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# Depression as a Mediator between Combat Deployment and Substance Use among Veterans

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# Depression as a Mediator between Combat Deployment and Substance Use among Veterans

by

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A Project submitted in partial satisfaction of
the requirements for the degree
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Each person whose signature appears below certifies that this doctoral project in his/her opinion is adequate, in scope and quality, as a doctoral project for the degree Doctor of Psychology.

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CONTENT

Appendices

FIGURES

Figures Page

# TABLES

Tables Page

ABBREVIATIONS

| | |
|---|---|
| OEF | Operation Enduring Freedom |
| OIF | Operation Iraqi Freedom |
| OND | Operation New Dawn |
| VA | Veterans Administration |
| AUD | Alcohol Use Disorder |
| DUD | Drug Use Disorder |
| DSM-IV | Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition |
| APA | American Psychiatric Association |
| DSM-5 | Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition |
| CDC | Center for Disease Control and Prevention |
| SAMHSA | Substance Abuse and Mental Health Services Administration |
| NVVRS | National Vietnam Veterans Readjustment Study |
| IED | Improvised Explosive Device |
| TBI | Traumatic Brain Injury |
| NSDUH | National Survey on Drug Use and Health |
| OUD | Opioid Use Disorder |
| CUD | Cannabis Use Disorder |
| PTSD | Posttraumatic Stress Disorder |
| DOD | Department of Defense |
| NMUPO | New-onset Non-medical Use of Prescription Opioid |

| | |
|---|---|
| HRBS | Health Related Behaviors Survey |
| CBHSQ | Center for Behavioral Health Statistics and Quality |
| SUDs | Substance Use Disorders |
| TUD | Tobacco Use Disorder |
| MDE | Major Depressive Episode |
| mTBI | Mild Traumatic Brain Injury |
| MDD | Major Depressive Disorder |
| CAI | Computer-Assisted Interviewing |
| ACASI | Audio Computer-Assisted Self-Interviewing |
| CAPI | Computer Assisted Personal Interviewing |
| NCS-R | National Comorbidity Survey-Replication |
| WMH-CIDI | WHO's Composite International Diagnostic Interview |
| NDSS | Nicotine Dependence Syndrome Scale |
| FTND | Fagerstrom Test of Nicotine Dependence |
| FTQ | Fagerstrom Tolerance Questionnaire |

ABSTRACT OF THE DOCTORAL PROJECT

Depression as a Mediator between Combat Deployment and Substance Use among Veterans

by

Brooke Kania Millham

Doctor of Psychology, Department of Psychology
Loma Linda University, September 2023
Dr. Holly E. R. Morrell, Chairperson

Individuals who deploy to combat zones often develop increased rates of substance use problems, which may be due to self-medication for depressive symptoms. This study used logistic simple mediation analyses with bootstrapping to test whether depression mediates the relationship between combat zone experience and substance dependence or abuse (alcohol, nicotine, marijuana, opioids, other illicit drugs, and concurrent substance misuse) among military veterans via secondary data analysis of the 2013 to 2018 National Survey on Drug Use and Health (NSDUH; $N$ = 14,121; 87.9% male; 54.4% age 50+; 75.2% white; 34.5% with combat zone experience). Analysis revealed that depression was only a significant mediator of the relationship between combat zone experience and alcohol dependence or abuse (OR = 1.020, 95% CI [1.002, 1.054], $p < .05$). Among the individual effects tested, the effect of combat zone experience on depression was only significant for alcohol ($b$ = .167, 95% CI [.008, .326], $p < .05$), the effect of depression on substance dependence or abuse was significant for all substance categories except marijuana (ORs = 1.125 to 1.473, $ps < .05$), and the direct effect of combat zone experience on all substance dependence or abuse categories was not significant, $ps > .05$. Clinicians may consider screening for depression in all veterans,

as well as screening for and emphasizing substance use prevention measures in those showing signs of depression. Our results also suggest the importance of combining treatments for depression and alcohol to improve treatment outcomes among veterans, regardless of combat zone experience.

# CHAPTER ONE

# LITERATURE REVIEW

## The Problem

There were 18.6 million veterans in the United States as of 2017 (Office of Enterprise Integration, 2017). Research has shown that service members are at a high risk for substance use and that this remains true after they separate from the military and become veterans (Derefinko et al., 2018; Hoopsick et al., 2017; Meadows et al., 2015b; National Institute on Drug Abuse [NIDA] 2019a; Seal et al., 2011). In fact, veterans who have separated from the military are actually at greater risk for substance use problems than both active duty service members and reserve members (Hoopsick et al., 2017). This may be due to the readjustment problems that many veterans face after leaving the military, or the fact that they are no longer closely monitored for substance use (Derefinko et al., 2018; Hoopsick et al., 2017).

Approximately two million service members have deployed to combat zones as part of Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) since September 11, 2001 (McDevitt-Murphy et al., 2014). Due to these recent wars in Afghanistan and Iraq, many of the veterans who are now leaving the military have been deployed to combat zones and many have even served multiple tours of duty, increasing the likelihood of having experienced traumatic events (Jordan, 2011; McDevitt-Murphy et al., 2014). One study found that among soldiers returning from Iraq, approximately 66.5% to 69.6% reported potentially traumatic experiences (Milliken et al., 2007). These high rates of deployment to combat zones and exposure to traumatic events have been associated with many negative outcomes.

Much research has shown that combat exposure is a risk factor for problematic substance use (Hassija et al., 2012; Jacobson et al., 2008; Larson et al., 2016; McDevitt-Murphy et al., 2014; Milliken et al., 2007; Vest et al., 2018; Wright et al., 2012). Studies conducted on Vietnam era veterans have found that combat veterans have increased risk for substance misuse compared to noncombat veterans (McDevitt-Murphy et al., 2014), which may hold true for veterans who have deployed to combat zones during more recent conflicts as well. Furthermore, research has shown that combat exposure is also associated with an increased risk for mental health problems such as depression (Hassija et al., 2012; Renshaw et al., 2009; Sampson et al., 2015). These findings are especially relevant to the veteran population, as negative effects of trauma exposure may increase significantly after separating from the military (Derefinko et al., 2018). Therefore, problematic substance use and mental health problems among combat veterans are particularly important to study, especially given the recent conflicts in Iraq and Afghanistan, which lasted over a decade.

Substance use among military personnel is very common, especially for those who have deployed to combat zones. The National Vietnam Veterans Readjustment Study found that combat veterans have higher prevalence rates for substance abuse and dependence than non-combat veterans (McDevitt-Murphy et al., 2014). More recently, a study utilizing information from a national Veterans Administration (VA) database examined prevalence rates among approximately 450,000 Iraq and Afghanistan veterans and found that 10% met criteria for an alcohol use disorder (AUD) diagnosis, which was similar to the AUD prevalence rate among Vietnam veterans and higher than the civilian prevalence rate, and that 4.5% met criteria a drug use disorder (DUD) diagnosis, which is

higher than prevalence rates for both Vietnam veterans and civilians (Seal et al., 2011). This study also found that 82% to 93% of these veterans with an AUD or DUD diagnosis had one or more comorbid mental health disorders, and 54% to 72% had a comorbid diagnosis of depression. While these statistics are already alarmingly high, it is also important to keep in mind that the data analyzed in this study were from the VA. Since neither the military nor the VA conducts universal screenings for substance misuse other than alcohol (Seal et al., 2011), the DUD prevalence rates and correlates reported in this study are likely an underrepresentation of the true rates among this population.

## Substance Use Disorders and Consequences

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; American Psychiatric Association [APA], 1994) contains two broad categories of substance related disorders; substance dependence and substance abuse. Substance dependence is defined as "a maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following [criteria], occurring at any time in the same 12-month period." These criteria include: (a) tolerance (a need for greater amounts of the substance to achieve the desired effect, or less effect with the same amount due to continued use); (b) withdrawal (defined as the typical withdrawal condition for the substance or taking the same or similar substance to avoid withdrawal symptoms); (c) the substance is taken for a longer time or in larger quantities than intended; (d) there are unsuccessful attempts or a continual desire to control or decrease substance use; (e) much time is spent on activities related to the substance; (f) important recreational, occupational, or social activities are reduced or abandoned due to the substance; and (g) the substance use persists despite knowledge that

continual psychological or physical problems are caused or worsened by the substance. Substance abuse is defined as, “a maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following [criteria], occurring within a 12-month period.” These criteria include: (a) continued substance use causing a failure to fulfill major obligations at school, work, or home; (b) continued use in situations where it is physically hazardous; (c) continued substance-related legal problems; (d) recurrent use despite recurrent interpersonal or social problems which are caused or worsened by the substance’s effects. To be diagnosed with substance abuse, the individual must never have met criteria for substance dependence within the same substance class.

The four criteria that comprise the substance abuse disorder diagnosis and the seven criteria that comprise the substance dependence disorder diagnosis were later combined to create the newer Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5; APA, 2013) diagnosis of “substance use disorder.” Therefore, its eleven criteria have largely remained the same with several exceptions. First, the recurrent substance-related legal problems criterion was dropped and a new criterion involving craving was added. Additionally, some details regarding the withdrawal criteria for each substance were updated.

Substance use can lead to many negative consequences and can impair functioning in many important areas of life, such as interpersonal relationships, communication, health, work, school, and so forth. According to the Centers for Disease Control and Prevention (CDC; 2019), excessive alcohol use includes binge drinking (four or more drinks on a single occasion for women, and five or more for men), heavy

drinking (eight or more drinks per week for women, and 15 or more for men), and any drinking by pregnant women or people younger than 21 years old. In the United States, 25.5% of adults over 18 years old had at least one binge drinking episode in the past year (CDC, 2017). Excessive alcohol use has short-term consequences that increase the risk of many damaging health conditions, such as injuries, violence, alcohol poisoning, risky sexual behavior, and pregnancy complications (CDC, 2019). Excessive alcohol use also has many long-term health risks, including learning and memory problems (including dementia), mental health problems, many different types of cancers, high blood pressure, heart disease, stroke, liver disease, digestive problems, and much more (CDC, 2019). From 2006 to 2010, excessive drinking caused 1 in 10 deaths among adults age 20 to 64 years old, shortening these individuals' lives by an average of 30 years (CDC, 2019).

In the United States, 19.7% of adults aged 18 years or older report tobacco use either "every day" or "some days" (Creamer et. al., 2018). Cigarette smoking damages almost every organ in the human body, reduces overall health, causes many diseases, and is responsible for nearly one in five deaths in the United States (CDC, 2018). Individuals who smoke cigarettes are two to four times more likely to have a stroke, two to four times more likely to develop coronary heart disease, and are 12 to 13 times more likely to die from COPD than nonsmokers (CDC, 2018). Smoking can cause cancer in almost any part of the body, and it also increases the risk that an individual will die from cancer and other diseases (CDC, 2018).

In 2018, 15.9% of adults in the United States reported using marijuana in the past year (Substance Abuse and Mental Health Services Administration [SAMHSA], 2019). Marijuana use has a wide range of physical and mental health effects. Physical effects

include breathing problems, increased heart rate, child development problems both during and after pregnancy, and intense nausea and vomiting with regular long-term use (NIDA, 2019b). Mental effects of long-term marijuana use have been linked to temporary paranoia, temporary hallucinations, and worsening symptoms in patients with schizophrenia (NIDA, 2019b).

In 2018, 3.7% of adults in the United States reported misusing opioids in the past year (SAMHSA, 2019). Prescription opioid use can have many harmful effects including confusion, drowsiness, constipation, nausea, euphoria, and slowed breathing, (NIDA, 2019c). This slowed breathing can cause hypoxia, which can lead to psychological and neurological effects such as coma, permanent brain damage, and even death (NIDA, 2019c). Additionally, heroin is chemically similar to prescription opioids and produces a similar high, but is cheaper and easier to acquire, so approximately 4-6% of people who misuse prescription opioids switch to heroin (NIDA, 2019c). Injecting opioids can increase the risk of contracting infectious diseases such as HIV and Hepatitis C (NIDA, 2019c). In 2018, 0.3% of adults in the United States reported using heroin in the past year (SAMHSA, 2019). Heroin use also leads to a vast array of long-term effects including liver and kidney disease, lung complications, sexual dysfunction, collapsed veins (if injected), damaged tissue inside the nostrils (if snorted), infections of the heart lining and valves, and more (NIDA, 2019d). Finally, substance dependence and abuse exacerbate other physical illnesses and mental disorders, including depression, and complicate treatment. All of these negative consequences are extremely expensive and place a large burden on our healthcare system.

## Substance Use Among Service Members

Much of our current knowledge on substance use among service members comes from research conducted on Vietnam-era veterans as part of the National Vietnam Veterans Readjustment Study (NVVRS), which was authorized in 1983 to collect data among Vietnam War veterans on prevalence rates of substance misuse and other psychological problems (Jordan et al., 1991; McDevitt-Murphy et al., 2014; Roszell et al., 1991). However, so much has changed over the past sixty years regarding war and its consequences, that it is imperative to study substance use patterns and consequences among veterans from more recent conflicts. Modern warfare places military members at an increased risk of harming noncombatants and being engaged in or exposed to other potentially morally injurious events such as mistreating civilians, using chemicals or bombs on villages, mutilating bodies, and torturing prisoners (Currier et al., 2014). Additionally, today, the United States military has fewer service members than it has in the past, which has led to an increased likelihood of repeated deployments (up to four), as well as extended deployments (12 to 18 months at a time), both of which increase the likelihood of trauma exposure (Jordan, 2011; McDevitt-Murphy et al., 2014). Recent conflicts involve fighting with insurgents whose primary weapon is the improvised explosive device (IED) which often results in traumatic brain injury (TBI) and losses of limbs (Jordan, 2011; Tanelian & Jaycox, 2008). Furthermore, survival rates among service members from recent wars have increased, and many of those injured return to active duty within three days (Jordan, 2011). All of these new and unique stressors have not been encountered in past wars and may result in unique consequences. Additionally, a large amount of research to date has only examined alcohol (Jacobson et al., 2008;

Sampson et al., 2015; Teachman et al., 2015) or has lumped all drug use together into one category (Kelley et al., 2015; Seal et al., 2011). Therefore, it is also important to examine the different categories of drugs independently, as doing so may shed light onto different trends that may exist among the different substances. Expanding upon research in this area would allow us to gain a more current and comprehensive understanding of the problem, which could be used to tailor and improve existing treatment, develop more effective treatments, and improve prevention efforts.

## Relevant Substances

The military has a vested interest in making sure soldiers are fit for service. Substance abuse and dependence negatively impact fitness levels and psychological readiness, and therefore the military attempts to monitor substance use among soldiers (Institute of Medicine, 2015; Jeffery et al., 2013). However, since alcohol is a large part of military culture, since the tobacco industry has blocked legislature to restrict tobacco use among service members, and since opioids are often prescribed for pain in this population, the military has struggled to control their use (Ames & Cunradi, 2004; Institute of Medicine, 2013; Singaraju et al., 2019). As a result, prevalence rates for these substances are fairly high among active duty service members, and these rates remain high after soldiers have left the military (Derefinko et al., 2018). On the other hand, since the military has a "zero tolerance" policy for most other drugs, since service members can be disciplined and dishonorably discharged for a positive drug test, and since the military occasionally conducts random drug screenings, the military has been able to keep the use of these other drugs to a minimum among service members (Hoopsick et al., 2017; Jeffery et al., 2013; NIDA, 2019a; Platteborze et al., 2013). However, once soldiers

leave the military and are no longer under strict regulations or subject to military drug tests, their use has been found to increase among veterans (Hoopsick et al., 2017; NIDA, 2019a; Seal et al., 2011). The proposed study will examine substance abuse and dependence for the following substances: alcohol, nicotine, marijuana, opioids, and other illicit drugs. Reasons for why each of these substances are important to study in this population are explained in detail below.

### *Relevant Substances: Alcohol*

The military does not forbid service members from consuming alcohol. Among military members, alcohol is the most commonly used drug (Derefinko et al., 2018; Meadows et al., 2015a; Teeters et al., 2017). Epidemiological findings show that 30.0% of active duty service members were binge drinkers compared to 24.7% of adult civilians, and 5.4% of active duty service members were heavy drinkers compared to 6.7% of adult civilians (Meadows et al., 2015b). Smaller-scale studies have even found that the majority of current members are binge drinkers, and almost half are considered heavy drinkers (Golub & Bennett, 2014) or that the majority of current members endorse alcohol use (Derefinko et al., 2018). Furthermore, AUD is the most prevalent form of SUD among active duty service members (NIDA, 2019a) with 35.3% of service members meeting criteria for hazardous drinking or possible AUD in 2015 (Meadows et al., 2015b). In recent years, studies have found that there has been a significant increase in heavy alcohol consumption rates among service members, which coincides with OEF and OIF, and that this is likely due to the military's socialization process and the stress of increased deployments to combat zones (Bray et al., 2013; Shirvani et al., 2017).

Drinking alcohol is an established part of military culture (Ames & Cunradi, 2004) and 68.2% of service members believe drinking is supported by military culture (Meadows et al., 2015b). The military seems to encourage men to consume alcohol in a variety of different ways, including through peer pressure experienced in social networks, through the role it plays as a rite of passage among this overwhelmingly young population, and since alcohol purchased on base is less expensive than alcohol purchased elsewhere (Teachman et al., 2015). Additionally, combat situations seem to play a role in alcohol use in this population (NIDA, 2019a; Russel et al., 2014).

The high rates of alcohol use during military service seem to continue when service members transition to the civilian world. A study that compared substance use rates while in the military and six months after discharge, found that rates of alcohol use were similarly elevated, with 91.5% of active duty members endorsing alcohol use and 88.6% of veterans endorsing alcohol use (Derefinko et al., 2018). Additionally, a study that compared past 30-day use and dependence among current reserves and former service members found that the overall odds of alcohol dependence were higher among veterans than current reserves, but that there were no statistically significant differences among the groups with regards to past month use (Hoopsick et al., 2017). Male veterans also report increased rates of alcohol consumption compared to nonveterans (Seal et al., 2011; Teachman et al., 2015). A study utilizing information from a national VA database examined prevalence rates among approximately 450,000 Iraq and Afghanistan veterans and found that 10% met criteria for an AUD diagnosis, while civilian AUD prevalence rates range from 3.1% to 8.5% (Hasin et al., 2007; Kessler et al., 2005; Seal et al., 2011). Another study of over 3,000 veterans found that 42.2% of veterans have a lifetime history

of AUD (Fuehrlein et al., 2016), while epidemiologic data show that only 29.1% of adult civilians have a lifetime AUD (McCabe et al., 2017).

