

**Pharmacological Management of Obesity in the National Health and Nutrition Examination Survey (NHANES) 2007-8**

**Short title: Pharmacological Management of Obesity**

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## **Abstract**

**Introduction:** The prevalence of obesity has been increasing in the United States. We set out to investigate the use of anti-obesity drugs in recent years.

**Methods:** We included 2630 men, and 2702 women who took part in NHANES. We analyzed their demographic, and anthropometric data, and their weight, and drug history. A person is a candidate for treatment of obesity if the initial body mass index  $\geq 30$  kg/m<sup>2</sup>, or  $\geq 27$  kg/m<sup>2</sup> in the presence of other risk factors (e.g. hypertension, diabetes or dyslipidemia). Sampling weights were used to adjust for non-response bias, and the oversampling of blacks, Mexican Americans, and the elderly.

**Results:** 45.9% of men, and 45.0% of women were candidates for treatment. Among these participants, 85.1% considered themselves overweight, 90.1% would like to lose weight, 61.9% had dietary changes, 36.5% exercised, 3.7% took non-prescription diet pills and 2.2% took prescription diet pills to control weight during the preceding year. During the preceding month, 0.5%, and 0.1% of participants were taking phentermine, and orlistat respectively. There were no participants on sibutramine.

**Conclusions:** Obesity is highly prevalent in the United States, but only a very small percentage is on anti-obesity medication. The withdrawal of sibutramine in October 2010 would have minimal impact on the general population. While improvements in pharmacological treatment of obesity are needed, our study also revealed that there is a need for more lifestyle changes in the majority of obese individuals.

## **Introduction**

Obesity is an epidemic world wide. The prevalence of obesity is accelerating in developed and developing countries. Studies have established that overweight, and obese people are at a higher risk of developing conditions like hypertension, dyslipidemia, type 2 diabetes, cardiovascular diseases, and obstructive sleep apnea<sup>1-3</sup>. Obesity is also a known risk factor

for a variety of more health conditions including cancer and reproductive abnormalities<sup>4</sup>. In the United States (US), approximately 300,000 people die annually due to obesity related causes. The morbidities associated with obesity accounts for a substantial amount of the national healthcare expenditure in US. Therefore it is time that obesity is accepted as a chronic disease and treatment directed towards achieving a sustainable, and healthy body weight<sup>5</sup>.

Lifestyle changes are an indispensable component in the treatment of obesity. A combination of dietary changes and exercise has shown to be more effective in achieving greater long term weight loss<sup>6</sup>. A recent study showed that a substantial proportion of obese Americans engaged in either diet changes or physical activities (73.5% women, and 60.3% men) but few adopted both<sup>7</sup>. Diet changes, and exercise are mainly short term remedies, and weight regain after one year of intervention is frequent<sup>8</sup>. On the other hand, environmental, and genetic factors make some people gain weight more easily than others<sup>9,10</sup>. Modern technologies that help people to perform daily tasks with less effort, central heating, sedentary jobs, are factors contributing to obesity<sup>10</sup>. As they cannot be changed easily, losing weight is difficult. The American College of Physicians recommends pharmacological therapy for people with a body mass index (BMI)  $\geq 30$  kg/m<sup>2</sup> or those with a BMI  $\geq 27$  kg/m<sup>2</sup>, and associated co-morbidities<sup>5,11</sup>.

Use of anti-obesity drug therapy alone causes only a modest weight loss (<5kg), although this change has been shown to improve cardiovascular risk factors, like insulin sensitivity, glycemic control, dyslipidemia, and hypertension in overweight patients<sup>12</sup>. Lifestyle changes including dietary changes, exercise, and behavioral therapy, enhances the effect of drug treatment<sup>13</sup>. Therefore, the patient on anti-obesity drug should continue lifestyle changes.

Accordingly, we analysed the use of pharmacological and non-pharmacological therapy for the treatment of obesity in the National Health and Nutrition Examination Survey (NHANES) study population.

### **Methods and procedures**

The NHANES was initiated in 1960 with the intention of assessing the health, and nutritional status of adults and children in US. After 1999, NHANES became a continuous study focusing on a variety of health and nutritional needs that concerns the US population. The methodology of this study, and the results are available online<sup>14</sup>. International Review Board Approval was obtained from the NCHS Research Ethics Review Board (ERB) as a continuation of protocol # 2005-06.

