HIGH LIGHT
CME

Migraine prevalence, disease burden, and the need for preventive therapy

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Abstract—*Objectives:* 1) To reassess the prevalence of migraine in the United States; 2) to assess patterns of migraine treatment in the population; and 3) to contrast current patterns of preventive treatment use with recommendations for use from an expert headache panel. *Methods:* A validated self-administered headache questionnaire was mailed to 120,000 US households, representative of the US population. Migraineurs were identified according to the criteria of the second edition of the International Classification of Headache Disorders. Guidelines for preventive medication use were developed by a panel of headache experts. Criteria for consider or offer prevention were based on headache frequency and impairment. *Results:* We assessed 162,576 individuals aged 12 years or older. The 1-year period prevalence for migraine was 11.7% (17.1% in women and 5.6% in men). Prevalence peaked in middle life and was lower in adolescents and those older than age 60 years. Of all migraineurs, 31.3% had an attack frequency of three or more per month, and 53.7% reported severe impairment or the need for bed rest. In total, 25.7% met criteria for "offer prevention," and in an additional 13.1%, prevention should be considered. Just 13.0% reported current use of daily preventive migraine medication. *Conclusions:* Compared with previous studies, the epidemiologic profile of migraine has remained stable in the United States during the past 15 years. More than one in four migraineurs are candidates for preventive therapy, and a substantial proportion of those who might benefit from prevention do not receive it.

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Migraine affects roughly 12% of the adults in occidental countries.[1,2] In US population studies, the prevalence of migraine is approximately 18% in women and 6% in men.[3-5] Approximately 90% of the migraineurs have moderate or severe pain, three quarters have a reduced ability to function during the headache attacks, and one-third require bed rest during their attacks.[6-9]

Migraine is also undertreated in the United States, though most studies have focused on acute treatment.[6-9] Most migraineurs treat their headaches with acute treatments to the exclusion of preventive drugs.[5,10,11] Patterns of use for migraine preventive treatment have rarely been studied in population samples.

The US Headache Consortium Guidelines discuss indications for the use of preventive medication, but do not provide operational criteria.[12] Because attack frequency and medication overuse are risk factors for headache progression, it is possible that preventive medication may also reduce the risk of progression.[13-16]

To better define the need for and patterns of use of preventive treatment, we conducted the American Migraine Prevalence and Prevention (AMPP) study. The AMPP aims to assess the epidemiology, the burden, and the patterns of treatment for migraine, using methods that allow comparisons with the findings of the American Migraine Studies I (AMS-I) and II (AMS-II).[3-5] As part of this effort, an expert panel defined operational criteria for preventive treatment. This panel defined three groups in terms of their need for preventive treatment. The first group should be *offered* preventive treatment. In the second group, prevention should be *considered*; prevention was an option, though patients could reasonably decide not to use preventives. In the third group, prevention was not indicated. Operational definitions are provided in the Methods section.

Herein we describe the epidemiology of migraine

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Table 1 *Total population surveyed and respondents, according to demographic features*

