OBJECTIVES: To document the recent dynamic changes in prevalence of obesity and medical comorbidities and costs for the U.S. general population. METHODS: This study analyzed data from the 2000 and 2004 Medical Expenditure Panel Survey (MEPS), a nationally representative panel data. Based on Body Mass Index (BMI), weight groups were defined as Underweight (UW, BMI < 18.5), Normal Weight (NW, BMI 18.5–24.9), Overweight (OW, BMI 25–29.9), Obese I (BMI 30–34.9), Obese II (BMI 35–39.9), and Obese III (BMI ≥ 40). Univariate analyses were conducted to examine changes in obesity prevalence, as well as the trend differentials in demographic and socioeconomic status. Trends in co-morbidities and medical costs were compared among different weight groups across years. All estimates are weighted to be nationally representative. RESULTS: The prevalence of obesity increased from 22.5% to 25.9% between year 2000 and 2004 (Obese I: 14.6% vs 16.4%, Obese II: 5.1% vs 6.1%, and Obese III: 2.8% vs 3.4%). Obesity increased more among African-Americans, individuals who had higher education, higher income, and public health insurance. For both years, obesity was consistently associated with the greatest risk of diabetes, high blood pressure, cardiovascular disease, asthma and joint pain (p < 0.001). In 2000 dollars, the change in total medical costs was from $3159 in 2000 to $3854 in 2004 for obese groups; $2324 to $3000 for NW; and $2345 to $3088 for OW, all at highly significant level of p < 0.001. Obesity related physician office-based costs, ER costs and RX costs were also increased as compared to other groups (p < 0.001). CONCLUSION: The prevalence of obesity has increased since 2000, resulting in an increase in obesity related comorbidities and medical costs. This study also showed that obesity may be associated with race, socioeconomic status, education, and health insurance.