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Obesity and Headache: Part I – A Systematic Review of the Epidemiology of Obesity and Headache

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Abstract

Individually, both obesity and headache are conditions associated with a substantial personal and societal impact. Recent data support that obesity is comorbid with headache in general and migraine specifically, as well as with certain secondary headache conditions such as idiopathic intracranial hypertension. In the current manuscript, we first briefly review the epidemiology of obesity and common primary and secondary headache disorders individually. This is followed by a systematic review of the general population data evaluating the association between obesity and headache in general, and then obesity and migraine and tension-type headache disorders. Finally, we briefly discuss the data on the association between obesity and a common secondary headache disorder that is associated with obesity, idiopathic intracranial hypertension. Taken together, these data suggest that it is important for clinicians and patients to be aware of the headache/migraine-obesity association, given that it is potentially modifiable. Hypotheses for mechanisms of the obesity-migraine association and treatment considerations for overweight and obese headache sufferers are discussed in the companion manuscript, as part II of this topic.

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INTRODUCTION

Individually, both obesity and headache are conditions associated with a substantial personal and societal impact. Recent literature has consistently demonstrated an association between obesity and headache, and with migraine in particular. Specifically, research has attempted to identify the populations in which the headache-obesity association is the strongest. In addition, specific links between various headache/migraine characteristics (eg, headache frequency, severity) have also been investigated in association with obesity. While a significant amount of data has emerged regarding the headache/migraine-obesity association, the direction of this relationship is not yet clear. In addition, questions remain regarding the modifiable nature of the obesity-headache relationship and its implications in clinical practice.

Hypotheses for mechanisms of the obesity-migraine association and treatment considerations for overweight and obese headache sufferers are discussed in the companion manuscript, as part II of this topic. In the current manuscript, we first briefly review the epidemiology of obesity and common primary headache disorders individually. This is followed by a systematic review of the general population data evaluating the association between obesity and headache in general, and then obesity and migraine and tension-type headache (TTH) specifically. Finally, we briefly review the data on the association between obesity and a common secondary headache disorder that is associated with obesity, idiopathic intracranial hypertension (IIH).

EPIDEMIOLOGY OF OBESITY

According to the World Health Organization, obesity is classified as having a total body fat (TBF) percentage greater than 35% in women and greater than 25% in men.¹ However, because cost and ease of use, most epidemiological studies utilize anthropometric indices (such as the body mass index [BMI] or waist circumference [WC]) to estimate the threshold for total body obesity (TBO) and abdominal obesity, respectively. General obesity or TBO, based on the BMI, is estimated as a BMI ≥ 30 kg/m², while abdominal obesity (abd-O), based on the WC, is estimated as a WC >88 cm in women or >102 cm in men^{2,3} (see Appendix 1 for body composition categories based on the BMI and WC).

The prevalence of obesity has increased globally over the past decades.^{4,5} In the United States, the prevalence of general obesity (BMI ≥ 30) increased from 33% (women) and 27% (men) in 1999–2000 to 35% (women) and 32% (men) by 2007–2008. Similarly, the prevalence of abd-O in the United States has increased over the past decade, with 62% of women and 43% of men fulfilling criteria for abdominal obesity in 2007–2008, as compared with 56% of women and 38% of men in 1999–2000.⁴

In addition to sex-specific differences, racial differences in adipose tissue distribution, as well as in obesity, have been identified.⁶ In the United States, obesity prevalence (based on BMI) has been reported to be greatest in African Americans, followed by Caucasians, and lowest in Asian Americans.^{4,7} However, notably given the same BMI, Asians have a higher TBF percentage compared with their Caucasian counterparts;⁸ and black women have a lower TBF percentage compared with white women.⁹

By itself, obesity is associated with substantial personal and financial burden.¹⁰ Further contributing to this burden, obesity has been shown to be comorbid with multiple medical disorders (eg, hyper-lipidemia, cardiovascular disease, depression).^{11,12} More recently, data also support an association between obesity and pain disorders,¹³ including nonstructurally related pain disorders such as headache, and migraine in particular.¹⁴

EPIDEMIOLOGY OF PRIMARY HEADACHE

Headache, in general, is incredibly common.¹⁵ The global lifetime prevalence of headache (all types), is 66% (male 65%, female 69%);¹⁵ while the 1-year period prevalence is approximately 47% (male 37%, female 52%).¹⁵

Of the primary headache disorders, TTH is the most common, with a lifetime prevalence of approximately 46% globally¹⁵ and a 1-year period prevalence of 38%.¹⁵ The 1-year incidence for TTH is between 14 and 44 per 1000 person-years.^{16,17} There is a female predilection for TTH, with a female to male ratio between 1.2:1 and 3:1.^{18,19}

Migraine, while less common than TTH in the general population, is the most common primary headache disorder presenting to a physician's office.²⁰ The lifetime prevalence of migraine is approximately 14% globally,¹⁵ with a 1-year period prevalence of 12–15%.^{15,21} Migraine incidence has been estimated between 3 and 18 cases per 1000 person-years.^{16,17} As with TTH, migraine is more common in women (17.6%) than men (6.5%). Additionally, in both sexes, migraine is most prevalent in those of reproductive age (between 20 and 50 years of age).^{15,21}

Migraine Incidence and Prevalence Rates Across Time

While it has been recognized that obesity incidence and prevalence rates have increased in the past several decades (particularly between 1999 and 2008),^{4,22} it is controversial as to if migraine incidence and prevalence rates have likewise increased in past decades. Several studies have reported that the incidence and/or prevalence of migraine in adolescents and adults have increased, particularly between the late 1980s to late 1990s and the mid-to-late 1990s to the early 2000s (Table 1).^{23–28} One study evaluating changes in migraine prevalence over time reported no increase in migraine prevalence between 1989 and 2001.¹⁷ However, study methodologies in the earlier studies, at least in part, limit our ability to draw firm conclusions. For example, some of these studies measured medically ascertained migraine (eg, clinician-diagnosed)^{23,24} and therefore are also likely measuring secular changes in medical consultation for migraine. Additionally, other studies used self-reported or non-International Classification of Headache Disorders (ICHD) migraine diagnoses (Table 1).^{25,29,30} Further, others have discussed an apparent increase^{29–31} or a lack of change^{21,32} in migraine prevalence over time without formal statistical evaluations being conducted. Regardless of whether the incidence and/or prevalence of migraine have increased, the existence or absence of such changes may be irrelevant to the validity of the migraine-obesity association, as such comparisons likely represent an example of an ecological fallacy³³ (see also <http://www.stanford.edu/class/ed260/freedman549.pdf> for further description and examples of ecological fallacies).