	No. in total population surveyed	Distribution in total population surveyed, respondents	No. of respondents	Response rate, %
Sex				
Men	124,665	48.4	77,185	62
Women	132,674	51.6	85,571	64
Race				
White	217,501	84.5	140,948	65
Black	21,307	8.3	11,950	56
Asian, Pacific Islander	3,898	1.5	1,923	49
American, Indian	1,791	0.7	1,019	56
Other	4,707	1.8	2,071	44
Unknown/no answer	8,135	3.2	4,832	59
Age, years				
12–17	23,933	9.3	13,951	58
18–29	45,238	17.6	22,963	51
30–39	42,947	16.7	22,618	53
40–49	47,242	18.4	29,168	62
50–59	41,870	16.3	29,201	70
60+	56,109	21.8	44,855	80
Region				
New England	13,239	5.1	8,364	63
Middle Atlantic	36,733	14.3	23,608	64
East North Central	41,288	16.0	27,356	66
West North Central	17,767	6.9	11,657	66
South Atlantic	47,913	18.6	30,399	63
East South Central	15,478	6.0	9,634	62
West South Central	28,529	11.1	17,499	61
Pacific	39,657	15.4	29,646	75
Mountain	16,735	6.5	10,593	63
Population density				
<100,000	35,545	13.8	22,873	64
100,000–499,999	43,231	16.8	26,997	62
500,000–1,999,999	57,711	22.4	36,572	63
2,000,000+	120,852	47.0	76,314	63
Household size				
1 Member	31,876	12.4	22,428	70
2 Members	79,139	30.8	55,941	71
3 Members	48,903	19.0	29,848	61
4 Members	52,113	20.3	29,755	57
5+ Members	45,308	17.6	24,784	55
Household income				
<$22,500	52,282	20.3	32,856	63
$22,500–39,999	49,267	19.1	30,921	63
$40,000–59,999	46,730	18.2	29,528	63
$60,000–89,999	51,371	20.0	32,514	63
$90,000+	57,689	22.4	36,937	64

in the United States. We also compare the patterns of preventive migraine treatment found in the population with recommendations drawn by a panel of headache experts.

Methods. *Sample and survey.* The AMPP was modeled on the methods of the AMS-I and AMS-II.[4,5] A validated self-administered headache questionnaire was mailed in June 2004 to a stratified random sample of 120,000 US households, drawn from a 600,000-household nationwide panel maintained by the National Family Opinion. The panel is comprised of sampling blocks, each with 5,000 households, which are constructed to be representative of the US population in terms of census region, population density, age of the head of the household, household income, and number of household members. Demographic and census information is obtained from each household during an initial recruitment mailing and routinely updated. Roughly 30% of each sampling block is updated or replaced every 2 years.

Initial screening questions were completed by the head of the household, who reported the total number of household members and the number of household members with at least occasional self-defined severe headache. Each household member with severe headaches was then asked to complete the remainder of the survey questions.

The validated questionnaire consisted of 21 questions assessing headache features. In addition, the survey included the Migraine Disability Assessment (MIDAS) questionnaire.[17] MIDAS was used to divide patients into four grades using previously validated and well-accepted scores based on lost time due to headaches. Finally, the questionnaire assessed use of health care and treatments for migraine. A diagnosis of migraine was assigned based on the criteria proposed by the second edition of the International Classification of Headache Disorders (ICHD-2), which is identical to the migraine criteria of the first edition (ICHD-1).[18,19] The survey had been previously shown to have a sensitivity of 100% and specificity of 82.3% for the diagnosis of migraine.[4]

Patterns of migraine preventive treatment. Participants were asked if they have ever taken prescription medication on a daily basis, to help prevent headache from occurring. Those who reported using preventive agents were asked whether they were currently taking such medications or when they stopped. Finally, subjects were asked about other medications they used on a daily basis from the following categories: water pills, other medications for high blood pressure, medications for seizure, medications for diabetes, medication for cholesterol, medication for diabetes, medications for depression, and medication for anxiety. Based on the responses, migraineurs were categorized as 1) never users of preventive medication; 2) current users; 3) previous users (had used preventive medications in the past, but were not currently); or 4) coincident users (reported medications for hypertension other than water pills, antiseizure medications, or prescription medications for depression). We recognize that this definition is overinclusive.

Candidates for migraine prevention. An expert panel of 12 physicians (neurologists and primary care doctors) as well as epidemiologists, psychologists, and statisticians with experience in headache research conducted several meetings in 2004 to develop guidelines for the use of preventive medication that could be operationalized in an epidemiologic study. Guidelines of the US Headache Consortium Guidelines were reviewed.[12] The panel based its recommendations on headache days per month experienced by migraineurs, as well as the level of attack-related impairment caused by the headaches. Impairment during a headache attack was categorized as severe impairment (unable to function or requiring bed rest), some impairment (able to function, but with reduced performance), or no impairment (able to function normally).