### *Relevant Substances: Nicotine*

Tobacco use is the primary cause of preventable disease in the military, costing the United States government approximately $6.5 billion annually (Singaraju et al., 2019). Epidemiological findings show that in 2015, 13.9% of active duty were current cigarette smokers and 7.4% were daily smokers (Meadows et al., 2015b). When comparing these rates to adult civilian smoking rates, some studies suggest that civilian smoking rates are higher (16.8% current cigarette smokers, 12.9% daily smokers; Meadows et al., 2015b), while other studies suggest that civilian rates are lower (Singaraju et al., 2019). While the 2015 smoking rates among active duty members were an improvement from 2011 data, which revealed that 24.0% of active duty were current cigarette smokers (Meadows et al., 2015b), there is still much room for improvement. Reasons for widespread use among this population may include the fact that tobacco restrictions are not heavily enforced and that smoke breaks are treated as a legitimate reason to rest during work hours (Singaraju et al., 2019). Studies have found that many service members who had never used tobacco before initiate tobacco use while in the military (Talcott et al., 2015), and tobacco use often begins or increases during deployments (Khan et al., 2015; Talcott et al., 2015).

These elevated rates of tobacco use during military service carry over into civilian life once these service members leave the military and become veterans. A study that compared substance use rates while in the military and six months after discharge, found

that rates of cigarette smoking were similarly elevated, with 40.7% of active duty endorsing smoking and 37.5% of veterans endorsing smoking (Derefinko et al., 2018). Another study that compared past 30-day use and dependence among current reserves and former service members found that the overall odds of both past month cigarette smoking and nicotine dependence were higher among veterans than current reserves (Hoopsick et al., 2017). Data also reveal that veterans smoke cigarettes at higher rates than civilians (NIDA, 2019a). An epidemiologic study using ten years of data from the National Survey on Drug Use and Health (NSDUH) found that among men ages 18 to 64, veterans have significantly higher rates of daily cigarette use compared to civilians (Hoggatt et al., 2017). Not only does this population have increased prevalence rates, but veterans are also at increased risk for nicotine dependence and tobacco use disorder (Baldassarri et al., 2019). Widespread tobacco use has been linked to an increased risk for many psychiatric and medical comorbidities among this population (Ashendorf et al., 2019; Baldassarri et al., 2019; Coughlin et al., 2019). Tobacco use in veterans was also found to be negatively related to cognitive processing speed, memory, and executive functioning (Ashendorf et al., 2019). Additionally, a study using data from the National Health Interview Survey found that the mortality differential seen in veterans from current war-era cohorts was partially to fully explained by smoking tendencies (Landes et al., 2018).

### *Relevant Substances: Marijuana*

Service members are forbidden from using marijuana while in the military. However, once service members leave the military they are no longer under such

stringent regulations, which may help explain the higher prevalence rate of marijuana use among veterans (Derefinko et al., 2018; Hoopsick et al., 2017; Jeffery et al., 2013; Platteborze et al., 2013). Several studies have documented the significant difference between the low levels of marijuana use during military service, compared to the significantly increased consumption after transitioning to the civilian world (Derefinko et al., 2018; Golub & Bennett, 2014). For example, a study that compared substance use rates while in the military and six months after discharge, found that only 3.7% of active duty endorsed marijuana use, while 26.2% of veterans endorsed marijuana use (Derefinko et al., 2018). These marijuana use rates among veterans are similar to those seen in the general US population (Davis et al., 2018).

Furthermore, there appears to be an increased tendency among veterans to use marijuana for medicinal purposes. According to the 2014 NSDUH data, in states where medical marijuana was legal, 41% of veterans who used marijuana in the past year used it medically, making medical marijuana use more than twice as prevalent among veterans compared to the general population (17%; Davis et al., 2018). One study found that most veterans reported using marijuana in an attempt to manage several mental and physical health symptoms and conditions, but that they mainly used higher risk marijuana formulations (such as low CBD, high THC, and smoked; Loflin et al., 2019), which implies a lack of regulation and education around how veterans use marijuana to self-medicate and that they may not be doing so in the safest manner. A growing number of studies indicates that people may be partially replacing opioids with marijuana as a means of medicating (Boehnke et al., 2016) and some researchers believe that veterans may be doing this as well (Corroon Jr. et al., 2017; Krawitz, 2015; Metrik, Bassett, et al.,

2018; Reinman et al., 2017). For example, one study among veterans receiving SUD or mental health treatment found that 78% reported using marijuana to treat chronic or severe pain (Davis et al., 2016). However, replacing or supplementing opioids with cannabis in an attempt to manage pain may not be as beneficial as some anticipate. One study found that being prescribed long-term opioid therapy and using medical cannabis together was significantly associated with an increased risk of prescription opioid misuse, as compared to long-term opioid therapy alone (Nugent et al., 2018). Another study found that compared to opioid use disorder (OUD) alone, OUD and cannabis use disorder (CUD) together were associated with fewer opioid prescriptions, but a higher likelihood of homelessness and inpatient psychiatric admission (De Aquino et al., 2019).

Expectancy Theory Framework, which poses that drug use tends to correlate with the drug's anticipated effects, may explain why medical marijuana use is so popular among veterans. Several studies have supported this in the context of Posttraumatic Stress Disorder (PTSD), finding that among veterans with PTSD symptoms, those that expect marijuana to assuage PTSD symptoms use more marijuana (Earleywine & Bolles, 2014; Grant et al., 2016). However, despite this widespread expectancy that marijuana will decrease PTSD symptoms, studies have shown that marijuana use is not actually associated with less severe PTSD symptoms (Johnson et al., 2016). These findings likely hold true for other mental health disorders as well, such as depression. High rates of marijuana use among veterans may also be due to the fact that the United States has been decreasing restrictions around marijuana over the past decade. Furthermore, the VA is now allowing its doctors to discuss the use of, and options surrounding, medical marijuana with patients (Katz, 2018), which may further promote its use among this

population. However, any increased use of a drug, and especially when used as a coping mechanism, has the potential to lead to problematic use. One study that examined CUD diagnoses among veterans in 2002, 2008, and 2009 found that CUD diagnoses increased more than 50%, and that states in which medical marijuana use was legalized had significantly higher CUD diagnoses rates (Bonn-Miller et al., 2012).

### *Relevant Substances: Opioids*

Opioid use is a problem among the current and former military population. In 2015, over 4% of current service members reported misusing one or more prescription drugs within the past year (Meadows et al., 2015b). Another study found that 26.4% of active duty service members received at least one opioid prescription and 0.7% received an over 90-day prescription for opioids (Jeffrey et al., 2014). In this population, opioid use typically begins with receipt of an opioid prescription after deployment-related injuries (NIDA, 2019a). A large study of active duty army soldiers found that 34.8% were prescribed opioids within a year of returning from OEF/OIF/OND, and 1.1% of these soldiers ended up using opioids long-term (i.e., opioids were prescribed for at least two thirds of days over 90 days or longer; Adams et al., 2019). From 2001 to 2009, military physicians more than quadrupled the number of prescriptions they wrote for pain medication (Institute of Medicine, 2013). Such regular use can lead to opioid use disorders due to the addictive potential of these drugs and the mental health struggles some service members experience (NIDA, 2019a). Therefore, the Department of Defense (DOD) began to intervene with clinical guidelines and directives, and 2011 became the turning point for which opioid use decreased among both active duty and civilian

populations (Kazanis et al., 2018). However, prescription pain relievers are still overused and misused at higher rates than other drugs in this population (NIDA, 2019a).

These high rates of prescription pain reliever use seem to remain steady or increase slightly once service members transition to the civilian world. A study that compared substance use rates while in the military and six months after discharge found that rates of prescription drug use were similarly elevated, with 11.1% of active duty members endorsing use and 15.0% of veterans endorsing use (Derefinko et al., 2018). Another study found that, during deployment, 6% of service members initiated misuse of prescription pain relievers and 7% misused prescription painkillers after separating from the military (Golub & Bennett, 2014), which may indicate a slight increase in use among veterans compared to current service members. Finally, a study that compared past 30-day use and dependence among current reserves and former service members found that the overall odds of past month nonmedical opioid use were higher among veterans than current reserves, but that there were no statistically significant differences among the groups with regards to dependence (Hoopsick et al., 2017). Given the elevated rates of prescription pain reliever misuse among veterans, and the current opioid crisis in the United States, studying opioid use among this population is both relevant and warranted.

After the DOD began to intervene to decrease opioid prescribing in 2011, there was reduced access to prescription opioids from medical sources, which led some people, including service members and veterans, to turn to diverted prescription opioids or heroin, since these forms of the drug are often easier to obtain, less expensive, and have high potencies (Banerjee et al., 2016; Bennett, Elliott, et al., 2017). Unfortunately, there is a very limited research examining heroin use among veterans and service members.

However, existent epidemiological data indicates that heroin use among veterans may be increasing. Data from the NSDUH reveal that among veterans, 0.3% reported past year heroin use in 2018, which increased from 0.1% in 2002 (SAMHSA, 2020). Additionally, 0.2% of veterans reported past year heroin use disorder (SAMHSA, 2020), compared to 0.1% of the general population (McCabe et al., 2017). A study was conducted among 3396 veterans enrolled in the Veterans Aging Cohort Study, half of which were HIV positive, and half of which were an age/race/site-matched control group without HIV, to examine the relationship between new-onset non-medical use of prescription opioid (NMUPO) and self-reported heroin initiation (Banerjee et al., 2016). While this study was somewhat controversial due to the potential sample bias (Ruan et al., 2017) and the way in which NMUPO was defined in the study (Osborne & Serdarevic, 2017), the researchers reported some interesting findings. First, this study found that receiving a prescription opioid was not significantly associated with NMUPO. Additionally, the study found that NMUPO is associated positively and independently with heroin initiation. This study provides some insight into the potential progression of opioid use. However, other studies have found that receipt of a pain reliever prescription is strongly associated with prescription misuse (Jeffery et al., 2013). Finally, while the epidemiological data show that heroin use rates are relatively low among this population, heroin use should not be overlooked because the ramifications of its use are fairly severe. According to a government report, 10.7% of veterans being admitted to treatment centers are admitted for heroin, which is second only to alcohol (SAMHSA, 2015). The fact that only 0.2% of veterans reported past year heroin use in 2015, yet heroin was the second most common drug veterans received treatment for, implies the severe consequences of

its use. Additionally, heroin carries a high risk of overdose since it is often illicitly manufactured, there is often uncertainty about its potency, and it is occasionally laced with fentanyl (Bennett, Elliott, et al., 2017). Among veterans, opioid overdose rates increased from 14% in 2010 to 21% in 2016, and this increase was mostly attributable to heroin and synthetic opioids (NIDA, 2019a).

### *Relevant Substances: Other Illicit Drugs*

In research and surveys, the term "illicit drugs" typically refers to the following substances, with occasional slight deviations: heroin, marijuana, cocaine (including crack), inhalants, hallucinogens, methamphetamine, and prescription tranquilizers, pain relievers, stimulants, and sedatives. Little research has been done on illicit drug use among active duty service members. One study indicated that most service members had used marijuana but no other illegal drugs (Golub & Bennett, 2014). On the 2015 Health Related Behaviors Survey (HRBS), less than 1% of enlisted personnel and officers across all service branches reported illicit drug use (Meadows et al., 2015b). For reference, on a large 2015 governmental self-report survey, 10.1% of civilians in the United States reported illicit drug use including marijuana in the past month (Center for Behavioral Health Statistics and Quality [CBHSQ], 2016b). The low prevalence rates among current service members is likely due to the stringent military regulations and penalties surrounding its use, and likely explains the lack of research in this area. However, there is also a lack of research on illicit drug use among veterans, despite fact that illicit drug use has been shown to significantly increase among veterans during the first six months after separating from the military (Derefinko et al., 2018). A study that compared past 30-day

use and dependence among current reserves and former service members found that the overall odds of both past month illicit drug use and illicit drug dependence were higher among veterans than current reserves (Hoopsick et al., 2017). Another study found that 1.7% of veterans report using illicit drugs other than marijuana in the past month, which is similar to civilian rates (Teeters et al., 2017). It is clear that veterans do engage in illicit drug use, and therefore more research needs to be done on this topic.

### *Relevant Substances: Concurrent Substance Misuse*

Few studies examine multiple or concurrent Substance Use Disorders (SUDs). To the best of our knowledge, only one large scale epidemiological study exists that compares multiple, or concurrent SUDs for a large range of different drug classes, and this study was conducted among civilians. A large epidemiological study conducted on U.S. adults examined multiple DSM-5 SUDs for ten different drug classes (McCabe et al., 2017). This study found that over 80% of US adults with a lifetime nonalcohol SUD had at least one other concurrent lifetime SUD. Additionally, past-year prevalence rates for multiple nonalcohol SUDs ranged from 56.8% for prescription opioid use disorder to 97.5% for inhalant use disorder. However, interestingly, this study found that only 25.5% of those with lifetime AUD, and 15.0% of those with past year AUD, had at least one other concurrent SUD. Furthermore, this study found evidence that people with multiple SUDs are less likely to remit from their SUDs than people with only one SUD. Other studies have found similar results indicating that the course of disease is more persistent among those with multiple SUDs compared to those with individual SUDs (McCabe & West, 2017).

Studies examining multiple or concurrent substance use rates among veterans and service members are less comprehensive and more piecemeal. To our knowledge, no studies exist that compare multiple DSM-5 SUDs across drug classes for this population. Instead, research on multiple SUDs among service members and veterans tends to compare only a couple of drug classes, and this comparison is not the main focus of the research. However, the existing literature does seem to suggest similar trends among this population as have been found by McCabe et al. (2017) in the civilian population, showing that drug use tends to co-occur. With regards to current service members, research on multiple SUDs is scarce. One large scale study among current service members found that those who reported harmful or hazardous drinking were more likely to report current cigarette smoking than those with low risk of alcohol dependency (Ulanday et al., 2017). Another study among active duty service members found that drug misuse was strongly predicted by receiving a past month, past year, or previous year pain reliever prescription (Jeffery et al., 2013). A study that compared substance use rates while in the military and six months after discharge found that endorsing the use of one substance often predicted endorsement of the use of another substance, both within military or civilian life and across the transition, with significant associations between marijuana, cigarettes, prescription misuse and illicit drugs (Derefinko et al., 2018)

Slightly more research exists that reveals information regarding multiple substance use rates among veterans. An internet-based survey found that veterans with lifetime AUD had significantly higher rates of DUD (Fuehrlein et al., 2016). A study among veterans who were referred to the VA for potential mental health reasons found that past year marijuana use was linked to other drug use, smoking status, and AUD, even

after controlling for age, race and gender (Goldman et al., 2010). More specifically, these researchers found that veterans with past year illicit drug use, AUD, and current smokers were 5.4, 2.3, and 1.5 times more likely to have used marijuana in the past year, respectively. As previously discussed, a growing number of studies indicate that people may be partially replacing opioids with marijuana as a means of self-medicating (Boehnke et al., 2016), and some researchers believe that veterans may be doing this as well (Corroon Jr. et al., 2017; Krawitz, 2015; Metrik, Bassett, et al., 2018; Reinman et al., 2017). However, this may be problematic, as research suggests that veterans with a medical marijuana card have significantly higher rates of several other forms of substance use (Davis et al., 2016). Another study among both veterans and civilians prescribed long-term opioid therapy found that those who endorsed using medical cannabis for pain were at significantly higher risk for hazardous alcohol use, nicotine use, and prescription opioid misuse (Nugent et al., 2018). However, a study using epidemiological data found that among veterans, those who had nicotine dependence and AUD had greater odds of past year cannabis use, but that veterans who used medicinal cannabis were less likely to have AUD or engage in recent heavy episodic drinking (Davis et al., 2018). These studies seem to indicate that non-medical marijuana use is associated with concurrent use of other substances, while medical marijuana may not necessarily be associated with concurrent use of other drugs.

The previously described study conducted by Banerjee et al. (2016) found that past year stimulant and cocaine use were significantly associated with NMUPO and that past year marijuana, cocaine, stimulant, and unhealthy alcohol use were significantly associated with heroin initiation. While this study was somewhat controversial, these

findings also point to the concurrent use of multiple substances. A large study examining VA electronic medical records among veterans who are current tobacco users found that those with AUD and DUD had lower smoking cessation rates and higher smoking relapse rates (Barnett et al., 2017). Studies among veterans have also found that veterans with tobacco use disorder (TUD) have significantly higher rates of both AUD and other DUDs (Manhapra & Rosenheck, 2017). This is problematic because comorbid AUD and TUD are associated with increased rates of homelessness, hepatic disease, receipt of VA disability pension, and outpatient services for substance use and mental health problems (MacLean et al., 2018). It is incredibly important to study multiple SUDs concurrently because research has shown that adverse consequences may be more severe for those experiencing multiple SUDs compared to those experiencing a single SUD (Abé et al., 2013; MacLean et al., 2018; McCabe et al., 2006).

### Combat Exposure and Substance Dependence/Abuse

As previously discussed, deployment to combat zones and the associated stress and exposure to potentially traumatic events increase the risk for many physical and psychological injuries, as well as other negative outcomes (Jordan, 2011; McDevitt-Murphy et al., 2014). Recent surveys among OEF and OIF veterans reveal that most have been exposed to one or more traumatic events (McDevitt-Murphy et al., 2014; Milliken et al., 2007; Tanielian & Jaycox, 2008). Additionally, veterans of these wars have often served multiple tours of duty, further increasing the likelihood of exposure to traumatic events (Jordan, 2011; McDevitt-Murphy et al., 2014) and associated negative outcomes, such as problematic substance use (Hassija et al., 2012; Jacobson et al., 2008; Larson et

al., 2016; McDevitt-Murphy et al., 2014; Milliken et al., 2007; Vest et al., 2018; Wright et al., 2012).

### *Combat Exposure and Alcohol*

Recently, there has been an increase in heavy alcohol consumption rates among service members, which corresponds to the conflicts in Afghanistan and Iraq (Bray et al., 2013; Shirvani et al., 2017). One study using Millennium Cohort data showed that among members of the Reserves and National Guard, those with combat exposure were significantly more likely to participate in new onset of heavy weekly drinking, binge drinking, and alcohol related problems when compared to service members who had no combat deployment experience (Jacobson et al., 2008). Another study conducted among members of a National Guard combat team revealed that prevalence rates of alcohol use before and after a combat deployment increased from 70.8% to 80.5%, and alcohol misuse increased from 8.51% to 19.15% (Russell et al., 2014). Combat exposure was also found to be significantly associated with alcohol misuse, even after accounting for lifetime interpersonal assault exposure (Hassija et al., 2012). Some studies point to a dose dependent relationship, in which increased combat exposure and its associated stress correlate with higher rates of alcohol use (Bartone et al., 2017; Bray et al., 2013; Brief et al., 2018). However, many aspects of the combat deployment experience seem to affect this relationship, above and beyond experiencing firsthand combat.

Research indicates that high exposure to atrocities and threatening situations (such as threat of injury or death) is associated with alcohol misuse (Wilk et al., 2010), indicating that several aspects of combat deployment influence this relationship. Another

study that examined different combat experiences found that changes in alcohol use from pre- to post-combat deployment were only affected by the experience of killing during combat, which actually led to a decrease in alcohol misuse (Russell et al., 2014). Additionally, a study among National Guard and Reserve members examined the relationship between alcohol problems and perceptions of combat experiences and found that perceiving combat experiences as traumatic was associated with an increased risk of alcohol problems, but that combat exposure itself showed no relationship with alcohol problems (Vest et al., 2018). Together, these findings suggest that other aspects of the combat deployment, rather than the direct combat itself, may influence the increase in alcohol misuse after deployment. This highlights the need for substance use research to examine all service members deployed to combat zones, rather than simply those engaging in firsthand combat. To our knowledge, little research has explored the effect of combat on alcohol consumption among veterans. However, one study found that having served in a combat zone was associated with increases alcohol consumption among enlisted service members, but not among veterans (Teachman et al., 2015).

