

The contribution of obesity to prescription opioid use in the United States

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Abstract

The prevalence of obesity has grown rapidly over the past several decades and has been accompanied by an increase in the prevalence of chronic pain and prescription opioid use. Obesity, through its association with pain, may represent an important contributor to opioid use. This cross-sectional study investigated the relationship between obesity and prescription opioid use among adults aged 35 to 79 years using data from the National Health and Nutrition Examination Survey (NHANES, 2003-2016). Relative to normal weight, body mass indices in the overweight {odds ratio (OR), 1.11 (confidence interval [CI], 0.88-1.39)}, obese I (OR, 1.26 [CI, 1.01-1.57]), obese II (OR, 1.69 [CI, 1.34-2.12]), and obese III (OR, 2.33 [CI, 1.76-3.08]) categories were associated with elevated odds of prescription opioid use. The association between excess weight and opioid use was stronger for chronic opioid use than for use with a duration of less than 90 days (P -value, <0.001). We estimated that 14% (CI, 9%-19%) of prescription opioid use at the population level was attributable to obesity, suggesting there might have been 1.5 million fewer opioid users per year under the hypothetical scenario where obese individuals were instead nonobese (CI, 0.9-2.0 million users). Back pain, joint pain, and muscle/nerve pain accounted for the largest differences in self-reported reasons for prescription opioid use across obesity status. Although interpretation is limited by the cross-sectional nature of the associations, our findings suggest that the obesity epidemic may be partially responsible for the high prevalence of prescription opioid use in the United States.

Keywords: Obesity, Chronic pain, BMI, NHANES, Opioids

1. Introduction

The prevalence of obesity has grown rapidly over several decades, with the proportion of U.S. adults with obesity

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increasing from 15% in 1976-1980 to 40% in 2015-2016.²³ Obesity is associated with heightened risk of diabetes, cardiovascular disease, and cancer, and is responsible for an estimated 380,000 deaths annually.³² The increase in obesity has been accompanied by a rise in the prevalence of chronic pain. Between 1998 and 2014, the proportion of U.S. adults reporting pain increased from 21.4% to 34.9% among men and 30.4% to 41.5% among women.⁵⁴ In 2015, 25.3 million adults (11.2%) reported experiencing chronic daily pain.³⁴

A report from the Institute of Medicine identified obesity as one of 5 major contributors to chronic pain.²⁶ Obesity raises risks of numerous conditions associated with chronic pain, including osteoarthritis,³ low back pain,^{46,47} diabetes-associated neuropathy,³⁸ fibromyalgia,⁵⁰ and migraine.^{5,41} This increased risk may be explained by several factors, including biomechanical strain on joints and stimulation of a systemic inflammatory state.^{43,49} Recent estimates indicate that low back pain and osteoarthritis are among the leading causes of years lived with disability in the United States.³² Obesity may also be associated with lower pain tolerance because weight loss has been shown to improve pain sensitization.⁴⁸

Dramatic increases in prescription opioid use have also occurred in recent years.^{1,19} Previously limited primarily to settings of end-of-life care, postsurgical care, and acute pain, prescription opioids have been increasingly used for chronic pain, with use rates quadrupling between 1999 and 2010.¹² The trend towards use of prescription opioids in chronic pain management has also contributed to rising levels of opioid dependence and overdose deaths.¹³ Prescription opioid dependence affected 2

million people and contributed to over 15,000 U.S. overdose deaths in 2015.¹⁹

Explanations for the opioid crisis have focused primarily on the role of supply-side factors, including shifts in pain assessment and treatment norms,^{6,29} insurers reducing coverage for behavioral pain therapy, and pharmaceutical innovation and marketing.^{20,21,29,52} Although the role of supply-side factors is well established, the underlying causes of demand for opioids are less clear. Some prior research has attributed the opioid crisis to increasing economic and social dislocation or to deteriorating mental health.^{7,8,17} Another possibility that has received less attention is that obesity has increased demand for prescription opioids through its complex associations with disability and pain.¹⁰

This study investigates this latter possibility using recent data from a nationally representative sample of the U.S. adult population. In our primary analysis, we examine the association of obesity with prescription opioid use and estimate the percentage of prescription opioid use attributable to obesity at the population level. Because long-term opioid therapy and stronger opioid regimens are associated with increased risks of opioid dependence and overdose,^{4,14,45} we additionally investigate the association of obesity with duration and strength of opioid use. Finally, we examine individuals' self-reported reasons for opioid use to identify the major types of pain underlying the differences in prescription opioid use by obesity status.

