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Breaking the Chain: Evaluating the Links Between Opioid Use Disorder, Overdose, and Suicide

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**Breaking the Chain:
Evaluating the Links Between Opioid Use Disorder, Overdose, and Suicide**

Amanda Nicole Stover

Dissertation submitted to the School of Pharmacy
at West Virginia University
in partial fulfillment of the requirements
for the degree of

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Keywords: opioid use disorder, overdose, suicide, safety screening, addiction treatment, trauma

Abstract

Breaking the Chain:

Evaluating the Links Between Opioid Use Disorder, Overdose, and Suicide

Amanda Nicole Stover

Previous research has estimated that 20–30% of individuals with opioid use disorder (OUD) have a history of both suicide attempt and unintentional opioid overdose. In 2018, more than 1.9 million adults 18 years and older had an OUD; while 1.4 million adults attempted suicide that same year (SAMHSA, 2019). The key to understanding this relationship is examining behaviors that precede these potentially fatal behaviors. One such precursory behavior is self-injury. Self-injurious behaviors (SIB) are one of the most important risk factors for future suicide (Cavanagh et al., 2003). Among individuals with OUD, previous research has found that those with OUD and SIB have a standardized mortality ratio approximately 14 times greater than those without OUD (Darke & Ross, 2002; Harris & Barraclough, 1997; Treméau et al., 2008; Wilcox et al., 2004).

This study has three primary objectives. The first is to conduct a systematic literature review to better understand the relationship between SIB, overdose and/or suicidal behaviors (i.e. suicidal ideation, suicide planning, or attempt) among people with OUD. The literature search was conducted in accordance with PRISMA guidelines for systematic reviews and meta-analyses. Forty-seven studies were included that examined the relationship between overdose, SIB, and/or suicidal behavior among people with OUD. Of these studies 46 were assessed using the NHLBI quality tool, 17.4% of studies were rated as poor, 32.6% were rated as fair, and 50.0% of studies were rated as good. Seven common themes were identified including: patterns

of substance use, psychological factors/diagnoses, sociodemographic characteristics, family history, traumatic life events, gender, and methods of suicide attempt. In general, patients with OUD who are at highest risk of suicide attempt and SIB tend to have more severe psychiatric profiles, increased rates of poly-drug use, tend to be female, experience significant life stressors and childhood maltreatment.

Results from the systematic review were used to inform the second and third aims of this study. The second aim was to evaluate the feasibility of a standardized screen for suicide and overdose among patients receiving addiction treatment. This was executed by conducting a cross-sectional study among a convenience sample of patients (n=113) recruited from two inpatient treatment programs. A modified version of the Patient Safety Screener (mPSS) was used to screen for suicidal ideation, suicide attempt, and overdose. The screen was administered in-person during treatment and administrative clinical data were extracted. Subjects (n=108) and members of their clinical care team (n=20) completed a screening acceptability survey. Approximately 60% of subjects had a positive mPSS screen, and 30.3% reported having suicidal ideation, suicide attempt, and overdose. Both subjects and clinical staff reported that it was acceptable to screen for suicide attempt(s) and overdose(s); however, a minority of clinical staff reported concerns about administration time (n=7) and impact on workflow (n=6).

The combined results of the systematic review and mPSS helped shape the final aim of this study. A cross-sectional study conducted in a subset of subjects who screened positive on the mPSS were used to assess clinical characteristics. Participants were categorized into three mutually exclusive groups: 1) unintentional overdose(s) (OD), 2) suicidal ideation or suicide attempt(s) (SI/SA), and 3) suicidal ideation or suicide attempt and unintentional overdose (SI/SA/OD). Multinomial logistic regression models were used to determine whether adverse

childhood experiences (ACE), self-injurious behaviors, substance use history, overdose history, and past year stressful life events were differentially associated with history of OD/SI/SA. All subjects categorized as having an unintentional OD only, reported having ever used cocaine, while only 72% of SI/SA subjects had ever used cocaine ($p=0.02$). Subjects in the unintentional OD group were more likely to have used heroin in the 24-hours preceding their most recent overdose (92.3%) compared to SI/SA (30.7%) and SI/SA/OD (75.0 %). In the multivariable model subjects with history of SI/SA had higher ACE scores and higher mean episodes of SIB than either of the other two participant groups.

Findings from this study support simultaneously screening for suicide and overdose in OUD inpatient treatment settings. Yet, upon further assessment of clinical and behavior characteristics, history of unintentional OD is distinct from SI/SA. Among patients who screen positive for all three outcomes, SI/SA/OD, there appears to be greater clinical severity. Therefore, it is important to evaluate patient history of suicidal ideation, suicide attempt(s), and overdose(s). More thorough evaluation of drugs involved in overdose and history of self-injury may help distinguish future risk and better inform treatment planning. Collectively this information has implications for resource needs, treatment, and prevention. However, additional research is needed to determine whether screening improves provision of services and reduces self-injurious behavior.

Dedication

“The sun is gone, but I have light.”

-Kurt Cobain

This dissertation is dedicated to the memory of Richard Anthony Piacquadio. A loving brother, father, son, and friend. He was taken from us too soon, but his light still shines brightly. He lives forever in our hearts. I carried his memorable smile with me throughout this journey and his memory in my heart with me every step of the way. You are loved and missed.

For Beth Anne Picard, an amazing daughter, sister, aunt, and friend. I will always remember your amazing spirit. Not a day goes by that I haven't thought of you. I wish you could be here to celebrate this final accomplishment with me. Your time was too short and left a huge hole in the world that no one can fill. You are loved and missed.

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List of Abbreviations

ACE	Adverse Childhood Experiences
AUD	Alcohol Use Disorder
CD	Cannot Determine
CI	Confidence Interval
CL	Checklist Item
EMR	Electronic Medical Record
IDU	Injection Drug Use
LEC	Life Events Checklist
mPSS	Modified Patient Safety Screen
N	No
NA	Not Applicable
NHLBI	National Heart Lung Blood Institute
NR	Not Reported
OD	Overdose
ODU	Opioid Use Disorder
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROMIS	Patient Reported Outcomes Measurement Information System
PSS	Patient Safety Scree
PTSD	Post-Traumatic Stress Disorder
SA	Suicide Attempt
SBQ-R	Suicide Behavior Questionnaire-Revised
SD	Standard Deviation
SI	Suicidal Ideation
SIB	Self-Injurious Behavior
SITBI-SF	Self-Injurious Thoughts and Behaviors Interview-Short Form
SMR	Standardized Mortality Ratio
SUD	Substance Use Disorder
US	United States
WV	West Virginia
Y	Yes

Chapter 1

1 Introduction

1.1 Background and Need for Study

Premature mortality associated with opioid-related overdose and suicide is a significant public health problem in the United States. In 2017, there were 47,600 opioid-related overdoses (14.9 per 100,000) and 47,173 (14.0 per 100,000) suicides reported in the U.S. (Hedegaard et al., 2018; Scholl et al., 2019; SAMHSA, 2019). Previous literature has found that people with OUD have a nearly fifteen times greater risk of all-cause mortality than demographically matched controls, with overdose being the leading cause of death (Degenhardt, et al., 2010). However, for every overdose resulting in death, there are many more nonfatal overdoses. Likewise, having one overdose substantially increases the risk of repeat overdose (Laroche et al., 2016; Hasegawa et al., 2014) and markedly elevates short-term risks of mortality (Kelty and Hulse, 2017; Stooze et al., 2009). One study, in a cohort of Austrian opioid users, found that following an overdose, people with OUD were nearly 50 times more likely to die than matched community controls, with most of the deaths involving an opioid (Risser et al., 2001). However, disentangling the complex relationship between intentional and unintentional overdoses, even among those overdoses that are nonfatal, remains difficult. In this context, repeated overdoses could be further complicated by history of self-injury, mental health diagnoses, and other life stressors.

Understanding the relationship between overdose and suicide may best be explained by examining key behaviors that precede these events. Approximately 50–60% of people who die by suicide have a documented prior history of self-injurious behavior (SIB) (Foster et al., 1997) with many instances of SIB occurring shortly before their fatal act (Gairin et al., 2003).

However, a majority of research studies conducted on SIB utilize adolescent samples, with far fewer studies focusing on adult populations under the assumption that these behaviors decrease in adulthood (Plener et al., 2016). Yet, previous research found individuals with SUDs have a 10-46% prevalence of SIB compared to 2-4% reported for the general population (Cummings et al., 2006; Evren & Evren, 2005; Harned et al., 2010; Maloney et al., 2010). Episodes of SIB are one of the most important risk factors for future suicide (Cavanagh et al., 2003). Still, limited information is available, specifically with regard to SIB and future risk for death by suicide, particularly with regard to the prevalence and relationship of lifetime SIB (O'Connor et al., 2016).

The relationship between overdose, suicide, and SIB is further complicated by co-occurring mental health diagnoses. In 2018, individuals with any mental health diagnosis are substantially more likely to misuse opioids in the past year than individuals without any comorbid mental health diagnosis (SAMSHA, 2019). According to the 2018 National Survey of Drug Use and Health, adults with a diagnosis of any mental illness were 9.2% more likely to have past year opioid misuse, and adults with a serious mental illness were 14.6% more likely to have past year opioid misuse; as compared to the 2.6% of the US population over 18 years old with past year opioid misuse and no co-occurring mental health diagnosis (SAMSHA, 2019). Studies consistently reported that depression scores were consistently higher, or history of major depressive episode was present among individuals with OUD for all outcomes of interest (i.e. SIB, suicidal ideation, suicide attempt). Commonly associated co-occurring psychiatric diagnoses reported for patients with SIB, suicidal ideation, and attempt included anxiety, PTSD, and borderline personality disorder. Collectively, these findings support greater psychiatric comorbidity with SIB and suicide attempt among those with OUD.

Likewise, prior to onset of attempted suicide many individuals with OUD reported significant life experiences. A study by Darke and Ross (2001) found that 82% of patients with OUD reported that a major life event had preceded their most recent suicide attempt. Research has found that the most commonly reported life events, prior to a suicide attempt among clients with OUD, was the conflict or dissolution of a primary relationship (Darke & Ross, 2001; Heale et al. 2003), bereavement (Darke & Ross, 2001; Heale et al. 2003), and impending incarceration (Darke & Ross, 2001). This finding highlights the complexity of the social dynamics; reinforcing that maintaining social relationships and a support system is key in attaining positive outcomes.

Overlap in SIB and suicide methods is important because SIB is associated with increased risk of a suicide attempt. Previous research has found that cutting is a common form of both SIB and suicide among individuals with OUD. One study found that cutting primary form of SIB for 25% of treatment seeking OUD patients (de los Cobos et al., 2007). A second study found that 74% of study participants with OUD engaged in cutting as their predominant form of SIB (Oyefeso et al., 2008). Additionally, three studies found cutting to be in the top three most common means of suicide attempt among individuals with OUD (Conner et al., 2007; Kazour et al., 2016; Neale, 2000). Although it is unknown if SIB is systematically assessed in OUD treatment, this overlap provides insight for means reduction and identifies a potential point for early intervention. Additionally, while a majority of studies utilized participants who primarily used heroin, however, heroin overdose was not a common method of suicide attempt (Vingoe et al., 1999). Likewise, although heroin was most frequently reported in overdoses, it was significantly more likely to be used in an accidental or unintentional overdose than an intentional overdose (Maloney et al., 2007; Neale, 2000). This is unclear whether this is due to lack of validated instruments to differentiate intentionality of overdose or if this is a result of assessment

bias. However, the most frequently cited methods of suicide attempt were overdose of non-opioid pills (Conner et al., 2007; Maloney et al., 2007), followed by cutting and hanging (Conner et al., 2007). Overall, firearms were the least likely to be used in attempted suicide among individuals with OUD, contrary to statistics normally reported on the US population. Although a study of veterans suggests firearms are the most common method used in a suicide attempt, they were more commonly used among individuals without a SUD diagnosis (Bohnert et al., 2017). This same study found that poisoning was the most common method of attempted suicide among individuals with a current SUD diagnosis (Bohnert et al., 2017). In 2017, firearms were the most common method of death by suicide, accounting for 50.6% of all suicide deaths (Kochanek et al., 2017), versus 13.9% for poisoning (Kochanek et al., 2017).