Based on expert consensus and the evidence, three groups were defined.

1. Prevention should be offered: migraine subjects reporting either 6 or more headache days per month, 4 or more headache days with at least some impairment, or 3 or more headache days with severe impairment or requiring bed rest.
2. Prevention should be considered: migraineurs with 4 or 5 migraine days per month with normal functioning, 3 migraine days with some impairment, or 2 migraine days with severe impairment.

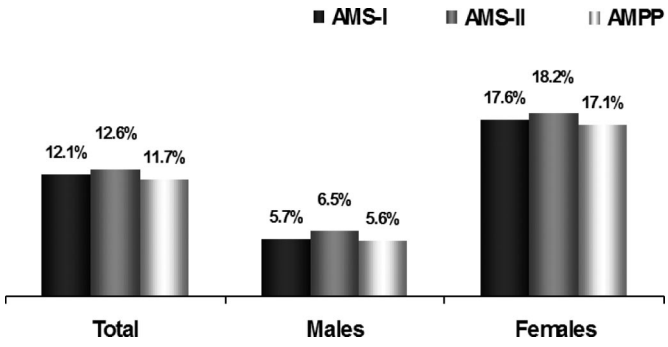

Figure 1. Prevalence of migraine in the American Migraine Study (AMS)-I, AMS-II, and American Migraine Prevalence and Prevention (AMPP) study for total sample and by sex.

3. Prevention is not indicated: migraineurs with less than 4 headache days per month and no impairment, or subjects with no more than 1 headache day per month regardless of the impairment.

Data analysis. Data from subjects aged 12 years and older were analyzed as previously described to estimate prevalence and variation in prevalence by demographic factors.[3-5] Sex-specific prevalence estimates of migraine (1-year period prevalence) were derived by age, race, urban vs rural residence, household income, and region of the country. GLIM Poisson regression (log-linear models) was used to model sex- and age-specific prevalence by income and to derived adjusted prevalence ratios. Data were modeled separately by sex. Age was divided into five categories, beginning with age 20 to 24 years and continuing to age 75 to 79 years. Those aged 12 to 19 years and those aged 80 years or older were treated as separate categories, and all age groups were modeled as a continuous variable. Two race groups (black and white), four population density groups (less than 100,000, 100,000 to 499,999, 500,000 to 1,999,999, and greater than or equal to 2,000,000), five income groups (less than $22,500, $22,500 to $39,999, $40,000 to $59,999, $60,000 to $89,999, and greater than or equal to $90,000), and nine US regions (Mountain, New England, Middle Atlantic, South Atlantic, East North Central, West North Central, East South Central, West South Central, and Pacific) were defined.

Adjusted estimates. Sex-specific regression models were used to adjust for possible confounding of demographic variables in estimating prevalence. Among men, age ($\chi^2 = 957.95$, $df = 5$, $p < 0.0001$), income ($\chi^2 = 311.65$, $df = 4$, $p < 0.0001$), race ($\chi^2 = 19.65$, $df = 1$, $p < 0.0001$), geographic region ($\chi^2 = 53.01$, $df = 8$, $p < 0.0001$), and population density ($\chi^2 = 71.85$, $df = 3$, $p < 0.0001$) improved the fit of the model to the data. Among women, age ($\chi^2 = 4{,}685.75$, $df = 5$, $p < 0.0001$), income ($\chi^2 = 324.23$, $df = 4$, $p < 0.0001$), race ($\chi^2 = 57.20$, $df = 1$, $p < 0.0001$, geographic region ($\chi^2 = 149.70$, $df = 8$, $p < 0.0001$), and population density ($\chi^2 = 259.51$, $df = 3$, $p < 0.0001$) each improved the fit of the model to the data. All covariates were included in the final model to derive adjusted prevalence ratios by race, age, income, urban vs rural residence, and region.

