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# Physical and Mental Comorbidity of Headache in a Nationally Representative Sample of U.S. Adults

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# Abstract

**BACKGROUND**—Comorbidity of headache with physical and mental disorders has been frequently reported in clinical samples, but few large scale population-based studies have investigated the contribution of comorbidity to health utilization and negative health perception.

**METHODS**—This question was addressed using combined six-year data from the 1999-2004 NHANES (n=31,126 adults), nationally representative datasets of the US population. Measures of physical disorders were based on standardized interviews of chronic conditions, and mental disorders were assessed by the Composite International Diagnostic Interview (CIDI) for DSM-IV.

**RESULTS**—The three-month prevalence of severe headaches or migraine in the US general population was 22.73%, with females and young adults having greater rates than males and older adults. Adults with headache had increased odds for a variety of physical disorders (including asthma, rheumatoid arthritis, and stroke), and mental disorders (including depression, generalized anxiety disorder and panic disorder). Adults with headache were more likely to rate their health as 'fair or poor' (17.9% vs. 6.1%), to seek healthcare four or more times in a year (43.3% vs. 22.7%) and to endorse physical and mental limitations. Health utilization and negative health perception were more strongly influenced by comorbid mental disorders than physical disorders.

**CONCLUSIONS**—The results from this nationally representative sample provide new information on the inter-relationships of headache with mental and physical disorders. The greater impact of comorbid mental compared to physical disorders on health care utilization and health perception has important implications for the clinical evaluation and treatment of headache in the population.

## Keywords

headache; migraine; comorbidity; psychiatric; disability; epidemiology

# BACKGROUND

Headaches are a common neurological complaint that rank among the top 10 most disabling conditions for men and women worldwide (1). The public health significance of headache is highlighted by its high prevalence, with approximately 46% of adults reporting a current headache disorder, (1), and dramatic personal and societal impact.

At the level of the affected individual, there is mounting evidence that persons with headaches have poor health-related quality of life (2-4) and serious functional impairment as a result of the nature and unpredictability of their headaches (5). For example, a Swedish survey revealed

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that more than 50% of migraine sufferers reported that their headache condition had a negative influence on their ability to attend work or school, and on their family life and leisure time (6). Severe headaches and migraine also have major economic impact due to medical expenses and employer costs (7). The annual US direct medical cost attributable to migraine was estimated at \$1 billion in 1999 (8), and migraine causes roughly 112 million bedridden days per year (8,9)Migraine costs employers approximately \$13 billion annually due to impaired work performance and employee absences (8).

Population based surveys have also found that migraine is often comorbid with several physical conditions, with the most consistent associations reported between migraine and asthma, epilepsy, chronic musculoskeletal pain and stroke (4,10,11), as well as with allergies, hypothyroidism, hypertension, and sleep disorders in clinical samples (12,13). Migraine has also been consistently shown to co-occur with mood and anxiety disorders in both clinical and community studies (14-20).

Despite the well-established patterns of comorbidity, however, few health economic studies have considered the role of comorbidity in estimating the costs of migraine and severe headaches. Because both major depression and migraine are among the leading causes of disability (DALY'S—(21-23)it is therefore essential to incorporate comorbidity in estimates of disability associated with either of these conditions alone. Recent studies that have studied a wide range of both physical and mental conditions suggest that there is an interactive influence of depression and physical disorders such as diabetes and heart disease (24-27).

Therefore, the goals of the present study are: (1) to investigate patterns of mental and physical comorbidity among people with severe headaches/migraine in a large population based survey of the U.S. general population; and (2) to examine the unique and combined impact of comorbid mental and physical disorders on the impact of severe headaches/migraine on health services and health perception in a large and representative sample of the U.S., the National Health Examination and Nutrition Survey (NHANES).

## METHODS

#### Sample

The NHANES surveys are conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention and constitute nationally representative samples of the noninstitutionalized U.S. civilian population obtained through a stratified, multistage probability sampling design. A detailed description of the sampling strategy and weighting methods are available online (28). The current study uses the combined six-year data derived from the NHANES 1999–2000, NHANES 2001-2002 and NHANES 2003-2004 surveys (total n=31,126). Response rates for the interview are 82%, 84% and 79% for the 1999-2000, 2001-2002, and 2003-2004 surveys, respectively.

#### Measures

Participants completed in-home interviews administered by trained lay interviewers where they answered a variety of questions on topics such as demographic characteristics, medical conditions, miscellaneous pain, physical functioning, health utilization, and health perception. The sociodemographic variables examined in this study included age, sex, race/ethnicity, marital status and education level.

Measures of severe headaches or migraine during the past three months are collected in the component of the NHANES interview on miscellaneous pain. The presence of anemia was assessed by asking the respondent if they had received treatment for anemia, such as transfusion, iron pills, iron shots, during the past three months. Other physical conditions were

assessed with a standard chronic condition checklist based on a standard interview. This method is used regularly by surveys conducted by the National Center for Health Statistics, including the NHANES and the US National Health Interview Survey (NHIS) (29).