THE EPIDEMIOLOGICAL ASSOCIATION BETWEEN OBESITY AND HEADACHE DISORDERS

Headache disorders, and migraine in particular, have long been recognized to be comorbid with multiple psychiatric (eg, depression, post-traumatic stress disorder) and medical conditions (eg, stroke, epilepsy).^{34,35} In the following sections, we review the existing literature examining the association between obesity and headache in general. We then

review the literature evaluating the relationship between obesity and specific primary headache disorders, migraine, and TTH, as well as the relationship between obesity and an obesity-related secondary headache disorder, IHH.

Search Method for Obesity and Common Primary Headache Disorders

A systematic search of PubMed database was conducted on August 1, 2013 using the keywords “headache,” “migraine,” “tension-type headache,” “cluster headache,” “paroxysmal hemicrania,” “trigeminal autonomic cephalalgia” AND “obese/obesity,” “body mass index/BMI,” “overweight,” or “body fat.” In addition, reference lists of relevant articles were reviewed for possible inclusion. All English language, cross-sectional and longitudinal, general population, and epidemiological studies of adult or adolescent (age >12) populations published between January 2000 and July 2013 were included. Over 500 studies were identified through the earlier search terms, of which 16 (including 2 on headache and migraine, 3 on TTH and migraine, and 11 on migraine only) fulfilled the earlier inclusion criteria and are reviewed later. No general population studies were identified evaluating the association between trigeminal autonomic cephalalgias and obesity, and thus, only headache in general, migraine, and TTH general population studies are reviewed later.

Obesity and Headache in General

Two studies have demonstrated a positive association between obesity and headache in general. In 2003, Scher et al conducted the first longitudinal, general population study evaluating the relationship between obesity and headache (see Table 2).³⁶ A total of 1192 adults, of predominantly reproductive age (18–65 years of age) with episodic headache (EH) (2–104 headache [HA] days/year) and chronic daily headache (CDH) (≥180 HA days/year) were evaluated at baseline and 11 months later. At baseline, obesity (self-reported: sr-BMI ≥30) was 34% more common in CDH participants (odds ratio [OR] 1.34, 95% confidence interval [CI] 1.0–1.8) than those with EH. Additionally, at the 11-month follow-up evaluation, EH participants with obesity were over 5 times more likely to have progressed to CDH than non-obese (sr-BMI <25) EH participants, (OR 5.28, 95% CI 1.3–21.1).³⁶

Subsequently, Keith et al conducted a cross sectional analysis of over 200,000 participants (16–90 years of age) drawn from 11 large general population databases that also demonstrated an increased risk of headache in those with obesity, as well as an increasing risk of headache with increasing obesity status. Headache in general was evaluated based on questionnaires from each of the 11 utilized databases (and will be reviewed here), while self-reported migraine was reported in a subgroup of older women (≥45 years of age), from only the Women’s Health Initiative database (and will be discussed in a later section). Participants with obesity (measured/sr: m/sr-BMI = 30) had an approximately 35% increased risk of headache as compared with those women with a normal BMI (BMI = 20). Those with morbid obesity (m/sr-BMI = 40) had an approximately 80% increased risk of headache.³⁷ Taken together these studies demonstrate that: (1) the risk of headache is increased in those with obesity and that this risk increases with increasing obesity status; (2) the association is stronger in those with chronic as compared with EH.

Obesity and Migraine

Reproductive-Age Migraine and Obesity Studies—The majority of general population studies of predominantly reproductive aged individuals (mean age <50) have demonstrated a significant association between obesity and migraine^{38–43} (see Table 2). The first cross-sectional population-based study demonstrating an association between obesity and headache of any kind was conducted in Australia by Brown et al in 2000.⁴⁴ This study included over 14,000 young women between the ages of 18 and 23. Controls included those

reporting no headache or migraine. Obese (sr-BMI ≥ 30) women were 47% more likely to report migraine or headache than non-obese (sr-BMI 25–29.9) women (OR 1.47, 95% CI 1.25–1.73).⁴⁴

Following the Brown et al and Scher et al studies, Bigal et al evaluated the prevalence of obesity in those with episodic migraine (EM) as compared with those with no headache, non-migraine headache, and possibly CDH, and found no association.⁴⁵ However, subgroup analyses evaluating just EM participants were also conducted. Although obese individuals were reported to be more likely to have high-frequency EM (HFEM; 10–14 HA days/month), as compared with those of normal weight (BMI 30–34.9: OR 2.9, 95% CI 1.9–4.4; BMI ≥ 35 : OR 5.7, 95% CI 3.6–8.8), those with obesity were not reported to be more likely to have lower frequencies of EM (ie, ≤ 9 HA days/month). Thus, in this study, obesity was not associated with increasing frequency of EM, but HFEM specifically.⁴⁵ A second cross-sectional study by Bigal et al in 2007 also supported an association between HFEM and obesity.⁴⁶

