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Prevalence of obesity for opioid- and stimulant-dependent participants in substance use treatment clinical trials

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ABSTRACT

Aims: To estimate obesity prevalence among drug-dependent individuals and to compare prevalence across different types of drug dependence.

Methods: 1596 opioid- and/or stimulant-dependent participants were extracted from six clinical trials within the National Drug Abuse Treatment Clinical Trials Network of the National Institute on Drug Abuse (NIDA CTN) to estimate obesity prevalence among drug-dependent users. Age-, sex-, and race-matched National Health and Nutrition Examination Survey (NHANES) samples were used as a general population reference. Standardized prevalence ratios (SPRs) were calculated to compare the CTN sample to NHANES as well as to compare within the CTN sample. Logistic regression estimated associations between the type of drug dependence and obesity.

Results: The standardized obesity prevalence among the drug-dependent CTN trial participants was 67% of expected for age-, sex- and race-matched NIHANES participants (SPR = 0.67, 95% CI: 0.60–0.74). Obesity was least prevalent among opioid-dependent-only participants (SPR = 0.36, 95% CI: 0.27–0.46 compared to the NHANES, and SPR = 0.33, 95% CI: 0.23–0.46 compared to the stimulant-dependent-only participants). Compared to stimulant-dependent-only users ($p < 0.0001$), the odds of obesity were 67% lower among opioid-dependent-only users (adjusted odds ratio [AOR] = 0.33, 95% CI: 0.23–0.46) and 33% lower among opioid and stimulant-co-dependent users (AOR = 0.67, 95%CI: 0.49–0.90) after controlling for age, sex, race, education and employment pattern.

Conclusions: The prevalence of obesity among drug-dependent clinical trial participants was lower than the general population, and lowest among opioid-dependent-only users, suggesting an inverse relationship between obesity prevalence and drug dependence, most notable among opioid-dependent-only users.

1. Introduction

Drug abuse and obesity are two significant public health threats that affect millions of Americans. Results from the 2014 National Survey on Drug Use and Health suggest that among people aged 12 or older, 4.3 million were current non-medical users of opioid pain medication, 0.4 million were current heroin users, 1.5 million were current cocaine users, and 1.6 million were non-medical users of stimulants (Center for Behavioral Health Statistics and Quality, 2015). More Americans aged 25–64 now die from drug overdose than from motor vehicle accidents (National Center for Injury Prevention and Control, 2014). Drug (mainly prescription opioid and heroin) overdose deaths are now an epidemic in the United States (Paulozzi et al., 2011). The age-adjusted drug overdose death rate involving prescription pain medication quadrupled, from 1.5 per 100,000 population in 2000 to 5.9 per 100,000 population in 2014; additionally, age-adjusted overdose rate involving heroin tripled during 2010–2014, from 1.0 per 100,000 population in 2010 to 3.4 per 100,000 population in 2014 and continues to increase in 2015 (Rudd et al., 2016a, 2016b). Obesity, defined as body mass index (BMI) $\geq 30\,kg/m^2$, is a major chronic health problem affecting more than one third of American adults (Flegal et al., 2012; Ogden et al., 2015). The sharp increase in the prevalence of obesity over the past two decades poses a public health challenge in the U.S. as it is associated with poor psychosocial health, poor quality of life and leading causes of deaths such as diabetes, cardiovascular disease, and certain cancers (Centers for Disease Control and Prevention, 2016).

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Obesity, thought to be mainly caused by excessive caloric intake that exceeds energy expenditure, has been associated with uncontrollable overeating behaviors (Vanbuskirk and Potenza, 2010). Substance use disorders (SUD) and certain eating disorders (ED) share similar impulsivity traits and disruptive brain functions such as blunted rewarding sensitivity and impaired self-control executive functions (Kenny, 2011; Volkow et al., 2013a, 2013b, 2012, 2008). There is a higher prevalence of "food addiction" in obese than in non-obese individuals (Gearhardt et al., 2014). Individuals with binge eating disorder (BED) are about 5 times more likely to have a BMI > 40 kg/m^2 than individuals without BED (Hudson et al., 2007). In addition, co-occurrence of SUD and ED, especially bulimia nervosa (BN) and BED among women and youth are frequently reported (Cohen et al., 2010; Denoth et al., 2011; Dunn et al., 2002; Gregorowski et al., 2013; Holderness et al., 1994; Jonas and Gold, 1986; Katzman et al., 1991; Root et al., 2010). Therefore, examining relationships between obesity and SUD may indicate underlying associations between ED and SUD.

Several epidemiological studies examined relationships between BMI and SUD, although results somewhat varied. A report from the National Co-morbidity Survey Replication (NCS-R) (Simon et al., 2006) suggests that obese people had about a 20% reduced odds of lifetime SUD (including abuse and dependence on alcohol or drugs) than normal weight people. Similarly, a study of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (Pickering et al., 2011) reported that obese people had 50% reduced odds of developing drug abuse and dependence; and those with drug abuse or dependence, compared to those without abuse and dependence, had 50% reduced odds of moving from normal weight to overweight or obese, and from overweight to obese. One limitation of these reports is that abused drugs were not characterized such that it is unclear whether different drugs have differing impact in BMI. Another NESARC study (Barry and Petry, 2009) explored the prevalence of various drug (marijuana, cocaine and opioid) use disorders among different BMI categories (normal weight, overweight, and obese), and found no significant association between these drug use disorders and BMI, but the analysis did not separate drug dependence from abuse. Another limitation with NESARC and NCS-R is that results may not be generalizable to the SUD population as the target population of these surveys was the general population.