### *Combat Exposure and Nicotine*

Many studies have found links between combat exposure and tobacco use. Combat exposure seems to increase the risk of smoking initiation among service members (NIDA, 2019a). Studies found that service members who were in combat units during deployment were more than twice as likely to use smokeless tobacco (Lin et al., 2019) and combat experience was associated with heavy smoking (over 20 cigarettes per day; Lopez et al., 2018). Another study of almost 40,000 service members found that

longer length of combat experience and certain job classifications, such as combat, maintenance, administrative, and food personnel, were associated with higher rates of cigarette smoking (Ulanday et al., 2017). However, research remains unclear on what may contribute to this relationship. Some studies suggest this relationship may be due to the fact that combat stress is associated with both initiation and increased tobacco use (Harte et al., 2014; Japuntich et al., 2016). Several studies have found a dose-dependent relationship among combat, its associated stress, and increased tobacco use (Japuntich et al., 2016; Lin et al., 2019). Talcott et al. (2015) also found that service members tend to initiate or increase tobacco use during combat deployments, and that many intend to reduce their use or completely quit after deployment, but only a few are able to achieve cessation post-deployment. Finally, another study found that the increase in cigarette smoking during combat deployments is attributable not just to trauma, but also to many other factors such as boredom, monotony, lack of recreation, and peer pressure (Khan et al., 2015).

### *Combat Exposure and Marijuana*

Existing research seems to show that combat exposure may be associated with increased marijuana use. One study in which Army members were followed for three years after OEF and OIF deployments found that between roughly 1.89% to 2.83% of these soldiers tested positive for marijuana (Larson et al., 2016), but unfortunately no comparisons were given for rates among service members without combat deployment experience. As previously discussed, many veterans use marijuana in an attempt to medicate for pain or psychiatric illnesses, and combat veterans may be no different. A

study conducted among OEF/OIF/OND veterans who reported using marijuana at least once in their lifetime found that the most commonly endorsed reasons for medical marijuana use were anxiety, PTSD, pain, depression, and sleep problems (Metrik, Bassett, et al., 2018). A recent anecdotal report reveals that OEF/OIF/OND veterans use marijuana instead of other drugs and believe it is less harmful than opioids (Krawitz, 2015). Another study found that veterans who identified as medical marijuana users, rather than recreational users, reported greater combat exposure and reported using more marijuana (Loflin et al., 2017). Studies have also found that combat veterans prefer to use marijuana rather than pharmaceutical medicine to reduce combat related anxiety, anger, and sleep disturbances (Croulet, 2019), implying that mental health disorders may mediate the relationship between combat exposure and marijuana use.

### *Combat Exposure and Opioids*

Current literature on the associations between opioid use and combat is mixed. Many studies suggest a link between combat deployment experience and opioid use (Adams et al., 2019; Kime, 2014). A large study of active duty army soldiers found that 34.8% were prescribed opioids within the year after returning from OEF/OIF/OND, and 1.1% of these soldiers ended up using opioids long-term (i.e., opioids were prescribed for at least two thirds of days over 90 days or longer; Adams et al., 2019). However, this literature also often suggests that combat exposure's relationship to pain reliever use among service members is likely due to additional factors that co-occur with combat exposure, such as pain or physical trauma, rather than the combat exposure itself. In this population, opioid use typically begins with receipt of an opioid prescription after

deployment-related injuries (NIDA, 2019a). Soldiers returning from deployment are significantly more likely to receive an opioid prescription than the general military population, and the most important predictors of opioid prescriptions are not demographics, but clinical symptoms of physical trauma or acute pain (Adams et al., 2019). In this population, opioids are often prescribed and taken in an attempt to alleviate severe pain while engaged in military operations (Kime, 2014). Some research has also found that these rates of prescription pain reliever use seem to remain elevated once service members leave the military (Derefinko et al., 2018). Research has also linked the elevated rates of opioid use among veterans to pain (Hudson et al., 2018; Petrakis et al., 2015).

However, a few studies have failed to find elevated rates of pain reliever use among combat veterans. One study found that opioid use among Iraq and Afghanistan veterans is lower than the overall veteran population (Hudson, 2016). Another study found that service during the recent Middle East conflicts was actually associated with a lower risk of high opioid use (20 or more prescriptions filled per year; Petrakis et al., 2015). Other studies have failed to find elevated rates among veterans when compared to civilians. A national epidemiological study found similar rates of lifetime opioid use disorders among veterans and nonveterans (2.0% and 2.7% respectively), but that individuals with OUD are five times more likely to have psychiatric comorbidities (Rhee & Rosenheck, 2019), including depression.

While use among this population seems to often begin in an attempt to alleviate the pain resulting from combat deployments, due to the addictive potential of these drugs, and the mental health struggles some service members experience, regular use can lead to

OUDs (NIDA, 2019a). Mixed findings in existent research highlight the importance of expanding research on opioid use among veterans and perhaps taking other factors into account as well. One promising avenue would be to examine mental health in order to better understand the relationship between opioids and combat exposure in this population.

Current literature on the association between heroin specifically and combat is extremely sparse. Research among Vietnam veterans has shown that 20% of troops were addicted to heroin at some point during their tour (Stanton, 1976). A more recent study in which Army members were followed for three years after OEF and OIF deployments found that between 0.032% and 0.045% of these soldiers tested positive for heroin (Larson, et al., 2016), but as mentioned previously, no comparisons were given for rates among service members without combat deployments.

### *Combat Exposure and Other Illicit Drugs*

Of the minimal research that has been done in this area, some findings point to the possibility that combat exposure may be associated with illicit drug use. One study conducted among Vietnam veterans found that combat exposure was modestly associated with illicit drug use (Reifman & Windle, 1996). A more recent study in which Army members were followed for three years after OEF and OIF deployments found that between roughly 1.02% to 1.33% of these soldiers tested positive for one or more illicit drug, not including marijuana (Larson et al., 2016), and other studies have shown similarly low rates of illicit drug use among service members as well (Golub & Bennett,

2014). For reference, approximately 4.7% of civilians in the United States reported illicit drug use not including marijuana in the past month (CBHSQ, 2016b).

In addition, a study conducted among recent OEF/OIF veterans returning to predominantly low-income and minority communities examined substance use rates at four time points: prior to military service, in the military, during the last deployment, and within the past 30 days (Golub & Bennett, 2014). Results from this study showed slight increases in all illicit substance use between the last deployment and the past 30 days (except for MDMA), but none of these increases were statistically significant. However, it is worth studying whether illicit drug use increases significantly when looking at the overall veteran population with combat deployment experience, rather than those specifically returning to predominantly low-income minority communities, especially since other research among the veteran population as a whole (not solely those with combat deployment experience) has shown that illicit drug use significantly increases among veterans during the first six months after separating from the military (Derefinko et al., 2018). Finally, to our knowledge, no studies have compared illicit drug use between active duty or veterans who have experienced a combat deployment and those who have no combat deployment experience.

### *Combat Exposure and Concurrent Substance Misuse*

Few studies examine the relationship between combat exposure and concurrent use of multiple substances among service members and veterans. The research that does exist is fairly piecemeal and tends to only compare a couple of drug classes, and these comparisons and their relationship to combat are not the main focus of the research.

However, the existing literature does seem to suggest that drug use often cooccurs for individuals who have experienced combat deployments. Among current service members with recent combat deployment experience, one study found that current daily smoking was associated with significantly increased alcohol misuse (Lopez et al., 2018). Another study among female OEF/OIF service members and veterans examined the prevalence and correlates of tobacco use, and revealed that current smoking was significantly associated with past year alcohol use and lifetime use of illicit drugs or prescription drugs not prescribed to them (Weg et al., 2015). Another study among OEF/OIF/OND veterans who reported using marijuana and alcohol together in the same day within the past 180 days found that heavy drinking tends to occur on days that marijuana is used, and that this is more likely to occur among veterans diagnosed with AUD or AUD and CUD, but not among veterans diagnosed with CUD alone (Metrik, Gunn, et al., 2018). Finally, a large-scale study of OEF and OIF veterans that examined the prevalence and independent correlates of AUD and DUD found that only 1% of veterans received an AUD diagnosis in isolation (without a DUD diagnosis nor any other mental health diagnosis), and only 0.2% of veterans received DUD diagnosis in isolation (without an AUD nor any other mental health diagnosis; Seal et al., 2011). These data reveal the importance of examining comorbid SUDs and mental health disorders among OEF/OIF veterans with an AUD or DUD.

### Combat Exposure and Depression

It is clear from previous research that combat exposure among current service members and veterans can be associated with an elevated risk for substance misuse. However, research findings indicate that combat exposure alone is likely not enough to

predict problematic substance use (Bailey & Stewart, 2014) because combat exposure is not independently nor directly associated with substance use (Scherrer et al., 2008; Trautmann et al., 2014). While combat exposure is likely to be a contributing factor, other factors must be taken into account in order to more comprehensively explain the relationship between combat and substance use. Research suggests that mental illness may help clarify our understanding of this relationship.

Some of the most common mental health disorders that combat veterans suffer from include PTSD, depression, anxiety, and adjustment disorder (Hoopsick et al., 2019; Seal et al., 2011). Depression has been found to be more prevalent among service members than among civilians. Data from 2015 show that 6.7% of civilian adults experienced one or more Major Depressive Episode (MDE) in the past year (CBHSQ, 2016b), while 9.4% of active duty service members experienced depression within the past year (Meadows et al., 2015a). These depression rates remain similarly elevated as service members leave the military (Derefinko et al., 2018; Meadows et al., 2015a; SAMHSA, 2020). Data from the 2018 NSDUH reveal that among veterans, 11.2% of those aged 26 to 49 have experienced a major depressive episode within the past year, while only 8.0% of the overall civilian population reports a past year major depressive episode (SAMHSA, 2020). In a population-based longitudinal study of soldiers returning from Iraq, mental health concerns, including depression, showed significantly higher rates six months after deployment than immediately upon return (Milliken et al., 2007). Additionally, this study found that among those who had mental health risks (which was measured by affirmative answers to questions regarding depression, PTSD, interpersonal aggressive ideation, or suicide ideation) six months after deployment, significantly more

left the military over the next five months. This suggests that post-combat mental health may worsen over time. Since many of these individuals leave the military and transition to the civilian world, it is especially important to study among veterans.

Research over the past twenty years has shown a strong co-occurrence among trauma, PTSD, and substance use disorders (Bailey & Stewart, 2014). However, PTSD does not appear to fully explain this relationship. First, past research on post-trauma effects may not be generalizable to veterans of more recent wars. Recent research comparing OEF/OIF veterans to Vietnam veterans reveals differences in PTSD symptom presentation among veterans of recent wars, such as lower levels of distress regarding symptoms of intrusion, defensive avoidance, anxious arousal, dissociation, and impaired self-reference (Erbes et al., 2009). Second, current DSM-5 PTSD diagnostic criteria may not accurately capture everyone suffering from the effects of trauma exposure; the full disease burden may be better exemplified by a sub-threshold PTSD definition (Hoge, 2015). Sub-threshold PTSD is important to examine as it is sometimes associated with even more severe problems than those faced by individuals who meet full diagnostic criteria for PTSD, such as higher levels of alcohol problems and similar levels of suicidality (Linn, 2019).

Recent research has also shown that different symptom clusters of PTSD relate differently to substance use disorders (Dworkin et al., 2018). More specifically, it seems as though this relationship between trauma and substance use disorders could be further explained by depressive symptoms. A recent study analyzed which clusters of PTSD symptoms predicted AUD and found that the frequency of negative alterations in cognition and mood predicted 4.9 times greater odds for alcohol abuse since deployment,

and that the intensity of these negative alterations in cognition and mood predicted 3.8 times greater odds, while the reexperiencing, hyperarousal, and avoidance clusters did not predict alcohol abuse (Boland et al., 2018). Another study conducted on combat veterans with PTSD and mild traumatic brain injuries (mTBI) found that the internalizing dimension symptoms, which are very similar to symptoms seen in depression and anxiety, most significantly predicted post-deployment functional impairment, and that mTBI history only affects functional impairment indirectly through these internalizing symptoms (Disner et al., 2017). Many symptoms from the PTSD symptom cluster involving negative changes in cognition and mood overlap with depressive symptoms, and there is evidence to show that depressive symptoms may play a more prominent role in explaining the lack of positive outcomes for OEF and OIF veterans (Bergmann et al., 2019). For example, a study of combat veterans with comorbid depression and PTSD revealed the distinctive contributions of depression in predicting mental and physical health related quality of life, even after accounting for the overlapping symptoms that PTSD and depression share (Pittman et al., 2012). Another study found that the relationship between trauma and drug use, as well as the mediation effect of depression, were statistically significant even after controlling for trauma symptom severity (Kelley et al., 2015). Examining depression may be a promising avenue to further explain the relationship between trauma exposure and negative outcomes such as substance use.

Among OEF/OIF veterans, after trauma, depression can be as prevalent as PTSD, and is highly comorbid with PTSD (Tanelian & Jaycox, 2008). As a result, current research has explored the relationship between combat exposure and depression. One study conducted on combat veterans found that 7.4% of current 12-month Major

Depressive Disorder (MDD) diagnoses could be attributable to combat exposure, but that the effect of combat on MDD was mainly an indirect effect mediated by a history of PTSD (Prigerson et al., 2002). Another study conducted on a small sample of National Guard soldiers who deployed to Iraq found that combat exposure was positively associated with depressive symptom severity (Renshaw et al., 2009). Another study found that combat exposure was significantly associated with depressive symptom severity, even after accounting for lifetime interpersonal assault exposure (Hassija et al., 2012). Other studies have managed to establish directionality between the two. One such study, a longitudinal study conducted on National Guard members for four years after deployment, found that those deployed to an area of conflict were more likely to endorse more symptoms of depression (Sampson et al., 2015).

Finally, there is evidence to suggest that different types of trauma may be associated with different resulting symptoms. A study that examined the impact of different types of trauma on OEF/OIF veterans found that exposure to personal life threat predicts symptoms of hyperarousal, while exposure to death or severe injury of others predicts depressive symptoms (Shea et al., 2017). Large percentages of these veterans reported exposure to death or severe injury of others during combat deployments: 55.8% of participants endorsed seeing dead bodies or human remains, 53.4% knew someone who was seriously injured or killed, 38.3% saw dead or seriously injured Americans, 29.6% witnessed an accident that resulted in serious injury or death, 28.2% had a member of their unit become a casualty, and 19.4% handled or uncovered human remains. Since the majority of service members who have deployed to a combat zone have been exposed to death or severe injury of others, and because this tends to be associated with depressive

symptoms, depression is an extremely important and pertinent mental health issue to study among veterans who have deployed to a combat zone.

## Self-Medication Model of Addiction

The self-medication model of addiction represents one attempt at explaining the relationship between depression and substance misuse, and has gained traction in the research. The self-medication model poses that substances are used in an attempt to reduce negative affect, such as depressive symptoms, and to increase positive affect, which reinforces the substance use (Dass-Brailsford & Myrick, 2010; Khantzian, 1985; Shiffman, 1982). It is possible that this phenomenon may be occurring among veterans, since research has shown high rates of comorbidity between depression and substance use disorders among veterans. A large-scale study of OEF and OIF veterans found that for veterans with AUD, DUD, or both AUD and DUD, 54% to 72% also had a diagnosis of depression (Seal et al., 2011). More specifically, a longitudinal study found that among veterans, having a current diagnosis of depression was associated with current engagement in cigarette smoking, stimulant use, heroin, marijuana, and opioids (Ruggles et al., 2017). Research has shown that depression can lead to substance abuse and dependence.

## Depression and Substance Dependence/Abuse

### *Depression and Alcohol*

Alcohol and depression seem to be closely linked among active duty service members and veterans. A large study of service members over several time points found

that those with baseline depression were at an increased risk for new-onset alcohol related problems (Jacobson et al., 2008). Another study conducted among veterans found that alcohol misuse is significantly more common among veterans reporting depressive symptoms (Jakupcak et al., 2010). Studies have offered various explanations for this relationship. One study found that, among service members previously deployed to Afghanistan or Iraq, hazardous drinkers, but also non-drinkers, were more likely to endorse clinically significant depression, compared to moderate drinkers (Calhoun et al., 2018). The authors explained that both groups were also more likely to report fair or poor health, as compared to moderate drinkers, which the researchers indicate may provide evidence for potentially beneficial effects of moderate alcohol consumption on both physical and mental health. Kelley et al. (2017) found that from pre- to post-deployment, increases in work-related stressors significantly predicted increases in depression symptoms, which then significantly predicted increases in hazardous drinking. While this study examined a non-combat deployment, other studies specifically examining service members with combat deployment experience indicate this may hold true for combat deployments as well (Sampson et al., 2015; Wright et al., 2012).

A study investigating depression trajectories over the four years following OEF/OIF combat deployments showed that AUD at all time points was associated with increases in depressive symptoms, and that AUD contributed to a steeper increase in depressive symptoms over time (Sampson et al., 2015). Another study among service members who participated in a fifteen-month deployment to Iraq examined the influence of combat experience on internalizing symptoms, including depression, and how this was related to externalizing symptoms, including alcohol problems, at four- and nine-months

following deployment (Wright et al., 2012). Results indicated that at both time points, internalizing symptoms, including depression, were significantly associated with externalizing behavior, including alcohol problems, and that combat exposure significantly predicted externalizing behavior, including alcohol problems.

The relationship between depression and alcohol use appears to remain once service members transition to a veteran status. Research conducted by Fuehrlein et al. (2016) found that veterans with a lifetime AUD had substantially higher rates of current and lifetime mood disorders compared to veterans without AUD, and that lifetime MDD was independently associated with past-year probable AUD among veterans. Another study among OIF veterans with combat deployment experience and a combat-related injury revealed that depressive symptoms significantly correlated with alcohol misuse (Heltemes et al., 2014).

### *Depression and Nicotine*

Studies among veterans have examined the relationship between depression and tobacco use specifically. A study conducted on a national sample of veterans found that those who have lifetime Nicotine Dependence were at an increased risk for several lifetime psychiatric disorders, including depression (Baldassarri et al., 2019). Studies have examined different theories to explain this relationship. One non-veteran specific study found that tobacco smokers tend to report increased rates of psychological distress, which contributes to the maintenance of smoking behavior (Chase et al., 2018). More specifically, MDD, which is often comorbid with smoking, involves dysregulated affect, and the nicotine in cigarettes enhances positive affect (Cook et al., 2017), which could

explain the high comorbidity rate between the two. Another study among post-9/11 combat veterans found that moderate to high nicotine dependence is associated with significantly increased three-way clustering of depression, PTSD, and pain (Fonda et al., 2019).