Subsequently, the migraine-obesity literature has consistently identified an association between migraine and obesity in general population studies evaluating those of reproductive age (the age when migraine is most prevalent)^{38–43} (see Table 2) and no association in those of perireproductive/postreproductive age^{37,39,43,47–49} (see Table 3). In 2008, Ford et al conducted a cross-sectional analysis from the National Health and Nutrition Examination Survey (NHANES). Notably, obesity status was estimated for the first time based on m-BMI. In this study, obese (m-BMI ≥ 30) participants had a 37% greater odds of migraine or severe headaches (OR 1.37, 95% CI 1.09–1.72) as compared with those of normal weight.³⁸ Following Ford et al's study, a 2010 cross-sectional study (also utilizing the NHANES) further defined the relationship between migraine and obesity.³⁹ In contrast with Ford et al's study, the odds of migraine in those with obesity were compared with those who were non-obese. Notably, this study was the first to suggest that the odds of migraine in those with obesity (by BMI) differed based on age, with a stronger association in younger individuals (<55 years) as compared with older individuals (55 years or older). Specifically, in participants 20–55 years of age, the prevalence and odds of migraine and severe headaches were increased in both women and men with obesity (m-BMI ≥ 30) as compared with non-obese individuals (women: 39.1% vs 30.2%, $P = .001$, OR 1.39, 95% CI 1.24–1.55; men: 20.2% vs 16.1%, $P = .001$, OR 1.38, 95% CI 1.20–1.59). However, in those older than 55 years of age, the risk of migraine in those with obesity was not increased. This study also extended the migraine–obesity relationship to include an association between migraine and abd-O in those ≥ 55 years old. Specifically, migraine was more prevalent in those with abd-O as compared with those without abd-O (women: 36.9% vs 28.8.2%, $P = .001$; men: 20.1% vs 15.9%, $P = .001$), and the risk of migraine was increased by 30–39% in those with abd-O as compared with those without abd-O (women: OR 1.39, 95% CI 1.25–1.56; men: OR 1.3, 95% CI 1.13–1.49)³⁹ (see Table 2).

The migraine-obesity association was also demonstrated in a general population study of younger reproductive-aged individuals.⁴⁰ In a cross-sectional analysis of 5847 adolescents (13–18 years old), Robberstad et al reported that those with migraine or probable migraine were 60% more likely to be overweight or obese (m-BMI) than those without migraine (OR 1.6, 95% CI 1.4–2.2).⁴⁰ Likewise, Vo et al also confirmed the obesity–migraine relationship in adult women of reproductive age in a cross-sectional, general population study of over 3700 premenopausal women.⁴¹ Similar to Keith et al's study evaluating obesity and headache in general,³⁷ this study also established that the risk of migraine increased with increasing obesity.⁴¹ While the overall odds of migraine in women with obesity (sr-BMI 30–34.9) was increased by almost 1.5-fold as compared with women without obesity (OR 1.48, 95% CI 1.12–1.96), those women with class II obesity (sr-BMI 35–39.9) demonstrated over

a 2-fold increased risk of migraine (OR 2.07, 95% CI 1.27–3.39), while women with morbid obesity (class III; sr-BMI ≥ 40) had almost a 3-fold increased risk of migraine (OR 2.75, 95% CI 1.60–4.70)⁴¹ (see Table 2).

Most recently, Peterlin et al conducted a general population, cross-sectional analysis of over 3800 participants evaluating the EM–obesity relationship.⁴³ This study extended the EM–obesity relationship to include those of all frequencies, including those with LFEM. In general, obese individuals had an 81% increased risk of EM as compared with those of normal weight (OR 1.81, 95% CI 1.27–2.57; $P = .001$). In addition, subgroup analyses demonstrated that the odds of LFEM (≥ 108 headache days/year) and very low headache frequency EM (VLFE; < 60 HA days/year) were increased by 83–89% in those with obesity (LFEM: OR 1.83, 95% CI 1.26–2.65; VLFE: OR 1.89, 95% CI 1.29–2.78) as compared with those with normal weight. However, there were no significant increases in the mean headache frequency (normal 43.8 ± 42.3 , overweight 39.2 ± 35.6 , obese 42.3 ± 45 headache days/year; $P = .37$) in participants with EM based on obesity status from normal to overweight to obese ($P = .37$), or between participants of normal weight and those with EM who were obese ($P = .67$). Finally, this study also substantiated the age variation in the migraine–obesity relationship. Specifically, age-stratified results showed that the risk of EM in those with obesity was increased by 86% in participants younger than 50 years of age, (OR 1.86, 95% CI 1.20–2.89; $P = .006$) but was not significantly increased in those older than 50 (OR 1.15, 95% CI 0.61–2.18)⁴³ (see Table 2).

Reproductive-Age Migraine and Obesity Studies in Asian Populations—The obesity-migraine association has also been demonstrated in at least 1 Asian general population study as well.⁴² Yu et al conducted a cross-sectional study of over 5000 participants evaluating the migraine-obesity association. Asians with morbid obesity (m-BMI ≥ 30) had a more than a 2-fold increased odds of EM (OR 2.10, 95% CI 1.39–3.12) as compared with normal-weighted (m-BMI 18.5–23) Asian individuals.⁴² However, an association between obesity and headache frequency was not found (Table 2).

Post-Reproductive-Age Migraine and Obesity Studies—In contrast with those studies evaluating predominantly reproductive-age individuals, all studies evaluating perimenopausal/postmenopausal populations have not found an association between migraine and TBO or abd-O^{37,39,43,47–49} (see Table 3).