2. Methods

2.1. Data

The National Health and Nutrition Examination Survey (NHANES) is a series of nationally representative cross-sectional samples of the noninstitutionalized U.S. population. The survey includes laboratory, physical examination, and questionnaire components.³⁵ Survey respondents provide detailed data on demographic characteristics, health behaviors, and prescription medications. Beginning in 1999, the NHANES has been implemented as a continuous survey released in 2-year cycles. The sampling methods are similar across survey waves, and the NHANES analytic guidelines recommend pooling multiple years of data to increase sample sizes for cross-sectional subgroup analyses.^{28,36}

For our primary analyses of the association of obesity with prescription opioid use, we pooled data from the 2003 to 2004, 2005 to 2006, 2007 to 2008, 2009 to 2010, 2011 to 2012, 2013 to 2014, and 2015 to 2016 waves of NHANES. These waves of data were the most recent for which information on prescription medications, including duration of use, was available. We used this sample throughout the study with the exception of the subanalysis of individuals' reported reasons for prescription opioid use for which the relevant questions were only available in 2013 to 2014 and 2015 to 2016. Across all analyses, the sample was restricted to adult participants aged 35 to 79 years with a body mass index (BMI) between 15 and 80 kg/m². Those who reported a recent cancer diagnosis, were pregnant, or were missing data on covariates were excluded from the analysis. The final analytic sample for the primary study endpoint included 25,424 individuals. The subanalysis of reasons for prescription opioid use included 7596 individuals. A flowchart of sample exclusion criteria and missing data in each study covariate is provided in Figure 1, supplemental digital content 1 (available at <http://links.lww.com/PAIN/A821>).

2.2. Assessment of body mass index

The key independent variable in our analysis, BMI (kg/m²), was calculated using height and weight measured at examination. A categorical measure of BMI was defined using the categories underweight (15 kg/m² \geq BMI < 20 kg/m²), normal weight (20 \geq BMI < 25), overweight (25 \geq BMI < 30), obese I (30 \geq BMI < 35), obese II (35 \geq BMI < 40), and obese III (40 \leq BMI \leq 80).

2.3. Covariates

Potential confounders were identified a priori to include socio-demographic and behavioral characteristics plausibly related to both BMI and prescription opioid use. These included education (less than high school, high school, some college, college or higher), insurance (yes, no), age (35-44, 45-54, 55-64, 65-79 years), sex (male, female), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, non-Hispanic other), and smoking status (never, former, current). We considered an individual a never smoker if he/she had smoked less than 100 cigarettes in their lifetime. Indicators of physical and mental health status were not included as potential confounders because they could potentially serve as important mediators of the association between BMI and opioid use.

2.4. Prescription opioid use

Interviewers asked participants, "In the past 30 days, have you used or taken medication for which a prescription is needed? Do not include prescription vitamins or minerals you may have already told me about." The medication name was recorded from the medication container (86.3%) or pharmacy receipt (1.1%) where available, or from the participant's verbal response (12.6%). Medications were coded using the Cerner Multum Lexicon Plus and classified using the Multum Lexicon Therapeutic Classification Scheme, a 3-level nested category system that assigns a therapeutic classification to each drug and each ingredient of the drug. Participants were also asked to report the length of time they had been taking each medication.

Participants reporting use of a narcotic analgesic (Multum Lexicon Classification: 57-central nervous system agents [level 1]; 58-analgesics [level 2]; 60-narcotic analgesics or 191-narcotic analgesic combinations [level 3]) were considered prescription opioid users. Opioids often used in treatment for opioid dependence or withdrawal (buprenorphine, naloxone) were excluded from our outcome variable.² In secondary analyses, prescription opioid use was further classified into categories of duration of use (<90 days, \geq 90 days), and 90 days of use or longer was considered chronic opioid use, consistent with prior analyses.^{12,39} We also classified prescription opioid use into 3 strength categories (weaker/equivalent/stronger than morphine) based on morphine equivalency criteria established by the Centers for Disease Control and Prevention (CDC) (see Table 1, supplemental digital content 1, which shows the classification of opioid prescriptions by morphine equivalency; available at <http://links.lww.com/PAIN/A821>).¹⁶

