2020

Identifying and Addressing Barriers to Accessing Treatment for Substance Use Disorders among Opioid-misusing Individuals Following Implementation of the Affordable Care Act

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A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University.

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ACKNOWLEDGEMENTS

I am incredibly thankful to Dr. Juan Lu, for all of the wisdom and support she provided while pushing me to complete this dissertation, and for giving me the opportunity to mentor and teach others along the way. I would also like to acknowledge Dr. Elizabeth Prom-Wormley, Dr. Robert Perera, and Dr. Andrew Barnes, whose contributions and advice helped make me a more confident and competent researcher. The final part of this project would not have been possible without the amazing work of Lt. Daniel Stamp, Dr. Allen Yee, and the community paramedicine program at Chesterfield Fire and Emergency Medical Services. Additionally, special thanks are owed to the Virginia Office of Emergency Medical Services, specifically Narad Mishra, who spent a great deal of time helping me get data for my projects. I am incredibly thankful to all of my friends and family who supported and encouraged me throughout the last four years. Finally, to my amazing husband Wesley; I am so thankful each and every day to have your unconditional love and support.

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COMMONLY USED ACRONYMNS

95% CI	95% Confidence Intervals
ACA	Patient Protection and Affordable Care Act
AIC	Akaike Information Criterion
aOR	Adjusted Odds Ratios
ARTS	Addiction Recovery and Treatment Services
BICss	Sample Size adjusted Bayes Information Criterion
BLRT	Bootstrapped Likelihood Ratio Test
EMS	Emergency Medical Services
ePCRs	Electronic Patient Care Reports
GSL	Good Samaritan Legislation
H+PPR	Heroin and Prescription Pain Relievers
HCV	Hepatitis-C
HIV	Human Immunodeficiency Virus
HO	Heroin Only
IDU	Injection Drug Use
IN	Intranasal
IV	Intravenous
LCA	Latent Class Analysis
LL	Log Likelihood
LRT	Lo-Mendel-Rubin Likelihood Ratio Test
mg	Milligrams
MITSA	Multiple Interrupted Time Series Analysis
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NSDUH	National Survey on Drug Use and Health
OOD	Opioid Overdose
OUD	Opioid Use Disorder
PMP	Prescription Monitoring Programs
PPR	Prescription Pain Relievers
PSTC	Peer Support and Treatment Connection
PSU	Polysubstance Use
PWID	People Who Inject Drugs
SITSA	Single Interrupted Time Series Analysis
SUD	Substance Use Disorder

Abstract

Background: This project utilized opioid-misusing adults to investigate the association between type of opioid misuse and perceived readiness, financial, structural, and stigma-related barriers to accessing SUD treatment; identified classes of PSU and the association between patterns of PSU and perceived barriers, and evaluated effectiveness of an out-of-hospital opioid-treatment connection program.

Methods: Respondents from 2015-2018 NSDUH included insured adults reporting past year opioid misuse. Multivariate logistic regression assessed relationship between type of opioid misuse and perceived barriers to SUD treatment. LCA identified patterns of PSU, and multivariate logistic regression assessed association between PSU classes and perceived barriers. EMS ePCRs for nonfatal OOD from February 1st 2016 – January 31st 2020 were utilized for SITSA and MITSA to evaluate association between implementation of an out-of-hospital opioid-treatment connection program and monthly trend of nonfatal OOD in the county of implementation and a control county.

Results: Of 6,095 individuals, 3.7% perceived at least one barrier. LCA identified: *Heroin injectors with high PSU, PPR users with low PSU*, and *PPR users with high PSU*. *Heroin injectors with high PSU* faced significantly greater odds of perceiving readiness, structural, and stigma-related barriers compared to *PPR users with low PSU*. The county of implementation reported an immediate decrease in nonfatal OOD by 0.34% each month post-intervention, however there were no significant differences in pre- to post-intervention level or slope between counties.

Conclusions: The findings of this study can be used to develop public-health interventions targeted towards subpopulations perceiving barriers, and continue evaluation of out-of-hospital intervention programs.

Chapter 1: Background

1.1 Human and Economic Toll of the United States Opioid Epidemic

In 2017, a total of 47,600 opioid-related fatalities occurred in the United States – approximately 130 Americans killed every day.[1] The annual number of drug overdose deaths in the United States has nearly tripled since 1999; with opioids, both prescription (oxycodone, oxycontin) and illicit (heroin, fentanyl), accounting for more than half of the lives claimed during that time period.[2] The mortality resulting from the opioid epidemic is responsible for destroying families, consuming public safety resources and burdening the U.S. healthcare system. In November of 2017 the White House Council of Economic Advisers reported the total economic cost of the opioid crisis at close to $504 billion,[3] with more than a third of that total economic burden likely made up of costs from reduced productive hours due to misuse/dependence, and expenses to the U.S. healthcare system.[4]

1.2 Opioid Addiction Treatment in the United States

The abrupt cessation of opioids may lead to strong cravings or intense symptoms of opioid withdrawal, which may encourage an individual to seek out and use opioids.[5] To break the cycle of abuse, there are a variety of therapies which can be used to treat Opioid Use Disorder (OUD), including pharmacotherapies, behavioral therapies, and a combination of both. These treatments take place in a variety of settings throughout in the US; overall the majority (91.3%) take place in outpatient programs, followed by residential programs (7%), and hospital inpatient program (1%).[6]

Pharmacotherapies. Evidence suggests that treating opioid addiction with medication is far more effective at keeping individuals in treatment and opioid-abstinent than using non-medication treatment.[7] Three medications are currently approved by the U.S. Food and Drug Administration to treat OUD: opioid-agonists methadone and buprenorphine, and the opioidantagonist naltrexone.[8] While sometimes mistaken as "heroin/opioid substitutes", the effects of these medications differ from those of heroin and other misused opioids.[9] Whereas the rapid onset of heroin produces immediate euphoria followed by a crash, methadone and buprenorphine have gradual onsets of action and maintain stable levels within the brain, decreasing an individual's craving for opioids without a euphoric high.[9] In 2017, facilities with opioid treatment programs reported more than a half-million individuals participated in medication-assisted opioid therapy, 73.9% received methadone, 21.7% buprenorphine, and 4.5% received Naltrexone.[6]

Behavioral therapies. Behavioral therapies help engage people in treatment for substance use disorder (SUD), enabling them to modify their attitudes toward opioid use, and help them develop coping mechanisms to handle physical and environmental cues that may trigger intense cravings for opioids.[9] Although maintenance on medication-assisted treatments alone has been effective at reducing overdose deaths,[10] research has also shown that both methadone and buprenorphine maintenance are more effective when included with some type of behavioral therapy.[9] This is likely why the American Society of Addiction Medicine recommends psychosocial treatment in conjunction with any pharmacological treatment for OUD.[5]

Despite the increased availability of treatment over the past decade,[11] most individuals with OUD report no use of OUD treatment.[12] Additional steps need to be taken to identify and address the variety of financial, structural, and stigma-related barriers that prevent individuals from accessing the treatment they need.

1.3 Barriers to Accessing Treatment for Substance Use Disorder

The gap for treatment of SUD is massive, that is, among those who need treatment for a SUD, few receive it.[9] Between 2016 and 2017, the National Survey on Drug Use and Health

(NSDUH) estimated 17,484 individuals needed but did not receive treatment for substance use in the past year.[13]

Perceived Need of Treatment. This gap primarily exists due to the substantial number of individuals who do not perceive a need for treatment of their substance use.[14,15] In a 2015 survey conducted by Ali et al., 97% of respondents with a SUD reported not feeling a need for treatment or counseling for their alcohol or substance use.[15] This perception persists because individuals are not be ready to stop using alcohol or drugs,[15] believe they can handle their addiction on their own,[16,17] or are not prepared to stop using alcohol or drugs.[15] Yet, even among the small group of individuals feeling a need for treatment, barriers to accessing treatment for SUD persist.

Financial barriers. Financial barriers are commonly cited by individuals acknowledging a need for SUD treatment,[10,18–20 21] with individuals not seeking help due to an inability to pay for treatment,[10,18,20,22] most often due to a lack of insurance.[20,22] One study estimated around 12 million uninsured Americans had a diagnosable mental or SUD,[23] and Wu et al. found that uninsured adults are disproportionately affected by OUD.[12]

Structural barriers. These financial barriers are likely exacerbated by the wide variation in the types of treatment for SUD and treatment coverage available in each state,[24] which contribute to a variety of structural/organizational barriers. Restrictions placed on medications used in treatment can lead to a shortage of providers available to provide treatment,[10,25–27] further impeding access by creating long waiting periods.[28] Limited availability of programs disproportionately affects individuals living in rural areas,[18] as well as vulnerable populations in need of special treatment accommodations, such as individuals who are pregnant,[29] or those with co-occurring psychiatric disorders[30] or disabilities.[31]

Stigma-related barriers. Lastly, stigma-related barriers are often cited for deterring individuals from seeking treatment, stemming primarily from a general lack of understanding about treatment for SUDs.[18,31–34] Some individuals report not seeking treatment due to a lack of community support,[18,31] and due to the belief that using medication assisted treatment was equilivant to substituting one addiction for another.[18,34] In other cases the treatment itself was an issue, as individuals reported not wanting to seek treatment due to stigmatization and judgement from clinicians and agency personnel.[31,32]

In order to address these barriers and reduce the treatment gap, strategies must be implemented to increase access to treatment for SUD, such as: achieving insurance parity, reducing stigma, and raising awareness among both patients and clinicians about value of addiction treatment.[9]

1.4 Addressing Barriers through the Patient Protection and Affordable Care Act

The United States government attempted to address many of these barriers to health care access through the Patient Protection and Affordable Care Act (ACA). The ACA aimed to increase healthcare access in three different ways: i) by extending insurance coverage through Medicaid expansion and state health insurance exchanges, ii) by requiring coverage of the essential health benefits package, including SUD screening and treatment services under both the Medicaid expansion program and the health plans offered on the state healthcare exchanges, and iii) by extending the 2008 mental health parity and addiction equity act: requiring insurers to cover SUD treatment in a no more restrictive way than medical and surgical services.[23,24]

Since full implementation of the ACA in 2014, significant strides to increase healthcare access have been made: 22 million Americans gained access to insurance, essentially decreasing the number of uninsured Americans by half, from 48.6 million in 2010 to 28.6 million in 2015,[35] and decreasing the rate of uninsurance for nonelderly adults to 10.2%.[36] Studies have shown that the provisions of the ACA have greatly expanded the ability of individuals with SUD to obtain and maintain coverage.[23]

In 2014, 81.5% of the respondents to the NSDUH with serious mental health or SUD reported insurance, a significant increase from all pre-2014 time periods,[37] and another study from Feder et al. reported the prevalence of uninsured individuals with heroin use disorder declined dramatically from 2010 to 2015, largely due to the increased prevalence of Medicaid coverage.[21]

Many researchers have credited the expansion of Medicaid as the driving force for many of the improvements in uninsurance;[24,36,38] [21]Medicaid insured 13 million Americans,[35] including 1.6 million with SUD who gained insurance coverage in the Medicaid expansion states.[24] Medicaid also accounted for the vast majority of new coverage among individuals with SUD, with use of Medicaid as a source of payment for SUD treatment increasing from 19.6% in 2011-2013 to 27% in 2014.[38]

Implementation of the ACA was not only instrumental in increasing the number of insured individuals with SUD, it also led to the proliferation of facilities offering SUD treatment and decreased the restrictions, requiring SUD treatments to be offered on par with medical and surgical procedures.[24] Across the US, coverage for addiction treatment generally improved from 2013-2017; the proportion of state plans providing benefits for residential SUD treatment and access to OUD medications dramatically increased, and annual service limits on outpatient addiction treatment decreased from 34% to 19% in standard plans.[39]

1.5 Enrollment in Substance Use Disorder Treatment following the ACA

Despite increases in insurance coverage and OUD medication availability following implementation of the ACA, the treatment rates for alcohol and SUDs have remained unchanged, as studies have reported no significant differences in SUD treatment utilization even up to three years following ACA implementation.[21,37,40]

One factor significantly impacting enrollment in SUD treatment is variation in the expansion of state Medicaid programs.[41,42] ACA allowed states to expand Medicaid to individuals whose incomes were at or below 138% of the federal poverty level;[41] however, a 2012 decision of the United States Supreme Court enabled states to choose whether or not to expand Medicaid, resulting in 19 states choosing not to expand.[41] In 2017 the rate of uninsurance in non-expansion states was 2.5 times higher than in the expansion states, as many low-income individuals who make too much money to qualify for Medicaid but not enough to be able to afford a plan on the health care exchange.[36] Medicaid was meant to play an important role in providing access to OUD treatment, as the program currently covers 30% of the 2.2 million Americans with prescription OUD.[7] Thus, one possible explanation for stagnant enrollment in SUD programs could be because individuals in need of SUD treatment remaining uninsured because they reside in a non-expansion state.

While many studies have focused on the persisting treatment access barriers of uninsured individuals, few have investigated the barriers experienced by insured individuals. While individuals who are insured are less likely to experience financial barriers to accessing treatment, they may continue to experience structural, motivational, and stigma-related barriers to accessing SUD treatment.[20] For example, insured individuals may face barriers to access due to a lack of treatment availability. A shortage of physicians able to provide SUD treatment limits treatment availability, and more than 30 million people live in U.S. counties without a single prescriber of medications for addiction treatment.[10] Although one study showed that the number of physicians able to prescribe buprenorphine dramatically increased between 2003-2012, the demand for treatment in 2012 continued to overwhelm the capacity of available programs, with the majority of states reporting a treatment gap of at least 3 patients per 1000 people, and an overall gap of nearly 1 million people nationally.[11]

Access to treatment among the insured may also be limited by service restrictions imposed by an individual's insurance, such as restrictions on OUD medications used in treatment.[43,44] One study sampling 100 policies on health insurance marketplaces found that plans were less likely to cover buprenorphine and naltrexone,[45] and reported that buprenorphine was more likely than methadone to be subject to prior authorization and restrictions.[45] In addition, clinicians report low reimbursement rates for OUD medications as a significant barrier to implementing addiction services program,[26] leading some clinicians to decline accepting insurance for addiction services at all.[25] Among those insured, those who are likely impacted most by service restrictions are individuals with Medicaid, as the benefits available vary widely from state-to-state.[39,43] One promising study by Andrews et al. reported that Medicaid benefits for addiction treatment generally improved between 2014 and 2017: the proportion of state plans providing benefits for residential treatment and OUD medications states increased and the proportion of services and medications subject to annual limits decreased.[39] Yet this study also reported that 15 states continued to prohibit coverage for short-term residential treatment, and only half provided coverage for long-term treatment.[39] Variation in the services reimbursed cause many Medicaid recipients difficulty locating treatment facilities,[22] especially facilities offering medications for addiction treatment.[43] Alas, even when individuals with Medicaid find a facility they may not be prioritized as patients or receive treatment equal to that received by individuals with private insurance, due to the lower fees reimbursement paid by Medicaid.[35]

1.6 Shortcomings of Strategies Currently Addressing the Opioid Epidemic

In addition to implementing the ACA, the United States has launched and promoted a variety of public health initiatives aimed at preventing opioid-related morbidity and mortality. Table 1.1 summarizes these strategies and their prevalence throughout the United States, and categorizes them as either "primary prevention" or "tertiary prevention" strategies, based on the three types of prevention strategies used by epidemiologists in response to disease epidemics.[46]

Primary prevention aims to reduce the incidence of a disease or condition.[46] Primary prevention strategies to address the opioid epidemic include *prescription monitoring programs* (PMP), which allow physicians to monitor the number of prescriptions a patient receives to deter overprescribing or "doctor shopping",[7,47,48] *prescription limits* which encourage physicians to limit the number of opioids in an initial opioid prescription,[7] and *prescription drug take-back programs*, which allow individuals to dispose of unused opioid medications to prevent diversion or misuse.[49] These initiatives aim to decrease the incidence of opioid misuse by limiting the number of prescribed opioids available for misuse.

Tertiary prevention aims to prevent further disease through therapeutic and rehabilitative measures after a disease has been diagnosed.[46] The majority of strategies addressing the opioid epidemic in the United States are tertiary prevention strategies, which aim to prevent future morbidity or morbidity associated with opioid misuse. Overdose fatalities could be further prevented by increasing public and layperson access to naloxone through *overdose education and naloxone distribution programs*[50–53] and *over-the-counter availability of naloxone,*[54,55] by ensuring overdose bystanders can call 911 without fear of arrest, as decreed in *Good Samaritan*

Legislation (GSL),[55] or by allowing individuals to use pre-obtained drugs under the watch of trained staff in *supervised drug consumption venues.*[56,57] In addition, the incidence of Human Immunodeficiency Virus (HIV) and Hepatitis C resulting from risky drug injection practices can be decreased through *syringe-needle access programs.*[46]

Although one or more of these programs has been implemented in nearly every state in the nation,[7] it is concerning that none of these initiatives employ *secondary prevention*, which emphasizes the screening of individuals for a health condition before it leads to serious complications.[46] Upon screening an individual with OUD, a clinician could connect that individual with further addiction treatment, assisting them to bypass the various treatment access barriers discussed previously. While tertiary strategies are critical to decreasing the morbidity and mortality associated with the opioid epidemic, these strategies often end with detoxification, the first stage of addiction treatment, which by itself does little to change long-term drug use.[9] To stop an addicted individual from compulsively seeking drugs and end the long-term cycle of abuse, drug treatment is a necessity,[9] and identifying ways to connect individuals with addiction treatment is critical.

1.7 Literature Summary

Opioid treatment is the most effective way to overcome an opioid addiction, yet the number of individuals receiving treatment remains low. In the past, many of the barriers preventing an individual from seeking care were financial, due to lack of insurance and inability to pay out of pocket for treatment. The ACA was implemented in order to decrease financial barriers to accessing healthcare, and while the ACA greatly expanded access to insurance, enrollment into treatment for substance use disorder has remained unchanged. Although some studies have investigated the relationship between treatment enrollment and Medicaid expansion, few have explored barriers to accessing treatment for SUD among insured individuals, and fewer still have focused on barriers to accessing OUD treatment. Additionally, although treatment initiatives in the United States have been effective in reducing the harm associated with opioid-use, very few initiatives have focused on promoting the screening of OUD and connecting individuals with OUD to the addiction treatment they require.

The aim of this dissertation was to address these research gaps by a) further investigating how sociodemographic and substance use characteristics are associated with barriers to accessing treatment for SUD, and b) evaluate the effectiveness of an out-of-hospital opioid treatment connection program on the number of nonfatal opioid overdoses.

This dissertation pursued these study objectives through the investigation of three aims:

1. Investigate the association between type of opioid misuse and perceived readiness, financial, structural, and stigma-related barriers to accessing treatment for substance use disorder among insured adults reporting past year opioid misuse.
2. Identify patterns of past year polysubstance use among a nationally representative sample of opioid-misusing adults in the U.S. and evaluate the association between class of polysubstance use and perceived readiness, financial, structural, and stigma-related barriers to accessing treatment for SUD.
3. Evaluate the impact of an out-of-hospital opioid treatment connection program on the number of nonfatal opioid overdoses 24-months post intervention.

Chapter 2. The association between type of opioid misuse and perceived barriers to accessing addiction treatment among insured opioid-misusing individuals

Abstract

Background: Little is known about the relationship between type of opioid misuse and access to treatment for substance use disorders. We investigated the association between type of opioid misuse and perceived readiness, financial, structural, and stigma-related barriers to accessing treatment for substance use disorder (SUD) among insured individuals reporting past year opioid misuse.

Methods: Participants from the 2015-2018 National Survey on Drug Use and Health included insured individuals reporting past year misuse of prescription pain relievers (PPR), heroin (HO), or both (H+PPR). Chi-square analyses determined the association between participant's predisposing, enabling, and need characteristics and type of opioid misuse. Multivariate logistic regression assessed the relationship between type of opioid misuse and all four perceived barriers to accessing treatment for SUD.

Results: Of the 6,095 individuals reporting past year opioid misuse, 244 (3.7%) perceived at least one barrier to accessing treatment for SUD. Whereas HO users most often perceived financial (50.5%) and stigma-related (39.8%) barriers, readiness (45.5%, 50.9%) and structural (41.2%, 44.9%) barriers were most cited by those using PPR or H+PPR. Misuse of H+PPR and HO (vs. PPR only) significantly increased the odds of perceiving readiness (OR=2.80, 95%CI=1.08-7.27), structural (OR=3.27, 95%CI=1.26-8.46), and stigma-related (OR=3.98, 95%CI=1.42-11.21) barriers. Severe mental health symptoms and increased number of SUD also significantly increased the odds of perceiving all four barriers.

Conclusions: Type of opioid misuse, mental health severity, and number of SUD are significantly associated with perceived barriers to accessing treatment for SUD. Targeted strategies that address individual-level factors (e.g., severe mental health problems, multiple SUD, type of opioid misuse) alongside population-level changes that increase availability of services may increase the likelihood of enrollment into treatment for SUDs.

2.1 Introduction

Treatment of Opioid Use Disorder (OUD) is the most effective way to treat opioid-related addiction and reduce the burden of this substance on the American health care system. Failure to enroll more individuals with OUDs into treatment has been costly to the U.S. healthcare system. In 2017 alone, a total of 47,600 opioid-related fatalities occurred in the United States. Further, the U.S. Council of Economic Advisors estimated the total economic cost of the opioid crisis in 2015 to be $504 billion.[3]

The 2010 implementation of the Patient Protection and Affordable Care Act (ACA) extended private and public insurance coverage to millions of Americans. It also included screening and treatment services for substance use disorders (SUD) as essential benefits in health insurance plans, and required insurers to cover behavioral health services, including SUD treatment.[23,58] Following implementation of the ACA, there were improvements in insurance rates among opioid-misusing individuals and increased availability of SUD treatment services.[39,59,60] [40] However, to date, there have been no significant differences in SUD treatment utilization even up to three years following implementation of the ACA.[21,37,40]

It is likely that the ACA did not fully address four main barriers that reduce the likelihood of seeking SUD treatment, including: motivational (not yet ready to quit substance use or believe they can handle the addition on their own),[17] financial (lack insurance or cannot afford treatment),[22] structural (medication restrictions, long waiting periods, lack of availability, transportation),[61–64] and stigma-related barriers (lack of community/family support, judgement from clinicians and healthcare providers)[65–67].

The recent shift in the type of opioid misuse from prescription opioids to heroin and synthetic opioids represents a structural barrier not fully addressed by the ACA and may have contributed to an increase in opioid use rather than encouraging accessing opioid treatment.[68,69] The mortality rate due to synthetic opioids increased by 45.2% between 2016-2017. In contrast, prescription-opioid mortalities plateaued during this same timeframe.[1] This is likely due to the influx of synthetic opioids such as fentanyl,[70] which made heroin and synthetic opioids a more accessible alternative to prescription opioids.[71] The shift in the type of opioid misuse had swift implications for the planning of harm reduction and SUD treatment initiatives.

Overall enrollment in SUD treatment programs remains low among opioid-misusing individuals, despite continued efforts to expand insurance coverage and access to SUD treatment. While there has been a great deal of research on the barriers to accessing SUD treatment, to date no study has investigated the barriers perceived by individuals who have insurance. In addition, the national shift in type of opioid misuse over the past decade could impact how opioid-misusing individuals perceive the accessibility of SUD treatment. No study has investigated the relationship between the type of opioid misuse and perceived barriers to accessing treatment for SUD. This study aimed to gain a better understanding of the relationship between type of opioid misuse and perceived barriers to accessing SUD treatment among insured adults in the United States. Therefore, the objective of this study was to investigate the association between type of opioid misuse and perceived barriers to accessing SUD treatment.

2.2 Methods

2.2.1 Data Source and Population

This study analyzed data from the 2015-2017 publicly available files of the National Survey on Drug Use and Health (NSDUH). The NSDUH is administered to the non-institutionalized civilian population aged 12 and older,[72] collecting detailed information on the use of alcohol, illicit drugs, mental illness, SUDs, utilization of behavioral health treatments, and treatment barriers for behavioral health conditions and treatments.[73] The NSDUH uses a stratified multistage area probability sample designed to represent each of the 50 states and the District of Columbia.[72] The methodological process for the NSDUH aims at increasing the accuracy of self-reports, through the use of computer-assisted personal interviewing, audio computer-assisted self-interviewing, and assurances that individual responses will remain confidential.[72] Data from 2015-2017 was chosen to represent the survey years when the ACA was fully implemented throughout the United States. Most provisions of the ACA were implemented by October of 2014, however there remained state-by-state variation for the implementation of others.[74] For example, although the ACA called for states to expand Medicaid to individuals whose incomes were at or below 138% of the Federal poverty line,[42,75] 19 states initially declined to do so. Thus, data from 2015 and beyond was chosen to give the most accurate representation of perceived barriers to treatment that continue to persist after implementation of the ACA.

The study population was made up of all individuals who reported past year misuse of prescription pain relievers (PPR), heroin (HO), or both heroin and PPR (H+PPR). The population included insured individuals between the ages of 18-64, to focus on the perceived barriers of individuals most likely to have obtained insurance as a result of the ACA.

2.2.2 Outcome Variables

The dependent variables in this study were four binary indicators (yes/no) for perceiving a readiness, financial, structural, or stigma-related barrier to accessing initial or additional treatment for SUD within the past 12 months. Membership in each barrier category was assigned from 11 responses to the question "Which of these statements explain why you did not get the treatment or counseling you needed for your use of [*substance*]?".[72] Responses used to assign barrier categories were similar to those used in previous studies, [21,37,73] these barriers are described in detail in Supplemental Table 2.1. Participants who responded yes to at least one of the responses assigned to a barrier were categorized as having perceived that barrier in the past 12 months.