Obesity and Chronic Migraine (CM)—In addition to EM, the current data also support an association between CM and obesity. In a cross-sectional analysis of more than 30,000 participants, Bigal and Lipton evaluated the odds of CM in those with obesity as compared with controls (those with no headaches and < 108 non-migraine headaches per year). The risk of CM was increased by 50% in those with BMI between 30 and 34.9 (OR 1.5, 95% CI 1.2–1.8) and by 100% in those with BMI > 35 (OR 2.0, 95% CI 1.4–2.4) compared with those of normal weight (BMI 18.5–24.9).⁵⁰

Finally, a recent cross-sectional, general population study of almost 7000 participants (migraine diagnosis based on ICHD-2) suggested that CM participants were 72% more likely to be obese (sr-BMI > 30) as compared with those without headache (OR 1.72, 95% CI 1.02–2.92).⁵¹ However, this finding was no longer significant after adjustments for frequent acute pain medication use (OR 1.85, 95% CI 0.54–6.27).⁵¹

Obesity and Migraine Conclusion—The current epidemiological literature on obesity and headache does not yet allow us to identify the direction of the headache/migraine–obesity relationship. However, taken together, the earlier studies support that the risk of both episodic and CM is increased in those with obesity, and that this risk may be strongest in

those of reproductive age. Further, although the existing data support that the risk of migraine increases with increasing obesity status, whether the migraine–obesity relationship is dose-dependent with increasing headache frequency has not been determined.

Obesity and TTH

Substantially less data exist examining the TTH and obesity association. Three general population studies have specifically evaluated this association.^{40,46,50} While Robberstad et al reported a 40% increased risk of TTH (episodic and chronic together) in adolescents 13–18 years of age who were overweight or obese (OR 1.4, 95% CI 1.1–1.6),⁴⁰ Bigal et al reported no association between ETTH and obesity in the predominantly adult population.⁴⁶ When evaluating CTTH, a 40% increased risk of CTTH was found in those with a BMI 35 as compared with those with a BMI 18.5–24.9 (OR 1.4, 95% CI 1.1–1.9) in another cross-sectional general population study by Bigal et al.⁵⁰

OBESITY AND SECONDARY HEADACHES

Secondary headaches are headaches that occur in close temporal relation to another disorder known to be able to cause headaches (eg, intracranial neoplasm, infection).⁵² IIH is a secondary headache condition with close links to both obesity and the female gender – both characteristics also associated with migraine and deserves special attention by physicians treating headaches.

Search Method for Obesity and Secondary Headache Disorders

A systematic search of PubMed database was conducted on August 1, 2013 using keywords “secondary headache,” “idiopathic intracranial hypertension,” “pseudotumor cerebri” AND “obese/obesity,” “body mass index/BMI,” “overweight,” or “body fat” for general population epidemiological studies published between January 2000 and July 2013. In addition, reference lists of relevant articles were reviewed for possible inclusion. Because of a paucity of data, search dates were extended to include those studies published between July 1983 and July 2013, as well as to include both general population and clinic-based epidemiological studies of adult or adolescent (age >12) populations. Over 300 studies were identified, of which 12 fulfilled the earlier inclusion criteria and are reviewed later.

Obesity and IIH

IIH, also known as pseudotumor cerebri, is most commonly characterized by a progressive headache associated with increased cerebral spinal fluid (CSF) pressure (>200 mm H₂O in the non-obese and >250 mm H₂O in the obese), normal CSF chemistry, and the absence of other structural, vascular, metabolic, toxic, or hormonal causes of increased intracranial pressure. These patients often present with enlarged blind spot, papilledema, visual field deficits, and occasionally 6th nerve palsies.⁵² Headache is reported by about 75–94% of IIH patients^{53,54} and is often the first symptom reported.^{55,56} With withdrawal of CSF and lowered pressure, headache usually improves.⁵² There is a substantial financial burden associated with IIH, and this cost may be increasing with the increasing incidence and prevalence of obesity. According to 1 report, 38% of IIH patients have been hospitalized, with a total economic cost of IIH patients exceeding more than \$400 million.⁵⁷

IIH is much more common in women than men, reported as 84–90% women in case-control studies.^{58,59} The association between obesity and IIH may be more robust in women as well, as case-control studies have shown that while 25–65% of male IIH sufferers are overweight, around 80% of females with IIH are overweight.^{59–61} However, even in men with IIH, the prevalence of obesity is higher than that of healthy male controls.⁶⁰

The average annual age-adjusted incidence rate for IHH had been estimated to be about 1–3 per 100,000 in the general female population,^{56,62,63} and in women with obesity, the incidence has been estimated to be as high as 12–19 per 100,000.^{58,63} Further, a lower incidence has been reported in populations with a lower prevalence of obesity,⁶⁴ while a higher incidence has been reported in a population of obese patients seeking bariatric surgery,⁶⁵ further supporting the role of obesity in IHH. The prevalence of IHH is around 11 per 100,000 in the general female population and 86 per 100,000 in obese women.⁶³ Small case-control studies have suggested that both BMI and weight gain are risk factors for IHH.^{54,55,66} Specifically, higher levels of percent weight gain was found to be associated with progressively greater risk of IHH (1 year 5–10% weight gain: OR 3.6, 95% CI 1.1–11.9, $P = .04$; 1 year 11–15% weight gain: OR 10.2, 95% CI 1.9–56.5, $P = .008$; 1 year >15% weight gain: OR 15.2, 95% CI 1.5–151.2, $P = .02$).⁶⁶ Finally, IHH patients with normal BMI may have better visual outcomes compared with those with obesity.⁶⁷ Taken together, the previous studies demonstrate that: (1) IHH is more common in women, especially obese women; (2) both higher BMI and higher annual percent weight gain are associated with greater risk of IHH; (3) IHH can occur in those of normal weight, and they may experience a less severe phenotype.

The precise cause of IHH is not known. It has been proposed that a deficiency in intracranial CSF absorption secondary to venous hypertension whether because of intracranial venous stenosis or because of raised intrathoracic pressure secondary to increased abdominal obesity may be the etiology.⁶⁸ However, abdominal adiposity is unlikely the sole cause of IHH, as studies have demonstrated significantly different CSF pressures when comparing patients with IHH with papilledema with patients with chronic TTH with similar BMIs.⁶⁹ In fact, instead of abdominal adiposity, 1 study found that lower body adiposity (defined as weight-to-hip ratio <0.76) was actually more than 6-fold more common in IHH than in control group of obese women.⁷⁰ Further, other comorbid conditions with obesity (ie, sleep apnea, systemic hypertension) have also been suggested as possible links between obesity and IHH.^{55,71,72} Large prospective studies are warranted to better define the causal relationship between obesity and IHH.