Respondents were asked a number of questions regarding their use of healthcare services. For this manuscript, we analyzed responses to two such questions: the first question asked about the number of times the respondent has received healthcare (zero, one, two, three, four or more) and the second question asked whether they have seen a mental health professional over the past year (yes or no). Responses to three additional questions on health perception and limitations were analyzed. The first question addressed the respondent's subjective impression of his/her own general health status (excellent, very good, good, fair or poor). The second question addressed whether the respondent had suffered from confusion or memory problems (yes or no). The third question asked whether the respondent had suffered from physical, mental or emotional problems (yes or no).

During a subsequent visit to a mobile examination center, a random sub-sample (50%) of participants aged 20-39 years were administered the computerized World Health Organization Composite International Diagnostic Interview Version 2.1 (WHO-CIDI Auto 2.1). The CIDI is a comprehensive, fully structured interview that is used by trained lay interviewers to assess mental disorders and provide diagnoses according to definitions and criteria of the tenth revision of the International Classification of Diseases (ICD-10, (30,31)) and the fourth edition of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-IV(32). Diagnoses of major depression, panic disorder and generalized anxiety disorder (GAD) within the past 12 months were constructed through computer algorithms based on the responses of the participant during the WHO-CIDI interview. In his review, Wittchen (33) reviewed the numerous reports documenting the good reliability and validity of the CIDI based on the WHO CIDI Field Trials carried out by the multinational CIDI editorial committee in both patient samples and in limited community samples throughout the world..Further details of the sub-sampling methodology is available online (28)

#### **Statistical Analysis**

All analyses were based on weighted data and implemented in SAS using the PROC SURVEY Procedures (SAS Institute Inc, Cary, NC). Significance tests and 95% confidence intervals were estimated using the Taylor Series method to adjust for the weighting and clustering of the NHANES data. All significance tests were made using Rao-Scott chi-square two-sided tests evaluated at the 0.05 level of significance, and Bonferroni corrections were applied to correct for multiple testing (defined as 0.05/number of comparisons).

For the first part of the analysis, respondents were classified into two groups based on the presence or absence of severe headaches or migraine. The frequency distribution of sociodemographic characteristics was compared between the headache and the no headache group. Simple and adjusted odds ratios (95% CI) were then calculated for each sociodemographic variable, where headache was the dependent variable and all the sociodemographic variables included as covariates. Marital status was omitted as a covariate from this analysis forward because of the large amount of missing data for this variable, and the absence of any notable confounding effect when included in the analysis.

The frequency distribution (95% CI) of physical conditions within the headache and no headache group were compared, and both simple and adjusted odds ratios (95% CI) were calculated. In the study of psychiatric comorbidity, the distribution of diagnoses of major depression, panic disorder and GAD was compared between those with and without headache. Logistic regression analysis was used to construct odds ratios of the association between

headache (independent variable) and each mental disorder diagnosis (dependent variable) in both an unadjusted model and a model adjusting for sociodemographic characteristics.

The analysis of health care utilization and health perception was also completed in the subsample of individuals who completed the WHO-CIDI interview. The frequency distribution of general health perception and health utilization was calculated in respondents without headache, and these percentages (95% CI) were compared across four additional groups: those with headache, those with headache comorbid with any physical disorder (as detailed above), those with headache comorbid with any mental disorder (major depression, panic disorder, GAD) and those with headache comorbid with any mental disorder and any physical disorder.

# RESULTS

Of the 31,126 respondents who completed the NHANES 1999-2004 surveys, we sampled only those adults 20 years of age or older who were asked whether they suffered from severe headaches or migraine during the past three months (Total n=15,332; NHANES 1999-2000: n=4880 out of 9965, NHANES 2001-2001: n= 5411 out of 11,039, NHANES 2003-2004: n=5041 out of 10,122). There were an additional two respondents who had missing values on this question, leaving a sample of 15,330 (n=12,275 with no headache and n=3045 with headache). The three-month prevalence rates of severe headaches or migraine were 27.62% for females, and 14.81% for males, yielding a total prevalence of 22.73% in the general population of U.S. adults.

A comparison of the sociodemographic characteristics of the headache and no headache sample are presented in Table 1. In agreement with previous reports, respondents reporting severe headaches or migraine were significantly more likely to be female (adjusted OR=2.32, 95% CI: 2.08, 2.59) and more likely to be young. Adjusted regression analysis showed an association between age group and severe headaches or migraine, and those respondents aged 20-39 years and 40-54 years had 4.52 and 4.33 increased odds of reporting severe headaches or migraine in comparison to respondents aged 75 years or more. Respondents with severe headaches or migraine were also more likely to be separated or divorced (adjusted OR=1.29, 95% CI: 1.13, 1.47), and report an education level of high school (adjusted OR=1.27, 95% CI: 1.09, 1.48) or less than high school (adjusted OR=1.76, 95% CI: 1.50, 2.06). A comparison of ethnicity showed that Mexican-Americans were less likely to report severe headaches or migraine (adjusted OR=0.83, 95% CI: 0.71, 0.98), whereas there were equal prevalence rates among non-Hispanic whites and non-Hispanic blacks.