2.2.3 Independent Variable

Type of opioid misuse was assigned to all respondents who reported "time since last used heroin" or "most recent pain reliever misuse" during the last 12 months and included three categories: individuals who reported use of heroin only (HO, N=127), individuals who only reported misuse of prescription pain relievers (PPR, N=5,580), and individuals who reported misuse of both heroin and prescription pain relievers (H+PPR, N=388).

2.2.4 Covariates

The theoretical framework for this study was based on Ronald Anderson's Behavioral Model of Health Services Use.[76,77] This model theorizes that an individual's use of healthcare services is a function of: the predisposition of the individual to use the services, an individual's ability to secure services; and the individual's need for such services.[76] Covariates chosen to represent the predisposing, enabling, and need factors that make up Anderson's model were selected based on previous literature.[12,78,79] <u>Predisposing characteristics</u> include "biological imperatives" and social factors that represent family relationships and status in society.[78] Predisposing characteristics included in the current study were age in years (18-25/26-34/35-49/50-64), sex (male, female), race/ethnicity (Non-Hispanic White/Non-Hispanic Black or African American/Non-Hispanic Asian/Hispanic/ other (including: Non-Hispanic native American or AK native, Non-Hispanic native HI or other pacific islander, and non-Hispanic more than one race)), sexual identity (heterosexual/ lesbian, gay, or bisexual), and education level (less high school or high school grad/some college, associates, or college graduate).

Enabling factors reflect financial and organizational factors that may enable service utilization.[78] These included: total family income (≤ $20,000/ >$20,000), urbanicity (large metro/small metro/non-metro), insurance type (Medicaid/private/other (e.g., TRICARE, CHAMPUS, CHAMPVA, VA, military, Medicare, or "covered by insurance-type other")), and survey year (2015/2016/2017).

The need factors embody the perceived need for health services and the evaluated need (as diagnosed by a clinician). These included severe psychological distress as indicated by past year psychological distress measured by the K6 scale (yes (≥13)/no(<13)), self-reported health (excellent, very good, good/fair or poor), past year injection drug use (IDU) (yes/no), and additional SUD. The K6 scale is a measure of how often a respondent experienced symptoms of psychological distress (e.g., nervous, hopeless, restless, depressed, worthless, or run-down) during the past 12 months.[72] Those with a score of 13 or greater were classified as having severe psychological distress in the past 12 months.

Additional SUD was the total sum of all of SUD reported by the individual. For example, if an individual reported alcohol use disorder and cocaine use disorder, his/her number of additional SUD would be 2. All SUD were logically assigned based on whether the respondent met the criteria as defined in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV).[72]

2.2.5 Ethical Considerations

Any analysis of publicly available secondary data, where information is recorded by the investigator in a manner that subjects cannot be identified (either directly or through identifiers) is considered exempt by the Virginia Commonwealth University School of Medicine Institutional Review Board.[80]

2.2.6 Analytic Strategy

All data analyses were performed using SAS 9.4 (SAS Institute Inc, NC). Analyses accounted for the complex survey design of the NSDUH, and pooling of data for three years was accounted for by dividing the weight from 2017 data by three.[72] Pearson Chi-square analyses were calculated to evaluate the association between predisposing, enabling, and need characteristics by type of opioid misuse. Bivariate logistic regression analyses were performed to assess the unadjusted association between the type of opioid misuse and all theoretical covariates with each of the perceived barriers to accessing SUD treatment (Supplemental Table 2.2). Multivariate logistic regression models were used to assess the association between type of opioid misuse and each perceived barrier, adjusting for all covariates (age, sex, race/ethnicity, sexual identity, education level, total family income, urbanicity, insurance type, survey year, self-reported health, severe psychological distress, past year IDU, and additional SUD).

2.3 Results

2.3.1 Study cohort

Table 2.1 reports the characteristics of the study population by type of past year opioid misuse. The number of individuals from each survey year was evenly distributed, with 34.5%, 34.3% and 31.3% in 2015, 2016, and 2017, respectively. The overall population was predominantly male (53.4%), white (69.6%), heterosexual (89.4%), and evenly distributed among the four age groups. The majority of the population had some college or graduated from college (62.6%), reported a total family income of less than $20,000 (78.4%), and lived in a large metropolitan community (56.9%). Nearly two-thirds (64.0%) reported having private insurance, while just over a quarter reported having Medicaid (27.3%). Half reported having good/fair/poor health (49.8%), nearly a third reported severe psychological distress (31.7%) and 12.3% reported past year IDU. Although the majority of participants reported no additional SUD (67.7%), nearly a third (32.3%) reported at least 1 additional SUD.

2.3.2 Sociodemographic characteristics by type of opioid misuse

The majority of the 6,095 insured adults reporting past year opioid misuse were PPR users (91.6%), followed by H+PPR users (6.4%) and HO users (2.1%). The proportion of males was significantly lower for PPR users (52.4%) compared to HO (67.4%) and H+PPR users (64.5%). Some college education was significantly more prevalent among PPR users (63.8%) compared to HO (44.2%) and H+PPR (51.1%) users, and the proportion earning less than $20,000 was significantly higher in HO (56.4%) compared to PPR (20.0%) and H+PPR (33.6%) users. In addition, two-thirds of PPR users (66.6%) were on private insurance, compared to only a third of HO (33.7%) and H+PPR users (35.0%), and the proportion of PPR users on Medicaid (24.8%) was nearly half that of HO (58.3%) and H+PPR (55.7%) users. The proportion of HO reporting fair/poor health (71.9%) was significantly higher compared to PPR (48.9%) and H+PPR (56.1%) users, and fewer PPR users reported severe psychological distress (30.4%), in contrast to HO (42.5%) and H+PPR (49.1%) users. Further, past year IDU was significantly more prevalent among HO (61.4%) and H+PPR (70.2%) users compared to PPR users (7.6%), and the prevalence of 1 additional SUD (32.5%) or 3 additional SUDs (10.6%) were significantly higher in H+PPR users as compared to HO (17.7%, 2.7%) and PPR users (22.9%, 2.1%).

The majority of the 244 respondents reporting at least one perceived barrier to accessing treatment for SUD were PPR users (70.4%), followed by H+PPR users (25%), and HO users (4.5%). Figure 2.1 illustrates the proportion of perceived barriers by type of opioid misuse among individuals reporting at least one perceived barrier. Half (50.5%) of the HO users reported a financial barrier, followed by stigma-related barriers (39.8%), readiness barriers (30.9%), and less than a quarter (23.4%) perceived a structural barrier. In contrast, PPR users most often perceived readiness (45.5%) and structural (41.2%) barriers, followed by financial (31.6%) and stigma-related (29.5%) barriers. Similar to the PPR group, the most perceived barriers among H+PPR were readiness (50.9%) and structural (44.9%) barriers, while less than a third reported financial (31.2%) and stigma-related barriers (30.6%).

2.3.4 Multivariable logistic regression of perceived barriers to treatment

2.3.4a Type of opioid misuse and perceived treatment barriers

Table 2.2 presents results from the multivariable logistic regression analysis of the adjusted association between type of opioid misuse and four perceived berries to assessing treatment. Type of opioid misuse was significantly associated with perceiving a readiness, structural, and stigma related barrier. Compared to individuals who only reported misuse of PPR, individuals reporting misuse of both H+PPR were at increased odds of perceiving a readiness (aOR=2.80, 95% CI=1.08-7.27), structural (aOR=3.27, 95% CI=1.26-8.46), or stigma-related (aOR=3.98, 95% CI=1.42-11.21) barrier to accessing treatment for SUD.

3.3.4b Covariates of interest associated with perceived barriers

Severe psychological distress. Individuals who reported severe psychological distress in the past year (as indicated by the K6 scale score $\geq$ 13) had an increased likelihood of perceiving all four barriers to accessing SUD treatment; reporting near triple the odds of perceiving a readiness (aOR=3.02, 95% CI=1.55-5.90), financial (aOR=2.45, 95% CI=1.05-5.70), structural (aOR=2.90, 95% CI=1.53-5.49), or stigma-related (aOR=2.90, 95% CI=1.42-5.92) barrier, compared to those not reporting severe psychological distress in the past year.

Additional SUD. Each additional SUD diagnoses increased the odds of perceiving a readiness (aOR=1.60, 95% CI=1.29-1.98), financial (aOR=1.25, 95% CI=1.08-1.44, or structural (aOR=1.34, 95% CI=1.11-1.62) barrier to accessing SUD treatment.

2.4 Discussion

Barriers to accessing treatment for SUD persist following nationwide implementation of the ACA in 2014. Among individuals reporting past year opioid misuse, 3.7% reported experiencing a barrier to accessing treatment for SUD. The findings of this study demonstrated that the association between perceiving barriers to accessing treatment and type of opioid misuse varied, and individuals reporting misuse of H+PPR during past year were more likely to perceive readiness, structural, and stigma-related barriers to care as compared to those reporting misuse of PPR only during the same period. Further, the results of this study identified two need characteristics (additional SUD and severe psychological distress) that increased the likelihood of perceiving each of the four barriers to accessing SUD treatment.

2.4.1 Misuse of H+PPR increased odds of experiencing readiness, structural, and stigma-related barriers

While past studies have focused on the association between type of opioid misuse and treatment outcomes,[81–84] this is the first study to investigate the relationship between type of opioid misuse and perceived barriers to accessing treatment for SUD. Misuse of H+PPR significantly increased the odds of perceiving readiness, structural, and stigma-related barriers compared to misuse of PPR only.

Readiness Barriers. Those misusing H+PPR had more than double the odds of perceiving a readiness barrier compared to those reporting PPR misuse alone. Among all substance users, perceived readiness to stop substance use is the most common reason for not engaging in treatment for SUD.[85] In Baltimore, over two-thirds (69.6%) of opioid overdose survivors reported not seeking treatment because they were not ready to stop substance use.[85] This is consistent with how individuals with OUD view their "need" for treatment; between 2015-2016 only 31.5% of individuals with OUD received treatment, and only 13.6% perceived the need for such treatment.[86] One possible explanation for the increased likelihood of readiness barriers in H+PPR compared to PPR alone is the increased severity of OUD among the H+PPR group compared to the PPR group. Studies report only 3.6-4.2% of individuals who misuse PPR start to use heroin,[87] suggesting that transitioning to heroin use appears to be part of the progression of addiction in a subgroup of nonmedical users of PPR.[87] Further, individuals with HO or H+PPR addiction are more likely to engage in co-occurring substance use, and be diagnosed with SUD in addition to OUD.[83,88] Thus, it might be possible that the stronger addiction severity in the small subgroup of H+PPR may influence their readiness to access SUD treatment. Very few studies have investigated how type of opioid misuse may influence readiness barriers to accessing SUD treatment. Future research should assess how type of substance use influences the reasons that opioid users are not ready for treatment, to improve efforts to motivate these individuals to engage in SUD treatment.

Structural Barriers. Individuals in the H+PPR group were three times more likely to perceive a structural barrier compared to those with PPR misuse only. One potential explanation for the increased odds of perceiving structural barriers is inadequate coverage for services; as over half of the H+PPR group had Medicaid compared to the PPR group (55.7% vs. 24.8%). However, although Medicaid recipients in the current study had an increased likelihood of experiencing a structural barrier compared to those with private insurance, this relationship was not statistically significant. This is surprising given the findings of previous studies, which reported that individuals with Medicaid were more likely to be turned away from care compared to those with employer-sponsored coverage,[89] and that SUD treatment facilities were not adequately prepared for an influx of patients with Medicaid.[60] However, the findings of the current study should also not be used to fully dismiss inadequate coverage of SUD services as a potential explanation, as the analysis could not account for the state-by-state differences in SUD service coverage for Medicaid recipients.

In addition, it is also possible that the increased severity of addiction in the H+PPR group would require more intensive SUD treatment that is often unavailable due to insurance restrictions on SUD services. The American Society of Addiction Medicine report that patients who engaged in co-occurring substance use might need additional supervision to consider methadone or inpatient/residential SUD treatment for additional monitoring during withdrawal.[90] Yet even after the implementation of the ACA these treatment options present challenges. For example, methadone can only be legally prescribed to patients who are able to make daily visits to an opiate treatment program, which limits accessibility to individuals who work or live in rural areas far away from the treatment program.[91] Further, these options may not be covered by insurance, as many states restrict coverage of methadone and residential services for individuals on Medicaid.[60,92] The findings of the current study provide additional support for the findings of previous researchers, who have concluded that implementation of the ACA has not altered the tiered nature of health care access.[89] State and local governments should work to decrease limits placed on SUD treatment, and increase the number of facilities accepting Medicaid.

Stigma-related Barriers. Individuals in the H+PPR group had nearly four times the odds of perceiving a stigma-related barrier compared to those reporting PPR misuse. Among individuals with any type of SUD, 10-23% report stigma as a barrier to seeking SUD treatment,[66] reporting stigmatization from healthcare providers,[65,66,93,94] family and friends, and self-stigma (e.g., feelings of shame).[66,93] Surprisingly, race/ethnicity and urbanicity, often reported as risk factors for stigmatization, were not significantly different among the groups.[95] One explanation for the increased likelihood of H+PPR to perceive barriers due to stigma compared to the PPR group may be related to the disproportionately high number of individuals who inject drugs in the H+PPR group compared to the PPR group (70.2% vs. 7.6%). Individuals who inject drugs often report negative interactions with healthcare professionals,[96,97] reporting that injecting carries a higher stigma than other methods of drug delivery like smoking or ingesting.[98] Further, studies show that clinicians often admit to stigma specifically concerning individuals who inject drugs.[99] Thus, the H+PPR group may feel more susceptible to privacy concerns while receiving treatment, and consequently may want to avoid a daily visit that might draw negative attention from others.[95]

It is difficult to assess the consistency of these findings with those of previous literature, as no previous studies have explored the association between type of opioid misuse and perceived stigma.

2.4.2: Covariates of interest associated with perceived barriers to accessing SUD treatment

Additional SUD. Each additional diagnosis of SUD increased the odds of experiencing readiness, financial, and structural barriers. Between 77.2-93.3% of individuals with OUD report an additional SUD,[100,101] and previous literature shows how detrimental additional SUDs can be on treatment outcomes, often increasing the risk of dropout.[102–104] It is not surprising that those with additional SUD are more likely to perceive a readiness barrier, as individuals with additional SUD are less likely to seek out treatment or end current substance use compared to individuals using opioids alone. In addition, as facilities are recommended to provide opioid-misusing individuals with co-morbid SUD with an individualized approach, these findings may indicate a continued demand for programs to meet this need.

Mental Health Severity. Mental health severity was the only characteristic that was significantly associated with the increased likelihood of perceiving all four barriers to accessing treatment for SUD. This is an important finding, as comorbid psychiatric disorders are highly prevalent, reported in 64.3-68.4% of individuals with OUD[100,105] and 78-78.5% of individuals receiving treatment for OUD.[103,106] These findings are supported by the results of previous studies which report that individuals on Medicaid are less likely to receive SUD treatment. In 2014 a study of Medicaid clients with OUD found that those with severe mental disorders, such as schizophrenia and/or bipolar were far less likely to receive medicated assisted treatment compared to individuals without those diagnoses.[107] These findings are also consistent with a previous analysis using the NSDUH data from 2008-2014, in which a high proportion of individuals with mild to serious mental illness and comorbid OUD reported not receiving needed SUD treatment; with over half reporting a perceived barrier due to affordability, and close to a third citing barriers due to stigma or lack of readiness.[108] The consistency between the results of the current study and previous literature may imply that changes following the ACA have not completely addressed treatment access barriers specific to those with severe mental illness. Further research is needed to understand how to address these barriers to help individuals with comorbid mental illness successfully participate in SUD treatment.

2.4.3 Strengths and Limitations

The NSDUH is the nationally representative source of annual estimates of drug use and mental illness among civilian members of the noninstitutionalized population in the United States.[109] This survey uses tools to assure privacy and confidentiality of all participant's responses, to increase the likelihood of honest reporting of illicit drug use and illegal activities. The response rate for each of the three years included here were relatively high, ranging between 69.7- 67.1%.[110–112] In addition, this study was strengthened by the use of the Behavioral Model of Health Services Use, making the findings easier to adapt to support the design of community-based interventions that could address the disparities in accessing SUD treatment faced by the OUD community.

These findings are also subject to several limitations. This survey is cross-sectional and not longitudinal; inferences for individuals cannot be made over the three-year period and direction of effect and causality cannot be determined. Additionally, questions about the use of illegal substances may discourage participant's candor, thus responses could be influenced by social desirability bias. Further, responses may be subject to recall bias, as many questions required participants to recall events taking place over the past 12 months.

The current study did not account for additional factors associated with stigma related barriers to treatment, such as pregnancy, parenthood, marital status, and Human Immunodeficiency Virus status. [21,66] Future investigation into this relationship should consider inclusion of these factors to expand on the work of this analysis.

Interpretation of these findings are limited to individuals with additional SUD, and should not be generalized to opioid-misusing individuals who may engage in the use of multiple substances but do not have an additional SUD. Additional information on these individual's patterns of substance use may be beneficial to the development of interventions for increasing treatment access. Future research should more accurately capture patterns of co-occurring substance use in order to better understand the relationship between patterns of substance use and perceived barriers to accessing SUD treatment.

Finally, generalizability of these findings are limited to the civilian, noninstitutionalized population of the United States. Although this only excludes approximately 3% of the U.S. population,[114] it likely excludes several subgroups considered to be at increased risk for OUD, including prisoners, military personnel, and the homeless. Additionally, the interview can only be conducted in English and Spanish, which excludes all non-English and Spanish speakers.[114] Exclusion of these groups may not only limits the generalizability of findings, but also result in the underestimation of the true prevalence of less commonly used drugs, including heroin.[114]

2.5 Conclusions

This study highlighted that different types of opioid misuse could be associated with perceived barriers to accessing treatment, and the association could be further impacted by severe psychological distress and additional SUD. The shift in opioid misuse from PPR to heroin and synthetic opioids has important implications for the development of effective treatment strategies for individuals with SUD. Further work is needed to better understand how these specific treatment barriers might influence type of opioid misuse.

Chapter 3. The influence of patterns of polysubstance use on perceived barriers to accessing treatment for substance use disorder

Abstract

Background: Opioid users engaging in polysubstance use (PSU) are at increased risk of overdose and mortality, yet little is known about the relationship between PSU and barriers to accessing substance use disorder (SUD) treatment. This study investigates the association between PSU classes and perceived readiness, financial, structural, and stigma-related barriers to accessing SUD treatment.

Methods: Data were included from the 2015-2017 National Survey on Drug Use and Health. Latent Class Analysis (LCA) determined patterns of PSU in 6,095 insured adults reporting past-year misuse of prescription pain relievers (PPR), heroin, or both. Multivariate logistic regression assessed the relationship between PSU classes and perceived barriers to accessing SUD treatment, adjusted for age, sex, race, sexual identity, education, total family income, urbanicity, insurance, survey year, self-reported health, severe psychological distress, average daily cigarette use, and accounting for complex survey design.

Results: LCA identified three patterns of past-year PSU: 1) Heroin injectors with high PSU (n=473, 7.8%), 2) PPR users with low PSU (n=4,000, 26.6%), and 3) PPR users with high PSU (n=1,622, 65.6%). Heroin injectors with high PSU faced significantly greater odds of perceiving readiness (aOR=3.11, 95%CI=1.43-6.77), structural (aOR=2.42, 95%CI=1.22-4.79), and stigma-related (aOR=3.13, 95%CI=1.31-7.48) barriers to accessing SUD treatment compared to PPR users with low PSU.

Conclusions: These findings highlight a subpopulation of opioid users at increased odds of perceiving readiness, structural, and stigma-related barriers to accessing SUD treatment. Targeted public health efforts are necessary to decrease perceived barriers to accessing treatment for SUD among opioid injecting individuals engaging in heavy PSU.

3.1 Introduction

Polysubstance use (PSU) is often defined as the concurrent or simultaneous consumption of more than one substance over a specified period of time.[115] Many studies consider the combined or subsequent use of both licit (alcohol, tobacco), and illicit (cocaine, methamphetamines, marijuana, sedatives, etc.) substances as PSU. PSU is increasingly being recognized as a problem by the public health community, due to increases in the number of multi-drug combination deaths. Jones et. al reported an increase in the rate of benzodiazepine involvement in opioid overdose deaths, from 18.0% in 2004 to 31.0% in 2011,[116] and Kandel et al., reported an increase in deaths resulting from a combination of prescription opioids with at least one additional psychoactive substance (benzodiazepines, antidepressants, heroin, alcohol, and cocaine) from 44.3% in 2002-2003 to 57.9% in 2014-2015.[117] In addition, PSU increases an individual's risk of a variety of adverse health outcomes, including: psychopathology,[118,119] chronic health conditions,[118] risk-taking behaviors,[119] criminal activity,[120,121] and nonfatal overdose.[122–124]

3.1.1 PSU use among opioid-misusing individuals

The increase in opioid-related fatalities over the past two decades may be partially explained by deaths resulting from the combination of opioid use and PSU.[117] Prevalence of PSU among opioid-misusing individuals is fairly high. Approximately 53-89.6% of opioid-misusing populations report PSU.[122,125–127] Opioid-misusing individuals most often report the co-use of tobacco,[120,128] alcohol,[129–133] cannabis,[130,132,133] cocaine,[122,127,131] benzodiazepines,[130–132] and methamphetamines[127]. While the high prevalence of PSU among opioid users may be due to an increased likelihood of opioid use among individuals with substance use disorders (SUD) (e.g. alcoholism, etc.), it is most likely due to the use of certain substances (i.e., cocaine, benzodiazepines, methamphetamines) to enhance opioid intoxication, or alleviate the symptoms of opioid withdrawl.[134–136]

Opioid-misusing individuals with PSU are less responsive to treatment for SUD than individuals without PSU disorders.[120,137] Many opioid-misusing individuals entering SUD treatment report co-occurring use of alcohol, marijuana, cocaine, and benzodiazepines,[138,139] and 75-86.0% of individuals entering opiate treatment report tobacco use.[140–142] Individuals continuing PSU during SUD treatment are at increased risk of relapse[143,144] and attrition.[82,139,145–147] Further, co-occurring PSU can significantly increase the likelihood of mortality during treatment; Ries et al. reported that the majority of deaths occurring during methadone treatments are attributed to polysubstance overdoses,[128] and Lofwall et al. reported buprenorphine-related deaths most often occurred due to the concomitant use of central nervous system depressants.[128,148]

Currently, the opioid-agonist methadone demonstrates the most comprehensive evidence of efficacy in individuals with co-occurring SUDs.[149] Studies investigating outcomes of methadone administration report statistically significant decreases in PSU following treatment.[150–152] In addition, in 2015 Ries et al. reported that individuals with Opioid Use Disorder (OUD) and PSU dependence could be effectively managed in an inpatient facility that offers 24-hour medical monitoring.[128] Nevertheless, individuals engaged in PSU have the lowest likelihood of opioid treatment success.

3.1.2 Barriers to accessing treatment for polysubstance users

Compared to studies of opioid treatment outcomes, there are few that investigate the association between PSU and opioid treatment enrollment and detail the role of barriers to seeking such care. Previous studies suggest that individuals engaged in opioid use and PSU actively seek treatment for emergency and behavioral health services[125]. For example, Calcaterra et. al. reported significantly higher incidence rate ratios for opioid users and individuals reporting multiple drug use accessing behavioral and emergent health care compared to those reporting no drug use[125]. Yet few studies detail how engagement and treatment seeking behaviors might differ between those using opioids and those engaging in PSU.

Opioid users with PSU are likely to experience barriers to accessing opiate treatment programs. This could be due to lingering guidelines of past programs, where continued use of additional substances during opiate treatment programs was considered grounds for dismissal from treatment. Although the Federal Drug Administration advised against the removal of patients engaging in PSU from treatment in 2017, stating that the harm caused by untreated opioid addiction could outweigh the risks of serious side effects from PSU.[153]

Despite this recommendation, individuals with PSU may still face structural barriers to accessing the most appropriate treatment for their needs. However, state and Federal control over these types of opioid treatment decrease their accessibility. Methadone remains the most restricted OUD medication in the US,[154] which may pose structural barriers to individuals seeking treatment. Moreover, inpatient SUD programs are the least likely to be funded by private insurance and Medicaid, creating financial deterrents to seeking treatment. Although addressing these barriers is crucial to make SUD treatment available to opioid users, to date no study has examined the barriers to accessing opioid treatment faced by individuals engaging in PSU.

3.1.3 Issues defining PSU

Examining treatment outcomes in the context of polysubstance or polydrug use is difficult, as it can involve a variety of licit and illicit substance configurations, making it challenging to identify salient categories.[155] As there is currently no standardized way to account for PSU, studies use a variation of definitions, such as "multiple drugs at the same time" ,[156] or "summing the total number of substances used",[157] while other studies provided no explanation for how PSU was defined.[144,158–160] Due to the variety of configurations for the types and frequency of substance use, it is not possible to directly observe "patterns" of polysubstance use, but these patterns may be determined through the observation of related variables.[161] One method used to identify substance use patterns is latent class analysis (LCA),[162] which can define a hidden or "latent" variable within which the manifest variables are locally independent.[162] In other words, if "polysubstance use" can be defined as a latent variable, then the classes of polysubstance use are taken to represent latent types of the polysubstance use as defined by measures of substance use within the sampled population. Identification of the polysubstance use latent variable could enable a better understanding of the socio-demographic and clinical differences between substance—using subgroups, and how perceived barriers to accessing treatment for SUD may differ among these substance-using subgroups.[163]

Previous studies have used LCA to identify patterns of substance use based on the substances used,[115,120,132,155,164–169] or routes of substance administration.[123,170–174] Previous LCA have examined the relationship between PSU classes and a variety of health-related outcomes, including: risky drug use behaviors,[155,167,172] Human-immunodeficiency virus (HIV) risk behaviors,[123,170,173] psychological distress,[167] recent overdose,[174] and mortality,[165] however only two studies explored the differences in healthcare utilization and treatment.[120,155] In 2018, Lorvick et al. reported that among women using 'hard drugs' – cocaine, methamphetamines, or heroin – the heavy polydrug class had significantly higher odds of unmet physical and mental healthcare needs.[155] These findings highlight the importance of identifying barriers that may keep individuals with PSU from accessing care.