CONCLUSION

Population studies have consistently identified an association between obesity and headache in general, as well as migraine specifically. The disease risk associated with obesity includes both episodic and CM. Specifically, obesity is estimated to increase the risk of migraine by 40–80%, and this risk increases with increasing obesity status from normal weight to overweight to obese. Further, the migraine-obesity disease risk is modified by age, being greatest in those of reproductive age – the age when migraine and headaches are most common and potentially most disabling. The association between obesity and TTH is less robust, and this association may be stronger in those with chronic TTH as compared with episodic TTH. Finally, IHH is a secondary headache condition that is significantly associated with obesity as well as the process of weight gain. Taken together, these data suggest that it is important for clinicians treating patients with headache disorders, and particularly migraine, who are obese or at risk of becoming obese, to be aware of the headache/migraine-obesity association, given that it is potentially modifiable. Hypotheses for mechanisms of the obesity-migraine association and treatment considerations for overweight and obese headache sufferers in light of these data are discussed in the companion manuscript, as part II of this topic.

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APPENDIX 1

Table A1

Appendix 1: WHO Criteria for Total Body Obesity & Abdominal Obesity

WHO Criteria for Total Body Obesity		
Women & Men		
BMI < 18.5	Underweight	
BMI 18.5–24.9	Normal weight	
BMI 25–29.9	Grade I obesity	Overweight
BMI 30–39.9	Grade II Obesity	Severe overweight
BMI ≥ 40	Grade III Obesity	Morbid Obesity
WHO Criteria for Abdominal Obesity		
Men		
WC < 94	Normal weight	
WC 94–102	Action Level 1	Overweight
WC > 102 cm	Action Level 2	Abdominal Obesity
Women		
WC < 80	Normal weight	
WC 80–88 cm	Action Level 1	Overweight
WC > 88 cm	Action Level 2	Abdominal Obesity

BMI = body mass index; WC = waist circumference.

Key Points

- Obesity is comorbid* with both episodic and chronic migraine.
- The risk of migraine may be strongest in those of reproductive age.
- The risk of migraine overall increases with increasing obesity status from normal to overweight to obese.
- Whether the migraine-obesity relationship is dose-dependent with increasing headache frequency has not been determined.
- Those with episodic headache who are obese have a greater risk of headache chronification than those with episodic headache who are not obese.

***By the seminal definition of Feinstein, the definition of comorbidity is: “any distinct additional entity that has existed or may occur during the clinical course of a patient who has the index disease under study.” {{431 Feinstein 1970;}}**

Table 1

Migraine Studies Evaluating Changes in Migraine Prevalence Across Time

Author Pub Year	Study Design	HA Dx	Age Range	1st Time Period (n)	2nd Time Period (n)	Migraine Prevalence (%)					
						Total Cohort		Women		Men	
						1st TP	2nd TP	1st TP	2nd TP	1st TP	2nd TP
Le et al ²⁵ 2012	Long-GP	SR	20–41	1994 (n = 22,053)	2002 (n = 14,810)	19	25*	24	31	13	16
Linde et al ²⁶ 2010	CS-GP	ICHD-Mod	>19	1995–97 (n = 51,383)	2006–08 (n = 39,690)	12	13*	—	15	—	7.4
Lyngberg et al ¹⁷ 2005	CS-GP	ICHD	25–36	1989 (n = 25)	2001 (n = 32)	11.3	15.5 [†]	15.6	23.5	7.1	5.4
Wang et al ²⁷ 2005	Long-GP	ICHD	13–15	1999 (n = 7942)	2001 (n = 7658)	5	7*	6	9	5	6
Laurell et al ²⁸ 2004	CS-GP	ICHD and ICHD-Mod	7–15	1955 (n = 8993)	1997 (n = 1371)	4	7*	—	12	—	10
Cheung ³¹ 2000	CS-GP	ICHD	>15	1992–93 (n = 7356)	1998 (n = 1436)	1.5	4.7 [‡]	—	—	—	—
Sillanpaa and Anttila ³⁰ 1996	CS-GP	Non-ICHD	<16	1974 (n = 1927)	1992 (n = 1436)	2	6 [†]	2	5	2	7
Centers for Disease Control and Prevention ²⁹ 1991	CS-GP	SR	>17	1979–1981 (n = 321,000)	1989 (n = 125,000)	2.6	4.1	—	—	—	—

* $P < .001$ as compared with 1st TP.

[†] Not significant.

[‡] P value not available.

The data from this study were collected by the Center for Disease Control (CDC) that reported that from 1980 through 1989, the prevalence of migraine in US increased from 25.8 per 1000 persons to 41.0 per 1000 persons. In addition, the CDC reported that prevalence among those under 45 years of age increased by 77% in women and 64% in men in this time period. P value not available.

CS-GP = cross-sectional general population; Dx = diagnosis; HA = headache; ICHD = International Classification of Headache Disorders; Long-GP = longitudinal general population; PP = period prevalence; SR = self report; TP = time-period; Yr = year.