A total of 5332 (2630 men, and 2702 women) subjects in NHANES 2007-2008 were included in this analysis. Participants aged  $\geq 20$  years, who were non-pregnant, and had valid data on BMI, and self-reported history of hypertension, diabetes, and hypercholesterolemia were included. Data extracted from the data set included demographic data such as age, gender, race/ethnicity, BMI, and self-reported history of weight, prescription medication, hypertension, hypercholesterolemia, and diabetes.

Obesity was defined as  $BMI \geq 30.0 \text{ kg/m}^2$ <sup>15</sup>. Sibutramine, orlistat, and phentermine were considered as drugs for the treatment of obesity. Candidates eligible for anti-obesity drugs were defined as participants with  $BMI \geq 30.0 \text{ kg/m}^2$  or  $BMI \geq 27.0 \text{ kg/m}^2$  in the presence of one or more risk factors (hypertension, diabetes or dyslipidemia)<sup>16-18</sup>. Participants who were told by a health professional to have high blood pressure were defined as having hypertension.

Similarly, those who were told to have high blood cholesterol and diabetes were defined as having hypercholesterolemia, and diabetes respectively.

Weight control was defined as participants who took measures to reduce weight, stop gaining weight or both. Dietary changes included eating less food, switching to low calorie foods, eating less fat, eating fewer carbohydrates, eating less sugar, candy & sweets, eating more fruits, vegetables, and salads, drinking a lot of water, having liquid diets, eating diet foods, following a special diet, changing eating habits, and skipping meals.

Data was analysed using SPSS version 18 (SPSS Inc, Chicago, IL), and data was stratified mainly according to the eligibility of participants for treatment with anti-obesity drugs, and gender. Participants with BMI  $\geq 30.0$  kg/m<sup>2</sup> and those with BMI between 27.0 and 29.9 kg/m<sup>2</sup> with risk factors were taken as the two categories eligible for anti-obesity drug treatment. Sampling weights were used to adjust for non-response bias and the oversampling of blacks, Mexican Americans, and the elderly.

## **Results**

Two categories, people with BMI  $\geq 30.0$  kg/m<sup>2</sup> (obese), and those with both BMI 27.0-29.9 kg/m<sup>2</sup>, and risk factors were identified as candidates for anti-obesity drug treatment (Table 1). Among all people 34.3%, and 11.1% were obese and had BMI 27.0-29.9 kg/m<sup>2</sup> with risk factors respectively (Table 1). A total of 46.0% men, and 44.9% women were candidates to be treated with anti-obesity drugs. The highest prevalence of subjects with BMI 27.0-29.9 kg/m<sup>2</sup>, and risk factors were among the subjects aged  $\geq 60$  years for both men, and women. The overall prevalence of obesity was highest in subjects aged 40-59 years, especially in women. Past studies have established that there is racial/ethnic difference in the prevalence

of obesity<sup>13</sup>. Non-Hispanic blacks showed the highest prevalence of obesity (44.1%), followed by Mexican Americans (39.3%), Non-Hispanic Whites (32.8), and others (26.9). Similar trends were found in both men, and women, but there was a trend of higher prevalence of obesity in women than in men among all ethnic groups. In contrast, the prevalence of people with BMI 27.0-29.9 kg/m<sup>2</sup>, and risk factors was higher in non-Hispanic whites than that in non-Hispanic blacks (p = 0.013), especially in men (p<0.001).

Table 2 shows the characteristics of candidates eligible for anti-obesity drugs. Obese people were younger (47.8 years) than people with BMI 27.0-29.9 kg/m<sup>2</sup>, and risk factors (56.1 years). The majority of the obese people were within the ages 20-59 while people with BMI 27.0-29.9 kg/m<sup>2</sup> with risk factors were above 40 years. Among the candidates for anti-obesity drug treatment, majority were non-Hispanic whites. More than 50% of the obese people had been told by a healthcare professional to have one or more risk factors. There was a higher prevalence of hypertension (42.6%), and diabetes (35.9%) compared to hypercholesteremia (15.8%) in obese people. The same trend was evident in people having BMI 27.0 -29.9 kg/m<sup>2</sup> with one or more risk factors.

Figure 1 shows the data on the self-reported weight history among people who were eligible for anti-obesity drugs. The majority (85.1%) were aware that they were overweight. 90.1% of them desired to weigh less. Only 61.9%, and 60.3 % of obese people, and people with BMI 27.0-29.9 kg/m<sup>2</sup> with risk factors changed their diet to control weight during the preceding 12 months respectively (Figure 2). An even lower percentage of people engaged in exercise to control weight in both categories during the preceding 12 months. A comparatively lower percentage of subjects used methods such as taking prescription diet pills (2.2%), and non-prescription diet pills (3.7%) to control weight during the preceding

year. Interestingly, a significantly higher number of women were engaged in diet changes, taking prescription and non prescription drugs, and other methods to control weight than men.

