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Impacts of Occupation and Urbanicity on Prescription Pain Reliever Abuse

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2014

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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Abstract

Impacts of Occupation and Urbanicity on Prescription Opioid Abuse
By Aaron Milloy

Introduction: In 2017, rural counties had higher age-adjusted rates of natural and semisynthetic (prescription) opioid overdose deaths (4.9 per 100,000) compared to urban counties (4.3 per 100,000). A Centers for Disease Control report suggested that one potential explanation for why prescription opioid rates are higher in rural counties is due to having higher rates of chronic pain, which has also been found to be associated with physical activity in the workplace. People working in physically strenuous jobs also have the highest rates of workplace injuries. This combination may cause individuals with more physically strenuous jobs to be more likely to be prescribed opioids.

Methods: This secondary analysis uses publicly available data acquired through the National Survey on Drug Use and Health in 2014. In addition to examining descriptive statistics of the sample population, we estimated adjusted prevalence ratios between past-year prescription pain reliever misuse and abuse/dependence, using logistic regression models with conditional margins.

Results: Adjusting for demographic and other covariates, neither exposure of interest, urbanicity and occupational injury risk, were found to have statistically significant association with past-year prescription pain reliever misuse or abuse/dependence. Other covariates were found to have statistically significant associations, including gender, education, marital status, insurance coverage, overall health, and past-year mental illnesses, which increased in magnitude as severity of illness increased. In an adjusted model examining past-year pain reliever abuse/dependence, compared to those with no mental illness, the prevalence ratio was 1.88 (95% CI: 1.59 – 2.22) for those with mild mental illness in the past year, 2.36 (95% CI: 1.91 – 2.92) for moderate mental illness, and 2.79 (95% CI: 2.23 – 3.47) for those with serious mental illness in the past year.

Discussion: Neither urbanicity nor occupational injury risk was found to have an association with prescription pain reliever misuse or abuse/dependence. Though mental illness was associated with pain reliever misuse and abuse/dependence, we are unable to infer a causal relationship. There were limitations in this study, including concerns that those misusing or being abusive/dependent on pain relievers may no longer be employed full-time.

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Chapter 1:
Introduction & Expanded Literature Review

Introduction

According to the CDC, there has been a rise in illicit drug abuse from 1999 to 2017. Neither urban nor rural areas have been immune to this epidemic. In 2017 the age-adjusted rate of drug overdose deaths was found to be 22.0 per 100,000 individuals in urban counties and 20.0 per 100,000 individuals in rural counties. In rural counties, this was an increase of 16.0 individuals per 100,000 since 1999, when the rate was 4.0 (1). Prescription opioids, which in 2017 accounted for 24.2% of all fatal drug overdoses, play a significant role in this epidemic and may impact rural counties more significantly than urban counties (2). The data shows that, in 2017, rural counties (4.9 per 100,000) had higher age-adjusted rates of natural & semisynthetic (prescription) opioid overdose deaths than urban counties (4.3 per 100,000) (1). Further research shows that 14 out of the 15 counties with the highest opioid prescription rates in 2017 were nonmetropolitan or rural (2).

In the CDC's January 2019 Morbidity & Mortality Report, researchers suggested that one potential explanation for why prescription opioid rates are higher in rural counties is due to having higher rates of chronic pain (2). In addition to being associated with age, chronic pain has also been found to be associated with the amount of physical activity in the workplace (3). Heuch et al. (2017) found that even after adjusting for age, men whose work involved "walking and heavy lifting" and "particularly strenuous physical work" were found to have 1.28 and 1.36 times the risk of low back pain compared to men with sedentary jobs (3). Many of the more physically strenuous jobs also have the highest rates of fatal work injuries, according to the Bureau of Labor Statistics' National Census of Fatal Occupational Injuries in 2017 (4). The combination of higher rates of chronic pain and higher rates of workplace injuries may cause individuals with more physically strenuous and dangerous jobs to be more likely to be prescribed opioids. As these more physically strenuous and dangerous jobs are more likely to be held by individuals living in rural counties, an association between job types and prescription opioid abuse may account for some of the differences we see in abuse rates between rural and urban counties (5).

There is a need to better understand the underlying factors related to why rural communities have been more significantly impacted by the prescription opioid epidemic than urban counties in the United States. The purpose of this thesis is to analyze whether underlying differences in the job types held by rural and urban individuals are independently linked to prescription opioid abuse, and whether job type confounds the observed association between county urbanicity and abuse rate.

Literature Review

Introduction

There are numerous underlying factors that help describe the characteristics, risks, and potential causes of the opioid epidemic that has occurred across the United States. While the CDC has already undertaken several steps to reverse the epidemic of opioid-related drug overdoses, especially when it comes to prescribing practices for chronic pain (6), it is important to better understand all underlying risk factors and how they may differ across communities and parts of the country.

The prescription opioid problem can be quantified in numerous ways. Much of the research, including work done by the CDC, describes the impact by accounting for the number of overdose deaths that have occurred. However other research describes the impact in other ways, including self-reported misuse, abuse, use disorder, and dependence, over various time frames.

Data including hospital admission, discharge, and opioid prescription rates have also been reviewed and included in researching the epidemic. While hospital-acquired data may be more accurate and reliable, it should be noted that studies have found that self-report data on drug use is valid and reliable (7). It is important to specify how each study described opioid use/abuse because it is possible that many of the potential risk factors may not be associated with the variables for use or abuse in the same way, or at the same magnitude.

The risk factors identified as being potentially associated with prescription opioid use/abuse include the two primary exposures being reviewed in this paper, urbanicity and occupation type, as well as demographic factors and other characteristics including age, gender, race, education, marital status, income, insurance, military service history, physical health, mental health, substance abuse, prescription practices, and pharmacy locations.

Rise in Prescription Opioid Abuse

The opioid epidemic shouldn't be described as a single problem, but as one involving several waves. The opioid drug class includes natural and semi-synthetic opioids, which are typically referred to as prescription opioids, but also heroin and synthetic opioids such as fentanyl. The CDC has described the opioid epidemic as occurring in 3 distinct waves, which they've displayed in a timeline shown in Figure 3WAVES below (8). The first wave was an increase in prescription opioid overdose deaths in the 1990s (8). The rapid acceleration of prescription opioid rates can partly be linked to the introduction of OxyContin in 1995 (9). Prior to this introduction, many physicians were reluctant to prescribe opioids for chronic conditions due to concerns about addiction. However, in 1995 Purdue Pharma funded more than 20,000 educational programs designed to encourage the long-term use of prescription opioids for chronic non-cancer pain (9). Many of the strategies the CDC has used to combat the epidemic have included re-education efforts and partnerships with healthcare providers and health systems to raise awareness about prescription opioid misuse and overdose (8). There is some evidence that these campaigns have been successful. The CDC's 2019 Surveillance Report of Drug-Related Risks and Outcomes notes that between 2006-2018, the annual prescribing rate decreased from 72.4 prescriptions per 100 persons to 51.4 prescriptions. Much of this decline occurred from 2014-2018. The report also notes an even larger decline in the prescription rate for high-dosage opioids, which are defined as having at least 90 morphine milligram equivalents (MME). The prescription rate per 100 persons decreased from 11.5 to 3.9 (10). The CDC has found that prescriptions that are at least 90 MME are found to have an increased risk of overdose and death. Though prescription rates, including high-dose rates, have declined, the impact of prescription opioids should not be minimalized. As of 2014, oxycodone and hydrocodone, the most commonly prescribed opioid pain relievers, were still the cause of more overdose deaths than any other opioid, including heroin and fentanyl (6).

Urbanicity

The Substance Abuse and Mental Health Services Administration's (SAMHSA) Treatment Episode Data Set provides descriptive data nationally about admissions to substance abuse providers for those aged 12 or older. An analysis of data from 2009 assessed the association between urbanicity and admissions for substance abuse treatment (11). In 2009 large central metropolitan areas, which they referred to as urban counties, accounted for 31.4% of all treatment facilities, while nonmetropolitan areas without a city, which they referred to as rural counties, accounted for 7.2%. As they expected, heroin admissions accounted for 21.8% of all urban admissions and only 3.1% or rural admissions. However, non-heroin opiates accounted for 4.0% of urban admissions and 10.6% of rural admissions, indicating that rural drug abusers may be more likely to report opiate pain reliever use. Additionally, 51.6% of rural admissions for substance abuse treatment were referred through the criminal justice system, compared to 28.4% of urban abusers (11). This may represent differences in substance abuse treatment and education resources in urban and rural counties.

In 2017 Han et al. analyzed data from the 2015 National Survey on Drug Use and Health (NSDUH). This survey collected representative data in the United States on prescription opioid use, misuse, and use disorders, as well as motivations/causes of misuse among those 12 or older years of age. They examined numerous variables, including county size, which was categorized in the same method as data from the 2014 NSDUH data set. The prevalence of prescription opioid misuse (without use disorder) among respondents was 11.3% in large metro counties, 9.7% in small metro counties, and 9.0% in nonmetro counties. When examining the prevalence of prescription use disorder, large metro counties reported 2.0%, small metro counties reported 2.1%, and nonmetro counties reported a prevalence of 2.3% (12).

Using the CDC Wide-Ranging ONline Data for Epidemiologic Research (WONDER) database for mortality data, researchers examined prescription opioid overdose death rates across the different county sizes. After adjusting for age, they found that across all county size groups the overdose death rate remained the same from 2016-2017, at 5.2 deaths per 100,000 individuals. In 2016, large central metro areas had a death rate of 4.7 per 100,000 individuals, large fringe metro areas had a rate of 5.2, medium metro areas had a rate of 6.0, small metro areas 5.2, micropolitan areas 5.7, and noncore areas 5.7. The only areas that had a different rate in 2017 included medium metro areas, with a death rate of 5.9, micropolitan areas with a rate of 5.6 and noncore areas with a rate of 5.3 (13).