### *Depression and Marijuana*

Studies among current service members and veterans have examined the relationship between depression and marijuana use specifically. A study conducted among current military members and found that marijuana use was associated with more severe depressive symptoms (Morgan et al., 2017). Research shows that OEF/OIF/OND veterans who have MDD are at higher risk for using marijuana, experiencing marijuana-related problems (according to the Marijuana Problems Scale), and having CUD (Metrik et al., 2016). Studies have also found that marijuana use among veterans is associated with depressive symptom severity, even after controlling for age, race, service era, and combat exposure (Gentes et al., 2016), and that marijuana use among veterans is individually associated with depressive disorders (Goldman et al., 2010). In fact, one of the most commonly reported conditions for medical marijuana use among a sample of OEF/OIF/OND veterans was depression (Metrik, Bassett et al., 2018). Research has attempted to explain this relationship. One study conducted on marijuana dependent veterans found that positive expectations about the effects of marijuana mediated the relationship between depressive symptoms and marijuana use (Farris et al., 2014). This research implies that veterans with greater depressive symptoms may hold stronger

beliefs that marijuana will help increase positive affect or assist with behavioral activation, which then predicts marijuana use.

### *Depression and Opioids*

Studies among veterans reveal that depression may help explain the relationship between combat experience and opioid use. A national epidemiological study found that individuals with OUD are five times more likely to have psychiatric comorbidities (Rhee & Rosenheck, 2019), including depression. Specifically, this study found that among veterans with an OUD, 41.2% had comorbid MDD, while among non-veterans with an OUD, 33.1% had comorbid MDD (Rhee & Rosenheck, 2019). Another study conducted on approximately five million veterans found that depressive disorders were independently associated with high prescription opioid use, which was defined as more than 20 prescriptions filled each year (Petrakis et al., 2015). Finally, not only is opioid use associated with higher rates of depression, but opioid use has been found to double the likelihood of depression recurrence (Scherrer et al., 2016). These studies suggest that among veterans, depression may facilitate the jump from using opioids as prescribed for pain management, to misusing them.

Research reveals similar findings when examining heroin specifically. Research among Vietnam Veterans has shown that 20% of troops were addicted to heroin at some point during their tour, and that one of the major contributing factors was the need for self-medication or escape (Stanton, 1976). A more recent qualitative study that examined Afghanistan and Iraq veteran narratives found that self-medicating with prescription opioids or heroin, especially after transitioning to civilian life, was one of the most

dominant themes, and that the stress of civilian life may play into this (Bennett, Elliott, et al., 2017). More specifically, a longitudinal study using data from the Veterans Aging Cohort Study found that among veterans, having a current diagnosis of depression was associated with current use of heroin (Ruggles et al., 2017). Another study conducted among over 3,000 veterans enrolled in the Veterans Aging Cohort Study, half of which were HIV positive, and half of which were an age/race/site-matched control group without HIV, found that participants with previous depression diagnoses had significantly higher chances of heroin initiation (Banerjee et al., 2016). Finally, research has also shown that both psychological and physical pain and distress are often associated with higher levels of opioid overdose (Bennett, Golub, et al., 2017).

### *Depression and Other Illicit Drugs*

To the best of our knowledge, only a few studies among military members or veterans has examined the relationship between depression and other illicit drug use. One such study was conducted among current military members and found that illicit drug use was associated with more severe depressive symptoms (Morgan et al., 2017). Another study using data from the Veterans Aging Cohort Study found that current depression was associated with current use of stimulants (Ruggles et al., 2017). However, studies conducted among the general population have shown that illicit drugs, specifically cocaine and ecstasy, are often used to reduce depressive symptoms (Khantzian, 1985; Scott et al., 2013).

### *Depression and Concurrent Substance Misuse*

Few studies examine the relationship between depression and concurrent use of multiple substances among service members and veterans. The research that does exist is fairly piecemeal and tends to only compare a couple of drug classes, and these comparisons and their relationship to depression are not the main focus of the research. However, the existing literature does seem to suggest that drug use often cooccurs when depression is involved. A large epidemiological study conducted among U.S. adults examined multiple DSM-5 SUDs for ten different drug classes and found that rates of multiple DSM-5 SUDs were significantly more prevalent among those with a lifetime mood disorder (16.4%) and past-year mood disorder (5.0%; McCabe et al., 2017). An epidemiological study examining OUD correlates found that both veterans and non-veterans with OUD were five times more likely to have substance use and other psychiatric comorbidities (Rhee & Rosenheck, 2019). With regards to veterans specifically, a large-scale study among veterans found that DUDs, depression, and antidepressant medications were all independently associated with extensive opioid use (Petrakis et al., 2015). A longitudinal study using data from the Veterans Aging Cohort Study in which half of the participants were HIV positive, and the other half were an age/race/site-matched control group without HIV, examined the temporal relationships between depression and different types of substance use. This study found several temporally concordant patterns among depression, cigarette smoking, unhealthy alcohol use, and other substance use, but only found one sequential temporal relationship in which cigarette smoking preceded unhealthy alcohol use but the inverse was not true (Ruggles et al., 2017). Finally, a large-scale study of OEF and OIF veterans that

examined the prevalence and independent correlates of AUD and DUD found that 53.6% with AUD, 58.1% with DUD, and 71.9% with both AUD and DUD also received a comorbid depression diagnosis (Seal et al., 2011) which points to a potential relationship between combat deployment experience, multiple SUDs, and depression.

## Consequences for Veterans

As previously discussed, veterans who have deployed to combat zones typically have high rates of trauma exposure and mental health conditions, such as depression. This can lead to a wide array of long-term consequences including substance abuse and dependence, physical health problems, suicide attempts, unhealthy behaviors, mortality, diminished productivity, and unemployment (Tanelian & Jaycox, 2008). Additionally, having a mental illness or a substance use disorder makes successful reintegration into civilian life more difficult for veterans, and is often associated with non-routine discharges from the military, which leads to loss of benefits, barriers to mental health care access, and worse post-discharge consequences on many fronts (Brignone et al., 2017; Brooks Holliday & Pedersen, 2017). Substance use disorders and mental health problems are also often related to an increased risk for self-injurious behavior, suicide attempts, and mortality among veterans (Bohnert et al., 2014; Bohnert et al., 2017; Kimbrel et al., 2017; Kimbrel et al., 2018). A study examining the circumstances surrounding military suicides found that the second most common proximal circumstance was mental health and substance use at 51.9% (Skopp et al., 2019). Furthermore, research has found that having a substance use disorder and a comorbid mental disorder often leads to more severe symptoms and poorer treatment outcomes than having either problem alone (Kessler et al., 2005; Seal et al., 2011; Watkins et al., 2001).

## The Current Study

Deployment to combat zones is often associated with an increased risk for stressful and traumatic experiences (Jordan, 2011; McDevitt-Murphy et al., 2014; Milliken et al., 2007; Tanelian & Jaycox, 2008). Individuals who deploy to a combat zone are also at increased risk for substance use problems (Hassija et al., 2012; Jacobson et al., 2008; Larson et al., 2016; McDevitt-Murphy et al., 2014; Milliken et al., 2007; Vest et al., 2018; Wright et al., 2012). However, research has yet to determine exactly how and why this happens. The majority of research in this area has examined PTSD as a contributing factor in the relationship between combat and problematic substance use due to its obvious relationship with trauma (Bailey & Stewart, 2014). However, as previously discussed, research shows that PTSD does not fully explain the relationship, and depressive symptoms may be a promising avenue to explore. Studies show that among individuals deployed to combat zones, exposure to death or severe injury of others, which is extremely commonplace in combat zones, predicts depressive symptoms (Shea et al., 2017). Studies have also found higher numbers of depressive symptoms among those who previously deployed to a combat zone (Sampson et al., 2015), and that depressive symptoms remain similarly elevated after leaving the military (Derefinko et al., 2018; Meadows et al., 2015a; SAMHSA, 2020). While the self-medication model of addiction has gained a fair amount of traction, to our knowledge it has not been validated among veterans with combat zone experience to explain how different types of substance use may be the result of an attempt to self-medicate for depressive symptoms. Therefore, it is important to study the potential role that depression plays in mediating the relationship between combat zone deployment and problematic substance use.

Additionally, since a large amount of research on this subject has focused on alcohol (Jacobson et al., 2008; Sampson et al., 2015; Teachman et al., 2015), or has combined all drugs into one category (Kelley et al., 2015; Seal et al., 2011), it is especially important to examine classes of substances independently, in order to gain more detailed insight into the relationship between combat exposure and substance misuse. Since alcohol, tobacco, marijuana, and opioids are especially pertinent to this population, they will be examined separately, along with an "other illicit drugs" category which will capture the remaining drugs. Furthermore, a substantial amount of the current knowledge on substance use among military members has been conducted on Vietnam veterans (Jordan et al., 1991; McDevitt-Murphy et al., 2014; Roszell et al., 1991). However, war has changed drastically over the past sixty years so it is likely that the effects of war have also changed. Therefore, it is important to study veterans from more recent wars in order to either ensure that past research findings still hold true, or to gather information on how current combat deployments may differentially affect depression and substance use.

Finally, most studies on this subject have used data collected by the military, the VA, or by an affiliate institution. In these contexts, respondents may be hesitant about candidly disclosing their mental health symptoms and substance use tendencies, as veterans may not want to be stigmatized for their mental health conditions, and active duty service members do not want to be stigmatized, subject to disciplinary action, or be dishonorably discharged from the military (NIDA, 2019a; Singaraju et al., 2019; Teeters et al., 2017). Furthermore, only 62% of separated OEF/OIF/OND veterans used the VA healthcare system from 2001 to 2015 (Department of Veterans Affairs, 2017), and

therefore studies that analyze data only from veterans who use the VA systematically do not account for over a third of the veteran population and thus results may not be generalizable to all veterans. Therefore, it is important to conduct this study in a manner that is not associated with the military nor VA to increase the likelihood of honest responding and generalizability.

This study will address the current gaps and shortcomings in the literature by exploring the potential effects that deployment to a combat zone have on abuse and dependence of different substances among veterans of the United States Armed Forces. Specifically, the study will examine whether this relationship is mediated by depression for the following substances: alcohol, nicotine, marijuana, opioids, other illicit drugs, and concurrent substance misuse. We predict that deployment to combat zones will be associated with higher rates of substance abuse or dependence for all of the listed substances, and that this relationship will be mediated by depression.

In this study, we controlled for covariates based on past literature in this arena. First, we controlled for assigned sex at birth. Research has shown that assigned sex is associated with a variety of substance use outcomes. For example, being a male is independently associated with alcohol use disorder diagnoses (Seal, Cohen, et al., 2011), lifetime AUD, and past year probable AUD (Fuehrlein et al., 2016), and that the odds of past month alcohol use are significantly greater among males (Hoopsick, Fillo et al., 2017). Research also indicates that being male is associated with higher rates of smoking cigarettes among active duty service members (Ulanday et al., 2017) and with increased odds of past year multiple substance use disorders (McCabe et al., 2017). Second, we controlled for government assistance programs, which we used as a proxy variable for

income level, as research has shown that income is associated with a variety of substance use outcomes. For example, research has shown that having a lower yearly income is independently associated with lifetime AUD (Fuehrlein et al., 2016), and that having an income greater than $41,000 is associated with a decreased likelihood of current smoking among veterans, and having an income over $75,000 is associated with having never smoked (Golden et al., 2018), implying that those with lower incomes are at increased risk for current smoking. Third, we controlled for age, as research shows that age is associated with a variety of substance use outcomes. For example, among military members and veterans, being younger than 25 years old is independently associated with alcohol use disorder (Seal, Cohen et al., 2011), younger members are at the highest risk for all alcohol related outcomes (including heavy weekly drinking, binge drinking, and alcohol related problems; Jacobson, Ryan et al., 2008), and that being younger is independently associated with lifetime and past year probable AUD (Fuehrlein et al., 2016). Research has also shown that among veterans, being younger than 65 years old is associated with current smoking (Golden et al., 2018). Finally, we controlled for race/ethnicity, as research shows that race/ethnicity is also associated with a variety of substance use outcomes. For example, identifying as non-Hispanic white is associated with higher rates of smoking cigarettes among active duty service members (Ulanday et al., 2017) and higher rates of heavy weekly drinking, binge drinking, and alcohol related problems (Jacobson et al., 2008).

# CHAPTER TWO

# METHODS

## Participants

Data from the 2013, 2014, 2015, 2016, 2017, and 2018 NSDUH public use data files was used for the purposes of this study (CBHSQ, 2018a; CBHSQ, 2018b; CBHSQ, 2018c; CBHSQ, 2019). Participants in this dataset are a representative sample of members of the United States civilian, noninstitutionalized population aged 12 or older. The total sample for the years under examination consisted of over 67,500 participants each year. For the purposes of this study, only data from United States veterans who provided usable responses to an item assessing combat deployment experience (described below) was analyzed.

Data from the 2013 to 2018 NSDUH data files was used when analyzing alcohol and marijuana, yielding a total of 14,121 participants. Our sample was primarily male (87.9%) and Non-Hispanic White (75.2%). The largest age-range category for our sample was age 50 and older (54.4%), followed by ages 35 to 49 (26.5%). Within our sample, 34.5% reported having been deployed to a combat zone. See Table 1.

Data from the 2015 to 2018 NSDUH data files were used when analyzing nicotine, opioids, other illicit drugs, and concurrent misuse, yielding a total of 9,661 participants. Our sample was primarily male (87.7%) and Non-Hispanic White (74.7%). The largest age-range category for our sample was age 50 and older (53.9%), followed by ages 35 to 49 (26.7%). Within our sample, 35.1% reported having been deployed to a combat zone. See Table 1.

**Table 1.** Demographics.

| Variable | 2013-2018 (*N* = 14121) | | 2015-2018 (*N* = 9661) | |
|---|---|---|---|---|
| | *N* | % | *N* | % |
| Combat | | | | |
| Yes | 4872 | 34.5 | 3389 | 35.1 |
| No | 9249 | 65.5 | 6272 | 64.9 |
| Depression | 7.05 (*M*) | 1.69 (*SD*) | 7.04 (*M*) | 1.67 (*SD*) |
| Alcohol Dependence/Abuse | | | | |
| Yes | 901 | 6.4 | - | - |
| No | 13220 | 93.6 | - | - |
| Nicotine Dependence | | | | |
| Yes | - | - | 1377 | 14.3 |
| No | - | - | 8284 | 85.7 |
| Marijuana Dependence/Abuse | | | | |
| Yes | 148 | 1.0 | - | - |
| No | 13973 | 99.0 | - | - |
| Opioid Dependence/Abuse | | | | |
| Yes | - | - | 76 | 0.8 |
| No | - | - | 9585 | 99.2 |
| Other Illicit Drug Dependence/Abuse | | | | |
| Yes | - | - | 82 | 0.8 |
| No | - | - | 9579 | 99.2 |
| Concurrent Dependence/Abuse | | | | |
| Yes | - | - | 288 | 3.0 |
| No | - | - | 9373 | 97.0 |
| Sex | | | | |
| M | 12412 | 87.9 | 8469 | 87.7 |
| F | 1709 | 12.1 | 1192 | 12.3 |
| Age | | | | |
| 18-25 | 946 | 6.7 | 594 | 6.1 |
| 26-34 | 1757 | 12.4 | 1282 | 13.3 |
| 35-49 | 3743 | 26.5 | 2577 | 26.7 |
| 50+ | 7675 | 54.4 | 5208 | 53.9 |
| Race/Ethnicity | | | | |
| White | 10620 | 75.2 | 7216 | 74.7 |
| Black/African American | 1584 | 11.2 | 1122 | 11.6 |
| Native American/AK Native | 209 | 1.5 | 134 | 1.4 |
| Native HI/Other Pacific | 218 | 1.5 | 152 | 1.6 |
| Islander/Asian | | | | |
| More than one Race | 514 | 3.7 | 362 | 3.7 |
| Hispanic | 976 | 6.9 | 675 | 7.0 |
| Government Program | | | | |
| Yes | 2173 | 15.4 | 1415 | 14.6 |
| No | 11948 | 84.6 | 8246 | 85.4 |

## Procedure

The NSDUH has been administered periodically since 1971 and annually since 1990. The NSDUH is conducted by RIT International, Research Triangle Park, North Carolina, and sponsored by the Center for Behavioral Health Statistics and Quality (CBHSQ) within SAMHSA. The primary purpose of the NSDUH is to gather information from members of the U.S. civilian, non-institutional population regarding the use of illicit drugs, alcohol, and tobacco, as well as to collect demographic and mental health information. The survey also monitors trends in specific drug use and mental health issues and assesses their effects by examining substance use, mental disorders, and treatment.

The survey uses a 50-state design with an independent, multistage area probability sample for each state. Participants are selected through a stratified sampling method called State Sampling Regions. Primary, secondary, and tertiary sampling units are then selected based on census tracts, census block groups, and area segments. Next, dwelling units are selected within each segment and Field Interviewers conduct a screening process to identify all survey eligible individuals. Finally, participants are selected by a computer program based on parameters specified for that area segment and a random number specified for the dwelling unit. Participants who complete a full interview are given an incentive of $30 to improve response rates. For all years between 2013 and 2018, strategies to elicit high response rates resulted in weighted screening response rates exceeding 73% and weighted interview response rates exceeding 66%.

The 2013, 2014, 2015, 2016, 2017, and 2018 NSDUH surveys were conducted using computer-assisted interviewing (CAI) in respondents' homes. Interviews were

carried out in two ways, depending on the nature of the question. All questions pertaining to substance use and other potentially sensitive topics were administered using audio computer-assisted self-interviewing (ACASI). The ACASI system was designed so participants had a private and confidential means of responding so as to increase the level of honest responses. Questions pertaining to less sensitive topics were administered by a human interviewer using computer-assisted personal interviewing (CAPI). Respondent anonymity was also protected throughout the study by separating survey responses from identifying information.

## Measures

Data from the 2013, 2014, 2015, 2016, 2017, and 2018 NSDUH public use data files was used for the purposes of this study, as they represent the most current comparable publicly available data and contain information regarding combat zone experience. To answer our research questions, we utilized data from the survey questions regarding depressive symptoms, and the use of alcohol, tobacco, marijuana, opioids, and other illicit drugs, specifically among veterans. We chose to use six years of data in order to ensure we had a sufficient number of participants endorsing each category of substance use.

### *Demographics*

Participants reported their age, assigned sex at birth, whether they were on a government assistance program, and race/ethnicity.

### *Veteran Status*

Veteran status was determined based on respondents' answers to the question, "Are you currently on active duty in the United States Armed Forces, are you in a Reserve Component, or are you now separated or retired from the military?" Respondents who answered "Now separated/retired from reserves/active duty" were included in our sample, while the remainder were excluded.

### *Combat Zone Experience*

To determine combat zone experience among participants, responses to the following question were analyzed: "Did you ever serve on active duty in the United States Armed Forces or Reserve components in a military combat zone or an area where you drew imminent danger pay or hostile fire pay?" Respondents who answered "yes" were categorized as having combat zone experience, while respondents who answered "no" were categorized as having no combat zone experience.