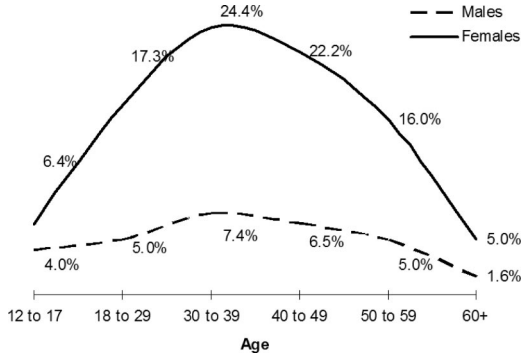

Figure 2. One-year period prevalence of migraine by age and sex adjusted for demographics.

Table 2 *Sex-specific migraine prevalence and prevalence ratios*

	Prevalence, %		Crude and adjusted prevalence ratios*			
	Men	Women	Men		Women	
	Crude	Crude	Crude	Adjusted	Crude	Adjusted
Race						
White	5.7	17.3	1.00	1.00	1.00	1.00
Black	4.1	13.7	0.73 (0.63–0.84)	0.62 (0.54–0.71)	0.79 (0.74–0.84)	0.69 (0.65–0.73)
Age, years						
12–17	4.9	7.3	1.00	1.00	1.00	1.00
18–29	6.2	20.4	1.27 (1.12–1.44)	1.26 (1.10–1.43)	2.79 (2.54–3.06)	2.72 (2.49–2.99)
30–39	9.0	28.1	1.85 (1.64–2.08)	1.86 (1.65–2.10)	3.85 (3.52–4.20)	3.84 (3.50–4.21)
40–49	7.9	25.5	1.63 (1.45–1.83)	1.63 (1.45–1.84)	3.49 (3.18–3.80)	3.49 (3.19–3.83)
50–59	5.9	18.2	1.22 (1.08–1.38)	1.25 (1.11–1.42)	2.48 (2.27–2.72)	2.51 (2.28–2.75)
60+	2.1	6.4	0.44 (0.38–0.50)	0.40 (0.34–0.46)	0.87 (0.79–0.96)	0.78 (0.71–0.87)
Region						
New England	4.9	15.0	1.00	1.00	1.00	1.00
Middle Atlantic	4.9	15.3	1.00 (0.85–1.18)	0.97 (0.83–1.15)	1.02 (0.94–1.11)	1.05 (0.97–1.14)
South Atlantic	5.2	15.9	1.07 (0.92–1.25)	0.99 (0.85–1.16)	1.06 (0.98–1.15)	1.04 (0.96–1.13)
East North Central	5.6	16.9	1.14 (0.85–1.35)	1.03 (0.87–1.23)	1.13 (1.03–1.25)	1.07 (0.98–1.17)
West North Central	5.9	17.9	1.21 (1.04–1.41)	1.16 (0.99–1.35)	1.19 (1.10–1.29)	1.20 (1.11–1.30)
East South Central	7.4	21.1	1.52 (1.28–1.80)	1.29 (1.08–1.54)	1.41 (1.29–1.54)	1.27 (1.17–1.39)
West South Central	6.3	18.8	1.28 (1.09–1.51)	1.15 (0.98–1.36)	1.26 (1.16–1.37)	1.21 (1.11–1.31)
Pacific	5.5	16.3	1.12 (0.96–1.31)	1.10 (0.94–1.30)	1.09 (1.00–1.18)	1.11 (1.02–1.20)
Mountain	5.6	18.3	1.15 (0.96–1.37)	1.01 (0.84–1.21)	1.23 (1.12–1.34)	1.13 (1.03–1.23)
Population density						
<100,000	6.6	20.0	1.00	1.00	1.00	1.00
100,000–499,999	6.4	19.2	0.98 (0.89–1.08)	1.03 (0.93–1.13)	0.96 (0.91–1.01)	0.99 (0.95–1.04)
500,000–1,999,999	6.0	18.0	0.91 (0.83–1.00)	1.03 (0.93–1.13)	0.90 (0.86–0.94)	0.97 (0.93–1.02)
2,000,000+	4.9	14.9	0.75 (0.69–0.81)	0.94 (0.86–1.03)	0.75 (0.71–0.78)	0.90 (0.86–0.95)
Household income						
<$22,500	8.8	20.1	1.00	1.00	1.00	1.00
$22,500–39,999	5.5	18.2	0.62 (0.57–0.68)	0.62 (0.57–0.68)	0.91 (0.87–0.94)	0.82 (0.79–0.86)
$40,000–59,999	5.3	17.2	0.59 (0.55–0.65)	0.55 (0.50–0.61)	0.86 (0.82–0.90)	0.73 (0.69–0.76)
$60,000–89,999	5.1	15.9	0.58 (0.53–0.63)	0.52 (0.47–0.57)	0.79 (0.75–0.83)	0.64 (0.61–0.67)
$90,000+	4.2	13.6	0.47 (0.43–0.52)	0.43 (0.39–0.47)	0.67 (0.64–0.71)	0.55 (0.52–0.57)

