

Body Mass Index and Episodic Headaches

A Population-Based Study

Marcelo E. Bigal, MD, PhD; Amy Tsang; Elizabeth Loder, MD; Daniel Serrano, PhD; Michael L. Reed, PhD; Richard B. Lipton, MD; for the American Migraine Prevalence and Prevention Advisory Group

Background: We investigated the influence of the body mass index (BMI [calculated as weight in kilograms divided by height in meters squared]) on the frequency, severity, and patterns of treatment of migraine, probable migraine (PM), and severe episodic tension-type headache (S-ETTH).

Methods: A validated questionnaire was mailed to 120 000 households selected to be representative of the US population. The participants were divided into 5 categories based on BMI: underweight (<18.5), normal weight (18.5-24.9), overweight (25.0-29.9), obese (30.0-34.9), and morbidly obese (>35.0). Analyses were adjusted by covariates that included demographic variables (age, sex, race, and income), duration of illness, comorbidities, use of preventive medication, and use of opioids.

Results: The response rate was 65%. We identified 18 968 individuals with migraine, 7564 with PM, and 2051 with

S-ETTH. The distribution of very frequent headaches (10-14 d/mo) was assessed by BMI. Among individuals with migraine, very frequent headaches (10-14 d/mo) occurred in 7.4% of the overweight ($P=.10$), 8.2% of the obese ($P<.001$), and 10.4% of the morbidly obese ($P<.0001$) subjects, compared with 6.5% of those with normal weight, in adjusted analyses. Among individuals with PM and S-ETTH, the differences were not significant ($P=.20$). The disability of migraineurs, but not of those with PM or S-ETTH, also varied as a function of BMI. Among migraineurs, 32.0% of those with normal weight had some disability compared with 37.2% of the overweight ($P<.01$), 38.4% of the obese ($P<.001$), and 40.9% of the morbidly obese ($P<.001$) subjects.

Conclusion: These findings support the concept that obesity is an exacerbating factor for migraine but not for other types of episodic headaches.

Arch Intern Med. 2007;167(18):1964-1970

Author Affiliations:

Departments of Neurology (Drs Bigal and Lipton) and Epidemiology and Population Health (Dr Lipton), Albert Einstein College of Medicine and The Montefiore Headache Center (Drs Bigal and Lipton and Ms Tsang), Bronx, New York; The New England Center for Headache, Stamford, Connecticut (Dr Bigal); Spaulding Rehabilitation Hospital, Boston, Massachusetts (Dr Loder); and Vedanta Research, Chapel Hill, North Carolina (Drs Serrano and Reed).

Group Information: A list of the members of the American Migraine Prevalence and Prevention Advisory Group appears at the end of this article.

HEADACHE AND OBESITY ARE prevalent and disabling disorders that are influenced by genetic and environmental risk factors.^{1,2} Individuals with episodic headache and obesity develop chronic daily headache (CDH) at more than 5 times the rate of normal-weight individuals.³ A large, cross-sectional population study confirmed the association between obesity and CDH and suggested that this association was relatively specific for chronic migraine (CM) but not for chronic tension-type headache.⁴ Among individuals with episodic migraine, the prevalence of episodic migraine did not vary significantly with the body mass index (BMI), suggesting that obesity is not associated with migraine itself.⁵ However, migraineurs with a high BMI had more frequent episodes of headache and higher levels of disability. These studies³⁻⁵ adjusted for potential sociodemographic and medical confound-

ers. Taken together, they suggest that obesity is not associated with migraine onset but that it is associated with increasing frequency and severity of migraine and with CM.

The relationship between obesity and frequency of episodic migraine has been demonstrated in a single population study.⁵ The specificity of the association has not been examined by assessing other headache types such as probable migraine (PM), a migraine subtype missing just 1 migraine feature, and episodic tension-type headache (ETTH). The American Migraine Prevalence and Prevention (AMPP) study has provided an excellent opportunity for further investigation of these relationships. The AMPP study is a multi-year, longitudinal, population-based study aiming to evaluate the prevalence, burden, and patterns of health care use for migraine as well as to assess the natural history of migraine and risk factors for CDH.⁶⁻⁸

We used the AMPP database to assess the relationship between BMI and episodic headaches, separately exploring the influence of BMI on the frequency and severity of migraine, PM, and severe ETTH (S-ETTH). We hypothesized that obesity is associated with higher migraine frequency and disability but not with S-ETTH frequency and disability, supporting the specific link between obesity and migraine. For PM, we expected an intermediate pattern of response because PM is a phenotype of intermediate severity. Among individuals with migraine and PM, we also assessed the influence of BMI on patterns of acute and preventive migraine treatment. In this article, we examine cross-sectional associations, without answering questions about temporality and causal sequence, which we hope to explore in the longitudinal phase of the study.