2.5. Reasons for prescription opioid use

In 2013 to 2014 and 2015 to 2016, the NHANES included data on the primary reason(s) for which an individual reported taking medications. For each prescription medication that an individual was taking, they self-reported up to 3 primary reasons for taking

the medication. Interviewers then classified each of the individual's self-reported reasons for use using *International Classification of Disease, 10th Revision, Clinical Modification (ICD-10-CM)* diagnosis codes. For purposes of this study, we adapted a previously developed typology³³ to categorize the *ICD-10-CM* codes into 8 major reasons for prescription opioid use: back pain, injury pain, joint pain, muscle/nerve pain, neck pain, and other (see Table 2, supplemental digital content 1, which shows the pain typology; available at <http://links.lww.com/PAIN/A821>).

2.6. Statistical analysis

We evaluated the association of BMI category with prescription opioid use using multivariable logistic regression, adjusting for age, sex, race/ethnicity, smoking status, insurance, and education. The normal weight category was specified as the reference group in this model. We also examined the association of BMI with the 3-level outcome for duration of prescription opioid use (no opioid use, < 90 days of use, ≥ 90 days of use) and prescription opioid strength (no opioid use, weaker than morphine, equivalent/stronger than morphine) using multinomial logistic regression. These 2 models were adjusted for the same set of covariates as used in the primary analysis. We then evaluated whether the slope of the association between BMI and prescription opioid use differed across outcome levels using a Wald test after refitting the models using continuous BMI.

We estimated the fraction of prescription opioid use that might have been averted under the hypothetical scenario in which the population with obesity had been nonobese using the population attributable fraction (PAF).^{30,44} We obtained the risk estimates for the PAF calculation from a multivariable logistic regression using a dichotomous obesity variable (nonobese, obese). Because our prescription opioid use outcome was rare (7.2%), our odds ratios approximate risk ratios.⁵³ Using the subpopulation option of the *svy* routine in Stata, we estimated the average annual size of the population using prescription opioids in the United States over the study period (2003-2016) and multiplied this total by the PAF to determine the average annual number of prescription opioid users whose use was attributable to obesity. In a sensitivity analysis, we estimated risk ratios from our odds ratios using the correction method proposed by Zhang and Yu⁵³ and repeated our PAF calculations using the corrected risk ratios.

Using the 2013 to 2016 subsample, we calculated the age-adjusted prevalence of prescription opioid use among obese and nonobese individuals. To investigate the underlying reasons for the differences in prescription opioid use by obesity, we then calculated the age-adjusted prevalence of reporting opioid use attributable to each category of pain reasons (back pain, injury pain, joint pain, muscle/nerve pain, neck pain, and other) among obese and nonobese individuals. For example, the prevalence of back pain-related opioid use among obese individuals was calculated by dividing the number of individuals reporting opioid use attributable to back pain by the total number of obese individuals in the sample. We then calculated the differences in prevalence between obese and nonobese individuals for each reason for use and evaluated the significance of these differences using Wald tests. To further examine the extent to which these reason-specific differences contributed to the overall difference in opioid use between obese and nonobese individuals, we divided the difference in probability for each reason by the overall difference in prescription opioid use for any reason between obese and nonobese individuals. Because respondents could report more than one prescription opioid and/or multiple reasons

for use per prescription, the total percent contributions to differences for all pain reasons exceeds 100%.

We used Stata 15 (StataCorp) for all analyses. All analyses were sample weighted using NHANES examination weights. We combined the 2-year sample weights for each survey cycle (NHANES 2003-2004, 2005-2006, 2007-2008, 2009-2010, 2011-2012, 2013-2014, and 2015-2016) according to recommendations provided in the NHANES analytic guidelines so that estimates were representative of the U.S. civilian noninstitutionalized population during an average year of the combined survey period.²⁸ We estimated variances using Taylor series linearization with the *SVY* routine and considered two-sided *P* values <0.05 statistically significant. The Stata package *punafoc* was used to generate PAFs.³⁷ Institutional review board approval was not required for this analyses of publicly available, deidentified data.

2.7. Role of funding source

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3. Results

The sample was 53.2 years old on average, 52.1% percent female, 70.8% non-Hispanic white, and 73.8% overweight or obese (Table 1). Prescription opioid use was reported among 7.2% of individuals. Furthermore, 5.3% of individuals reported using prescription opioids for ≥90 days, and 5.1% reported use of a prescription opioid equivalent to morphine or stronger.