One large limitation of previous LCA characterizing patterns of PSU is a lack of generalizability, either due to the choice of population or limited inclusion of substances included in the LCA. Of the 8 previous LCA which reported patterns of PSU among opioid users,[123,132,164,165,171,173,174] only 2 use a population from the United States.[164,171] Yet the patterns of PSU among these populations are likely different to what would be observed in a nationwide population of opioid users. For instance, Kuramoto et al. performed an LCA using responses from participants reporting weekly use of heroin or cocaine in a large U.S. city,[171] and Bobashev et al. recruited heroin-using individuals from a syringe exchange program in a large U.S. city.[164]

Previous LCA are further limited in the information they provide due to variation in the substances chosen for inclusion in the LCA. Among the LCA in opioid-misusing populations, substances most often included were methamphetamines, marijuana, cocaine, and heroin.[123,132,164,165,171,175] Only half (50.0%) included misuse of prescription pain relievers (PPR)/prescription opioids and alcohol.[123,164,165,175] Very few studies included the use of benzodiazepines, barbiturates, crack, hallucinogens, ketamine, power cocaine, speedball, stimulants, tranquilizers, and inhalants.[123,132,171,175] The aforementioned limitations of previous LCA highlight gaps which may limit accurate characterization of PSU patterns, and support the need for an additional LCA to characterize patterns of PSU in a nationwide sample of opioid-misusing individuals.

The lack of consensus of the definition of PSU among opioid users limits the generalizability of previous studies that identify the barriers to seeking opioid treatment. Additionally, although past research has indicated poorer treatment engagement among polysubstance users, no study has yet examined the relationship between patterns of substance use and barriers to accessing treatment for SUD among opioid-misusing individuals. The objectives of this study were twofold: 1) identify patterns of past year PSU among a nationally representative sample of opioid-misusing adults in the U.S., and 2) evaluate the association between membership in PSU classes and perceived readiness, financial, structural, and stigma-related barriers to accessing treatment for SUD.

3.2 Methods

3.2.1 Data Source and Study Design

This study utilized data from the 2015-2017 National Survey on Drug Use and Health (NSDUH), a survey sponsored by the Substance Abuse and Mental Health Services Administration, within the U.S. Department of Health and Human Services.[176] The survey is administered to the non-institutionalized civilian population aged 12 and older, collecting detailed information on the use of alcohol, illicit drugs, mental illness, SUDs, utilization of behavioral health treatments, and treatment barriers for behavioral health conditions and treatments.[73]

The NSDUH uses a stratified multistage area probability sample designed to represent each of the 50 States and the District of Columbia. Each sampled individual was scheduled for a 60-minute interview conducted in a private area of the home on a laptop provided by the field investigator. To increase cooperation and honest reporting about sensitive topics, the NSDUH employs methodological practices aimed at increasing the accuracy of self-reports, using a combination of computer-assisted personal interviewing and audio computer-assisted self-interviewing, and by providing assurances that individual responses will remain confidential.[177] Upon completion of a full interview, each respondent is given $30.[178]

3.2.2 Study Population

Similar to Chapter 2, this study used publicly available data from the NSDUH from 2015-2017, which represents the period after the Patient Protection and Affordable Care Act (ACA) was implemented throughout the U.S. Inclusion in this study was also limited to insured adults between the ages of 18-64, who reported past year use of heroin, past year misuse of PPR, or both.

3.2.3 Measures

Past year Substance Use. Indicator variables included in the LCA model were binary indicators for the past year use of 12 substances (based on the question "Most recent use of [*substance])*, and binary measures reporting past year injection of substances (based on the question: "Time since last used needle to inject [*substance*]?").

The substances assessed included: binge alcohol use, (defined as drinking 5 or more drinks on the same occasion for males and four or more drinks on the same occasion for females), crack, cocaine, hallucinogens (LSD, PCP, Ecstasy, DMT/AMT/Foxy, Ketamine, and Salvia), heroin, inhalants, methamphetamines, marijuana, PPR, sedatives, stimulants, and tranquilizers. Injection of four substances was also assessed, including: cocaine, heroin, methamphetamines, or "other" substances.

Binge alcohol use was selected to distinguish between less harmful occasional alcohol use and more problematic binge drinking. As a recent study reported that the prevalence of opioid misuse increases with the frequency of binge drinking,[179] it is reasonable to expect that binge drinking adults would be at greater risk for an overdose due to an interaction between alcohol and opioids.

All substances selected for inclusion in the current LCA were also included in previous studies for classifying subtypes of PSU. Surprisingly, of the 8 previous studies characterizing PSU in opioid-misusing populations, none included tobacco use as an indicator variable, despite the high prevalence of tobacco use among opioid users.[128] This is likely because the high prevalence of tobacco use among opioid-users would not be a distinguishing factor between classes. To ensure comparison of our classes to classes of other studies, tobacco use was not included as an indicator variable in the LCA, but instead was accounted for in the final regression analyses.

Use of PPR, stimulants, tranquilizers, and sedatives were only included if the respondent indicated past year misuse, defined as: Use of [*medication*] in a way the doctor did not direct, including: using it without a prescription, using it in greater amounts, more often, or longer, or using it in any other way a doctor did not direct.[178] These categories are created by the NSDUH to represent a combination of prescriptions commonly misused. Further information on substances included in the prescription drug categories is available in Supplemental Table 3.1.

Sociodemographic Variables. Covariates were selected to match the model previously described in Chapter 2, and included; sex (male/female), age (18-25/26-34/35-64), race/ethnicity (Non-Hispanic White/Non-Hispanic Black, African American/Non-Hispanic Asian/Hispanic/Other), sexual identity (heterosexual/lesbian, gay, or bisexual), education level (less high school or high school grad/some college, associates, or college graduate), total family income (≤ $20,000/ >$20,000), urbanicity (large metro/small metro/non-metro), type of health insurance (Medicaid/Private/ other (e.g., TRICARE, CHAMPUS, CHAMPVA, VA, military, Medicare, or "covered by insurance-type other")), survey year (2015/2016/2017), severe psychological distress as indicated by the K6 scale (yes (≥13)/no(<13)), self-reported physical health (excellent, very good, good/fair or poor), past year tobacco use (defined as any reported past year use of cigarettes, cigars, pipes, or smokeless tobacco), and average number of cigarettes used per week (≥1-1 per day/2 to 5 per day/6 to 15 per day/16 to > 35 per day).

Barriers to SUD Treatment. The dependent variables for this study were perceived readiness, financial, structural, or stigma-related barriers to accessing initial or additional treatment for SUD within the past 12 months. Additional information on these barriers was previously described in Chapter 2, and is also available in Supplemental Table 2.1. Data were collected from 11 responses to create the four dichotomous barrier variables (yes/no), as demonstrated in previous studies.[29,37,73] Respondents who said yes to one or more of the statements asked in any group were categorized as having perceived that barrier in the past 12 months.

3.2.4 Statistical Analysis

LCA were conducted using Mplus 7.4, and multivariate regression analyses were conducted using SAS 9.4. The statistical analysis for this project occurred in three steps: 1) LCA was used to identify distinct classes of polysubstance use based on the unweighted frequency of past year substance use in the population, 2) individual cases were assigned to each class of polysubstance use, and 3) multivariate logistic regression was used to assess the association between predicted polysubstance class membership and perceived barriers to accessing treatment for substance use disorder.

Step 1: Latent Class Analysis. LCA was utilized to identify hidden subpopulations of PSU that reflected distinct subgroups of substance use in a population of opioid-misusing individuals. LCA is unique from other “mixture model” types of cluster analysis as it is intended for use with categorical data.[180] This is likely one of the reasons so many researchers have used

LCA to describe PSU, as substance use is typically measured at the categorical level.[180] The LCA model posits the existence of two or more unobservable population subtypes, or *latent classes*.[180] A *latent variable* is measured indirectly by means of two or more observed variables within a population.[163] Figure 3.1 illustrates a hypothetical latent variable. In Figure 3.1 an oval represents the latent variable, three squares (X_1, X_2, X_3) represent the observed indicator variables used to measure the latent variable, and three circles (e_1, e_2, e_3) represent the error component associated with each indicator variable. Note the arrows in this diagram show the causal flow stems from the latent variable to the indicator variable; this illustrates the concept that observed indicator variables measure latent variables, but they do not cause the latent variable.[163]

In LCA the latent variable is categorical, or made up of classes, and each class has a set of probabilities for various responses to each indicator variable. The first equation in latent class modeling expresses the probability of observing response pattern y defined by:

$$P(Y=y) = \sum_{c=1}^{C} p\,(X=c) \ \text{x} \ p(Y=y/X=c)$$

X represents the categorical latent variable, c is a specific latent class among C classes, y is the realization of the vector Y measuring the response patterns ($X \rightarrow Y$), p(X=c) represents the *latent class probability*, or the probability of belonging to class c, and p(Y=y/X=c) is the *conditional response probability*, or the conditional probability of having response pattern y, given that X belongs to specific class c.[181] To illustrate, Figure 3.2 provides a schematic representation of a 3 class model. In Figure 3.2, the circle at top represents a case selected from the population at random, X represents latent classes 1-3, and S_x are three indicator variables. The probability of being in latent class 1 is represented by p(X=1), and p(Y=1/X=1) is the conditional probability of reporting indicator 1 for latent class 1. For example, if $p(X=1) = 0.4$ and $p(Y=1/X=1) = 0.2$, then an individual chosen at random would have a 40% chance of belonging to latent class 1, and a 20% chance of reporting indicator 1 given membership in latent class 1.

In the current study, LCA was performed using 16 indicators, which reported the unweighted prevalence of past-year substance use for: binge alcohol use, crack, cocaine, hallucinogens, heroin, inhalants, methamphetamines, marijuana, PPR, sedatives, stimulants, tranquilizers, and routes of substance administration (use of a needle to inject methamphetamines, cocaine, heroin, or other drugs).

An important assumption of the LCA model is the assumption of local independence, or that conditional on the latent variable, the observed variables are independent.[163] This assumption is visually represented in Figure 3.1; which shows that each indicator variable is a function of the latent variable and an error term, and only connected through the latent variable. Thus, if each indicator conditioning on the latent variable is independent, then the joint probability of all the elements making up the y vector for latent class c can be found by multiplying the individual probability parameters corresponding to a particular latent class. This leads to the second equation for LCA, which expresses the probability of observing the response pattern as a function of the latent class probabilities and the conditional response probabilities.

$$P(Y=y) = \sum_{c=1}^{C} p\,(X=c) \times \prod_{k=1}^{K} p(Y_k=y_k/X=c)$$

In this equation, K represents the number of mutually independent indicator variables given the class, and the parameters of this model can be estimated through implementation of a maximum likelihood method.

Step 2: Case assignment to latent classes. Membership in a latent class is determined through an individual's *posterior probability* of belonging to class c given observed response pattern y. Posterior probabilities can be derived using Bayes' theorem:

$$P(X=c/Y=y) = \frac{p(Y=y/X=c) \times p(X=c)}{p(Y=y)}$$

Here, posterior probabilities are the product of the latent class probability p(X=c) and the conditional response probability p(Y=y/X=c) over the probability of a particular response pattern p(Y=y). Using posterior probabilities, cases are assigned to classes of the latent variable using *modal assignment*, where each case is assigned to the class with the largest posterior probability. Modal assignment is optimal, as it produces the smallest classification errors,[181] and is particularly beneficial in instances where there may be little or no information in the item response probabilities. In the context of the current study, the probability of PPR misuse alone would be expected to contribute little to class assignment, due to the high prevalence in the population, thus membership would be expected to rely more heavily on the latent class probability.

Assessing LCA model fitness. The latent class model will be performed for multiple classes, thus it is important to choose the model which has the best empirical fit. As there is currently no standardized way to assess LCA model fitness, researchers suggest using a variety of statistical indicators to determine fitness. The current study utilized four evaluative indicators to determine which number of classes best fit the model, including: Sample-size adjusted Bayesian Information Criterion (BIC_{SS}), entropy, Lo-Mendell-Rubin likelihood ratio test (LRT), and the parametric bootstrapped likelihood ratio test (BLRT).

Even using an optimal method for assigning class membership, it is possible that some individuals may be assigned to the wrong class. For this reason, it is important to assess the separation between the classes, or how well the classes can be distinguished based on existing empirical information.[181] This can be done by measuring how much membership of posterior probabilities deviate from uniform using entropy, a standardized measure of the accuracy of placing participants into classes based on their model-based posterior probabilities.[163,182] Values for entropy range from 0 – 1, and larger values indicate better latent class separation and subsequently lower class error.

The sample size adjusted Bayesian Information Criterion was created to aid model selection by penalizing the number of factors in a model.[163,183] Models with the lowest BIC_{SS} are considered to have the best fit.[182] The LRT and BLRT are used to compare nested latent class models. LRT uses an approximation to the likelihood ratio test distribution, and BLRT also uses a likelihood-based technique, p-values for both tests can be used to compare the increase in model fit between the *k-1* and *k* class models.[183,184]

Step 3: Multivariate regression analysis. After determining the model with the best empirical fit, results of the LCA were exported to SAS 9.4. Chi-square analyses were used to determine differences in sociodemographic characteristics by class. Association between the PSU classes and each of the perceived barriers to accessing treatment for SUD (readiness, financial, structural, stigma-related) were assessed using multivariate logistic regression, adjusting for age, sex, race/ethnicity, sexual identity, education level, total family income, urbanicity, insurance type, survey year, self-reported health, severe psychological distress, and average cigarette use per day. All SAS analyses accounted for the complex sampling design of the NSDUH. Evaluative indicators used to assess regression model fit included the Log Likelihood (LL), Akaike Information Criterion (AIC), and adjusted R^2.

3.3 Results

3.3.1 Study Cohort

There were 6,095 insured respondents reporting past year opioid misuse. The cohort was evenly distributed among the age groups, with 26.0% aged 18-25, 24.1% aged 26-34, 27.9% aged 35-49, and 22.1% aged 50-64. Respondents were predominantly male (53.4%), white (69.6%), and heterosexual (89.4%), with some college or a college degree (62.3%), a total family income above $20,000 (78.4%), and lived in a large metro area (56.9%). The majority reported having private insurance (64.0%), over a quarter reported Medicaid (27.3%). Half of the respondents reported very good/excellent health (50.2%), yet nearly a third reported severe psychological distress occurring within the past year (31.7%).

The majority of respondents reported past year misuse of PPR (97.5%), far fewer reported heroin use (8.4%). The majority of respondents reported use of tobacco (60.8%), while nearly half reported binge alcohol and marijuana use (53.1% and 56.4%, respectively). Tranquilizers were the second most often misused prescription medication (26.8%), followed by stimulants (20.4%), while few respondents reported misuse of sedatives (5.6%). Cocaine was the most often reported illicit substance (18.0%), followed by hallucinogens (16.0%), while very few reported past year misuse of methamphetamines (6.3%), crack (3.6%), and inhalants (4.0%). Approximately 12.3% of the sample reported any type of injection drug use within the past year, Heroin injection occurred most frequently (4.5%), followed by injection of other drugs (2.6%), methamphetamines (2.3%), and cocaine (1.6%).

3.3.2 Number of Classes

Fit statistics for classes 2-6 are described in Table 3.1. The three-class model was selected based on high entropy (0.837), and significant p-values from both the LMR and the

BLRT. The 3-class model was also deemed preferable to the 4-class model due to ease of class interpretability and theoretical considerations.

3.3.3 Characteristics of the three-class model

Table 3.2 reports the response probabilities for endorsing each type of substance use, categorized by most likely class membership for a three-class model, and Figure 3.3 illustrates the latent classes of past year PSU. Class 1 was deemed the "Heroin injectors with high PSU", as individuals in this class had the highest probability of reporting illicit (heroin (89.5%), cocaine (54.4%), crack (33.3%), methamphetamines (37.0%)) and injection (cocaine (19.1%), heroin (57.3%), methamphetamines (27.6%), and other (29.7%)) substance use compared to other classes.

Class 2 ("PPR users with low PSU"*)* contained the largest proportion of the study sample (n=4000, 64.2%), and was composed of individuals reporting misuse of PPR (99.4%), who reported moderate use of licit/near licit substances (binge alcohol (42.6%), marijuana (37.5%)), low use of illicit substances, and almost no injection substance use.

Class 3 (27.9% of the sample) was the "PPR with high PSU" class, made up of individuals misusing PPR (99.8%) who also reported disproportionately high misuse of prescription medications (tranquilizers (52.6%), stimulants (50.2%)), licit/near licit substances (binge alcohol use (80.9%), marijuana (95.6%)), and several illicit substances (cocaine (46.6%), hallucinogens (47.8%)), but little to no injection substance use.

3.3.4 Comparison of sociodemographic characteristics by latent class membership

Table 3.3 reports sociodemographic characteristics of the study population by type of latent class PSU. The age distribution was significantly different in each class. *Heroin injectors with high PSU* were closer to middle age, with 33.5% between 26-34 and 26.5% between 35-49, while the *PPR users with high PSU* had a higher proportion of older individuals, with 26.5% between 50-64 and 32.0% between 35-49. In contrast, the *PPR users with low PSU* had a disproportionately higher prevalence of younger respondents, as 51.7% reported being 18-25. In addition, while males were more prevalent among the *Heroin injectors with high PSU* (65.9%) and *PPR users with high PSU* (64.2%), females made up over half (51.1%) of the *PPR users with low PSU*.

PPR users with low PSU and *PPR users with high PSU* appeared to be similar with respect to education level, total family income, and insurance type. Individuals in these classes were more likely to have some college (64.0%, 63.1%), report a total family income of more than $20,000 (81.6%, 75.7%), and were insured by private insurance (65.9%, 69.7%). In contrast, *Heroin injectors with high PSU* were more likely to have a lower education (51.9%), and make less than $20,000 (44.2%). Further, *Heroin injectors with high PSU* were far more likely to be Medicaid recipients (59.1%).

3.3.5 Association between latent class membership and barriers to accessing treatment for SUD

Table 3.4 reports the adjusted odds of perceiving a barrier to SUD treatment for each PSU class (odds ratios for all covariates provided in Supplemental Table 3.2). Compared to *PPR users with low PSU*, readiness barriers were significantly more likely to be perceived by both *PPR users with high PSU* (aOR=2.89, 95%CI=1.41-5.93) and *Heroin injectors with high PSU* (aOR=3.11, 95%CI=1.43-6.77). Additionally, *Heroin injectors with high PSU* also had significantly increased odds of perceiving structural (aOR=2.42, 95%CI=1.22-4.79) and stigma-related barriers (aOR=3.13, 95%CI=1.31-7.48) compared to *PPR users with low PSU.*

3.4 Discussion

The findings of this study identified three distinct classes of PSU within a nationally representative sample of individuals reporting opioid misuse in the past year: (1) *Heroin injectors with high PSU*, (2) *PPR users with low PSU* and (3) *PPR users with high PSU*. The type of substances most often misused varied by class: whereas *PPR users with low PSU* only reported a high probability of PPR misuse, *PPR users with high PSU* were characterized by high probabilities of licit/near licit (binge alcohol and marijuana) and prescription drug misuse (tranquilizers, stimulants). In contrast, *Heroin injectors with high PSU* reported high probabilities of illicit (cocaine, crack, methamphetamines) and injection substance use, and moderate probabilities of licit/near licit (binge alcohol, marijuana) and prescription misuse (PPR tranquilizers, stimulants, and sedatives). The likelihood of perceiving barriers to accessing SUD treatment also varied between PSU classes. Compared to the *PPR users with low PSU*, both the *Heroin injectors with high PSU* and *PPR users with high PSU* class had significantly greater odds of perceiving a readiness barrier. *Heroin injectors with high PSU* also reported significantly increased odds of perceiving structural and stigma-related barriers to accessing SUD treatment. The findings of this study highlight how barriers to accessing SUD treatment differ by distinct PSU subgroups within the opioid-misusing population, and may require appropriately targeted interventions to help decrease barriers to accessing treatment for SUD.

3.4.1 Differences between classes

The classes of PSU in this study may differ from those of previous LCA for a variety of reasons. First, this study is unique as it provides patterns of PSU among opioid-misusing individuals in the U.S. In contrast to previous studies, which investigated patterns of PSU among heroin users,[164,171] the current study reports patterns of PSU among individuals reporting past year use of heroin, PPR misuse, or both. Further, the patterns of PSU are likely different as this study uses a nationally representative sample. This is different from previous studies, which recruited people who inject drugs (PWID),[166,168,185,186] or recruited from only one urban city, where the increased availability of certain substances (i.e., methamphetamines, cocaine) might have influenced the observed patterns of PSU, but not be reflective of substance use trends throughout the nation[168].

Previous U.S. studies have investigated the associations between patterns of PSU and various health-related outcomes, including: healthcare utilization,[155] overdose training,[185] risk behaviors (e.g., injection practices, sex risk behaviors, HIV/Hepatitis-C (HCV) risk factors),[123,155,167,170,172,173] psychological distress,[167] drug overdose,[186] and mortality.[165] This study is unique in that it examines the relationship between patterns of PSU and perceived barriers to accessing treatment for SUD, which may provide insight into what obstacles continue to persist, and which populations are most likely impacted. In addition, only one other U.S. study has investigated the association between insurance status and class of PSU; reporting a high prevalence (83%) of health insurance among a group of polysubstance using women, and no significant differences in the prevalence of health insurance by classes of PSU.[155] The findings of the current study go further by identifying significant differences in types of insurance by classes of PSU; *Heroin injectors with high PSU* contained the highest proportion of Medicaid recipients, while private insurance was highly prevalent among *PPR users with high PSU* and *PPR users with low PSU*. The high prevalence of Medicaid recipients in the *Heroin injectors with high PSU* class relative to the other classes is consistent with the findings of previous literature, which show a high prevalence of heroin use or dependence among individuals with Medicaid.[187]

Understanding how type of insurance differs by class of PSU may further inform the discussion of how to decrease barriers to accessing SUD treatment, as discussed in more detail below.

3.4.2 Substances of interest

Binge Alcohol Use. Conditional probabilities for binge alcohol use were highest for *PPR users with high PSU* (80.9%). Previous studies have also reported the highest probabilities of binge alcohol use in classes characterized by heavy PSU. Lorvick et al. found that binge drinking was significantly higher in a "heavy polydrug class" where ≥ 75% of members reported use of heroin, crack, non-heroin opioids, and benzodiazepines, with moderate use of cocaine and methamphetamines.[155] In addition, in an analysis of PSU among lifetime cocaine users, the highest probabilities of binge drinking were reported in a class with high probabilities of marijuana, prescription opioid, stimulant, and sedative misuse.[188]

The comparably low probability of binge alcohol use among *Heroin injectors with high PSU* is also consistent with the results of previous studies, where the lowest conditional probabilities of alcohol use were reported in classes characterized by heroin injectors.[170,171] Yet, while in the findings of the current study binge drinking appears to be lower among *Heroin injectors with high PSU*, research suggests co-occurring alcohol use is becoming more prevalent among heroin users. A 2015-2016 analysis assessing combinations of substance use among heroin users reported alcohol as one of the most simultaneously co-used substances with both heroin and prescription drugs.[164] Further, a study of heroin and cocaine users in a methadone-maintenance program reported that drinking alcohol was associated with heroin craving and use of other drugs.[189] The moderate to high prevalence of binge alcohol use within each class highlights the importance of screening for alcohol use in all opioid-misusing individuals entering treatment for SUD, so that they may receive services best tailored to their needs.

Marijuana Use. The probability of past year marijuana use was relatively high for *Heroin injectors with high PSU* (71.3%) and *PPR users with high PSU* (95.6%). High probability of marijuana use among heroin users was expected based on the results of previous studies. Past month marijuana use was reported by 40-61.0% of PWID in the U.S.,[155,164,185] and one analysis of heroin users in Cleveland, OH reported that marijuana was one of the most common simultaneously co-used substances with heroin.[164] Previous studies in the U.S. have reported high probabilities of marijuana use among individuals who report both illicit drug and prescription opioid misuse,[170,171,185,188] and two Canadian studies reported conditional probabilities of marijuana use ≥ 50% within all classes of opioid users.[132,175]

Although the prevalence of marijuana use among *PPR users with low PSU* is comparably low (37.5%), it is noteworthy that marijuana is one of two substances of moderate use in the class containing the largest proportion of the population. This may be due to the rise in clinical evidence supporting the use of marijuana to treat opioid withdrawal, reduce opioid use/misuse, and improve outcomes for SUD treatment.[190] Although findings of the current study show marijuana use is most prevalent among *Heroin injectors with high PSU* and *PPR users with high PSU*, future research should continue to monitor these patterns as legislation to decriminalize and legalize recreational use spread throughout the U.S.

Tobacco use. Moreover, the findings of the current study are consistent with the conclusions of previous studies, which stated that while smoking has decreased in the overall population, it remains highly prevalent among opioid-misusing individuals.[128] It is possible that SUD treatment facilities may continue to avoid addressing nicotine dependence, believing it may cause additional stress for patients. Yet studies have demonstrated that smoking cessation can be effectively carried out during methadone maintenance,[128] and one systematic review concluded that implementation of a smoking cessation intervention during SUD treatment often had no significant impact on opioid or illicit drug use.[191] Although the American Society of Addiction Medicine recommends a tobacco use query and cessation counseling be performed during the diagnosis of OUD, they also state that further research on tobacco cessation during opiate treatment programs is needed before specific evidence-based recommendations can be made.[90] The high prevalence of tobacco use among these groups highlights the necessity of investigating tobacco use in these patients, in order to monitor and reduce use within this population. Surveillance of tobacco use among opioid-users could better inform the development and evaluation of interventions promoting smoking cessation. Future research should consider accounting for tobacco use when assessing patterns of substance use among opioid-misusing populations.