The 2019 CDC Annual Surveillance Report provided further evidence that mortality and misuse prevalence data may differ across county sizes. Excluding heroin and methadone overdoses, in 2016 the age-adjusted opioid overdose hospitalization rates were estimated as 16.3 per 100,000 individuals for large central metro counties, 17.1 for large fringe metro counties, 21.3 for medium metro counties, 21.1 for small metro counties, 19.7 for micropolitan counties, and 18.8 among noncore metro counties (10). In 2017, among persons 12+, the prevalence of reported misuse of prescription pain relievers in the past year was found to be 3.9% among large metro counties, 4.3% among small metro, and 4.0% among non-metro counties. Among non-metro counties, those areas categorized as "Completely Rural" had a prevalence of 4.3%. These misuse prevalence rates declined in 2018, to 3.4% among large metro residents, 4.0% among small metro residents, and 3.7% among non-metro residents (10).

Occupation Type

There is evidence that not only are various occupation types, as well as occupation industries, associated with higher rates of injuries, but also higher rates of prescription opioid use/abuse. We also know that the prevalence of job types and industries differ between various county sizes. The research outlining these findings is described below.

Without displaying exact analyses, several sources have described a difference in the association between risk of injury and job type. In 2019 the financial news organization 24/7 Wall St analyzed the Bureau of Labor Statistics 2017 data from the annual National Census of Fatal Occupational Injuries report. The analyses calculating fatality rates per 100,000 individuals, which helped identify the 25 most dangerous jobs in the United States. These jobs included fishers, loggers, pilots & flight engineers, roofers, refuse collectors, iron/steel workers, truck drivers, farmers/ranchers, landscaping/groundskeeping, electrical installer/repairers, agriculture, construction, extraction, maintenance, mechanics, patrol officers, operators, miners, taxi drivers, athletes, painters, firefighters, & electricians (14). The National Safety Council has also completed extensive research into workplace injuries, and they concluded that the top 5 occupations with the largest number of workplace injuries resulting in days away from work included service industries (including police/firefighters), transportation/shipping, manufacturing/production, installation/maintenance, and construction. They report that most workplace injuries are due to overexertion, contact with objects and equipment, and slips, trips, or falls (15). The World Bank has also conducted research on workplace injuries, and in their 2017 Disease Control Priorities report on Injury Prevention and Environmental Health, concluded that workplace sectors including agriculture, forestry, fishing, construction, manufacturing, and transportation accounted for approximately 50% of all serious accidents at work (16).

With evidence that certain occupations and industries place workers at a higher risk of injury, and likely chronic pain, we should also examine if these occupations and industries lead to higher rates of prescription opioid use. Some research has already examined this topic. Thumula et al. (2017) examined nonsurgical workers' compensation claims in 26 states for individuals prescribed pain medications and had missed more than seven days of work. What they found was that 52-80% of these individuals were prescribed opioids for their pain management, and that after using Manufacturing as a reference, individuals that worked in construction had 1.191 times the odds of receiving opioids. The other industries used in this research, clerical/professional, trade, high-risk services, low-risk services, and "other" industries, all had statistically significant lower odds of receiving opioids, compared to manufacturing (17). In addition to higher rates of prescriptions, there is also evidence that certain industries see higher rates of misuse and abuse. Cerda et al. (2017) examined prescription opioid poisoning hospital discharges among residents in California. They found that as the density of manual labor industries within ZIP codes increased by 1 standard deviation, discharges for prescription opioid poisonings occurred at higher rates. Per standard deviation increase in density, the rate ratio for prescription opioid poisoning discharges was 1.15 (95% CI: 1.10-1.19) as density of construction employment increased and 1.12 (95% CI: 1.04-1.20) as density of manufacturing employment increased (18). Morano et al. (2018) discovered similar results in their findings. They examined mortality from unintentional or undetermined drug overdoses from data pulled from the National Occupational Mortality Surveillance in the U.S. from 2007-2012. They found that healthcare practitioners, healthcare support staff, personal care and service staff, construction, extraction, unpaid workers, and workers with "unknown" occupations all had statistically significant proportionate mortality ratios (PMR). Each of these occupations observed significantly more prescription opioid overdose deaths than expected (19).

There is also evidence that occupation types differ among counties of varying sizes. Peek-Asa, et al. (2004) noted in their research that traumatic occupational fatality rates are higher among rural than urban populations. However, this difference is also found within occupations as well, as they report that injury mortality rates in the construction industry are 40% higher in more rural states (5). It is possible that this is due to other factors, such as the fact that those injured in rural areas reach the hospital less quickly than urban areas. The Pew Research Center reported in 2018 that rural residents live, on average, 17.0 minutes away from a hospital, if traveling by car. Urban residents lived, on average, 10.4 minutes away from a hospital (20). So, for those injured in rural counties, it may take longer for them to receive treatment for their injury in a hospital, making the injury more likely to be fatal. Overall, Peek-Asa et al. (2004) conclude that many of the most dangerous occupations are found in rural areas, most notably mining and agriculture (5).

Age

Rates of overall use, as well as medical use, of prescription opioids appear to increase with age. By examining 2015 National Survey on Drug Use and Health (NSDUH) data, Han et al. (2017) found that older adults, aged 50+ were more likely to use (medically & nonmedically) prescription opioids, compared to 18-29 and 30-49 year olds. 39.5% (95% CI: 38.31-40.69) of adults 50 or older used prescription opioids in the previous 12 months at the time of the survey, compared to 37.0% (95% CI: 36.05-37.93) of 30-49 year olds and 35.7% (95% CI: 34.81-36.52) of 18-29 year olds (12). Durand et al. (2019) found similar differences while examining workers' compensation claims records of Tennessee residents from 2013-2015. It was discovered that middle and older age groups in the cohort were more likely than younger age groups to receive an opioid after injury. Those older than 55 had an odds ratio of 2.6 (95% CI: 1.81-3.87) when compared to odds of adults < 26 years of age (21).

While overall use and odds of being prescribed opioids may be higher among older individuals, the evidence suggests that younger individuals are more likely to misuse and abuse. Included in Han et al.'s (2017) analysis of 2015 NSDUH data was prevalence of prescription opioid misuse and use disorder. Among adults who have used prescription opioids in the previous 12 months, 20.1% of 18-29 year olds and 11.8% of 30-49 year olds were found to have misused, compared to only 5.3% of those 50 and older. There were also differences in prevalence of use disorder among prescription opioid users, with 3.5% of 18-29 year olds, 2.8% of 30-49 year olds, and 1.0% of those 50 or older being categorized as having a prescription opioid use disorder in the past 12 months (12). Rice et al. (2012) found similar results. Using 12-19 year olds as the reference group, they observed that 50-59 year olds had an odds ratio of 0.74 and 60-64 year olds had an odds ratio of 0.59, when examining the probability of being diagnosed as a prescription opioid abuser (22). The CDC also reported that in 2017 that reported misuse of prescription pain relievers was highest among 18-25 (7.2%) and 26-34 (6.0%) year olds (10).

While prescription opioid misuse and use disorder is more prevalent among young age groups, the evidence suggests that overdose rates are higher among older age groups. In California, from 2001-2011 there were greater rates of prescription opioid related hospital discharges in ZIP codes that had higher concentrations of arthritis-related hospital discharges. Per standard deviation increase in the arthritis discharge rate, there was an 8% increase in prescription opioid related discharges (18). Prescription overdose rates have continued to increase among older adults, at a rate faster than other age groups since 2010 (23). From 1999-2014 the prescription overdose mortality rate was highest among birth cohorts born in 1951-1962 (23). The CDC has further confirmed the association between age and prescription opioid mortality. The findings in the 2019 Surveillance Report included prescription opioid overdose death rates per 100,000 persons, which were highest among 45-54 (10.0), 35-44 (9.1), and 55-64 (8.4) year olds (10).

There is also evidence that age varies across counties of different sizes. The U.S. Census Bureau’s 2011-2015 American Community Survey found a median age of 43 years among rural and 36 years among urban residents (24). When only considering adults 18 or older, the median age was found to be 51 for rural and 45 for urban residents (25).

Gender

Research suggests that males are much more likely to misuse or overdose on prescription opioid medications, despite a higher percentage of females receiving an opioid prescription (10). Rice et al. (2012) found that from 2007-2009 males had 1.35 times the odds of being diagnosed as a prescription opioid abuser (22). Among prescription opioid users, 12.8% of males misused and 2.9% had an opioid use disorder, compared to 8.5% and 1.4% of females (12). Reported misuse may be declining among both genders. In 2017 4.6% of males self-reported misuse of prescription pain relievers, compared to 3.6% of females. The prevalence decreased to 3.9% of males and 3.4% of females in 2018 (10).

Race – Ethnicity

There is an association between race/ethnicity and prescription opioid misuse/abuse. In 2018 the CDC found that Native-Hawaiian/Pacific Islander and American Indian/Alaskan Native ethnicity groups self-reported the highest rates of prescription pain reliever misuse (10). Han et al. (2017) also found racial differences, with 14.1% of Hispanic prescription opioid users misusing within the past 12 months, compared to 10% of non-Hispanic white, 9.1% of non-Hispanic black, and 10.6% of "other" prescription opioid users (12). However, overdose death rates do not follow the same trends. In 2011 the age-adjusted opioid-analgesic overdose rate was 7.3 per 100,000 for non-Hispanic white persons, 2.3 for non-Hispanic black persons, and 2.0 for Hispanic persons (26).

Race and ethnicity differ greatly based on geographic location across the United States. The Pew Research Center analysis of 2012-2016 American Community Survey data found that among urban counties were comprised of 44% white, 27% Hispanic, and 17% black persons. Suburban counties were comprised of 68% white, 14% Hispanic, and 11% black persons. Rural counties were comprised of 79% white, 8% Hispanic, and 8% black persons (20).

Education

Prior evidence suggests that educational level is associated with prescription opioid abuse. The 2015 NSDUH survey found that respondents with higher educational levels were less likely to have prescription opioid misuse or use disorders in the last 12 months (12). Cochran et al. (2017) also found that rural respondents with a high school education or less had significantly greater odds of abusing prescription opioids, with an adjusted odds ratio of 6.68 (27).

Educational level has also been found to vary based on urbanicity. The 2011-2015 American Community Survey found that 29% of respondents in urban areas had a bachelor’s degree or higher educational level, compared to just 19.5% of respondents in rural areas (25). These differences have been further confirmed by the Pew Research Center, who found 35% of urban respondents to have a bachelor’s degree or higher level, compared to just 31% of suburban and 19% of rural residents (20).