Overall, the relationship between self-injurious behaviors, suicidal ideation, suicide planning, and suicide attempt has been investigated to varying degrees throughout the published literature. However, there is still a lack of prospective longitudinal data that provide adequate temporal information between onset of OUD and SIB and/or suicide outcomes. Moreover, the relationship between SIB, suicidality, and overdose remains under-researched. In general, patients with OUD at highest risk of attempted suicide and SIB tended to have more severe psychiatric profiles, have increased rates of poly-drug use, experienced significant life stressors and childhood maltreatment. These findings provide critical information for treatment paradigms, including points for intervention and increased services. In order to address the complex nature of overlapping SIB, suicidality, and overdose among individuals with OUD this study has proposed three specific aims to further elucidate this relationship.

1.2 Specific Aims

Specific Aim 1: Conduct a systematic literature review of self-harm behaviors among people with illicit opioid use or opioid use disorder.

Specific Aim 2: Assess the feasibility and acceptability of a standardized screen to measure self-harm and suicide for individuals in OUD treatment.

Sub-aim 2A: Develop a standardized assessment of self-injury and suicide for patients receiving addiction treatment services.

Sub-aim 2B: Evaluate the acceptability of a standardized screening tool to identify self-injury and suicide risk in addiction treatment facilities.

Hypothesis 1: For patients, if the time burden is low and understandability is high, we anticipate that their willingness to complete the assessment will be high.

Hypothesis 2: For clinical staff, if screening does not impose increased clinical burden and can provide information perceived as useful their willingness to integrate the screening tool into clinical practice will be more likely than if perceived burden to clinical staff is high.

Specific Aim 3: Assessment of clinical profiles for three patient groups: 1) unintentional overdose only, 2) suicidal ideation and suicide attempt (SI/SA), and 3) suicidal ideation, suicide attempt, and unintentional overdose (SI/SA/OD). In order to determine group differences multinomial logistic regression models will be employed to evaluate the relationship between groups with age of onset of substance use, age of initiation of SIB, last episode of self-injury, ACE domain scores, and past year stressful life experiences for each of the three groups.

Hypothesis 1: Previous research has related ACEs to earlier age of initiating opioid use, recent injection drug use, and lifetime overdose (Stein et al., 2017). Likewise, studies have reported that accumulation of ACEs increases the odds of both suicidal ideation and

suicide attempt. Based on previous research, it is believed that perceived stressful life events will be associated with SI/SA while ACE domain scores will be an overlapping factor in both SI/SA (Chen et al., 2009) and the unintentional overdose groups (Stein et al., 2017).

Hypothesis 2: Furthermore, subjects with more recent episodes of SIB will represent the group with a more severe behavioral profile (i.e SI/SA/OD) who engage in more high-risk behaviors and require higher levels of care.

Chapter 2

2. Factors Associated with Self-Injurious Behavior, Overdose, and Suicide Among

Individuals with Opioid Use Disorder: A Systematic Review

2.1 Abstract

Background: Both suicide and opioid use disorder (OUD) represent significant threats to public health. In 2018, more than 1.9 million US adults 18 years and older had an OUD; while 1.4 million adults attempted suicide that same year. The key to understanding this relationship is examining behaviors that often precede these potentially fatal acts, such as self-injurious behavior (SIB). The overall objective of this systematic review is to better understand the relationship between SIB, overdose and/or suicidal behaviors among people with OUD.

Methods: A systematic literature review was conducted of research studies that examined overdose, SIB, suicide, and OUD. The literature search was conducted in accordance with PRISMA guidelines for systematic reviews and meta-analysis.

Results: Forty-seven studies were included that examined the relationship between overdose, SIB, and/or suicidal behavior among people with OUD. Of these studies 46 were assessed using the NHLBI quality tool, of which 17.4% were rated as poor, 32.6% were rated as fair, and 50.0% of studies were rated as good. Seven common themes were identified including: patterns of substance use, psychological factors/diagnoses, sociodemographic characteristics, family history, traumatic life events, sex, and methods of suicide attempt.

Conclusions: In general, patients with OUD who are at highest risk of suicide attempt and SIB have more severe psychiatric profiles, are female, have increased rates of poly-drug use, and experienced significant life stressors and childhood maltreatment. Collectively this information has implications for resource needs, treatment, and prevention.

2.2 Introduction

Both suicide and opioid use disorder (OUD) represent significant threats to public health. In 2018, more than 1.9 million adults 18 years and older in the United States (US) had an OUD. That same year, 1.4 million adults ages 18 or older attempted suicide (SAMHSA, 2019). However, a key to understanding the relationship between these two conditions is to examine key behaviors that precede these potentially fatal behaviors. Approximately 50–60% of people who die by suicide have a documented prior history of self-injurious behavior (SIB) (Foster et al., 1997) with many instances of SIB occurring shortly before their fatal act (Gairin et al., 2003). Yet, limited information is available with regard SIB and future risk for death by suicide, specifically, in terms of the prevalence and relationship with lifetime SIB (O'Connor et al., 2018). To date, four articles have assessed the published literature in a systematic review of the relationship between substance use disorders (SUDs) and suicide (Bohnert et al., 2010; Colledge et al., 2020; Harris & Barraclough, 1997; Wilcox et al., 2004). To varying degrees, each has expanded upon the connection between SUDs and mental health disorders. However, until the recent meta-analysis published by Colledge and colleagues (2020), no review has systematically investigated precursors of suicide and SUDs or a specific SUD (other than alcohol use disorder) and risk factors highly correlated with suicide. Specifically, Colledge colleagues explore the relationship between depression, post-traumatic stress and injection drug use (IDU) (2020). Findings from their analysis indicate that adding suicide prevention to harm-reduction services should be a considered priority based on the strong relationship between self-harm, depression, and IDU (Colledge et al., 2020). Intentionality of overdose is often hard to ascertain and is an outcome that can blur the lines between SIB and suicide attempts. In order to better understand

the relationship between SIB and/or risk of suicide among people with OUD, a systematic review of published literature was conducted to gauge the current body of literature.

Self-injurious behavior (SIB) is defined as the deliberate destruction of body tissue without suicidal intent, for purposes not deemed socially acceptable. Included are such behaviors as cutting, burning, head banging, picking at wounds, and self-biting (ISSS, 2007). SIB and suicide attempts are linked to increased risk of death by suicide (Cooper et al., 2005; Hawton et al., 2012; O'Connor & Nock, 2014; O'Connor et al., 2016; Turecki & Brent, 2016). A majority of research studies conducted on SIB utilize adolescent samples, with far fewer studies focusing on adult populations under the assumption that these behaviors decrease in adulthood (Plener et al., 2016). However, an early study conducted by Briere and Gill (1998) using a stratified, random sample of adults estimated the 6-month prevalence of SIB in adults to be 4% in the United States (US). Although substantially less attention is paid to co-occurring SIB and SUDs, rates of these behaviors are also elevated in this population. Previous research found individuals with SUDs have a 10-46% prevalence of SIB compared to 2-4% reported for the general population (Evren & Evren, 2005; Harned et al., 2010; Maloney et al., 2010). Episodes of SIB are one of the most important risk factors for future suicide (Cavanagh et al., 2003). When specifically looking at people with OUD, previous research has found these individuals have a standardized mortality ratio approximately 14 times greater than those without OUD (Darke & Ross, 2002; Harris & Barraclough, 1997; Tremblay et al., 2008; Wilcox et al., 2004).

A previous meta-analysis by Harris and Barraclough (1997) broadly examined the relationship between 44 mental health diagnoses and their standardized mortality ratio (SMR) for suicide. The overall analysis found that 36 of these diagnoses had excess SMRs relative to the overall population. Specifically, they found that substance abuse was associated with two-fold

higher risk of mortality when compared to other mental health diagnoses (Harris & Barraclough, 1997). In 2004, Wilcox and colleagues expanded upon the previous work of Harris and Barraclough in estimating SMRs and SMRs stratified by sex. Their updated review also included evaluation of subcategories of SUDs focusing on alcohol use disorder (AUD), OUD, intravenous drug use (IDU), mixed drug use, and heavy drinking (Wilcox et al., 2004). However, this review did not account for behavioral precursors to suicide or behaviors highly correlated with suicide. Wilcox and colleagues (2004) make a point in their review to address the dearth of literature on AUD and suicide, distinguishing that only a somewhat moderate amount of attention is paid to OUD and suicide. They concluded that limited prospective data on the use of other specific substances of abuse and associations with suicidal behavior manifests in published research. A 2010 review assessed the overlap and risk factors of unintentional overdose and suicide among substance users (Bohnert et al., 2010) and identified substance use as a risk factor for suicide, suicide attempts, and both fatal and non-fatal overdoses.

Previous literature has found that people with OUD have a nearly fifteen times greater risk of all-cause mortality than demographically matched controls, with overdose being the leading cause of death (Degenhardt, et al., 2010). In the US, 70,237 people died from overdose in 2017 (Hedegaard et al., 2018). Of these deaths, opioids were responsible for 47,600 (67.8%) (Hedegaard et al., 2018). However, for every overdose resulting in death, there are many more nonfatal overdoses. Likewise, having one overdose substantially increases the risk of repeat overdose (Laroche et al., 2016; Hasegawa et al., 2014) and markedly elevates short-term risks of mortality (Kelty and Hulse, 2017; Stooze et al., 2009). One study, in a cohort of Austrian opioid users, found that following an overdose, people with OUD were nearly 50 times more likely to die than matched community controls, with most of the deaths involving an opioid

(Risser et al., 2001). However, disentangling the complex relationship between intentional and unintentional overdoses, even among those overdoses that are nonfatal, remains difficult. In this context, repeated overdoses could straddle the line of SIB and suicide attempt(s).

The overall objective of this systematic review is to improve our understanding of relationship between self-injurious behavior (SIB), overdose and/or suicidal behaviors (i.e. suicidal ideation, suicide planning, and suicide attempt) among people with OUD. To achieve this end, the systematic review has two aims: (1) to examine the association between a history of SIB, overdose and/or suicidal behavior in people with OUD and (2) to examine the potential overlapping factors and clinical implications of these behaviors among people with OUD. Thus, the innovation of this review is the aim to address behaviors associated with increased risk for suicidality and OUD to more effectively potential risks and treatment implications associated in populations with multiple morbidities. Furthermore, this review addresses the overlap of overdose with SIB and suicidality, which hitherto has not been explored. Finally, a thematic analysis of research evidence, limitations, and future directions will be discussed.

2.3 Methods

Search Strategy

The literature search followed PRISMA guidelines for systematic reviews and meta-analysis (Moher et al., 2009). Articles were retrieved through a systematic search of electronic peer-review literature across three databases: the U.S. National Library of Medicine's PubMed electronic database, the American Psychological Association's PsycINFO electronic database, and the Institute for Scientific Information's Web of Science electronic database. All databases were searched for articles published between January 1, 1998 and August 31, 2018. A 20-year timeframe was selected to overlap intentionally with the review published by Bohnert and

colleagues (2010), and to capture new, relevant studies on this topic and to expand to include literature addressing SIB.

Each database had a slightly different search structure. To accommodate varying search parameters, terms were coupled with relevant MeSH/thesaurus terms and truncated, with spelling variations as appropriate. A combination of the following terms “self-harm,” “self- injury,” “deliberate self-harm,” “self-directed violence,” “self-injurious behavior,” “non-suicidal self-harm,” “suicide,” “opioid abuse,” “opioid misuse,” “heroin abuse,” “narcotics abuse,” “opiate abuse,” “opiate misuse,” “opiate use disorder,” and “opioid use disorder” were used within the search parameters for article retrieval.