### *Past Year Major Depressive Episode*

Presence of depressive symptoms was defined using the DSM-IV for NSDUH 2015 and 2016, and the DSM-5 for NSDUH 2017 and 2018. Research has shown that the NSDUH questions pertaining to MDE can be used to determine MDE under both the DSM-IV and DSM-5 criteria (CBHSQ, 2016a). More specifically, the NSDUH MDE questions were based on the depression section of the National Comorbidity Survey-Replication (NCS-R; Harvard School of Medicine, 2005). The NCS-R used a modified version of the WHO's Composite International Diagnostic Interview (WMH-CIDI),

which has been shown to be a reliable and valid method of generating DSM-IV psychological diagnoses (Wittchen, 1994).

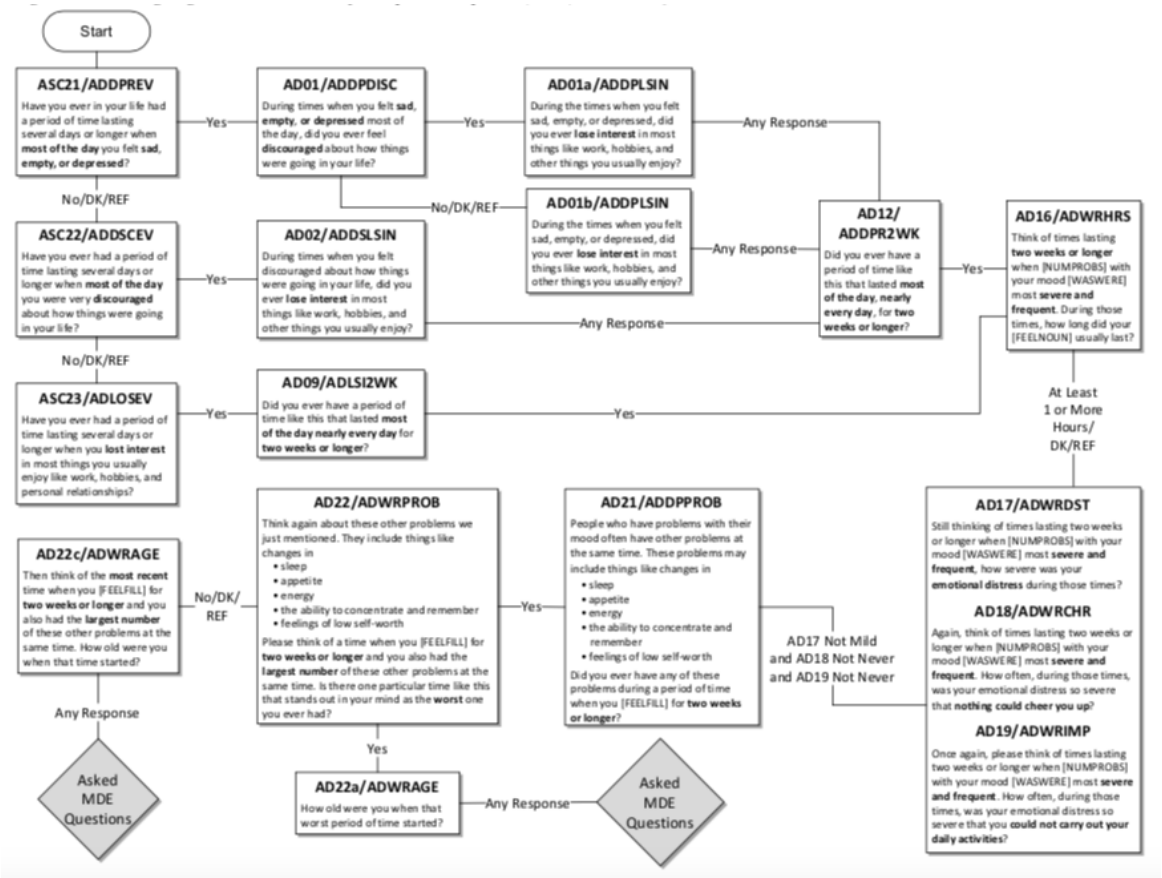


***Figure 1.*** Routing Logic Prior to Adult Major Depressive Episode (MDE) Attribute Questions

Before the MDE questions were presented, respondents were asked a series of related introductory questions detailed in Figure 1. If respondents did not meet criteria according to the routing logic of these introductory questions, they were categorized as not having an MDE in the past year and were not asked the MDE questions. If respondents met the routing logic criteria of the introductory questions, they were then asked the MDE questions. All MDE questions were related to the nine criteria of MDE

and can be found in Appendix A. For the majority of questions, participants simply selected “yes” or “no,” with the exception of two questions pertaining to weight loss or gain, in which participants were asked to select a weight range. For the purposes of the present study, based on the number of affirmative responses to these questions, participants were given a Past Year MDE score ranging from 0 to 9, with higher scores indicating the more depressive symptoms.

### *Substance Abuse and Dependence*

In this study, we examined participants’ self-reported Nicotine Dependence, Alcohol Abuse and Dependence, Marijuana Abuse and Dependence, Opioid Abuse and Dependence, and Other Illicit Drug Abuse and Dependence. For the purposes of this study, Other Illicit Drugs refer to any of the following: hallucinogens, inhalants, methamphetamine, prescription tranquilizers, cocaine, prescription stimulants, or prescription sedatives. Please see Appendix B for detailed information regarding the questions that comprise the following scales.

Before any questions pertaining to dependence or abuse were presented, respondents were asked a series of introductory questions. With regards to nicotine dependence, if respondents did not report cigarette smoking within the past month, they were categorized as not having nicotine dependence and were not asked the dependence questions. If respondents reported they had smoked a cigarette within the past month, they were then asked the nicotine dependence questions. With regards to marijuana, alcohol, opioids, and other illicit drug dependence or abuse, if respondents did not use the respective substance in the past twelve months (or for alcohol and marijuana, if

participants used it less than five days in the past twelve months) they were categorized as not having dependence or abuse for that substance and were not asked the corresponding dependence and abuse questions. If respondents reported they had used the respective substance within the past twelve months, they were then asked the corresponding dependence or abuse questions.

For the purposes of this study, we described substance use in terms of the DSM-IV diagnoses "dependence" and "abuse" since the NSDUH has chosen to continue using these terms. However, it is important to keep in mind that the four criteria that comprise the substance abuse disorder diagnosis and the seven criteria that comprise the substance dependence disorder diagnosis were essentially combined to create the newer DSM-5 diagnosis of "substance use disorder," and therefore its eleven criteria have largely remained the same, with several exceptions. First, the recurrent substance-related legal problems criterion was dropped and a new criterion involving craving was added. Additionally, some details regarding the withdrawal criteria for each substance were updated. Therefore, while the NSDUH continues to assess substance use in terms of dependence and abuse, this area of study is still very relevant, since, when combined, these disorders largely mirror substance use disorder and its criteria.

**Alcohol**

Past year alcohol dependence was defined based on the DSM-IV dependence criteria. Ten questions pertaining to the seven dependence criteria were asked. For the majority of questions, participants simply selected "yes" or "no." One exception was for the question "were you able to keep the limits you set, or did you often drink more than

you intended to?" in which participants selected from the following responses: "usually kept to the limits set" or "often used more than intended." The participants were given an Alcohol Dependence score, ranging from one to seven, based on their answers to the seven dependence criteria, with higher scores indicating more dependence. Based on the DSM-IV diagnostic criteria, participants who endorsed three or more of the seven dependence criteria were categorized as having Alcohol Dependence in the past year (APA, 1994).

Past year alcohol abuse was defined using the DSM-IV abuse criteria. Five questions pertaining to the four abuse criteria were asked and participants had the ability to select "yes" or "no." The participant was given an Alcohol Abuse score, ranging from one to four, based on their answers to the four abuse criteria, with higher scores indicating more abuse. Based on the DSM-IV diagnostic criteria, participants who endorsed one or more of the four abuse criteria, and who did not meet criteria for dependence for alcohol, were categorized as having Alcohol Abuse in the past year (APA, 1994).

For the purposes of this study, participants were categorized as having Past Year Alcohol Dependence or Abuse if they were categorized as having Alcohol Dependence or Alcohol Abuse; otherwise, they were categorized as *not* having Past Year Alcohol Dependence or Abuse.

**Nicotine**

Nicotine dependence was defined based on the dependence criteria contained in the Nicotine Dependence Syndrome Scale (NDSS; Shiffman et al., 1995; Shiffman et al.,

2004) and the Fagerstrom Test of Nicotine Dependence (FTND; Fagerstrom, 1978; Heatherton et al., 1991) for participants who reported cigarette smoking within the past month. The FTND displays adequate reliability and validity (Burling & Burling, 2003; Etter et al., 1999; Kozlowski et al., 1994). The NDSS is a valid measure of nicotine dependence, as it has been found to correlate with a variety of other nicotine dependence measures, including the original version of the FTND and the Fagerstrom Tolerance Questionnaire (FTQ; Fagerstrom, 1978), and has adequate test-retest reliability (Shiffman et al., 2004).

The NDSS is based on DSM-IV criteria for nicotine dependence (Edwards & Gross, 1976) and contains 17 questions pertaining to the five aspects of dependence. A Nicotine Dependence score was created for each participant by averaging the responses to the 17 NDSS questions (1 = *not at all true*, 2 = *somewhat true*, 3 = *moderately true*, 4 = *very true*, 5 = *extremely true*; four questions will be reverse coded; Shiffman et al., 2004). Scores on the NDSS range from 1 to 5, with higher Nicotine Dependence scores indicating higher levels of nicotine dependence. Participants with scores greater than or equal to 2.75 meet criteria for nicotine dependence (Shiffman et al., 1994).

The FTND is a multi-item measure of nicotine dependence. However, the majority of its ability to distinguish nicotine dependence is based on a single item assessing the time period in which the first cigarette is smoked after waking up (Heatherton et al., 1989). Since the majority of nicotine is eliminated from the bloodstream during the night, individuals dependent on nicotine often smoke soon after awakening. Therefore, the NSDUH simply uses this one item from the FTND: “On the days that you smoke, how soon after you wake up do you have your first cigarette?”

Participants answer on a four-point Likert scale: 1 denoting “within the first 5 minutes after you wake up,” 2 denoting “between 6 and 30 minutes after you wake up,” 3 denoting “between 31 and 60 minutes after you wake up,” and 4 denoting “more than 60 minutes after you wake up.” Based on this measure, participants were defined as “dependent” on nicotine if they indicated that they smoked their first cigarette within thirty minutes of waking up on days in which they smoked (Heatherton et al., 1991).

For the purposes of this study, participants who smoked a cigarette in the past month were defined as having Nicotine Dependence in the past month if they met dependence criteria on either the NDSS or FTND or both.

**Marijuana**

Past year marijuana dependence was defined based on the DSM-IV dependence criteria. Nine questions pertaining to the six dependence criteria were asked. For the majority of questions, participants simply selected “yes” or “no.” One exception was for the question “were you able to keep the limits you set, or did you often use marijuana or hashish more than you intended to?” in which participants selected from the following responses: “usually kept to the limits set” or “often used more than intended.” The participant was given a Marijuana Dependence score, ranging from one to six, based on their answers to the six dependence criteria, with higher scores indicating more dependence. Based on the DSM-IV diagnostic criteria, participants who endorse three or more of the six dependence criteria were categorized as having Marijuana Dependence in the past year (APA, 1994).

Past year marijuana abuse was defined using the DSM-IV abuse criteria. Five questions pertaining to the four abuse criteria were asked and participants had the ability to select "yes" or "no." The participant was given a Marijuana Abuse score, ranging from one to four, based on their answers to the four abuse criteria, with higher scores indicating more abuse. Based on the DSM-IV diagnostic criteria, participants who endorsed one or more of the four abuse criteria, and who did *not* meet criteria for dependence for marijuana, were categorized as having Marijuana Abuse in the past year (APA, 1994).

For the purposes of this study, participants were categorized as having Past Year Marijuana Dependence or Abuse if they were categorized as having either Marijuana Dependence or Marijuana Abuse; otherwise, they were categorized as *not* having Past Year Marijuana Dependence or Abuse.

**Opioids**

Past year opioid dependence was defined based on the DSM-IV dependence criteria for prescription pain relievers or heroin. Ten questions pertaining to the seven dependence criteria for each of the two substances were asked. For the majority of questions, participants simply selected "yes" or "no." One exception was for the question "were you able to keep the limits you set, or did you often use [prescription pain relievers or heroin] more than you intended to?" in which participants selected from the following responses: "usually kept to the limits set" or "often used more than intended." The participant was given a prescription pain reliever dependence score, ranging from one to seven, based on their answers to the seven dependence criteria, with higher scores

indicating more dependence. The participant was given a heroin dependence score, ranging from one to seven, based on their answers to the seven dependence criteria, with higher scores indicating more dependence. Based on the DSM-IV diagnostic criteria, participants who endorsed three or more of the seven dependence criteria for prescription pain relievers or heroin or both were categorized as having Opioid Dependence in the past year (APA, 1994).

Past year opioid abuse was defined using the DSM-IV abuse criteria for prescription pain relievers or heroin. Five questions pertaining to the four abuse criteria for each of the two substances were asked, and participants had the ability to select "yes" or "no." The participant was given a prescription pain reliever abuse score, ranging from one to four, based on their answers to the four abuse criteria, with higher scores indicating more abuse. The participant was given a heroin abuse score, ranging from one to four, based on their answers to the four abuse criteria, with higher scores indicating more abuse. Based on the DSM-IV diagnostic criteria, participants who endorsed one or more of the four abuse criteria for prescription pain relievers or heroin or both, and who did not meet criteria for dependence for the same substance, were categorized as having Opioid Abuse in the past year (APA, 1994).

For the purposes of this study, participants were categorized as having Past Year Opioid Dependence or Abuse if they were categorized as having Opioid Dependence or Opioid Abuse; otherwise, they were categorized as *not* having Past Year Opioid Dependence or Abuse.

**Other Illicit Drugs**

Past year other illicit drug dependence was defined based on the DSM-IV dependence criteria for any of the following substances: hallucinogens, inhalants, methamphetamine, prescription tranquilizers, cocaine, prescription stimulants, or prescription sedatives. For each substance, ten questions pertaining to the seven dependence criteria were asked. For the majority of questions, participants simply selected "yes" or "no." One exception was for the question "were you able to keep the limits you set, or did you often use [illicit drug name] more than you intended to?" in which participants selected from the following responses: "usually kept to the limits set" or "often used more than intended." The participant was given an Other Illicit Drug Dependence score for each substance, ranging from one to seven, based on their answers to the seven dependence criteria, with higher scores indicating more dependence. Based on the DSM-IV diagnostic criteria, participants who endorsed three or more of the seven dependence criteria for one or more of the other illicit drugs were categorized as having Other Illicit Drug Dependence in the past year (APA, 1994).

Past year other illicit drug abuse was defined using the DSM-IV abuse criteria. For each substance, five questions pertaining to the four abuse criteria were asked and participants had the ability to select "yes" or "no." The participant was given an Other Illicit Drug Abuse score for each substance, ranging from one to four, based on their answers to the four abuse criteria, with higher scores indicating more abuse. Based on the DSM-IV diagnostic criteria, participants who endorsed one or more of the four abuse criteria for one or more of the illicit drugs, and who did not meet criteria for dependence

for the same substance, were categorized as having Other Illicit Drug Abuse in the past year (APA, 1994).

For the purposes of this study, participants were categorized as having Past Year Other Illicit Drug Dependence or Abuse if they were categorized as having Other Illicit Drug Dependence or Other Illicit Drug Abuse; otherwise, they were categorized as *not* having Past Year Other Illicit Drug Dependence or Abuse.

### Concurrent Substance Misuse

Participants were categorized as having concurrent substance use if they were categorized as having substance dependence or abuse for more than one substance in the past 12 months. For the purposes of examining polysubstance use, each illicit drug was examined separately.

## Statistical Analysis

We used logistic simple mediation analyses with bootstrapping to test whether depression mediated the relationship between combat zone experience and substance misuse (dependence or abuse), after controlling for a series of covariates identified in the literature: age, assigned sex, government assistance program, and race/ethnicity (Jacobson et al., 2008; Rhee & Rosenheck, 2019; Sahker et al., 2016; Sampson et al., 2015; Seal et al., 2011; Teeters et al., 2017; Ulanday et al., 2017). Prior to analysis, we ran descriptive statistics, tested for outliers, and tested the assumptions of both linear and logistic regression.

Power analysis for logistic mediation models with bootstrapping is not well developed. These models include both linear and logistic components. Therefore, we

used GPower (version 3.1; Faul et al., 2009) to calculate power across a range of effect sizes and numbers of predictor variables (to determine how many covariates we can reasonably include in our analysis) for the linear components of the model, and we calculated the minimum sample size required for the logistic components of the model using an equation based on a simulation study by Peduzzi et al. (1996): $N = 10k/p$, where $N$ = sample size, $k$ = number of predictors, and $p$ = the proportion of "successful" events, or in our case the proportion of individuals who qualified for a diagnosis of substance abuse or dependence according to the criteria described above. Based on our data, the values of $p$ for the proposed analyses are: 0.0613 for alcohol misuse, 0.1425 for nicotine misuse, 0.0107 for marijuana misuse, 0.0085 for opioid misuse, 0.0098 for other illicit drug misuse, and 0.0298 for concurrent substance misuse.

For the linear components of the model, results indicated that we needed a minimum of 29 participants to detect a large effect size and a maximum of 347 participants to detect a small effect size, with 80% power and six predictors at $\alpha = .05$. For the logistic component of the model, results indicated that we would need a range of sample sizes depending on the substance in question and the number of covariates we chose to analyze. After merging data sets across survey years, we calculated actual sample sizes and then selected covariates for each statistical model with the goal of maximizing power while still including the most important covariates identified in previous research. This meant that for those analyses with small sample sizes (i.e. marijuana and opioids) we were limited to no additional covariates beyond the primary predictors of interest, while for other analyses with larger sample sizes (i.e., nicotine and alcohol) we were able to analyze all covariates of interest.

# CHAPTER THREE

## RESULTS

Depression was only a significant mediator of the relationship between combat zone experience and alcohol dependence or abuse, such that the odds of having alcohol dependence or abuse were 2% greater for those with combat zone experience than for those without combat zone experience, after controlling for all covariates (OR = 1.020, 95% CI [1.002, 1.054], $p < .05$). Depression was not a significant mediator of the relationship between combat zone experience and nicotine, marijuana, opioid, other illicit, and concurrent substance dependence or abuse, $p$s > .05 (see Table 2).

**Table 2.** Indirect Effect of Depression on the Relationship between Combat Zone Exposure and Substance Dependence or Abuse

| Substance | Indirect Effect (OR) | 95% CI |
|---|---|---|
| Alcohol | 1.020* | [1.002, 1.054] |
| Nicotine | 1.021 | [0.999, 1.064] |
| Marijuana | 1.019 | [0.998, 1.077] |
| Opioids | 1.041 | [0.977, 1.153] |
| Other Illicit Drugs | 1.037 | [0.981, 1.152] |
| Concurrent Substance Misuse | 1.023 | [1.000, 1.079] |

*$p < .05$.