Marital Status

Marriage has been found to have a protective effect on prescription opioid abuse. 7.4% of married respondents, compared to 18.3% of never married respondents, were found to have misused opioids in the past 12 months in one survey (12). In the same survey, a lower percentage of married respondents were also found to have prescription opioid use disorder (12). Tetrault (2007) also found evidence of a protective effect. Married women had an unadjusted odds ratio of 0.84 and married men had an unadjusted odds ratio of 0.68, compared to unmarried respondents (28).

Marital status also varies based on geographic location. The 2011-2015 American Community Survey found that 61.9% of rural respondents and 50.8% of urban respondents reported being currently married (25).

Income

As household income increases, the likelihood of prescription opioid abuse or misuse decreases. Cerda (2017) found prescription opioid related hospital discharges were increased in postal codes that had lower average incomes (18). In addition to increased discharges, lower incomes are also associated with a higher prevalence of prescription opioid misuse and use disorder (12). This association with income is present even after stratifying for gender. One study found that both men and women with lower incomes were found to be more likely to have used prescription opioids nonmedically in the past year (28).

Income, as well as poverty rates, differ based on urbanicity. The 2011-2015 American Community Survey found the median income of rural respondents to be $52,386, compared to $54,296 for urban respondents (25). Despite a higher median income, urban residents are more likely to be considered in poverty due to cost of living differences. The same survey found a 14% poverty rate in urban areas, compared to 11.7% in rural areas (25).

Insurance

The evidence shows that being uninsured presents a significant increase in the risk of prescription opioid abuse. The 2015 NSDUH survey results show that 21.1% of those who were uninsured met the criteria for prescription opioid misuse over the previous 12 months, compared to approximately 11% of those on private insurance or Medicaid (12). Becker (2008) also found a significant increase in risk when comparing uninsured respondents to those with "other public" insurance, finding an unadjusted odds ratio of 3.2 (29). However, when controlling for other factors, these statistically significant differences disappear. No statistically significant differences were observed based on type of insurance (29). There may be other factors that confound the association between insurance and prescription opioid abuse.

From 2011-2015 there doesn't appear to be a vast difference in the prevalence of uninsured residents in rural and urban counties, however the data described wasn't tested for statistical significance. The American Community Survey from 2011-2015 found that 15.3% of urban residents were uninsured, compared to 13.6% of rural residents (25).

Physical Health

Physical health problems, particularly chronic pain, are some of the most common reasons that individuals initially use prescription opioids, as well as one of the risk factors for prolonged use. From 1980 to 2000, the percentage of patient visits where opioids were prescribed to patients with chronic pain increased from 8 to 16% (30). Shah (2017) also found that in their study population, the most common indication for receiving a prescription for opioids was due to chronic pain conditions, at 25.1%, nearly double the percentage for surgery (31). Although not exclusive to chronic pain, Han (2017) found, while analyzing the 2015

NSDUH survey, that 63.4% of prescription opioid misusers reported physical pain as motivation for their misuse (12).

There are also differences in the physical health of residents depending on geographic location. While it could very likely be influenced by the fact that rural residents have a higher median age, residents living in noncore counties were 9% more likely to report having a disability, compared to residents in large metro counties (32). The difference is even more staggering when examining reports of multiple disabilities, where residents of noncore counties were 24% more likely to report 3 or more (32).

Mental Health

The evidence supports an association between various mental health disorders and prescription opioid abuse. Webster et al. (2018) discovered, when examining prescription opioid DUI offenders, that they were more likely to report depression, anxiety, and other mental health problems (33). The 2015 NSDUH survey also found increased prevalence of major depressive episode among users who have misused or have a use disorder involving prescription pain relievers (12). Those with post-traumatic stress disorders may also have an increased risk, with one study among rural residents finding an adjusted odds ratio of 5.44 for prescription opioid misuse (27). Most other studies in the available literature found increased risk among those with mental health disorders overall. In 2001, those classified as having a “Common Mental Health Disorder” had 1.96 times the odds of using prescription opioids than those without such disorders (34). Rice et al. (2012) also found increased odds among those with mental health issues, with an adjusted odds ratio of 2.45 (22). Tetrault et al. (2007) examined gender differences among mental health and prescription opioid abuse. Among those with a serious mental illness, they found that women had an OR of 1.67 (1.29-2.17) and men had an OR of 1.25 (0.91-1.70), when it comes to non-medical use of prescription opioids (28).

Differences in the prevalence in mental health disorders have also been examined based on urbanicity. While examining NSDUH data from 2009-2011, Breslau et al. (2014) found that, while using large metro areas as the reference, that respondents from small metro (OR=1.14) and semi-rural (OR=1.18) areas had an increased odds of reporting Major Depression or other serious mental illness. While rural respondents had an OR of 1.11, this was not statistically significant (35).

Presence of other Substance Abuse

Many studies examining prescription opioid use/abuse found an association with abuse of other substances. The 2015 NSDUH survey found increased prevalence of an alcohol use disorder among both prescription opioid use disorder and misuse in the past year (12). Among both men and women with past-year non-medical use of prescription opioids, Tetrault et al. (2007) also found increased adjusted odds ratios of past year alcohol abuse (28). Illicit drug use was also found to have an association with prescription opioid misuse, with rural respondents seeing an adjusted odds ratio of 14.34 (95% CI: 2.16 – 95.38) and urban respondents an adjusted odds ratio of 4.33 (95% CI: 1.12 – 16.58), compared to residents in those areas who did not exhibit illicit drug use (27).

Evidence suggests that the prevalence of substance abuse varies based on urbanicity. A 2012 report from the SAMHSA 2009 Treatment Episode Data Set found that the prevalence of alcohol and marijuana-related hospital admissions were increased in rural areas, compared to urban areas. Methamphetamine use admissions were similar in both urban and rural areas, accounting for approximately 6% of total substance use admissions in both areas. However, cocaine and heroin admissions were more likely in urban areas (11).

Pharmacy & Prescription Practices

Multiple studies have examined pharmacy and prescription practices and their associations with prescription opioid abuse. One study, which examined pharmacy location and pharmacy density, found that in postal codes with a greater pharmacy density, there were larger numbers of prescription opioid-related hospital discharges (18). Prescription practices, which have been a significant target of the CDC to decrease prescription opioid abuse rates, have shown significant risks. Herzig et al. (2014) found that from 2009-2010, 51% of all nonsurgical patient admissions were prescribed opioids, which may be due to rises in chronic pain (36). The type of drug-release may also be associated with an increased risk in abuse, with one study finding that a higher percentage of abusers were prescribed extended-release opioid pain relievers compared to non-abusers (37). Overall, it is apparent that the length of the prescription, strength of the dose, and type of dose all show an increased risk of using prescription opioids longer than 1 year (31).

It should be noted that the CDC's efforts to improve prescription practices have shown significant effects. The CDC's 2018 Annual Surveillance Report indicates that the number of prescriptions overall since 2006 have decreased, in addition to the average daily MME (Morphine Milligram Equivalents) per prescription. However, rates of 30 day or greater prescriptions have continued to increase since 2006 (13).

Military Service

While perhaps associated with physical and mental health problems, studies have shown that respondents that have served in the military are more likely to use and misuse prescription opioids. From 2001-2009, the percentage of veterans prescribed opioids increased from 17 to 24%. Chronic use increased over that time period as well, from 3% to 4.5% (38). Kelley et al. (2018) found that 46.2% of the military veterans wounded in combat in their study misused prescription opioids in the past year (39). The increase in use and misuse may only apply to veterans however, as one study noted that use of prescription opioids among active duty servicemen was lower than the general population (40).

Chapter 2:
Manuscript

Introduction

According to the Centers for Disease Control (CDC), there was an increase in illicit drug abuse from 1999 to 2017. Neither urban nor rural areas have been immune to this epidemic. In 2017 the age-adjusted rate of all drug overdose deaths was 22.0 per 100,000 individuals in urban counties and 20.0 per 100,000 individuals in rural counties. In rural counties, this was an increase of 16.0 individuals per 100,000 since 1999, compared to a 15.6 per 100,000 increase in urban counties (1). Prescription opioids, which in 2017 accounted for 24.2% of all fatal drug overdoses, play a significant role in this epidemic and may affect rural counties more significantly than urban counties (2). In 2017, rural counties had higher age-adjusted rates of natural and semisynthetic (prescription) opioid overdose deaths (4.9 per 100,000) than urban counties (4.3 per 100,000) (1). Further, 14 out of the 15 counties with the highest opioid prescription rates in 2017 were nonmetropolitan or rural (2).

One potential explanation for why prescription opioid rates are higher in rural counties is higher prevalence of chronic pain, which is the most common indication for an opioid prescription (2, 31). In addition to being associated with age, chronic pain has also been found to be associated with the amount of physical activity in the workplace (3). Heuch et al. (2017) found that even after adjusting for age, men whose work involved “walking and heavy lifting” and “particularly strenuous physical work” were found to have 1.28 and 1.36 times the risk of low back pain, respectively, compared to men with sedentary jobs (3). Many of the more physically strenuous jobs also have the highest rates of work injuries, according to the Bureau of Labor Statistics’ National Census of Fatal Occupational Injuries in 2017 (4). This may lead to higher rates of prescription opioid misuse, as the research suggests that physical pain is the most common reason for misuse (12). The combination of higher rates of chronic pain and higher rates of workplace injuries may cause individuals with more physically strenuous and dangerous jobs to be more likely to be prescribed and misuse opioids. As these more physically strenuous and dangerous jobs are more likely to be held by individuals living in rural counties, an association between job types and prescription opioid abuse may account for some of the differences we see in abuse rates between rural and urban counties (5).

This analysis examines whether there are links between prescription opioid abuse and misuse and urbanicity and occupation, and whether differences in occupation held by rural and urban individuals confounds the observed association between urbanicity and prescription opioid abuse and/or misuse.