The aims of this study were 1) to estimate the prevalence of obesity for opioid- and stimulant-dependent users from clinical trials and compare to the U.S. general population sample; and 2) to compare the prevalence of obesity across groups with different types of drug dependence.

2. Methods

2.1. Study populations

Drug-dependent users were participants in one of the six drug abuse treatment clinical trials within the National Drug Abuse Treatment Clinical Trials Network of the National Institute on Drug Abuse (NIDA CTN), where measurement data on height and weight at study entry were available (https://datashare.nida.nih.gov/data). The CTN protocols included: CTN-0001, CTN-0002, CTN-0003, CTN-0037, CTN-0046, and CTN-0048. To focus on specific SUD, this analysis only included past-year opioid- and/or stimulant-dependent participants, diagnosed at the baseline visit by the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV). Table 1 summarizes the sample sizes by the types of drug dependence.

The National Health and Nutrition Examination Survey (NHANES) was used to represent the U.S. general population. NHANES was conducted in two-year cycles. To match the survey years and participants' age range with the CTN trials, four cycles were selected: 2001–2002, 2003–2004, 2005–2006, and 2009–2010. As the NHANES intentionally oversampled certain group of Hispanic population (i.e., Mexican Americans) before 2007 and then oversampled the entire Hispanic population since 2007 (Zipf et al., 2013), to simplify, the current analysis included only non-Hispanic Whites and non-Hispanic Blacks/African Americans (AA) aged 20–71 years within the respective NHANES cycles that matched the CTN trials (referred to as "cohort-matched").

Four cohort-matched samples between the NHANES and CTN samples were compared: 1) overall CTN sample and 2001–2006 and 2009–2010 NHANES samples; 2) stimulant-dependent-only CTN sample and 2009–2010 NHANES sample; 3) opioid-dependent-only CTN sample and 2001–2006 NHANES sample; and 4) opioid-stimulant-co-dependent CTN sample and 2001–2006, 2009–2010 NHANES samples. Additionally, comparisons were performed within the CTN sample.

2.2. Statistical analysis

Standardized prevalence ratio (SPR) was used to measure the relative prevalence of obesity for the CTN sample using the NHANES participants as the references. SPR is a ratio of the observed cases in the sample of interest to the expected cases, had the prevalence in the sample of interest been the same as in the reference sample (Last, 1983). Two age subgroups (20–40 years, and > 40 years), two sex subgroups (female and male), and two race subgroups (Black/AA and White) were used for standardizing the prevalence ratios. An SPR > 1 suggests higher age-, sex- and race-standardized prevalence in the sample of interest compared to the reference population. Confidence intervals (CIs) of the SPRs were computed using Byar's approximation (Breslow and Day, 1987; Liddell, 1984; Sahai and Khurshid, 1993). This same methodology was applied to calculating SPRs for obesity within the CTN subgroups with the stimulant-dependent-only subgroup as the reference. To assess the association between the odds of obesity and the type of drug dependence, a logistic model was applied to the CTN sample. In addition to drug dependence type, age, sex, race, education years and employment patterns in the past three years were included as covariates. Generalized linear models (GLM) were used to compare BMI values between drug dependence and non-dependence, adjusting for age, sex and race.

Unlike the NHANES, clinical trials may exclude, as part of the exclusion criteria, individuals perceived to be unsafe to participate. In one CTN trial (CTN-0037) with exercise as an intervention, individuals with BMI > 40 had to be cleared by a medical personnel for the trial enrollment. A review of the BMI values of the CTN and NHANES samples suggests that the lowest BMI values of these two samples were similar (15.1 kg/m^2 and 14.7 kg/m^2 respectively), but not the highest (56.2 kg/m^2 and 130.0 kg/m^2 respectively). To avoid a potential overestimation of the differences between the CTN and NHANES samples, a sensitivity analysis was conducted to only compare the CTN and NHANES samples by removing the NHANES participants with a BMI greater than 60.0 kg/m^2.

3. Results

3.1. Participant demographic and characteristics

A total of 1596 opioid-dependent-only, stimulant-dependent-only, or opioid-stimulant-co-dependent participants from six NIDA CTN trials and 10,966 participants from the referent NHANES were identified. Age, sex and race distributions of the CTN and NHANES samples differed (Table 2), indicating that the standardization of demographics across these two samples prior to comparing the obesity prevalence was necessary. The overall crude mean BMI of the CTN sample was 26.9 kg/m^2, lower than the NHANES sample (29.0 kg/m^2). All 3 CTN subgroups had lower crude mean BMI than the cohort-matched NHANES participants, but the opioid-dependent-only subgroup had the lowest crude mean BMI (24.9 kg/m^2, Table 2) and showed the largest difference