METHODS

SAMPLE AND SURVEY

As a part of the AMPP study, a validated self-administered headache questionnaire was mailed to a stratified random sample of 120 000 US households, drawn from a 600 000-member panel maintained by the National Family Opinion Survey. The survey has been described in detail elsewhere.^{6,7} The sample was constructed to be representative of the US population in terms of demographics. 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 who have at least occasional self-defined severe headache. All household members 12 years or older were asked to complete the remainder of the survey questions.

The validated questionnaire consisted of 21 questions assessing headache features. Also, the survey included the Migraine Disability Assessment (MIDAS) questionnaire⁹ and evaluated the use of health care and treatments for migraine. Headache diagnosis was assigned based on the criteria proposed by the second edition of the *International Classification of Headache Disorders (ICHD-2)*.¹⁰ The survey had been previously shown to have a sensitivity of 100% and a specificity of 82.3% for the diagnosis of migraine.¹ However, because the screening question asked about severe headaches, herein we report only on S-ETTH. Finally, the questionnaire asked about weight and height at the time of the survey. Weight and height were obtained only in the individuals who responded positively to the screening headache question.

PATTERNS OF MIGRAINE TREATMENT

Subjects with migraine and PM were asked a series of questions about their patterns of acute and preventive treatment. The acute treatment options were (1) no treatment, (2) treatment with over-the-counter medications (OTCs) only, (3) treatment with prescription medications only, or (4) treatment with both OTCs and prescription medications. Subjects were then asked if they had ever taken prescription medication for a headache on a daily basis to help prevent headache. Those who responded positively were asked if they were currently taking such medications. Finally, subjects were asked about daily medications they were using for reasons other than to treat their headaches. Based on the answers, subjects were divided into 4 categories: (1) never users of preventive medications; (2) current users (were taking preventive drugs specifically prescribed for their headaches at the time of the survey); (3) lapsed users (had

used preventive medications for headache in the past but were not using at the time of the survey); and (4) coincident users (were using medications accepted to be effective preventive migraine medications but for medical reasons other than headache).

DATA ANALYSIS

Analyses were performed using SPSS version 13.0 (SPSS Inc, Chicago, Illinois). Data were summarized using frequency counts and descriptive statistics. The BMI was calculated according to the following formula: (weight in pounds divided by height in inches squared) \times 703, or weight in kilograms divided by height in meters squared. We defined 5 categories based on BMI: underweight (<18.5), normal weight (18.5-24.9), overweight (25.0-29.9), obese (30.0-34.9), and morbidly obese (>35.0). The χ^2 test was used to compare percentages. We modeled frequent headaches (10-14 d/mo) and disability, as measured by the MIDAS questionnaire, as dependent variables, with BMI, use of acute or preventive medication, age, race, and socioeconomic status as independent variables in logistic regression. The odds ratio (OR) was estimated for each explanatory variable, after controlling for confounders. Continuous independent variables were evaluated for nonlinearity using squared and higher-order terms. Logistic regression was also used to identify the influence of obesity on patterns of acute medication use and, in separate models, on patterns of preventive treatment. For these analyses, patterns of acute medication use were dichotomized into nonprescription acute treatment (no medication or OTCs only) and prescription medication (usually prescription or prescription plus OTCs). Similarly, patterns of preventive treatment were grouped as current and lapsed vs never used. The coincident and current groups were modeled separately. For the modeling, covariates included demographic variables (age, sex, race, and income), duration of illness, comorbidities, use of preventive medication, and use of opioids. The degrees of freedom for each test equaled the number of categories for that predictor minus 1. Ninety-five percent confidence intervals (CIs) are provided for all ORs. All CIs not containing the value 1 indicate that that factor is a statistically significant predictor, with $P < .05$.

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 12 years or older. Response rates were similar in men (62%) and women (64%). They were higher in whites (65%) than in African Americans (56%, $P < .001$) and in individuals older than 50 years ($P < .01$). Response rates did not differ significantly ($P = .14$) by geographic region, population density, or household income and are detailed elsewhere.⁶

EPISODIC HEADACHE TYPE ACCORDING TO BMI

A total of 30 703 individuals (18.8%) screened positive for episodic headaches in the past year. Of these subjects, 18 968 met ICHD-2 criteria for migraine, yielding an unadjusted 1-year period prevalence estimate of 11.7%. A total of 7564 individuals (4.6%) met the criteria for PM, while 2051 (1.2%) had S-ETTH. Finally, there were 2120 individuals (1.3%) with other types of episodic head-