Methods

This study uses cross-sectional data acquired through the National Survey on Drug Use and Health (NSDUH) conducted in 2014 (41). Survey data from this year included the collection of respondents' employment industry and job type. Yearly surveys following the one completed in 2014 no longer include this information. The nationally representative survey has been conducted annually in all 50 states since 1971 through the Substance Abuse and Mental Health Services Administration (SAMHSA), an agency in the United States Department of Health and Human Services (DHHS). The survey contains questions regarding tobacco, alcohol, and substance use and abuse; mental health and other health issues; illicit behavior questions; as well as demographic questions including income, gender, race, ethnicity, age, education, employment status, and veteran status (42). The data collected in this survey makes it ideal to examine the associations between prescription opioid abuse, urbanicity, and occupation. The data is deidentified and publicly available at datafiles.SAMHSA.gov. After consultation with the

Institutional Review Board, it was determined that this analysis did not meet the criteria for "human subjects research", and therefore was exempt from Institutional Review Board approval.

Study Population

The 2014 NSDUH survey was administered to 67,901 individuals aged 12 or older from all 50 states and the District of Columbia. Sampling was conducted to get an accurate representation of the United States by sampling from residents of households, persons in noninstitutionalized residences, and civilians living on military bases. The 8 largest states had a target sample size of 3,600 respondents, and the remaining 43 states, as well as D.C., had a target sample size of 900 respondents. The survey was found to have an approximate 82% weighted screening response rate and approximately 71% weighted interview response rate. After restricting the sample population to adults employed in full-time positions, the sample size was reduced to 21,642.

Variable Selection

<u>Dependent Variables</u>

The 2014 NSDUH survey does not measure prescription opioid use; however, it includes several outcomes related to prescription pain reliever misuse/abuse over the past year. The majority of pain relievers included in the survey questions are classified as prescription opioids, and the majority of pain relievers identified as being misused by respondents were opioids. The pain reliever outcomes used in this analysis were previously created by survey researchers and include 1) Any nonmedical use of prescription pain relievers in the prior year of the respondents answers to the survey and 2) Pain reliever abuse or dependence in the prior year of the respondents answers to the survey. Nonmedical use is defined as using pain relievers they are not prescribed or only taking for the feelings and experience they caused. Abuse is defined in the survey as having a positive response to 1 or more of the following criteria: 1) Serious problems at home, work, or school due to substance use 2) using regularly and then did something where substance use may have put them in physical danger, 3) substance use causing actions that repeatedly got them in trouble with the law, and 4) substance use caused problems with family or friends and they continued to use. Dependence is defined as meeting 3 of the following criteria: 1) spent a great deal of time over a period of a month getting, using, or getting over the effects of the substance, 2) unable to set limits on use or used more than intended, 3) needed to use more of the substance to get the desired effects or noticed that the usual amount had less effect, 4) unable to cut down or stop using the substance when they tried or wanted to, 5) continued to use the substance even thought it was causing nerves and/or emotional, mental health, or physical problems, 6) reduced or discontinued participation in important activities due to using the substance, and 7) experienced withdrawal symptoms lasting more than a day after cutting back or stopping use of the substance. In this survey abuse and dependence were mutually exclusive, with dependence taking precedence.

Covariates of Interest

Urbanicity is categorized based on county size as “large metro”, “small metro”, and “non-metro” using the US Department of Agriculture’s Rural Urban Continuum Codes (RUCC) (43). While the RUCC codes include 9 population levels, the 2014 NSDUH data set condenses these levels into three categories. “Large metro” areas are defined as having a densely populated center with 1,000,000 or more inhabitants, “small metro” areas are defined as having population center between 50,000 and 1,000,000 inhabitants, and "nonmetro areas" are defined as having less than 50,000 inhabitants.

In addition to employment status, respondents' current employment industry is included in this survey. As previously described, certain industries may be associated with higher rates of chronic pain and injuries. Based on literature review, participants were categorized as working in an industry with a higher risk of injury and chronic pain if they worked in the agriculture, forestry, fishing, hunting, construction, manufacturing, transportation, or utilities industries. All others were considered to have a low-risk occupation, making this a dichotomous variable.

Demographic Variables

Demographic Variables were chosen after conducting a literature review and determining characteristics that may be associated with the chosen outcome variables. Age is categorized as 18-25, 26-34, 35-49, 50-64, & 65+. Race and ethnicity are categorized as Hispanic, non-Hispanic Black, non-Hispanic White, Native American/Alaskan Native, Native Hawaiian/Other Pacific Islander, Asian, or multiple races. Additional demographic characteristics included in regression models are gender (male, female), education (less than high school, high school graduate, some college, college graduate), marital status (married, widowed, divorced/separated, never married), insurance status (covered, not covered), income (less than $20,000, $20,000-$49,999, $50,000-$74,999, $75,000 or more), military status (have ever served, haven't ever served), mental illness in the past year (no mental illness, mild mental illness, moderate mental illness, serious mental illness), overall health (excellent, very good, good, fair/poor).

Statistical Analysis

Frequencies of all independent and dependent variables, stratified by urbanicity, were conducted in this analysis. Using “Large Metro” counties as the reference group, chi-square tests were conducted to examine frequency differences between county sizes, with the statistical significance was set at $\alpha = 0.05$. Frequencies were also determined based on the respondents’ employment industry as well as for the new dichotomous variable examining risk of injury and chronic pain based on employment industry, stratified by urbanicity. Unadjusted analyses examining differences in employment industry risk based on urbanicity were conducted through logistic regression analysis with conditional margins test to obtain prevalence ratios.

Unadjusted and adjusted multivariable analyses, examining prescription pain reliever misuse and abuse/dependence variables of interest, were conducted through logistic regression analyses with conditional margins tests to obtain prevalence ratios. Following multivariable analyses, the occupational injury risk variable was assessed to see if it confounded the association between urbanicity and each dependent outcome variable. Confounding was considered present if the removal of the independent variable in the model caused a +- 10% difference in the prevalence ratio for urbanicity. Lastly, multicollinearity was assessed between all variables within the multivariate regression analyses of each outcome variable. Results of confounding and multicollinearity assessments are found in the appendices. All analyses were completed in SAS v9.4 (44).

Results

Table 1 describes the demographic composition, stratified by urbanicity (county size), of individuals that are included in the multivariable logistic regression model (adults employed full-time). An additional table displaying the frequencies for all adults in the dataset is included in

Appendix A. While we cannot conclude on which specific groups or levels within each variable statistically vary, the prevalence of age groups was found to vary by urbanicity in this sample, with a higher percentage of adults reporting being age 65 and older in nonmetro areas in this sample. 2.4% of nonmetro residents in the sample reported being 65 or older, compared to 1.6% of small metro and 1.9% of large metro respondents. Differences are also notable in this sample among race/ethnicity between county sizes, with larger metro areas containing a higher percentage of respondents reporting being of non-white descent. Among large metro respondents, 14.3% reported their race as Black and 21.4% reported being of Hispanic descent, compared to 9.2% Black and 13.3% Hispanic among small metro respondents and 6.2% Black and 7.9% Hispanic among nonmetro respondents. Other independent variables that were found to differ across county sizes included marital status, educational level, insurance coverage, yearly income, military or veteran status, and self-reported overall health. Gender was not found to vary significantly across county size. Prevalence of a mental illness in the past year also did not significantly vary across county sizes.

Table 2 displays the prevalence of job industries that respondents were employed in. Chi-square analyses were not conducted, so a statistical conclusion cannot be made regarding differences across county sizes. However, some of the more noticeable differences include agriculture, forestry, fishing, & hunting industries, where 5.58% of nonmetro respondents reporting working in these industries, compared to 1.49% of small metro respondents and 0.41% of large metro respondents.

Table 3 displays the prevalence of respondents that are considered working in industries that are associated with higher rates of workplace injuries and more physically strenuous jobs (risk for chronic pain). As described in the introduction, injuries and workplace physical activity has previously been noted to be associated with higher rates of pain reliever prescriptions and higher rates of abuse. Nonmetro respondents, as hypothesized, were more likely to work in the industries that place them at a higher risk of injury and chronic pain. 33.7% of nonmetro respondents, compared to 27.3% of small metro and 23.3% of large metro respondents, were employed full-time in industries with a higher risk of workplace injury. The unadjusted prevalence of small metro respondents holding jobs in high-risk industries was 1.17 (95% CI: 1.11 - 1.23) times the prevalence of large metro respondents. The unadjusted prevalence of nonmetro respondents holding jobs in high-risk industries was 1.45 (95% CI: 1.37 - 1.53) times the prevalence of large metro respondents.

Table 4 displays unadjusted and adjusted prevalence ratios for any pain reliever abuse or dependence in the previous year, among adults employed full-time. In the unadjusted models, neither exposure of interest, urbanicity and high-risk jobs, were found to have statistically significant associations with pain reliever use or dependence. Female respondents were less likely to experience pain reliever abuse or dependence compared to male respondents (PR = 0.68, 95% CI: 0.50 – 0.93). Married respondents had a lower prevalence of abuse or dependence compared to those who were never married (PR = 0.32, 95% CI: 0.22 – 0.46) Compared to college graduates, those with less than a high school education (PR = 2.92, 95% CI: 1.72 – 4.96), those that were high school graduates (PR = 2.07, 95% CI: 1.32 – 3.24), and those with some college education (PR = 2.58, 95% CI: 1.68 – 3.97) had an increased prevalence of abuse or dependence. Respondents without insurance coverage (PR = 2.45, 95% CI: 1.75 – 3.43), those who made less than $20,000 (PR = 2.87, 95% CI: 1.80 – 4.58), or made between $20,000 and $49,999 (PR = 2.38, 95% CI: 1.61 – 3.51), and respondents with past-year presence of a mental illness were also found to have a statistically significant unadjusted association with pain reliever abuse/dependence.