Studies were limited to research articles published in peer-reviewed journals available in English. The search results were imported into a bibliographic software program (EndNote X9), and duplicated articles were removed. Articles were excluded if they: (1) failed to provide new data (e.g., review articles), (2) data were limited to case reports or only descriptive in nature, (3) their sample was limited to children (i.e., the sample age cutoff was <18 years), (4) their sample excluded persons who used opioids or had a sub-group of participants with opioid use, abuse, or OUD (i.e., clustered substances of abuse together), (5) they did not examine SIB and/or suicide and opioid use/OD, (6) the study examined both SIB and/or suicide and opioid use/OD but did not test for an association between these outcomes (i.e., did not provide data on outcomes relative to one another beyond prevalence), and/or (7) the study was conducted using toxicology or post-mortem data only. Titles and abstracts were independently screened, and then full texts were reviewed to identify eligible studies. Reference lists from eligible research articles were searched for further studies that might be included in the final review. Any disagreements in article inclusion were resolved by discussion or between the co-authors.

Quality Assessment

The quality of studies was examined using the National Heart, Lung, and Blood Institute (NHLBI) quality assessment tool (2014). This tool was chosen because it evaluates quality based on study design. The tool employs one check list tailored for observational cohort and cross-sectional studies and another checklist for case-control studies. Both checklists were developed to address internal validity (i.e., risk of bias) in an equivalent manner. Each checklist item was rated as “yes,” “no,” “not applicable (NA),” “cannot determine (CD),” or “not reported (NR).” These items then inform an overall quality rating for each study as “good,” “fair,” or “poor.”

2.4 Results

The PubMed search resulted in 672 articles, the PsycINFO search identified 970 articles, and the Web of Science search yielded 972 articles. After deletion of duplicate articles, a total of 1,631 unique articles remained. Following an initial article inspection (i.e. title and keywords), 143 abstracts were reviewed and a total of 47 articles remained that were relevant to this systematic review (Figure 2.1).

Twenty-six of the 47 studies examined more than one outcome. Ten studies examined overdose and suicide attempt (Best et al., 2000; Bradvik et al., 2007; Conner et al., 2007; Darke & Ross, 2001; Heale et al., 2003; Neale, 2000; Ross et al., 2005; Rossow & Lauritzen, 1999; Ravndal & Vaglum, 1999; Vingoe et al., 1999), one additional study examined overdose with SIB and suicide attempts (de los Cabos et al., 2007), and another included all drug poisonings (Olsson et al., 2016). Five studies reported on suicidal ideation and suicide attempt (Cheek et al., 2016; Kazour et al., 2016; Kuramoto et al., 2012; Maloney et al., 2009; Wines et al., 2004). Four studies assessed suicide planning, in addition to suicidal ideation and suicide attempt (Ashrafioun et al., 2017; Darke et al., 2015; Havens et al., 2004; Marchand et al., 2017). Five

studies examined SIB and suicide attempt (Baykara & Alban, 2018; Darke et al., 2010; Darke et al., 2012; Harned et al., 2006; Maloney et al., 2010). One study examined suicide attempt, overall suicide risk, fatal accidental intoxication, and injury/intoxication of undetermined intent (Olsson et al., 2016) (Table 2.1).

Quality of Studies

Forty-six studies in the present review used quantitative methods that could be evaluated using the NHLBI quality assessment tool. One study employed a mixed methods design and primarily reported qualitative data (Neale, 2000). Hence it was not assessed for quality. Of the studies assessed using the NHLBI quality tool, 17.4% had an overall rating of poor, 32.6% were rated as fair, and 50.0% good. Forty-two of the studies relied on self-report measures, 66.7% of which did not use validated measure for suicide, overdose, or SIB outcomes. Recall bias was the predominant research limitation across all studies included in the review. Seventy-two percent of studies use statistical modeling to address potential confounding by controlling for known covariates associated with the outcome of interest. However, only 21.7% (n=10) of the studies provided calculations for sample or effect sizes (Table 2.2).

Themes

Patterns of Substance Use

Twenty-six studies reported on patterns of substance abuse associated with SIB and suicidal behaviors. Four studies analyzed the relationship between SIB and OUD. Of these studies, three found that SIB was associated with increased likelihood of having OUD (Darke et al., 2010, Lavania et al., 2012, & Maloney et al., 2010). Two of these studies also found an increased rate of AUD and OUD (Darke et al., 2010 and Maloney et al., 2010). One study found that patients with a dually diagnosed AUD and OUD were more likely to report SIB. However, they were less

likely to report suicide attempts than participants with other SUDs (Darke et al., 2010). Five studies assessed the relationship between suicidal ideation and OUD. Three studies found that OUD was associated with a statistically increased likelihood of suicidal ideation (Ashrafioun et al., 2017, Kuramoto et al., 2012, & Jin et al., 2013), specifically among samples with individuals who predominantly used heroin.

Eighteen examined suicide attempts or risk and OUD. The most common overlapping risk factor between OUD and suicide attempt(s)/risk of suicide was poly-drug use (Darke & Ross, 2001; Darke et al., 2004; Darke et al., 2015; Hakansson et al., 2010; Harned et al., 2006; Havens et al., 2004; Rossow & Lauritzen, 1999). Additionally, four studies found the likelihood of recent heroin overdose (Darke et al., 2004), history of overdose (Hankansson et al., 2010), and history of a suicide attempt increased with the number of previously reported heroin overdoses (Bradvik et al., 2007; Rossow & Lauritzen, 1999).

Psychological Factors/Diagnoses

Twenty-four studies reported specific psychological symptom and /or psychiatric diagnoses associated with suicidal behaviors, SIB, and OUD. Fifty-four percent of studies reported an association with suicidal behaviors and/or SIB and major depressive disorder or depressive episodes. Two studies found that study participants who met the criteria for both OUD and SIB also were more likely to have met the criteria for a depressive episode (Maloney et al., 2010) and had significantly higher scores on the Beck Depression Scale than patients without SIB (Baykara & Alban, 2018). In addition, one study found that treatment with antidepressant medication was a significant predictor of suicide attempt among those with OUD (Roy, 2010). Two studies found that participants with OUD, suicide attempts, and SIB were more likely to have been diagnosed with borderline personality disorder (Darke et al., 2004;

Maloney et al., 2010). Another frequently reported psychiatric diagnosis was posttraumatic stress disorder (PTSD). Two studies found that a recent suicide attempt among participants with OUD was associated with a diagnosis of PTSD (Darke et al., 2004; Darke et al., 2015). One of these studies found PTSD to be significantly associated with SIB among those with OUD (Darke et al., 2004). Three additional studies reported overall increased reporting of overall history of mental health problems: one specifically with regards to intentional overdose (Neale, 2000), another reported higher odds of suicidal ideation (Marchand et al., 2017), and a third found that patients with a history of both a suicide attempt and overdose had increased psychiatric problems—specifically anxiety, depression, and suicidal ideation (Rossow & Lauritzen, 1999).

Family History

Six studies investigated the association between family history of suicidal behaviors and suicidal behaviors, SIB, and OUD. Two studies found that people with OUD were more likely to report a history of suicide attempts among family members (Dragisic et al., 2015; & Roy, 2002). One more found that family history of suicidal behavior predicted a suicide attempt in people with OUD (Roy, 2010). Additionally, another study found that maternal alcohol use or psychiatric problems and paternal alcohol problems were significantly associated with a suicide attempt in patients with OUD (Hakansson et al., 2010).

Role of Gender

Fifteen studies investigated the role of gender and suicidal behaviors or SIB and OUD. Three studies found that females with OUD were significantly more likely to report a history of SIB than males (Darke et al., 2010; Darke et al., 2012; Maloney et al., 2010). Seven reported an association between gender and a suicide attempt among participants with OUD. Similar to the studies that examined this relationship to SIB, females with OUD were significantly more likely

to have a history of a suicide attempt(s) than males (Bohnert et al., 2017; Hakansson et al., 2010; Kazour et al., 2016). Females with OUD who attempted suicide also were more likely to be younger than those with no such history (Dark et al., 2012; Roy 2012), attempt suicide more frequently than males (Darke et al., 2001; Darke et al., 2015; Maloney et al., 2007; Tremereau et al., 2005), and use less lethal methods (Icick et al., 2017). Two studies found that females were more likely than males to have attempted suicide prior to the onset of heroin use (Darke & Ross, 2001; Maloney et al., 2007), with one finding that males were more likely than females to be using heroin at the time of their most recent suicide attempt (Darke & Ross, 2001).

Sociodemographic Factors

Ten studies examined sociodemographic characteristics associated with the relationship between suicidal behaviors, SIB, and OUD. Four studies investigated age at time of suicide attempt and/or SIB. Overall, younger OUD patients were more likely than older counterparts to have attempted suicide (Baykara & Alban, 2018; Roy 2010). Consistent with previous research, OUD patients engaged in SIB at a significantly younger than their age of a first suicide attempt (Darke et al., 2012), primarily beginning in adolescence (Maloney et al., 2010). Conversely, another study reported that risk of suicide attempt was associated with older age among patients with OUD (Hakansson et al., 2010). Two studies found that suicidal ideation was significantly more common among OUD patients who lived alone (Darke et al., 2015; Maremmani et al., 2007). Similarly, overdoses were reported more frequently among people who were homeless, had only drug-using friends, or no friends at all (Rossow & Lauritzen, 1999). Marital status, specifically being unmarried or divorced was also significantly associated with an increased risk of suicide attempt/suicidal ideation and OUD (Darke et al., 2015; Dragisic et al., 2015; Jin et al., 2013). Additionally, two of the studies found that participants with OUD, who more frequently

reported suicidal ideation and suicide attempts, were significantly more likely than those who reported less frequency to be unemployed (Darke et al., 2015; Maremanni et al., 2007).

Childhood and Adulthood Life Events

Eleven studies evaluated the contribution of both childhood and adult life events and their association with suicidal behaviors and SIB among patients with OUD. Participants with OUD who experienced childhood maltreatment/trauma (i.e. emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect) were more likely to report a history of suicide attempt(s) (Kalyoncu et al., 2007; Maloney et al., 2007; Maloney et al., 2010; Roy 2002). One study reported that for each unit increase in the childhood emotional neglect score, the adjusted odds of suicidal ideation increased by nine percent (Marchand et al., 2017). Participants with OUD and a self-reported history of SIB were also more likely to report every subtype of childhood maltreatment, particularly sexual abuse and neglect (Maloney et al., 2007). Individuals who reported experiencing a violent physical assault, before age sixteen were significantly more likely to self-report a history of SIB and a suicide attempt (Darke et al., 2012). Furthermore, participants with OUD and prior sexual assault were more likely to report severe suicidal ideation (Gilmore et al., 2008). History of emotional, physical, and sexual abuse was also positively and independently associated with a history of attempted suicide (Hakansson et al., 2010). In adulthood, the number of stressful or traumatic life events was significantly associated with that outcome (Chen et al., 2009; Marchand et al., 2017). One study of young IDUs found that the odds of a suicide attempt increased by 22% with each violent exposure reported (Havens et al., 2004). Similarly, the number of stressful life events experienced by a person was positively associated with self-reported SIB (Lavania et al., 2012).

Triggers for Behavior and Methods of Suicide Attempt

Eight studies reported on behaviors associated with methods of suicide attempts and/or SIB or triggers for engaging in those behaviors. The most commonly reported method of attempted suicide was overdose using non-opioid pills (Conner et al., 2007; Maloney et al., 2007; Vingoe et al., 1999). In the two studies that did report opioids as the primary method of suicide attempt, the sample was predominately heroin users who attempted suicide via heroin overdose (Kazour et al., 2016; Neale, 2000). The two most commonly reported triggers of attempted suicide were a conflict or dissolution in the primary relationship and bereavement (Darke & Ross, 2001; Heale et al., 2003).

2.5 Discussion

Main Findings

This systematic review included 47 studies that examined the relationship between overdose, SIB, suicidal ideation, and suicide attempts among patients with OUD. To date, four review articles have reviewed the literature examining the association between substance use disorders (SUDs) and suicide (Bohnert et al., 2010; Colledge et al., 2019; Harris & Barraclough, 1997; Wilcox et al., 2004). To varying degrees, each has expanded upon this connection; however, until Colledge and colleagues (2019), no review has systematically investigated precursors of suicide and SUDs or at a specific SUD (other than alcohol use disorder) and risk factors highly correlated with suicide. Understanding these precursors of suicidal behavior and the overlapping risk factors between OUD and SIB are key in examining risks for potentially fatal behaviors.