3.1. Association of obesity with prescription opioid use

Increasing BMI was associated with a marked increase in the use of prescription opioids (see Table 3, Supplemental Digital Content 1, which shows the prevalence of primary and secondary opioid outcomes by BMI category; available at <http://links.lww.com/PAIN/A821>). Adjusting for covariates, obese I, obese II, and obese III individuals had elevated odds of prescription opioid use compared with normal weight individuals (odds ratio [OR] for obese I, 1.26 confidence interval [CI], 1.01-1.57; OR for obese II, 1.69 [CI, 1.34-2.12]; OR for obese III, 2.33 [CI, 1.76-3.08]) (Table 2).

The association between excess weight and prescription opioid use was stronger for chronic opioid use than for opioid use with a duration of less than 90 days (*P*-value for the Wald test comparing continuous BMI coefficients across duration levels, <0.001). Individuals with the most elevated BMIs were more likely to report chronic prescription opioid use. Obese I individuals had 1.36 (CI, 1.06-1.75) times the odds, obese II individuals had 1.89 (CI, 1.44-2.48) times the odds, and obese III individuals had 2.87 (CI, 2.12-3.88) times the odds of reporting chronic opioid use (Table 3). Figure 1 shows that the adjusted proportion of adults reporting chronic opioid use increased with increasing BMI from 3.9% among underweight adults (CI, 2.5%-5.4%) to 10.3% among obese III individuals (CI, 8.4%-12.1%). Comparatively, the proportion of less than 90-day opioid use remained fairly constant across BMI category, from 2.3% among those with an underweight BMI (CI, 0.9%-3.7%) to 2.1% among those with an obese III BMI (CI, 1.4%-2.9%).

The association between BMI and prescription opioid use was consistently observed across categories of opioid strength (*P*-value for the Wald test comparing continuous BMI coefficients across

Table 1
Sample characteristics, NHANES 2003 to 2016 (n = 25,424).

	n	U.S. population (million)	%*
Age, y			
35-44	6364	41.5	27.7
45-54	6384	44.1	29.4
55-64	6095	34.5	23.0
65-79	6581	29.9	19.9
Sex			
Female	13,000	78.0	52.1
Male	12,424	71.9	47.9
Race/ethnicity			
Non-Hispanic white	11,011	106.1	70.8
Non-Hispanic black	5645	16.5	11.0
Hispanic	6482	17.4	11.6
Non-Hispanic other	2286	9.9	6.6
Education			
Less than high school	7063	25.8	17.2
High school or equivalent	5803	34.9	23.3
Some college	6931	45.4	30.3
College or higher	5627	43.8	29.2
Insurance status			
Uninsured	4819	22.2	14.8
Insured	20,605	127.7	85.2
Smoking status			
Never	12,968	76.4	50.9
Former	6989	42.3	28.2
Current	5467	31.3	20.8
BMI, kg/m²			
Underweight (15-19.9)	837	5.4	3.6
Normal (20-24.9)	5517	34.0	22.7
Overweight (25-29.9)	8713	51.7	34.5
Obese I (30-34.9)	5778	33.1	22.1
Obese II (35-39.9)	2635	14.9	10.0
Obese III (40-80)	1944	10.8	7.2
Prescription opioid use			
No opioid use	23,562	139.1	92.8
Opioid use	1862	10.8	7.2
Duration of opioid use			
No opioid use	23,562	139.1	92.8
< 90 d of use	486	2.9	1.9
≥ 90 d of use	1376	8.0	5.3
Strength of opioid use†			
No opioid use	23,562	139.1	92.8
Weaker than morphine	584	3.2	2.1
Equivalent to morphine	900	5.1	3.4
Stronger than morphine	378	2.5	1.7

* Sample weighted based on NHANES analytic guidelines.

† Opioids were classified into 3 strength categories (weaker/equivalent/stronger than morphine) based on morphine equivalency criteria established by the Centers for Disease Control and Prevention (Frenk SM, Porter KS, Paulozzi LJ. Prescription opioid analgesic use among adults: United States, 1999-2012. NCHS Data Brief 2015;189:1-8).

