1.33) *	1.16 (1.02-1.33) *	1.16 (1.02-1.33) *
Problems paying medical bills	1.67 (1.47-1.89) ***	1.67 (1.47-1.90) ***	1.67 (1.47-1.90) ***	1.67 (1.47-1.89) ***
Comorbidities				
Depression/Anxiety problems	2.43 (1.83-3.21) ***	2.43 (1.84-3.21) ***	2.43 (1.84-3.21) ***	2.43 (1.84-3.21) ***
Hypertension	1.27 (1.11-1.45) ***	1.27 (1.11-1.44) ***	1.27 (1.11-1.44) ***	1.27 (1.11-1.45) ***
High cholesterol	1.10 (0.98-1.22)	1.11 (0.98-1.23)	1.10 (0.98-1.23)	1.10 (0.98-1.23)
Former drinker	1.04 (0.92-1.18)	1.04 (0.92-1.19)	1.04 (0.92-1.18)	1.04 (0.92-1.18)
Current smoker	1.31 (1.16-1.47) ***	1.31 (1.16-1.47) ***	1.31 (1.16-1.48) ***	1.30 (1.16-1.47) ***
Neck pain	2.63 (2.32-2.97) ***	2.52 (2.17-2.91) ***	2.63 (2.33-2.97) ***	2.64 (2.33-2.99) ***
Low back pain	1.79 (1.60-2.00) ***	1.79 (1.60-2.00) ***	1.67 (1.45-1.92) ***	1.79 (1.61-2.00) ***
Pain in jaw/front ear	3.44 (2.89-4.10) ***	3.46 (2.90-4.12) ***	3.43 (2.88-4.08) ***	3.20 (2.59-3.95) ***
Interactions with each variable [#]				
Hispanic White	-	1.06 (0.81-1.39)	1.34 (1.03-1.75) *	0.89 (0.53-1.50)
Black	-	1.14 (0.81-1.61)	1.02 (0.75-1.39)	1.64 (0.93-2.86)
Asian	-	1.62 (1.04-2.51) *	1.57 (1.04-2.37) *	2.08 (0.87-5.00)
Bi/Multiracial	-	1.04 (0.53-2.01)	1.35 (0.74-2.46)	0.75 (0.28-2.03)
AIAN	-	0.78 (0.35-1.75)	0.97 (0.42-2.22)	8.94 (2.16-37.00) **

[#] Interaction terms between race/ethnicity and single variable were included in only one model. [ψ] CI=Confidence Interval.
[θ] AIAN=American Indian and Alaska Natives. *P<0.05; ** P<0.01; ***P<0.001.

Table 12c. Additional multivariable logistic regressions on migraine with precipitating factors (continued)