In 2018, individuals with any mental health diagnosis are substantially more likely to misuse opioids in the past year than individuals without any comorbid mental health diagnosis (SAMSHA, 2019). According to the 2018 National Survey of Drug Use and Health, adults with a

diagnosis of any mental illness were 9.2% more likely to have past year opioid misuse and adults with a serious mental illness were 14.6% more likely to have past year opioid misuse; this is compared to the 2.6% of the US population over 18 years old with past year opioid misuse and no co-occurring mental health diagnosis (SAMSHA, 2019). Consistent with these findings, fifty-one percent of the studies in this review reported associations between psychiatric diagnoses, SIB, and suicidality among individuals with OUD. Studies consistently reported that depression scores are consistently higher, or history of major depressive episode is present among individuals with OUD for all outcomes of interest (i.e. SIB, suicidal ideation, suicide attempt). Commonly associated co-occurring psychiatric diagnoses reported for patients with SIB, suicidal ideation, and attempt included anxiety, PTSD, and borderline personality disorder. Collectively these findings support greater psychiatric comorbidity with SIB and suicide attempt among those with OUD.

Overall, females were more likely to report a history of SIB, suicidal ideation, and suicide attempt, which is similar to that found in the general population (Bohnert et al., 2017; Hakansson et al., 2010; Kazour et al., 2016; Olfson et al., 2017). Females were also more likely to make multiple attempts (Darke et al., 2012; Darke et al., 2015; Treméau et al., 2005). Females were also more likely to report recent episodes of SIB (past 12-months) despite older age compared to males (Darke et al., 2012), though age of onset of SIB consistently occurred in adolescents and before the first suicide attempt was made for both males and females (Darke et al., 2012; Maloney et al., 2010). One study reported that females with OUD were 2-3x more likely to die by suicide than males (Bohnert et al., 2017). This is contrary to statistics reported among the general population in the US where men are 3.54 times more likely to die by suicide than women (Kochanek et al., 2017). Specifically, with regards to heroin use, it was noted the

females were more likely to attempt suicide prior to the onset of heroin use compared to males (Maloney et al., 2007), with one study reporting that females were 18 times more likely to attempt suicide before initiation of heroin use compared to males (Darke & Ross, 2001). These studies suggest that females with OUD are not only at higher risk of suicide attempt, but at higher risk for making multiple attempts when compared to males irrespective of transition to heroin use. This could in part be due to co-occurring risks for other psychiatric diagnoses; however, given higher reporting rates of SIB among females suicide risk remains a significantly greater threat among females.

Nationally representative samples have found that adults in the US reporting recent suicide attempts are more likely to be female, white, unemployed, and have a family history of suicide attempt irrespective of any other comorbid health diagnoses (Olfson et al., 2017). Additionally, being widowed, divorced, or unmarried was also significantly associated with suicide attempt independent of mental health or SUD diagnosis (Olfson et al., 2017). Findings from several studies reporting on demographic characteristics in combination with suicidality among individuals with OUD are consistent with those reported in the general population. Specifically, being unmarried (Dragisic et al., 2015; Jin et al., 2013; Maremmani et al., 2007), unemployed (Darke et al., 2015; Jin et al., 2013), living alone (Darke et al., 2015; Maremmani et al., 2007) and homeless (Rossow & Lauritzen, 1999) were all significantly correlated with increased history of suicidal ideation. Likewise, one study included in this review also reported that irrespective of diagnosis of OUD patients with history of suicide attempt were more likely to have a family member with a history of suicide attempt (Maloney et al., 2007) which coincides with reports from research done in general samples. Although these factors were not consistently examined across studies included in the review, several consistencies are present in demographic

characteristics associated with suicidality independent of OUD diagnosis. This overlap in employment status, marital status, and family history can potentially help identify global characteristics of suicidality that remain constant irrespective of diagnosis of OUD.

An important finding from this review is the role of treatment. Although few studies measured the impact of treatment with respect to the outcomes of interest (i.e. SIB, suicidal ideation, and/or suicide attempt); several studies did provide some key points. Patients with OUD in treatment settings who reported suicide attempts generally tended to be in overall poorer health or have chronic medical conditions (Darke et al., 2015; Hakansson et al., 2010; Roy, 2010). Likewise, previous number of times detoxed was positively associated with number of suicide attempts (Kazour et al., 2016). Similarly, patients with deliberate overdoses were more likely to be in treatment at the time of overdose (Best et al., 2000).

Prior to onset of suicide attempt many individuals with OUD reported significant life experiences. A study by Darke and Ross (2001) found that 82% of patients with OUD reported that a major life event had preceded their most recent suicide attempt. Research has found that the most commonly reported life events prior to suicide attempt among clients with OUD was the breakdown of a primary relationship or dissolution of a primary relationship (Darke & Ross, 2001; Heale et al. 2003), bereavement (Darke & Ross, 2001; Heale et al. 2003), and impending incarceration (Darke & Ross, 2001). This highlights the complexity of the social dynamics; particularly, as mentioned earlier, that living alone, and poor social functioning are also associated with increased risk for both suicidal ideation and suicide attempt. Maintaining social relationships and having support is key in attaining positive outcomes.

While a majority of studies utilized participants who primarily used heroin, interestingly, heroin overdose was not a common method of suicide attempt (Vingoe et al., 1999). Likewise,

even though heroin was most frequently reported in overdoses, it was significantly more likely to be used in an accidental overdose than a deliberate overdose (Maloney et al., 2007; Neale, 2000). This is unclear whether this is due to lack of validated instruments to differentiate intentionality of overdose or if this is a result of assessment bias. However, the most frequently cited methods of suicide attempt were overdose of non-opioid pills (Conner et al., 2007; Maloney et al., 2007), followed by cutting and hanging (Conner et al., 2007). Overall, guns were the least likely to be used to attempt suicide among individuals with OUD contrary to statistics normally reported among suicide attempts in US population. Although a research done among veterans suggests that firearms are the most common method used in suicide attempt, firearms were more commonly used among individuals without any SUD diagnosis (Bohnert et al., 2017). This same study found that the most common methodology for suicide attempt among individuals with any current SUD diagnosis was poisoning (Bohnert et al., 2017). In 2017, firearms were the most common method of death by suicide accounting for 50.6% of all suicide deaths (Kochanek et al., 2017); whereas poisoning accounted for 13.9% of suicide deaths in the US (Kochanek et al., 2017).

Overlap in SIB and suicide methodology are of importance because SIB is associated with increased risk of suicide attempt. Previous research has found that cutting is a common form of both SIB and suicide among individuals with OUD. One study found that 25% of treatment seeking OUD patients primary form of SIB was cutting (de los Cobos et al., 2007). A second study found that 74% of study participants with OUD engaged in cutting as their predominant form of SIB (Oyefeso et al., 2008). Additionally, three studies found cutting to be in the top three most common forms of suicide attempt among individuals with OUD (Conner et al., 2007; Kazour et al., 2016; Neale, 2000). Although it is unknown if SIB is systematically

assessed in OUD treatment, this overlap provides insight for means reduction and a potential point for early intervention.

Implications

A total of two studies reported an overall increased risk of suicide specifically associated with OUD. One of these studies found that inpatients with heroin use had a 16-fold increase in standardized mortality ratio due to suicide compared to the general population (Pan et al., 2014). A second, reported 1.76 odds of death by nonviolent suicide among individuals with OUD compared to those without OUD (Ilgent et al., 2009). Two indicators of substance use severity were found to be associated with suicide attempt in this review: age of onset of opioid use and IDU. Several studies reported that an earlier onset of substance use was associated with increased risk of suicide attempt among people with OUD (Dragisic et al., 2015; Havens et al., 2004; Ickick et al., 2017; & Kazour et al., 2016). Likewise, IDUs with OUD also had an increased risk for suicide attempt (Dragisic et al., 2015; Hakansson et al., 2010; Masferrer et al., 2016). Both of these factors overlap with risk of suicide attempt and risk for potential overdose marking increased severity of substance use. Furthermore, as summarized by previous studies those who maintain relationships with only friends in the drug use community are further at risk of suicidal behaviors. The connection between these factors indicates that poor social functioning, psychiatric decline, and substance use not only correlate to suicidality but represent key factors for intervention.

Limitations

Twenty-six studies were cross section, thus temporal conclusions could not be drawn linking onset of OUD with SIB, suicidal ideation, and/or suicide attempt. Five studies included longitudinal data limiting the ability to identify true causal relationships between OUD and SIB

and/or suicidal behaviors due to lack of temporal information. Furthermore, a majority of this research was conducted among inpatient or outpatient treatment samples which limits generalizability. It is also unknown whether treatment seeking individuals have more functional impairments or experience more symptom severity than non-treatment seeking individuals. Likewise, limited studies are conducted in low-income, rural areas which may have different patterns of substance use and barriers to treatment further contributing to the variability in estimation of SIB and suicide among people with OUD. Only one study in this review examined overdose and SIB indicating a need for further investigation of this relationship in future research, especially given the strong connection between SIB and future risk for suicide attempt.

2.6 Conclusions

Overall, the relationship between self-injurious behaviors, suicidal ideation, suicide planning, and suicide attempt has been investigated to varying degrees throughout the published literature. However, there is still lack of prospective longitudinal data providing adequate temporal information between onset of OUD and SIB and/or suicide outcomes. Furthermore, the relationship between SIB, suicidality, and overdose still remains under researched. In general, patients with OUD who are at highest risk of suicide attempt and SIB tend to have more severe psychiatric profiles, increased rates of poly-drug use, tend to be female, experience significant life stressors, and childhood maltreatment. These findings provide crucial points for treatment paradigms including points for intervention and increased services to address the complex nature overlapping SIB, suicidality, and OUD.

2.7 Acknowledgements

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Figure 2.1: Prisma Flow Diagram