* Adjusted for age, sex, race, region, population density, household income, and household size.

Results. A total of 120,000 households were contacted, encompassing 257,399 household members. Surveys were returned from 77,879 households (65% response) yielding data for 162,576 household members aged 12 years or older. Response rates (table 1) were similar in men (62%) and women (64%) and were higher in white (65%) than in black (56%, $p < 0.001$) individuals and in those aged older than 50 years ($p < 0.01$). Response rates did not differ significantly by geographic region, population density, or household income. In comparison to nonresponders, responders were older and more likely to be women. There were no differences by geographic region, population density, or household income.

Migraine prevalence. There were 18,968 individuals aged 12 years or older who met ICHD-2 criteria for migraine yielding an unadjusted 1-year period prevalence estimate of 11.7% (5.6% for men and 17.1% for women; figure 1). Age-specific migraine prevalence curves adjusted for demographics are provided in figure 2. Migraine prevalence was highest in those aged 30 to 39 years for both men (7.4%), and women (24.4%). Prevalence was lowest in those aged 60 years or older at 1.6% in men and 5.0% in women. At the other end of the lifespan, prevalence was 4.0% in men and 6.4% in women aged between 12 and 17 years.

For both men and women (table 2), prevalence was significantly higher in whites than in blacks (women, 17.3% vs 13.7%; men, 5.7% vs 4.1%). Finally, for both sexes, the prevalence of migraine was higher in those of lower income. In those with a household income higher than

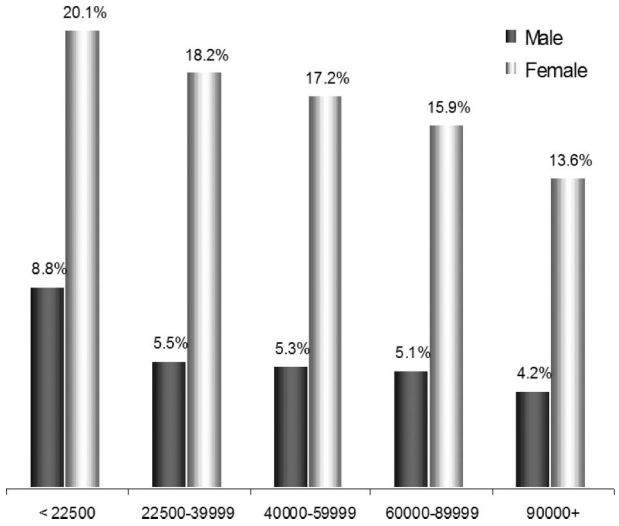

Figure 3. One-year period prevalence of migraine by sex and household income.