Table 2
Headache and Obesity General Population Studies of Predominantly Reproductive-Age Participants

Author (Year)	Study Analysis (Database) Size	Population Inclusion	Sex	Mean Age (Range)	Race	Exposure Categories	Outcome	HA & BMI Dx (sr vs m)	Statistical Adjustments	Findings
Brown et al ⁴⁴ (2000)	CS-GP (AL-SWH) n = 12,855 (HA/Mig 7229)	1. No HA/Mig 2. HA/Mig (Controls; Participants with no HA/Mig) Note: Freq not reported	W	20 (18–23)	NR Birth Origin: 88.6% Australian 3.6% Asian 7.8% Other	BMI <17 (n = 377) BMI 17–<18.5 (n = 1104) BMI 18.5–<20 (n = 2240) BMI 20–<25 [†] (n = 6536) BMI 25–<30 (n = 1817) BMI >30 (n = 738)	OR HA or Mig	HA: Non-ICH BMI: sr	1. Age 2. Education 3. Smoking 4. Exercise 5. Area of residence	The OR of HA or Mig were increased in women with sr-BMI 25–<30 (OR 1.12, CI 1.00–1.25) and sr-BMI >30 (OR 1.47, CI 1.25–1.73) compared with women with normal weight (sr-BMI 20 to <25). No conclusion can be drawn regarding obesity and HA freq
Scher et al ³⁶ (2003)	Long-GP n = 1932 (EH 798)	1. EH: 2–104 HA/year 2. CDH: 180 + HA/year (Controls; EH)	M & W Combined	40 (18–65)	White 73% Non-white 25% Unknown 2%	BMI <25 [†] (n = 599) BMI 25–30 (n = 390) BMI 30 (n = 316)	1) OR of prevalent CDH 2) OR CDH incidence in EH participants	HA: Non-ICH BMI: sr	1. Age 2. Sex 3. Race 4. Education 5. Marital status 6. BMI 1. BMI 2. Baseline headache frequency	The odds of new onset CDH was 5-fold greater in those EH participants with sr-BMI 30 (OR 5.28, CI 1.3–21.1) compared with EH participants with normal weight (sr-BMI <25). The OR of CDH were increased in headache participants (ie, EH + CDH) with sr-BMI 25–30 (OR 1.26, CI 1.0–1.7) and sr-BMI 30 (OR 1.34, CI 1.0–1.8) as compared with headache participants with normal weight.

Author (Year)	Study Analysis (Database) Size	Population Inclusion	Sex	Mean Age (Range)	Race	Exposure Categories	Outcome	HA & BMI Dx (sr vs m)	Statistical Adjustments	Findings
Bigal et al ⁴⁵ (2006)	CS-GP (Master Health Study) n = 30,215 (EM: 3791)	1. 14 or < nonmigraine HA days/month 2. No HA 3. CDH 4. EM (Controls: CDH, non-migraine HA and No HA)	M & W Combined & Stratified	39 (18–89)	White 72% Black 25%	BMI <18.5 (n = 941) BMI 18.5–24.9 [†] (n = 15,501) BMI 25–29.9 (n = 9,258) BMI 30–34.9 (n = 3,133) BMI 35 (n = 1,382)	OR of EM in all BMI categories evaluate as compared to those with non-migraine HA, CDH, no HA	HA: ICHD-1 BMI: sr	1. Income 2. Marital status 3. Use of acute or preventative medications 4. Depression	Among those with EM, the odds of HFEM (ie, 10–14 headache days/month) were increased in those with sr-BMI 25–29.9 (OR 1.3, CI 1.1–1.9), sr-BMI 30–34.9 (OR 2.9, CI 1.9–4.4), and sr-BMI 35 groups (OR 5.7, CI 3.6–8.8) compared with those with normal weight (sr-BMI 18.5–24.9). The OR of LFEM were not increased in those with sr-BMI 30–34.9 vs those with sr-BMI 18.5–24.9, including those with <3 HA days/month (OR 0.8; CI 0.6–0.99) and those with 3–9 HA days/month (OR 0.8; CI 0.7–1.1).
Ford et al ³⁸ (2008)	CS-GP (NHANES) n = 7,601 (Mig: 1649)	1. Sev HA or Mig 2. No Sev HA or Mig (Controls: No Sev HA or Mig) Note: Freq not reported	M & W Combined & Stratified	46 (20–85)	White 50% Black 18% Mex Am 24%	BMI <18.5 (n = 121) BMI 18.5–24.9 [†] (n = 2313) BMI 25–29.9 (n = 2784) BMI 30 (n = 2383)	OR Mig	HA: Non-ICHD BMI: m	1. Age 2. Sex 3. Race 4. Education 5. Marital status 6. Physical activity 7. Smoking 8. Alcohol 9. SBP 10. CRP 11. Cholesterol 12. Diabetes	The OR of migraine or severe HA was increased in those with m-BMI 30 (OR 1.37, CI 1.09–1.72) compared with those with normal weight (m-BMI 18.5–25). No conclusion can be drawn regarding obesity and HA freq.

Author (Year)	Study Analysis (Database) Size	Population Inclusion	Sex	Mean Age (Range)	Race	Exposure Categories	Outcome	HA & BMI Dx (sr vs m)	Statistical Adjustments	Findings
Peterlin et al ³⁹ (2010)	CS-GP (NHANES) n = 15,631 (Mig: 3915)	1. Severe HA or Mig 2. No severe HA or Mig (Controls: No Sev HA or Mig) Note: Freq not reported	M & W Stratified	38 (20–55)	Men: White 70% Black 11% Women: White 82% Black 8%	1) BMI 30 (n = 4,585) BMI <30 [†] (n = 11,046) 2) Abd ob (n = 6,631) No Abd-O [†] (n = 9,000) Abd OB defined as WC 88 cm in women and WC 102 cm in men	OR Mig	HA: Non-ICHD BMI: m	1. Age 2. Education 3. Race 4. Smoking 5. Alcohol 6. Income 7. Diabetes 8. Abd-O or TBO	1. The OR of migraine or severe HA were increased in women with m-BMI 30 (OR 1.39, CI 1.25–1.56) and men with m-BMI 30 (OR 1.38, CI 1.20–1.59) compared with those with BMI <30. 2. The OR of migraine or severe HA were increased in women with Abd-O compared with women without Abd-O (OR 1.26, CI 1.1–1.45), and in men with Abd-O compared with men without Abd-O (OR 1.3, CI 1.13–1.49). No conclusion can be drawn regarding obesity and HA freq.
Robberstad et al ⁴⁰ (2010)	CS-GP (Head-Hunt Youth) n = 5847 (Mig: 392)	1) Mig 2) TTH 3) Non-classifiable HA 4) No HA (Controls: No migraine or non-migraine HA) Note: Freq not reported	M & W Combined & Stratified	<18 (13–18)	White 98% Non-white <3%	Overweight (based on pediatric cut BMI offs per sex and age) (n = 891) Number of participants of normal weight and obese were not given)	OR Mig	HA: Non-ICHD BMI: m	1. Age 2. Sex 3. Smoking 4. Physical activity	The OR of migraine were increased in overweight or obese adolescents and young adults (per pediatric cut-off points) compared with those not overweight or obese (OR 1.6, CI 1.4–2.2). No conclusion can be drawn regarding