Table 2.1 Study Characteristics							
Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Ashrafioun et al. (2017)/USA	Cross Sectional Study	41,053 (365)	2014 National Survey on Drug Use and Health (NSDUH).		Prescription opioids, alcohol, hallucinogens, inhalants, stimulants, marijuana, sedatives, tranquilizers	Suicide ideation, suicide planning, SAs (past 12- months)	<ul style="list-style-type: none"> Adjusted models found that prescription opioid misuse was significantly associated with SI for each frequency category. Individuals who reported an average of weekly or more use had a significant association with suicidal planning and attempts.
Baykara & Alban (2018)/Turkey	Cross Sectional Study	100 (100)	Inpatients between 18-65 yrs old diagnosed with OUD.	<ul style="list-style-type: none"> DSM-V 	Opioids	Self-Injurious Behavior (SIB), SAs (4-6 weeks after last use of substance; lifetime history)	<ul style="list-style-type: none"> Patients with history of OUD & SIB had higher subscale scores for passive aggression, somatization, and immature factor. Beck depression and Beck anxiety inventory scores were higher for patients with both OUD and history of SA. Logistic regression analysis found that passive aggression subscale scores and younger age were related to SIB. History of SA was associated with younger age, suppression, dissociation, somatization, higher Beck anxiety inventory, low idealization, projection, devaluation, splitting, and rationalization scores.
Best et al. (2000)/UK	Cross Sectional Study	200 (200)	Patients in methadone treatment in Edinburgh and south London.		Methadone	Accidental OD; deliberate OD (lifetime)	<ul style="list-style-type: none"> Patients with a deliberate OD were more likely to currently be taking diazepam, have higher depression scores, hopelessness scores, more lifetime ODs, & OD more recently. The deliberate OD group was more likely to be in treatment at the time of OD and more frequently reported SI in the past-month than individuals who reported accidental OD.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Bohnert et al. (2017)/USA	Cross Sectional Study	4,836,086 (37,908)	Veteran Health Association (VHA) users from the 2005 fiscal year and alive at the beginning of the 2006 fiscal year.	<ul style="list-style-type: none"> National Death Index (NDI) & ICD-10 (suicide mortality) VHA National Patient Care Database (NPCD) and ICD-9 CM (SUDs) 	Any SUD, AUD, cocaine use disorder, cannabis use disorder, OUD, amphetamine use disorder, sedative/hypnotic use disorder	Suicide Mortality (2006-2011)	<ul style="list-style-type: none"> 9,087 individuals died by suicide (34.7 per 100,00). For men, OUD was the third largest risk for suicide For women, OUD was the second largest risk for suicide Adjusting for mental health factors, the only substance specific diagnoses to remain statistically significant were alcohol and OUD for women; for men, any SUD, and all specific SUDs, remained significant risk factors for suicide. Post-hoc analyses found a 2-3x greater suicide rate for women than men; especially with respect to alcohol use disorder, cocaine use disorder, OUD, or a general SUD diagnosis.
Borges et al. (2000)/USA	Cross Sectional Study	8,098 (NR)	1990-1992 National Comorbidity Survey (NCS), individuals aged 15-54.	<ul style="list-style-type: none"> CIDI DSM-III-R 	Alcohol, analgesics, sedatives, tranquilizers, stimulants, marijuana, cocaine, inhalants, hallucinogens, heroin	SA (lifetime prevalence)	<ul style="list-style-type: none"> Heroin users were 3.5 times more likely to attempt suicide than non-users. Current heroin users had an OR of 6.1 associated with first-time SA
Bradvik et al. (2007)/ Sweden	Cross Sectional Study	149 (149)	Heroin users recruited from the needle exchange program and the Addiction Cent fall of 2003.		Heroin, alcohol, benzodiazepines, cannabis, central stimulants	Intentional OD, unintentional OD, SAs	<ul style="list-style-type: none"> Likelihood of reporting a SA increased with the number of heroin ODs. Of the 51 persons where heroin was not used as a means of SA, 18 (29%) made multiple attempts. When accounting for depressed mood and other substances of use (alcohol, benzodiazepines, cannabis, and central stimulants) neither showed a statistically significant impact on SA.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Cheek et al. (2016)/USA	Cross Sectional Study	10,203 (NR)	Adults 18 yrs + with lifetime history of major depression and IDU.	<ul style="list-style-type: none"> 2008- 2013 National Survey on Drug Use and Health (NSDUH) DSM-IV 	Heroin, cocaine, stimulants	Substance use (past 12- months); SI, suicide plan(s), SA(s) (2008- 2013; 6 years)	<ul style="list-style-type: none"> IDUs are more likely to have increased depressive symptoms, SI, plan, and attempt(s). Compared non-heroin IDUs, those who inject heroin are less likely to attempt suicide (OR: 0.92); however, they are more likely to have SI and develop a suicide plan (not statistically significant).
Chen et al. (2009)/Taiwan	Cross Sectional Study	488 (488)	Heroin-dependent patients recruited from a methadone program enrolled between Sept. 2006-Jan.2008.	<ul style="list-style-type: none"> Clinical Interview ("Have you attempted suicide in the preceding one-month? Have you attempted suicide in your lifetime?") 	Heroin, alcohol	SA(s) (previous month and lifetime)	<ul style="list-style-type: none"> 10.9% of patients had a recent SA (past 30 days) and 17.8% reported a lifetime SA. Severity of heroin dependence, depression score, levels of family support, and number of stressful life events, were associated with recent SA(s). Multivariable analyses found that severity of heroin dependence and needle sharing were significantly associated with recent SA.
Conner et al. (2007)/USA	Cohort Study	131 (131)	Patients from a methadone program at an urban university hospital in upstate New York.		Methadone, history of OUD	SA(s) (lifetime and past year), unintentional OD (lifetime and past year)	<ul style="list-style-type: none"> 37.4% (n=49) of patients reported lifetime history of SA(s). Of those with a lifetime history of SA, 33 (67.4%) had 2+ attempts and 7 (14.3%) made an attempt in the last year. Most common methods of SA were intentional OD (29, 59.2%), cutting (9, 18.4%), and hanging (5, 10.2%). Multivariable analysis found that higher belonging score (i.e. greater perceived belonging) was associated with decreased probability of history of SA.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Darke & Ross (2001)/Australia	Cross Sectional Study	223 (223)	Methadone patients recruited from February- July 2000.		Heroin, polydrug use	Non-fatal heroin OD, SA(s) (lifetime)	<ul style="list-style-type: none"> • 40% of participants reported at least one SA in their lifetime. • Males were significantly more likely to be using heroin at the time of their most recent SA compared to females. • 8% of participants were receiving psychiatric or psychological treatment at the time of their most recent SA. • 31% of participants had a history of both an OD (intentional or unintentional) and SA(s). • Multiple logistic regression analysis found that being female, parental absence during childhood, earlier age of first intoxication, and higher levels of polydrug use were associated with history of SA.
Darke et al. (2004)/Australia	Cross Sectional Study	1,230 (1,230)	Current heroin users and patients recruited from different treatment modalities.	<ul style="list-style-type: none"> • DSM-IV (heroin dependence) 	Heroin, alcohol, benzodiazepines, total number of drug classes used	Lifetime and recent attempted suicide	<ul style="list-style-type: none"> • 34% of patients had a history of SA; females are significantly more likely than males to report an attempt (44% vs 28%). • Recurrent SI was reported by 23% of patients and 15% reported having a current plan. • Residential rehabilitation patients had a significantly higher level of recurrent SI compared to other groups. • Recent SA was associated with lifetime and recent polydrug use, recent heroin OD, and benzodiazepine use. • Recent history of SA was also associated with current major depression, current SI, diagnosis of borderline personality disorder, and diagnosis of PTSD.
Author	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary

(Pub year)/ Country							
Darke et al. (2010) /Australia	Cross Sectional Study	400 (300)	Treatment and non-treatment seeking drug users.		Alcohol, opioids, psychostimulants , cannabis	SA(s), SIB, (lifetime, past 12-months)	<ul style="list-style-type: none"> • One third of the sample reported a lifetime history of SIB, 20% had engaged in SIB on more than one occasion, and 10% had SIB in the past 12-months. • Individuals with alcohol and opioid use were significantly more likely to have a history of SIB. • Females, PTSD diagnosis, younger age of first intoxication, and history of SA were significantly associated with SIB. • About 33% of the sample reported a history of SA, 17% reported multiple SAs, and 15% made an attempt in the past 12-months. • 23% of opioid users reported a history of SA.
Darke et al. (2012)/Australia	Cross Sectional Study	191 (50)	Patients receiving treatment services between January 2009-Januray 2010.	• Opiate Treatment Index	Alcohol, opioids, psychostimulants , cannabis	SA(s), SIB, (lifetime, past 12-months)	<ul style="list-style-type: none"> • Females were more likely than males to have engaged in SIB in the preceding year, attempted suicide, to have multiple attempts, have an attempt in the 12-months, and be younger at their first SA. • 43% of patients had either engaged in SIB and/or attempted suicide, 18% reported both. • Individuals who experienced physical assault before age 16 were significantly more likely to have engaged in SIB and have a history of SA compared to those who experienced an assault after age sixteen. • There were no differences in weekly psychostimulant users, weekly heroin users, or combination users in either lifetime or 12-month histories of self-harm.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Darke et al. (2015)/Australia	Cohort Study	615 (413)	Australian Treatment Outcomes Study (ATOS), 11-year follow-up study.	<ul style="list-style-type: none"> • Composite International Diagnostic Interview 2.1 (CIDI) • Opiate Treatment Index 	Heroin, nicotine, alcohol, cannabis, benzodiazepines, prescription opioids	SA(s) (lifetime, 12-months, 24-months, 36-months), current SI, suicidal plan(s)	<ul style="list-style-type: none"> • 34.7% of participants used heroin in the 12-months prior to follow-up, 24.8% used in the month prior, and 9.7% reported daily heroin use. • 42.2% of ATOS participants reported ever having made a SA and 18.6% reported making multiple attempts at 11-year follow-up. • Participants that reported a recent SA (12 months prior to follow-up), having a current plan, and/or SI were more likely to live alone, be unemployed, meet criteria for Major Depression and PTSD, be in poorer health, and report more extensive polydrug use. • Diagnosis of Major Depression increased the odds of SA by 1.68 times, each extra drug class used increased odds by 1.39 times
de los Cobos et al. (2007)/Spain	Cross Sectional Study	164 (164)	Opioid-abstinent or hospitalized patients with OUD.	<ul style="list-style-type: none"> • Clinical evaluation conducted by psychiatrist 	Heroin	SIBs and ODs (during course of patients reported heroin dependence); history of bulimia, SA(s) (lifetime)	<ul style="list-style-type: none"> • 87.8% of the heroin-dependent patients interviewed had a history of SIB. • Most common SIB: hitting extremities (77.4%), picking scabs (52.4%), head-butting (43.3%), cutting (25%), biting (20.7%), carving signs (15.2%), scratching (14.6%), burns (14%) and pulling out hair (9.1%). • 25.6% had a history of SA(s), 59.1% had an accidental OD(s)

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Dragisic et al. (2015)/Bosnia and Herzegovina	Case-Control Study	200 (200)	Individuals recovering from OUD with and without history of SA.	<ul style="list-style-type: none"> • ICD-10 	Opioids	SA(s) (lifetime)	<ul style="list-style-type: none"> • Individuals with OUD who attempted suicide were more likely to be unmarried or divorced compared to those with OUD who have not attempted suicide. • Clients with history of SA more commonly had psychotic disorders, drug addiction, and family history of SAs. • Persons with OUD and attempted suicide also have a significantly longer history of addiction duration (i.e. substance use) and IDU.
Ghaffari-Nejad et al. (2011)/Iran	Case-Control Study	70 (70)	Hospitalized patients for SUD.	<ul style="list-style-type: none"> • DSM-V • California Suicide Risk Assessment Questionnaire 	Opioids	Suicide Risk	<ul style="list-style-type: none"> • Cases were patients with OUD; controls were peers without OUD • Suicide risk wasn't statistically significant between the case and control group. • Individuals with OUD had a significantly higher depression scores than controls
Gilmore et al. (2018)/USA	Cross Sectional Study	60 (24)	Patients who received sexual assault treatment in the ED.	<ul style="list-style-type: none"> • Self-report • Patient Health Questionnaire-9 (SI) 	Opioids	SI (past 2 weeks)	<ul style="list-style-type: none"> • Linear regression analysis found a significant association between prescription opioid use and SI. • Those with a prior sexual assault and OUD reported more severe SI
Hakansson et al. (2010)/Sweden	Cross Sectional Study	6,836 (2,346)	Entrants in the Swedish criminal justice system databased between 2001 and August 2006.	<ul style="list-style-type: none"> • Addiction Severity Index 	Alcohol, heroin, methadone, opioids, tranquilizers, amphetamines, cocaine, cannabis, solvents, hallucinogens	SA(s) (lifetime)	<ul style="list-style-type: none"> • 21% (n=1,453) of persons reported a SA. • Logistic regression found: older age, female gender, history of binge drinking, IDU, delirium tremens, OD, chronic medical problems, maternal alcohol or psychiatric problems, paternal alcohol problems, history of emotional, physical, and sexual abuse, history of depression, anxiety, hallucinations, eating disorders, and difficulty controlling violent behavior

							were independently associated with history of SA.
Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Harned et al. (2006)/USA	Cross Sectional Study	65 (9)	A sample of outpatient women with PTSD and SUD.	<ul style="list-style-type: none"> • DSM-IV • Traumatic History Questionnaire • Suicidal Behaviors Questionnaire, 13-item revised version 	Alcohol, cocaine, cannabis, opioids, sedative-hypnotics, amphetamines, hallucinogens	Self-harm ideation, self-harm, SI, SA(s) (past three months)	<ul style="list-style-type: none"> • 13.8% engaged in SIB, 10.8% attempted suicide, and 7.7% had both SIB and attempted suicide (n=21 total). • Of these 21 women, 61.9% reported drinking alcohol or using drugs immediately before or during the SA/self-harm episode. • Recent history of SIB and/or attempted suicide were more likely to have diagnoses of AUD and polysubstance dependence and less likely to meet criteria OUD.
Havens et al. (2004)/USA	Cross Sectional Study	2,219 (NR)	IDUs 15-30 yrs old recruited from 1997 to 1999.		Heroin, cocaine, marijuana, alcohol	SI, SA(s), and suicide plan(s)(6-months)	<ul style="list-style-type: none"> • 68.9% of participants were using heroin daily. • In the past 6-months, receiving money for sex was associated with recent SA(s) • Daily heroin, speedball, marijuana, or IDU was not associated with recent SA(s) • Polydrug use was significantly associate with recent SA
Heale et al. (2003)/Australia	Cross Sectional Study	256 (256)	Heroin OD survivors resuscitated by paramedics between July 1999-May 2001.		Heroin, benzodiazepines, alcohol	SA(s), intentional OD (lifetime, past 6-months)	<ul style="list-style-type: none"> • 17% reported an intentional OD (n=42); 67% reporting at least one in the past 6-months. • Primary reasons for intentional OD included: relationship breakdown (3/9), family problems (2/9), and treatment discharge • Survivors of recent intentional ODs reported using a statistically significantly higher mean amount of heroin