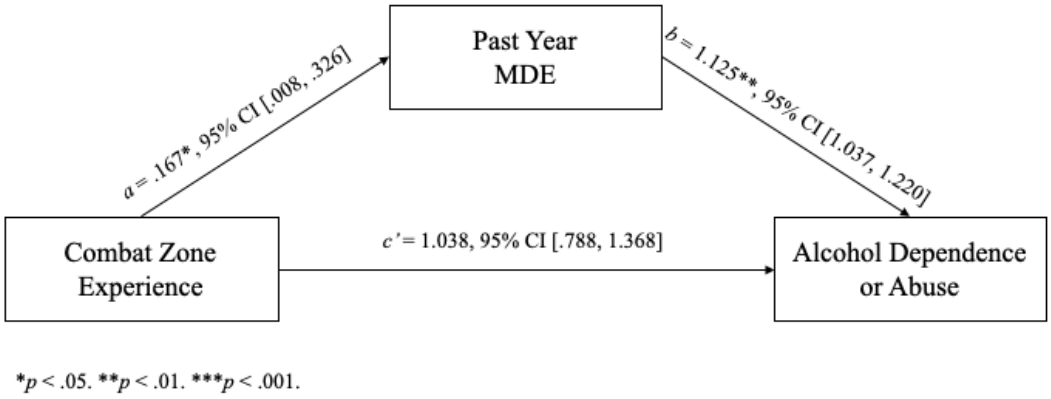


***Figure 2.*** Depression as a Mediator of the Relationship between Combat Zone Exposure and Alcohol Dependence or Abuse

In the model where depression was tested as the mediator between combat zone experience and alcohol dependence or abuse, individual effects were also tested (Figure 2). The individual effect of combat zone experience on depression was significant, such that people who do have combat zone experience had a .167-point greater past year MDE score, on average, than people who do not have combat zone experience ($a$ = .167, 95% CI [.008, .326], $p$ < .05). The individual effect of depression on alcohol dependence or abuse was significant, such that for every one-unit increase in depression, the odds of alcohol dependence or abuse increased by 12.5% (OR = 1.125, 95% CI [1.037, 1.220], $p$ < .01). The direct effect of combat zone experience on alcohol dependence or abuse was not significant, $p$ > .05.

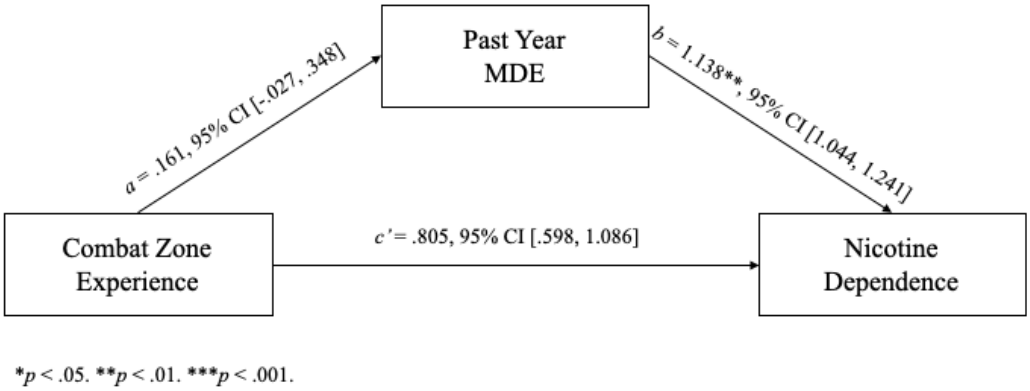


***Figure 3.*** Depression as a Mediator of the Relationship between Combat Zone Exposure and Nicotine Dependence

In the model where depression was tested as the mediator between combat zone experience and nicotine dependence, individual effects were also tested (Figure 3). The individual effect of combat zone experience on depression was not significant, $p > .05$. The individual effect of depression on nicotine dependence was significant, such that for every one-unit increase in depression, the odds of nicotine dependence increased by 13.8% (OR = 1.138, 95% CI [1.044, 1.241], $p < .01$). The direct effect of combat zone experience on nicotine dependence was not significant, $p > .05$.

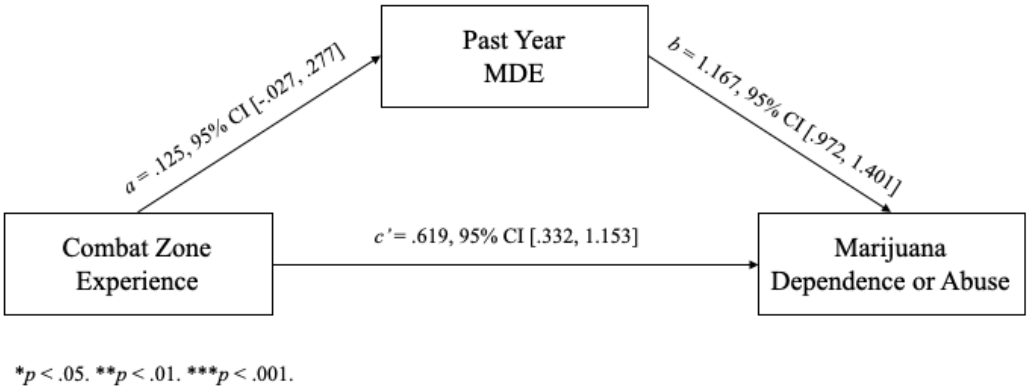


***Figure 4.*** Depression as a Mediator of the Relationship between Combat Zone Exposure and Marijuana Dependence or Abuse

In the model where depression was tested as the mediator between combat zone experience and marijuana dependence or abuse, individual effects were also tested (Figure 4). The individual effect of combat zone experience on depression was not significant, $p > .05$. The individual effect of depression on marijuana dependence or abuse was not significant, $p > .05$. The direct effect of combat zone experience on marijuana dependence or abuse was not significant, $p > .05$.

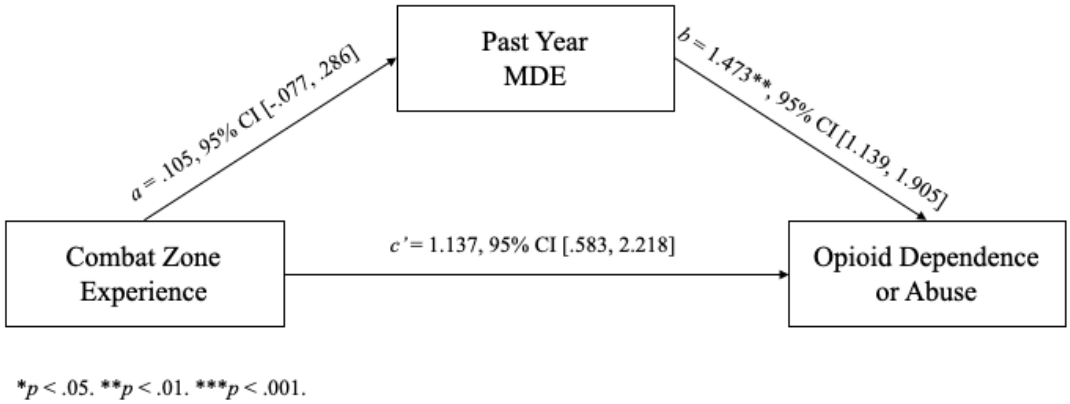


***Figure 5.*** Depression as a Mediator of the Relationship between Combat Zone Exposure and Opioid Dependence or Abuse.

In the model where depression was tested as the mediator between combat zone experience and opioid dependence or abuse, individual effects were also tested (Figure 5). The individual effect of combat zone experience on depression was not significant, $p > .05$. The individual effect of depression on opioid dependence or abuse was significant, such that for every one-unit increase in depression, the odds of opioid dependence or abuse increased by 47.3% (OR = 1.473, 95% CI [1.139, 1.905], $p < .01$). The direct effect of combat zone experience on opioid dependence or abuse was not significant, $p > .05$.

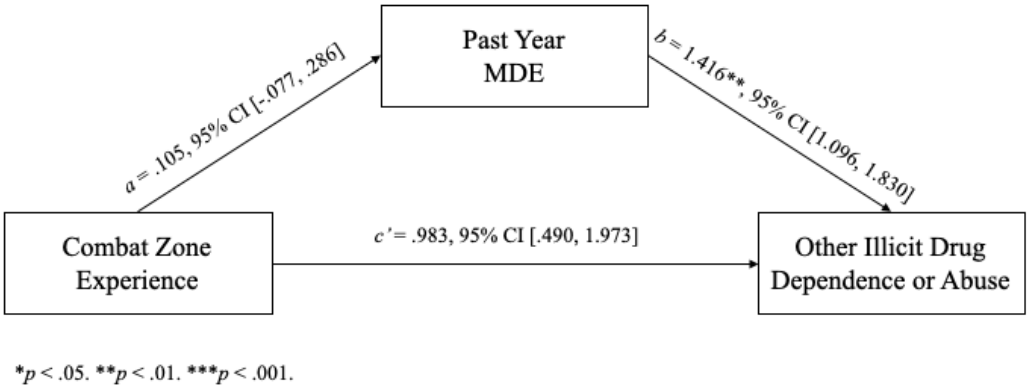


***Figure 6.*** Depression as a Mediator of the Relationship between Combat Zone Exposure and Other Illicit Drug Dependence or Abuse.

In the model where depression was tested as the mediator between combat zone experience and other illicit drug dependence or abuse, individual effects were also tested (Figure 6). The individual effect of combat zone experience on depression was not significant, $p > .05$. The individual effect of depression on other illicit drug dependence or abuse was significant, such that for every one-unit increase in depression, the odds of other illicit drug dependence or abuse increased by 41.6% (OR = 1.416, 95% CI [1.096, 1.830], $p < .01$). The direct effect of combat zone experience on other illicit drug dependence or abuse was not significant, $p > .05$.

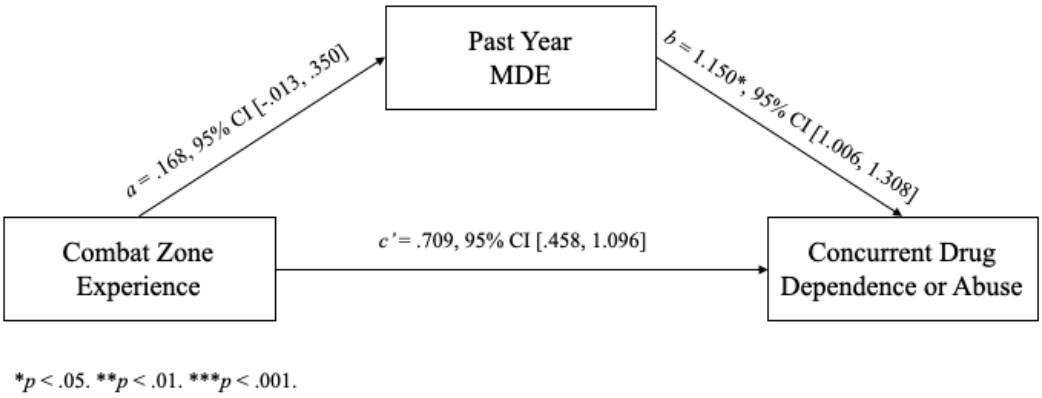


***Figure 7.*** Depression as a Mediator of the Relationship between Combat Zone Exposure and Concurrent Drug Dependence or Abuse.

In the model where depression was tested as the mediator between combat zone experience and concurrent substance dependence or abuse, individual effects were also tested (Figure 7). The individual effect of combat zone experience on depression was not significant, $p > .05$. The individual effect of depression on concurrent substance dependence or abuse was significant, such that for every one-unit increase in depression, the odds of concurrent substance dependence or abuse increased by 15% (OR = 1.150, 95% CI [1.006, 1.308], $p < .05$). The direct effect of combat zone experience on concurrent substance dependence or abuse was not significant, $p > .05$.

Several covariates were controlled for when testing mediation (Table 3). Assigned sex significantly predicted dependence or abuse, such that males reported between 65.7% and 114% greater odds of alcohol, nicotine, and concurrent substance dependence or abuse ($OR_{alcohol}$ = 1.817, 95% CI [1.294, 2.551], $p < .05$; $OR_{nicotine}$ = 1.657, 95% CI [1.170, 2.347], $p < .05$; $OR_{concurrent}$ = 2.140, 95% CI [1.247, 3.670], $p < .05$). Government assistance programs significantly predicted nicotine dependence and concurrent substance dependence or abuse, such that those on a government assistance program

reported 143.5% to 193.9% greater odds of dependence or abuse ($OR_{nicotine}$ = 2.435, 95% CI [1.797, 3.300], $p < .05$; $OR_{concurrent}$ = 2.939, 95% CI [1.939, 4.457], $p < .05$). However, this was not true for alcohol dependence or abuse, *ps* > .05. Age significantly predicted alcohol dependence or abuse, such that those 26 years and older reported 41.3% to 73.2% lower odds of alcohol dependence or abuse than those 18 to 25 years old ($OR_{Age26-34}$ = .587, 95% CI [.384, .897], $p < .05$; $OR_{Age35-49}$ = .420, 95% CI [.283, .624], $p < .05$; $OR_{Age50+}$ = .268, 95% CI [.175, .411], $p < .05$). However, this was not true for nicotine dependence, *ps* > .05. Race/ethnicity only significantly predicted nicotine dependence in two instances, such that the odds of having nicotine dependence were 43.3% lower for those who identified as NonHispanic Black/African American than those who identified as NonHispanic White (OR = .567, 95% CI [.341, .944], $p < .05$), and the odds of reporting nicotine dependence were 47.5% lower for those who identified as Hispanic than those who identified as NonHispanic White (OR = .525, 95% CI [.284, .970], $p < .05$). Race did not significantly predict nicotine dependence among the other racial/ethnic groups. Race/ethnicity did not significantly predict alcohol dependence or abuse, *ps* > .05.

**Table 3.** Effects of Covariates on Substance Dependence or Abuse

| Covariates | Alcohol OR [95% CI] | Nicotine OR [95% CI] | Marijuana OR [95% CI] | Opioid OR [95% CI] | Other Illicit OR [95% CI] | Concurrent OR [95% CI] |
|---|---|---|---|---|---|---|
| Assigned Sex at Birth | 1.817*** [1.294, 2.551] | 1.657** [1.170, 2.347] | -- | -- | -- | 2.140** [1.247, 3.670] |
| Government Program | 1.120 [.826, 1.520] | 2.435*** [1.797, 3.300] | -- | -- | -- | 2.939*** [1.939, 4.457] |
| Black or African American | 1.446 [.962, 2.176] | .567* [.341, .944] | -- | -- | -- | -- |
| Native American/AK Native | 1.103 [.373, 3.259] | .408 [.092, 1.801] | -- | -- | -- | -- |
| Asian/Native HI/Other Pacific Islander | .574 [.172, 1.915] | 1.177 [.454, 3.051] | -- | -- | -- | -- |
| More than one race | .927 [.513, 1.674] | .604 [.316, 1.157] | -- | -- | -- | -- |
| Hispanic | 1.240 [.782, 1.967] | .525* [.284, .970] | -- | -- | -- | -- |
| Age 26 to 34 | .587* [.384, .897] | 1.049 [.615, 1.791] | -- | -- | -- | -- |
| Age 35 to 49 | .420*** [.283, .624] | .828 [.500, 1.372] | -- | -- | -- | -- |
| Age 50+ | .268*** [.175, .411] | .654 [.389, 1.100] | -- | -- | -- | -- |

*Note.* Reference groups include: Assigned Sex at Birth (Female), Government Program (No), Race/Ethnicity (White), Age (18 to 25); dashes indicate predictors that were not included in the corresponding regression model due to low statistical power.
*$p < .05$. **$p < .01$. ***$p < .001$

# CHAPTER FOUR

# DISCUSSION

## Mediation: Alcohol

Depression was found to be a significant mediator of the relationship between combat zone experience and alcohol dependence or abuse, which is consistent with our hypothesis. Additionally, we found that the individual effect of combat zone experience on depression was significant, the individual effect of depression on alcohol dependence or abuse was significant, and the direct effect of combat zone experience on alcohol dependence or abuse was not significant. All these findings are in line with prior research conducted on this topic.

Recently, there has been an increase in heavy alcohol consumption rates among service members, which corresponds with the conflicts in Afghanistan and Iraq (Bray et al., 2013; Shirvani et al., 2017). Studies have shown that, among this population, those with combat exposure are significantly more likely to participate in new onset of heavy weekly drinking, binge drinking, and alcohol related problems when compared to service members who have no combat deployment experience (Jacobson et al., 2008), and that prevalence rates of alcohol use and misuse both increase before and after a combat deployment (Russell et al., 2014). Combat exposure was also found to be significantly associated with alcohol misuse, even after accounting for lifetime interpersonal assault exposure (Hassija et al., 2012). Some studies point to a dose dependent relationship, in which increased combat exposure and its associated stress correlate with higher rates of alcohol use (Bartone et al., 2017; Bray et al., 2013; Brief et al., 2018). However, many aspects of the combat deployment experience seem to affect this relationship, above and

beyond experiencing firsthand combat, including high exposure to atrocities and threatening situations (Wilk et al., 2010). In fact, a study among National Guard and Reserve members examined the relationship between alcohol problems and perceptions of combat experiences and found that perceiving combat experiences as traumatic was associated with an increased risk of alcohol problems, but that combat exposure itself showed no relationship with alcohol problems (Vest et al., 2018). Together, these findings suggest that other aspects of the combat deployment, rather than the direct combat itself, may influence the increase in alcohol misuse after deployment. This research was consistent with our finding that the direct effect of combat zone experience on alcohol dependence or abuse was not significant, while the other individual effects were significant, as well as the overall mediation model.

Alcohol and depression seem to be closely linked among active duty service members and veterans. A large study of service members over several time points found that those with baseline depression were at an increased risk for new-onset alcohol related problems (Jacobson et al., 2008). Research conducted by Fuehrlein et al. (2016) found that veterans with a lifetime AUD also had substantially higher rates of current and lifetime mood disorders compared to veterans without AUD, and that lifetime MDD was independently associated with past-year probable AUD among veterans. Another study conducted among veterans found that alcohol misuse is significantly more common among veterans reporting depressive symptoms (Jakupcak et al., 2010). This research is consistent with our finding that the individual effect of depression on alcohol dependence or abuse was significant.

While we are not aware of any studies that examine depression as a mediator between combat zone experience and alcohol dependence or abuse, a link between depression and alcohol use problems has been observed among combat service members and combat veterans. One study among service members who participated in a fifteen-month deployment to Iraq examined the influence of combat experience on internalizing symptoms, including depression, and how this was related to externalizing symptoms, including alcohol problems, at four and nine months following deployment (Wright et al., 2012). Results indicated that at both time points, internalizing symptoms, including depression, were significantly associated with externalizing behavior, including alcohol problems, and that combat exposure significantly predicted externalizing behavior, including alcohol problems. A study investigating depression trajectories over the four years following OEF/OIF combat deployments showed that AUD at all time points was associated with increases in depressive symptoms, and that AUD contributed to a steeper increase in depressive symptoms over time (Sampson et al., 2015). Another study among OIF veterans with combat deployment experience and a combat-related injury revealed that depressive symptoms significantly correlated with alcohol misuse (Heltemes et al., 2014). This research is consistent with our finding that the individual effect of combat zone experience on depression was significant, as well as the overall mediation.