Author (Year)	Study Analysis (Database) Size	Population Inclusion	Sex	Mean Age (Range)	Race	Exposure Categories	Outcome	HA & BMI Dx (sr vs m)	Statistical Adjustments	Findings
Vo et al ⁴¹ (2011)	CS-GP (OMEGA) n = 3733 (Mig: 672)	1) Physician DxMig 2) No Lifetime Physician MigDx (Controls: Participants with no lifetime physician MigDx) Note: Freq not reported	W	<40 (18–40 s)	White 86% Other 14%	BMI < 18.5 (n = 160) BMI 18.5–24.9 [†] (n = 2623) BMI 25–29.9 (n = 612) BMI 30 (n = 338)	OR Mig	HA: Non-ICH BMI: SR	1. age 2. Race 3. Education 4. Marital status 5. Smoking 6. Exercise status 7. History of chronic hypertension 8. Diabetes	obesity and HA freq. The OR of migraine were increased in women with sr-BMI 30–34.9 (OR 1.48, CI 1.12–1.96), sr-BMI 35–39.9 (OR 2.07, CI 1.27–3.39), and sr-BMI 40 (OR 2.75, CI 1.60–4.70) compared with women with normal weight (BMI 18.5–24.9). No conclusion can be drawn regarding obesity and HA freq.
Yu et al ⁴² (2012)	CS-GP n = 5029 (EM: 467)	Those with: 1) EM (<15 HA days/month) 2) No EM (excluded those with headache 15 days/month) (Controls: No EM)	M & W Combined	43 (18–65)	Han Chinese 94% Other 6%	BMI < 18.5 (n = 262) BMI 18.5–<23 [†] (n = 2,469) BMI 23–<25 (n = 1,064) BMI 25–<30 (n = 1,044) BMI 30 (n = 190)	OR EM	HA: ICHD2 BMI: M	1. Age 2. Sex 3. Education 4. Marital status 5. Occupation 6. Urban or rural habitation	The OR of EM was increased in Asians with m-BMI 30 (OR 2.10, CI 1.39–3.12) compared to Asians with normal weight (m-BMI 18.5–23). Headache frequency among different BMI categories showed no significant difference.
Peterlin et al ⁴³ (2013)	CS-GP (NCS-R) n = 3862 (EM: 188)	1) EM 2) No HA (controls: No HA)	M & W Combined & Stratified	<46.6 (18–50+)	White 85.5% Black 14.5%	BMI < 18.5 (n = 129) BMI 18.5–24.9 [†] (n = 1424) BMI 25–29.9 (n = 1306) BMI 30 (n = 1004)	OR EM	HA: ICHD2 BMI: SR	1. Age 2. Race 3. Sex 4. Smoking 5. Depression 6. Poverty index 7. Diabetes	The OR of EM was increased in those with sr-BMI 30 (OR 1.81, CI:1.27–2.57) compared with those with normal weight (sr-BMI 18.5–24.9). The OR of

Author (Year)	Study Analysis (Database) Size	Population Inclusion	Sex	Mean Age (Range)	Race	Exposure Categories	Outcome	HA & BMI Dx (sr vs m)	Statistical Adjustments	Findings
										low-frequency EM (LFEM [108 HA days/year]) and very low HA frequency EM (VLFEM [60 HA days/year]) were increased in those with obesity (LFEM: OR 1.83, 95% CI 1.26–2.65; VLFEM: OR 1.89, 95% CI 1.29–2.78) as compared with those with normal weight. Additionally, this study substantiated that the risk of EM in those with obesity was stronger in those younger than 50 years of age (OR 1.86, 95% CI 1.20–2.89; $P = .006$) than in those older than 50 (OR 1.15, 95% CI 0.61–2.18). Headache frequency among different BMI categories showed no significant difference.

No additional information regarding location, frequency, severity, or accompanying symptoms of HA were given.

[†]Reference BMI.

Abd-O = abdominal obesity (defined as WC 102 cm in men; WC 88 cm in women); BMI = body mass index; CI = confidence interval; CDH = chronic daily headache; CS = cross-sectional; EH = episodic headache; EM = episodic migraine; GP = general population study; HA = headache; HFEM = high-frequency episodic migraine; ICHD = International Classification of Headache Disorders; LFEM = low-frequency episodic migraine; Long = longitudinal; m = measured; M = men; Mex Am = Mexican American; Mig = migraine; NHANES = National Health and Nutrition Examination Survey; NR = not reported; OR = odds ratio; Prob-EM = probable episodic migraine; Sev-ETTH = severe episodic tension type HA; sr = self-reported; TBO = total body obesity; VLFEM = very low headache frequency EM; W = women; WC = waist circumference.