In the adjusted model displayed in Table 4, there was no effect of urbanicity or job type on abuse or dependence of opioids in the past year. Females respondents had a lower prevalence of abuse or dependence (PR = 0.52, 95% CI: 0.38 – 0.72). Married respondents had a lower adjusted prevalence of abuse or dependence compared to those who were never married (PR = 0.59, 95% CI: 0.40 – 0.88). Having "Excellent" overall health was associated with a lower prevalence of abuse or dependence compared to respondents reporting poor health (PR = 0.38, 95% CI: 0.19 – 0.77). Respondents with less than high school education (PR = 2.15, 95% CI: 1.20 – 3.85) or only some college (PR = 2.07, 95% CI: 1.33 – 3.24) had an increased prevalence of abuse or dependence compared to college graduates. Respondents without insurance coverage (PR =1.52, 95% CI: 1.04 – 2.21) were found to have an increased prevalence of abuse or dependence. Mental illness in the past year was found to have an association that increased in magnitude as severity of mental illness increased. Individuals with mild mental illness (PR = 3.24, 95% CI: 2.15 – 4.89), moderate mental illness (PR = 5.49, 95% CI: 3.40 – 8.87) and severe mental illness (PR = 9.13, 95% CI: 5.93 – 14.05) all had statistically significant increases in prevalence of abuse or dependence.

Table 5 displays the unadjusted and adjusted prevalence ratios for any nonmedical use of prescription pain relievers. Neither primary exposure, urbanicity and high-risk jobs, were found to have an association with nonmedical use. Females were found to have a lower prevalence of nonmedical use (PR = 0.74, 95% CI: 0.65 – 0.83). Respondents in excellent (PR = 0.43, 95% CI: 0.33 – 0.55) or very good (PR = 0.70, 95% CI: 0.56 – 0.87) overall health were found to have a lower prevalence, compared to those with poor health. Individuals without insurance coverage

(PR = 1.75, 95% CI: 1.51 – 2.02) were found to have an increased prevalence of nonmedical use. Similar to table 4, past year mental illness increased in prevalence as mental illness severity increased.

In the Table 5 adjusted model, individuals that were married (PR = 0.61, 95% CI: 0.52 – 0.71) were found to have a lower prevalence of nonmedical pain reliever use compared to those that were never married. Respondents in “Excellent” (PR = 0.55, 95% CI: 0.42 – 0.71) overall health were found to have a lower prevalence of past year nonmedical use of prescription pain relievers compared to those in “Poor” health. Individuals without insurance coverage (PR = 1.20, 95% CI: 1.02 – 1.40) were found to have an increased prevalence of nonmedical use. Using “No mental illness” in the past year as the reference group, the prevalence ratio was 1.88 (95% CI: 1.59 – 2.22) for those with mild mental illness in the past year, 2.36 (95% CI: 1.91 – 2.92) for those with moderate mental illness, and 2.79 (95% CI: 2.23 – 3.47) for those with serious mental illness in the past year.

After regression analyses were complete the occupational job risk variable was assessed to see if it confounded the relationship between urbanicity and the dependent variables. The results are presented in Appendices C and D. Occupational job risk was found to confound the relationship between urbanicity and the outcome indicating abuse/dependence, but only the prevalence ratio among respondents in small metro counties, compared to large metro respondents. The inclusion of the occupational risk variable caused the prevalence ratio of prescription pain reliever abuse or dependence to decrease from 0.89 to 0.71, however the statistical significance of this prevalence ratio remained unchanged and included the null ratio (1.00).

Discussion

Summary of Study

We did not observe an association between the exposures of interest, county size and workplace physical risk, and the 2 outcome variables measuring prescription pain reliever use and abuse. In both the adjusted and unadjusted analyses the confidence intervals were wide, likely due to the low number of participants who had abused or been dependent on prescription pain relievers. A larger sample size would provide a more precise estimate of association. While neither exposure of interest was found to have an association with prescription pain reliever misuse or abuse/dependence, our examination found evidence that workplace physical risk confounded the association between pain reliever use/abuse and county size.

Discussion of Other Key Results

Identifying as female, being married, having completed higher levels of education, having medical insurance, and reporting excellent overall health were all found to be associated with lower prevalence of prescription pain reliever nonmedical use and abuse/dependence in adjusted analyses. One key finding in this secondary analysis was the magnitude of the association pain reliever nonmedical use and abuse/dependence outcomes had with the presence of a mental illness in the past year, and how it increased in magnitude as mental illness severity increased. The magnitude was particularly high in the model that included individuals identified as being abusive or dependent on prescription pain relievers. Compared to people without mental illness, prevalence ratios ranged from 3.24 (mild mental illness) to 9.13 (serious mental illness) in adjusted analyses. However, because these data are cross-sectional, we are unable to make any conclusions regarding causation.

Limitations

This secondary analysis included many limitations. All analyses were restricted to respondents with full-time employment. This reduced the sample size from 41,671 to 21,642 adult respondents. The demographic make-up of the entire adult sample is included in Appendix A. There are several reasons excluding those with no job or part-time jobs may have limited our analyses. By only including those employed full-time at the time of the survey, we may be excluding those who were employed full-time and needed to reduce work hours or could no longer work due to workplace injury, chronic pain, or the effects of pain reliever abuse or dependence.

Another limitation in this analysis is how counties are classified. The 2014 NSDUH survey included 2 variables classifying the county size that respondents lived in. The variable chosen for this analysis included “Large Metro”, “Small Metro”, and “Nonmetro”, based on the defined metropolitan statistical area used by the Office of Management and Budget (OMB). While respondents may report being residents of a county classified as “Large Metro” or “Small Metro”, not all parts of a county may be heavily populated and may more resemble “rural” environments. The Health Resources & Services Administration (HRSA) points out that these measurement challenges have led to the Grand Canyon being classified as being located in a metro county (45). Examining urbanicity using census tracts or ZIP codes might provide more nuanced results.

One of the more concerning limitations in these analyses is that prescription pain reliever abuse, dependence, and overall use are determined from questions that assessed “nonmedical” use. NSDUH survey designers consider nonmedical use as taking medications respondents were not prescribed or if respondents took the medications only for the experience or feelings they caused. This may limit the number of respondents that are classified as using/abusing nonmedically because 1) Many may be using medications they were prescribed, 2) They may consider their use, even if not using as prescribed, as "medical" use if they are using to relieve pain. This is important because the most commonly reported motivation for misuse of prescribed opioids is to relieve physical pain (12). Other limitations of the outcome variables used in these analyses include the fact that respondents are self-reporting their use, introducing recall bias, and there were several prescription pain relievers that are not technically opioids, making it difficult to compare these analyses with other studies that examine specifically prescription opioids. However, it was rare that respondents reported use of prescription pain relievers not considered opioids.

Public Health Implications

Further studies are needed to continue exploring rural/urban differences in prescription opioid use and misuse. Results from previous studies have varied, with some finding higher rates of the outcome of interest in more populated urban counties, and others finding higher rates of outcomes in rural counties. This may be due to the variedness in study design and outcomes being examined. Future studies are needed to re-examine the association between urbanicity and prescription opioid use and misuse. The role of injury risk in the workplace also needs to be re-examined due to limitations in this secondary analysis. Evidence suggests that certain industries and job types are associated with higher rates of workplace deaths and injuries, which may lead to medical problems that require prescription opioid use. Further studies are needed to examine if this is the case and if job types with higher rates of injuries is associated with prescription opioid abuse, dependence, and misuse.

One of our key findings was the magnitude of the association between the presence of mental illness and prescription pain reliever misuse, abuse, and dependence. This association also increased in magnitude as severity of mental illness increased. Previous studies have shown similar associations, but future research needs to examine the association to determine causation, as it would be important to understand whether prescription opioid use contributes to mental illness or is a result of mental illness, whether prescribed for medical reasons or obtained for nonmedical use.

Chapter 3:
Extended Conclusion

Conclusions

Prescription opioid abuse, and addiction in general, is a complicated problem in our society. Many of the underlying factors for prescription opioid outcomes are not well understood, and results from previous studies have been varied, and sometimes contradictory, with respect to many of the potential underlying factors. Another reason why it may remain difficult to accurately assess some of the underlying factors is the possibility that the factors may vary depending on the outcome under study: prescription opioid overall use, misuse, abuse, overdose, or death. Although we did not observe evidence of an association between urbanicity and prescription opioid misuse and abuse, it is possible that urbanicity is associated with other facets of the opioid epidemic. Further research is needed to determine if urbanicity plays a role in prescription use, misuse, abuse, as well as other negative health outcomes.

While questions remain about the significance of many underlying factors for prescription opioid abuse, several others have been identified and addressed. The CDC has had great success educating healthcare providers on safe prescription practices, leading to a steady decrease in the number of opioid prescriptions filled per 100 people and a lower Morphine Milligrams Equivalent (MME) daily dose per prescription. Since 2006, the number of opioid prescriptions filled per 100 people reduced from 72.4 to 51.4 in 2018. Over that same time, the average daily MME dose per prescription reduced from 59.7 to 42.9 MME (10). Much of this decline has occurred since 2010. Despite significant changes in prescription practices in most of the country, additional work is needed. In 2018 the CDC found that 11% of counties in the country still dispensed enough prescriptions for every resident to have at least one prescription filled (46).

Similar to prescribing practices, we may be able to take steps to reduce the impact of prescription opioid abuse by addressing other issues. We identified significant associations between prescription opioid abuse/misuse and insurance coverage, physical health, and the presence of mental illnesses. All these areas are interconnected and addressable in ways that could help reduce prescription opioid use and abuse. By providing better and broader healthcare coverage and insurance, promoting more healthy lifestyles, and better addressing mental illness in the United States we may also indirectly be helping reduce prescription opioid misuse and abuse.

The COVID-19 Pandemic has brought death and other terrible health outcomes around the world, and yet additional consequences may be overlooked. The American Medical Association issued a brief in September 2020 detailing the numerous national and state media reports about the rise in opioid-related mortality since the start of the pandemic in the United States (47). Media reports may be numerous, but research is needed to identify which opioids are being used more, and whether that includes prescription opioids. However, some of the societal and public health effects resulting from the pandemic can lead to an environment where prescription opioid misuse and abuse can rise. The pandemic has caused significant rises in unemployment, mental health issues, physical health problems, as well as a reduction in insurance coverage, all of which are associated with an increase in prescription opioid misuse and abuse. The situation is even more dire due to the recent research showing that individuals with a substance use disorder are at a higher risk of pulmonary infections such as COVID-19 (48).

Though we did not identify an association between urbanicity and prescription opioid misuse and abuse/dependence, different approaches to categorizing urbanicity might provide more meaningful results. One such possible alternative is using Rural-Urban Commuting Area (RUCA) codes, which uses measures of population density, urbanization, and daily commuting (49). These RUCA codes are then applied to every ZIP code around the country, providing a more specific rating of urbanization than a categorization of county size. The 2020 census may also help improve the accuracy of our categorizations, especially for data collected more recently.