Analysis of the prescription medication data shows that only 0.6% of eligible people were on anti-obesity drug treatment (Table 3). Surprisingly, majority of them were on phentermine, followed by orlistat. There were no subjects on sibutramine which was withdrawn by the Food and Drug Administration (FDA) in October 2010.

## **Discussion**

Our study reports the use of pharmacological and non-pharmacological therapy in the treatment of obesity among US adults in recent years. It is evident that the majority of American men and women are candidates for anti-obesity drug treatment. However, an important finding of this study was that very few of these candidates were on medication for obesity; the use of prescription or non-prescription medications were disappointingly low.

Given that sibutramine and orlistat were the drugs of choice for the treatment of obesity in 2007-08, it was interesting to find that the majority of candidates were on phentermine followed by orlistat. Although phentermine is the most widely prescribed and cheapest anti-obesity drug in the US<sup>19</sup>, its use is obsolete in some parts of the world due to its adrenergic responses resulting in increasing blood pressure and heart rate<sup>20,21</sup>. In fact, phentermine is recommended only for short term use, and therefore of limited use in long term weight management<sup>18</sup>. It is of interest to note that none of the participants were on sibutramine. This drug was withdrawn in October 2010 as a result of the findings of the SCOUT study, which revealed that subjects with pre-existing cardiovascular conditions on long term sibutramine

may have an increased risk of developing non-fatal myocardial infarction or non-fatal stroke<sup>22</sup>. Even though the decision to withdraw sibutramine was controversial, it is reassuring to find that only a very small proportion of obese individuals would have been exposed to the alleged risks of sibutramine in the US. Presently orlistat is the only choice for the pharmacologic treatment of obesity. Its efficacy has been established in previous studies.<sup>20,23</sup> In practice, orlistat is not widely used, despite the fact that it is also available over the counter. This may be attributable to its unpleasant side effects<sup>19</sup>. There is clearly a need for new and effective drugs for the treatment of obesity. However, these new treatments need careful evaluation of their risks and benefits.

It was encouraging that the majority of candidates for anti-obesity drug treatment perceived themselves overweight, particularly as self perception of overweight is known to be a strong predictor to pursue weight control activities<sup>7</sup>. A large percentage of these candidates desired to lose weight indicating the need for a sustainable weight control plan.

Non-pharmacologic interventions are an integral component in a weight control plan. However, adherence to lifestyle changes was low, and engaging in exercise seemed less popular than dietary changes among this sub-population. Another study using NHANES 1988 – 2006 data showed that the proportion of participants engaging in physical activity 12 times a month or more has decreased from 53% to 43%, and eating 5 or more fruits and vegetables a day has decreased from 42% to 26%<sup>24</sup>. Poor adherence to lifestyle changes may be a result of unawareness of its importance among subjects, reluctance to change or in some cases discouragement by the futility of weight control efforts.

There are some limitations in our study. The estimates of the percentage of anti-obesity drug treatment may be inaccurate due to the small number of participants on anti-obesity drugs. Nevertheless, this is in itself evidence for the under treatment of obesity.

### **Conclusions**

Obesity is highly prevalent in the United States, but only a very small percentage is on anti-obesity medication. Finding that none of the subjects were on sibutramine shows that its withdrawal in October 2010, would have minimal impact on the general population. While improvements in pharmacological treatment of obesity are needed, our study also revealed that there is a need for more lifestyle changes in the majority of obese individuals.

### **Disclosure statement**

None

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Figure 1: Weight perceptions and desire to lose weight among participants who were eligible for anti-obesity drug treatment