There are several reasons why we believe depression was found to be a significant mediator of the relationship between combat zone experience and alcohol dependence or abuse. First, these significant findings may be in part due to the fact that active duty service members and veterans both consume alcohol at high rates. The military does not forbid service members from consuming alcohol. In fact, alcohol is an established part of

military culture (Ames & Cunradi, 2004) and the majority of service members believe drinking is supported by military culture (Meadows et al., 2015b). Among military members, alcohol is the most commonly used drug (Derefinko et al., 2018; Meadows et al., 2015a; Teeters et al., 2017). Studies have found that the majority of current members are binge drinkers and almost half are considered heavy drinkers (Golub & Bennett, 2014), and that the majority of current members endorse alcohol use (Derefinko et al., 2018). Furthermore, AUD is the most prevalent form of SUD among active duty service members (NIDA, 2019a), with 35.3% of service members meeting criteria for hazardous drinking or possible AUD in 2015 (Meadows et al., 2015b). These high rates of alcohol use during military service seem to continue when service members transition to the civilian world. A study that compared substance use rates while in the military and six months after discharge, found that rates of alcohol use were similarly elevated, with 91.5% of active duty members endorsing alcohol use and 88.6% of veterans endorsing alcohol use (Derefinko et al., 2018). Studies also show that veterans have increased prevalence rates for AUD diagnoses compared to civilians (Fuehrlein et al., 2016; Hasin et al., 2007; Kessler et al., 2005; McCabe et al., 2017; Seal et al., 2011)

Second, these findings are in line with the self-medication model of addiction. The self-medication model of addiction represents one attempt at explaining the relationship between depression and substance misuse, and has gained traction in the research. The self-medication model poses that substances are used in an attempt to reduce negative affect, such as depressive symptoms, and to increase positive affect, which reinforces the substance use (Dass-Brailsford & Myrick, 2010; Khantzian, 1985; Shiffman, 1982). One study among OEF/OIF veterans found that alcohol misuse is

significantly more common among those who also report depressive symptoms (Jakupcak et al., 2010). Another study that compared German service members recently deployed to Afghanistan to those never deployed, found a significant association between mental disorders (including depressive disorders) and heavy drinking among recently deployed service members (Trautmann et al., 2014). Trautmann and colleagues (2014) concluded that their findings imply that deployment to combat zones may promote different pathways involved in the progression of substance use and mental disorders, such as using substances in an attempt to self-medicate negative deployment-related psychological symptoms.

### Mediation: Nicotine, Marijuana, Opioids, Other Illicit Drugs, Concurrent Misuse

Depression was not found to be a significant mediator of the relationship between combat zone experience and dependence or abuse for the following substances: nicotine, marijuana, opioids, other illicit drugs, and concurrent substance misuse. These findings were inconsistent with our hypothesis that combat zone experience would be associated with higher rates of substance dependence or abuse for these substances, and that this relationship would be mediated by depression. While we are not aware of any studies that examine depression as a mediator between combat zone experience and dependence or abuse specifically for these substances, our findings were inconsistent with the literature that is available in this area, which we detailed in our literature review.

There are several possible reasons that may explain this lack of significant findings. First, our study had speculative amounts of power. Having a low probability of avoiding a Type II error may have contributed to some of our nonsignificant findings. Second, due to statistical power limitations, we were unable to examine all relevant

covariates, and for the substance categories of marijuana, opioids, and other illicit drugs, we were unable to examine any demographic covariates. Third, our study was restricted to cross-sectional data, which led to several potential limitations regarding timing.

Based on the nature of the data, we were unable to determine when participants were deployed to combat zones (i.e., we were unable to differentiate between those who were in a combat zone decades ago versus last year). Taking into account how much time has passed since the participant was deployed may be important, as research shows that time can be a relevant factor impacting mental health after deployments. For example, one study showed that for those with more depressive symptoms, the addition of an alcohol use disorder contributed to a sharper increase in depressive symptoms as more time elapsed since the deployment (Sampson et al., 2015), and this may be true for other drugs as well. Furthermore, we were not able to account for the presence of depression and/or substance use prior to combat zone deployment. Pre-combat exposure data would have been useful for creating baselines for the participants, as it is possible that some participants experienced a certain degree of depressive symptoms or substance dependence or abuse before the deployment, or that the deployment prolonged or exacerbated these symptoms. For example, other researchers have concluded that preexisting disorders may become aggravated due to stressful deployment events and the stressful process of returning home afterwards (Trautmann et al., 2014). Finally, we were also not able to examine lifetime depression or substance use; we were limited to examining these variables within the past year. However, denying these symptoms within the past year does not mean that this relationship never existed for the person, simply that

it did not exist within the past year. Therefore, we may have missed participants for whom this relationship existed more than one year prior to survey administration.

Another possible reason for our nonsignificant findings may be that, given that we were restricted to the existing variables in the dataset, we were not able to take other potentially relevant pieces of information into account. This includes many factors associated with the combat zone deployment experience. As previously discussed, deployment to combat zones and the associated stress and exposure to potentially traumatic events increase the risk for many physical and psychological injuries, as well as other negative outcomes (Jordan, 2011; McDevitt-Murphy et al., 2014). Recent surveys among OEF and OIF veterans reveal that most have been exposed to one or more traumatic events (McDevitt-Murphy et al., 2014; Milliken et al., 2007; Tanielian & Jaycox, 2008). Additionally, veterans of these wars have often served multiple tours of duty, further increasing the likelihood of exposure to traumatic events (Jordan, 2011; McDevitt-Murphy et al., 2014) and associated negative outcomes, such as problematic substance use (Hassija et al., 2012; Jacobson et al., 2008; Larson et al., 2016; McDevitt-Murphy et al., 2014; Milliken et al., 2007; Vest et al., 2018; Wright et al., 2012). Furthermore, modern warfare places military members at an increased risk of potentially morally injurious events (Currier et al., 2014).

Given this, there were many factors associated with the combat zone deployment experience that would have been beneficial to include in our analysis, but that we were unable to include due to the limited variables in our data set. One such variable was moral injury, which is sometimes the result of participating in or observing events that violate beliefs about the self (Bravo et al., 2019). Research has shown that moral injury

mediates the associations between atrocities of war and leadership failure/betrayal and symptoms of depression and hazardous alcohol use (Battles et al., 2018). Research has also found that psychological distress mediates the relationship between different types of moral injury and substance use (Feingold et al., 2018). Given the connections found between moral injury, depression, and substance use, it likely would have been beneficial to examine moral injury in our study.

Second, length and number of combat zone deployments would also possibly have been important factors to have taken into account in our study. Research has shown that longer combat experience is a correlated of higher smoking rates among active duty members (Ulanday et al., 2017), and higher rates of drinking are attributable to longer length and increased number of deployments (Shirvani et al., 2017). Therefore, length and number of combat zone deployments would have been useful variables to use as covariates. Third, the era or war in which the participant's combat zone deployment took place may have also been helpful information to have had, as research has shown that this may make a difference in terms of depression rates and substance use. For example, studies have shown that military service location and era has a significant interactive effect on post-service marijuana use rates (Ritter et al., 1985) and that depression is significantly worse for service members who were deployed to Iraq as compared to those deployed to Afghanistan (Hoge et al., 2004). Finally, the number, severity, and nature of the combat deployment related traumas experienced may have also been helpful information to have had.

In addition to these combat zone deployment related variables, there were a few additional variables that would have been useful for our study to take into account, had it

not been for our data set restrictions. One such variable is other lifetime stressors or lifetime traumatic events that were not combat deployment related. Research shows that, among service members after a combat deployment, a high number of lifetime stressors is associated with greater depression (Sampson et al., 2015). Second, we were unable to account for whether participants had or were engaging in any treatment for depression or substance use. Some of these individuals may have developed a substance problem or had depression prior to the past year, but participated in treatment or were otherwise able to overcome their substance dependence or abuse and/or depression before participating in our study. If a person is receiving or has received treatment for depression or substance use, they may have been less likely to report symptoms of depression or substance use for our study. However, this does not mean that the relationship does not exist for these individuals, simply that the relationship did not exist at the time of the study and they are receiving effective treatment.

Another possible contributor to the lack of significant findings in our study may have been our focus on depression instead of anxiety. Upon further reflection, it is possible that anxiety may be a more fitting mediator in the relationship between combat zone experience and substance dependence or abuse. As discussed previously in the literature review section, research over the past twenty years has shown a strong co-occurrence among trauma, PTSD, and substance use disorders (Bailey & Stewart, 2014). However, PTSD does not appear to fully explain this relationship, as past research on post-trauma effects may not be generalizable to veterans of more recent wars (Erbes et al., 2009) and current DSM-5 PTSD diagnostic criteria may not accurately capture everyone suffering from the effects of trauma exposure; the full disease burden may be

better exemplified by a sub-threshold PTSD definition (Hoge, 2015). Sub-threshold PTSD is important to examine as it is sometimes associated with even more severe problems than those faced by individuals who meet full diagnostic criteria for PTSD, such as higher levels of alcohol problems and similar levels of suicidality (Linn, 2019). In hindsight, given the similarities between PTSD and anxiety, anxiety may have been a better mediator to explore for this relationship between combat deployment exposure and substance dependence or abuse.

Existing research supports the strong link between substance use and anxiety among veterans. For example, among the VA population, those receiving over 20 opioid prescriptions a year were more likely to be diagnosed with anxiety (Petrakis et al., 2015). Additionally, another study shows that significant covariates of current smoking among service members includes high anxiety (Ulanday et al., 2017). Existing research also supports the strong link between substance use and anxiety among veterans with combat deployment experience. Among a German military sample, heavy drinking and regular smoking were both related to higher risk for anxiety disorders among those who were deployed to Afghanistan 12 months prior (Trautmann et al., 2014). Additionally, another study found that returning combat veterans prefer to use marijuana rather than pharmaceutical medicine to relieve anxiety (Croulet, 2019), and one of the most commonly endorsed conditions for medical marijuana was anxiety (Metrik, Bassett, et al., 2018).

We also have several theories as to why our mediation analysis was not significant based on the specific substances. With regards to nicotine, our study only examined traditional cigarette smoking. However, the CDC found that electronic-

cigarette smoking is very popular among younger populations, with 7.6% of Americans ages 18 to 24 identifying as current e-cigarette users, while only 4.3% of those ages 25 to 44, 2.1% of those ages 45 to 64, and 0.8% of those 65 and older were identifying as e-cigarette users (Villarroel, Cha, & Vahratian, 2020). Additionally, smokeless tobacco use is much more prevalent among military members than the general population, and even higher among those members who have been deployed to a combat zone (Lin et al., 2019). Therefore, it would likely have been important to expand our study to include all forms of nicotine including electronic cigarette use, which is very popular in the younger cohorts, as well as smokeless tobacco, which is popular among military members and veterans.

In terms of marijuana, our study did not differentiate between medicinal marijuana use and recreational marijuana use, which potentially could have made a difference in our results. As previously discussed, a growing number of studies indicate that people may be partially replacing opioids with marijuana as a means of self-medicating (Boehnke et al., 2016), and researchers believe that veterans may be doing this as well (Corroon Jr. et al., 2017; Krawitz, 2015; Metrik, Bassett, et al., 2018; Reinman et al., 2017). Studies have found that veterans who use marijuana medicinally use larger amounts and endorse significantly more arousal symptoms after combat trauma experience prompts, as compared to veterans who use it recreationally (Loflin et al., 2017). Research has also found that veterans deployed after 9/11 that use medicinal marijuana differ significantly in mental health functioning as compared to those who use it recreationally (Metrik, Bassett, et al., 2018). These findings indicate that testing medical marijuana use and recreational marijuana use separately may have led to

different results. Finally, only a small portion of our population endorsed marijuana dependence or abuse, which may have also contributed to the lack of significant findings.

With regards to opioid dependence or abuse, it is important to consider the downturn in opioid use as of December 2011, among both active duty military members and civilians, which was likely a result of policy directives and cultural changes that were made in an effort to combat the opioid crisis in the United States (Kazanis et al., 2018). Only a small portion of our sample endorsed opioid dependence or abuse, which likely contributed to the lack of significant findings.

Finally, with regards to other illicit substances, separating the different drugs may have revealed significant trends; however, due to the small portion of our sample that endorsed other illicit drug dependence or abuse, we had to include these drugs in the same category and examine them as one group. Similarly, with regards to concurrent substance misuse, examining the specific pairings of drugs, or how many substances the participant was misusing concurrently may have also revealed significant trends. However, due to the small portion of our sample endorsed concurrent substance dependence or abuse, we were unable to do this.

### Individual Paths: Combat Zone Experience Predicting Substance Dependence or Abuse

Combat zone experience did not directly predict dependence or abuse for any substance. Prior research indicates that combat exposure among current service members and veterans can be associated with an elevated risk for substance misuse. However, research findings also indicate that combat exposure alone is likely not enough to predict problematic substance use (Bailey & Stewart, 2014) because combat exposure is not

directly nor independently associated with substance use (Scherrer et al., 2008; Trautmann et al., 2014). While combat exposure is likely to be a contributing factor, other factors must be taken into account in order to more comprehensively explain the relationship between combat and substance use. The fact that our findings indicated that combat zone experience did not directly predict dependence or abuse for any substance further corroborates these prior research findings. These nonsignificant findings are actually a very important finding, as this confirms that the relationship is not simple, and that there are other factors at play that may be moderating or mediating this relationship.

### Individual Paths: Combat Zone Experience Predicting Depression

Prior research suggests that mental illness may help explain the relationship between combat zone experience and depression. Some of the most common mental health disorders that combat veterans suffer from include PTSD, depression, anxiety, and adjustment disorder (Hoopsick et al., 2019; Seal et al., 2011). As previously discussed in our literature review, PTSD has already been widely studied and does not fully explain this relationship, especially for veterans of more recent wars. Among OEF/OIF veterans, after trauma, depression can be as prevalent as PTSD, and is highly comorbid with PTSD (Tanelian & Jaycox, 2008). Studies have also found that those deployed to an area of conflict are more likely to endorse more symptoms of depression years later (Sampson et al., 2015). Finally, there is evidence to suggest that different types of trauma may be associated with different resulting symptoms, such that exposure to personal life threat predicts hyperarousal symptoms, while exposure to death or severe injury of others predicts depressive symptoms (Shea et al., 2017). Large percentages of these veterans reported exposure to death or severe injury of others during combat deployments, and

because this tends to be associated with depressive symptoms, depression is an extremely important and pertinent mental health issue to study among veterans who have deployed to a combat zone.

As previously discussed, combat zone experience directly predicted past year major depressive episode in the regression model for alcohol abuse/dependence, but not in the models predicting any other substance. This may be partially due to the different reasons detailed above regarding why the mediation analyses were nonsignificant for these same substances, including speculative amounts of power, cross-sectional data, statistical limitations involving covariates, and being limited to existing variables in the dataset (which excluded us from examining deployment related variables, lifetime stressors, and treatment history).

### Individual Paths: Depression Predicting Substance Dependence or Abuse

Past year major depressive episode predicted dependence or abuse for almost every substance. These findings make sense, given prior research on the self-medication model of addiction. According to the self-medication model, substances are used in an attempt to increase positive affect and decrease negative affect, such as depressive symptoms, which reinforces the substance use (Dass-Brailsford & Myrick, 2010; Khantzian, 1985; Shiffman, 1982). Our findings show that this phenomenon may also be occurring among veterans. This makes sense, given that research has shown high rates of comorbidity between depression and substance use disorders among this population.

However, past year major depressive episode did not predict marijuana dependence or abuse. Research on military members shows that marijuana use is associated with more severe depressive symptoms (Morgan et al., 2017), that those with

MDD are at higher risk for using marijuana (Metrik et al., 2016), and that marijuana use is associated with depressive symptom severity, even after controlling for relevant demographic factors (Gentes et al., 2016). However, unlike the other substances examined in this study, marijuana has also been used medically by members of this population in a conscious attempt to medicate depressive symptoms. In fact, one of the most commonly reported conditions for medical marijuana use among a sample of OEF/OIF/OND veterans was depression (Metrik, Bassett et al., 2018). Research has attempted to explain this relationship. Studies have found that positive expectations about the effects of marijuana mediated the relationship between depressive symptoms and marijuana use (Farris et al., 2014). These findings imply that veterans with greater depressive symptoms may hold stronger beliefs that marijuana will help increase positive affect or assist with behavioral activation. Given our finding that past year major depressive episode did not predict marijuana dependence or abuse, coupled with past research findings that those with depression tend to use marijuana more often and do so in a conscious attempt to medicate the depression, it is possible that marijuana either does sufficiently decrease depressive symptoms, or that its placebo effect is strong enough to decrease depressive symptoms. Further research in this area is warranted, as the findings could have far reaching clinical implications.

## Covariates

While we were unable to examine all covariates for all of our substances due to power limitations, it is important to examine each covariate, and whether it predicted dependence or abuse of each substance we were able to examine it for. We controlled for assigned sex when examining nicotine dependence, and alcohol and concurrent substance

dependence or abuse. Assigned sex significantly predicted dependence or abuse for all three drug categories, such that males were at greater odds for substance dependence or abuse. These findings are consistent with prior research on this population, which indicates that being a male is independently associated with alcohol use disorder diagnoses (Seal, Cohen, et al., 2011), lifetime AUD and past year probable AUD (Fuehrlein et al., 2016), and that the odds of past month alcohol use are significantly greater among males (Hoopsick, Fillo et al., 2017). These findings are also consistent with prior research on nicotine, which indicates that being male is associated with higher rates of smoking cigarettes among active duty service members (Ulanday et al., 2017). Finally, these findings are consistent with prior research on concurrent substance misuse, which shows that being male is associated with increased odds of past year multiple substance use disorders (McCabe et al., 2017).

We also controlled for government assistance programs, which we used as a proxy variable for income level, when examining nicotine dependence, and alcohol and concurrent substance dependence or abuse. Government assistance programs significantly predicted both nicotine dependence and concurrent substance dependence or abuse, such that those on government assistance programs were at greater odds for nicotine dependence and concurrent substance dependence or abuse. Research has shown that one factor associated with a decreased likelihood of current smoking among veterans is having an income greater than $41,000, while another factor associated with having never smoked is having an income over $75,000 (Golden et al., 2018), implying that those with lower incomes are at increased risk for current smoking. We are unaware of any research on concurrent substance misuse that controlled for income; however, given

that much prior research on these individual drugs indicates higher rates of independent dependence or abuse among those in lower income brackets, we can assume this to also be true of their concurrent misuse. However, this was not true of alcohol dependence or abuse, such that being on a government assistance program did not place our participants at greater odds for alcohol dependence or abuse. One study that evaluated the correlates of both lifetime and past year probable AUD found that having a lower yearly income was independently associated with lifetime AUD but not with past year probable AUD (Fuehrlein et al., 2016), which could explain our findings, as our study assessed past year alcohol dependence or abuse, not lifetime.