	OR (95% CI) [Ψ]		
	Model 11 (+Sleep disturbances)	**Model 11a (+Race x Inadequate sleep)**	**Model 11b (+Race x Excessive sleep)**
Non-Hispanic White	1	1	1
Hispanic White	0.97 (0.85-1.12)	0.98 (0.85-1.13)	0.96 (0.83-1.11)
African American / Black	1.04 (0.89-1.20)	1.08 (0.92-1.27)	1.04 (0.90-1.21)
Asian	0.92 (0.74-1.14)	0.93 (0.75-1.16)	0.92 (0.74-1.14)
Biracial or Multiracial	1.17 (0.88-1.55)	1.15 (0.84-1.58)	1.18 (0.88-1.57)
AIAN [θ]	1.16 (0.73-1.83)	1.31 (0.76-2.24)	1.20 (0.76-1.92)
18-24 years old	1	1	1
25-44 years old	1.03 (0.86-1.23)	1.03 (0.86-1.23)	1.03 (0.86-1.23)
45-64 years old	0.65 (0.53-0.79) ***	0.65 (0.53-0.79) ***	0.65 (0.53-0.79) ***
65+ years old	0.24 (0.19-0.30) ***	0.24 (0.19-0.30) ***	0.24 (0.19-0.30) ***
Female	2.21 (1.99-2.45) ***	2.21 (1.99-2.45) ***	2.21 (1.99-2.45) ***
Poverty	1.18 (1.03-1.36) *	1.18 (1.03-1.36) *	1.18 (1.03-1.35) *
Problems paying medical bills	1.53 (1.35-1.74) ***	1.53 (1.35-1.74) ***	1.53 (1.35-1.74) ***
Depression/Anxiety problems	2.01 (1.51-2.68) ***	2.00 (1.50-2.67) ***	2.03 (1.52-2.71) ***
Hypertension	1.18 (1.04-1.35) *	1.19 (1.04-1.35) *	1.18 (1.04-1.35) *
Current smoker	1.25 (1.10-1.41) **	1.24 (1.09-1.41) **	1.24 (1.10-1.41) **
Neck pain	2.41 (2.11-2.74) ***	2.40 (2.11-2.74) ***	2.41 (2.11-2.74) ***
Low back pain	1.60 (1.43-1.79) ***	1.60 (1.43-1.79) ***	1.61 (1.44-1.80) ***
Pain in jaw/front ear	3.16 (2.64-3.78) ***	3.16 (2.65-3.78) ***	3.16 (2.64-3.77) ***
Inadequate sleep	1.31 (1.12-1.53) **	1.40 (1.14-1.72) **	1.31 (1.12-1.53) **
Excessive sleep	1.48 (1.05-2.08) *	1.47 (1.05-2.08) *	1.48 (1.05-2.08) *
Troubles in falling asleep	1.58 (1.42-1.76) ***	1.58 (1.42-1.77) ***	1.58 (1.42-1.76) ***
Troubles in staying asleep	1.38 (1.24-1.55) ***	1.38 (1.24-1.54) ***	1.38 (1.24-1.55) ***
Taking sleep medications	1.33 (1.17-1.52) ***	1.33 (1.16-1.52) ***	1.33 (1.16-1.52) ***
Interactions with each variable [#]			
Hispanic White	-	0.94 (0.65-1.35)	2.11 (0.80-5.59)
Black	-	0.79 (0.53-1.16)	0.86 (0.40-1.83)
Asian	-	0.90 (0.46-1.75)	1.35 (0.28-6.55)
Bi/Multiracial	-	1.07 (0.48-2.36)	0.41 (0.05-3.33)
AIAN	-	0.45 (0.16-1.26)	0.06 (0.00-1.16)

[#] Interaction terms between race/ethnicity and single variable were included in only one model. [Ψ] CI=Confidence Interval.
[θ] AIAN=American Indian and Alaska Natives. *P<0.05; ** P<0.01; ***P<0.001.

Table 12d. Additional multivariable logistic regressions on migraine with precipitating factors (continued)