Table 1. Demographic Characteristics of Subjects by Headache Type

Characteristic	Individuals, No. (%)		
	With Migraine (n = 18 968)	With Probable Migraine (n = 7564)	With Severe Episodic Tension-Type Headache (n = 7564)
Age Range, y			
12-19	1178 (6.21)	536 (7.08)	103 (5.02)
20-29	2808 (14.80)	904 (11.95)	222 (10.82)
30-39	4318 (22.76)	1392 (18.40)	281 (13.70)
40-49	5073 (26.74)	1748 (23.10)	357 (17.40)
50-59	3612 (19.04)	1562 (20.65)	448 (21.84)
60-69	1409 (7.42)	834 (11.02)	289 (14.09)
≥70	570 (3.00)	588 (7.77)	351 (17.11)
Sex			
Male	4364 (23.00)	3038 (40.16)	940 (45.83)
Female	14 604 (76.99)	4526 (59.83)	1111 (54.16)
Race			
White	16 568 (87.34)	6214 (82.15)	1702 (82.98)
Black	1180 (6.22)	786 (10.39)	215 (10.48)
Other	650 (3.42)	289 (3.82)	58 (2.82)
Unknown	570 (3.00)	275 (3.63)	76 (3.70)
BMI			
Underweight, <18.5	536 (3.35)	154 (2.86)	57 (4.30)
Normal weight, 18.5-24.9	5487 (34.38)	1883 (35.02)	445 (33.58)
Overweight, 25.0-29.9	4449 (27.87)	1628 (30.28)	408 (30.79)
Obese, 30.0-34.9	2797 (17.52)	917 (17.05)	226 (17.05)
Morbidly obese, ≥35.0	2689 (16.85)	794 (14.76)	189 (14.26)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

Table 2. Percentage of Headache Sufferers With Very Frequent Headaches (10 to 14 d/mo) as a Function of BMI Category

BMI Category	Individuals With Migraine (n = 15 958)		Individuals With Probable Migraine (n = 5376)		Individuals With Severe Episodic Tension-Type Headache (n = 1325)	
	n/N (%)	OR ^a (95% CI)	n/N (%)	OR ^a (95% CI)	n/N (%)	OR ^a (95% CI)
Underweight	43/536 (8.0)	1.44 (0.98-1.96)	12/154 (7.7)	1.12 (0.60-1.41)	2/57 (3.5)	1.29 (0.29-1.62)
Normal weight	358/5487 (6.5)	1 [Reference]	127/1883 (6.7)	1 [Reference]	9/445 (2.0)	1 [Reference]
Overweight	331/4489 (7.4)	1.15 (0.98-1.132)	100/1628 (6.1)	0.91 (0.72-1.26)	6/408 (1.4)	0.75 (0.32-1.92)
Obese	228/2787 (8.1)	1.31 (1.10-1.56)	52/917 (5.6)	0.83 (0.61-1.23)	11/226 (4.8)	0.61 (0.27-2.26)
Morbidly obese	279/2689 (10.3)	1.74 (1.41-1.93)	74/794 (9.3)	1.53 (1.16-1.96)	3/189 (1.5)	0.74 (0.23-2.79)

Abbreviations: BMI, body mass index; CI, confidence interval; n, number of individuals in the headache category and BMI group with a headache frequency of 10 to 14 per month; N, number of individuals in the headache category in the specified BMI group; OR, odds ratio.

^aThe ORs were adjusted by demographic variables (age, sex, race, and income), duration of illness, comorbidities, use of preventive medication, and use of opioids.

aches. **Table 1** shows the demographic characteristics of the respondents by headache type.

FREQUENCY AND DISABILITY BY HEADACHE TYPE AND BMI

Next, we examined the distribution of very frequent episodic headaches (10-14 d/mo) by BMI category. For migraine, the percentage of frequent headaches increased as a function of BMI (**Table 2**). Compared with the percentage of normal-weight subjects with episodic migraine (6.5% had very frequent headaches), the percentage of subjects with very frequent migraine was higher in the overweight

category (7.4%; OR, 1.15; 95% CI, 0.98-1.13; $P=.06$) and higher still in the obese (8.2%; OR, 1.3; 95% CI, 1.1-1.5; $P<.001$) and the morbidly obese (10.4%; OR, 1.7; 95% CI, 1.4-1.9; $P<.001$) categories. For PM, the differences were significant only in the morbidly obese group (9.3% vs 6.7% in the normal-weight group; OR, 1.5; 95% CI, 1.1-1.9; $P=.02$). For S-ETTH, the percentage of subjects with 10 to 14 headache days per month did not vary as a function of BMI. Adjustment for demographic variables (age, sex, and race) did not alter these relationships. Very frequent headaches were overrepresented in the obese and morbidly obese groups for migraine, in the morbidly obese group for PM, but not in the S-ETTH group.