We also controlled for age when examining nicotine dependence and alcohol dependence or abuse. Age significantly predicted alcohol dependence or abuse, such that those 26 years and older reported lower odds of alcohol dependence or abuse than those aged 18 to 25. This finding was consistent with the research, which indicated that among military members and veterans, younger members are at the highest risk for all alcohol related outcomes (including heavy weekly drinking, binge drinking, and alcohol related problems; Jacobson, Ryan et al., 2008), that being younger than 25 years old is independently associated with alcohol use disorder (Seal, Cohen et al., 2011), and that being younger is independently associated with lifetime and past year probable AUD (Fuehrlein et al., 2016). However, our study found that this was not true of nicotine dependence. This may be because prior research has shown that one factor associated with a decreased likelihood of current smoking among veterans is service in May of 1975 or later (Golden et al., 2018), implying that older veterans are at an increased risk for current smoking. Additionally, those 26 years and older may have reported higher odds

of nicotine dependence than those age 18 to 25 due to the fact that our study asked about traditional cigarette smoking specifically, while many younger people are now consuming nicotine in various other forms, such as through the use of electronic cigarettes (Villarroel, Cha, & Vahratian, 2020).

Finally, we controlled for race/ethnicity when examining nicotine dependence and alcohol dependence or abuse. Race/ethnicity only significantly predicted nicotine dependence in two instances, such that the odds of having nicotine dependence were lower for those who identified as non-Hispanic Black/African American and Hispanic, as compared to non-Hispanic white. Race did not significantly predict nicotine dependence among other racial/ethnic groups, nor did it significantly predict alcohol dependence or abuse. This finding is somewhat consistent with prior research on nicotine, which indicated that identifying as non-Hispanic white was associated with higher rates of smoking cigarettes among active duty service members (Ulanday et al., 2017). However, this finding was inconsistent with prior research regarding alcohol, which found that among this population, identifying as white and non-Hispanic was associated with higher rates of heavy weekly drinking, binge drinking, and alcohol related problems (Jacobson et al., 2008). Our sample demographics are similar to those of the 2018 veteran population with regards to racial and ethnic breakdown, suggesting that the racial and ethnic breakdown of our sample does not explain our inconsistent findings (Office of Enterprise Integration, 2020). We are unsure of what may be causing these inconsistent findings, but it is possible that the people who felt comfortable disclosing information about their substance use are somehow different from the general population.

## Implications and Conclusions

Our study examined whether depression mediates the relationship between combat zone experience and substance dependence or abuse (alcohol, nicotine, marijuana, opioids, other illicit drugs, and concurrent substance misuse) among veterans of the United States Armed Forces. Depression was the only significant mediator of the relationship between combat zone experience and alcohol dependence or abuse. Among the individual effects tested, the effect of combat zone experience on depression was only significant for alcohol, the effect of depression on substance dependence or abuse was significant for all substance categories except marijuana, and the direct effect of combat zone experience on all substance dependence or abuse categories was not significant.

Our study has provided a more current and comprehensive understanding of substance abuse and dependence among veterans. Our findings could be used to improve preventive and assessment measures, tailor and improve existing treatments, develop new treatments, and direct future research. Assessment and prevention could be improved by having clinicians screen for depression and substance use among all veterans and by having clinicians emphasize substance use prevention measures in those showing signs of depression. More universal screening could assist in identifying depression in earlier stages, so that clinicians could potentially intervene before depression worsens and before alcohol becomes a means of self-medication. Our results show that clinicians should be especially watchful of depression and specifically alcohol use among veterans with combat zone experience.

With regards to treatment, while current interventions recognize that depression and substance use exacerbate one another and lead to worse treatment outcomes, they are

still often treated as two separate entities (Watkins et al., 2001). Our results confirm the importance of combining treatments specifically for depression and alcohol may improve treatment outcomes among veterans, regardless of combat zone experience. Treating these issues in tandem allows clinicians to address the root of the problem, which may prove more effective. Furthermore, knowing that this relationship exists among this population allows for the opportunity of tailoring treatment efforts to the specific needs of veterans. Additional clinical trials comparing single versus combined treatments in this population are warranted. These improvements could enhance the quality of life and mental health outcomes for veterans. Given that alcohol is consumed at high rates and is the most commonly used substance among this population, these results could prove highly applicable to veterans with combat zone experience.

These implications are also important because having a mental illness or a substance use disorder makes successful reintegration into civilian life more difficult for veterans, and is often associated with non-routine discharges from the military, which leads to loss of benefits, barriers to mental health care access, and worse post-discharge consequences on many fronts (Brignone et al., 2017; Brooks Holliday & Pedersen, 2017). Substance use disorders and mental health problems are also often related to an increased risk for self-injurious behavior, suicide attempts, and mortality among veterans (Bohnert et al., 2014; Bohnert et al., 2017; Kimbrel et al., 2017; Kimbrel et al., 2018). Furthermore, research has found that having a substance use disorder and a comorbid mental disorder often leads to more severe symptoms and poorer treatment outcomes than having either problem alone (Kessler et al., 2005; Seal et al., 2011; Watkins et al., 2001). Therefore, using our findings to improve prevention, assessment, and treatment may be

critical, not only for veterans being treated at the VA, but also for those being treated in other settings.

These findings also have implications with regards to future research. As previously discussed, it may be worthwhile to research anxiety as a mediator of the relationship between combat zone experience and substance dependence and abuse for the different substance categories. Examining anxiety in this context seems promising and may also have wide reaching implications, similar to those discussed previously for our research on depression. Additionally, future research on this topic should examine previously discussed deployment related variables, lifetime stressors, and treatment history, as doing so may shed light onto more nuanced findings. Finally, our findings suggest it would likely be beneficial to examining this relationship using longitudinal data, as using cross-sectional data may have limited our ability to examine the true nature of this relationship.

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## APPENDIX A

## MAJOR DEPRESSIVE EPISODE ITEMS

During that [worst/most recent] period of time…

1) **Depressed mood most of the day**
   a) …did you feel sad, empty, or depressed **most of the day nearly every day?**
   b) …did you fell discouraged about how things were going in your life **most nearly every day**?

   A respondent was assigned a positive response to this symptom if he or she answered yes to either of the above questions.

2) **Markedly diminished interest or pleasure in all or almost all activities most of the day**
   a) …did you lose interest in almost all things like work and hobbies and things you like to do for fun?
   b) …did you lose the ability to take pleasure in having good things happen to you, like winning something or being praised or complimented?

   A respondent was assigned a positive response to this symptom if he or she answered yes to either of the above questions.

3) **Weight**
   a) Did you have a much smaller appetite than usual nearly every day during that time?
   b) Did you have a much **larger** appetite than usual nearly every day?
   c) Did you gain weight without trying to during that period of time?
      i) …because you were growing?
      ii) …because you were pregnant?
   d) How many pounds did you gain?
   e) Did you **lose** weight without trying to?
      i) …because you were sick or on a diet?
   f) How many pound did you lose?

   A respondent was assigned a positive response to this symptom if he or she answered yes to questions ‘a’ or ‘b’ above, or the answer to either question ‘d’ or ‘f’ was greater than or equal to 10. (Note that ‘d’ was only asked if ‘c1’ and ‘c2’ were not ‘yes,’ and ‘f’ was only asked if ‘e1’ was not ‘yes.’)

4) **Insomnia or hypersomnia**
   a) Did you have a lot more trouble than usual falling asleep, staying asleep, or walking too early nearly every night during that [worst/most recent] period of time?
   b) During that [worst/most recent] period of time, did you sleep a lot more than usual nearly every night?

A respondent was assigned a positive response to this symptom if he or she answered yes to either of the above questions.

5) **Psychomotor agitation or retardation**
   a) Did you talk or move more slowly than is normal for you nearly every day?
      i) Did anyone else notice that you were talking or moving slowly?
   b) Were you so restless or jittery nearly every day that you paced up and down or couldn't sit still?
      i) Did anyone else notice that you were restless?

   A respondent was assigned a positive response to his symptom if he or she answered yes to either of the above 'a1' or 'b1' questions. (Note that 'a1' was only asked if 'a' was 'yes' and 'b1' was only asked if 'b' was 'yes.')

6) **Fatigue or loss of energy**
   a) During that [worst/most recent] period of time, did you feel tired or low in energy nearly every day, even when you had not been working very hard?

   A respondent was assigned a positive response to this symptom if he or she answered yes to either of the above 'a1' or 'b1' questions. (Note that 'a1' was only asked if 'a' was 'yes' and 'b1' was only asked if 'b' was 'yes.')

7) **Feelings of worthlessness**
   a) Did you feel that you were not as good as other people nearly every day?
      i) Did you feel totally worthless nearly every day?

   A respondent was assigned a positive response to his symptom if he or she answered yes to question 'a1.' (Note that 'a1' was only asked if 'a' was 'yes.')

8) **Diminished ability to think or concentrate or indecisiveness**
   a) During that [worst/most recent] period of time, did your thoughts come much more slowly than usual or seem confused nearly every day?
   b) Did you have a lot more trouble concentrating than usual nearly every day?
   c) Were you unable to make decisions about things you ordinarily have no trouble deciding about?

   A respondent was assigned a positive response to his symptom if he or she answered yes to any of the above questions.

9) **Recurrent thoughts of death or recurrent suicide ideation**
   a) Did you often think about death, either your own, someone else's, or death in general?
   b) During that period, did you ever think it would be better if you were dead?
   c) Did you think about committing suicide?
      i) Did you make a suicide plan?
      ii) Did you make a suicide attempt?

A respondent was assigned a positive response to this symptom if he or she answered yes to and of the above questions.

## APPENDIX B

## SUBSTANCE DEPENDENCE AND ABUSE ITEMS

### Nicotine Dependence Syndrome Scale (NDSS)

The conceptual roots of the NDSS are similar to those behind the DSM-IV concept of dependence (Edwards & Gross, 1976). The 2018 NSDUH contains 19 NDSS questions that address five aspects of dependence:

(1) Smoking drive (compulsion to smoke driven by nicotine craving and withdrawal)
   (a) After not smoking for a while, you need to smoke in order to feel less restless and irritable.
   (b) When you don't smoke for a few hours, you start to crave cigarettes.
   (c) You sometimes have strong cravings for a cigarette where it feels like you're in the grip of a force you can't control.
   (d) You feel a sense of control over your smoking – that is, you can "take it or leave it" at any time.
   (e) You sometimes worry that you will run out of cigarettes.

(2) Nicotine tolerance
   (a) Since you started smoking, the amount you smoke has increased.
   (b) Compared to when you first started smoking, you need to smoke a lot more now in order to be satisfied.
   (c) Compared to when you first started smoking, you can smoke much, much more now before you start to feel anything.

(3) Continuous smoking
   (a) You smoke cigarettes fairly regularly throughout the day.
   (b) You smoke about the same amount on weekends as on weekdays.
   (c) You smoke just about the same number of cigarettes from day to day.
   (d) It's hard to say how many cigarettes you smoke per day because the number often changes.
   (e) It's normal for you to smoke several cigarettes in an hour, then not have another one until hours later.

(4) Behavioral priority (preferring smoking over other reinforcing activities)
   (a) You tend to avoid places that don't allow smoking, even if you would otherwise enjoy them.
   (b) There are times when you choose not to be around your friends who don't smoke because they won't like it if you smoke.
   (c) Even if you're traveling a long distance, you'd rather not travel by airplane because you wouldn't be allowed to smoke.

(5) Stereotypy (fixed patterns of smoking)
   (a) Do you have any friends who do not smoke cigarettes?
   (b) The number of cigarettes you smoke per day is often influenced by other things – how you're feeling, or what you're doing, for example.

(c) Your smoking is not affected much by other things. For example, you smoke about the same amount whether you're relaxing or working, happy or sad, alone or with others.

**Fagerstrom Test of Nicotine Dependence (FTND)**

How soon after you wake up do you have your first cigarette?
On the days that you smoke, how soon after you wake up do you have first cigarette?

How soon after you wake up do you have your first cigarette?

1 = Within the first 5 minutes after you wake up……..
2 = Between 6 and 30 minutes after you wake up…….
3 = Between 31 and 60 minutes after you wake up……
4 = More than 60 minutes after you wake up…….
85 = BAD DATA Logically assigned……
91 = NEVER USED NIGARETTES…….
93 = DID NOT USE CIGARETTES IN THE PAST 30 DAYS…
94 = DON'T KNOW……..
97 = REFUSED……..
98 = BLANK (NO ANSWER)……..

**Alcohol Dependence Items**

To be defined with alcohol dependence, a respondent must have met three or more of these alcohol dependence criteria:

1) Spent a great deal of time over a period of a month or more getting, using, or getting over the effects of alcohol.
2) Used alcohol more often than intended or was unable to keep set limits on alcohol use
3) Needed to use alcohol more than before to get desired effects or noticed that same amount of alcohol use had less effect than before.
4) Inability to cut down or stop using alcohol every time tried or wanted to.
5) Continued to use alcohol even though it was causing problems with emotions, nerves, mental health, or physical problems.
6) Alcohol use reduced or eliminated involvement or participation in important activities.
7) Reported experiencing two or more alcohol withdrawal symptoms at the same time that lasted longer than a day after alcohol use was cut back or stopped. Symptoms include (i) sweating or feeling that heart was beating fast; (ii) having hands tremble; (iii) having trouble sleeping; (iv) vomiting or feeling nauseous; (v) seeing, hearing, or feeling things that were not really there; (vi) feeling like could not sit still; (vii) feeling anxious; and (viiii) having seizures or fits,

**Marijuana Dependence Items**

To be defined with marijuana dependence, a respondent must have met three or more of these marijuana dependence criteria:

1) Spent a great deal of time over a period of a month or more getting, using, or getting over the effects of marijuana.
2) Used marijuana more often than intended or was unable to keep set limits on marijuana use.
3) Needed to use marijuana more than before to get desired effects or noticed that same amount of marijuana use had less effect than before.
4) Inability to cut down or stop using marijuana every time tried or wanted to.
5) Continued to use marijuana even though it was causing problems with emotions, nerves, mental health, or physical problems.
6) Marijuana used reduced or eliminated involvement or participation in important activities.

**Prescription Pain Reliever Dependence Items**

To be defined with prescription pain reliever dependence, a respondent must have met three or more of these pain reliever dependence criteria:

1) Spent a great deal of time over a period of a month or more getting, using, or getting over the effects of pain relievers.
2) Used pain relievers more often than intended or was unable to keep set limits on pain reliever use.
3) Needed to use pain relievers more than before to get desired effects or noticed that same amount of pain reliever use had less effect than before.
4) Inability to cut down or stop using pain relievers every time tried or wanted to.
5) Continued to use pain relievers even though they were causing problems with emotions, nerves, mental health, or physical problems.
6) Pain reliever use reduced or eliminated involvement or participation in important activities.
7) Reported experiencing three or more pain reliever withdrawal symptoms at the same time that lasted longer than a day after pain reliever use was cut back or stopped. Symptoms include (i) feeling kind of blue or down; (ii) vomiting or feeling nauseous; (iii) having cramps or muscle aches; (iv) having teary eyes or a runny nose; (v) feeling sweaty, having enlarged eye pupils, or having body hair standing up on skin; (vi) having diarrhea; (vii) yawning; (viii) having a fever; and (ix) having trouble sleeping.

**Heroin Dependence Items**

To be defined with heroin dependence, a respondent must have met three or more of these heroin dependence criteria:

1) Spent a great deal of time over a period of a month or more getting, using, or getting over the effects of heroin.
2) Used heroin more often than intended or was unable to keep set limits on heroin use.
3) Needed to use heroin more than before to get desired effects or noticed that same amount of heroin use had less effect than before.
4) Inability to cut down or stop using heroin every time tried or wanted to.
5) Continued to use heroin even though it was causing problems with emotions, nerves, mental health, or physical problems.
6) Heroin use reduced or eliminated involvement or participation in important activities.
7) Reported experiencing three or more heroin withdrawal symptoms at the same time that lasted longer than a day after heroin use was cut back or stopped. Symptoms include (i) feeling kind of blue or down; (ii) vomiting or feeling nauseous; (iii) having cramps or muscle aches; (iv) having teary eyes or a runny nose; (v) feeling sweaty, having enlarged eye pupils, or having body hair standing up on skin; (vi) having diarrhea; (vii) yawning; (viii) having a fever; and (ix) having trouble sleeping.

**Alcohol Abuse Items**

To be defined with abuse of alcohol, a respondent must have met one or more of these alcohol abuse criteria in the past year and must not have been dependent upon alcohol in the past year:

(1) Serious problems at home, work, or school caused by using alcohol, such as

-neglecting their children
-missing work or school
-doing a poor job at work or school
-losing a job or dropping out of school

(2) Used alcohol regularly and then did something that might have put you in physical danger.

(3) Use of alcohol caused you to do things that repeatedly got you in trouble with the law.

(4) Problems with family or friends that were probably caused by using alcohol and continued to use alcohol even though you thought using alcohol caused these problems.

**Marijuana Abuse Items**

To be defined with abuse of marijuana, a respondent must have met one or more of these marijuana abuse criteria in the past year and must not have been dependent upon marijuana in the past year.

(1) Serious problems at home, work, or school caused by using marijuana, such as

-neglecting their children
-missing work or school

-doing a poor job at work or school
-losing a job or dropping out of school

(2) Used marijuana regularly and then did something that might have put you in physical danger

(3) Use of marijuana caused you to do things that repeatedly got you in trouble with the law.

(4) Problems with family or friends probably caused by using marijuana and continued to use marijuana even though you thought using marijuana caused these problems.

**Prescription Pain Reliever Abuse Items**

To be defined with abuse of prescription pain relievers, a respondent must have met one or more of these pain reliever abuse criteria in the past year and must not have been dependent upon prescription pain relievers in the past year:

(1) Serious problems at home, work, or school caused by using pain relievers, such as
-neglecting their children
-missing work or school
-doing a poor job at work or school
-losing a job or dropping out of school

(2) Used pain relievers regularly and then did something that might have put you in physical danger.

(3) Use of pain relievers caused you to do things that repeatedly got you in trouble with the law.

(4) Problems with family or friends probably caused by using pain relievers and continued to use pain relievers even though you thought using pain relievers caused these problems.

**Heroin Abuse Items**

To be defined with abuse of heroin, a respondent must have met one or more of these heroin abuse criteria in the past year and must not have been dependent upon heroin in the past year:

(1) Serious problems at home, work, or school caused by using heroin, such as
-neglecting their children
-missing work or school
-doing a poor job at work or school
-losing a job or dropping out of school

(2) Used heroin regularly and then did something that might have put you in physical danger.

(3) Use of heroin caused you to do things that repeatedly got you in trouble with the law.

(4) Problems with family or friends probably caused by using heroin and continued to use heroin even though you thought using heroin caused these problems.