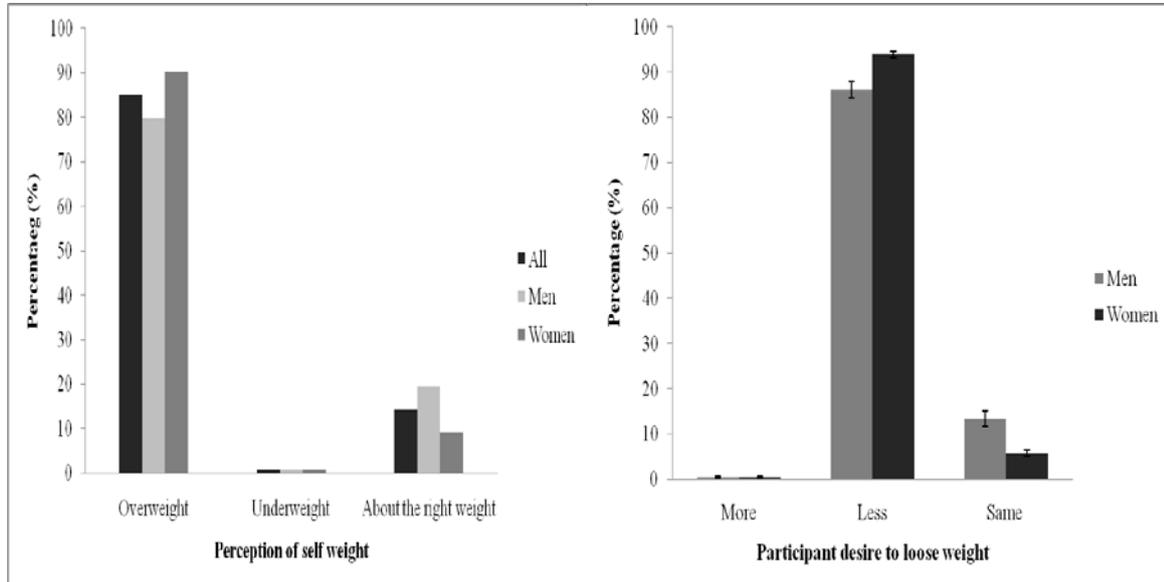
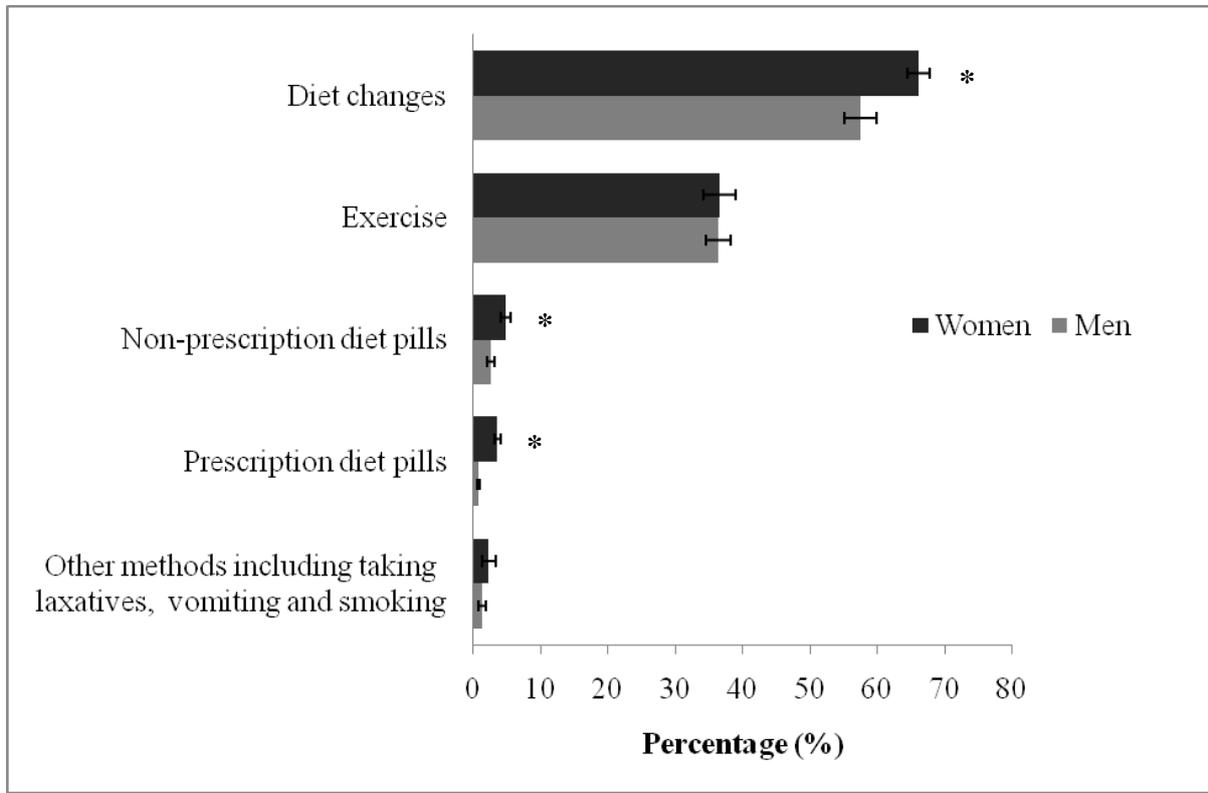


Figure 2: Methods used to control weight.