Table 3. Percentage of Individuals With Some Level of Disability, as Measured by the MIDAS Scale,^a According to Headache Type and BMI Category

BMI Category	Individuals With Migraine		Individuals With Probable Migraine		Individuals With Severe Episodic Tension-Type Headache	
	% With Disability	OR ^b (95% CI)	%	OR ^b (95% CI)	%	OR ^b (95% CI)
Underweight	36.8	1.27 (1.00-1.53)	17.5	0.87 (0.53-1.35)	22.8	1.54 (0.86-3.03)
Normal weight	32.1	1 [Reference]	19.7	1 [Reference]	16.0	1 [Reference]
Overweight	37.2	1.34 (1.28-1.43)	18.6	0.94 (0.81-1.17)	16.9	1.13 (0.75-1.62)
Obese	38.4	1.37 (1.27-1.57)	19.6	1.07 (0.89-1.24)	18.1	1.12 (0.75-1.89)
Morbidly obese	40.9	1.54 (1.33-1.66)	22.9	1.23 (0.99-1.57)	19.6	1.34 (0.86-2.01)

Abbreviations: BMI, body mass index; CI, confidence interval; MIDAS, Migraine Disability Assessment; OR, odds ratio.

^aThe MIDAS questionnaire stratifies headache-related disability in 4 levels: I, none or minimal; II, mild; III, moderate; and IV, severe.

^bThe ORs were adjusted by demographic variables (age, sex, race, and income), duration of illness, comorbidities, use of preventive medication, and use of opioids.

Table 4. Patterns of Acute Medication Use Among Individuals With Migraine and Probable Migraine, According to BMI^a

BMI Category	No Medication	Usually OTC Medication	Usually Prescription Medication	Both OTC and Prescription Medication	Sometimes Prescription Medication	OR (95% CI)
Migraine						
Underweight	15 (2.81)	245 (45.97)	114 (21.39)	159 (29.83)	273 (51.22)	1.00 (0.81-1.23)
Normal weight	108 (1.98)	2568 (47.06)	1183 (21.68)	1598 (29.28)	2781 (50.96)	1 [Reference]
Overweight	83 (1.87)	2067 (46.66)	913 (20.61)	1367 (30.86)	2280 (51.47)	1.02 (0.91-1.13)
Obese	52 (1.87)	1269 (45.70)	568 (20.45)	888 (31.98)	1456 (52.43)	1.14 (0.96-1.19)
Morbidly obese	58 (2.17)	1155 (43.18)	635 (23.74)	827 (30.92)	1462 (54.65)	1.16 (1.05-1.27)
Probable Migraine						
Underweight	6 (3.95)	103 (67.76)	22 (14.47)	21 (13.82)	43 (28.29)	1.15 (0.72-1.54)
Normal weight	60 (3.21)	1301 (69.50)	224 (11.97)	287 (15.33)	511 (27.30)	1 [Reference]
Overweight	43 (2.66)	1122 (69.43)	186 (11.51)	265 (16.40)	451 (27.91)	1.02 (0.91-1.27)
Obese	33 (3.63)	596 (65.64)	120 (13.22)	159 (17.51)	279 (30.73)	1.10 (0.94-1.19)
Morbidly obese	19 (2.43)	516 (65.90)	97 (12.39)	151 (19.28)	248 (31.67)	1.24 (1.05-1.51)

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio; OTC, over-the-counter.

^aValues other than OR (95% CI) are expressed as number (percentage) of individuals. Medication refers to symptomatic medication (used to treat established headache attacks).

We also assessed the percentage of individuals with some level of disability (MIDAS grades II to IV) according to BMI group and headache type. Among migraineurs, 32% of those with normal weight had some level of headache-related disability, compared with 37.2% of the overweight (OR, 1.3; 95% CI, 1.2-1.4; $P < .01$), 38.4% of the obese (OR, 1.3; 95% CI, 1.2-1.5; $P < .001$), and 40.9% of the morbidly obese (OR, 1.5; 95% CI, 1.3-1.6; $P < .001$) subjects. The differences just missed statistical significance for the underweight subjects (36.8%; OR, 1.27; 95% CI, 1.0-1.5; $P = .05$) (**Table 3**). For individuals with PM and S-ETTH, the overall distribution of MIDAS scores was skewed toward less disability. For PM, 19.7% of the subjects with normal weight had some disability, compared with 17.5% of the underweight (OR, 0.8; 95% CI, 0.5-1.3), 18.6% of the overweight (OR, 0.9; 95% CI, 0.8-1.1), 19.6% of the obese (OR, 1.0; 95% CI, 0.8-1.2), and 23% of the morbidly obese (OR, 1.2; 95% CI, 1.0-1.5; $P < .05$) subjects. Finally, for S-ETTH, the relationship was not seen. A total of 16% of the individuals with normal weight had some disability, and the percentages were not significantly different in the other

weight groups (overweight group, $P = .36$; obese group, $P = .72$; and morbidly obese group, $P = .51$) (**Table 3**).