BMI, body mass index; NHANES, National Health and Nutrition Examination Survey.

strength levels, 0.69). Individuals in the obese II category (OR, 1.59 [CI, 1.09-2.31]) and obese III category (OR, 2.10 [CI, 1.39-3.17]) were more likely to have a prescription opioid that was weaker than morphine compared with those who were in the normal BMI category (see Table 4, supplemental digital content 1, which shows opioid strength as a function of BMI using multinomial logistic regression; available at <http://links.lww.com/PAIN/A821>). The relation of excess BMI to increase in opioid use was slightly more pronounced for morphine equivalent/stronger opioids: obese I individuals were 1.31 (CI, 0.99-1.74) times as likely, obese II were

Table 2
Multivariable logistic regression: association between BMI and prescription opioid use among adults aged 35 to 79 years, NHANES 2003 to 2016 (n = 25,424).

	OR*	95% CI	P
BMI, kg/m²			
Underweight (15-19.9)	1.06	0.75-1.48	0.75
Normal (20-24.9)	1.00 (Ref)	—	—
Overweight (25-29.9)	1.11	0.88-1.39	0.38
Obese I (30-34.9)	1.26	1.01-1.57	0.04
Obese II (35-39.9)	1.69	1.34-2.12	<0.001
Obese III (40-80)	2.33	1.76-3.08	<0.001
Age, y			
35-44	1.00 (Ref)	—	—
45-54	1.22	1.00-1.48	0.045
55-64	1.47	1.22-1.76	<0.001
65-79	1.32	1.08-1.63	0.008
Sex			
Female	1.00 (Ref)	—	—
Male	0.76	0.68-0.86	<0.001
Race/ethnicity			
Non-Hispanic white	1.00 (Ref)	—	—
Non-Hispanic black	0.75	0.63-0.89	0.001
Hispanic	0.66	0.54-0.81	<0.001
Non-Hispanic other	0.86	0.65-1.15	0.31
Education			
Less than high school	1.00 (Ref)	—	—
High school or equivalent	0.86	0.71-1.03	0.10
Some college	0.84	0.72-0.97	0.02
College or higher	0.42	0.33-0.53	<0.001
Insurance status			
Uninsured	1.00 (Ref)	—	—
Insured	1.83	1.46-2.28	<0.001
Smoking status			
Never	1.00 (Ref)	—	—
Former	1.49	1.27-1.75	<0.001
Current	2.56	2.20-2.99	<0.001
Survey year			
2003	1.00 (Ref)	—	—
2005	0.93	0.68-1.27	0.65
2007	1.04	0.75-1.43	0.83
2009	0.98	0.75-1.27	0.87
2011	1.13	0.84-1.53	0.42
2013	1.15	0.82-1.59	0.42
2015	0.97	0.74-1.27	0.81

* Sample weighted based on NHANES analytic guidelines.

BMI, body mass index; CI, confidence interval; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio.

1.73 (CI, 1.32-2.27) times as likely, and obese III were 2.44 (CI, 1.76-3.38) times as likely to use strong opioids compared with normal BMI individuals. Figure 2, Supplemental Digital Content 1, shows how the adjusted proportions of weaker than morphine opioid use and equivalent/stronger than morphine both increase with increasing BMI (available at <http://links.lww.com/PAIN/A821>).

3.2. Prescription opioid use attributable to obesity at the population level

Overall, obese individuals had 1.45 (CI, 1.27-1.66) times the odds of prescription opioid use compared with nonobese individuals (see Table 5, Supplemental Digital Content 1, which shows the underlying regression model for the PAF

Table 3
Multinomial logistic regression: association between BMI and prescription opioid duration among adults aged 35 to 79 years, NHANES 2003 to 2016 (n = 25,424).

	< 90 d of opioid use			≥ 90 d of opioid use		
	RRR*	95% CI	P†	RRR*	95% CI	P†
BMI, kg/m ²						
Underweight (15-19.9)	1.21	0.64-2.28	0.55	0.99	0.66-1.50	0.98
Normal (20-24.9)	1.00 (Ref)	—	—	1.00 (Ref)	—	—
Overweight (25-29.9)	0.92	0.60-1.41	0.69	1.20	0.94-1.54	0.15
Obese I (30-34.9)	1.04	0.72-1.48	0.85	1.36	1.06-1.75	0.02
Obese II (35-39.9)	1.28	0.83-1.96	0.27	1.89	1.44-2.48	<0.001
Obese III (40-80)	1.24	0.77-1.98	0.38	2.87	2.12-3.88	<0.001

* Model sample weighted based on NHANES analytic guidelines and adjusted for age (35-44, 45-54, 55-64, 65-79 years), sex (male, female), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, non-Hispanic other), education (less than high school, high school or equivalent, high school, some college, college or higher), insurance status (uninsured, insured), smoking status (never, former, current), and survey year (2003, 2005, 2007, 2009, 2011, 2013, 2015). No opioid use was used as the base outcome for the multinomial logistic regression.