The rates and comorbidity of physical disorders in respondents in the headache and no headache sample are presented in Table 2. Overall, 84.61% of individuals with severe headaches or migraine had at least one comorbid physical condition, 55.70% had at least two, and 31.77% had at least three comorbid conditions as opposed to the 68.76%, 37.90%, and 19.05%, respectively, in the no headache sample (p<0.001 for all). After Bonferroni correction for multiple comparisons, respondents reporting severe headaches or migraine were significantly more likely (p<0.006) to suffer from a range of physical disorders, including asthma (adjusted OR=1.52, 95% CI: 1.29-1.79), low back pain (adjusted OR=2.77, 95% CI: 2.49-3.09), rheumatoid arthritis (OR=1.95, 95% CI: 1.68-2.25), and a variety of cardiovascular disorders, including angina (OR=2.15, 95% CI: 1.62-2.84) and congestive heart failure (adjusted OR=1.81, 95% CI: 1.36-2.40). In addition, respondents with severe headaches or migraine were more likely to report trouble seeing even with glasses (adjusted OR=2.02, 95% CI: 1.80-2.28), treatment for anemia (adjusted OR=2.11, 95% CI: 1.60-2.78), thyroid problems (adjusted OR=1.39, 95% CI: 1.16-1.67), chronic bronchitis (adjusted OR=2.21, 95% CI: 1.80-2.71), liver problems (adjusted OR=1.69, 95% CI: 1.38-2.07), and being overweight (adjusted OR=1.51, 95% CI: 1.35-1.69). When the frequency of respondents in the headache

and no headache sample suffering from two or more conditions within a given physical grouping were compared, we found that respondents with headache were more likely to have at least two comorbid respiratory conditions (5.69% versus 2.65%), and at least two comorbid pain conditions (7.92% vs. 4.51%). Overall, headache sufferers had an increased odds of at least one (OR=2.84), two (OR=2.56) and three (OR=2.69) comorbid conditions.

There were a total of 598 with headache and 1667 respondents with no headaches among respondents, ages 20-39 years, who completed the WHO-CIDI. As reported in Table 3, respondents reporting severe headaches or migraine were significantly more likely to meet criteria for major depression (14.61% vs. 5.42%), panic disorder (5.62% vs. 1.55%), and/or GAD (5.78% vs. 1.97%). After adjusting for age, race, sex, and education, respondents with severe headaches or migraine had 2.84 increased odds of major depression, 3.29 increased odds of panic disorder and 3.03 increased odds of GAD. Overall, individuals with severe headaches or migraine had 2.30 (95% CI: 1.37, 3.85) increased odds of having a single mental disorder, and 6.28 (95% CI: 2.05, 19.26) increased odds of at least two disorders (both p<0.001).

The association between headache, comorbid mental disorders and comorbid physical disorders on health utilization and general health perception is presented in Table 4. As a group, respondents with severe headaches or migraine were less likely to rate their general health condition as excellent (17.54% vs. 27.06), and more likely to rate their health as 'fair or poor' (17.87% vs. 6.11%). Respondents with severe headaches or migraine plus at least one comorbid physical disorder were even less likely to rate their health as excellent (13.87% vs. 27.06%) and more likely to rate their health as fair or poor (21.47% vs. 6.11%). It was the addition of a comorbid mental disorder, however, that caused the greatest shift in general health perception; respondents with headache plus at least one mental disorder (n=102) or at least one mental disorder coupled with at least one additional physical disorder (n=79) were less likely to rate their health as excellent (5.81% and 4.59%, respectively, vs. 6.11%). These differences were all significant at p<0.001.

Similarly, respondents with headache were more likely to endorse physical, mental or emotional problems and confusion or memory problems than their non headache counterparts (19.75% vs. 8.94% and 5.90% vs. 2.53%, respectively). Although these problems were accentuated among those with comorbidity in general, the contribution of mental disorders outweighed that of comorbid physical disorders.

There was a direct association between severe headaches or migraine and use of healthcare four or more times in the past year (43.32% vs. 22.71%), an effect which increased linearly up to 53.45% in the headache group with both a comorbid mental and physical condition. Comorbidity was also associated with an increase in the number of respondents who had visited a mental health professional in the previous year, with the headache plus any comorbid mental disorder group reporting the highest rates (33.42% vs. 6.82% in the no headache sample).

# DISCUSSION

The results presented here supply new information on the effect of mental and physical disorder comorbidity on health utilization and general health perception. In agreement with previous large population-based studies (34), severe headaches or migraine affect a substantial proportion of our sample. Approximately 23% of respondents endorsed severe headaches or migraine within the past three months. Comorbidity was pervasive; 84.61% of the headache sample had at least one comorbid physical disorder and 19.22% had at least one comorbid mental disorder.

Our results confirm the high magnitude of physical comorbidity associated with headache in a similar but larger study of the US population (35). Furthermore, we found that respondents with severe headaches or migraine were more likely to have clusters of respiratory and pain conditions rather than increased rates of all physical conditions assessed in this survey.

Similar to prior epidemiologic surveys worldwide, we found strong associations between severe headaches or migraine and major depression, panic disorder and GAD (36). Respondents with severe headaches or migraine were approximately three times as likely to receive a diagnosis of these disorders, and were almost five times as likely to have at least two disorders. Additionally, we examined the mental and physical disorder comorbidity simultaneously and their relative and joint impact on health care utilization and negative health perception.