3.4.3 Association between classes of PSU and barriers to accessing treatment for SUD

Readiness Barriers. The *Heroin injectors with high PSU* and *PPR users with high PSU* were significantly more likely to perceive a readiness barrier to treatment compared to *PPR users with low PSU*. These findings are consistent with those of earlier studies reporting readiness and motivation to stop using opioids as a persisting issue. Over a third of opioid misusing adults throughout the U.S. report they are not yet ready to stop using opioids.[86] Among PWID, not being ready for treatment, and not viewing drug use as a problem are common reasons for not seeking treatment for SUD.[192] Education and targeted interventions to connect opioid-misusing individuals with treatment are crucial in order to increase enrollment in SUD treatment. By identifying distinct groups of opioid users with a high likelihood of perceiving readiness barriers (*PPR users with high PSU* and *Heroin users with high PSU*) the findings of this study could be used to develop more targeted interventions that can be implemented in areas frequented by these high-risk populations.

Structural Barriers. The *heroin injectors with high PSU* were nearly two and a half times more likely to perceive a structural barrier to treatment in comparison to *PPR users with low PSU*. One likely explanation is that *heroin injectors with high PSU* are more likely to be covered by Medicaid, as over half (59.1%) were Medicaid recipients, and as such may be more likely to experience coverage-related barriers to treatment access. Although Medicaid coverage has increased substantially among individuals with SUD following the implementation of the ACA, the supply of SUD treatment available to Medicaid covered individuals has not kept pace.[21,38] This is likely because many states' Medicaid programs restrict coverage of addiction treatment; requiring prior authorization for medications used to treat opioid addiction or imposing lifetime treatment caps that limit accessibility.[193,194] In addition, poor reimbursement rates in comparison to private insurance may lead to decreased acceptance of Medicaid among SUD treatment providers; between 2014-2017, only 52.0% of buprenorphine-prescribing physicians accepted Medicaid for buprenorphine-related office visits,[194] and Saloner et al. found that opioid addiction treatment utilization was nearly 30% higher among Medicaid enrollees in states where Medicaid reimbursed methadone, compared to states with no public funding for methadone.[195] Further research is needed to better understand the relationship between perceived barriers and SUD treatment Medicaid coverage policies.

In addition, *Heroin injectors with high PSU* may face more barriers finding appropriate treatment. PWID often report medical[196] and psychiatric[197] comorbidities that may complicate their ability to find treatment for SUD. Although policies such as prescription guidelines and prescription monitoring programs may have contributed to the rise in PWID, treatment coverage for PWID in the U.S. continues to be far below international standards, as the ratio between the availability of treatment services and the number of PWID who could use those services remains low.[198] In addition, resources to address psychiatric comorbidity during treatment for SUD are often limited.[199] One study assessing addiction treatment programs between 2004-2011 found only 18% were capable of dual diagnosis of addiction and mental health treatment.[200] Taken together, these findings emphasize that additional work is needed to decrease structural barriers that prevent individuals with high heroin, PSU and injection substance use from accessing treatment for SUD.

Stigma-Related Barriers. Heroin injectors with high PSU had three times the odds of experiencing a stigma-related barrier compared to *PPR users with low PSU*. Whereas non-injecting individuals who misuse PPR may be able to conceal their addiction, PWID are more likely to bear physical symptoms (i.e., open sores, "track marks") or comorbidities (i.e., HIV, HCV, Endocarditis) that reveal their addiction. Many PWID report experiencing stigma due to family, community, and healthcare professionals.[201] Negative interactions with healthcare providers are a leading reason PWID are hesitant to access SUD treatment.[96,97] In one study, PWID perceived attitudes from healthcare professionals that were based solely on their knowledge of the participants' injection drug use, stating that they felt "looked down on" by medical personnel, and reporting that medical staff often prioritized care for others, placing PWID "at the back of the line".[97] In addition, clinician attitudes towards PWID could influence quality of care. Medical staff report that their colleagues are less supportive of harm reduction services for PWID,[202] and a significant predictor of support for discriminatory behavior are the attitudes and concerns that clinicians have about PWID.[67] In one study of syringe access programs, although 60.6% of PWID reported seeing a primary care provider within the past year, results indicated they were not receiving adequate preventative services or education about harm reduction.[203] Additional work remains to decrease the amount of stigma perceived by opioid-misusing PWID. These findings provide further support for the conclusions of previous studies, which have called for continued efforts to educate clinicians and the community at large in order to destigmatize treatment for SUD.

Financial barriers. PSU class was not significantly associated with perceiving a financial barrier to accessing treatment. In contrast to the previous results, this finding might reflect the success of current interventions. It was notable that PSU class was not significantly associated with perceiving a financial barrier to accessing treatment. As this study only included individuals with insurance, this result could indicate that provisions under the ACA to make coverage of SUD services equitable to other healthcare services are making SUD treatment more affordable for insured adults. This supports the results of a previous study, which reported a decrease in perceived financial barriers to accessing SUD treatment following implementation of the ACA.[73]

3.4.4 Public health implications

First, understanding the relationship between patterns of PSU and access barriers can be used to inform public health efforts to address these barriers, and highlight appropriate locations for resource allocation. *Heroin injectors with high PSU* were most likely to perceive readiness, structural, and stigma-related barriers to accessing SUD treatment, therefore interventions to decrease these barriers should focus on places where *Heroin injectors with high PSU* are found, such as needle exchange sites, supervised injection sites, or clinics preventing the spread of HIV/HCV. In addition to harm reduction sites, efforts to decrease barriers and increase treatment connection might be provided at emergency departments. Previous literature shows that individuals with PSU patterns similar to *Heroin injectors with high PSU* and *PPR users with* *high PSU* are more likely to be treated in an emergency room as compared to *PPR users with low PSU*. In one LCA identifying patterns of substance use among overdose survivors admitted to a U.S. emergency department between 2017-2018, a significant number of patients fell within the "mostly heroin overdose" (45%) or "opioid, polysubstance" (11%) classes, while less than a third (27.3%) fell into the "mostly non-heroin opioid overdose" class.[188] Several studies have reported that interventions initiated in the emergency department (e.g., initiation of medication assisted treatment, peer support) to connect overdose survivors with treatment can increase the engagement in SUD treatment or harm reduction services following discharge.[204–206]

3.4.5 Strengths and limitations

Strengths. This study was the first to characterize patterns of PSU within a nationally representative population of opioid-misusing adults in the U.S. The NSDUH assures privacy and confidentiality of answers to increase the likelihood of honest reporting of illicit drug use and illegal activities, and the response rate for each of the three years included in this study were high, ranging between 69.7-67.1%.[207]

As opposed to previous studies where substances were required to have a prevalence of 15-20% to be included as an indicator variable in LCA,[132,155,165,166,168,170] this study included past year use of all licit/near licit, illicit, and prescription misuse reported to the NSDUH. In addition, in contrast to all other U.S. studies investigating patterns of PSU, this study included information about tobacco use and smoking.

Limitations. The findings of this study should also be viewed within the context of several limitations. First, the data are cross-sectional and derive from self-reported substance use within the past 12 months, which may be limited due to recall bias and/or social desirability bias. In addition, these patterns of PSU derived from indicators of past year substance use from a nationally representative population. Thus, results may not be generalizable to specific cities or regions within the U.S. where increased availability of certain street drugs (e.g., crack, cocaine, methamphetamines) or legality of substance use (i.e. marijuana) might alter observed patterns of PSU.

Second, the LCA did not account for the complex sampling design of the NSDUH, which may have resulted in biased parameters and underestimated standard errors.[208] In addition, the findings of the current study may not directly compare to those of previous LCA due to variation in how alcohol use is captured. For example, several studies included indicators of any alcohol drinking or use,[164,170,171] which makes it difficult to distinguish between less harmful occasional alcohol use and more problematic binge drinking. Additionally, the definitions for "binge drinking" varied, including "4 or more drinks on a single occasion"[155] and "≥5 of more drinks in one sitting".[168] Only three studies used indicator variables for binge drinking as defined by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) (five drinks for men and four for women in one sitting).[166,188,209] Future researchers should consider using the NIAAA definition of binge drinking to ensure comparability between studies, and aid the development of strategies to prevent opioid overdoses involving alcohol.

Finally, these findings may be limited due to an inability to differentiate between all modes of drug administration (i.e., snorting, smoking), and the inability to differentiate between concurrent vs. simultaneous substance use. In addition, this study did not differentiate between misuse of prescription opioids primarily prescribed for pain (e.g., oxycodone, fentanyl, morphine, oxymorphone) and opioids prescribed for treatment of OUD (e.g., buprenorphine, methadone).

3.5 Conclusions

Participation in treatment is a necessary step towards ending opioid addiction. This study demonstrated an association between patterns of PSU and perceived barriers to accessing SUD treatment among opioid-misusing individuals. These findings highlighted a subpopulation of opioid users at increased odds of experiencing readiness, structural, and stigma-related barriers to accessing SUD treatment, and provided strong evidence that additional steps are necessary to decrease barriers to treatment perceived by individuals reporting high PSU. These findings also underscored the importance of re-evaluating the admissions process for SUD treatment, and providing further education to clinicians and the community to decrease stigma towards individuals with SUD. The current study added information to the contributions of previous literature that could be used to encourage the development of interventions that help opioid-misusing individuals seeking SUD treatment to overcome the barriers that they are most likely to face. Decreasing perceived barriers to accessing care are necessary in order to increase enrollment in SUD treatment.

Chapter 4. Evaluating the impact of an out-of-hospital initiated opioid treatment connection program on the number of nonfatal opioid overdoses 24-months post intervention

Background: The steady rise in opioid-related mortality has led to rise in interventions aimed at connecting opioid-misusing individuals to treatment for substance use disorder (SUD). On February 1st 2018 the Chesterfield Fire and EMS Community Paramedicine Program implemented an out-of-hospital intervention aimed at connecting survivors of nonfatal opioid overdose (OOD) to treatment for SUD. The objective of this study was to evaluate the association between the implementation of this out-of-hospital intervention and the trend of monthly nonfatal OOD in the county of implementation.

Methods: We utilized EMS electronic patient care records in Virginia from February 1, 2016 to January 31, 2020. Incidents where naloxone was administered with patient improvement were included for Virginians aged 18-89. Two interrupted time series (ITS) analyses were conducted using Poisson regression to assess changes to the trend of monthly nonfatal OOD from pre-intervention to post-intervention. Analyses included single ITS of Chesterfield County and multiple ITS comparing trends in both Chesterfield County and a comparable control county.

Results: Of the 16,719 911 responses to a nonfatal OOD in Virginia during the study period, 1,034 (6.0%) occurred in Chesterfield County and 879 (5.3%) in the control county. Single ITS showed an immediate decrease in nonfatal OOD by 0.33% each month (p=0.0857), and no statistically significant difference between the post-intervention trend and the pre-intervention trend (p=0.9195). There were no statistically significant differences in the pre-intervention level or trend of monthly nonfatal OOD between counties, indicating comparability. The post-intervention level was approximately 0.18% lower for Chesterfield (p=0.5150), and the difference in the differences of slopes between counties from pre-to-post intervention was 0.02% (p=0.2404).

Conclusions: These findings provide initial support for the effectiveness of an out-of-hospital intervention that links survivors of nonfatal OOD to treatment for SUD.

4.1 Introduction

4.1.1 The Opioid Epidemic in Virginia

In 2017, the opioid epidemic caused the deaths of 1,445 Virginians, an 8% increase in fatalities from 2016.[210] Opioid-related incidents have burdened healthcare and public safety resources throughout the Commonwealth, resulting an annual average of 10,000 emergency department visits and 4,000 emergency medical services (EMS) responses[211] in 2017, and one opioid-related criminal arrest every two hours.[212] Accumulating costs from the impact of opioid misuse on public safety and other state services has had a broad impact on the Virginia's economy, with one study estimating the per capita cost of the opioid epidemic at $1,624 per resident, equivalent to nearly 3% of the overall gross domestic product in Virginia.[213] Although the continued needs of the opioid epidemic have pushed the General Assembly of Virginia to invest a great deal of money between 2017 and 2018[214] to fund public health initiatives aimed at decreasing opioid-related morbidity and mortality, the steady increase in fatalities despite these efforts highlight the need to address potential gaps that may persist.

4.1.2 VA Initiatives to Decrease Opioid-Related Morbidity

Similar to many states throughout the nation, Virginia has acknowledged the serious consequences of the opioid epidemic, declaring that "a public health emergency resulting from opioid addiction exists in the Commonwealth, affecting the health and safety of Virginians" on November 21st, 2016.[215] Virginia officials addressed the public health emergency through implementation of interventions aimed at preventing future addiction and decreasing overdose fatalities. To promote the appropriate use of controlled substances, in July of 2017 Virginia mandated all prescribers to register for the prescription monitoring program (PMP), an online database which enabled prescribers to monitor their patient's use of controlled substances, and more effectively deter potential misuse and diversion.[216] To decrease deaths due to accidental overdoses, Virginia took steps to increase civilian access to the opioid-antidote naloxone. The Commonwealth medical director released standing order in 2016 which allowed for the over-the-counter prescription of naloxone,[217–219] and in 2017 the opioid overdose and naloxone education program REVIVE! was initiated, which dispensed naloxone at no cost through community trainings and local health departments throughout Virginia.[220,221] Finally, to decrease the incidence of Human Immunodeficiency Virus (HIV) and Hepatitis C among injection drug users, in 2018 the Commonwealth opened two needle exchange programs.[222–224]

Various key public health initiatives have been implemented successfully throughout the nation, each recommended by the Centers for Disease Control as a key strategy to decrease opioid overdose (OOD) morbidity and mortality.[225] Despite these efforts, the number of opioid-related fatalities in Virginia has continued to rise, from 1,284 in 2016 to 1,445 in 2017.[210]

One explanation for the rise in deaths could be due to the increased presence of fentanyl in Virginia. As previously mentioned, fentanyl use has significantly increased throughout the nation since 2013, accounting for 77% of the total increase in deaths attributed to heroin.[226] This trend was also reported in Virginia according to Attorney General Mark Herring, who stated in a press briefing that “fentanyl has become the biggest driver of the rise in overdose deaths in Virginia”.[227] Deaths due to fentanyl in the Commonwealth have increased by 1,337% since 2009[227] and continue to rise, increasing by 23.4% from 2016 to 2017.[228]

However, the upward trending of opioid-related fatalities could also be attributed to the policy emphasis on implementing initiatives rooted in primary and tertiary prevention-based approaches, rather than secondary prevention approaches which would emphasize screening and treatment. PMP are a primary prevention strategy, allowing surveillance of individuals who use prescription opioids to prevent and deter further misuse; whereas both needle exchange and naloxone distribution programs represent tertiary prevention strategies, reducing either risk of blood-born pathogen transmission or risk of fatal overdose among individuals already misusing opioids.[229,230] Although multiple studies have demonstrated the effectiveness of these strategies in decreasing opioid-related morbidity,[225,229] these initiatives are ultimately limited in that they do not directly address treatment for opioid addiction. Virginia Governor Dr. Ralph Northam highlighted the importance of both treatment and prevention in a 2018 address to medical students discussing the opioid epidemic, emphasizing that state efforts to address the opioid crisis must involve both prevention and treatment, stating "…when prevention does fail, treatment works".[231] However, since this address no additional funds or programs have been initiated to increase access to treatment, and as 464,000 Virginians reported needing but not receiving treatment for substance use in 2016, additional initiatives to ensure better access to treatment were clearly warrented.[232]

4.1.3 VA Initiatives to Increase Access to Addiction Treatment

One program aimed at increasing access to addiction treatment for Virginians' was the Addiction Recovery and Treatment Services or ARTS program, implemented in April of 2017.[214] ARTS increased the number of available addiction treatment providers by making addiction treatment more cost effective for practitioner to provide, resulting in increased access to treatment for Medicaid members with opioid and other substance use disorders.[214,233–235] Following ARTS implementation the number of outpatient opioid treatment services in Virginia increased from 6 to 108,[234] and evaluators reported a 51% increase in the treatment rate of Medicaid members with Opioid Use Disorder (OUD) over the first five months of the program.[233] Though initially restricted due to the limited number of individuals covered by

Medicaid in a non-expansion state, access through ARTS is expected to further increase in January of 2019, when the expansion of Medicaid throughout the Commonwealth will increase Medicaid coverage to an additional 400,000 individuals.[236]

In addition to expanding access to addiction recovery and treatment services for Medicaid recipients through ARTS, in May 2018 Governor Ralph Northam accepted a Federal grant of over 9.7 million dollars for the Department of Behavioral Health and Developmental Services, expected to help fund the Virginia Community Services Boards, which provide prevention, treatment, and recovery services to all Virginians.[211]

4.1.4 Limitations to VA Initiatives

While initiatives to improve access to addiction treatment in Virginia have yielded promising results, limitations remain. The continued rise of opioid-related fatalities despite implementation of the ARTS program could be attributed to the restricted number of individuals eligible for Medicaid who qualify for participation in the program.[214] Although increased access is expected with Medicaid expansion in 2019, the benefits of the program will remain limited only to individuals covered by Medicaid, likely excluding a significant proportion of the opioid addicted population who are in need of addiction treatment but are either not qualified for Medicaid,[237] or are eligible but unable to enlist.[238] Further, although the 2014 passage of the Patient Protection and Affordable Care Act (ACA) expanded insurance to many Americans,[45] passage of the ACA was not associated with increased use of treatment for substance use disorder (SUD) among individuals with substance use disorders,[21] indicating additional initiatives to engage these individuals may still be warranted.[38] Low treatment enrollment in this population could persist due to logistical barriers to access (ie. transportation),[239] or lack knowledge on where to access these resources.[21] Finally, these interventions will likely have little impact on individuals declining to seek treatment due to motivational or stigmatization barriers, which are more common among the insured population.[22]

4.1.5 Healthcare Partnerships Connecting Addicts with Treatment

To better address these remaining gaps, additional efforts should focus on connecting opioid-abusing individuals to treatment and supporting them throughout the treatment process. Governor Northam highlighted the importance of these programs by allocating additional funding from his $9.7 million dollar Federal grant to "support the development of partnerships with the hospital that will connect individuals who overdose with peers in recovery".[211] Although hospital partnerships connecting individuals with peers during the recovery period have demonstrated early success,[240] limiting inclusion to hospital-based partnerships could potentially exclude a significant proportion of the opioid-abusing population, as prehospital research reports 63-69% of patients refuse transport to the hospital following an OOD,[241,242] or depart prior to physician discharge against medical advice.[243] Further, as studies suggested that individuals with access to naloxone could be less likely to call for assistance following an overdose,[244] the increased availability of naloxone in the Commonwealth could lead to a decrease in the number of individuals seeking treatment at a hospital following an overdose. Thus, to expand the effort of treatment-connection initiatives in the opioid-abusing community, it may be beneficial to explore not only hospital partnerships, but also partnerships with public safety personnel, specifically, emergency medical services (EMS).

4.1.6 Feasibility of EMS Personnel Connecting Patients to Addiction Treatment

The recent expansion of EMS personnel into non-emergent healthcare roles further supports their partnership viability. Although designed to respond to emergency situations, many EMS agencies now participate in mobile integrated health care or community paramedicine;

programs which enable EMS personnel to provide individualized patient care in a non-emergent role.[245] Many of these programs were designed to use EMS personnel to help patients navigate the healthcare system to find and access available resources.[246] Individualized to the needs of the patient, community paramedicine programs provide a variety of services, including: management of chronic diseases, assessing and addressing hazards in the home, or accessing and arranging medical appointments.[245,246] Research has demonstrated these programs are extremely effective at connecting patients with healthcare resources, resulting in decreased use of EMS, decreased visits to the emergency department, decreased hospital readmissions.[247,248] Further, participants of these programs report being highly satisfied with the care they receive from the community paramedics.[246] The success of these programs demonstrate EMS personnel can effectively connect patients with healthcare resources in the community, providing further support for the use of EMS personnel in connecting opioid-misusing patients with treatment.

Although few studies have reported the implementation of overdose related intervention and treatment connection programs by public safety personnel, emerging results from these studies are promising. A 2017 survey in Massachusetts reported that 21% of public safety agencies were administering some form of outreach program for opioid addicts.[249] Administered primarily by law enforcement and fire, some interventions reported encouraging results; with one program of police-led referrals successfully placing 75% of those seeking addiction treatment services into care.[250] However, no study has yet evaluated the effectiveness of programs using EMS personnel to connect patients with treatment for SUD. The promising results of programs implemented by other public safety officials further support the feasibility of a program implemented by EMS personnel.

4.1.7 Study Aims and Hypothesis

Although various interventions have aimed to increase the availability of addiction treatment throughout the nation, many individuals in need of addiction treatment remain without. Programs where health-care providers connect opioid-misusing individuals to addiction treatment and peers in addiction recovery are currently recommended, but underutilized in the out-of-hospital environment. While early research has demonstrated that public-safety outreach programs can be effective in referring individuals to addiction treatment facilities, at the date of this writing no programs have evaluated the effectiveness of an intervention implemented by EMS personnel. This is the first evaluation of an out-of-hospital intervention implemented by EMS personnel to link survivors of OOD with treatment for substance use disorders.

The objective of this study was to evaluate the impact of the Chesterfield Fire & EMS Community Paramedicine Peer Support and Treatment Connection (PSTC) program on the trend of monthly nonfatal OODs, 24 months after implementation of the program. We hypothesized that Chesterfield County would see a significant decrease in the level of monthly nonfatal OODs immediately after implementation of the PSTC program, and a gradual decrease in the trend of monthly nonfatal OODs over the 24-month post-intervention period, as compared to the 24-month pre-intervention period. Additionally, we hypothesized that pre- to post implementation differences in the trend of monthly nonfatal OODs would be significantly lower for Chesterfield County in comparison to an adjacent "control" county.

4.2 Methods

4.2.1 Study Design

This study used a quasi-experimental interrupted time-series design to compare changes in the trend of monthly nonfatal OODs before and after implementation of the PSTC program. Observations of nonfatal OODs were collected simultaneously in Chesterfield County and an adjacent county over four years and split into two time periods: pre-intervention (February 1st 2016 – January 31st 2018) and post-intervention (February 1st 2018 – January 31st 2020).

4.2.2 Study Intervention

On February 1st 2018 the Chesterfield County Fire and Rescue Community Paramedicine Program partnered with a peer support specialist for an opioid outreach intervention that aimed to connect survivors of nonfatal OOD treated by Chesterfield EMS with an addiction treatment program within Chesterfield County or the surrounding area. Following an EMS response for an OOD, a Chesterfield Community Paramedic and peer support specialist follow up with the patient by phone to schedule a meeting. During the meeting, the team encourages the individual to seek treatment for opioid misuse, and offers to help connect them to local treatment programs within the county or surrounding area. If the individual agrees, the peer support specialist works one-on-one to enroll them in treatment programs. The services provided by the community paramedicine team and the peer support specialist vary, as services are individualized to meet the needs of each participant. The team may call to follow up with the participant if they need counseling or may attend the mental health evaluations with the participant at their request. Once a participant completes a mental health evaluation, they become eligible for the community health services provided by the Chesterfield County Community Services Board, and their participation in the program ends.

4.2.3 County Populations and Emergency Medical Services

Chesterfield County is the 4th most populous county in Virginia, with an estimated 2018 population of 348,556. Chesterfield County Fire and Rescue is the largest provider of EMS in Chesterfield County, and responded to 69.6-81.2% of the nonfatal OODs during the study period. In addition to Chesterfield Fire and EMS, EMS are provided by four volunteer rescue squads, and a large metropolitan service from a neighboring county, which responded to 19.3-21.0% of nonfatal OOD during the study period.

The control county was chosen due to the similarities in demographic characteristics and the provision of EMS within the county. Supplemental Table 4.1 summarizes the population characteristics and OOD characteristics for each county in 2018. Located adjacent to Chesterfield County, the control county is the 5th most populous county in Virginia, with an estimated 2018 population of 329,261. Similar to Chesterfield, the control county-run fire department is the primary provider of EMS, and responded to 65.4-75.3% of nonfatal OODs during the study period. EMS in the control county is also supplemented by five volunteer rescue squads, and a large metropolitan service in a neighboring county, which responded to 12.6-23.4% of nonfatal OOD during the study period. Up to the time of this writing, the county-run fire department had not yet implemented a program aimed at connecting survivors of nonfatal OOD with resources for addiction treatment.

4.2.4 Data Source and Study Population

Adults between the ages of 18 and 89 were eligible for inclusion in the study if they were treated by EMS personnel for a nonfatal OOD in Chesterfield County or the control county during the study period (February 1st 2016 – January 31st 2020). Incidents meeting criteria that were the result of a non-911 response (interfacility transport, standby, assist) were excluded from analysis.

Data was extracted from EMS electronic patient care reports (ePCRs) for all incidents of nonfatal OODs within both counties occurring between February 1st, 2016 and January 31st 2020. An ePCR is required to be completed by a Virginia certified paramedic or emergency medical technician after every EMS incident in the Commonwealth of Virginia, then submitted to the

Virginia Pre-Hospital Information Bridge program located within the Virginia Department of Health Office of Emergency Medical Services, Division of Trauma and Critical Care.[251] All protected health information was removed using de-identification methods recommended by the U.S. Health and Human Services.[252]

Annual estimates for county population were obtained from the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research.

4.2.5 Measures

The primary dependent variable of the study was the monthly count of nonfatal OOD for Chesterfield County and the control county between February 1st, 2016 and January 31st 2020. A nonfatal OOD was defined as any EMS incident where an individual was administered naloxone and their condition "improved".