	OR (95% CI) [ψ]		
	Model 11c (+Race x Trouble falling asleep)	**Model 11d (+Race x Trouble staying asleep)**	**Model 11e (+Race x Taking sleep medications)**
Non-Hispanic White	1	1	1
Hispanic White	1.02 (0.84-1.23)	1.03 (0.85-1.25)	0.98 (0.84-1.14)
African American / Black	1.09 (0.88-1.36)	1.01 (0.82-1.24)	1.03 (0.87-1.22)
Asian	0.82 (0.61-1.10)	0.85 (0.63-1.14)	0.92 (0.73-1.15)
Biracial or Multiracial	1.12 (0.70-1.79)	1.38 (0.89-2.13)	1.06 (0.77-1.47)
AIAN [θ]	1.17 (0.62-2.18)	1.46 (0.80-2.65)	1.25 (0.75-2.06)
18-24 years old	1	1	1
25-44 years old	1.03 (0.86-1.23)	1.03 (0.86-1.23)	1.03 (0.86-1.23)
45-64 years old	0.65 (0.53-0.79) ***	0.65 (0.53-0.79) ***	0.65 (0.53-0.79) ***
65+ years old	0.24 (0.19-0.30) ***	0.24 (0.19-0.30) ***	0.24 (0.19-0.30) ***
Female	2.21 (1.99-2.46) ***	2.21 (1.99-2.46) ***	2.21 (1.99-2.45) ***
Poverty	1.18 (1.03-1.36) *	1.18 (1.03-1.36) *	1.18 (1.03-1.35) *
Problems paying medical bills	1.53 (1.35-1.74) ***	1.53 (1.35-1.74) ***	1.53 (1.35-1.74) ***
Depression/Anxiety problems	2.01 (1.51-2.68) ***	2.01 (1.51-2.68) ***	2.00 (1.50-2.67) ***
Hypertension	1.19 (1.04-1.35) *	1.18 (1.04-1.35) *	1.18 (1.04-1.35) *
Current smoker	1.25 (1.10-1.41) **	1.25 (1.10-1.42) **	1.25 (1.10-1.42) **
Neck pain	2.41 (2.11-2.74) ***	2.41 (2.11-2.75) ***	2.41 (2.11-2.74) ***
Low back pain	1.60 (1.43-1.80) ***	1.60 (1.43-1.79) ***	1.60 (1.43-1.79) ***
Pain in jaw/front ear	3.16 (2.65-3.78) ***	3.16 (2.65-3.78) ***	3.15 (2.64-3.77) ***
Inadequate sleep	1.31 (1.12-1.54) **	1.31 (1.12-1.53) **	1.30 (1.11-1.53) **
Excessive sleep	1.48 (1.05-2.08) *	1.48 (1.05-2.08) *	1.47 (1.05-2.08) *
Troubles in falling asleep	1.60 (1.41-1.82) ***	1.58 (1.42-1.77) ***	1.58 (1.42-1.76) ***
Troubles in staying asleep	1.39 (1.24-1.55) ***	1.40 (1.23-1.59) ***	1.39 (1.24-1.55) ***
Taking sleep medications	1.33 (1.17-1.52) ***	1.33 (1.17-1.52) ***	1.32 (1.12-1.55) **
Interactions with each variable [#]			
Hispanic White	0.91 (0.70-1.20)	0.88 (0.67-1.16)	0.99 (0.69-1.43)
Black	0.90 (0.66-1.22)	1.06 (0.81-1.38)	1.05 (0.73-1.50)
Asian	1.31 (0.88-1.96)	1.24 (0.80-1.93)	1.01 (0.53-1.95)
Bi/Multiracial	1.08 (0.59-1.97)	0.73 (0.41-1.30)	1.61 (0.81-3.22)
AIAN	0.98 (0.44-2.19)	0.65 (0.27-1.55)	0.63 (0.24-1.69)

[#] Interaction terms between race/ethnicity and single variable were included in only one model. [ψ] CI=Confidence Interval.
[θ] AIAN=American Indian and Alaska Natives. *P<0.05; ** P<0.01; ***P<0.001.

CHAPTER 5: DISCUSSION

This chapter analyzes the results from the previous chapter, and is divided into the following sections: yearly trend of migraine prevalence, differences in migraine prevalence among races and ethnicities, effects of explanatory variables on racial/ethnic migraine prevalence, limitations of the study, implications of this study, future research, and conclusions.

1. Yearly trend of migraine prevalence

This study obtained the latest data on migraine prevalence in the vast US adult population from the NHIS.

The age and sex adjusted prevalence is 14.95% in 2015. It is almost exactly the average value from previous large-scale US government studies. [4] We can estimate that 36 million American adults are suffering from migraine nationwide, which is equivalent to approximately 1 out of every 7 people in the US. Since migraine prevalence varies substantially depending on age and gender, it is important to compare the proportions in subgroups or with adjustment.

When looking at the annual tendency, we can say the overall migraine prevalence remained relatively stable in the United States from 2010 to 2015 (Figure 2), as opposed to the global tendency. [5] Trends in non-Hispanic Caucasians, Hispanic Caucasians and African Americans are very close to each other. As for American Indians and Alaska Natives, the proportion of

people having migraine was higher than overall prevalence throughout the 6 years, and a greater fluctuation was also noticed.

This study is among the few currently available reports that include data from minority populations in the United States; it sheds light on the migraine prevalence among these residents, especially Asians and people with 2 or more races, otherwise concealed by the majority group of non-Hispanic Whites.

2. Differences in migraine prevalence among races and ethnicities

Comparison of migraine prevalence among different subgroups resulted in interesting findings.