The respondents endorsing severe headaches or migraine were more likely to rate their health as 'fair or poor', receive healthcare four or more times in the past year, and report seeing a mental health professional within the past year. The greater proportion of respondents reporting limitations because of physical, mental or emotional problems and confusion and memory problems supports prior studies that document decreased health-related quality of life and health perception in individuals with headache or migraine (34,37). When the sample was restricted to those respondents with at least one additional physical disorder, at least one mental disorder, or both, there was a decline in general health perception and an increase in healthcare utilization. A similar finding was reported in a study of health-related quality of life (HRQOL), where migraineurs had a poor HRQOL that was further reduced in the presence of comorbid asthma or chronic musculoskeletal pain (4).

Additionally, our results build upon previous findings of reduced HRQOL in subjects when migraine was comorbid with depression as compared to migraine alone (37), and a later study which reported that individuals with migraine comorbid with mood disorders had lower HRQOL in all domains with pronounced effects on emotional role, social functioning and general health in comparison to those with migraine alone (38). Although there was a decline in health perception and an increase in health utilization with increasing physical or mental comorbidity, the most intriguing result is the greater influence of comorbid mental, as opposed to physical, conditions. This suggests that special attention should be paid to symptoms of mood and anxiety disorders in the evaluation and treatment of migraineurs due to the pronounced effect on perceived quality of life. A review by Bair and colleagues (39), for example, reported that neglecting to treat any underlying depression might explain some pain treatment failures.

There are many potential reasons for high rates of comorbidity in headache. It may result from common biologic pathways, or it may be causal in that disturbances in one system may provoke disturbances in another. Severe headaches or migraine could also be a secondary effect of medication used to treat other mental or physical conditions. Greater sensitivity to pain and/or a lower tolerance for symptoms among people with headaches is another possible explanation for comorbidity. More focused longitudinal studies are needed in order to determine the order of onset of comorbid conditions, identify the biological, environmental and social factors that precipitate or aggravate the comorbidity, and determine how comorbidity shapes the course and severity of each disorder as well as the response to treatment. Although we are unable to distinguish between the possibilities here, there was notable clustering of disorders within the diagnostic groups of mood and anxiety disorders, respiratory and pain conditions. Given the implications of this clustering, special attention should be paid to the assessment of these disorders during evaluation.

There are several strengths of this study. The NHANES 1999-2004 data represents the compilation of three large, nationally representative cross-sectional surveys (NHANES 1999-2000, 2001-2002 and 2003-2004). Comparison across years made it possible to examine any possible temporal trends in frequency of severe headaches or migraine, of which none were apparent. The NHANES dataset also collects extensive information on physical conditions, health perception and utilization, and full WMH-CIDI diagnostic criteria for depression, panic disorder and GAD, which distinguishes it from other epidemiologic datasets such as the Epidemiologic Catchment Area Study and National Comorbidity Study that focus more exclusively on mental conditions.

Several limitations also need to be considered. Diagnostic criteria for specific subtypes of headache (40) could not be assessed, nor could their age at onset, frequency, severity, or treatment history. This limited our ability to investigate possible explanations for comorbidity in this sub-sample. However, prior prospective research has shown that the onset of anxiety disorders generally precede the onset of migraine, which in turn precedes the onset of depression (18). We also cannot discern whether the headaches occurred as a consequence of treatment; however, it could be argued that individuals who do develop severe headaches or migraine in response to treatment differ from those who do not. Although there is no specific information on headache severity, the question on headache only addresses frequent and severe headaches or migraine occurring within the past three months. Therefore, it is likely that the sample who endorsed headaches are suffering from what they perceive as a current and severe condition.

Another limitation is the use of self-reported medical conditions. Although widely used in epidemiological surveys, the conditions could not be verified by a clinician so it is possible that a small percentage of respondents may have been misclassified. Additionally, we could not assess the severity of self-reported mental or physical disorders, which may be related to both comorbidity and disability. Several subtypes of mood or anxiety disorders with established associations to disability and severe headaches, such as specific phobia, social phobia, or bipolar disorder (16,20,36)were also not assessed. Finally, the restricted age range of the subsample limited the analyses that could be completed regarding the inter-relationship between physical and mental comorbidity.

Comorbidity has implications for the prevention and treatment of disorders. It can alter the clinical course of patients with the same diagnosis by affecting the time of detection, prognostic anticipations, therapeutic selection and post-therapeutic outcome of an index diagnosis (41). In addition, it can also affect the length of hospital stay, response to somatic treatment and mortality (24). The results presented here suggest that severe headaches or migraine are often accompanied by at least one additional comorbid physical and mental disorder, which results in a more negative outcome in terms of health perception and utilization. Comorbidity is an indication of disturbances in multiple systems, so its inclusion in clinical evaluation and treatment is essential. By considering not only the index disorder, but the deleterious effects that comorbid disorders, particularly mood and anxiety disorders, can have on severity and course, the effectiveness of any intervention or treatment will be enhanced.

This study provides new information on the significant role of comorbid mood and anxiety disorders on the impact of severe headaches or migraine on health care utilization and perception in the general population. The findings support converging evidence of the importance of mental disorders as an equal or greater source of disability than general physical conditions (25,42), and the impact of comorbid mental and physical disorders on work loss, disability and diminished quality of life (27,43). Likewise, the strength of the health impact of comorbidity also supports the need for integration of both mental and physical disorders in the clinical evaluation, and treatment of patients with headaches and/or depression, panic or GAD,

as well as the importance of establishing strategies to minimize the disability associated with these conditions.