Although we did not observe an association between jobs in which workers are more at risk of injury and prescription opioid misuse and abuse, additional research is warranted. There is evidence that injuries or trauma lead to prescription opioids being dispensed to treat acute pain. In fact, CDC even points out that much of the long-term opioid use often begins with the treatment of acute pain (31, 50). We have also seen a rise in the use of prescription opioids for chronic pain (51). Taking these factors into account, more research needs to be conducted to determine whether certain jobs that place workers at a higher risk of injury additionally place workers at risk of long-term prescription opioid use and potential abuse. Unfortunately, this analysis may have been unable to prove that association, possibly due to multiple limitations discussed earlier, as well as the nature of how employment is recorded in the survey. The 2014 National Survey on Drug Use and Health (NSDUH) recorded the type of industry as well as the kind of work each current employed respondent does. This analysis used the type of industry, rather than type of work, to create a new variable categorizing the industries as having an increased risk of injury, due to the fact evidence discovered during literature review, including 2014 nonfatal injury rate data from the U.S. Bureau of Labor Statistics, supported using a variable assessing industry. Further research should specifically investigate risk based on the respondents' type of work.

Recommendations

Of available data through 2018, 2014 was the last year that the National Survey on Drug Use and Health (NSDUH) included questions regarding employment industry and type of work. We recommend that the survey include these questions in future surveys. Other recommendations for the NSDUH include questions regarding the medical use of prescription opioids as prescribed (in addition to misuse and abuse), since many individuals transition from a prescription for an acute or chronic health problem to abuse. Second, NSDUH researchers should examine urbanicity and consider including alternatives to the 3-level classification based on Rural Urban Continuum Codes. The Centers for Disease Control and Prevention (CDC) often uses the 2013 National Center for Health Statistics (NCHS) Urban-Rural Classification Scheme for Counties, a 6-level categorization method that classifies counties as large central metro, large fringe metro, medium metro, small metro, micropolitan, and noncore. These 6 levels can additionally be re-classified as metropolitan and nonmetropolitan (micropolitan & noncore) (52).

An additional limitation of surveys using misuse and abuse variables is that it relies on respondents' memory, effort, and honest opinion regarding their misuse. This can lead to several biases, including the under-report of stigmatized behaviors, survey fatigue, as well as recall bias. An alternative, more objective research dataset may be emergency department admission and/or discharge data for prescription opioid overdoses. Data regarding address and/or ZIP codes of patients would be required to assess urbanicity and determine if there are associations with non-fatal and fatal overdoses. However, this method of data collection may not include workplace data, which would have to be collected by contacting the patient. The workplace data would need to include current and past workplace history to capture those who are no longer employed or changed employment due to workplace injuries, chronic pain, and/or prescription opioid abuse.

In addition to research recommendations, it is also recommended that preventative measures be put in place to address previous conclusions regarding differences in prescription opioid abuse among various occupations and county sizes. Nonmetro and rural counties should receive an increase in prescription opioid education and surveillance. Counties with disproportionately greater jobs in industries with an increased risk for injury, such as construction and manufacturing, should also be targeted for an increase in education and surveillance. Public health officials should also provide educational materials to employees in these industries, warning them of the dangers of prescription opioid use and potential abuse for those injured or experiencing chronic pain.

These recommendations, in addition to taking preventative measures to help curb prescription opioid abuse, are necessary to continue to assess whether there are underlying differences in urbanicity and employment in prescription opioid misuse and abuse. This may be especially important if there is a rise in prescription opioid use due to the COVID-19 pandemic. The more we understand about the underlying characteristics of prescription opioid abuse, the better able we will be to combat this epidemic in our country and prevent future abuse.

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Tables & Figures

Table 1: Sample Demographics

Variable	Total N (%)	Nonmetro N (%)	Small Metro N (%)	Large Metro N (%)
Age				
18-25	5282 (24.0%)	1073 (24.6%)	1917 (25.2%)	2292 (22.7%)
26-34	5459 (24.8%)	942 (21.6%)	1885 (24.8%)	2632 (26.1%)
35-49	7889 (35.8%)	1556 (35.7%)	2690 (35.4%)	3643 (36.1%)
50-64	3012 (13.7%)	681 (15.6%)	984 (13.0%)	1347 (13.3%)
65+	411 (1.9%)	103 (2.4%)	120 (1.6%)	188 (1.9%)
Chi-Sq (p)	62.6 (<.0001)			
Race				
White	14198 (64.4%)	3365 (77.3%)	5289 (69.6%)	5544 (54.9%)
Black	2407 (10.9%)	269 (6.2%)	696 (9.2%)	1442 (14.3%)
Native Amer/AK Native	278 (1.3%)	154 (3.5%)	81 (1.1%)	43 (0.4%)
Native HI/Pac Island	121 (0.6%)	32 (0.7%)	51 (0.7%)	38 (0.4%)
Asian	966 (4.4%)	70 (1.61%)	264 (3.5%)	632 (6.3%)
2 or More Races	567 (2.6%)	120 (2.8%)	208 (2.7%)	239 (2.4%)
Hispanic	3516 (15.9%)	345 (7.9%)	1007 (13.3%)	2164 (21.4%)
Chi-Sq (p)	1324.3 (<.0001)			
Gender				
Male	11912 (54.0%)	2390 (54.9%)	4050 (53.3%)	5472 (54.2%)
Female	10141 (46.0%)	1965 (45.1)	3546 (46.7%)	4630 (45.8%)
Chi-Sq (p)	2.9 (0.24)			
Education				
Less than High School	2087 (9.5%)	486 (11.2%)	683 (9.0%)	918 (9.1%)
High School Graduate	6009 (27.3%)	1558 (35.8%)	2139 (28.2%)	2312 (22.9%)
Some College	6090 (27.6%)	1250 (28.7%)	2225 (29.3%)	2615 (25.9%)
College Graduate	7867 (35.7%)	1061 (24.4%)	2549 (33.6%)	4257 (42.1%)
Chi-Sq (p)	510.3 (<.0001)			
Marital Status				
Married	10712 (48.6%)	2289 (52.6%)	3718 (49.0%)	4705 (46.6%)
Widowed	268 (1.2%)	53 (1.2%)	98 (1.3%)	117 (1.2%)
Divorced/Separated	2663 (12.1%)	552 (12.7%)	976 (12.9%)	1135 (11.2%)
Never Married	8410 (38.1%)	1461 (33.6%)	2804 (36.9%)	4145 (41.0%)
Chi-Sq (p)	83.6 (<.0001)			
Insurance Status				
Covered	19068 (86.5%)	3707 (85.1%)	6554 (86.3%)	8807 (87.2%)
Not Covered	2985 (13.5%)	648 (14.9%)	1042 (13.7%)	1295 (12.8%)
Chi-Sq (p)	11.4 (.0034)			
Income				
Less than $20,000	2478 (11.2%)	529 (12.2%)	880 (11.6%)	1069 (10.6%)

$20,000-$49,999	6905 (31.3%)	1586 (36.4%)	2497 (32.9%)	2822 (27.9%)
$50,000-$74,999	4233 (19.2%)	883 (20.3%)	1504 (19.8%)	1846 (18.3%)
$75,000 or More	8437 (38.3%)	1357 (31.2%)	2715 (35.7%)	4365 (43.2%)
Chi-Sq (p)	230.1 (<.0001)			
Military Service - Ever				
Yes	1307 (5.9%)	314 (7.2%)	500 (6.6%)	493 (4.9%)
No	20733 (94.1%)	4039 (92.8%)	7092 (93.4%)	9602 (95.1%)
Chi-Sq (p)	38.5 (<.0001)			
Mental Illness - Past Year				
None	18317 (83.1%)	3622 (83.2%)	6276 (82.6%)	8419 (83.3%)
Mild	2070 (9.4%)	412 (9.5%)	703 (9.3%)	955 (9.5%)
Moderate	930 (4.2%)	179 (4.1%)	367 (4.8%)	384 (3.8%)
Serious	736 (3.3%)	142 (3.3%)	250 (3.3%)	344 (3.4%)
Chi-Sq (p)	11.8 (0.0662)			
Overall Health				
Excellent	5599 (25.4%)	946 (21.7%)	1931 (25.4%)	2722 (27.0%)
Very Good	9094 (41.3%)	1843 (42.3%)	3090 (40.7%)	4161 (41.2%)
Good	5906 (26.8%)	1244 (28.6%)	2087 (27.5%)	2575 (25.5%)
Fair/Poor	1447 (6.6%)	322 (7.4%)	487 (6.4%)	638 (6.3%)
Chi-Sq (p)	53.1 (<.0001)			

Table 2: Among those employed full-time, prevalence of employment Industries stratified by urbanicity

	Total N (%)	**Nonmetro N (%)**	**Small Metro N (%)**	**Large Metro N (%)**
Type of Industry				
Agriculture/Forestry/Fishing/ Hunting	397 (1.80%)	243 (5.58%)	113 (1.49%)	41 (0.41%)
Mining	208 (0.94%)	119 (2.73%)	63 (0.83%)	26 (0.26%)
Construction	1843 (8.36%)	384 (8.82%)	671 (8.83%)	788 (7.80%)
Manufacturing (Nondurable Goods)	975 (4.42%)	259 (5.95%)	356 (4.69%)	360 (3.56%)
Manufacturing (Durable Goods)	1660 (7.53%)	380 (8.73%)	592 (7.79%)	688 (6.81%)