PATTERNS OF TREATMENT

Use of prescription acute treatment did not significantly vary by BMI (**Table 4**). Among migraineurs who were of normal weight, 50.9% sometimes used prescription medications to treat their attacks. In the underweight group, the percentage was 51.2%; in the overweight group, it was 51.5%; in the obese group, it was 52.4%; and in the morbidly obese group, it was 54.6%. In adjusted analyses, the BMI did not correlate with patterns of acute treatment among migraineurs. Similar findings were seen in the PM group.

Regarding preventive treatment, about 51% of the normal-weight subjects ever used preventive medication (pooling together the current, lapsed, and coincident user groups). In contrast, 57% of the overweight (OR, 1.3, 95% CI, 1.2-1.4), 62% of the obese (OR, 1.6; 95% CI, 1.4-1.8), and 72% of the morbidly obese (OR, 2.5; 95% CI, 2.3-2.8) subjects ever used preventive medication. The

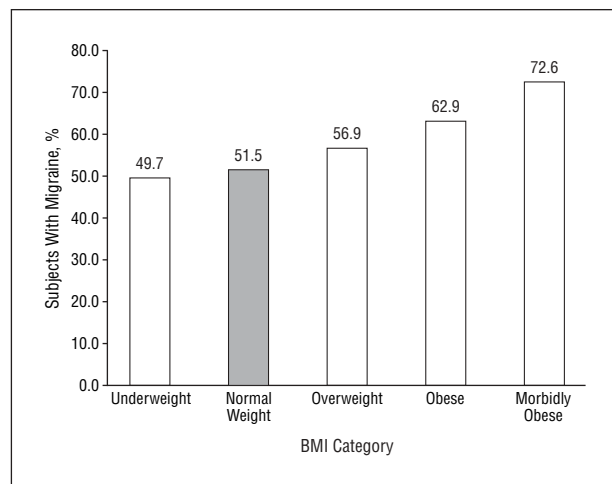


Figure 1. Percentage of subjects with migraine who ever used a migraine prevention medication (for migraine purposes or for other medical reasons) according to body mass index (BMI) category.

differences between the normal weight and the underweight groups (OR, 0.9; 95% CI, 0.7-1.1) were not significant ($P = .41$) (**Figure 1**). When the coincident group was excluded, ever using a preventive treatment specifically for migraine was still significantly more common in the obese and the morbidly obese groups (**Table 5**). Finally, current use of preventive medication was more common among the obese (15.3%, OR, 1.4, 95% CI, 1.2-1.6) and the morbidly obese (17.3%, OR, 1.5; 95% CI, 1.3-1.7) groups (Table 5) than among the normal-weight group (12.8%). For PM, the patterns were very similar. About 42% of the normal-weight subjects ever used preventive medication (for migraine or as a coincident treatment). Preventive medications were used by 45% of the overweight (OR, 1.1; 95% CI, 0.9-1.3), 58% of the obese (OR, 1.8; 95% CI, 1.6-2.2), and 63% of the morbidly obese (OR, 2.3; 95% CI, 1.9-2.7) subjects (**Figure 2**).

Coincident use of a medication with potential preventive effectiveness increased with BMI in both the migraineurs and the PM subjects. Of normal-weight migraineurs, 12.5% used migraine prevention medications for reasons other than migraine, increasing to 17.6% of the overweight (OR, 1.5, 95% CI, 1.3-1.6), 21.8% of the obese (OR, 1.7; 95% CI, 1.3-1.9), and 27.2% of the morbidly obese (OR, 2.6; 95% CI, 2.3-2.9) subjects. Among PM subjects, coincident prevention use occurred in 14.7% of those who were of normal weight, 18.3% of those who were overweight (OR, 1.3, 95% CI, 1.1-1.5), 25.1% of those who were obese (OR, 1.9; 95% CI, 1.5-2.3), and 30.1% of those who were morbidly obese (OR, 2.4; 95% CI, 2.0-3.0).

COMMENT

There is an epidemic of obesity in the United States. In 2000, 64% of the adults in the United States were overweight or obese.^{2,11} In 2002, the prevalence of obesity had increased by 16% compared with 1988 to 1994.¹² Our findings show that among migraineurs, 62.3% of the subjects were overweight or obese, and among individuals

with PM or S-ETTH, the percentage was 62.1%, dovetailing the distribution in the general population in the United States and supporting our sampling strategy. Because a previous population study showed that obesity was not comorbid to migraine,⁵ we did not expect to see differences in the prevalence of migraine, PM, and S-ETTH by BMI.