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### Abbreviations

NHANES	National Health Examination and Nutrition Survey
WHO-CIDI	World Health Organization Composite International Diagnostic Interview
GAD	Generalized Anxiety Disorder
HRQOL	health-related quality of life

#### REFERENCES

- 1. Stovner L, Hagen K, Jensen R, Katsarava Z, Lipton R, Scher A, Steiner T, Zwart JA. The global burden of headache: a documentation of headache prevalence and disability worldwide. Cephalalgia 2007;27 (3):193-210. [PubMed: 17381554]
- 2. Kryst S, Scherl E. A population-based survey of the social and personal impact of headache. Headache 1994;34(6):344-50. [PubMed: 7928313]
- 3. de Velasco, I Ruiz; Gonzalez, N.; Etxeberria, Y.; Garcia-Monco, JC. Quality of life in migraine patients: a qualitative study. Cephalalgia 2003;23(9):892–900. [PubMed: 14616931]
- 4. Terwindt GM, Ferrari MD, Tijhuis M, Groenen SM, Picavet HS, Launer LJ. The impact of migraine on quality of life in the general population: the GEM study. Neurology 2000;55(5):624-9. [PubMed: 10980723]
- 5. Leiper DA, Elliott AM, Hannaford PC. Experiences and perceptions of people with headache: a qualitative study. BMC Fam Pract 2006;7:27. [PubMed: 16670013]
- 6. Linde M, Dahlof C. Attitudes and burden of disease among self-considered migraineurs-- a nationwide population-based survey in Sweden. Cephalalgia 2004;24(6):455–65. [PubMed: 15154855]
- 7. Stang P, Von Korff M, Galer BS. Reduced labor force participation among primary care patients with headache. J Gen Intern Med 1998;13(5):296-302. [PubMed: 9613884]
- 8. Hu XH, Markson LE, Lipton RB, Stewart WF, Berger ML. Burden of migraine in the United States: disability and economic costs. Arch Intern Med 1999;159(8):813-8. [PubMed: 10219926]
- 9. Lafata, J Elston; Moon, C.; Leotta, C.; Kolodner, K.; Poisson, L.; Lipton, RB. The medical care utilization and costs associated with migraine headache. J Gen Intern Med 2004;19(10):1005–12. [PubMed: 15482552]
- 10. Merikangas, KR.; Rasmussen, BK. Migraine Comorbidity. In: Olesen, J.; Tfelt-Hansen, P.; Welch, KMA., editors. The Headaches. Williams & Williams; Philadelphia, Lippincott: 2000.
- 11. Welch KM. Relationship of stroke and migraine. Neurology 1994;44(10 Suppl 7):S33-6. [PubMed: 7969944]
- 12. Bigal ME, Sheftell FD, Rapoport AM, Tepper SJ, Lipton RB. Chronic daily headache: identification of factors associated with induction and transformation. Headache 2002;42(7):575-81. [PubMed: 12482208]
- 13. Peres MF, Young WB, Kaup AO, Zukerman E, Silberstein SD. Fibromyalgia is common in patients with transformed migraine. Neurology 2001;57(7):1326-8. [PubMed: 11591860]
- 14. Bag B, Hacihasanoglu R, Tufekci FG. Examination of anxiety, hostility and psychiatric disorders in patients with migraine and tension-type headache. Int J Clin Pract 2005;59(5):515–21. [PubMed: 15857345]