$90,000, the prevalence of migraine was 13.6% in women and 4.2% in men. In those with an income lower than $22,500, the prevalence was 20.1% in women and 8.8% in men (figure 3). After adjusting for other factors, the prevalence ratio for migraine was significantly lower with every increase in income strata, and in the highest stratum ($90,000+), prevalence was reduced by nearly half.

The majority of the migraineurs (62.7%) had 1 to 4 headache days per month (table 3). During migraine attacks, most migraineurs reported severe impairment or the need for bed rest (53.7%); just 7.2% reported no attack-related impairment. During a 3-month period, 35.1% of the migraineurs had at least 1 day of activity restriction related to headache. Although most (63.7%) were classified as MIDAS grade 1 (no or little migraine-related disability), 22% had moderate or severe disability levels (MIDAS grades 3 or 4).

Distribution of frequency and impairment. Table 4 provides the distribution of monthly headache frequency and attack-related impairment for those with migraine. As indicated by a single asterisk in table 4, prevention should be offered to approximately one quarter of the migraineurs (25.7%). Of those, 60% have severe impairment or require bed rest. An additional 13.1% met criteria for considering preventive treatment.

Details on the use of migraine prevention among the individuals surveyed were described in a separate article.[20] In brief, only 13% of the migraineurs were currently taking preventive medication for migraine. In our survey, 43.3% had never used a migraine preventive treatment, 25.5% were previous users, and 18% were coincident users. Among those who had never used a preventive, approximately one-third (32.4%) met expert guideline criteria for offering it (19.3%) or considering it (13.1%). Women were more likely than men to need preventive therapy (34.0% vs 27.5%, chi = 30.7, $p < 0.001$).

Discussion. Herein, we report on the prevalence and distribution of migraine in the United States. We then evaluate the frequency of headache attacks and migraine-related impairment as a prelude to evaluating indications for preventive treatment. In this study, the 1-year period prevalence of migraine was 17.1% in women and 5.6% in men.

Based on a report from the US Centers for Disease Control and Prevention, it was suggested that the prevalence of migraine in the United States increased by 60%, from 25.8 per 1,000 person-years to 41 per 1,000 person-years between 1981 and 1989.[21] A study of migraine prevalence based on medical record review also suggested that migraine prevalence was increasing.[22] Three methodologically identical studies during a 15-year period with samples of more than 20,000 (AMS-I), 30,000 (AMS-II), and 160,000 (AMPP) demonstrate that migraine prevalence has been stable in the United States. Studies that rely on self-report or medical record review may reflect increasing awareness, consultation, and diagnosis of migraine, rather than changing prevalence.

Our study confirms major findings of the AMS-I and AMS-II.[3-5] In all three studies, migraine prevalence was higher in whites than in blacks. There was

Table 3 *Migraine frequency and impact*

Variable	n (%)
Monthly headache frequency	
<1 per month	4,279 (23.4)
1–4 per month	11,481 (62.7)
5–9 per month	1,761 (9.6)
9–14 per month	777 (4.2)
Headache-related impairment during severe headache	
Function normally	1,366 (7.2)
Some impairment	7,299 (39.1)
Severe impairment or bed rest required	10,035 (53.7)
Days of activity restriction per headache	
0	3,113 (16.8)
<1	8,909 (48.1)
1–2	5,556 (30.0)
3–5	779 (4.2)
6+	171 (0.9)
School/work/social impact in previous 3 months	
Missed at least 1 day of work/school	4,790 (25.3)
Work/school productivity reduced by at least 50%	5,311 (28.1)
Did no household work	9,050 (47.7)
Household productivity reduced by at least 50%	6,512 (34.3)
Missed family or social activity	5,519 (29.1)
MIDAS grade	
1	12,078 (63.7)
2	2,719 (14.3)
3	2,032 (10.7)
4	2,139 (11.3)

MIDAS = Migraine Disability Assessment.