We found that among migraineurs, obesity was associated with very frequent headaches as well as with higher disability grades, associations that were consistent with previous findings.^{4,5} We also found that obesity was associated with very frequent headaches among individuals with PM, although only morbid obesity was associated with high disability scores. Finally, BMI was not associated with headache frequency or disability of headaches among individuals with S-ETTH. These findings support the concept that obesity is related to migraine in particular, not with headaches overall. They are also consistent with the findings of another population study, in which obesity was associated with chronic migraine but not with chronic tension-type headache.⁴ If obesity was associated with an increase in the frequency of S-ETTH, we would expect that obesity and chronic tension-type headache would be linked as well.

Although the frequency of attacks tended to be higher in obese migraineurs, the use of acute prescription treatment occurred at similar rates by BMI group. There was a significant increase in prescription medication use in the morbidly obese group compared with the normal-weight group, but the difference was very small. Patterns were similar for PM. As acute medications are not believed to contribute to obesity, it may be that frequent headache motivates consultation or that obesity and its comorbidities motivate consultation. The relationship between obesity and use of preventive medication for migraine and PM has several possible explanations. First, since obesity is associated with frequent and more disabling attacks among individuals with migraine,^{4,5} severity of illness may motivate consultation and appropriate preventive treatment. Also, migraine is associated with comorbidities¹³⁻¹⁵ that may increase the probability of treatment of migraine or the probability of coincidental treatment that is associated with weight gain. It is also possible that the causal sequence is reversed and that obesity is a consequence of treatment with migraine prevention medications that may potentially increase weight.¹⁶

Our study has limitations. First, we used a validated questionnaire to diagnose headaches only in individuals with self-defined severe headaches. Although the questionnaire has high sensitivity and specificity for migraine, it was not designed to identify most patients with ETTH. Nonetheless, we elected to present information on the S-ETTH group that it did identify because it confirms previous findings, especially the observation that obesity seems to be particularly linked to headaches in the migraine spectrum but not to tension-type headache. A second and important limitation regards our definition of coincident users of preventive medication and was discussed above. Third, our results may have some participation bias if migraineurs with lower disability are less likely to participate in the survey, leading to inflated estimates of preventive therapy use. Strengths of

Table 5. Patterns of Preventive Medication Use Among Individuals With Migraine and Probable Migraine, According to BMI^a

BMI Category	Medication Use ^b					OR (95% CI)
	Never	Lapsed	Coincident	Current	Ever for Migraine (Lapsed + Current)	
	Migraine					
Underweight	269 (50.3)	136 (25.4)	57 (10.7)	73 (13.6)	209 (64.1)	1.03 (0.81-1.24)
Normal weight	2650 (48.5)	1432 (26.2)	687 (12.6)	691 (12.7)	2123 (63.6)	1 [Reference]
Overweight	1902 (43.1)	1168 (26.4)	781 (17.7)	566 (12.8)	1734 (64.6)	1 (0.91-1.16)
Obese	1041 (37.1)	760 (27.1)	606 (21.6)	402 (14.3)	1162 (70.6)	1.20 (1.13-1.36)
Morbidly obese	733 (27.4)	753 (28.1)	729 (27.2)	462 (17.3)	1215 (83.1)	1.32 (1.21-1.40)
Probable Migraine						
Underweight	86 (56.6)	38 (25.0)	17 (11.2)	11 (7.2)	49 (10.1)	1.02 (0.81-1.23)
Normal weight	1082 (58.0)	382 (20.5)	277 (14.8)	126 (6.7)	508 (10.3)	1 [Reference]
Overweight	942 (55.0)	312 (18.2)	313 (18.3)	145 (8.5)	457 (11.5)	1.12 (0.95-1.18)
Obese	384 (42.1)	195 (21.4)	229 (25.1)	104 (11.4)	299 (11.9)	1.25 (1.19-1.34)
Morbidly obese	293 (37.4)	186 (23.8)	235 (30.0)	69 (8.8)	255 (10.5)	1.32 (1.24-1.49)

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio.

^aValues other than OR (95% CI) are expressed as number (percentage) of individuals.