- Breslau N. Psychiatric comorbidity in migraine. Cephalalgia 1998;18(Suppl 22):56–8. discussion 58-61. [PubMed: 9793713]
- Breslau N, Lipton RB, Stewart WF, Schultz LR, Welch KM. Comorbidity of migraine and depression: investigating potential etiology and prognosis. Neurology 2003;60(8):1308–12. [PubMed: 12707434]
- Guidetti V, Galli F, Fabrizi P, Giannantoni AS, Napoli L, Bruni O, Trillo S. Headache and psychiatric comorbidity: clinical aspects and outcome in an 8-year follow-up study. Cephalalgia 1998;18(7): 455–62. [PubMed: 9793697]
- Merikangas KR, Angst J, Isler H. Migraine and psychopathology. Results of the Zurich cohort study of young adults. Arch Gen Psychiatry 1990;47(9):849–53. [PubMed: 2393343]
- Merikangas KR, Merikangas JR, Angst J. Headache syndromes and psychiatric disorders: association and familial transmission. J Psychiatr Res 1993;27(2):197–210. [PubMed: 8366469]
- Swartz KL, Pratt LA, Armenian HK, Lee LC, Eaton WW. Mental disorders and the incidence of migraine headaches in a community sample: results from the Baltimore Epidemiologic Catchment area follow-up study. Arch Gen Psychiatry 2000;57(10):945–50. [PubMed: 11015812]
- Knight M, Stewart-Brown S, Fletcher L. Estimating health needs: the impact of a checklist of conditions and quality of life measurement on health information derived from community surveys. J Public Health Med 2001;23(3):179–86. [PubMed: 11585189]
- 22. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006;3(11):e442. [PubMed: 17132052]
- 23. Stewart WF, Ricci JA, Chee E, Morganstein D, Lipton R. Lost productive time and cost due to common pain conditions in the US workforce. Jama 2003;290(18):2443–54. [PubMed: 14612481]
- 24. Buist-Bouwman MA, de Graaf R, Vollebergh WA, Ormel J. Comorbidity of physical and mental disorders and the effect on work-loss days. Acta Psychiatr Scand 2005;111(6):436–43. [PubMed: 15877710]
- 25. Kessler RC, Ormel J, Demler O, Stang PE. Comorbid mental disorders account for the role impairment of commonly occurring chronic physical disorders: results from the National Comorbidity Survey. J Occup Environ Med 2003;45(12):1257–66. [PubMed: 14665811]
- Merikangas KR, Ames M, Cui L, Stang PE, Ustun TB, Von Korff M, Kessler RC. The impact of comorbidity of mental and physical conditions on role disability in the US adult household population. Arch Gen Psychiatry 2007;64(10):1180–8. [PubMed: 17909130]
- Stewart-Brown S, Layte R. Emotional health problems are the most important cause of disability in adults of working age: a study in the four counties of the old Oxford region. J Epidemiol Community Health 1997;51(6):672–5. [PubMed: 9519131]
- 28. CDC: Centers for Disease Control and Prevention. The National Health and Nutrition Examination Survey, Analytic and Reporting Guidelines. Centers for Disease Control and Prevention; 2006.
- 29. Schoenborn CA, Adams PF, Schiller JS. Summary health statistics for the U.S. population: National Health Interview Survey, 2000. Vital Health Stat 10 2003;(214):1–83. [PubMed: 15786609]
- World Health Organization. The ICD-10 Classification of Mental and Behavioural Disorders: clinical Descriptions and Diagnostic Guidelines. World Health Organization; Geneva, Switzerland: 1992. p. 50-51.
- World Health Organization. The ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research. World Health Organization; Geneva, Switzerland: 1993. p. 36-40.
- 32. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Washington, DC: 1994.
- Wittchen HU. Reliability and validity studies of the WHO--Composite International Diagnostic Interview (CIDI): a critical review. J Psychiatr Res 1994;28(1):57–84. [PubMed: 8064641]
- 34. Carson AP, Rose KM, Sanford CP, Ephross SA, Stang PE, Hunt KJ, Brown CA, Szklo M. Lifetime prevalence of migraine and other headaches lasting 4 or more hours: the Atherosclerosis Risk in Communities (ARIC) study. Headache 2004;44(1):20–8. [PubMed: 14979879]
- 35. Strine TW, Chapman DP, Balluz LS. Population-based U.S. study of severe headaches in adults: psychological distress and comorbidities. Headache 2006;46(2):223–32. [PubMed: 16492231]
- Radat F, Swendsen J. Psychiatric comorbidity in migraine: a review. Cephalalgia 2005;25(3):165– 78. [PubMed: 15689191]

- Lipton RB, Hamelsky SW, Kolodner KB, Steiner TJ, Stewart WF. Migraine, quality of life, and depression: a population-based case-control study. Neurology 2000;55(5):629–35. [PubMed: 10980724]
- Brna P, Gordon K, Dooley J. Health-related quality of life among Canadians with migraine. J Headache Pain 2007;8(1):43–8. [PubMed: 17361382]
- 39. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: a literature review. Arch Intern Med 2003;163(20):2433–45. [PubMed: 14609780]
- 40. International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Headache Classification Committee of the International Headache Society. Cephalalgia 1988;8(Suppl 7):1–96.
- 41. Kaplan MH, Feinstein AR. The importance of classifying initial co-morbidity in evaluatin the outcome of diabetes mellitus. J Chronic Dis 1974;27(7-8):387–404. [PubMed: 4436428]
- 42. Druss BG, Marcus SC, Olfson M, Tanielian T, Elinson L, Pincus HA. Comparing the national economic burden of five chronic conditions. Health Aff (Millwood) 2001;20(6):233–41. [PubMed: 11816664]
- 43. Rijken M, van Kerkhof M, Dekker J, Schellevis FG. Comorbidity of chronic diseases: effects of disease pairs on physical and mental functioning. Qual Life Res 2005;14(1):45–55. [PubMed: 15789940]

Three-month weighted prevalence rates and adjusted odds ratios of sociodemographic characteristics by severe headaches/ migraine in the NHANES 1999-2004