†The association between continuous BMI and opioid use was stronger for chronic opioid use than for opioid use with a duration of less than 90 d (P-value for the Wald test comparing the BMI coefficients across duration levels, <0.001).

BMI, body mass index; CI, confidence interval; NHANES, National Health and Nutrition Examination Survey; RRR, relative risk ratio.

calculations; available at <http://links.lww.com/PAIN/A821>). At the population level, our analysis indicated that the fraction of prescription opioid use attributable to obesity was 14% (CI, 9%-19%). Extrapolating estimates from our sample to the U.S. population, 10.8 million adults aged 35 to 79 years were prescription opioid users, on average for each year of the study period, suggesting there might have been 1.5 million fewer opioid users under the hypothetical scenario where obese individuals were instead nonobese (CI, 0.9-2.0 million users). The sensitivity analysis using corrected risk ratios in PAF calculations yielded comparable estimates (PAF, 14%).

3.3. Self-reported reasons for prescription opioid use by obesity

Figure 2 shows the age-adjusted prevalence of prescription opioid use associated with specific reasons for obese and nonobese individuals. Overall, 9.3% (CI, 7.7%-11.0%) of obese individuals and 5.9% (CI, 4.6%-7.2%) of nonobese individuals in our sample reported prescription opioid use for any reason, a difference of 3.4% (CI, 2.0%-4.9%). Differences in the prevalence of prescription opioid use by obesity status were most pronounced for back pain (prevalence difference of 1.8% [CI, 0.8%-2.8%]; ie, 4.3% of obese and 2.5% of nonobese individuals reported prescription opioid use and attributed the reason for use to back pain), joint pain (prevalence difference of 1.3% [CI, 0.3%-2.3%]), and muscle/nerve pain (prevalence difference of 1.2% [CI, 0.4%-2.0%]) (Table 6, Supplemental Digital Content 1; available at <http://links.lww.com/PAIN/A821>). The prevalence of opioid use associated with other pain and injury was also higher in obese as compared to nonobese individuals; however, the differences were not statistically significant for these reasons for use. In contrast to the other reasons, the prevalence of opioid use associated with neck pain was higher in nonobese as compared to obese individuals; however, the difference was not statistically significant.

4. Discussion

This study of obesity and opioid prescription patterns had 4 principal findings. First, we found a significant association of obesity with prescription opioid use, with the strength of the association increasing in magnitude across increasing BMI categories. Second, we found that the associations were

especially pronounced when prescription opioid use was differentiated into long-term vs shorter-term use, indicating that obesity may represent an important factor driving long-term opioid therapy. Third, we estimated that 14% (CI, 9%-19%) of opioid prescription use may be attributable to obesity, equivalent to 1.5 million (CI, 0.9-2.0 million) individuals in the population using prescription opioids as a result of obesity, on average, for each year of the study period. Fourth, we found that several types of pain were especially important in explaining differential prescribing practices by obesity status, with the most prominent contributions coming from back pain, joint pain, and muscle/nerve pain.

Individuals with obesity were significantly more likely to receive prescription opioids and use opioids for longer periods, underscoring the significant burden of pain in this population. Long-duration use of prescription opioids is a major risk factor for opioid use disorder and opioid-related mortality.⁴⁵ In one study, individuals with a new episode of chronic noncancer pain who used low-dose prescription opioids for more than 90 days had nearly 15 times the odds of developing an opioid use disorder relative to those who were not prescribed an opioid.¹⁴

Recent CDC guidelines recommend several other drug classes for first-line treatment of chronic pain and encourage nonpharmacologic approaches, including cognitive behavioral therapy (CBT).¹² Suggested first-line pharmacologic treatments include acetaminophen and NSAIDs for osteoarthritis and back pain and gabapentinoids for neuropathic pain. Reductions in pain with acetaminophen, however, are limited, and NSAIDs are contraindicated for several common obesity-related conditions, including cardiovascular disease, as well as other common medical issues such as renal insufficiency and gastrointestinal ulceration.¹² Gabapentinoids, which include gabapentin and pregabalin, pose their own unique risks,¹⁸ especially in combination with certain other classes of drugs commonly prescribed among individuals with obesity. With respect to nonpharmacologic approaches, CBT and other approaches have shown promise but are generally underused or used in combination with, rather than as a substitute for, pharmacotherapy.