\* indicates p value <0.05 for differences between men and women

Table 1: Prevalence of obesity and subjects with both BMI 27.0 -29.9 kg/m<sup>2</sup> and risk factors

	Prevalence of subjects with BMI ≥30.0 kg/m <sup>2</sup> (obesity), % (SE)			Prevalence of subjects with BMI 27.0 -29.9 kg/m <sup>2</sup> and risk factors, % (SE)		
	All	Men	Women	All	Men	Women
N	5332	2630	2702	5332	2630	2702
Overall	34.3(1.2)	32.8(1.6)	35.8(1.1)	11.1(0.6)	13.1(1.0) †	9.2(0.7) †
Age group, year						
20 – 39	31.5(2.1)	28.5(2.0)†	34.7(2.6)†	3.7(0.7)	4.1(1.0)	3.2(0.6)
40 – 59	36.4(1.8)	34.7(2.5)	38.1(2.2)	12.8(0.9)	17.5(1.8)†	8.3(0.8)†
≥60	35.3 (1.1)	37.3 (2.0)	33.7 (1.8)	19.7(1.3)	21.2(1.5)	18.5(2.1)
Race/ethni city						
Non- Hispanic white	33.2(1.8)	33.1 (2.1)	33.3 (1.7)	12.4(0.8)	15.4(1.2)†	9.6(1.1)†
Non- Hispanic black	44.1 (2.2)	37.4 (2.8)†	49.5 (2.1)†	9.3(0.8)	7.5(1.0)†	10.9(0.9)†
Mexican American	39.7 (3.7)	36.0 (4.4)†	44.3 (3.2)†	5.8(0.4)	6.0(0.8)	5.6(0.9)
Others	27.6 (3.4)	24.4 (3.9)	30.9 (3.7)	8.5(1.6)	10.1(2.5)	6.9(1.6)

† indicates p value <0.05 for the prevalence between men and women

Table 2: Characteristics of candidates for anti-obesity drugs among participants

	Participants with BMI $\geq 30.0$ kg/m <sup>2</sup> (obesity)	Participants with BMI of 27.0-29.9 kg/m <sup>2</sup> and risk factors
N	1983	614
Age, year	47.8(0.5)	56.1(0.6)
Age group, %		
20 – 39 year	33.5 (1.8)	12.0(1.9)
40 – 59 year	42.0 (1.6)	45.7(2.9)
$\geq 60$ year	24.5 (1.2)	42.3(2.6)
BMI, kg/m <sup>2</sup>	35.7(0.1)	28.5(0.05)
Race/ethnicity, %		
Non Hispanic white	67.7 (5.0)	78.2(3.2)
Non Hispanic black	14.4 (3.0)	9.5(2.2)
Mexican American	9.4 (2.4)	4.2(0.8)
Other	8.5 (1.8)	8.1(1.7)
Risk Factors, %		
Diabetes	35.9 (1.3)	63.7 (2.2)
Hypertension	42.6(1.5)	68.3 (1.9)
Hypercholesterolemia	15.8 (1.7)	10.7 (0.9)
Any of the above	57.7 (1.1)	100 (0.0)

Data are expressed as mean or percent (SE).

Table 3: Anti-obesity drug treatment in obese and subjects with BMI 27.0 -29.9 kg/m<sup>2</sup> with risk factors

Anti-obesity drug treatment	All (n=2597)		Participants with BMI ≥30.0 kg/m <sup>2</sup> (obesity) (n=1983)		Participants with BMI of 27.0-29.9 kg/m <sup>2</sup> and risk factors (n=614)	
	cases	%(SE)	cases	%(SE)	cases	%(SE)
Sibutramine	0	0.0 (0.0)*	0	0.0 (0.0)*	0	0.0 (0.0)*
Orlistat	1	0.1 (0.1)*	1	0.1 (0.1)*	0	0.0 (0.0)*
Phentamine	9	0.5 (0.1)*	9	0.4 (0.1)*	1	0.3 (0.2)*
Total	10	0.6 (0.2)*	10	0.6 (0.2)*	1	0.3 (0.2)*

\*Estimates are unreliable due to coefficient of variation >0.3