	% (95% CI) am	ong adults with:	
	No Severe Headaches/Migraine (n=12275)	Severe Headaches/Migraine (n=3045)	aOR <sup>a</sup> (95% CI)
Sex			
Female	48.11 (47.33, 48.88)	67.04 (64.94, 69.13)	2.32 (2.08, 2.59) *
Male	51.89 (51.12, 52.67)	32.96 (30.87, 35.06)	REF
Age			
20-39	37.38 (35.58, 39.18)	47.27 (45.46, 49.08)	4.52 (3.38, 6.05) *
40-54	30.23 (28.93, 31.52)	35.67(33.69, 37.64)	4.33 (3.26, 5.75) *
55-74	23.41 (21.99, 24.84)	14.19 (12.64, 15.75)	2.04 (1.59, 2.61) *
75+	8.98 (8.21, 9.75)	2.87 (2.18, 3.56)	REF
Marital Status			
Never Married	22.25 (20.39, 24.11)	26.70 (23.47, 29.92)	1.13 (0.95, 1.33)
Widowed	7.50 (6.70, 8.30)	4.30 (3.45, 5.15)	0.90 (0.66, 1.22)
Separated/Divorced	11.36 (10.48, 12.24)	15.28 (13.66, 16.89)	1.29 (1.13, 1.47) ‡
Married	58.89 (56.72, 61.07)	53.73 (50.67, 56.79)	REF
Ethnicity			
Non-Hispanic black	10.75 (8.76, 12.73)	12.29 (9.75, 14.83)	0.94 (0.81, 1.10)
Mexican American	7.10 (5.42, 8.78)	7.97 (5.97, 9.97)	$0.83~(0.71,0.98)~^\dagger$
Other Race	3.97 (3.19, 4.76)	4.49 (3.26, 5.73)	1.05 (0.80, 1.38)
Other Hispanic	5.30 (3.24, 7.35)	7.56 (4.11, 11.02)	1.18 (0.88, 1.57)
Non-Hispanic white	72.9 (69.71, 76.07)	67.68 (63.03, 72.33)	REF
Education			
Less than high school	19.77 (18.34, 21.21)	24.80 (22.66, 26.95)	1.76 (1.50, 2.06) *
High school/GED	25.87 (24.19, 27.55)	26.72 (24.49, 28.96)	1.27 (1.09, 1.48) ‡
More than high school	54.36 (52.05, 56.66)	48.47 (25.57, 51.38)	REF

 $a^{a}$  aOR=Adjusted Odds Ratios of the effect of each demographic variable in a model containing every other sociodemographic variable in Table 1 but the poverty income ratio.

\*p<0.001

‡p<0.01

 $^{\dagger}p < 0.05$ 

Rates and adjusted odds ratio of the associations between severe headaches/migraine and physical disorders

	% (9	5% CI) among adults w	ith:		
	No Severe Headaches/Migraine (n=12275)	Severe Headaches/Migraine (n=3045)	Total	OR (95% CI)	aOR <sup>d</sup> (95% CI)
Respiratory Disease	14.45 (13.51, 15.40)	23.25 (20.87, 28.65	16.35 (15.37, 17.32)	1.79 (1.57, 2.07) *	1.74 (1.49, 2.02) *
Cardiovascular Disease	8.32 (7.35, 9.28)	8.19 (6.96, 9.43)	8.29 (7.47, 9.11)	0.98 (0.81, 1.20)	$1.79\ (1.47, 2.19)^{*}$
Pain Conditions	37.55 (36.26, 38.87)	60.66 (58.67, 62.66)	42.53 (41.25, 43.81)	2.56 (2.35, 2.80) *	2.67 (2.43, 2.93) *
Gastrointestinal Disease	11.55 (10.05, 13.04)	14.83 (12.75, 16.91)	12.25 (10.78, 13.72)	$1.33\ (1.16, 1.53)^{*}$	$1.37  (1.17, 1.60)^{*}$
Other					
Anemia	2.25 (1.94, 2.56)	4.94 (3.86, 6.02)	2.83 (2.50, 3.16)	2.25 (1.74, 2.92) *	2.11 (1.60, 2.78) *
Cancer	8.15 (7.55, 8.75)	8.21 (7.05, 9.37)	8.16 (7.60, 8.73)	1.01 (0.86, 1.18)	$1.55 \left(1.31, 1.84\right)^{*}$
Thyroid problems	7.93 (7.31, 8.55)	9.87 (8.62, 11.12)	8.34 (7.83, 8.86)	1.27 (1.07, 1.51)	$1.39 \left( 1.16, 1.67  ight)^{*}$
Trouble Seeing even w/glasses	16.07 (15.22, 16.93)	26.54 (24.26, 28.83)	18.32 (17.31,19.34)	$1.89\ (1.69,\ 2.11)^{*}$	$2.02 \ (1.80, 2.28)^{*}$
AT LEAST 1 CONDITION b	68.76 (67.33, 70.19)	84.61 (82.79, 86.44)	72.14 (70.85, 73.43)	2.50 (2.16, 2.89) *	2.84 (2.46, 3.28) *
AT LEAST 2 CONDITIONS $c$	37.90 (36.49, 39.30)	55.70 (53.18, 58.23)	41.70 (40.20, 43.19)	2.06 (1.89, 2.25) *	2.56 (2.34, 2.81) *
AT LEAST 3 CONDITIONS	19.05 (17.88, 20.22)	31.77 (29.60, 33.95)	21.77 (20.58, 22.96)	1.98 (1.79, 2.19) *	2.69 (2.39, 3.02) *

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Respiratory Diseases include asthma, chronic bronchitis, and emphysema

Cardiovascular Diseases include angina, congestive heart failure, coronary heart disease, heart attack and stroke

Pain Conditions include low back pain, osteoporosis, and rheumatoid arthritis

Gastrointestinal Diseases include diabetes, liver problems, being overweight and stomach, duodenal, or peptic ulcers

 $^{a}$ Adjusted for sex, age, race and education status.

 $b_{\rm Total}$  values did not include the presence of ulcers due to the high missingness of this variable (present in 1999-2000 survey only).