Transportation/Utilities	998 (4.53%)	197 (4.52%)	332 (4.37%)	469 (4.64%)
Information/Comms	411 (1.86%)	45 (1.03%)	142 (1.87%)	224 (2.22%)
Wholesale Trade (Durable Goods)	263 (1.19%)	38 (0.87%)	102 (1.34%)	123 (1.22%)
Wholesale Trade (Nondurable Goods)	290 (1.32%)	39 (0.90%)	88 (1.16%)	163 (1.61%)
Retail Trade	2123 (9.63%)	429 (9.85%)	744 (9.79%)	950 (9.40%)
Finance/Insurance/Real Est./Rental/Leasing	1391 (6.31%)	156 (3.58%)	442 (5.82%)	793 (7.85%)
Professional/Scientific/Mgmt/ Admin/Waste Mgmt	2490 (11.29%)	260 (5.97%)	756 (9.95%)	1474 (14.59%)
Education/Health/Social Services	4804 (21.78%)	967 (22.20%)	1746 (22.99%)	2091 (20.70%)
Arts/Entertainment/Rec/Accommodation/Food Services	2029 (9.20%)	390 (8.96%)	712 (9.37%)	927 (9.18%)
Public Admin	1136 (5.15%)	247 (5.67%)	386 (5.08%)	503 (4.98%)
Other	961 (4.36%)	185 (4.25%)	329 (4.33%)	447 (4.42%)
Not Reported/Don't Know/Refused/Blank	74 (0.003%)	17 (0.004%)	22 (0.003%)	35 (0.003%)

Table 3: Prevalence of High-Risk Job Types stratified by Urbanicity

	Total **N (%)**	**Nonmetro** **N (%)**	**Small Metro** **N (%)**	**Large Metro** **N (%)**
Occupational Injury Risk				
Yes	5873 (26.72%)	1463 (33.7%)	2064 (27.3%)	2346 (23.3%)
No	16106 (73.28%)	2875 (66.3%)	5510 (72.8%)	7721 (76.7%)
Prevalence Ratio		1.45	1.17	1.00 (Ref)
95% Wald CI		1.37 – 1.53	1.11 – 1.23	

Table 4: Logistic Regression Model - Full Model – Abuse/Dependence in Past Year

Variable	Unadjusted Prevalence Ratio	95% Wald Confidence Interval	Adjusted Prevalence Ratio	95% Wald Confidence Interval
County Size				
Large Metro	1.00 (Ref)		1.00 (Ref)	
Small Metro	0.83	0.58 – 1.18	0.71	0.50 – 1.02
Nonmetro	1.04	0.71 – 1.54	0.87	0.57 – 1.33
Occupational Injury Risk				
Yes	1.08	0.77 – 1.52	1.02	0.71 – 1.45
No	1.00 (Ref)		1.00 (Ref)	
Age				
18-25	4.67	0.65 – 33.61	1.93	0.30 – 12.38
26-34	4.74	0.66 – 34.12	2.43	0.38 – 15.41
35-49	1.51	0.21 – 11.07	0.97	0.15 – 6.24
50-64	1.77	0.23 – 13.53	1.42	0.20 – 9.83
65+	1.00 (Ref)		1.00 (Ref)	
Race				
White	1.00 (Ref)		1.00 (Ref)	
Black	0.68	0.39 – 1.18	0.60	0.34 – 1.06
Native American/Alaskan Native	0.42	0.06 – 3.01	0.40	0.05 – 2.85
Native Hawaiian/Other Pac Island	2.91	0.94 – 9.02	2.07	0.66 – 6.45
Asian	0.73	0.32 – 1.65	0.98	0.44 – 2.19
2+ Races	1.03	0.42 – 2.52	0.76	0.31 – 1.85
Hispanic	0.53	0.32 – 0.90	0.39	0.23 – 0.65
Gender				
Male	1.00 (Ref)		1.00 (Ref)	
Female	0.68	0.50 – 0.93	0.52	0.38 – 0.72
Education				
Less than High School	2.92	1.72 – 4.96	2.15	1.20 – 3.85
High School Graduate	2.07	1.32 – 3.24	1.54	0.94 – 2.52
Some College	2.58	1.68 – 3.97	2.07	1.33 – 3.24
College Graduate	1.00 (Ref)		1.00 (Ref)	
Marital Status				
Married	0.32	0.22 – 0.46	0.59	0.40 – 0.88
Widowed	0.61	0.15 – 2.46	0.98	0.23 – 4.08
Divorced/Separated	0.58	0.36 – 0.95	0.75	0.44 – 1.28
Never Married	1.00 (Ref)		1.00 (Ref)	
Insurance				
Covered	1.00 (Ref)		1.00 (Ref)	
Not Covered	2.45	1.75 – 3.43	1.52	1.04 – 2.21
Income				
Less than $20,000	2.87	1.80 – 4.58	1.27	0.73 – 2.20
$20,000-$49,999	2.38	1.61 – 3.51	1.28	0.84 – 1.96

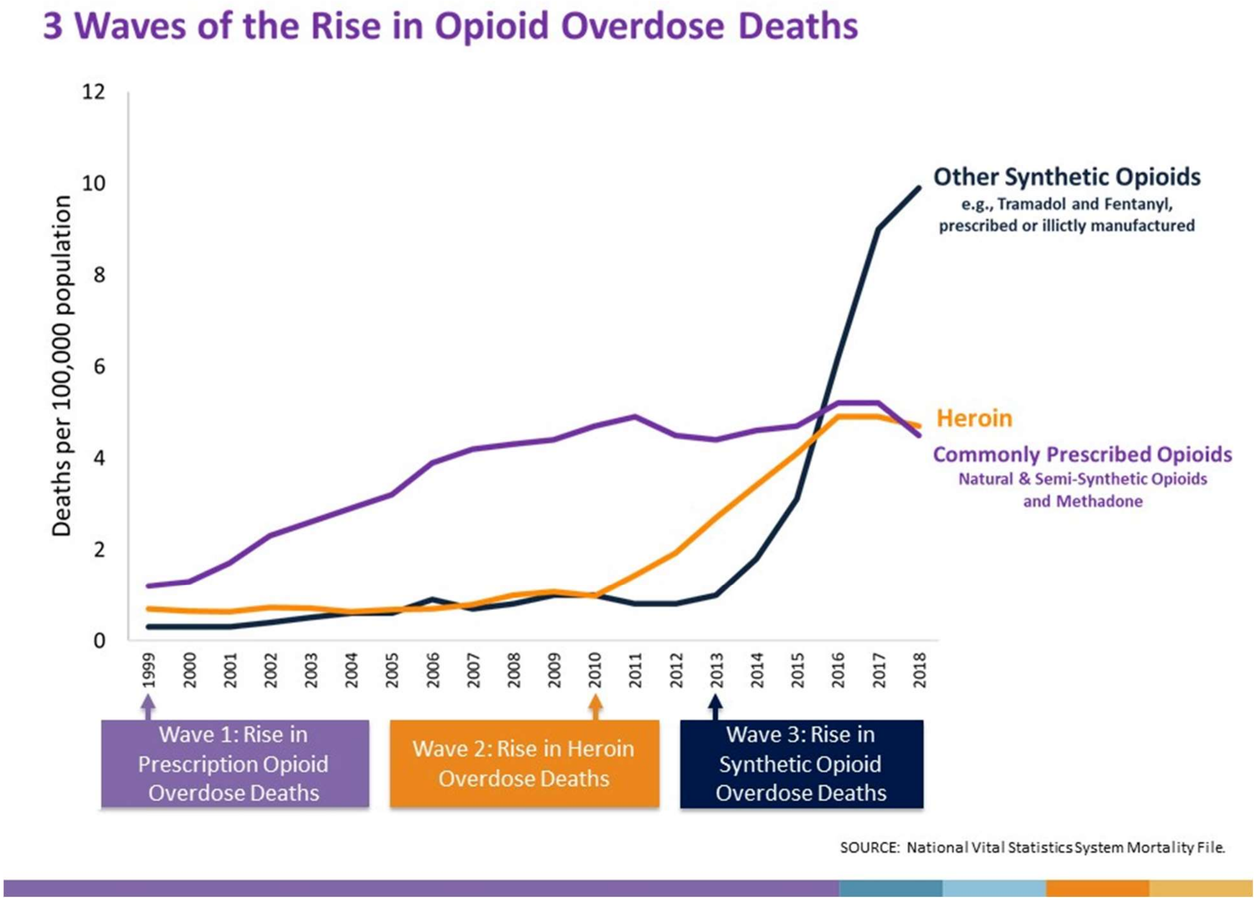
$50,000-$74,999	1.15	0.68 – 1.95	0.84	0.50 – 1.43
$75k +	1.00 (Ref)		1.00 (Ref)	
Military Service – Ever				
Have served	0.39	0.15 – 1.06	0.41	0.16 – 1.07
Have not Served	1.00 (Ref)		1.00 (Ref)	
Overall Health				
Excellent	0.21	0.11 – 0.40	0.38	0.19 – 0.77
Very Good	0.52	0.31 – 0.85	0.80	0.47 – 1.37
Good	0.80	0.48 – 1.31	1.05	0.62 – 1.77
Poor	1.00 (Ref)		1.00 (Ref)	
Mental Illness Past Year				
No Mental Illness	1.00 (Ref)		1.00 (Ref)	
Mild Mental Illness	3.83	2.53 – 5.78	3.24	2.15 – 4.89
Moderate Mental Illness	6.65	4.25 – 10.42	5.49	3.40 – 8.87
Serious Mental Illness	11.77	7.93 – 17.48	9.13	5.93 – 14.05

Table 5: Logistic Regression Model - Full Model – Overall Nonmedical Use in Past Year

Variable	Unadjusted Prevalence Ratio	95% Wald Confidence Interval	Adjusted Prevalence Ratio	95% Wald Confidence Interval
County Size				
Large Metro	1.00 (Ref)		1.00 (Ref)	
Small Metro	1.01	0.89 – 1.16	0.93	0.81 – 1.07
Nonmetro	0.92	0.78 – 1.09	0.84	0.71 – 1.01
Occupational Injury Risk				
Yes	0.98	0.86 – 1.13	0.89	0.77 – 1.03
No	1.00 (Ref)		1.00 (Ref)	
Age				
18-25	4.92	2.21 – 10.94	2.74	1.23 – 6.07
26-34	3.93	1.76 – 8.75	2.65	1.20 – 5.86
35-49	2.08	0.93 – 4.66	1.64	0.74 – 3.61
50-64	1.61	0.71 – 3.69	1.43	0.63 – 3.21
65+	1.00 (Ref)		1.00 (Ref)	
Race				
White	1.00 (Ref)		1.00 (Ref)	
Black	0.93	0.76 – 1.14	0.81	0.66 – 1.00
Native American/Alaskan Native	0.69	0.36 – 1.31	0.62	0.33 – 1.16
Native Hawaiian/Other Pac Island	2.10	1.22 – 3.61	1.54	0.90 – 2.64
Asian	0.50	0.33 – 0.76	0.57	0.38 – 0.86
2+ Races	1.16	0.82 – 1.64	0.90	0.64 – 1.27
Hispanic	0.95	0.80 – 1.13	0.70	0.58 – 0.85
Gender				
Male	1.00 (Ref)		1.00 (Ref)	