Table 4 *Distribution of headache frequency and attack-related impairment, and corresponding prevention need based on headache expert recommendations*

	Headache frequency, days per month					
Headache-related impairment	≤1	2	3	4–5	6–10	11–14
No impairment	4.5%	0.6%	0.7%	0.6%†	0.5%*	0.4%*
Some impairment	22.6%	3.5%†	4.4%†	3.5%*	3.1%*	2.0%*
Severe impairment or bed rest required	33.0%	4.6%†	5.2%*	4.1%*	3.9%*	2.9%*

* Panel of experts recommended *offering* migraine prevention (25.7%).
† Panel of experts recommended *considering* migraine prevention (13.1%).

also a striking inverse relation between family income and migraine prevalence. All three studies report a three-to-one women preponderance.

Like earlier studies in the United States, most migraineurs had from one to four headache attacks per month.[3-6] Our study also confirms the burden of migraine in the population and shows that more than 50% of all migraineurs report severe impairment or require bed rest during their headaches. There is no evidence that migraine severity or attack frequency has increased.

Nonetheless, attack frequency and impairment are part of the public health burden of migraine and are potential targets for treatment. Attack-related impairment can be addressed with acute treatment, whereas attack frequency is best addressed with behavioral methods and preventive pharmacotherapy. To assess the need for preventive therapy, an expert panel developed operational criteria for offering or considering prevention based on headache frequency and attack-related disability.

The criteria applied for "offer" or "consider" preventive treatment are intended as an operational rule for epidemiologic research and not as a clinical management guideline. They were admittedly somewhat arbitrary. In practice, the decision to prescribe a preventive therapy is multifactorial and depends on previous treatment history, patient preference, comorbidities, and a range of other factors. Therefore, the criteria presented in table 4 are incomplete. For those who want to use different criteria to assess the need for prevention, we provided a detailed breakdown of patients (table 4). We acknowledge that there are patients in the "offer prevention" group who might be well-managed by modifying acute treatment, and there are patients with infrequent severe attacks, perhaps with persistent neurologic deficits, who may be best treated with a preventive. It is not possible to operationalize the complex dialogue and judgment for prevention in this study. These data are intended only to provide a benchmark.

With these caveats, we found that a sizeable subset of patients meeting criteria for offering (25.7%) or considering (13.1%) preventive therapy do not receive it. The proportion of subjects who were candidates for or should be considered for preventative treatment was 38.8%. Only 12.4% of the migraineurs currently used a preventative, indicating that this form of treatment is underutilized. Comparable data are not available from population studies in the United States.

Use of preventive treatment varies with region of the world. Although the disability of migraine in the United States, France, and Latin America is similar, just 6% of the migraineurs in France and 2% in Latin America were current preventive users.[23,24]

Our study has limitations. First, we used a validated questionnaire to diagnose migraine just in those with self-defined severe headaches. However, migraine attacks do not have to be severe. Limits of our criteria for migraine prevention were discussed above. Second, our definition of coincident users of preventive medication is overly broad. We assume that antihypertensive treatments (other than diuretics), antiepileptic medications, and antidepressant drugs have antimigraine properties, which may not necessarily be true. For example, individuals taking beta blockers, calcium channel blockers, lisinopril, and candesartan, as well as persons using antihypertensive treatments not tested for migraine, are in the coincident category. As a consequence, our coincident category provides an upper-boundary estimate in the number of individuals using medications potentially effective for migraine. Another limitation is that information on nutraceutical medications such as magnesium and vitamin B_2 was not captured in the screening questionnaire. In the AMPP follow-up study, we plan to capture details of medication and nutraceutical use. Strengths of this study include the size of the sample, its representativeness of the US population regarding demographic characteristics, and the use of questionnaires that allow comparisons with the AMS-I and AMS-II.[3-6]

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