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Leick et al. (2017)/France	Cross Sectional Study	433 (217)	Treatment seeking outpatients recruited between April 2008 & April 2016.	<ul style="list-style-type: none"> • DSM-IV-TR • Diagnostic Interview for Genetic Studies v4.0, "suicide section" (DIGS 4.0) 	Opioids, nicotine, cocaine, alcohol, sedatives, cannabis, multiple SUDs	SA(s) (lifetime)	<ul style="list-style-type: none"> • Patients reporting serious and non-serious SAs had earlier onset of OUD and tobacco smoking. • Women were less likely to have a serious SA when they reported any history of MOUD. • Women with current mood disorder and OUD were less likely to present with a serious SA.
Ilgen et al. (2009)/USA	Cross Sectional Study	488 (488)	Individuals, 18-63 yrs old receiving SUD treatment.	<ul style="list-style-type: none"> • National Death Index (NDI) • ICD-10 • ICD-9-CM 	Alcohol, cocaine, cannabis, opioids, amphetamine, barbiturate, multiple substances	Violent suicide, nonviolent suicide (FY 2002-2006)	<ul style="list-style-type: none"> • OUD and polysubstance use were associated with greater likelihood of nonviolent suicide. • Logistic regression analyses found that among those who died by suicide, cocaine, OUD, and multiple SUDs were all associated with greater risk of nonviolent compared to violent suicide. • Patients with OUD who died by suicide have an odds ratio of 0.76 of using violent means compared to an odds ratio of 1.67 for nonviolent means.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Jin et al. (2013)/China	Case-Control Study	607 (406)	HIV+ (n=204) and HIV- (n=202) patients with history of heroin IDU in methadone treatment.	<ul style="list-style-type: none"> Chinese version of the Composite International Diagnostic Interview (CIDI v3.0) Item 9 of the Beck Depression Inventory-II 	Heroin, alcohol	SI (past 2 weeks)	<ul style="list-style-type: none"> Factors significantly associated with current SI included being unmarried or unemployed, having a lifetime (past) history of major depression, or lifetime alcohol use disorder or heroin use disorder. Among treated IDUs (n = 407), past history of major depression, or past AUD, and higher BDI-II total score were associated with current suicidality Longer duration of IDU and poor social support were also significantly associated with current suicidality Multivariable predictors of suicidality were HIV-related stress, social support, and prior history of major depression. Suicidality among HIV- treated IDUs, was best predicted by prior history of major depressive disorder and prior history of AUD. Prior major depression increased risk by 6-fold and past AUD increased risk by 3-fold.
Kalyoncu et al. (2007)/Turkey	Cross Sectional Study	108 (108)	Patients 18-24 yrs old receiving inpatient treatment for OUD.	<ul style="list-style-type: none"> DSM-IV 	Alcohol, heroin, overall drug use	SA(s) (past month)	<ul style="list-style-type: none"> 37.0% (n=40) had a history of SA. Childhood trauma questionnaire scores were significantly higher among patients with a history of SA than patients without a history of SA. Patients with a SA also had a greater likelihood of meeting DSM-IV criteria for another current psychiatric disorder, specifically antisocial personality disorder.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Kazour et al. (2016)/Lebanon	Case-Control Study	122 (61)	Patients with OUD.	<ul style="list-style-type: none"> • DSM-IV • Beck SI Scale (BSI) 	Opioids, cocaine, cannabis, ecstasy (MDMA), LSD, amphetamines, benzodiazepines, alcohol	SA(s) (lifetime), SI (current)	<ul style="list-style-type: none"> • 37.7% (n=23) of the heroin dependent group had a personal history of SA; the most frequent method was intentional heroin OD, oral medication OD and cutting. • History of SA was associated with females, had younger age of first substance use, and OUD. • Number of SAs was significantly associated with number of previous detox admissions and number SAs among family. • Subjects with OUD, 9 had current SI. • Patients with current SI did not have higher rates of OD, but they did have significantly higher rates of intentional OD.
Kuramoto et al. (2012)/USA	Cross Sectional Study	37,933 (7,468)	2009 National Survey on Drug Use and Health (NSDUH).	<ul style="list-style-type: none"> • DSM-IV 	Non-medical prescription opioids	SI, SA(s) (past 12-months)	<ul style="list-style-type: none"> • Approximately 7% of the former nonmedical prescription opioid users (n = 310), 11% of the persistent users (n = 287), and 9% of the recent-onset users (n = 178) reported SI compared to the 3% of never users who reported ideation. • A greater proportion of persistent (17%) and recent-onset (19%) users with ideation also reported SA as compared with former and never users. • 23% of nonmedical users with past-year prescription opioid disorder reported SI • Individuals with OUD had more than threefold increased odds for reporting SI.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Lavania et al. (2012)/India	Cross Sectional Study	60 (27)	Nondepressed, male inpatients 18-60 yrs old with SUD.	<ul style="list-style-type: none"> Addiction Severity Index (ASI) ICD-10 	Opioids, alcohol, unspecified others	Self-injurious behavior (SIB) (lifetime)	<ul style="list-style-type: none"> Higher rates of OUD were found in people who reported SIB. Individuals with SIB had significantly higher rates of OUD, risk of isolation, the number of life events, anger trait and anger expression, personality disorder, number of substance use problems, and lower social function.
Maloney et al. (2009)/Australia	Case-Control Study	1,125 (726)	Individuals receiving MOUD treatment.	<ul style="list-style-type: none"> DSM-IV 	Opioids, cannabis, sedatives, stimulants, cocaine, alcohol, tobacco	SI (lifetime), persistent SI (lifetime), suicide plan (lifetime), SA(s) (lifetime, past 12- months)	<ul style="list-style-type: none"> Cases were recruited from opioid maintenance treatment. Controls were recruited from the community in the same geographic area as the treatment centers. Female cases were significantly more likely to attempt suicide prior to the onset of heroin use compared to male cases (68% vs 46%). Cases who reported a lifetime SA were significantly more likely to meet DSM-IV criteria for dependence for each drug class examined and psychiatric disorders assessed. OUD was not a significant risk factor for SAs over and above the other identified risk factors.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Maloney et al. (2010)/Australia	Case-Control Study	966 (686)	Individuals with and without OUD.	<ul style="list-style-type: none"> • DSM-IV 	Cannabis, sedatives, opioids, stimulants, cocaine, nicotine, alcohol	SA(s), Self-injurious behavior (SIB), Both SIB & SA(s) (lifetime)	<ul style="list-style-type: none"> • Female cases were significantly more likely to report a history of SIB compared to male cases. • The SIB group were significantly more likely to be female, younger, completed more than 10 years of schooling, report every childhood maltreatment subtype, meet criteria for alcohol dependence, and criteria for dependence on more lifetime drug classes. • The SIB and SA were more likely to report multiple lifetime SAs compared to those in the SA only group and had a significantly increased risk for screening positively for BPD.
Marchand et al. (2017)/Canada	Cross Sectional Study	176 (176)	Long-term opioid dependent individuals recruited between December 2011 and June 2013.	<ul style="list-style-type: none"> • Composite International Diagnostic Interview-Major Depression Module 	Opioids, illicit stimulants	SI, suicide plan(s), SA(s) (lifetime)	<ul style="list-style-type: none"> • Of those with lifetime SI (n=77), plans for suicide were reported by 62.3% (n=48), and 75.3% (n=58) reported SAs. • Each unit increase in childhood emotional neglect score and number of potentially traumatic life events, the adjusted odds of lifetime SI increased by 9% and 13%, respectively. • History of depression, anxiety, childhood emotional neglect, and the number of lifetime traumatic events were significantly associated with higher odds of SI. • For women histories of depression and anxiety remained independently associated with lifetime SI among women • For men, childhood emotional neglect and number of lifetime traumatic events were independently associated with lifetime SI.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Maremmanni et al. (2007)/Italy	Cross Sectional Study	616 (616)	Individuals with OUD requesting outpatient treatment between 1995 and 2003.	<ul style="list-style-type: none"> • DSM-IV • Drug Addiction History Rating Scale (DAH-RS) • SCL-90-item 15 (SI) 	Alcohol, opioids, CNS depressants, CNS stimulants, hallucinogens, phencyclidine, cannabis, inhalants, poly-substance use	SI (past week)	<ul style="list-style-type: none"> • Suicidal thoughts during the past week were reported by 199 patients (29.1%). • SI did not correlate with patterns of heroin use (presence of periodic self-detoxification vs. uninterrupted use), frequency of intake (daily vs. sporadic), age of first substance use or age at first treatment. • A significant association was present between duration of addiction and SI. • Odds of SI were higher for patients receiving welfare benefits (OR = 1.69), with bipolar spectrum disorder (OR = 1.42), the unemployed (OR = 1.37), those with early onset of OUD (OR = 1.36), those living alone (OR = 1.33), and those with problems in organizing.
Masferrer et al. (2016)/Spain	Cross Sectional Study	196 (36)	Bereaved SUD patients, abstinent for at least 30- days.	<ul style="list-style-type: none"> • DSM-IV-TR • Spanish version of the Risk of Suicide (RS) (Plutchick et al., 1989) (suicide risk) 	Alcohol, cocaine, heroin	Suicide Risk	<ul style="list-style-type: none"> • There was no relationship between main SUD diagnosis and risk of suicide. • Subjects who injected or nasally administered drugs had a higher risk of suicide than those who took drugs orally or smoked.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Neale (2000)/ Scotland	Mixed-Methods	77 (62)	Individuals with history of nonfatal OD.	<ul style="list-style-type: none"> Self-report/Qualitative interviews 	Heroin, alcohol, temazepam, diazepam, methadone	Intentional OD, accidental OD (lifetime)	<ul style="list-style-type: none"> 49% of the 77 participants reported suicidal thoughts or feelings (suicidal intent) prior to their current OD. A significant association was found between intentional overdosing and self-reported history of mental health problems (p, 0.001). Mean number of types of drug taken prior to OD was 2.3 for individuals with an intentional OD and 2.1 for accidental ODs. Most commonly used drugs prior to OD were heroin (46 respondents); alcohol (23 respondents); temazepam (18 respondents); diazepam (17 respondents); and methadone (16 respondents). Heroin was the most frequently used drug by both intentional (n=16) and accidental ODs (n=30) but was significantly more likely to be used in the accidental than in the intentional incidents.
Olsson et al. (2016)/Sweden	Prospective Cohort Study	6,744 (NR)	Criminal justice clients with SUDs.	<ul style="list-style-type: none"> Addiction Severity Index National Causes of Death Registry (Mortality data) ICD-10 (classification of injury/death) 	Alcohol(binge-drinking), heroin, other opioids, sedatives/tranquilizers, cocaine, amphetamines, cannabis	SA(s), suicide risk, fatal accidental intoxication, injury/intoxication of undetermined intent	<ul style="list-style-type: none"> Cox regression analyses found death from a fatal accidental OD was associated with use of heroin and cannabis; male gender was marginally significant. Cox regression analysis found that death from injury/intoxication of undetermined intent was positively associated with use of heroin, binge drinking alcohol, and previous psychiatric hospitalization. Sensitivity analysis found that death from intoxication of undetermined intent was positively associated with use of heroin and binge drinking