Female	0.74	0.65 – 0.83	0.66	0.58 – 0.75
Education				
Less than High School	2.17	1.77 – 2.65	1.70	1.35 – 2.13
High School Graduate	1.67	1.42 – 1.97	1.31	1.10 – 1.57
Some College	1.59	1.35 – 1.87	1.31	1.10 – 1.56
College Graduate	1.00 (Ref)		1.00 (Ref)	
Marital Status				
Married	0.40	0.35 – 0.46	0.61	0.52 – 0.71
Widowed	0.42	0.21 – 0.84	0.69	0.35 – 1.38
Divorced/Separated	0.58	0.47 – 0.70	0.77	0.61 – 0.96
Never Married	1.00 (Ref)		1.00 (Ref)	
Insurance				
Covered	1.00 (Ref)		1.00 (Ref)	
Not Covered	1.75	1.51 – 2.02	1.20	1.02 – 1.40
Income				
Less than $20,000	2.21	1.83 – 2.66	1.15	0.93 – 1.43
$20,000-$49,999	1.79	1.54 – 2.08	1.12	0.95 – 1.32
$50,000-$74,999	1.38	1.15 – 1.66	1.07	0.89 – 1.29
$75k +	1.00 (Ref)		1.00 (Ref)	
Military Service – Ever				
Have served	0.67	0.50 – 0.92	0.78	0.58 – 1.06
Have not Served	1.00 (Ref)		1.00 (Ref)	
Overall Health				
Excellent	0.43	0.33 – 0.55	0.55	0.42 – 0.71
Very Good	0.70	0.56 – 0.87	0.84	0.67 – 1.06
Good	0.96	0.77 – 1.19	1.07	0.85 – 1.34
Poor	1.00 (Ref)		1.00 (Ref)	
Mental Illness Past Year				
No Mental Illness	1.00 (Ref)		1.00 (Ref)	
Mild Mental Illness	2.11	1.78 – 2.49	1.88	1.59 – 2.22
Moderate Mental Illness	2.74	2.23 – 3.37	2.36	1.91 – 2.92
Serious Mental Illness	3.32	2.69 – 4.08	2.79	2.23 – 3.47

Figure 1


3 Waves of the Rise in Opioid Overdose Deaths
Deaths per 100,000 population
0
2
4
6
8
10
12
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
Other Synthetic Opioids
e.g., Tramadol and Fentanyl, prescribed or illictly manufactured
Heroin
Commonly Prescribed Opioids
Natural & Semi-Synthetic Opioids and Methadone
Wave 1: Rise in Prescription Opioid Overdose Deaths
Wave 2: Rise in Heroin Overdose Deaths
Wave 3: Rise in Synthetic Opioid Overdose Deaths
SOURCE: National Vital Statistics System Mortality File.

Appendices

Appendix A: Supplemental Demographics – Entire adult survey sample

Variable	Total N (%)	Nonmetro N (%)	Small Metro N (%)	Large Metro N (%)
Age				
18-25	13069 (31.4%)	2648 (30.4%)	4762 (32.9%)	5659 (30.6%)
26-34	8390 (20.1%)	1558 (17.9%)	2932 (20.2%)	3900 (21.1%)
35-49	11235 (27.0%)	2297 (26.4%)	3772 (26.0%)	5166 (28.0%)
50-64	5361 (12.9%)	1267 (14.6%)	1801 (12.4%)	2293 (12.4%)
65+	3616 (8.7%)	929 (10.7%)	1224 (8.5%)	1463 (7.9%)
Chi- Sq (p)	136.5 (<.0001)			
Race				
White	26012 (62.4%)	6550 (75.3%)	9763 (67.4%)	9699 (52.5%)
Black	4925 (11.8%)	591 (6.8%)	1441 (9.9%)	2893 (15.7%)
Native Amer/AK Native	681 (1.6%)	406 (4.7%)	189 (1.3%)	86 (0.5%)
Native HI/Pac Island	224 (0.5%)	55 (0.6%)	97 (0.7%)	72 (0.4%)
Asian	1844 (4.4%)	142 (1.6%)	525 (3.6%)	1177 (6.4%)
2 or More Races	1251 (3.0%)	277 (3.2%)	480 (3.3%)	494 (2.7%)
Hispanic	6734 (16.2%)	678 (7.8%)	1996 (13.8%)	4060 (22.0%)
Chi-Sq (p)	2865.0 (<.0001)			
Gender				
Male	19412 (46.6%)	4071 (46.8%)	6659 (46.0%)	8682 (47.0%)
Female	22259 (53.4%)	4628 (53.2%)	7832 (54.1%)	9799 (53.0%)
Chi-Sq (p)	3.6 (0.1624)			
Education				
Less than High School	5627 (13.5%)	1409 (16.2%)	1836 (12.7%)	2382 (12.9%)
High School Graduate	12537 (30.1%)	3209 (36.9%)	4448 (30.7%)	4880 (26.4%)
Some College	11965 (28.7%)	2511 (28.9%)	4398 (30.4%)	5056 (27.4%)
College Graduate	11542 (27.7%)	1570 (18.1%)	3809 (26.3%)	6163 (33.4%)
Chi-Sq (p)	819.5 (<.0001)			
Marital Status				
Married	17785 (42.7%)	4025 (46.3%)	6213 (42.9%)	7547 (40.8%)
Widowed	1289 (3.1%)	328 (3.8%)	431 (3.0%)	530 (2.9%)
Divorced/Separated	4801 (11.5%)	1091 (12.5%)	1754 (12.1%)	1956 (10.6%)
Never Married	17796 (42.7%)	3255 (37.4%)	6093 (42.1%)	8448 (45.7%)
Chi-Sq (p)	181.5 (<.0001)			
Insurance Status				
Covered	35576 (85.4%)	7356 (84.6%)	12430 (85.8%)	15790 (85.4%)
Not Covered	6095 (14.6%)	1343 (15.4%)	2061 (14.2%)	2691 (14.6%)
Chi-Sq (p)	6.6 (0.0378)			
Income				

Less than $20,000	9257 (22.2%)	2226 (25.6%)	3393 (23.4%)	3638 (19.7%)
$20,000-$49,999	13240 (31.8%)	3086 (35.5%)	4752 (32.8%)	5402 (29.2%)
$50,000-$74,999	6823 (16.4%)	1442 (16.6%)	2390 (16.5%)	2991 (16.2%)
$75,000 or More	12351 (29.6%)	1945 (22.4%)	3956 (27.3%)	6450 (34.9%)
Chi-Sq (p)	542.8 (<.0001)			
Military Service - Ever				
Yes	2739 (6.6%)	682 (7.8%)	1065 (7.4%)	992 (5.4%)
No	38904 (93.4%)	8013 (92.2%)	13416 (92.7%)	17475 (94.6%)
Chi-Sq (p)	80.6 (<.0001)			
Mental Illness - Past Year				
None	33312 (79.9%)	6884 (79.1%)	11519 (79.5%)	14909 (80.7%)
Mild	4198 (10.1%)	896 (10.3%)	1477 (10.2%)	1825 (9.9%)
Moderate	2165 (5.2%)	468 (5.4%)	798 (5.5%)	899 (4.9%)
Serious	1996 (4.8%)	451 (5.2%)	697 (4.8%)	848 (4.6%)
Chi-Sq (p)	15.3 (0.0184)			
Overall Health				
Excellent	9785 (23.5%)	1748 (20.1%)	3418 (23.6%)	4619 (25.0%)
Very Good	15816 (38.0%)	3286 (37.8%)	5491 (37.9%)	7039 (38.1%)
Good	11307 (27.1%)	2479 (28.5%)	3965 (27.4%)	4863 (26.3%)
Fair/Poor	4748 (11.4%)	1184 (13.6%)	1614 (11.1%)	1950 (10.6%)
Chi-Sq (p)	121.4 (<.0001)			

Appendix B: Collinearity Assessment

	Abuse / Dependence		**Dependence**		**Abuse**		**Use**	
Variable Name	VDP1	VDP2	VDP1	VDP2	VDP1	VDP2	VDP1	VDP2
CONDINDX	68.118	40.344	7364.56	43.569	18019.39	266067	60.8061	34.3517
AGEFINAL1	0.442	0.5161	1.00	0.00	0.00	0.807	0.6517	0.3053
AGEFINAL2	0.447	0.5149	1.00	0.00	0.00	0.807	0.6557	0.3008
AGEFINAL3	0.443	0.4988	1.00	0.00	0.00	0.737	0.6565	0.2914
AGEFINAL4	0.432	0.4674	1.00	0.00	0.00	0.00	0.6266	0.2660
MILSERVICE	0.455	0.5191	0.00	0.964	1.00	0.00	0.2170	0.7340

Collinearity assessments were made between all control and exposure variables for each dependent outcome. Multicollinearity was found to exist between age categories and military service.

Appendix C: Confounding Assessment in Abuse/Dependence Model

	Large Metro	Small Metro	Nonmetro
Full Model Urbanicity OR's	1.00 (Ref)	0.71 0.50 – 1.02	0.87 0.57 – 1.33
Remove Occupational Risk	1.00 (Ref)	**0.89** **0.70 – 1.12**	0.83 0.62 – 1.10

*Bold indicates a change +- 10% from Gold Standard Model OR

Appendix D: Confounding Assessment in Overall Nonmedical Use Model

	Large Metro	Small Metro	Nonmetro
Full Model Urbanicity OR's	1.00 (Ref)	0.93 0.81 – 1.07	0.84 0.71 – 1.01
Remove Occupational Risk	1.00 (Ref)	0.97 0.88 – 1.06	0.87 0.77 – 0.98