The Asian population showed much lower prevalence of migraine (10.68%) than any other race group in the United States, which is consistent with the results from Loder and Sheikh [15]. Both Asian women (14.69%) and Asian men (6.44%) held the lowest prevalence. We also discovered notably higher migraine prevalence in people with 2 or more races (20.91%), especially in women (27.91%), compared to non-Hispanic Whites and Hispanic Whites, which was seldom discussed before.

When adjusted by age and sex, there is no remarkable difference found between non-Hispanic Whites, Hispanic Whites and Blacks in the US. This is opposed to several previous studies, which concluded that Caucasians had significantly larger proportion of migraineurs compared to

other races. [10] [13] [14] It is likely that the category "non-White race" consisted of considerably diverse subgroups, including Asians with lower prevalence, therefore interpretation of the variance could be complicated. Appropriate subdivision of the category would help further understanding of the difference. Blacks and AIANs had female to male ratios of prevalence lower than 2, probably due to the higher proportions of migraineurs in men.

Although the 3-month migraine prevalence of American Indians and Alaska Natives was above the overall level in the United States (17.36%), the difference between them and other race subgroups is not considered statistically significant, possibly due to their relatively small sample number which resulted in a large standard error. Still, their migraine prevalence was the highest in men (14.82%).

3. Effects of explanatory variables on racial/ethnic migraine prevalence

This section analyzes the association between each candidate variable — sociodemographic characteristics, medical care quality factors, migraine comorbidities and triggers — and racial/ethnic migraine prevalence.

3.1. Sociodemographic factors

Younger age (<45 years) and female are positive predictors of migraine in all study populations, regardless of race or Hispanic ethnicity. It is likely that younger people face more changes in their life and triggers of migraine as well, compared to the older ones. Ovarian hormone

fluctuations by oral contraceptives or during menstruation, pregnancy and menopause are well known to render women susceptible to migraine. [75] - [81] A recent study also showed that women with a history of migraine have faster decline of estradiol prior to menstruation, no matter whether they have experienced a headache in that cycle. [92]

Married status and higher education are somewhat protective against migraine. Married people without adverse outcomes could receive support and positive feedback from their family; since death of spouse, divorce, and marital separation are top 3 stressful life events in adults according to the Holmes-Rahe Stress Inventory, [93] [94] [95] these major stressors may put the individuals at a higher risk of migraine, too. Highly educated people tend to be more aware of their health conditions and medical care; they are also associated with generally higher socioeconomic status and more satisfactory treatment of migraine. However, in Hispanic and AIAN groups higher education turned out to be exerting the opposite effects: those people with Bachelor's degree or above are more likely to have migraine. Further research is needed to explain this relationship. That being said, the negative effects of adverse marriage events and lower education are no longer significant when poverty and medical bill payment problems are taken into consideration.

People in poverty are more likely to suffer from migraine, partly due to their generally poor health conditions and limited access to medical care. They may be forced to live in an unfavorable environment and skip meals or eat less because of insufficient budgets, which could trigger migraine. Poverty itself can also contribute as a stressor and a risk factor of depression/anxiety, too. Although positive correlation between poverty and migraine is seen in

the multivariate models, the intensity varies among racial and ethnic groups: Hispanic Whites and African Americans showed a little weaker association than non-Hispanic Whites; within American Indians and Alaska Natives there is even evidence that individuals in poverty may suffer less from migraine, without convincing reasons.

3.2. Quality of medical care

Neither insurance coverage nor English proficiency is correlated with migraine prevalence, but medical bill payment problems are significantly associated with migraine throughout the US adult population. On one hand, problems in paying medical bills are more direct challenges in health care for people, compared to uninsured status and language barriers. On the other hand, such challenges add to pressure on the individuals and may render them more susceptible to migraine attacks.

3.3. Comorbidities of migraine

3.3.1. Depression and anxiety

In the regression models, depression and anxiety problems are strongly associated with migraine prevalence, which is consistent with the results from previous studies. [47] [63] [64] [65] [66] The lowest proportion of depression/anxiety problems in Asians and the highest proportion in bi-/multiracial people may partly explain their significantly different migraine prevalence. However, we should be aware that cultural differences may have resulted in under-reporting of depression by Asians. Previous studies suggested under-diagnoses and under-treatment of depression among the Asian population, partly due to the stigma of mental illness. [96] [97] [98]

Cultural influence in interpreting medical conditions and utilizing health care is an important issue, which physicians and policy makers should seriously take into consideration.