							alcohol; negatively associated with depression. • Death from suicide was positively associated with previous SA(s) and use of sedatives/tranquilizers was marginally significant.
Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Oyefeso et al. (2008)/England	Cohort Study	80 (80)	OUD patients receiving inpatient and outpatient treatment.	• ICD-10 • 2 items from Nonadaptive and Adaptive Personality (SIB)	Opioids	Patterns and prevalence of self-injurious behavior; predictors of self-injurious behavior (SIB) (lifetime, past 12-months)	• 69% of patients reported using heroin in the past 30-days • 39 patients endorsed SIB; lifetime SIB prevalence of 49. • 10 patients endorsed the question “Have you hurt yourself on purpose in the last 12 months?” prior year prevalence of 13%. • Reasons for SIB among opiate addicts was affect-regulation followed by self-punishment. • Most frequently reported SIB types were cutting (74%), nail biting (51%), chewing inside mouth (44%), and self-beating (36%). • The most frequently cited reasons for SIB were to cope with emotional pain (84%), to express hatred for self (68%), to express feelings of helplessness and powerlessness (63%) and to stop feelings of emptiness, numbness and depression (58%). • 76% of patients reported persistent drug and/or alcohol problems as a trigger for SIB.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Pan et al. (2014)/Taiwan	Cohort Study (with Nested Case-Control)	2,750 (2,750)	OUD inpatients admitted between 1990 and 2010.	<ul style="list-style-type: none"> • DSM-III & DSM-IV (heroin dependence) • ICD-9 & ICD-10 (suicide mortality) 	Heroin	Suicide mortality (January 1,1990- December 31, 2010)	<ul style="list-style-type: none"> • Suicides among inpatients with heroin dependence, had a 16-fold greater standardized mortality ratio (SMR=16.2) compared to the general population and the highest SMR among all specified cause of death categories. • Mean interval from the index admission to suicide was 5.8 years (SD = 4.2). • Methods include: hanging(n = 27), charcoal burning/gases other than in domestic use (n = 17),drugs/poisons (n = 14), jumping from a high place (n = 3), drowning (n = 2), cutting (n = 2), gases in domestic use (n = 1), and others (n = 3); no one used firearms. • Multivariable analysis found that SA at index admission and lifetime depressive syndrome were significantly associated with suicide risk.
Penney et al. (2012)/Canada	Case-Control Study	5,990 (NR)	Individuals seeking addiction treatment between 2001-2008 with and without past year SA.		Alcohol, amphetamines, stimulants, barbiturates, benzodiazepines, cannabis, cocaine/crack, ecstasy, glue, inhalants, hallucinogens, opioids	Hospitalized SA(s) (past 12-months)	<ul style="list-style-type: none"> • No relationship between opioids and hospitalization for SA.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Ravndal & Vaglum (1999)/Norway	Prospective Cohort Study	200 (112)	Individuals receiving treatment for SUDs between 1986-1988.		Alcohol, cannabis, psychoactive drugs, opioids, amphetamines	Prevalence of lifetime non-fatal ODs and SAs (baseline, 5-year follow- up)	<ul style="list-style-type: none"> • 43% (n=85) reported being hospitalized once or several times because of ODs. • There was a weak relationship between OD and SA(s). • Daily use of opiates and number of months in inpatient treatment were significant correlates of OD. • Clients who had spent up to 1 year altogether in inpatient treatment had 4.17 times greater chance of an OD than clients who had not been in treatment • Clients who had spent 1 year or more in inpatient treatment had 8.74 times greater chance of OD than clients without inpatient treatment. • 47% (n=94) of clients reported having one or more SAs. • Individuals with SA reported greater consumption of alcohol (17 vs. 13 liters pure alcohol) and a more frequent use of opioids (43% daily use vs. 32%) in the last 6-months. • Individuals with a SA had more frequent use of benzodiazepines, reported more ODs, had more in- and outpatient treatment and spent less time in prison.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Ross et al. (2005)/Australia	Prospective Cohort Study	825 (825)	Current heroin users entering different treatment modalities between February 2001 through August 2002.	<ul style="list-style-type: none"> • DSM-IV 	Heroin	SA(s) (lifetime); OD(s) (past 12-months; lifetime)	<ul style="list-style-type: none"> • 58% of participants had experienced a heroin OD (OD), with 28% occurring in the preceding 12-months. • In the 12-months prior to interview, the RR group was more likely to have ODd in than the MT, DTX and NT groups. • 37% of the sample reported a SA, 14% having made an attempt in the past 12-months and 6% in the preceding month. • Prevalence of attempted suicide in the past 12-mos did not differ by treatment modality. • Females were significantly more likely to have a SA in the past year.
Rossow & Lauritzen (1999)/Norway	Cross Sectional Study	2,051 (1,367)	National sample of individuals with SUD seeking treatment from 1992-1993.		Alcohol, cannabis, opioids, amphetamines, inhalants, tranquilizers, other substances	Prevalence of non-fatal ODs and SA(s); predictors of covariation between OD and SA(s) (lifetime)	<ul style="list-style-type: none"> • 45.5% reported having experienced one or more ODs. • About 70% who experienced an ODs had two or more • 16% reported having 9+ ODs • 32.7% reported having made one or more SAs, • Among those who reported SAs, 56.1% reported 2+ attempts. • Odds of having attempted suicide were six times higher among those who had experienced ODs (OR=6.3 • The number of SAs was also positively and significantly associated with the number of ODs. • Individuals with both SAs and ODs were characterized as older; more often homeless; displayed poor social functioning and mostly maintaining social relations in the drug scene; daily use of opiates, alcohol and tranquilizers; HIV risk-taking

							behavior, having more psychiatric problems (depression and anxiety) and more severe SI.
Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Roy (2002)/USA	Case-Control Study	246 (246)	OUD patients with and without SA.	<ul style="list-style-type: none"> • DSM-IV 	Opioids, alcohol, cocaine	SA(s), first- and second- degree relative history of suicide (lifetime)	<ul style="list-style-type: none"> • 105 of the 246 patients with OUD reported a lifetime SA. • 21 patients attempted suicide by deliberate heroin OD with intent to die, and 12 of those made at least one additional attempt using other methods. • OUD patients with history of SA had significantly higher childhood trauma scores for emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect than compared to OUD patients without history of suicide. Significantly more patients with SA had a history of cocaine dependence and alcohol dependence. • Significantly more people with SA had history of major depressive disorder and higher ASI composite scores. • Of the 105 patients with a SA, 31 had a family history of suicidal behavior. • Multivariable analysis also found that neuroticism with significantly and independently associated with SA and had higher hostility scores.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Roy (2010)/USA	Case-Control Study	527 (527)	Abstinent OUD patients.		Opioids, alcohol, cocaine	SA(s) & familial history of suicide (lifetime)	<ul style="list-style-type: none"> • 207 of the 527 OUD patients (39.3%) attempted suicide. • Patients who had attempted were younger than those who had no history of SA and a majority were female. • Significant predictors of SA were family history of suicidal behavior, alcohol or cocaine dependence, and receiving antidepressant medication.
Tremeau et al. (2005)/France	Case-Control Study	160 (160)	OUD patients receiving methadone or buprenorphine treatment.	<ul style="list-style-type: none"> • DSM-IV • Urine toxicology (confirm opioid use at intake) 	Opioids	Characteristics of SA(s), familial history of SA	<ul style="list-style-type: none"> • 27% of patients (10 men and 11 women) made their first SA before they experienced heroin. • Women made more attempts and they resorted to non-heroin drug ODs more frequently.
Vingoe et al. (1999)/England	Cross Sectional Study	48 (48)	Outpatients receiving treatment for SUDs, with a history of opioid IDU.		Heroin	Non-intentional OD(s); intentional OD(s) or SA(s) (lifetime, past 12- months)	<ul style="list-style-type: none"> • 54% (n=26) of patients had experienced a heroin OD in the past, 10 had only overdosed once; 16 had multiple ODs. • 60% (n=29) patients had a history of suicidal thoughts • 26 had a suicide plan; plans include: 6 had thoughts about heroin OD, 14 had considered OD of other drugs, 3 had thought of cutting, 2 of shooting and 1 of jumping. • 35% (n=17) patients had made SAs in the past. Methods of attempt include: 2 took a heroin OD, 12 took an OD of other drugs, 2 by cutting, and 1 by jumping. • History of heroin OD, half (13/26) made a SA at some time in their lives. • OD of heroin was not a common method for attempting suicide: of the 13 subjects who had a history of both heroin OD and of a SA, 2 used intentional heroin OD.

Author (Pub year)/ Country	Study Design	Overall Sample (OUD)	Sample Characteristics	Data Sources & Measure(s)	Substances Examined	Outcomes (Time frame)	Key findings/ Summary
Wines et al. (2004)/USA	Cohort Study (Prospective)	470 (470)	Adults admitted to an inpatient treatment.	<ul style="list-style-type: none"> 2-questions from ASI (suicidal behavior) 	Alcohol, heroin, benzodiazepines, cocaine, sedatives, stimulants	SI, SA(s) (6, 12, 18, & 24-months, lifetime)	<ul style="list-style-type: none"> No significant associations between frequency of recent alcohol, heroin, benzodiazepines or cocaine use and SAs, whether or not depressive symptoms were present Alcohol, heroin, benzodiazepines or cocaine were not significantly associated with either SI or SA.
Abbreviations: BPD =Borderline Personality Disorder; DSM =Diagnostic and Statistical Manual; OD =Overdose; OUD = Opioid Use Disorder; SA = Suicide Attempt; SI = Suicidal Ideation; SIB = Self-Injurious Behavior(s); SUD =Substance Use Disorder							

TABLE 2.2: Quality Assessment and Rating of Systematic Review Studies															
2.2A). Evaluation of Case-Control Studies															
Author (Pub year)	Study Design	CL1	CL2	CL3	CL4	CL5	CL6	CL7	CL8	CL9	CL10	CL11	CL12		Quality Rating
Dragisic (2015)	Case-Control	Y	N	N	Y	N	Y	NA	Y	Y	Y	N	N		Poor
Ghaffari- Nejad (2011)	Case-Control	Y	N	Y	Y	N	N	N	Y	Y	Y	NR	Y		Poor
Jin (2013)	Case-Control	Y	Y	N	Y	Y	Y	NR	N	Y	Y	NR	Y		Good
Ilgen (2009)	Case-Control	Y	Y	N	Y	Y	Y	Y	N	Y	Y	NR	Y		Good
Kazour (2016)	Case-Control	Y	Y	N	Y	Y	Y	NR	N	Y	Y	NR	Y		Good
Maloney (2009)	Case-Control	Y	Y	Y	Y	Y	Y	NR	N	Y	Y	Y	Y		Good
Maloney (2010)	Case-Control	Y	Y	Y	Y	Y	Y	NR	N	Y	Y	NR	Y		Good
Penney (2012)	Case-Control	Y	Y	N	Y	Y	Y	NA	NA	NA	Y	N	Y		Fair
Roy (2002)	Case-Control	Y	Y	N	Y	Y	N	NA	N	NA	Y	NR	Y		Fair
Roy (2010)	Case-Control	Y	Y	N	Y	Y	Y	NR	NR	N	Y	NR	Y		Good
Tremeau (2005)	Case-Control	Y	Y	N	Y	Y	N	NR	NR	Y	Y	N	Y		Good
<p>Abbreviation definitions: Y=Yes; N=No; NR=Not Reported; NA= Not Applicable; CD= Cannot Determine; CL=Checklist Item</p> <p>Key for Case-Control Studies:</p> <p>CL1. Was the research question or objective in this paper clearly stated?</p> <p>CL 2. Was the study population clearly specified and defined?</p> <p>CL 3. Was the participation rate of eligible persons at least 50%?</p> <p>CL 4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?</p> <p>CL 5. Was a sample size justification, power description, or variance and effect estimates provided?</p> <p>CL 6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?</p> <p>CL 7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?</p> <p>CL 8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?</p> <p>CL 9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?</p> <p>CL 10. Was the exposure(s) assessed more than once over time?</p> <p>CL 11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?</p> <p>CL 12. Were the outcome assessors blinded to the exposure status of participants?</p>															