The significant challenges inherent in treating chronic pain in the setting of obesity, particularly given its contribution to various chronic pain conditions, highlight the critical importance of primary and secondary obesity prevention. Evidence from clinical trials and observational studies indicate that weight loss

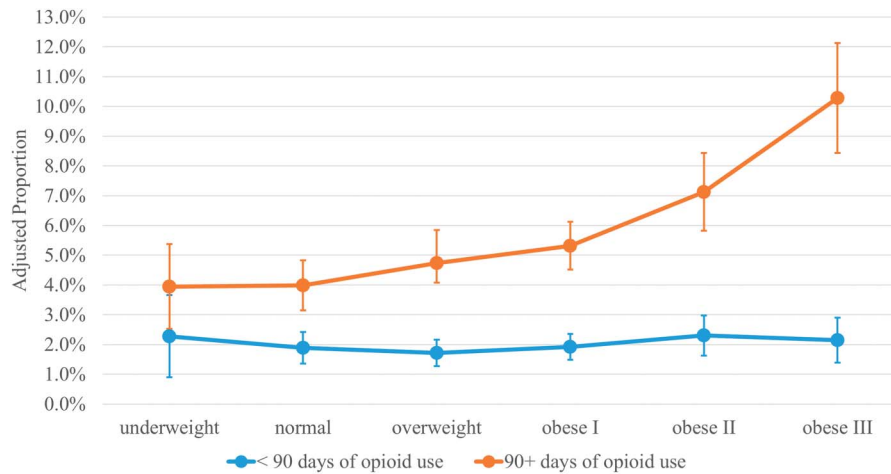


Figure 1. The proportion of reporting < 90 days of opioid use and ≥ 90 days of opioid use (chronic use) by BMI category in the sample of US adults ages 35–79 years. Estimates were generated using the margins command in Stata following a multinomial logistic regression of duration of opioid use (see Table 3). Estimates were sample weighted according to NHANES analytic guidelines and adjusted for age (35–44 years, 45–54 years, 55–64 years, 65–79 years), sex (male, female), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, non-Hispanic other), education (less than high school, high school or equivalent, high school, some college, college or higher), insurance status (uninsured, insured), smoking status (never, former, current) and survey year (2003, 2005, 2007, 2009, 2011, 2013, 2015). Error bars show the 95% confidence intervals for the estimates.

can lead to substantial reductions in osteoarthritic pain.^{9,15} Reductions in chronic pain have also been identified in cohorts with surgically induced weight loss.^{25,31,40,48} In one study of patients with severe obesity and knee osteoarthritis who underwent gastric bypass surgery, biomarker measures showed substantial improvement in cartilage synthesis and declines in systematic inflammation, cartilage degradation, and self-reported knee pain.^{42,48}

The limitations of our study merit acknowledgement. First, due to the cross-sectional nature of the study, it was not possible to determine the directionality of the associations or whether the associations between obesity and prescription opioid use were causal in nature. Conditions associated with opioid use may lead to weight gain or weight loss, possibly leading to confounding by illness.^{22,27} For example, serum vitamin D levels, which have an inverse association with opioid use, obesity, inflammation, and

pain,^{11,24,51} may serve as a confounder of associations we investigate in this study. In the light of the potential for confounding, future research should confirm the findings of this study using incident study designs in which it is possible to establish the temporal precedence of weight status with respect to prescription opioid use. Second, our PAF calculations are based on an assumption of causality between exposure (BMI) and outcome (prescription opioid use) despite the aforementioned limitation of using observational data. Thus, our population-level estimates of the opioid use attributable to obesity are provisional and should be interpreted with caution. Third, the NHANES did not assess prescription opioid dosage, and we were therefore limited to evaluating broad categories of strength based on morphine equivalency criteria established by the CDC. Fourth, although the ability to directly link prescription opioid use to underlying reasons for use represented a strength of