There is no interaction detected except in American Indians and Alaska Natives, who actually showed negative correlation between depression/anxiety problems and migraine. We noticed that the prevalence of depression or anxiety problems causing difficulties is very low in all racial/ethnic subgroups (less than 6%), and when it is combined with the originally small population of AIANs, only 11 cases of AIANs with depression/anxiety are found from the primordial dataset. This limited case number is predisposed to sample bias and might have resulted in the contradiction.

3.3.2. Obesity

Even though obesity shows positive association in a univariate analysis, which agrees with preceding conclusions, [14] [47] [49] [68] [69] it is not a statistically significant predictor of migraine when adjusted by other comorbidities. It is possible that obesity affects frequency and intensity of migraine, rather than its prevalence, as supposed by Bigal et al. [70] There is no interaction found between obesity and race/ethnicity.

3.3.3. Hypertension and high cholesterol

Hypertension and high cholesterol are both positively associated with migraine prevalence regardless of gender. Although Hispanic Whites and Asians had the lowest prevalence of

hypertension (22.90% and 23.34%, respectively), when it does exist, the association with migraine is even greater (OR=1.89 and 2.28, in comparison with other racial groups 1.34). High cholesterol status does not interact with races or Hispanic ethnicities, and its association with migraine is no longer present when pain and sleep disturbances join the regression models.

3.4. Precipitating factors of migraine

3.4.1. Alcohol drinking

Alcohol consumption showed positive correlation with migraine prevalence in the univariate analyses. We know that alcohol functions as a direct vasodilator and a natural diuretic. Some individuals may be vulnerable to vasodilation and/or dehydration with electrolyte imbalances, therefore migraine occurs afterwards. The association of former drinkers is stronger than current drinkers, suggesting a possible impact of alcohol withdrawal. However, such associations of alcohol consumption are not significant compared to pain or sleep disturbances.

3.4.2. Smoking

Both smoking status and nicotine intake appear to adversely impact headache activity. [99] The number of cigarettes smoked per day ($r = 0.471$; $P < 0.001$) has been a significant predictor of carboxyhemoglobin (COHb) levels, which at 10% or above can impede blood oxygenation in brain and trigger headaches. [100] Also, epidemiologic studies have suggested that depression is common among smokers. [101]

Despite these exacerbating factors, African Americans seem to interact with smoking uniquely: for Black people who currently smoke, their odds ratio of suffering from migraine is 0.95 compared to Blacks who do not smoke. This is an unprecedented result and will need further investigation.

3.4.3. Pain

Pain in neck, low back, jaw or front ear all revealed significantly positive associations with migraine prevalence in each of the racial/ethnic groups. These different types of pain could be the precipitating factors, manifestation, or postdrome syndromes of migraine. [102] They influence Asians, Hispanics, and AIANs more significantly than other groups. People with 2 or more races show very high proportions of each type of pain, which may be responsible for their higher migraine prevalence.

3.4.4. Sleep disturbances

Sleep disturbances are also strong migraine predictors, and no race/ethnicity is particularly affected. Since the Asian people have the lowest proportions of troubles in falling/staying asleep, sleep medication usage, pain in neck/low back/jaw/front ear, former/current drinkers and current smokers, these precipitating factors may have sufficiently mediated between their race and migraine prevalence.

In summary, strong correlations with racial/ethnic migraine prevalence were found in age, sex, poverty status, problems in paying medical bills, serious depression and anxiety, hypertension, current smoking, pain in neck/lower back/jaw/front ear, inadequate or excessive sleeping hours, troubles in falling or staying asleep, and sleep medication usage. Marital status, higher education, obesity, alcohol drinking and high cholesterol also showed some associations with migraine, but not so significant as other variables.

4. Limitations of the study

We should be aware of several limitations of this study, too.