 $^{\rm C}$  Values represent any 2 conditions either within a grouping or between groupings

\* Significant after Bonferroni Correction, p=0.0045

Weighted 12-month month prevalence rates of mental disorders and adjusted odds ratios of association between severe headaches/migraine with mental disorders  $^a$ .

Kalaydjian and Merikangas

	% (95	% CI) among adults with			
	No Severe Headaches/Migraine (n=1667)	Severe Headaches/Migraine (n=598)	Total	OR (95% CI)	aOR <sup>b</sup> (95% CI)
Major Depression	5.42 (3.61, 7.22)	14.61 (10.72, 18.50)	7.80 (6.17, 9.43)	2.99 (1.82, 4.91) *	2.84(1.71, 4.73) *
Panic Disorder	1.55 (0.80, 2.31)	5.59 (3.35, 7.83)	2.60 (1.77, 3.43)	3.75 (1.99, 7.10) *	3.29 (1.63, 6.62) *
Generalized Anxiety Disorder	1.97 (1.08, 2.85)	5.74 (2.94, 8.54)	2.95 (2.00, 3.90)	3.04 (1.51, 6.12) *	$3.03 \ (1.43, 6.38)^{*}$
Only 1 disorder	6.35~(4.64, 8.06)	13.91 (9.85, 17.98)	8.31 (6.96, 9.66)	2.38 (1.43, 3.97) *	2.30 (1.37, 3.85) *
Only 2 disorders	$0.57\ (0.11,\ 1.03)$	3.99 (1.97, 6.02)	1.46 (0.86, 2.05)	7.27 (2.67, 19.83) *	6.28 (2.05, 19.26) *
Three conditions	0.48 (0.00, 0.97)	1.31 (0.06, 2.56)	0.69 (0.21, 1.17)	2.78 (0.67, 11.44)	2.74 (0.71, 10.63)

<sup>1</sup>All analysis conducted in the sub-sample of adults, 20-39 years, who were administered the CIDI

 $\boldsymbol{b}_{\mbox{Adjusted}}$  for age, race, sex, and education status

\* Significant after, Bonferroni Correction=0.0083

Health perception and utilization by severe headaches/migraine and comorbid physical and mental disorders<sup>a</sup>

		20(2	oz% CI) among adults w	1th:	
	No Severe Headaches/Migraine (n=1667)	Severe Headaches/Migraine (n=598)	Severe Headaches/Migraine + Any Physical <sup>a</sup> (n=427)	Severe Headaches/Migraine +Any Mental <sup>a</sup> (n=102)	Severe Headaches/Migraine +Any Physical + Mental Psych (n=79)
General Health Condition					
Excellent	27.06 (24.87, 29.23)	17.54 (12.45, 22.62) *	13.87 (8.81, 18.94) *	5.81 (0.05, 11.57) *	$4.59\ (0.00, 9.67)^{*}$
Good or Very good	66.83 (64.67, 68.99)	64.59 (58.60, 70.58)	64.66 (58.27, 71.05)	72.89 (63.21, 82.58)	71.61 (58.92, 84.30)
Fair or Poor	6.11 (4.96, 7.25)	17.87 (14.12, 21.62)	21.47 (16.48, 26.46)	21.30 (11.48, 31.12)	23.80 (12.81, 34.79)
Functional Limitations					
Confusion or memory	2.53 (1.60, 3.45)	5.90~(3.51, 8.28)	6.67 (3.66, 9.68) ‡	14.05 (6.73, 21.38) *	15.17 (7.01, 23.32) *
Physical, mental or emotional problems	8.94 (6.81, 11.08)	19.75 (15.76, 23.74) *	23.17 (18.32, 28.01) *	33.45 (23.69, 43.22) *	35.10 (25.49, 44.72) *
Healthcare past year (# of visits)					
Zero	26.34 (23.59, 29.10)	$16.55\ (12.86,\ 20.25)\ ^{*}$	12.67 (8.46, 16.87) *	$13.30~(6.08, 20.51)^{*}$	$11.38$ (3.38, 19.39) $^{*}$
One to three	50.95 (48.05, 53.84)	40.13 (35.65, 44.60)	39.28 (34.01, 44.55)	36.16 (26.34, 45.98)	35.19 (24.81, 44.57)
Four or more	22.71 (20.54, 24.88)	43.32 (38.67, 47.97)	48.05 (42.47, 53.63)	50.54 (38.93, 62.16)	53.43 (42.00, 64.85)
Seen mental health professional in past year	6.82 (5.12, 8.52)	$13.95\ (9.60,\ 18.30)\ ^*$	14.75 (9.82, 19.68) *	33.42 (22.35, 44.50) *	$30.95~(17.41, 44.50)^{*}$

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 $^{a}$ All analysis conducted in the sub-sample of adults, 20-39 years, who were administered the CIDI

b-values calculated against those with no headache. Medical Conditions included the presence of arthritis, asthma, chronic bronchitis, low back pain, thyroid disorder and overweight (conditions relevant for respondents in this age group). Psychiatric disorders included a diagnosis of major depression, panic disorder or GAD.

\* p<0.001

<sup>‡</sup>p<0.01

 $^{\dagger}\mathrm{p<0.05}$