The primary independent variable was the study period: the period of February 1st 2016 – January 31st 2018 (pre-intervention period) vs. the period of February 1st 2018 – January 31st 2020 (post-intervention period).

Demographic and incident-related measures were extracted to assess differences in demographic and incident-related characteristics between the two counties. These included: sex (male or female), age in years (18-24, 25-34, 35-44, 45-54, 55-64 or ≥65), and race (Non-Hispanic White, Non-Hispanic Black, or other (Hispanic, Asian, American Indian or Alaska native, native Hawaiian or other Pacific Islander, "other race", or selections of multiple races)). Incident-related characteristics included year of overdose, location of incident (private residence, residential facility, or public location), route of naloxone administration (intranasal (IN), intravenous (IV), other (intramuscular, intraosseous, oral, endotracheal tube, topical, other/miscellaneous), or combined (receiving naloxone through a combination of IN, IM, IV or other routes)) and the dose of naloxone administered in milligrams (mg) (0.4-0.9 mg, 1.0-1.9 mg, 2.0-2.9 mg, 3.0-4.9 mg, or ≥ 5.0 mg)).

4.2.6 Analytic Strategy

All statistical analyses were performed using R Studio v3.6.3. Descriptive statistics were calculated to assess differences in the distribution of demographic and incident-related characteristics between the two counties, using T-tests for continuous variables and Pearson Chi-square tests for categorical variables.

Interrupted time-series analysis using a Poisson regression model was used to assess the changes in the level and trend of monthly nonfatal OOD before and after implementation of the PSTC program. Development of the model and analysis were based on an interrupted time series regression tutorial developed by Bernel et. al.[253]

This times series analysis was performed using two models: a single interrupted time series (SITSA) model which assessed changes in the pre- and post-intervention trend of monthly nonfatal OOD before and after intervention implementation in Chesterfield, and a multiple interrupted time series (MITSA) model, which assessed changes in the pre- and post-intervention trends of monthly nonfatal OOD between Chesterfield County and the control county.

The equation for SITSA is based on segmented linear regression:[254]

$$y_T = \beta_0 + \beta_1 T + \beta_2 X + \beta_3 XT + \varepsilon$$

In this model, y_T is the average of nonfatal OODs at month T, T is the continuous time (in months) from the start of the pre-intervention period on February 1st 2016 to the end of the implementation period on January 31st 2020. X is a binary variable that indicates intervention implementation (0=pre-intervention, 1=intervention), and XT is an interaction term that represents time after intervention implementation. β_0 is an estimate of the baseline count of monthly nonfatal OODs, β_1 estimates the average change in monthly nonfatal OOD during the pre-intervention period, β_2 estimates the level change in monthly nonfatal OOD immediately after intervention implementation, β_3 estimates the average change in monthly nonfatal OOD from pre- to post-intervention, and ε is an error term that represents random variability that was not accounted for in the model. In addition, β_{1+3} was calculated to show change in the average monthly nonfatal OOD during the post-intervention period.

The equation for the MITSA model is an expansion of the SITSA equation that adds in a control series. This control series was used to assess whether the level and slope changes observed in the treatment county (Chesterfield) are significantly different from those observed in the control county.[254]

$$y_T = \alpha + \beta_1 T + \beta_2 X + \beta_3 XT + \beta_4 Z + \beta_5 ZT + \beta_6 ZX + \beta_7 ZXT + \varepsilon$$

In this equation, Z is a binary variable that codes treatment status (1=treatment, 0=control), and ZT, ZX, and ZXT are all interaction terms among the aforementioned variables.[255] In this model the purpose of coefficients $\beta_0 - \beta_3$ are the same as those described in the SITSA model, but now provide estimates for the control county. β_4 estimates the pre-intervention difference in the level of the outcome between treatment and control, β_5 estimates the pre-intervention difference in the slope of the outcome between treatment and control, β_6 indicates the difference between treatment and control in the level immediately following introduction of the intervention, and β_7 indicates the difference between treatment and control groups in the trend of the outcome variable after initiation of the intervention compared to the pre-intervention trend.[255]

Results of the observed and predicted trends for each model were plotted to visually demonstrate the curve-shifting. The Pearson-based dispersion statistic was used to assess for overdispersion in each model.[256] If overdispersion was found, models were adjusted in a quasipoisson model, which allows variance in the model to be proportional rather than be equal to the mean. In addition, autocorrelation, or the correlation of a variable with itself at different time periods, was assessed in both the SITSA and MITSA models through visual inspection of the sample autocorrelation and residual plots, and use of the Breusch-Godfrey test statistic.

4.2.7 Statement of Ethics

This study utilized de-identified data; no variables in the assessment could be used to identify patients, or indicate status of vulnerable patient populations (i.e., pregnant women or prisoners). This study was therefore approved as exempt from review by the Institutional Review Board at Virginia Commonwealth University, ID= HM20016514.

4.3 Results

Of the 16,719 911 responses to a nonfatal OOD during the study period, 1,034 (6.0%) occurred in Chesterfield County and 879 (5.3%) in the control county. Table 4.1 describes the demographic and incident-related characteristics for nonfatal OODs by county. In comparison to nonfatal OOD responses in the control County, Chesterfield County reported a higher prevalence of female patients (38.9% vs. 33.1%), a lower prevalence of Non-Hispanic Black patients (22.5% vs. 32.1%), and reported more overdoses occurring in a private residence (67.9% vs. 59.5%). Further, in contrast to patients in the control county, patients in Chesterfield were predominately administered naloxone intra-nasally (60.4% vs. 28.2%). Additionally, the average total dose of naloxone administered to patients was significantly higher in Chesterfield (3.2 mg vs. 1.8 mg), and over half (54.2%) of Chesterfield patients received a dose of 3.0mg or higher, compared to 15.5% of patients in the control county.

The dispersion statistic for the SITSA quasipoisson model was 2.18, indicating that the conditional variance was at least two times larger than the conditional mean. Adjusted estimates showing trends in observed and predicted monthly nonfatal OOD in Chesterfield County are included in Table 4.2, and are further illustrated in Figure 4.1. Pre-adjustment estimates were included in Supplemental Table 4.2. The pre-intervention trend (β_1) in Chesterfield County showed an increase in monthly nonfatal OODs by about 0.01% each month. There was an immediate decrease in monthly nonfatal OOD by 0.33% following implementation of the intervention, however this estimate was not statistically significant (p=0.0857). Additionally, there was no statistically significant difference between the post-intervention trend and the pre-intervention trend (p=0.9195), and the estimated post-intervention trend (β_{1+3}) appeared very similar to the pre-intervention trend, showing an increase in monthly nonfatal OOD by 0.02%. On visual inspection the residuals appear to be randomly distributed, showing no patterns (Supplemental Figure 4.1), further the correlogram for autocorrelation revealed no lags in time where autocorrelation was statistically significant (Supplemental Figure 4.2).

The dispersion statistic for the MITSA quasipoisson model was 2.02, indicating that the conditional variance was approximately two times larger than the conditional mean. Adjusted estimates of the MITSA are reported in Table 4.3, and predicted pre- and post-intervention trends for both counties are presented in Figure 4.2. Unadjusted estimates are available for comparisson in Supplemental Table 4.3.

Table 4.3 reports the results of the MITSA between Chesterfield and the control county. Monthly averages of nonfatal OOD for both counties are plotted in Figure 4.2. In contrast to Chesterfield, the pre-intervention trend (β_1) in the control county showed a decrease in monthly nonfatal OOD by .003% each month (p=0.7512). Immediately following initiation of the intervention, monthly nonfatal OOD decreased by 0.15% (p=0.4702). There was no statistically significant difference between the pre-intervention trend and the post-intervention trend (β_3), showing an approximate 0.02% increase in the monthly average nonfatal OODs ($p=0.0953$). Chesterfield and the control county did not show any statistically significant differences in the pre-intervention level (β_4) or trend (β_5) of monthly nonfatal OOD, indicating that the two series were comparable prior to intervention implementation. There were no statistically significant differences in the pre- to post-intervention differences in level (β_6) or trend (β_7) between Chesterfield and the control county. The post-intervention level was approximately 0.18% lower for Chesterfield compared to the control county ($p=0.5150$), and the difference in the differences of slopes between counties from pre-to-post intervention was 0.02% ($p=0.2404$).

Residuals from the MITSA appeared to be randomly distributed with no clustering or patterns (Supplemental Figure 4.3), and visual inspection for autocorrelation revealed no lags in time where autocorrelation was statistically significant (Supplemental Figure 4.4).

4.4 Discussion

The SITSA found no statistically significant pre- to post-intervention differences in the average monthly number of nonfatal OODs in Chesterfield County. An immediate reduction was observed in the average monthly nonfatal OOD following program implementation, however this difference was not statistically significant. Additionally, there was no significant difference in the trend of average monthly nonfatal OOD from pre- to post-intervention. In the MITSA, there was a difference observed in the pre- to post-intervention trends for the control county. The post-intervention trend showed a minimal increase in monthly nonfatal OOD compared to the trend of nonfatal OOD pre-intervention, however this difference was not statistically significant. There were no statistically significant differences for both the pre-intervention trend and the pre-intervention level between Chesterfield and the control county. Chesterfield saw a greater reduction in monthly nonfatal OODs immediately following program implementation compared to the control county, however this difference was not statistically significant. In addition, there was no statistically significant difference in the differences between the pre- to post-intervention trends for each county.

4.4.1 Results of MITSA model

The trend of monthly average nonfatal OODs in Chesterfield County did not significantly change from pre-intervention to post-intervention. A lack of significant change between the pre-intervention and post-intervention trends usually indicate that the intervention under investigation may not be sustainable over time. However, the MITSA showed the trend of nonfatal OODs in the control county significantly increased from pre-intervention to post-intervention. The key assumption when using MITSA is that change in the level or trend in the outcome would be similar for the control and for the treatment group, had the intervention not been implemented[255]. This suggests that implementation of the intervention may have delayed or slowed a rise in the trend of nonfatal OODs in Chesterfield County that would have been expected if the intervention had not been implemented.

4.4.2 Unmeasured potential confounders impacting analysis

Overall, the differences between the two counties for the estimates of pre- to post-intervention change for the level and trend of nonfatal OODs were not statistically significant. This could be due to the co-occurring implementation of other opioid-related interventions, which may impact one county more than the other. The key assumption behind comparison with a control county, is that confounding omitted variables would affect the treatment and control groups similarly.[255] Yet it is possible that some of the co-occurring opioid-related interventions had a differential impact on the counties.

The disproportionate prevalence of fentanyl between the counties could impact the monthly average of nonfatal OODs. In Virginia, fentanyl-related mortality spiked at the beginning of the study period, increasing by 177.3% from 2015 to 2016.[228] Data from the Office of the Virginia Medical Examiner show that the 2016-2018 fentanyl-related mortality rate per 100,000 was 8.0 to 13.8 in Chesterfield, compared to 6.4 to 11.2 in the control county.[257] Ideally, fentanyl would be accounted for through stratification,[258] which would allow for evaluation of the differential impact of the intervention on subpopulations of nonfatal OODs with and without fentanyl. Unfortunately, EMS ePCRs lack a standardized way of reporting fentanyl involvement during a nonfatal OOD. Even if documented, the accuracy of self-reported data would still be questionable, as many individuals may not know the heroin they purchased had been cut with fentanyl.[259] Further research is needed to determine whether this intervention would have a differential impact on the monthly average nonfatal OODs after controlling for fentanyl.

Legislation increasing the availability of naloxone in Virginia, such as naloxone distribution programs and over-the-counter availability of naloxone, may also impact the counties differently.[260] Prevalence of bystander naloxone may impact the monthly average of nonfatal OOD, as individuals administering naloxone may be less willing to call 911, either out of fear for police involvement,[261,262] or because they feel they can handle the overdose themselves.[263,264] Thus, prevalence of bystander naloxone may increase the likelihood of an individual overdosing without summoning 911, which would underestimate the true count of nonfatal OODs in the community. Accounting for the presence of bystander naloxone in Virginia would be challenging. To the author's knowledge, the REVIVE! program does not keep a record of the number of residents receiving naloxone training, or the number of naloxone units distributed in each county. However, prior naloxone administrations, or naloxone administered prior to the arrival of EMS personnel, could be used as a proxy to account for the presence of bystander naloxone within the community. A previous analysis of 2016-2018 nonfatal OODs in both counties revealed that Chesterfield had a disproportionately high number of prior naloxone administrations compared to the control county. Thus, it is possible that individuals in Chesterfield could be less likely than those in the control county to summon 911 to the scene of an overdose. This would result in the underestimation of the true count of OOD each month, and have a differential impact on the monthly average of nonfatal OODs in the two counties.

4.4.3 Strengths

This study has several strengths. Interrupted time series allows researchers to perform a robust analysis of a dependent variable without incurring the cost and work associated with a randomized control trial.[258] The interrupted time series approach enables us to evaluate the effect of the Chesterfield intervention program on the monthly average of nonfatal OODs in Chesterfield County, while accounting for the pre-implement trend for the monthly average of nonfatal OODs.

An additional strength of this study is the inclusion of a non-equilivant control group in our MITSA, which enhances the internal validity of the analysis by allowing the researcher to control for omitted confounding variables.[253,255]

4.4.4 Limitations

However, the results of this study should also be viewed in the context of several limitations. The data used for this study were de-identified and unlinked, meaning it is possible that an individual could have been treated multiple times during the study period. However, it is unlikely that the occurrence of a "repeat overdose" would differ between counties. In addition, the analysis was limited to records from two counties in the Commonwealth of Virginia, which may limit the generalizability of these results to other jurisdictions.

In addition, on January 1st, 2017 the Virginia Office of EMS stopped accepting ePCRs from EMS agencies not using data submission standards for National Emergency Medical Services Information System version 3.4. This initially resulted in the exclusion of all incidents from Chesterfield Fire and EMS, and all volunteer rescue squads in Chesterfield County for January and February of 2017. While Chesterfield Fire and EMS was able to provide researchers with the cumulative number of eligible cases for those two months, data from volunteer rescue squad responses were not available; which may have slightly underestimated the true count of nonfatal OODs in Chesterfield County for those two dates.

Further, previous researchers have questioned the accuracy of using EMS naloxone administrations as a proxy for nonfatal OODs, reporting low sensitivity and positive predictive value for the use of naloxone administrations alone.[265] While our definition (i.e., EMS patients who received naloxone and improved) increased precision by excluding false-positive cases (i.e., OOD patients who received naloxone with no improvement), it likely still underestimates the true number of nonfatal overdoses during the study period, by excluding any individual with an OOD who was not administered naloxone. This definition also would have excluded individuals who had an OOD but did not improve until additional naloxone was administered at the hospital, or individuals who did not improve due to comorbidities secondary to an OOD or pharmacokinetic effects of a secondary drug unaffected by naloxone administration.

Finally, the accuracy of these findings are dependent upon the accuracy of the ePCRs created by EMS professionals documenting these incidents.

4.5 Conclusions

Implementation of an opioid treatment connection program did not appear to have a statistically significant impact on the monthly average of nonfatal OODs. Although the monthly average of nonfatal OODs was reduced following program implementation, this association was not statistically significant. Increasing the number of months for post-intervention analysis may be needed to more accurately determine whether this intervention has a sustained effect on the average number of nonfatal OODs each month. Further research is needed to evaluate the effectiveness of public health interventions implemented by EMS personnel as a part of the public health strategy to address the opioid crisis.

Chapter 5: Conclusions

Increasing the enrollment of opioid-misusing individuals into treatment for substance use disorder (SUD) is necessary in order to achieve sustainable long-term decreases in opioid-related morbidity and mortality. For this reason, addressing barriers to accessing treatment for SUD is critically important to increase treatment enrollment. The goal of this dissertation was to produce results that would provide insight into the persisting barriers to accessing SUD treatment in opioid-misusing individuals by: testing the association between type of opioid misuse and perceived readiness, financial, structural, and stigma-related barriers in insured adults reporting past year opioid misuse (Chapter 2); identifying classes of past year polysubstance use among opioid-misusing adults in the U.S. and assessing the association between polysubstance use classes and perceived barriers to accessing treatment for SUD (Chapter 3); and evaluating the effectiveness of an out-of-hospital opioid treatment connection program on the number of nonfatal opioid overdoses 24-months post intervention (Chapter 4).

5.1 Type of opioid misuse and perceived barriers to accessing treatment

Chapter 2 provided insight into the degree to which those reporting opioid misuse and perceived a need for treatment perceived a barrier to accessing treatment. Results from Chapter 2 indicated that 3.7% of insured Americans reporting past-year opioid misuse perceived at least one barrier to accessing treatment for SUD. Further, individuals with combined heroin and prescription pain reliever (PPR) misuse were nearly 3 times more likely to perceive readiness and structural barriers, and nearly 4 times more likely to perceive stigma-related barriers to accessing treatment for SUD in comparison to individuals who only reported past year misuse of PPR.

Results from Chapter 2 could help inform the strategic placement of public-health interventions aimed at connecting opioid-misusing individuals to treatment for SUD. For example, interventions could be implemented in areas with a traditionally high prevalence of heroin injectors or individuals with high polysubstance use (PSU), such as clean needle syringe services, supervised injection sites, homeless shelters, halfway houses, and the emergency department. In addition, these findings should serve to further support guidelines for the routine screening of substance misuse currently recommended by the American Society of Addiction Medicine[5]. Individuals with high PSU and people who inject drugs are at greater risk for psychiatric and medical comorbidities, and often seek emergency or acute care to treat those conditions.[266] Thus, increasing identification of SUD through routine screening during treatment for psychiatric and medical comorbidities may increase access to treatment for SUD in these populations.

5.2 Type of opioid misuse and perceived barriers to accessing treatment

In Chapter 3, latent class analysis (LCA) identified three distinct classes of PSU within a nationally representative sample of individuals reporting opioid misuse in the past year: (1) *Heroin injectors with high PSU*, (2) *PPR users with low PSU* and (3) *PPR users with high PSU*. Compared to *PPR users with low PSU*, *Heroin injectors with high PSU* and *PPR users with high PSU* had 3 times the odds of perceiving readiness barriers, and *Heroin injectors with high PSU* were also nearly 2.5 times more likely to perceive structural barriers and 3 times more likely to perceive stigma-related barriers. No subpopulations in this opioid-misusing population had a statistically significant association with financial barriers.

Taken together, the results of Chapter 3 further demonstrate how accounting for patterns of PSU during the assessment of treatment outcomes is crucial for the design and implementation of interventions addressing barriers to accessing treatment. For example, in Chapter 2, individuals with H+PPR were more likely to perceive barriers to treatment compared to individuals with PPR. However, in Chapter 3 classifying individuals into groups based on their past year substance use enabled the identification of two distinct subgroups of individuals with H+PPR that were more likely to perceive barriers to accessing treatment (*PPR users with high PSU, Heroin injectors with PSU)*. The unique sociodemographic characteristics and substance use profiles of these two subgroups could be used to more efficiently target interventions aimed at connecting individuals to treatment. For example, an intervention addressing readiness barriers may increase opportunities for individuals in both subgroups to interact with social workers or peer recovery specialists, who could provide counseling or motivational interviewing and discuss resources for treatment. Although some locations, such as the emergency department, might offer access to both populations, this intervention could better target *Heroin injectors with high PSU* through additional implementation at harm reduction services (e.g., clean needle exchange sites, supervised injection facilities).

Results of the LCA also identified a class of PSU that might be difficult to connect to treatment, further supporting the recommendation for physicians to increase routine screening of SUD. *PSU users with high PSU* might be more difficult to access for two reasons: 1) *PPR users with high PSU* would not be expected to participate in the same harm reduction initiatives as *Heroin injectors with high PSU* (e.g., clean needle exchange sites, supervised injection facilities), and 2) the high prevalence of older adults and lack of any physical signs of addiction may make this group 'less identifiable' as individuals with a SUD. Thus, increasing routine screening for substance misuse at emergency and acute care facilities could increase the identification of this hard-to-reach group that accounted for nearly a quarter of the population, and enable clinicians to link those individuals to needed resources.

5.3 Type of opioid misuse and perceived barriers to accessing treatment

Chapter 4 discusses an out-of-hospital intervention implemented by emergency medical services (EMS) personnel and a peer support specialist that connects survivors of nonfatal opioid overdoses (OOD) to treatment for SUD. Initial findings of this study demonstrated that, on average, the County of implementation (Chesterfield) showed an immediate decrease in the monthly number of nonfatal OOD compared to a control county where the intervention was not implemented. In addition, the difference in the differences in pre- to post-intervention trend showed that the control county had a slight increase in the post-intervention trend of monthly opioid overdoses. However, Chesterfield County saw no difference in the trend between pre- and post-intervention. Thus, although this small sample yielded small effect sizes and no statistical significance, these findings suggest that in the absence of the intervention, Chesterfield County may have also experienced an increase in monthly nonfatal OODs. Therefore, these results provide preliminary evidence that encourages the use of out-of-hospital opioid treatment connection programs to prevent further increases in the trend of monthly nonfatal OODs.

Many of the services offered by Chesterfield County and other EMS-implemented programs directly address the barriers identified in the current study. Similar to Chesterfield County, community paramedics in a Houston program conduct home visits with a peer recovery coach, who uses motivational interviewing to address readiness barriers in survivors of nonfatal OOD[268]. Peer support and recovery specialists could also be used to help patients overcome stigma-related barriers, as they can offer counseling and support through the treatment initiation process based on their own lived experiences.

Out-of-hospital programs can also address financial and structural barriers by connecting opioid-misusing individuals to available treatment programs most appropriate for their care. In Chesterfield, a community paramedic is responsible for determining treatment availability and ensuring program participants are placed in treatment appropriate for their care. This is also similar to previous programs; in Houston, community paramedics are also responsible for following up with patients and scheduling all clinical visits.[268]

In addition, collaborations formed between out-of-hospital programs and treatment facilities may further decrease barriers to treatment access by enabling program patients to gain immediate access to treatment. For example, Chesterfield program participants initially had a 10-day waiting period to receive a mental health evaluation necessary for entering treatment. However, six months after program implementation, participants no longer had to wait to receive this evaluation. Other EMS programs prevent structural delays to accessing treatment by taking it upon themselves to initiate the initial treatment. In Houston, patients enrolled in the program following an outreach visit are assessed by a nurse practitioner and provided with a one or two-week prescription for suboxone as interim treatment until the patient can be connected to a long-term program[268]. In New Jersey, paramedics can request permission from medical oversight physicians to provide buprenorphine to eligible patients immediately following an overdose[269].

To date, many of the out-of-hospital programs currently available to address barriers to accessing treatment for SUD are still in the pilot stages, and at the time of this project, none have assessed the effects of program participation on treatment or population-level outcomes. In this respect, the final aim of this project is unique as it offers findings for the association between implementation of an out-of-hospital intervention and a population level outcome (nonfatal opioid overdoses). Other programs have reported difficulty evaluating the effects of their program on treatment outcomes due to small sample sizes[269] or difficulty obtaining data due to data-sharing agreements and/or privacy concerns.[268] Future researchers should continue to evaluate the effects of out-of-hospital programs on treatment outcomes.

5.4 Conclusions

Although barriers to accessing treatment for SUD continue to persist following implementation of the ACA, the development and implementation of public-health interventions can be targeted towards the subpopulations most likely to perceive barriers. The findings of this project identify these subpopulations, and also report encouraging initial findings for an out-of-hospital intervention that might be used to address these barriers. Future research should expand upon the findings of this project through continued evaluation of innovative intervention programs that can be used to help opioid-misusing individuals overcome persisting obstacles and obtain life-saving treatment.