Table 3

Migraine and Obesity General Population Studies of Periparturient and Postparturient-Age Participants

Author (Year)	Study Analysis (Database) Size	Population Inclusions	Sex	Mean Age (range)	Race	Exposure Categories	Outcome	HA & BMI Dx (sr vs m)	Statistical Size Adjustments	Findings
Mattsson et al ⁴⁷ (2007)	CS-GP [†] n = 684 (EM: 130)	1. Active Mig (1 Mig Attack In Prev Yr) 2. Inactive Mig (No Mig Past Yr But Prev Mig Hx) 3. No Mig	W	54 (40–74)	NR	Active migraine (n = 130) Inactive migraine (n = 95) No migraine (n = 459) [§]	Mean BMI Obesity Status	HA: ICHD BMI: (m)	1. Age 2. Education	The mean (m)-BMI was not significantly different in older women with active migraine (26.7 ± 4.7), inactive migraine (27.2 ± 4), and no migraine (26.7 ± 4.5), $P = .32$. Active and inactive migraine were not associated with obesity (LR chi-square = 0.07, 2 d.f., $P = .96$).
Keith et al ³⁷ (2008)	CS-GP (WHS) [‡] n = 220,370 (EM: NR)	1) Severe/ Freq HA or Mig 2) No Severe/ Freq HA or Mig	W	>50 (50–79)	White 83%	BMI ~20 [§] BMI ~30 BMI ~40	OR Mig	HA: non-ICHD BMI: (m)	1. Age 2. Race 3. Smoking	As compared with those with (m)-BMI = 20, the odds of migraine were not increased in older women with BMI = 30 (OR 1.00, 95% CI 0.96–1.04) or those with BMI = 40 (OR 0.99; 95% CI 0.92–1.07).
Winter et al ⁴⁹ (2009)	CS-GP (WHS) n = 63,467 (Mig: 9195)	1) Active Mig (1 Mig Attacks In Prev Yr) 2) Inactive Mig (No Mig Past Yr But Prev Hx Mig) 3) No Mig [§]	W	54 (45)	NR	BMI < 23 (n = 18,301) BMI 23–24.9 [§] (n = 12,475) BMI 25–26.9 (n = 9744) BMI 27–29.9 (n = 10,105)	OR Mig	HA: non-ICHD BMI: (sr)	1. Age 2. Smoking 3. Exercise 4. Alcohol 5. HTN 6. Menopausal status 7. Hormone use 8. Hypercholesterolemia	The OR of migraine in older women with (sr)-BMI 35 (OR 1.03, CI 0.95–1.12) was not increased as compared with those with BMI < 23(ref).

Author (Year)	Study Analysis (Database) Size	Population Inclusions	Sex	Mean Age (range)	Race	Exposure Categories	Outcome	HA & BMI Dx (sr vs m)	Statistical Size Adjustments	Findings
Peterlin et al ³⁹ (2010)	CS-GP (NHANES) n = 15,631 (Mig: 3915)	1) Severe HA or Mig 2) No severe HA or Mig [§]	M & W Stratified	68 (55)	M: White 81.8% Black 8.2% W: White 79.8% Black 9.1%	BMI 30–34.9 (n = 8338) BMI 35 (n = 4504) 1) BMI 30 (n = 4585) BMI < 30 [§] (n = 11,046) 2) Abd ob (n = 6631) No Abd-O (n = 9000) Abd OB defined as WC 88 cm in women and WC 102 cm in men	OR Mig	HA: non-ICHD BMI: (m)	1. Age 2. Education 3. Race 4. Smoking 5. Alcohol 6. Income 7. Diabetes 8. abd-O or TBO	The OR of migraine were not increased in older women or older men with (m)-BMI 30, (Women: OR 0.85, CI 0.67–1.08; Men: OR 0.82, CI 0.58–1.16) as compared with those with BMI < 30. The OR of migraine were decreased in older women with Abd-O (OR 0.73, CI 0.56–0.97) as compared with those without Abd-O; there was no difference in OR of migraine in men with Abd-O as compared with without Abd-O (OR 0.97; CI 0.70–1.34).
Winter et al ⁴⁸ (2012)	Long-GP (WHS) n = 19,162 (EM: 3483)	Baseline: BMI 18.5–< 25 After 12.9 years 1) BMI 18.5 to <25 [§] 2) BMI 25 3) BMI 30	W	54 (45)	White 95%	No migraine (n = 15,679) Any migraine (n = 3483)	HR over-wt (BMI 25) or obese (BMI 30)	HA: Non-ICHD BMI: (sr)	1. Age 2. Race 3. Smoking 4. Exercise 5. Alcohol 6. HTN 7. Menopausal status 8. Hormone use 9. Hypercholesterolemia 10. Depression 11. Calorie intake	The HR for older women with any history of migraine (HR 1.00, CI 0.83–1.19) to become obese (1st)-BMI 30) was not increased compared with

Author (Year)	Study Analysis (Database) Size	Population Inclusions	Sex	Mean Age (range)	Race	Exposure Categories	Outcome	HA & BMI Dx (sr vs m)	Statistical Size Adjustments	Findings
Peterlin et al ⁴³ (2013)	CS-GP (NCS-R) n = 3862 (EM: 188)	1) EM 2) No HA [§]	M & W Combined & Stratified	>50 (50–98)	White 85.5% Black 14.5%	BMI < 18.5 (n = 129) BMI 18.5–24.9 [§] (n = 1424) BMI 25–29.9 (n = 1306) BMI 30 (n = 1004)	OR EM	HA: ICHD BMI: (sr)	1. Age 2. Race 3. Sex 4. Smoking 5. Depression 6. Poverty index 7. Diabetes	women without migraine. The OR of episodic migraine was not increased in older men and women with (sr)-BMI 30 (OR 1.15, CI 0.61–2.18) as compared with those with normal weight ((sr)-BMI 18.5–24.9).

[†] This study utilizes a Swedish database of women invited for mammography screening.

[‡] This study was a meta-analysis evaluating the association between headache in general and obesity; only the WHI database was used when evaluating the association between obesity and migraine specifically.

[§] Reference group.

BMI = body mass index; cs = cross-sectional; CI = confidence interval; EM = episodic migraine; GP = general population study; HA = headache; HR = hazard ratio; hx=history; ICHD = International Classification of Headache Disorders; long = longitudinal; Mig = migraine; (m)-BMI = measured-BMI; M = men; NHANES = National Health and Nutrition Examination Survey; NR = not reported; OR = odds ratio; prev = previous; sr-BMI = self-reported BMI; W = women, WC = waist circumference; WHI = Women's Health Initiative; yr = year.