^bMedication used on a daily basis (to prevent onset of headache).

this study include the robust sample size, known to be representative of the US population regarding the demographic characteristics and the use of questionnaires that allow comparisons with the American Migraine Study I and American Migraine Study II.^{1,17} Finally and most important, BMI was calculated based on weight and height that were self-reported. Recent research has investigated this particular issue. Differences between self-reported (over the telephone) and measured BMI were investigated for a sample of 3797 adolescents. It was concluded that self-reports of stature, weight, and BMI are valid representations of their measured counterparts.¹⁸ In adults, the National Health Interview Survey interviewed 68 556 adults and calculated their BMI using computer-assisted telephone interview assessments of weight and height that were identical to ours, generating data adopted by health-policy makers.¹⁹ Computer-assisted telephone interviews with self-reported weight have also been used to assess comorbidity between obesity and other health problems.²⁰ Nonetheless, it is reasonable to suppose that obese individuals would tend to underestimate their reported weight, creating a bias that is difficult to assess in our results.

This study suggests that obesity is related to migraine and, to a lesser extent, to PM but not to S-ETTH. The specificity of this association can be explained by several hypotheses and creates an opportunity to generate a mechanistic hypothesis.²¹ Obesity and migraine may be associated in several ways. First, both are influenced by genetic and environmental risk factors.²² Second, migraine, like obesity, has been reported as a risk factor for stroke and cardiovascular illnesses.^{11,12,15} Several of the inflammatory mediators that are increased in obese individuals are important in the pathogenesis of migraine, and they may increase the frequency, severity, and duration of migraine attacks.^{22,23} Shared biological predisposition may also play a significant role. Orexins modulate appetite control, metabolism, and pain, and dysfunction in their pathways seems to predispose to obesity and

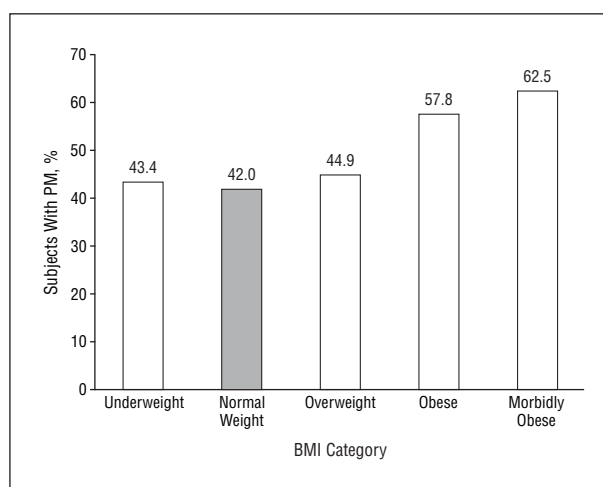


Figure 2. Percentage of subjects with probable migraine (PM) who ever used a migraine prevention medication (for migraine purposes or for other medical reasons) according to body mass index (BMI) category.

chronic pain.²⁴ Finally, conditions that are comorbid with both states (eg, depression) may also make the relationship between both diseases more complex.²⁵

Identifying factors and mechanisms that contribute to the onset of chronic migraine has emerged as a priority in headache research and is one of the main goals of the AMPP project. Exploring the links between headache and obesity may make a substantial contribution to this effort.

Accepted for Publication: January 8, 2007.

Correspondence: Marcelo E. Bigal, MD, PhD, Department of Neurology, Albert Einstein College of Medicine, 1300 Morris Park Ave, Rousso Bldg, Room 330, Bronx, NY 10461 (mbigal@acom.yu.edu).

Author Contributions: Study concept and design: Bigal, Tsang, Loder, Serrano, and Lipton. Acquisition of data: Bigal, Reed, and Lipton. Analysis and interpretation of data: Bigal, Loder, Serrano, and Lipton. Drafting of the manu-

script: Bigal, Serrano, and Reed. *Critical revision of the manuscript for important intellectual content*: Bigal, Tsang, Loder, Serrano, and Lipton. *Statistical analysis*: Bigal, Serrano, and Lipton. *Obtained funding*: Bigal and Lipton. *Administrative, technical, and material support*: Tsang and Reed. *Study supervision*: Lipton.

The AMPP Advisory Group Members: Richard B. Lipton, MD (principal investigator), Marcelo E. Bigal, MD, PhD, Dawn Buse, PhD, Michael L. Reed, PhD, Walter F. Stewart, PhD, Merle Diamond, MD, Frederick Freitag, DO, Elisabeth Hazard, PhD, Jonathan Tierce, CPhil, Elizabeth Loder, MD, Paul Winner, MD, Stephen Silberstein, MD, and Seymour Diamond, MD.

Financial Disclosure: None reported.

Funding/Support: This study was sponsored by the National Headache Foundation through a grant from Ortho-McNeil Neurologics, Inc.

Additional Contributions: Kristina M. Fanning, PhD, and Kathy Ward helped with data management and analysis.