Because this is a cross-sectional study, it is not possible to determine causal relationships between migraine prevalence and individual variables. For example, shorter than usual sleep hours can induce migraine, while migraine attacks during nighttime may result in inadequate sleep as well. It is also difficult to differentiate triggers, manifestation and postdrome syndromes of migraine, as mentioned above.

There may be also sampling and recalling biases in the self-reported results. The survey contained a large number of questions which can be time-consuming, and asked about the past 3-month prevalence of migraine. Because headaches can only be perceived by patients themselves, the interpretation of suffering from migraine is considerably subjective, which may have resulted in over-reporting or under-reporting of migraine.

In addition, since this study uses data from the NHIS which covered generally broad health topics, some migraine-specific variables were unavailable to be identified in the analyses. For example, no information was found regarding stress levels, usage of oral contraceptives, whether the respondent received accurate diagnosis of migraine, or whether effective medication for migraine was given. On the other hand, several variables had to be discarded because of too many missing values, such as stress from work and confidence in obtaining affordable coverage.

Lastly, although race/ethnicity summarizes main physiological traits, each subgroup in this study is potentially heterogeneous. For example, the Asian population can be classified into Chinese, Japanese, Korean, Filipino, Vietnamese, etc. Hispanics are also divided into Mexican, Dominican, Puerto Rican and so forth. Further careful subdivision may be helpful to better understand the conditions of migraine across different ethnicities.

5. Implications of this study

Taking all the above into consideration, we can summarize the implications – involving epidemiology, clinical practice, and even health policy – of this study.

This study revealed a relatively stable prevalence of migraine during 2010-2015 in the United States, which indicates somewhat good control of the disorder.

Compared to the non-Hispanic White population, differences in migraine prevalence were only detected in Asians and bi-/multi-racial people after adjustment by age and gender, demonstrating the strong impact of the two physiological factors. It is also a novel discovery that people with 2 or more races, who were seldom studied before, had significantly higher migraine prevalence than Caucasians. This result will help raise awareness of neurological health in such a population.

Still, the significant association between race and migraine disappeared when adjusted by precipitating factors of migraine. It is good news that many of the contributing factors are relatively changeable or controllable, compared to congenital characteristics such as race, age and sex. Lifestyle adjustment and control of chronic conditions may help prevent or alleviate migraine attacks, especially for bi-/multi-racial people.

Interactions of races/ethnicities and contributing factors are another new finding from this study. They will assist physicians in considering the susceptibility of migraine within specific racial or ethnic groups. For example, although migraine prevalence is lower among Asians, when they have hypertension, neck pain, or lower back pain, the effects of these contributing factors on migraine are even greater. Therefore, physicians should pay more attention to those Asian patients with such conditions. Also, related patient education programs should be implemented more actively, such as hypertension prevention for Hispanic people, in order to better improve health conditions.

6. Future research

Our next step is to establish a full migraine-specific study on races and ethnicities, hopefully including sufficient variables and cases into analyses, which may meet the need for targeted interventions. Since there is a large number of immigrants in the United States, the impact of acculturation (especially on minority populations) and dietary factors on migraine will be other research objects to be examined.

7. Conclusions

- The overall prevalence of migraine declined from 2010 to 2015 in the US adult population; a slight increase was seen in Asians and people with 2 or more races, but the changes were not statistically significant.

- Significant differences were found in Asians (lower) and people with 2 or more races (higher) compared to non-Hispanic Whites regarding age and sex adjusted racial/ethnic differences.

- Strong correlations with racial/ethnic migraine prevalence were found in age, sex, poverty status, problems in paying medical bills, serious depression and anxiety, hypertension, current smoking, pain, and sleep disturbances.

- Marital status, higher education, obesity, alcohol drinking and high cholesterol also showed some associations with migraine, but not so significant as other variables.

- A lower proportion of contributing factors in Asians and a higher proportion in people with 2 or more races may partly explain the racial differences in migraine prevalence.

- Interactions between contributing factors and races/ethnicities suggest clinicians to consider susceptibility of migraine within specific patient groups.

- More specific research and further careful subdivision may be helpful to better understand the conditions of migraine across different populations.

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