APPENDIX

APPENDIX A: Tables and Figures

Table 1.1: Public Health Initiatives Addressing the Opioid Epidemic in the United States

Initiative	Aim	Effectiveness	Implementation
PRIMARY PREVENTION			
Prescription Drug Monitoring Programs	Allow physicians and pharmacists access to a patient's history of controlled substance prescriptions to prevent aberrant drug-seeking by the patient (visits to multiple providers) or aberrant prescribing practices by doctors[7]	Studies have suggested that PMP are associated with significant declines in visits to multiple providers[47], and correlated with declines in overall opioid prescribing in states requiring PMP utilization[48]	All 50 states have PMP • 23 mandate clinician enrollment • 13 require use prior to writing a prescription[7]
Prescription Limits	Limit the number of opioid pills written in an initial prescription to decrease the risk of diversion and physical dependence and reduce the overall volume of prescriptions[7]	No studies were found which evaluate effectiveness of state prescription limits, but studies of hospital-based prescriber limits have been associated with modest reductions in mortality[270]	25 states have enacted prescription limits[7]
Prescription Drug Take-Back Programs	Allow easy disposal of leftover medications to reduce availability of unused controlled medications at risk for diversion or misuse[49]	Take-back programs only gather a small fraction of existing opioids, and are not likely have a minimal impact on reducing unused prescription opioids within a community[49]	At least 40 states publicize locations for collection boxes[7]
TERTIARY PREVENTION			
Overdose Education and Naloxone Distribution Programs	Distribute naloxone to community laypersons and individuals at high risk of opioid overdose to prevent overdose deaths[50]	Overdose education programs are effective in improving knowledge related to recognizing and responding to an overdose, and bystanders and individuals who use opioids can administer naloxone to reverse an opioid overdose[51,52]	There are NDPs in 15 states and DC[46], or 8% of U.S. counties[53]
Over-the-counter availability of Naloxone	Increase availability of naloxone to opioid-users and laypersons to increase access in the event of an opioid overdose[7]	Pharmacies in states with standing orders stock naloxone and dispense it without a prescription[54], and adoption of naloxone access laws has been associated with significant reduction in opioid-related deaths[55]	49 states allow OTC prescription of naloxone[7†]
Good Samaritan Laws	Enable bystanders to an opioid overdose to call 911 without fear of being arrested[7]	Good Samaritan laws decrease the proportion of opioid-related deaths, but not significantly[55], Good Samaritan laws were also not associated with an increase in the use of prescription opioids[55]	39 states have enacted GSLs[7]
Syringe-Needle Access Programs	Limit the spread of blood borne infections by providing injection drug users with clean needles[7]	Evidence suggests that access to syringe exchange programs decreases the risk of disease transmission[7], though some studies report less effectiveness at preventing Hepatitis C infection[46]	41 states have syringe access programs[7]
Supervised Drug Consumption Venues	Enable use of pre-obtained drugs in hygienic settings where trained staff are able to respond to overdoses, decreasing risk of fatal overdose[56]	Overdoses were rare (one per 1,287 injections), but were successfully reversed by program staff. Participants in the program also reported more hygienic disposal of syringes[57]	None[‡]

Abbreviations: GSL=Good Samaritan laws, **NDP**=naloxone distribution programs, **OTC**=over the counter, **PMP**=prescription monitoring programs
[†]Nebraska is the only state that does not allow over-the-counter prescription of naloxone
[‡]Supervised drug consumption venues are currently not legal in the US, evaluation of the program mentioned was performed at an un-sanctioned site in the US[57]

Table 2.1: Characteristics of insured U.S. adults by type of opioid misuse (NSDUH 2015-2017) (N=6,095)

	TOTAL (N=6,095)	HO (N=127)	PPR (N=5,580)	H+PPR (N=388)
	N ($\%_w$)	**N ($\%_w$)**	**N ($\%_w$)**	**N ($\%_w$)**
Age				
18-25 years	2783 (26.0)	**43 (15.0)**‡	**2566 (26.1)**‡	**174 (29.1)**‡
26-34 years	1451 (24.1)	**42 (33.0)**‡	**1286 (23.2)**‡	**123 (35.0)**‡
35-49 years	1386 (27.9)	**23 (20.5)**‡	**1288 (28.3)**‡	**75 (23.3)**‡
50-64 years	475 (22.1)	**19 (31.5)**‡	**440 (22.4)**‡	**16 (12.7)**‡
Sex				
Male	3067 (53.4)	**77 (67.4)**†	**2762 (52.4)**†	**228 (64.5)**†
Female	3028 (46.6)	**50 (32.6)**†	**2818 (47.6)**†	**160 (35.5)**†
Race/ethnicity				
Non-Hispanic White	3979 (69.6)	90 (72.2)	3587 (69.2)	302 (75.9)
Non-Hispanic Black	664 (10.2)	13 (14.8)	635 (10.1)	16 (8.8)
Hispanic	572 (6.3)	10 (4.0)	535 (6.5)	27 (4.2)
Other	880 (13.9)	14 (9.2)	823 (14.1)	43 (11.2)
Sexual identity				
Heterosexual	5188 (89.4)	110 (90.8)	4760 (89.6)	318 (86.7)
Lesbian, gay or bisexual	841 (10.6)	15 (9.2)	764 (10.4)	62 (13.3)
Education level				
HS graduate or less	2544 (37.4)	**79 (55.8)**‡	**2252 (36.2)**‡	**213 (48.9)**‡
Some college-graduate	3551 (62.6)	**48 (44.2)**‡	**3328 (63.8)**‡	**175 (51.1)**‡
Total family income				
< $20,000	1590 (21.6)	**65 (56.4)**‡	**1390 (20.0)**‡	**135 (33.6)**‡
> $20,000-$49,000	4505 (78.4)	**62 (43.6)**‡	**4190 (80.0)**‡	**253 (66.4)**‡
Urbanicity				
Large metro	2707 (56.9)	62 (64.0)	2481 (56.7)	164 (56.7)
Small metro	2224 (30.7)	43 (27.5)	2026 (30.7)	155 (32.8)
Non-metro	1164 (12.4)	22 (8.5)	1073 (12.6)	69 (10.5)
Insurance type				
Private insurance	3704 (64.0)	**41 (33.7)**‡	**3527 (66.6)**‡	**136 (35.0)**‡
Medicaid	1882 (27.3)	**74 (58.3)**‡	**1588 (24.8)**‡	**220 (55.7)**‡
Other[b]	509 (8.7)	**12 (8.0)**‡	**465 (8.7)**‡	**32 (9.5)**‡
Survey year				
2015	2190 (34.5)	33 (24.2)	2029 (34.8)	128 (32.4)
2016	1988 (34.3)	53 (37.6)	1795 (34.0)	140 (37.4)
2017	1917 (31.3)	41 (38.2)	1756 (31.2)	120 (30.2)
Self-reported health				
Fair/poor	2971 (49.8)	**87 (71.9)**‡	**2664 (48.9)**‡	**220 (56.1)**‡
Excellent/very good	3123 (50.2)	**40 (28.1)**‡	**2915 (51.1)**‡	**168 (44.0)**‡
Severe psychological distress[c]				
No < 13	3877 (68.3)	**72 (57.5)**‡	**3622 (69.6)**‡	**183 (50.9)**‡
Yes ≥ 13	2218 (31.7)	**55 (42.5)**‡	**1958 (30.4)**‡	**205 (49.1)**‡
Past year IDU				
No	5366 (87.7)	**50 (38.6)**‡	**5195 (92.4)**‡	**121 (29.8)**‡
Yes	729 (12.3)	**77 (61.4)**‡	**385 (7.6)**‡	**267 (70.2)**‡
Additional SUD				
None	3863 (67.7)	**83 (69.2)**‡	**3606 (69.0)**‡	**174 (45.5)**‡
1 additional SUD	1573 (23.3)	**24 (17.7)**‡	**1433 (22.9)** ‡	**116 (32.5)**‡
2 additional SUD	449 (6.4)	**15 (10.4)**‡	**373 (6.0)**‡	**61 (11.4)**‡
3 or more SUD	197 (2.6)	**5 (2.7)**‡	**158 (2.1)**‡	**34 (10.6)**‡

$\%_w$=weighted percent, **H+PPR**=heroin and prescription pain reliever use, **HS**=high school, **H**=heroin use only, **IDU**=injection drug use, **N**=sample size, **NSDUH**=National Survey on Drug Use and Health, **PPR**=prescription pain relievers use, **SUD**=substance use disorder.

NOTE: **Boldface** indicates value of statistical significance; *α<.05, †α<.01, ‡α<.0001

[a]Comprised of Non-Hispanic native American or AK native, Non-Hispanic native HI or other Pacific Islander, and non-Hispanic more than one race

[b]Comprised of Medicare, CHAMPUS, Military Plans, and "any other health insurance not already listed"

[c]K6 scale measures symptoms of psychological distress during the past 30 days, a score ≥ 13 indicates severe psychological distress within the past year

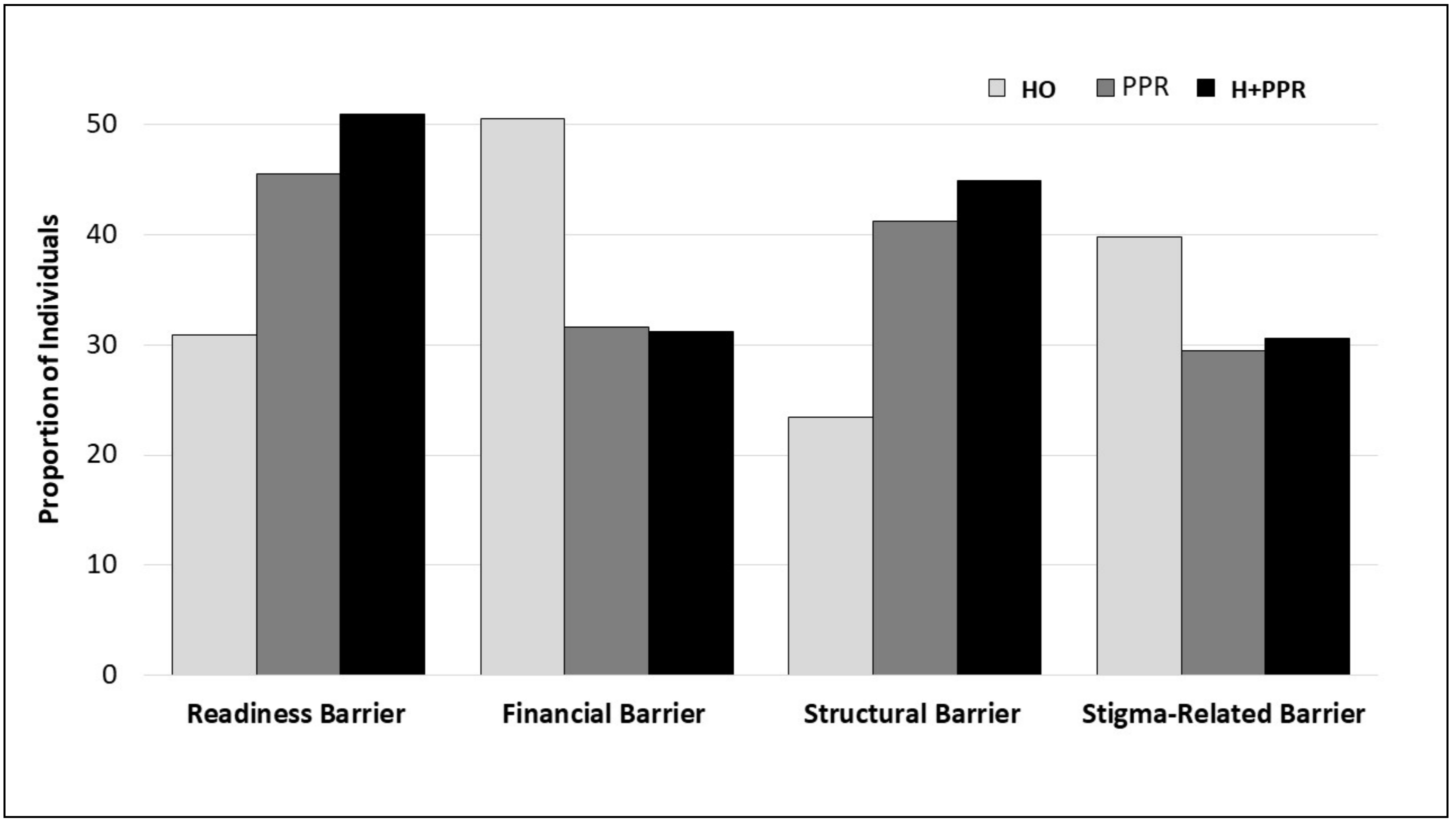


Figure 2.1: Perceived barriers by type of opioid misuse among respondents who reported at least one perceived barrier to accessing substance use disorder treatment (NSDUH 2015-2017) (N=244)

Table 2.2: Adjusted odds ratios for perceived barriers to accessing substance use disorder treatment in the past year by insured adults with past year opioid misuse (NSDUH 2015-2017) (N=6,029)

	Readiness Barrier aOR[a] (95% CI)	Financial Barrier aOR[a] (95% CI)	Structural Barrier aOR[a] (95% CI)	Stigma-Related Barrier aOR[a] (95% CI)
Age				
18-25 years	*Referent*	*Referent*	*Referent*	*Referent*
26-34 years	1.19 (0.58-2.42)	1.85 (0.81-4.24)	**1.89 (1.07-3.33)***	1.03 (0.52-2.06)
35-49 years	1.12 (0.59-2.12)	1.28 (0.61-2.69)	1.14 (0.58-2.21)	0.90 (0.35-2.31)
50-64 years	0.52 (0.20-1.36)	0.25 (0.03-2.52)	0.73 (0.22-2.43)	0.58 (0.12-2.76)
Sex				
Male	0.81 (0.43-1.51)	0.88 (0.49-1.57)	0.77 (0.40-1.52)	0.78 (0.42-1.44)
Female	*Referent*	*Referent*	*Referent*	*Referent*
Race/ethnicity				
Non-Hispanic White	*Referent*	*Referent*	*Referent*	*Referent*
Non-Hispanic Black	0.43 (0.18-1.05)	0.69 (0.18-2.69)	0.82 (0.35-1.94)	0.46 (0.08-2.71)
Hispanic	1.10 (0.49-2.48)	1.22 (0.34-4.32)	1.98 (0.85-4.58)	1.84 (0.60-5.62)
Other[a]	1.12 (0.57-2.19)	**0.17 (0.05-0.54)†**	1.14 (0.47-2.76)	0.70 (0.26-1.88)
Sexual identity				
Heterosexual	*Referent*	*Referent*	*Referent*	*Referent*
Lesbian, gay, or bisexual	**1.70 (1.00-2.90)***	1.17 (0.54-2.50)	1.52 (0.79-2.92)	1.36 (0.64-2.88)
Education level				
HS graduate or less	*Referent*	*Referent*	*Referent*	*Referent*
Some college-graduate	1.40 (0.83-2.37)	0.78 (0.36-1.67)	0.87 (0.48-1.57)	1.37 (0.58-3.27)
Total family income				
< $20,000	1.31 (0.73-2.33)	1.85 (0.79-4.33)	1.16 (0.60-2.23)	**2.82 (1.43-5.56)†**
> $20,000	*Referent*	*Referent*	*Referent*	*Referent*
Urbanicity				
Large metro	*Referent*	*Referent*	*Referent*	*Referent*
Small metro	0.78 (0.43-1.41)	0.95 (0.50-1.77)	0.94 (0.57-1.57)	1.88 (0.97-3.65)
Non-metro	0.91 (0.47-1.75)	1.17 (0.52-2.65)	1.33 (0.66-2.65)	1.77 (0.63-4.93)
Insurance type				
Private insurance	*Referent*	*Referent*	*Referent*	*Referent*
Medicaid	1.54 (0.88-2.70)	2.32 (0.88-6.16)	1.66 (0.66-4.15)	1.06 (0.36-3.13)
Other[b]	**3.12 (1.43-6.81)†**	1.25 (0.52-3.01)	**2.03 (1.05-3.94)***	0.50 (0.19-1.27)
Survey year				
2015	*Referent*	*Referent*	*Referent*	*Referent*
2016	0.78 (0.41-1.49)	0.75 (0.37-1.52)	1.16 (0.60-2.26)	0.64 (0.24-1.75)
2017	1.22 (0.65-2.28)	1.02 (0.52-2.01)	0.80 (0.44-1.46)	0.98 (0.52-1.84)
Self-reported health				
Excellent/very good	*Referent*	*Referent*	*Referent*	*Referent*
Fair/poor	1.25 (0.70-2.21)	1.04 (0.59-1.82)	1.51 (0.97-2.36)	1.33 (0.59-3.00)
Severe psychological distress[c]				
No < 13	*Referent*	*Referent*	*Referent*	*Referent*
Yes ≥ 13	**3.02 (1.55-5.90)†**	**2.45 (1.05-5.70)***	**2.90 (1.53-5.49)†**	**2.90 (1.42-5.92)†**
Past year IDU				
No	*Referent*	*Referent*	*Referent*	*Referent*
Yes	1.43 (0.54-3.81)	1.85 (0.62-5.46)	1.00 (0.44-2.27)	1.34 (0.47-3.80)
Additional SUD	**1.60 (1.29-1.98)‡**	**1.25 (1.08-1.44)†**	**1.34 (1.11-1.62)†**	1.14 (0.86-1.49)
Type of opioid misuse				
PPR	*Referent*	*Referent*	*Referent*	*Referent*
HO	1.08 (0.26-4.46)	1.98 (0.39-9.97)	0.89 (0.15-5.27)	2.25 (0.42-12.14)
H+PPR	**2.80 (1.08-7.27)***	2.03 (0.89-4.60)	**3.27 (1.26-8.46)***	**3.98 (1.42-11.21)***

$\%_w$=weighted percent, **aOR**=adjusted odds ratio, **H+PPR**=heroin and prescription pain reliever use, **HS**=high school, **HO**=heroin use only, **IDU**=injection drug use, **N**=sample size, **NSDUH**=national survey on drug use and health, **PPR**=prescription pain relievers use, **SUD**=substance use disorder.

NOTE: **Boldface** indicates value of statistical significance; *α<.05, †α<.01, ‡α<.0001

[a]Comprised of Non-Hispanic native American or AK native, Non-Hispanic native HI or other Pacific Islander, and non-Hispanic more than one race

[b]Comprised of Medicare, CHAMPUS, Military Plans, and "any other health insurance not already listed"

[c]K6 scale measures symptoms of psychological distress during the past 30 days, a score ≥ 13 indicates severe psychological distress within past year

Supplemental Table 2.1: Reasons why individuals felt they didn't need treatment or additional treatment in the past year (N=382)

Barrier	Explanation	N (%w)	Overall†
Readiness Barrier	Because not ready to stop use	21 (4.6)	4.6
Financial Barrier	Because of cost	11 (2.1)	6.2
	Because no insurance	17 (4.3)	
Structural Barrier	Because no transportation	8 (2.0)	4.9
	Because treatment wanted not offered	6 (1.7)	
	Because No openings in the program	6 (1.2)	
	Because didn't have time	6 (1.4)	
	Because didn't know where to go	4 (0.8)	
Stigma Barrier	Because neighbors have negative opinion	13 (3.2)	4.4
	Because have negative effect on job	14 (2.6)	
	Because didn't want others to find out	7 (1.5)	

These responses are given for the question: "Which of these statements explain why you did not get the treatment or counseling you needed for your use of [*substance*]?"

†Weighted percentages

Supplemental Table 2.2: Bivariate associations between predisposing, enabling, and need characteristics with perceived treatment barriers among insured adults with past year opioid misuse (NSDUH 2015-2017) (N=6,029)

	Readiness Barrier OR (95% CI)	Financial Barrier OR (95% CI)	Structural Barrier OR (95% CI)	Stigma-Related Barrier OR (95% CI)
Age				
18-25 Years	*Referent*	*Referent*	*Referent*	*Referent*
26-34 Years	1.13 (0.62-2.05)	1.79 (0.86-3.74)	**1.76 (1.05-2.95)**†	0.88 (0.51-1.52)
35-49 Years	0.83 (0.48-1.43)	1.10 (0.57-2.13)	0.84 (0.42-1.69)	0.67 (0.28-1.61)
50-64 Years	**0.33 (0.12-0.88)***	0.23 (0.02-2.24)	0.48 (0.16-1.44)	0.39 (0.09-1.65)
Sex				
Male	0.74 (0.43-1.26)	0.84 (0.50-1.40)	0.69 (0.38-1.25)	0.67 (0.37-1.22)
Female	*Referent*	*Referent*	*Referent*	*Referent*
Race/Ethnicity				
Non-Hispanic White	*Referent*	*Referent*	*Referent*	*Referent*
Non-Hispanic Black	**0.45 (0.21-0.98)***	0.66 (0.20-2.17)	0.87 (0.38-2.00)	0.36 (0.08-1.75)
Hispanic	1.15 (0.53-2.52)	1.30 (0.32-5.24)	2.04 (0.85-4.87)	1.61 (0.50-5.20)
Other	1.06 (0.59-1.91)	**0.19 (0.06-0.59)***	1.12 (0.43-2.94)	0.56 (0.21-1.50)
Sexual Identity				
Heterosexual	*Referent*	*Referent*	*Referent*	*Referent*
Lesbian, Gay, or Bisexual	**2.67 (1.74-4.12)**‡	1.63 (0.84-3.19)	**2.35 (1.27-4.35)**†	**2.21 (1.07-4.57)***
Education Level				
Less than HS or HS grad	*Referent*	*Referent*	*Referent*	*Referent*
Some college, AS, or CG	1.19 (0.72-1.95)	0.67 (0.33-1.34)	0.69 (0.37-1.27)	1.22 (0.54-2.79)
Total family income				
< \$20,000	**1.81 (1.12-2.92)***	**2.55 (1.30-5.03)**†	**2.01 (1.20-3.38)**†	**3.05 (1.71-5.45)**†
> \$20,000	*Referent*	*Referent*	*Referent*	*Referent*
Urbanicity				
Large metro	*Referent*	*Referent*	*Referent*	*Referent*
Small metro	1.03 (0.59-1.81)	1.31 (0.73-2.36)	1.17 (0.71-1.92)	2.27 (1.15-4.46)
Non-metro	1.11 (0.63-1.94)	1.68 (0.70-4.02)	1.62 (0.77-3.42)	2.04 (0.72-5.74)
Insurance Type				
Private Insurance	*Referent*	*Referent*	*Referent*	*Referent*
Medicaid	**2.47 (1.53-4.00)***	**2.73 (1.56-4.82)**†	**3.79 (2.16-6.64)**†	1.29 (0.74-2.22)
Other[a]	**3.54 (1.73-7.25)***	**2.95 (1.06-8.17)**†	2.28 (0.85-6.10)	1.61 (0.54-4.79)
Year				
2015	*Referent*	*Referent*	*Referent*	*Referent*
2016	0.88 (0.47 – 1.68)	0.82 (0.40-1.68)	1.26 (0.64-2.46)	0.72 (0.27-1.98)
2017	1.41 (0.77 – 2.57)	1.53 (0.61-2.19)	0.92 (0.50-1.69)	1.13 (0.58-2.21)
Self-Reported Health				
Excellent/Very Good	*Referent*	*Referent*	*Referent*	*Referent*
Fair/Poor	**1.70 (1.05-2.74)***	1.49 (0.94-2.37)	**2.17 (1.34-3.50)**†	1.67 (0.84-3.36)
Severe psychological distress				
No < 13	*Referent*	*Referent*	*Referent*	*Referent*
Yes ≥ 13	**5.51 (3.13-9.73)**‡	**3.85 (1.73-8.60)**†	**4.73 (2.55-8.77)**‡	**4.31 (2.07-8.96)**†
Past Year IDU				
No	*Referent*	*Referent*	*Referent*	*Referent*
Yes	**3.67 (1.88-7.18)**†	**4.41 (2.24-8.70)**‡	**18.12 (9.90-33.17)**†	**3.30 (1.66-6.56)**†
Additional SUD	**1.90 (1.60-2.25)**‡	**1.52 (1.33-1.73)**‡	**1.60 (1.38-1.86)**‡	**1.42 (1.19-1.71)**†
Past Year Opioid Misuse				
PPR	*Referent*	*Referent*	*Referent*	*Referent*
HO	1.56 (0.46-5.32)	3.74 (0.88-15.81)	1.29 (0.21-7.90)	3.14 (0.70-14.02)
H+PPR	**6.20 (3.20-12.01)**†	**5.34 (2.76-10.27)***	**5.91 (3.11-11.22)**†	**5.60 (2.68-11.69)***

HO=heroin use, **PPR**=pain reliever use, **H+PPR**= heroin and pain reliever use, **SUD**=substance use disorder, **IDU**=injection drug use, **HS**=high school, **N**=sample size, **%w**=weighted percent, **NSDUH**=national survey on drug use and health, **OR**=odds ratio, **95% CI**=95% confidence interval

NOTE: Boldface indicates statistical significance; *α<.05, †α<.01, ‡α<.0001

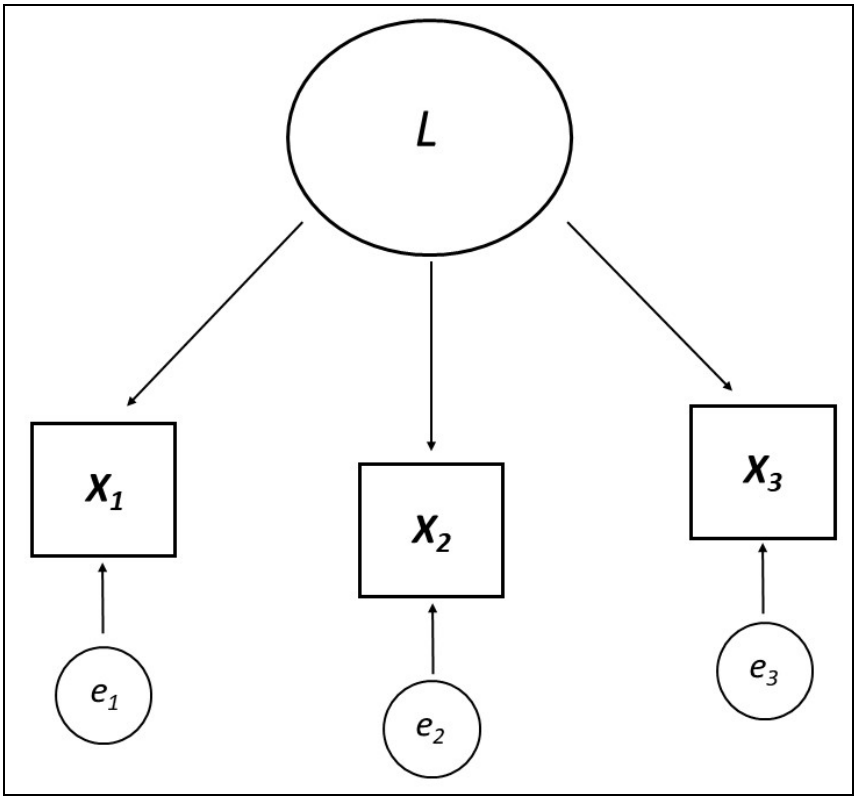


Figure 3.1: Schematic representation of the latent variable
Adapted from Uebersax, 1994

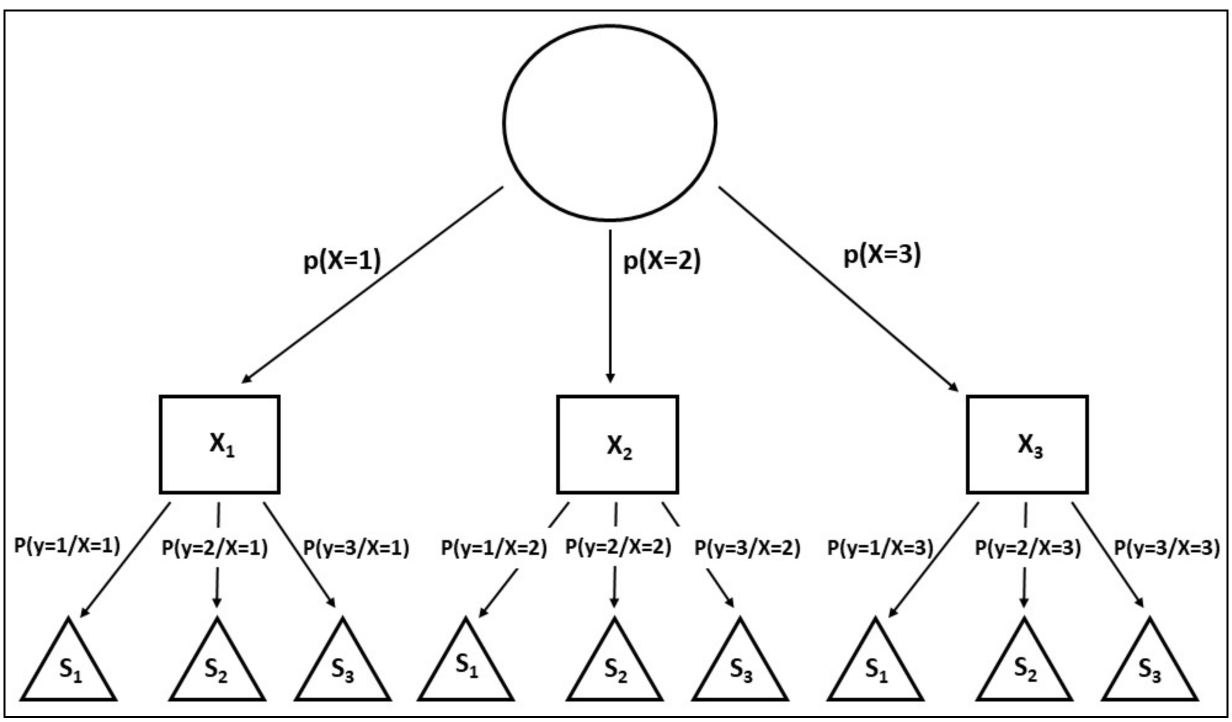


Figure 3.2: Schematic representation of the latent class model
Adapted from Uebersax, 1994

Table 3.1: Latent class analysis model fit statistics for classes 2-6

Classes	BIC_{ss}	Entropy	p-value for LMR[a]	Loglikelihood	Npar	p-value for BLRT[a]
2-CLASS	55384.4	0.787	<.0001	-27600.8	33	<.0001
3-CLASS	52734.0	0.837	<.0001	-26228.6	50	<.0001
4-CLASS	52502.9	0.709	<.0001	-26066.0	67	<.0001
5-CLASS	52121.0	0.747	0.0001	-25827.9	84	<.0001
6-CLASS	52078.8	0.768	0.2054	-25759.8	101	<.0001

BIC_{ss}=Sample Size Adjusted Bayes Information Criteria, **BLRT**=Bootstrapped Likelihood Ratio Test, **LCA**=Latent Class Analysis, **LMR**=Lo-Mendell-Rubin Adjusted Likelihood Ratio Test, **Npar**=Number of parameters

[a]LMR and BLRT compare the increase in model fit between the *k-1*and *k* class models. Significant values indicate that the model has a statistically better fit than the model that preceeded it.