REFERENCES

1. Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache*. 2001;41(7):646-657.
2. National Center for Chronic Disease Prevention and Health Promotion. Overweight and obesity: obesity trends. Centers for Disease Control and Prevention Web site. <http://www.cdc.gov/nccdphp/dnpa/obesity/trend/maps/index.htm>. Accessed April 18, 2005.
3. Scher AI, Stewart WF, Ricci JA, Lipton RB. Factors associated with the onset and remission of chronic daily headache in a population-based study. *Pain*. 2003;106(1-2):81-89.
4. Bigal ME, Lipton RB. Obesity is a risk factor for transformed migraine but not for chronic tension-type headache. *Neurology*. 2006;67(2):252-257.
5. Bigal ME, Liberman JN, Lipton RB. Obesity and migraine: a population study. *Neurology*. 2006;66(4):545-550.
6. Lipton RB, Bigal ME, Diamond M, Freitag F, Reed M, Stewart WF. Migraine prevalence, disease burden and the need of preventive therapy: migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. 2007;68(5):343-349.
7. Diamond S, Silberstein S, Loder E, Reed M, Bigal ME, Lipton RB. Patterns of diagnosis and acute and preventive treatment of migraine in the United States: results from the American Migraine Prevalence and Prevention Study. *Headache*. 2007;47(3):355-363.
8. Silberstein SD, Loder E, Diamond S, Reed M, Bigal ME, Lipton RB; AMPP Advisory Group. Probable migraine in the United States: results of the American Migraine Prevalence and Prevention (AMPP) study. *Cephalalgia*. 2007;27(3):220-234.
9. Stewart WF, Lipton RB, Dowson AJ, Sawyer J. Development and testing of the Migraine Disability Assessment (MIDAS) Questionnaire to assess headache-related disability. *Neurology*. 2001;56(6)(suppl 1):S20-S28.
10. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders, ed 2. *Cephalgia*. 2004;24(suppl 1):1-15.
11. Barnes P, Schiller JS. Early release of selected estimates based on data from the 2006 National Health Interview Survey. National Center for Health Statistics Web site. <http://www.cdc.gov/nchs/nhis.htm>. Accessed July 16, 2007.
12. The obesity epidemic: fat, fact and fiction. National Institute for Medical Research Web site. <http://www.nimr.mrc.ac.uk/millhill essays/2002/obesity.htm>. Accessed May 8, 2006.
13. Breslau N, Lipton RB, Stewart WF, Schultz LR, Welch KM. Comorbidity of migraine and depression: investigating potential etiology and prognosis. *Neurology*. 2003;60(8):1308-1312.
14. Haut SR, Bigal ME, Lipton RB. Chronic disorders with episodic manifestations: focus on epilepsy and migraine. *Lancet Neurol*. 2006;5(2):148-157.
15. Kurth T, Gaziano JM, Cook NR, Logroscino G, Diener HC, Buring JE. Migraine and risk of cardiovascular disease in women. *JAMA*. 2006;296(3):283-291.
16. Young WB, Rozen TD. Preventive treatment of migraine: effect on weight. *Cephalalgia*. 2005;25(1):1-11.
17. Lipton RB, Stewart WF, Simon D. Medical consultation for migraine: results from the American Migraine Study. *Headache*. 1998;38(2):87-96.
18. Himes JH, Hannan P, Wall M, Neumark-Sztainer D. Factors associated with errors in self-reports of stature, weight, and body mass index in Minnesota adolescents. *Ann Epidemiol*. 2005;15(4):272-278.
19. Schoenborn CA, Adams PF, Barnes PM. Body weight status of adults: United States, 1997-98. *Adv Data*. 2002;6(330):1-15.
20. Luder E, Ehrlich RI, Lou WY, Melnik TA, Kattan M. Body mass index and the risk of asthma in adults. *Respir Med*. 2004;98(1):29-37.
21. Lipton RB, Silberstein SD. Why study the comorbidity of migraine? *Neurology*. 1994;44(10)(suppl 7):S4-S5.
22. Bigal ME, Lipton RB, Holland P, Goadsby PJ. Obesity, migraine and chronic migraine: possible mechanisms of interaction. *Neurology*. 2007;68(21):1851-1861.
23. Zelissen PM, Koppeschaar HP, Lips CJ, Hackeng WH. Calcitonin gene-related peptide in human obesity. *Peptides*. 1991;12(4):861-863.
24. Mohamed-Ali V, Pinkney JH, Coppack SW. Adipose tissue as an endocrine and paracrine organ. *Int J Obes Relat Metab Disord*. 1998;22(12):1145-1158.
25. Holland PR, Akerman S, Goadsby PJ. Orexin 1 receptor activation attenuates neurogenic dural vasodilation in an animal model of trigeminovascular nociception. *J Pharmacol Exp Ther*. 2005;315(3):1380-1385.