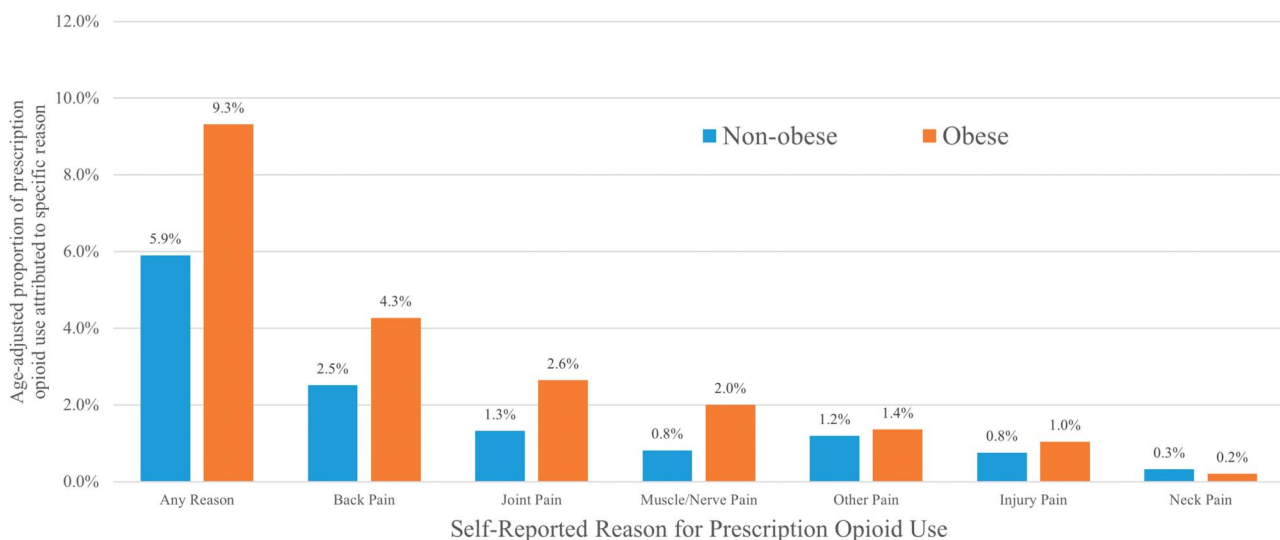


Figure 2. The age-adjusted prevalence of prescription opioid use for any reason and for each category of pain reasons specifically, stratified by obese vs non-obese. See Table 6, Supplemental Digital Content 1 for complete estimates (<http://links.lww.com/PAIN/A821>). *Sample interpretation:* 4.3% of the sample with obesity and 2.5% of the sample without obesity reported using prescription opioids and attributed that use to back pain.

the analysis, the reasons were based on respondent self-report, potentially reducing their accuracy and clinical specificity. Nonetheless, these were the reasons for which the individuals thought they were using those opioids.

In conclusion, this cross-sectional study suggests that individuals with obesity receive prescription opioids at significantly higher rates than nonobese individuals. Given the link with receipt of prescription opioids to progression to opioid dependence and overdose, this higher prevalence of opioid prescription among obese individuals indicates that they are likely at an increased risk of such adverse outcomes. At the population level, the obesity epidemic, through its association with chronic pain, may be partially responsible for the high prevalence of prescription opioid use in the United States and its population health consequences. Interventions and policies aimed at reducing prescription opioid use may therefore benefit from increased consideration of and integration with obesity prevention and treatment efforts aimed at these prevalent comorbidities that contribute to chronic pain.

Conflict of interest statement

A. Stokes and S. Lee have received research funding from Ethicon, Inc. (a subsidiary of Johnson & Johnson, Inc.). C. Hsiao, J.R. Waggoner, and R.F. Scamuffa are employees of Ethicon, Inc. S.S. Johnston and E.M. Ammann are employees of Epidemiology, Medical Devices, Johnson & Johnson, Inc. The remaining authors have no conflicts of interest to declare.

Acknowledgements

Author contributions: A. Stokes designed the study, interpreted the data, and wrote the manuscript. K.M. Berry and J.M. Collins performed the analyses and contributed to interpreting the data and writing the manuscript. S.S. Johnston, C. Hsiao, J.R. Waggoner, E.M. Ammann, R.F. Scamuffa, D.J. Lundberg, and S. Lee contributed to the study design and interpretation of the data, and reviewed and edited the manuscript. D.H. Solomon, D.T. Felson, T. Neogi, and J.E. Manson reviewed the manuscript and contributed to the introduction and discussion. A. Stokes and K.M. Berry had full access to all the data in the study and take full responsibility for the integrity of the data and the accuracy of the data analysis.

Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at <http://links.lww.com/PAIN/A821>.

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