Table 3.2: Conditional probabilities of past year substance use among individuals reporting past year opioid misuse for three classes of polysubstance use (NSDUH 2015-2017) (N=6095)

	Overall[a] (n=6095, 100%)	**C1: Heroin injectors with high PSU** (n=473, 7.8%)	**C2: PPR users with low PSU** (n=4000, 65.6%)	**C3: PPR users with high PSU** (n=1622, 26.6%)
Licit/Near licit Substance Use	n (%)	n ($\%_c$)	n ($\%_c$)	n ($\%_c$)
Binge alcohol	3235 (53.1)	188 (39.8)	1704 (42.6)	1312 (80.9)
Marijuana	3437 (56.4)	337 (71.3)	1500 (37.5)	1551 (95.6)
Prescription Drug Misuse				
PPR	5934 (97.5)	350 (74.1)	3976 (99.4)	1619 (99.8)
Tranquilizers	1627 (26.8)	202 (42.7)	548 (13.7)	853 (52.6)
Stimulants	1242 (20.4)	122 (25.8)	276 (6.9)	814 (50.2)
Sedatives	340 (5.6)	49 (10.3)	136 (3.4)	151 (9.3)
Illicit Substance Use				
Heroin	511 (8.4)	423 (89.5)	32 (0.8)	63 (3.9)
Cocaine	1097 (18.0)	257 (54.4)	44 (1.1)	756 (46.6)
Crack	221 (3.6)	158 (33.3)	0 (0)	57 (3.5)
Hallucinogens	976 (16.0)	113 (23.8)	48 (1.2)	775 (47.8)
Inhalants	243 (4.0)	38 (8.0)	44 (1.1)	152 (9.4)
Methamphetamines	385 (6.3)	175 (37.0)	44 (1.1)	157 (9.7)
Injection Drug Use				
Used Needle to Inject Cocaine	98 (1.6)	90 (19.1)	0 (0)	3 (0.2)
Used Needle to Inject Heroin	277 (4.5)	271 (57.3)	0 (0)	0 (0)
Used Needle to Inject Methamphetamines	142 (2.3)	131 (27.6)	0 (0)	8 (0.5)
Used Needle to Inject Other Drug	159 (2.6)	140 (29.7)	8 (0.2)	6 (0.4)

$\%_c$=Conditional probability of class membership, **N**=Sample size, **NSDUH**=National survey on drug use and health, **PPR**=Prescription pain reliever, **PSU**=Polysubstance use

[a]Overall column provides the past-year substance and injection drug use for the entire population.

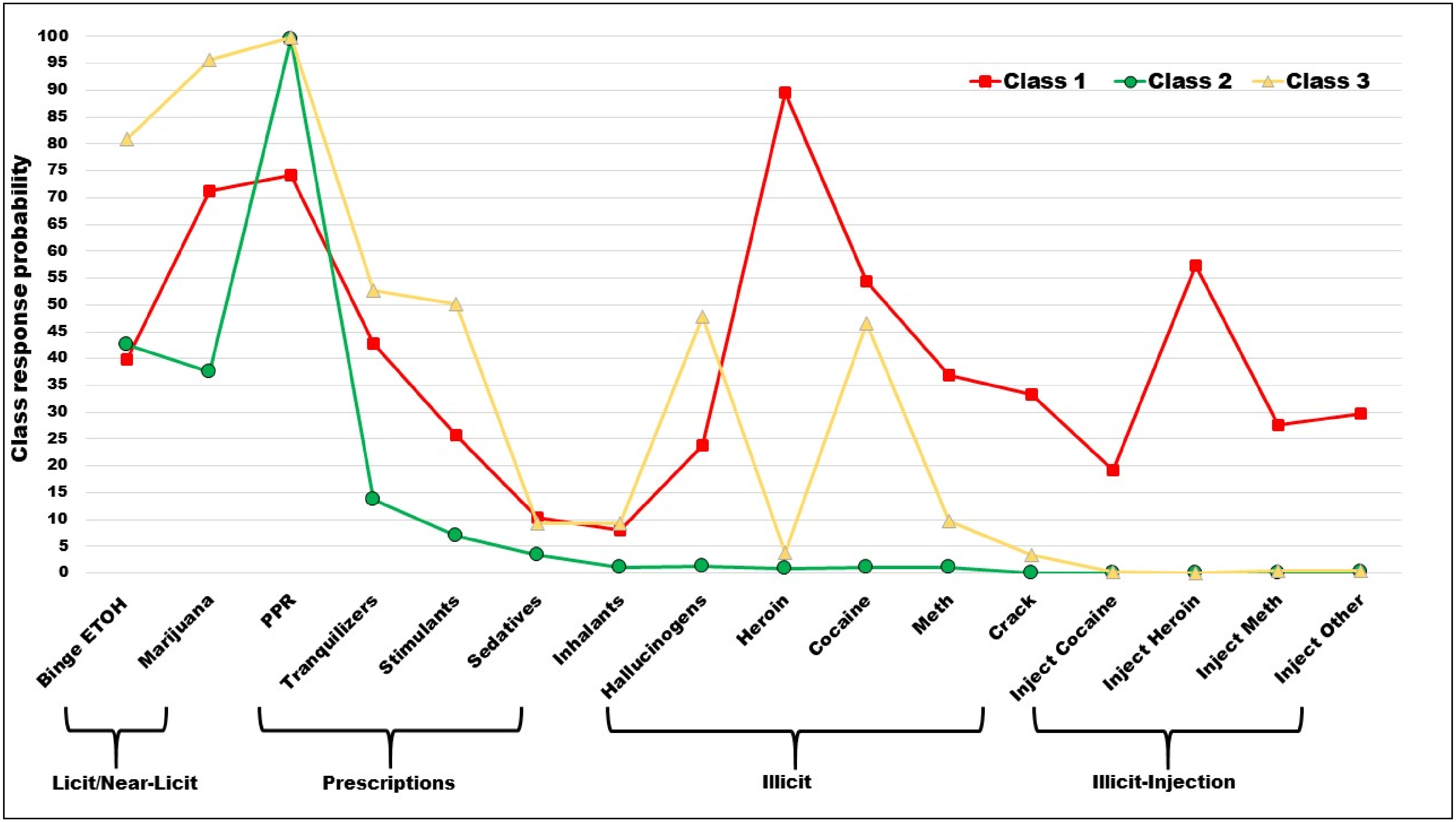


Figure 3.3: Latent classes of past year polysubstance use
ETOH=alcohol, **PPR**=prescription pain relievers

Table 3.3: Sociodemographic characteristics of insured opioid-misusing adults by latent class of polysubstance use (NSDUH 2015-2017) (N=6,095)

	TOTAL (N=6,095)	C1: Heroin injectors with high PSU (N=473)	C2: PPR users with low PSU (N=4000)	C3: PPR users with high PSU (N=1622)
	N ($\%_w$)	N ($\%_w$)	N ($\%_w$)	N ($\%_w$)
Age[‡]				
18-25 years	2783 (26.0)	**178 (20.7)**	**1495 (19.0)**	**1110 (51.7)**
26-34 years	1451 (24.1)	**150 (33.5)**	**987 (22.6)**	**314 (26.0)**
35-49 years	1386 (27.9)	**105 (26.5)**	**1119 (32.0)**	**162 (14.4)**
50-64 years	475 (22.1)	**40 (19.4)**	**399 (26.5)**	**36 (7.9)**
Sex[‡]				
Male	3067 (53.4)	**284 (65.9)**	**1830 (48.9)**	**953 (64.2)**
Female	3028 (46.6)	**189 (34.1)**	**2170 (51.1)**	**669 (35.8)**
Race/ethnicity[†]				
Non-Hispanic White	3979 (69.6)	**354 (73.1)**	**2480 (68.0)**	**1145 (73.8)**
Non-Hispanic Black	664 (10.2)	**29 (11.6)**	**532 (11.2)**	**103 (6.2)**
Hispanic	572 (6.3)	**39 (4.2)**	**386 (6.6)**	**147 (6.3)**
Other[a]	880 (13.9)	**51 (11.1)**	**602 (14.2)**	**227 (13.6)**
Sexual identity[‡]				
Heterosexual	5188 (89.4)	**397 (89.2)**	**3470 (90.9)**	**1321 (84.6)**
Lesbian, gay or bisexual	841 (10.6)	**68 (10.8)**	**484 (9.1)**	**289 (15.4)**
Education level[‡]				
HS graduate or less	2544 (37.4)	**274 (51.9)**	**1620 (36.0)**	**650 (36.9)**
Some college-graduate	3551 (62.6)	**199 (48.1)**	**2380 (64.0)**	**972 (63.1)**
Total family income[‡]				
< $20,000	1590 (21.6)	**198 (44.2)**	**939 (18.4)**	**453 (24.3)**
> $20,000-$49,000	4505 (78.4)	**275 (55.8)**	**3061 (81.6)**	**1169 (75.7)**
Urbanicity				
Large metro	2707 (56.9)	199 (56.1)	1796 (57.5)	712 (55.0)
Small metro	2224 (30.7)	174 (31.2)	1439 (30.0)	611 (32.9)
Non-metro	1164 (12.4)	100 (12.7)	765 (12.5)	299 (12.1)
Insurance type[‡]				
Private insurance	3704 (64.0)	**147 (31.4)**	**2463 (65.9)**	**1094 (69.7)**
Medicaid	1882 (27.3)	**283 (59.1)**	**1211 (25.2)**	**388 (22.9)**
Other[b]	509 (8.7)	**43 (9.5)**	**326 (9.0)**	**140 (7.4)**
Survey year				
2015	2190 (34.5)	132 (28.8)	1463 (34.8)	595 (35.3)
2016	1988 (34.3)	180 (36.3)	1283 (34.1)	525 (34.0)
2017	1917 (31.3)	161 (34.9)	1254 (31.1)	502 (30.7)
Self-reported health[‡]				
Fair/poor	2971 (49.8)	**303 (63.7)**	**1976 (50.0)**	**692 (44.3)**
Excellent/very good	3123 (50.2)	**170 (36.3)**	**2023 (50.0)**	**930 (55.7)**
Severe psychological distress[c‡]				
No < 13	3877 (68.3)	**240 (52.1)**	**2725 (72.7)**	**912 (59.3)**
Yes ≥ 13	2218 (31.7)	**233 (47.9)**	**1275 (27.3)**	**710 (40.7)**
Past year tobacco use[‡]				
No	2037 (39.2)	**26 (8.2)**	**1789 (49.4)**	**222 (15.6)**
Yes	4058 (60.8)	**447 (91.8)**	**2211 (50.6)**	**1400 (84.4)**
Average cigarette use per day for past 30 days[‡]				
Never used/don't smoke	2990 (53.8)	**59 (16.6)**	**2411 (63.3)**	**520 (34.9)**
<1 – 1 per day	572 (7.7)	**26 (6.1)**	**278 (6.0)**	**268 (14.3)**
2 to 5 per day	834 (12.3)	**6 (15.2)**	**437 (9.9)**	**331 (19.4)**
6 to 15 per day	893 (12.5)	**153 (25.7)**	**442 (9.5)**	**298 (18.1)**
16 to > 35 per day	803 (13.6)	**169 (36.4)**	**430 (11.3)**	**204 (13.4)**

$\%_w$=weighted percent, **HS**=high school, **N**=sample size, **NSDUH**=National survey on drug use and health, **PPR**=prescription pain relievers use, **PSU**=Polysubstance use NOTE: **Boldface** indicates value of statistical significance; [*]α<.05, [†]α<.01, [‡]α<.0001

[a]Comprised of Non-Hispanic native American or AK native, Non-Hispanic native HI or other Pacific Islander, and non-Hispanic more than one race

[b]Comprised of Medicare, CHAMPUS, Military Plans, and "any other health insurance not already listed"

[c]K6 scale measures symptoms of psychological distress during the past 30 days, a score ≥ 13 indicates severe psychological distress within the past year

Table 3.4: Association between classes of polysubstance use and perceived barriers to accessing treatment for substance use disorder (NSDUH 2015-2017) (N=6,029)

	Readiness Barrier	**Financial Barrier**	**Structural Barrier**	**Stigma-Related Barrier**
	aOR[a] (95% CI)	**aOR[a] (95% CI)**	**aOR[a] (95% CI)**	**aOR[a] (95% CI)**
Classes of PSU				
C1: Heroin injectors with high PSU	**3.11 (1.43-6.77)**[†]	1.76 (0.64-4.85)	**2.42 (1.22-4.79)**[*]	**3.13 (1.31-7.48)**[*]
C2: PPR users with low PSU	*Referent*	*Referent*	*Referent*	*Referent*
C3: PPR users with high PSU	**2.89 (1.41-5.93)**[†]	1.58 (0.75-3.33)	1.65 (0.83-3.26)	2.28 (0.99-5.24)

95%CI=95% confidence interval, **aOR=**adjusted odds ratio, **N=**sample size, **NSDUH=**national survey on drug use and health, **PPR=**prescription pain reliever, **PSU=**polysubstance use, **SUD=**substance use disorder.
[a]Model adjusted for age, sex, race/ethnicity, sexual identity, education level, total family income, urbanicity, insurance type, year, self-reported health, severe psychological distress, and average number of cigarettes/day.
NOTE: **Boldface** indicates value of statistical significance; [*]α<.05, [†]α<.01, [‡]α<.0001

Supplemental Table 3.1: Specific drugs making up substance use categories[114]

	Classification Question for Misuse	Drugs Included
Hallucinogens	"How long has it been since you have used any hallucinogen?"	**LSD**, also called 126 "acid"; **PCP**, also called "angel dust" or phencyclidine; **peyote**; **mescaline**; **psilocybin**, found in mushrooms; **"Ecstasy"** or **"Molly,"** also known as MDMA; **ketamine**, also called "Special K" or "Super K"; **DMT**, also called imethyltryptamine, AMT, also called alpha-methyltryptamine, or Foxy, also called 5-MeO-DIPT; **Salvia divinorum**; and **any other hallucinogen** besides the ones that have been listed.
Inhalants	"Have you ever inhaled any of the following substances, even once, for kicks or to get high?"	amyl nitrite, "poppers," locker room odorizers, or "rush"; correction fluid, degreaser, or cleaning fluid; gasoline or lighter fluid; glue, shoe polish, or toluene; halothane, ether, or other anesthetics; lacquer thinner or other paint solvents; lighter gases, such as butane or propane; nitrous oxide or "whippets"; felt-tip pens, felt-tip markers, or magic markers; spray paints; computer keyboard cleaner, also known as air duster; some other aerosol spray; and any other inhalant besides the ones that have been listed.
Pain Relievers	"Have you ever, even once, used any prescription pain reliever in a way that a doctor did not direct the respondent to use it"	**Hydrocodone products** (Vicodin®, Lortab®, Norco®, Zohydro® ER, or generic hydrocodone); **Oxycodone products** (OxyContin®, Percocet®, Percodan®, Roxicodone®, or generic oxycodone); **Tramadol products** (Ultram®, Ultram® ER, Ultracet®, generic tramadol, or generic extended-release tramadol); **Codeine products** (Tylenol® with codeine 3 or 4 or generic codeine pills); **Morphine products** (Avinza®, Kadian®, MS Contin®, generic morphine, or generic extended-release morphine); **Fentanyl products** Duragesic®, Fentora®, or generic fentanyl); **Buprenorphine products** (Suboxone®, generic buprenorphine, or generic buprenorphine plus naloxone); **Oxymorphone products** (Opana®, Opana® ER, generic oxymorphone, or generic extended-release oxymorphone), 148 Demerol®; **Hydromorphone products** (Dilaudid® or generic hydromorphone, or Exalgo® or generic extended-release hydromorphone); **Methadone; Any other prescription pain reliever***
Sedatives	"Have you ever, even once, used any prescription sedatives in a way that a doctor did not direct the respondent to use it"	**Zolpidem products** (Ambien®, Ambien® CR, generic zolpidem, or generic extended-release zolpidem); **eszopiclone products** (Lunesta® or generic eszopiclone); **zaleplon products** (Sonata® or generic zaleplon); **benzodiazepine sedatives** (flurazepam [also known as Dalmane®], **temazepam products** [Restoril®, or generic temazepam], or triazolam [Halcion® or generic triazolam]); **barbiturates** (Butisol®, Seconal®, or phenobarbital); or any other Prescription sedative.
Stimulants	"Have you ever, even once, used any prescription stimulants in a way that a doctor did not direct the respondent to use it"	**Amphetamine products** (Adderall®, Adderall® XR, Dexedrine®, Vyvanse®, generic dextroamphetamine, generic amphetaminedextroamphetamine combinations, or generic extended-release amphetamine-dextroamphetamine combinations); **methylphenidate products** (Ritalin®, Ritalin® LA, Concerta®, Daytrana®, Metadate CD, Metadate ER, Focalin, Focalin XR, generic methylphenidate, generic extended-release methylphenidate, generic dexmethylphenidate, or generic extended-release dexmethylphenidate); **anorectic (weight-loss) stimulants** (Didrex®, benzphetamine, Tenuate®, diethylpropion, phendimetrazine, or phentermine); **Provigil®**; **or any other prescription stimulant.**
Tranquilizers	"Have you ever, even once, used any prescription tranquilizers in a way that a doctor did not direct the respondent to use it"	**benzodiazepine tranquilizers** (including alprazolam products [Xanax®, Xanax® XR, generic alprazolam, or generic extendedrelease alprazolam]; **lorazepam products** [Ativan® or generic lorazepam]; **clonazepam products** [Klonopin® or generic clonazepam]; or **diazepam products** [Valium® or generic diazepam]); **muscle relaxants** (cyclobenzaprine [also known as Flexeril®] or Soma®); **or any other prescription tranquilizer.**

Supplemental Table 3.2: Adjusted odds ratios for perceived barriers to accessing substance use disorder treatment in the past year by insured adults reporting past year opioid misuse (NSDUH 2015-2017)

	Readiness Barrier aOR[a] (95% CI)	Financial Barrier aOR[a] (95% CI)	Structural Barrier aOR[a] (95% CI)	Stigma-Related Barrier aOR[a] (95% CI)
Age				
18-25 years	*Referent*	*Referent*	*Referent*	*Referent*
26-34 years	1.41 (0.74-2.69)	1.69 (0.79-3.62)	1.76 (0.95-3.26)	1.16 (0.53-2.54)
35-49 years	1.49 (0.83-2.67)	1.22 (0.63-2.37)	1.16 (0.58-2.31)	1.08 (0.36-3.21)
50-64 years	0.62 (0.22-1.72)	0.28 (0.03-2.86)	0.76 (0.21-2.73)	0.76 (0.11-4.99)
Sex				
Male	0.89 (0.49-1.61)	0.87 (0.51-1.51)	0.75 (0.39-1.46)	0.74 (0.42-1.32)
Female	*Referent*	*Referent*	*Referent*	*Referent*
Race/ethnicity				
Non-Hispanic White	*Referent*	*Referent*	*Referent*	*Referent*
Non-Hispanic Black	0.44 (0.19-1.02)	0.96 (0.29-3.17)	1.01 (0.38-2.67)	0.53 (0.09-3.16)
Hispanic	1.02 (0.47-2.21)	1.36 (0.39-4.71)	2.22 (0.95-5.17)	1.82 (0.59-5.57)
Other[a]	1.00 (0.50-2.00)	**0.24 (0.07-0.77)***	1.43 (0.50-4.08)	0.77 (0.27-2.22)
Sexual identity				
Heterosexual	*Referent*	*Referent*	*Referent*	*Referent*
Lesbian, gay, or bisexual	1.66 (0.99-2.80)	1.26 (0.62-2.54)	1.61 (0.84-3.06)	1.51 (0.71-3.21)
Education level				
HS graduate or less	*Referent*	*Referent*	*Referent*	*Referent*
Some college-graduate	1.36 (0.81-2.29)	1.03 (0.49-2.16)	1.02 (0.59-1.77)	1.55 (0.66-3.61)
Total family income				
< $20,000	1.21 (0.70-2.11)	1.80 (0.81-3.98)	1.02 (0.53-1.97)	**2.53 (1.27-5.03)**[†]
> $20,000	*Referent*	*Referent*	*Referent*	*Referent*
Urbanicity				
Large metro	*Referent*	*Referent*	*Referent*	*Referent*
Small metro	0.81 (0.44-1.51)	0.97 (0.55-1.70)	0.97(0.58-1.61)	1.90 (0.93-3.88)
Non-metro	0.94 (0.51-1.74)	1.00 (0.48-2.09)	1.19 (0.60-2.36)	1.66 (0.61-4.50)
Insurance type				
Private insurance	*Referent*	*Referent*	*Referent*	*Referent*
Medicaid	**3.47 (1.67-7.23)**[†]	2.16 (0.80-5.84)	1.53 (0.61-3.83)	1.08 (0.38-3.10)
Other[b]	**1.88 (1.06-3.34)**[*]	1.15 (0.49-2.71)	1.85 (0.98-3.49)	0.55 (0.23-1.34)
Survey year				
2015	*Referent*	*Referent*	*Referent*	*Referent*
2016	0.81 (0.42-1.55)	0.80 (0.41-1.59)	1.15 (0.60-2.21)	0.68 (0.25-1.82)
2017	1.32 (0.72-2.42)	1.10 (0.56-2.17)	0.82 (0.44-1.52)	0.99 (0.52-1.86)
Self-reported health				
Excellent/very good	*Referent*	*Referent*	*Referent*	*Referent*
Fair/poor	1.35 (0.74-2.45)	0.86 (0.48-1.53)	1.32 (0.85-2.07)	1.22 (0.52-2.88)
Severe psychological distress[c]				
No < 13	*Referent*	*Referent*	*Referent*	*Referent*
Yes ≥ 13	**3.48 (1.92-6.29)**[‡]	**2.51 (1.15-5.48)**[*]	**2.90 (1.58-5.34)**[†]	**2.77 (1.44-5.34)**[†]
Average cigarette use per day for past 30 days				
Non-Smoker	*Referent*	*Referent*	*Referent*	*Referent*
<1-1 per day	1.51 (0.61-3.76)	1.53 (0.31-7.55)	2.77 (0.85-9.04)	0.73 (0.15-3.53)
2-5 per day	**2.45 (1.12-5.35)**[*]	1.49 (0.34-6.48)	**5.52 (1.90-16.03)**[‡]	**3.59 (1.06-12.22)**[*]
6-15 per day	1.57 (0.70-3.53)	**4.98 (2.21-11.23)**[‡]	**4.93 (1.74-13.98)**[†]	1.72 (0.53-5.51)
16->35 per day	0.85 (0.35-2.02)	**6.86 (3.07-15.36)**[†]	**5.74 (2.50-13.16)**[†]	**3.40 (1.27-9.15)**[*]
Classes of PSU				
C1: Heroin injectors with high PSU	**3.11 (1.43-6.77)**[†]	1.76 (0.64-4.85)	**2.42 (1.22-4.79)**[*]	**3.13 (1.31-7.48)**[*]
C2: PPR users with low PSU	*Referent*	*Referent*	*Referent*	*Referent*
C3: PPR users with high PSU	**2.89 (1.41-5.93)**[†]	1.58 (0.75-3.33)	1.65 (0.83-3.26)	2.28 (0.99-5.24)

%$_w$=weighted percent, **aOR**=adjusted odds ratio, **H+PPR**=heroin and prescription pain reliever use, **HS**=high school, **HO**=heroin use only, **IDU**=injection drug use, **N**=sample size, **NSDUH**=national survey on drug use and health, **PPR**=prescription pain relievers use, **SUD**=substance use disorder.

NOTE: **Boldface** indicates value of statistical significance; [*]α<.05, [†]α<.01, [‡]α<.0001

[a]Comprised of Non-Hispanic native American or AK native, Non-Hispanic native HI or other Pacific Islander, and non-Hispanic more than one race

[b]Comprised of Medicare, CHAMPUS, Military Plans, and "any other health insurance not already listed"

[c]K6 scale measures symptoms of psychological distress during the past 30 days, a score ≥ 13 indicates severe psychological distress within the past year

Table 4.1: Demographic and incident-related characteristics for nonfatal opioid overdoses in Chesterfield County and the Control County 2016-2020[e] (N=1,888)

	Chesterfield N=1,009 (6.0%)	Control N=879 (5.3%)	Total N=1,888
Age[‡]			
18-24 years	**120 (11.9)**	**122 (13.9)**	242 (12.8)
25-34 years	**385 (38.2)**	**264 (30.0)**	649 (34.4)
35-44 years	**211 (20.9)**	**178 (20.3)**	389 (20.6)
45-54 years	**151 (15.0)**	**161 (18.3)**	312 (16.5)
55-64 years	**86 (8.5)**	**96 (10.9)**	182 (9.6)
≥ 65 years	**56 (5.6)**	**58 (6.6)**	114 (6.0)
Sex[d*]			
Female	**392 (38.9)**	**287 (33.1)**	679 (36.2)
Male	**617 (61.2)**	**579 (66.9)**	1196 (63.8)
Race/ethnicity[d‡]			
Non-Hispanic White	**740 (74.1)**	**554 (65.3)**	1294 (70.0)
Non-Hispanic Black	**225 (22.5)**	**272 (32.1)**	497 (29.9)
Other	**34 (3.4)**	**22 (2.6)**	56 (3.0)
Overdose year[‡]			
2016	224 (22.2)	191 (21.7)	415 (22.0)
2017	244 (24.2)	223 (25.4)	467 (24.7)
2018	244 (24.2)	214 (24.4)	458 (24.2)
2019	275 (27.3)	231 (26.3)	506 (26.8)
2020	22 (2.2)	20 (2.3)	42 (2.2)
Overdose location[d†]			
Private residence	**684 (67.9)**	**521 (59.5)**	1205 (64.0)
Public area	**308 (30.6)**	**322 (36.8)**	630 (33.5)
Residential facility	**15 (1.5)**	**33 (3.8)**	48 (2.5)
Route of naloxone administration[d‡]			
IV	**285 (28.6)**	**483 (56.0)**	768 (41.3)
IN	**602 (60.4)**	**243 (28.2)**	845 (45.4)
IM/ other[b]	**16 (1.6)**	**24 (2.8)**	40 (2.2)
Combined[c]	**94 (9.4)**	**113 (13.1)**	207 (11.1)
Total dose of naloxone			
0.4 – 0.99 mg	**86 (8.6)**	**118 (13.9)**	204 (11.1)
1.0 – 1.9 mg	**134 (13.5)**	**264 (31.1)**	398 (21.6)
2.0 – 2.9 mg	**236 (23.7)**	**335 (39.5)**	571 (31.0)
3.0 – 4.9 mg	**437 (43.9)**	**122 (14.4)**	559 (30.3)
≥ 5.0 mg	**103 (10.3)**	**9 (1.1)**	112 (6.1)

%= percent, **IM=**intramuscular, **IN=**intranasal**, IV=**intravenous, **mg=**milligrams**, N=**sample size
[*]α<.05, [†]α<.01, [‡]α<.0001
[a] All values reported as percentages within each column as N (%)
[b] Other included all intra-muscular routes and any other routes of medication administration not already mentioned, including ET tubes, etc.
[c] Combined is any individual who was administered naloxone through multiple routes
[d]Frequencies may not add up due to missing values
[e]February 1[st] 2016 – January 31[st] 2020

Table 4.2: Single interrupted time series of monthly nonfatal opioid overdoses in Chesterfield County[a] (2016-2020)

	P	Estimate	SE	p-value
Intercept	β_0	2.877163	0.140802	<.0001
Pre-Intervention Slope	β_1	0.013664	0.009478	0.1565
Change in Level (pre-post interruption)	β_2	-0.326317	0.185637	0.0857
Change in Slope (pre-post interruption)	β_3	0.001356	0.013343	0.9195
Post-Intervention Slope	$\beta_1 + \beta_3$	0.01502	0.002959	---

SE=standard error, **P**=parameter
NOTE: Pre-intervention = February 1st 2016 – January 31st 2018, Post-Intervention = February 1st 2018 – January 31st 2020.
[a]Estimates adjusted for overdispersion

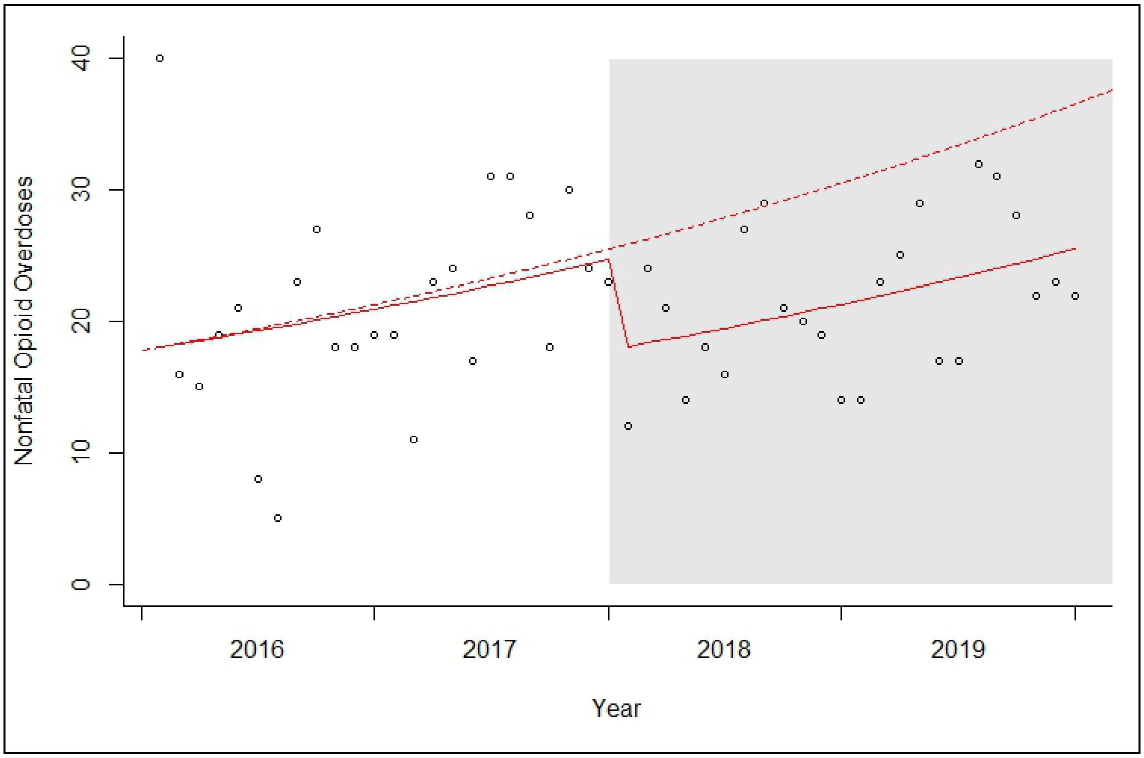


Figure 4.1: Single interrupted time series analysis of nonfatal opioid overdoses in Chesterfield County
Solid line= modeled trend for the monthly number of nonfatal opioid overdoses, dashed line = counterfactual, or predicted trend if no intervention had been implemented.
Area shaded in gray represents the post-intervention period (February 1st 2018 – January 31st 2020).

Table 4.3: Multiple interrupted time series for monthly nonfatal opioid overdoses comparing Chesterfield County to Control County[a] (2016-2020)

	Parameter	Estimate	SE	p-value
Intercept	β_0	2.851519	0.145439	<.0001
Pre-Intervention slope (Control)	β_1	-0.003269	0.010277	0.7512
Δ Level (pre-post interruption) (Control)	β_2	-0.148562	0.204838	0.4702
Δ Slope (pre-post interruption) (Control)	β_3	0.024081	0.014280	0.0953
Δ Pre-intervention level (Treatment vs. Control)	β_4	0.025645	0.198878	0.8977
Δ Pre-intervention slope (Treatment vs. Control)	β_5	0.016933	0.013748	0.2214
Δ Differences in level (pre-to-post intervention) (Treatment vs. Control)	β_6	-0.177755	0.271924	0.5150
Δ Differences in slope (pre-to-post intervention) (Treatment vs. Control)	β_7	-0.022725	0.019214	0.2401

SE=standard error
NOTE: Pre-intervention = February 1st 2016 – January 31st 2018, Post-Intervention = February 1st 2018 – January 31st 2020.
[a]Estimates adjusted for overdispersion

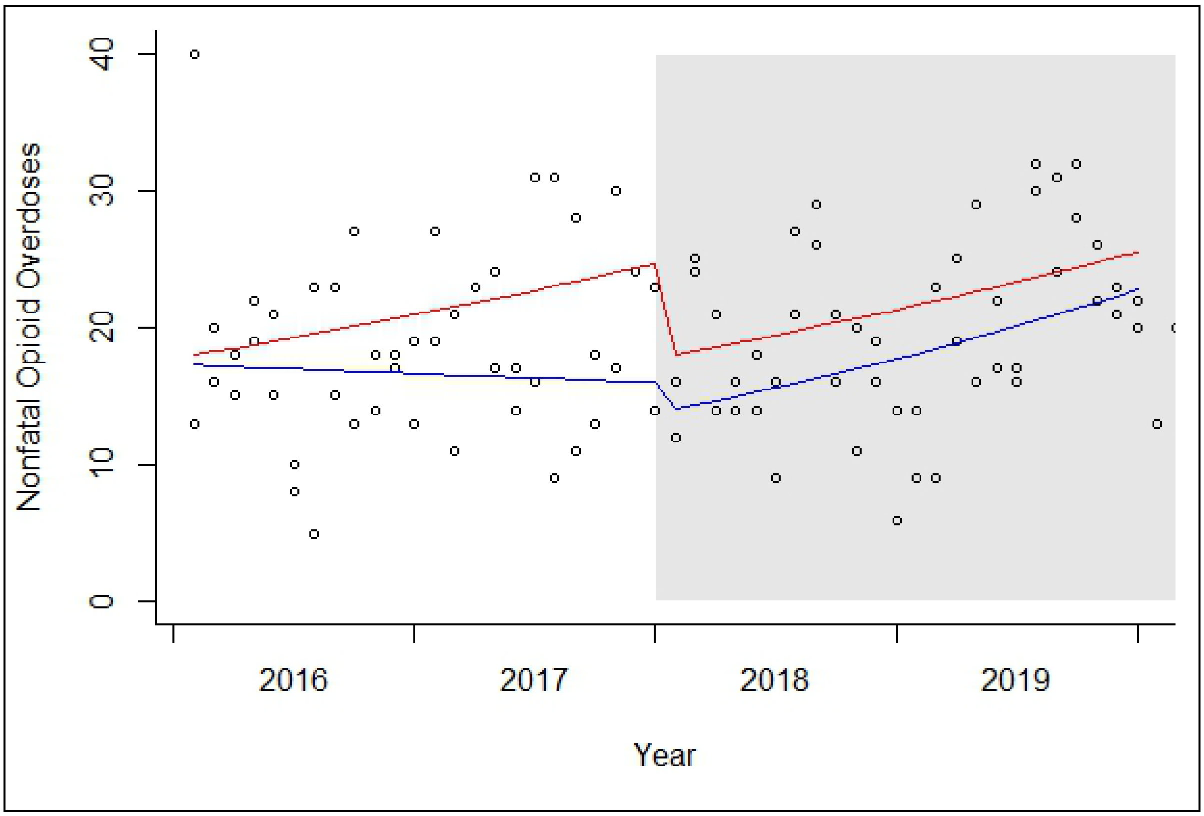


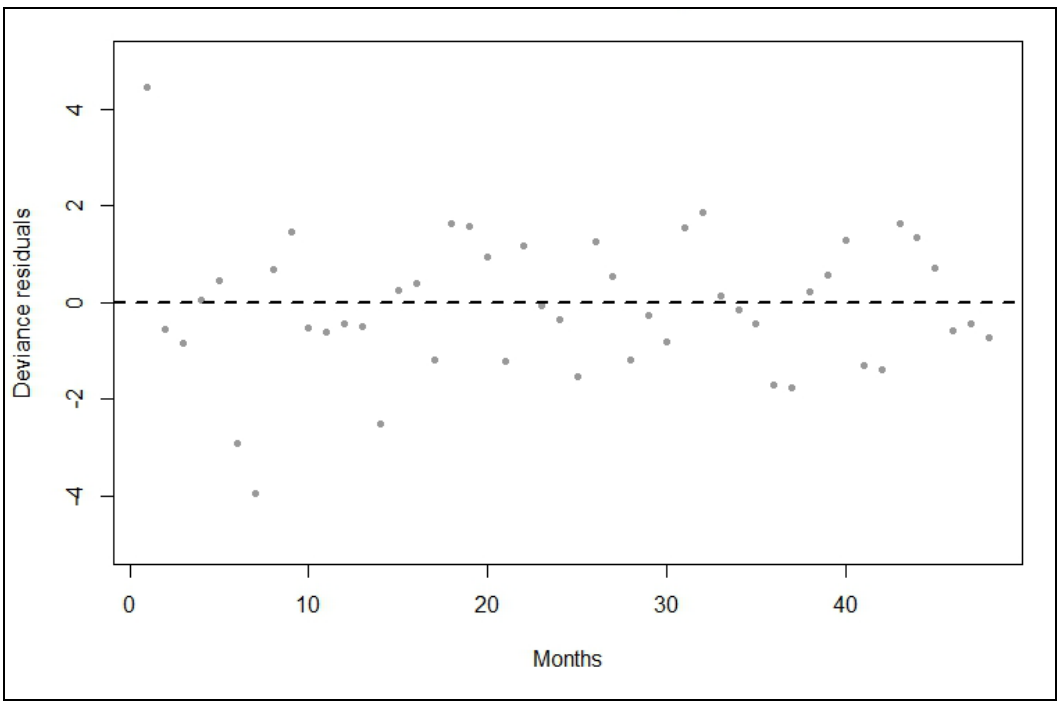
Figure 4.2: Multiple iteration time series analysis for Chesterfield County and the Control County

Solid red line= modeled trend for the number of monthly nonfatal opioid overdoses for Chesterfield County, **Solid blue line** = modeled trend for the number of monthly nonfatal opioid overdoses in the control county
Area shaded in gray represents the post-intervention period (February 1st 2018 – January 31st 2020).

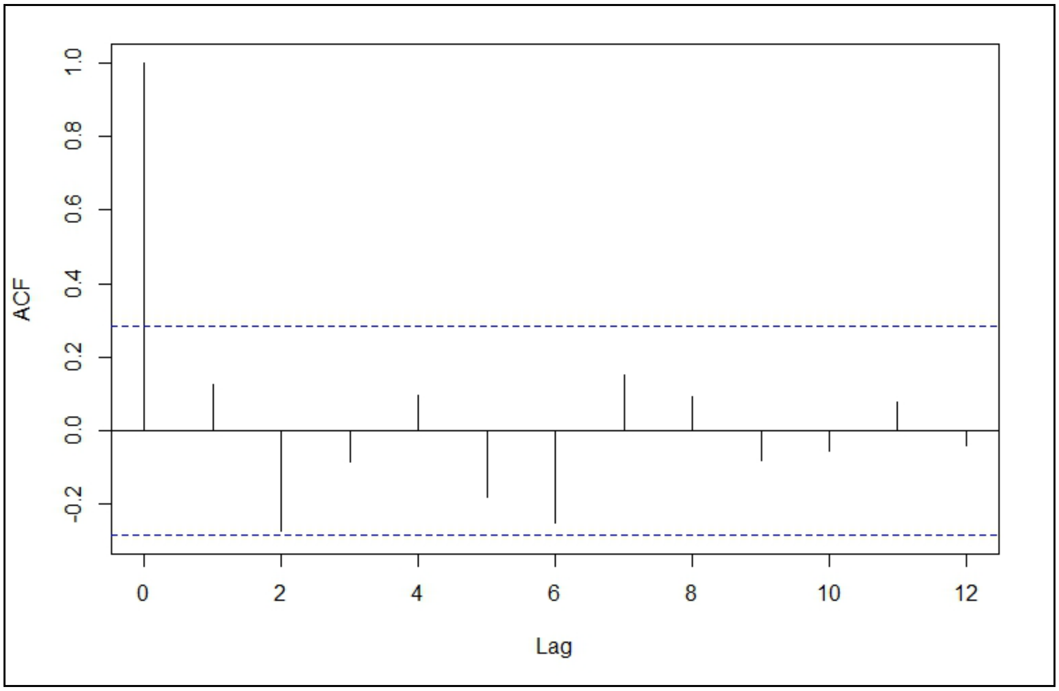
Supplemental Table 4.1: Demographic and population characteristics for Chesterfield County and the Control County (2018)

	Chesterfield County[a]	Control County[a]
Total population	348,556	329,261
Age (years)		
19-24 years	91365 (26.2%)	76767 (23.3%)
25-34 years	122578 (35.2%)	140009 (42.5%)
35-44 years	137517 (39.5%)	131226 (39.9%)
45-54 years	146533 (42.0%)	134387 (40.8%)
55-64 years	137025 (39.3%)	127513 (38.7%)
≥ 65 years	148957 (42.7%)	147537 (44.8%)
Sex		
Male	168,039 (48.2%)	156,230 (47.4%)
Female	180,517 (51.8%)	173,031 (52.6%)
Race		
White	243,545 (69.9%)	192,633 (58.5%)
Black or African American	88,221 (25.3%)	104,312 (31.7%)
American Indian and Alaska Native	2,337 (1.0%)	1,356 (0.4%)
Asian or Pacific Islander	14,453 (4.1%)	30,960 (9.4%)

[a]2018 Bridged-Race Population Estimates 1990-2018 Results, CDC WONDER



Supplemental Figure 4.1: Residual plot to assess for autocorrelation in the single interrupted time series analysis of Chesterfield County



Supplemental Figure 4.2: Estimates of autocorrelation for the single interrupted time series model of Chesterfield County

ACF=autocorrelation function, resCF=residuals for Chesterfield
Horizontal blue lines represent 95% confidence intervals

Supplemental Table 4.2: Single interrupted time series of the monthly number of nonfatal opioid overdoses in Chesterfield County (not adjusted for overdispersion)

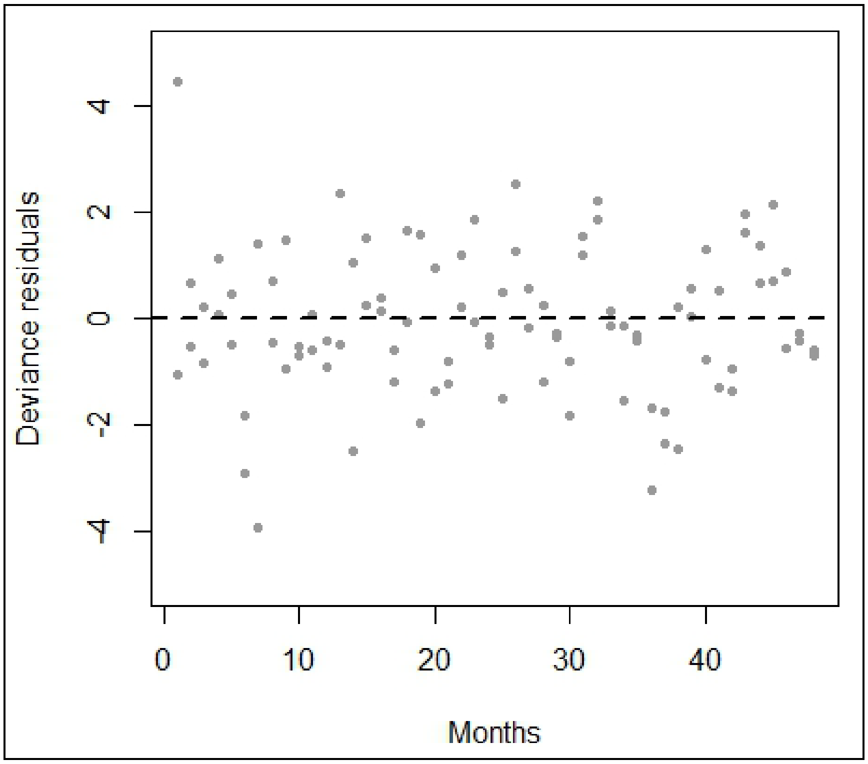
	P	Estimate	SE	p-value
Intercept	β_0	2.877163	0.095470	<.0001
Pre-Intervention Slope	β_1	0.013664	0.006427	0.03350
Change in Level (pre-post interruption)	β_2	-0.326317	0.125870	0.00953
Change in Slope (pre-post interruption)	β_3	0.001356	0.009047	0.88084
Post-Intervention Slope	$\beta_1 + \beta_3$	0.01502	0.0102873	0.15093

SE=standard error, **P**=parameter
NOTE: Pre-intervention = February 1st 2016 – January 31st 2018, Post-Intervention = February 1st 2018 – January 31st 2020.

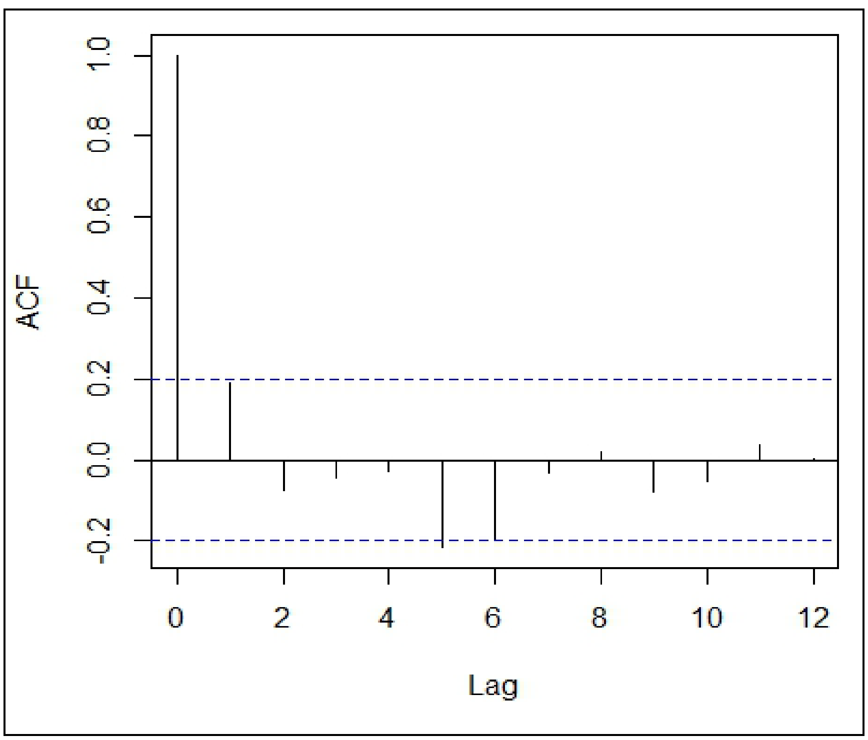
Supplemental Table 4.3: Multiple interrupted time series for the number of monthly nonfatal opioid overdoses comparing Chesterfield County to Control County (not adjusted for overdispersion)

	P	Estimate	SE	p-value
Intercept	β_0	2.851519	0.102361	<.0001
Pre-Intervention slope (Control)	β_1	-0.003269	0.007233	0.6513
Δ Level (pre-post interruption) (Control)	β_2	-0.148562	0.144167	0.3028
Δ Slope (pre-post interruption) (Control)	β_3	0.024081	0.010050	0.0166
Δ Pre-intervention level (Treatment vs. Control)	β_4	0.025645	0.139972	0.8546
Δ Pre-intervention slope (Treatment vs. Control)	β_5	0.016933	0.009676	0.0801
Δ Differences in level (pre-to-post intervention) (Treatment vs. Control)	β_6	-0.177755	0.191383	0.3530
Δ Differences in slope (pre-to-post intervention) (Treatment vs. Control)	β_7	-0.022725	0.013523	0.0929

SE=standard error, **P**=parameter
NOTE: Pre-intervention = February 1st 2016 – January 31st 2018, Post-Intervention = February 1st 2018 – January 31st 2020.



Supplemental Figure 4.3: Residual plot to assess for autocorrelation in the multiple interrupted times series analysis of Control County and Chesterfield County



Supplemental Figure 4.4: Estimates of autocorrelation for the multiple interrupted time series model for Chesterfield County and Control County

ACF=autocorrelation function, MITSAres=residuals for multiple interrupted time series
Horizontal blue lines represent 95% confidence intervals

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Vita

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