2.2B). Evaluation of Cohort and Cross-Sectional Studies																
Author (Pub year)	Study Design	CL1	CL2	CL3	CL4	CL5	CL6	CL7	CL8	CL9	CL10	CL11	CL12	CL13	CL14	Quality Rating
Ashrafioun (2017)	Cross Sectional	Y	Y	Y	Y	Y	N	N	Y	Y	N	Y	NA	NA	Y	Good
Baykara (2018)	Cross Sectional	Y	Y	NR	Y	N	N	N	N	Y	N	Y	N	NA	N	Poor
Best (2000)	Cross Sectional	Y	Y	NA	Y	N	N	N	Y	Y	N	Y	Y	NA	N	Fair
Bohnert (2017)	Cohort Study (Retrospective)	Y	Y	Y	Y	Y	Y	Y	N	Y	NA	Y	N	NA	Y	Good
Borges (2000)	Cross Sectional	Y	Y	Y	Y	Y	N	N	N	Y	N	Y	N	NA	Y	Fair
Bradvik (2007)	Cross Sectional	Y	Y	Y	N	N	N	N	N	Y	N	Y	N	NA	N	Poor
Cheek (2016)	Cross Sectional	Y	Y	Y	Y	Y	N	N	N	Y	N	Y	N	NA	Y	Good
Chen (2009)	Cross Sectional	Y	Y	CD	Y	N	N	N	N	Y	Y	Y	N	NA	Y	Fair
Conner (2007)	Cohort (Prospective)	Y	Y	CD	Y	N	N	N	N	Y	N	Y	N	N	Y	Fair
Darke (2001)	Cross Sectional	Y	Y	CD	Y	N	N	N	Y	Y	N	Y	N	NA	Y	Fair
Darke (2004)	Cross Sectional	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	N	NA	Y	Good
Darke (2010)	Cross Sectional	Y	Y	CD	Y	N	N	N	Y	N	Y	Y	N	NA	Y	Good
Darke (2012)	Cross Sectional	Y	Y	CD	Y	N	N	N	N	Y	N	Y	N	NA	Y	Fair
Darke (2015)	Cohort (Prospective)	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	N	Y	Good
2.2B). Evaluation of Cohort and Cross-Sectional Studies (Continued)																
Author (Pub year)	Study Design	CL1	CL2	CL3	CL4	CL5	CL6	CL7	CL8	CL9	CL10	CL11	CL12	CL13	CL14	Quality Rating
de los Cobos (2007)	Cross Sectional	Y	N	CD	Y	N	N	N	N	Y	N	Y	Y	NA	Y	Fair
Gilmore (2018)	Cross Sectional	Y	Y	NR	Y	N	N	N	N	Y	N	Y	N	NA	Y	Good
Hakansson (2010)	Cross Sectional	Y	Y	N	Y	Y	N	N	NA	N	N	Y	N	Y	N	Good
Harned (2006)	Cross Sectional	Y	Y	NR	Y	N	N	N	N	Y	N	Y	NR	NA	N	Poor

2.2B). Evaluation of Cohort and Cross-Sectional Studies (Continued)

Author (Pub year)	Study Design	CL1	CL2	CL3	CL4	CL5	CL6	CL7	CL8	CL9	CL10	CL11	CL12	CL13	CL14	Quality Rating
Havens (2004)	Cross Sectional	Y	Y	CD	Y	N	N	N	Y	Y	N	N	N	NA	Y	Good
Icick (2017)	Cross Sectional	Y	Y	CD	Y	N	Y	Y	Y	Y	N	Y	CD	NA	Y	Good
Kalyoncu (2007)	Cross Sectional	Y	N	CD	CD	N	N	N	N	Y	N	Y	NR	NA	Y	Poor
Kuramoto (2012)	Cross Sectional	Y	Y	Y	Y	NA	N	N	Y	Y	N	Y	N	NA	Y	Good
Lavania (2012)	Cross Sectional	Y	Y	CD	Y	Y	N	N	N	Y	N	Y	CD	NA	Y	Good
Marchand (2017)	Cross Sectional	Y	Y	CD	Y	N	N	N	N	Y	N	Y	CD	NA	Y	Fair
Maremman i (2007)	Cross Sectional	Y	Y	NR	NR	N	N	N	N	Y	N	Y	NR	NA	CD	Poor
Masferrer (2016)	Cross Sectional	Y	Y	Y	Y	Y	N	N	N	Y	N	Y	NR	NA	Y	Good
Olsson (2016)	Cohort	Y	Y	Y	Y	NA	Y	Y	NA	Y	N	Y	N	Y	Y	Good
Oyefeso (2008)	Cohort	Y	Y	Y	Y	NR	Y	Y	N	Y	N	Y	NR	NA	CD	Fair
Pan (2014)	Cohort (Nested Case-Control)	Y	Y	CD	Y	NA	Y	Y	N	Y	N	Y	N	NA	Y	Good
Ravndal (1999)	Cohort	Y	Y	NR	Y	N	Y	Y	N	Y	N	Y	NR	N	CD	Fair
Ross (2005)	Cohort Study	Y	Y	NR	Y	N	Y	Y	Y	Y	Y	Y	CD	NR	NR	Good
Rossow (1999)	Cross Sectional	Y	Y	N	Y	CD	N	N	N	Y	Y	N	Y	NR	NA	Fair
Vingoe (1999)	Cross Sectional	Y	N	NR	CD	N	N	N	CD	Y	N	Y	NR	NA	N	Poor

2.2B). Evaluation of Cohort and Cross-Sectional Studies (Continued)																
Author (Pub year)	Study Design	CL1	CL2	CL3	CL4	CL5	CL6	CL7	CL8	CL9	CL10	CL11	CL12	CL13	CL14	Quality Rating
Wines (2004)	Cohort	Y	Y	NR	Y	N	Y	Y	N	Y	N	Y	N	NR	Y	Fair
Neale (2000)	Mixed Methods	-	-	-	-	-	-	-	-	-	-	-	-	-	-	N/A
<p>Abbreviation definitions: Y=Yes; N=No; NR=Not Reported; NA= Not Applicable; CD= Cannot Determine; CL=Checklist Item</p> <p>Key for Cross Sectional/Cohort Studies:</p> <p>CL1. Was the research question or objective in this paper clearly stated?</p> <p>CL 2. Was the study population clearly specified and defined?</p> <p>CL 3. Was the participation rate of eligible persons at least 50%?</p> <p>CL 4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?</p> <p>CL 5. Was a sample size justification, power description, or variance and effect estimates provided?</p> <p>CL 6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?</p> <p>CL 7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?</p> <p>CL 8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?</p> <p>CL 9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?</p> <p>CL 10. Was the exposure(s) assessed more than once over time?</p> <p>CL 11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?</p> <p>CL 12. Were the outcome assessors blinded to the exposure status of participants?</p> <p>CL 13. Was loss to follow-up after baseline 20% or less?</p> <p>CL 14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?</p>																

Chapter 3

3 Feasibility and Acceptability of Safety Screening Among Patients Receiving Addiction Treatment

3.1 Abstract

Background: Premature mortality associated with opioid-related overdose and suicide is a significant public health problem in the United States (U.S.). Approximately 20–30% of individuals with opioid use disorder have a history of both suicide attempt and unintentional opioid overdose. *Objective:* The objective of this study is to evaluate the feasibility of a standardized screen for suicide and overdose among patients receiving addiction treatment.

Design: A cross-sectional study was conducted using a convenience sample of patients (n=113) recruited from two inpatient treatment programs. *Methods:* A modified version of the Patient Safety Screener (mPSS) was used to screen for suicidal ideation, suicide attempt, and overdose. The screen was administered in-person during treatment, and results were linked to administrative clinical data. Subjects (n=108) and members of their clinical care team (n=20) completed a screening acceptability survey. A positive mPSS was recorded if a patient reported suicidal ideation in the past two weeks, a suicide attempt, and/or an overdose in the past six months. *Results:* Fifty-eight percent of subjects had a positive mPSS screen, and 30.3% reported suicidal ideation, suicide attempt, and overdose. Subjects and clinical staff reported that it was acceptable to screen for suicide attempt(s) and overdose(s). About a third of the clinical staff reported concerns about administration time (n=7) and impact on workflow (n=6). *Conclusions:* Both suicide and overdose are important patient safety factors that should be incorporated into treatment and discharge planning. The findings of this study support simultaneously screening

for suicide and overdose in OUD inpatient treatment settings. Future research needs to determine whether screening improves provision of services and reduces self-injurious behavior.

3.2 Introduction

Premature mortality associated with opioid-related overdose and suicide are significant public health problems in the United States (U.S.) (Bohnert and Ilgen, 2019; Cunningham et al., 2018; Oquendo and Volkow, Rockett et al., 2016; 2018; VanHouten et al., 2019). In 2018, there were 46,802 opioid-related overdoses (14.3 per 100,000) and 48,344 (14.2 per 100,000) suicides reported in the U.S. (Wilson, 2020; Xu et al., 2020). Previous research has estimated that 20–30% of individuals with opioid use disorder (OUD) have reported a history of both a suicide attempt(s) and unintentional opioid overdose(s) (Darke et al., 2015; Maloney et al., 2010). People with OUD have elevated mortality rates, with suicide being one major contributor to premature mortality (Darke et al., 2011; Degenhardt et al., 2011; Darke et al., 2007; Wilcox et al., 2004). Additionally, overdose also plays a significant role in morbidity and mortality among individuals with OUD (Bohnert et al., 2010; Darke et al., 2015; Ravndal & Vaglum, 1999). While previous reports have estimated that 25% of opioid overdose deaths are intentional (Oquendo & Volkow, 2018), this is likely an underestimate given that suicide rates due to poisoning are underreported by approximately 30% (Donaldson et al., 2006). Furthermore, with the true proportion of non-fatal ODs identified as intentional being unknown, there exists a relationship between suicide and overdose that is difficult to ascertain.

Several studies have examined individuals with a history of both unintentional overdose(s) and suicide attempt(s) (Maloney et al., 2010; Rossow and Lauritzen, 1999). Subjects with this joint history manifest worse psychological and social functioning, as well as more severe drug-related problems than those without a history of both unintentional overdose(s) and suicide attempt(s) (Bohnert et al., 2010). Ravndal and Vaglum found that 47% of clients in addiction treatment reported at least one suicide attempt, and 43% had at least one overdose-related

hospitalization (1999). Patients with a history of suicide attempt(s) were more likely to report polydrug use, non-fatal overdose, and higher healthcare utilization (Ravndal & Vaglum, 1999). The higher clinical severity observed among patients with a history of suicide and overdose reflects that these individuals need a broader range of services and intensive case management (Bohnert et al., 2010). Despite evidence of the overlap between overdose and attempted suicide, clinical screening and intervention have not been integrated.

Accurate identification of patients with a history or at risk of suicide and overdose is critical for treatment planning. In higher acuity treatment settings, there may be regulatory requirements to conduct universal suicide screening; however, there are no regulations to screen for a history of non-fatal overdose, and it is unknown whether overdose history is routinely assessed. The Joint Commission has recognized the importance of identifying suicide risk as part of routine clinical care and emphasizes the documentation of suicide assessments (both positive and negative findings), particularly in behavioral health care settings (The Joint Commission, 2016). However, suicide documentation in electronic medical records (EMRs) is often inconsistent or incomplete (Tanguturi et al., 2017). An estimated 83% of suicide decedents utilized healthcare in the year prior to their death, and 24% had a documented mental health diagnosis within 4-weeks prior to death (Ahmedani et al., 2014). Missing or incomplete suicide documentation in the EMR may have led to missed opportunities to deliver prevention services. The mental health and addiction treatment systems are not integrated, and at a regulatory level, this may discourage simultaneous screening for overdose and suicide. Some behavioral health programs may be unable to treat patients with active suicidal ideation because their physical environment does not meet the requirements to ensure safety. Individuals with substance use disorders (SUDs) frequently have co-occurring mental health problems (Swendsen et al., 2010; Harris &

Barraclough, 1997), which can be very difficult to distinguish in the early phase of treatment, especially as withdrawal causes dysphoria. As many as 40% of patients seeking SUD treatment have a history of suicide attempt(s) (Roy & Janal, 2007; Roy, 2009; Roy, 2010). Patients frequently present with depressive symptoms and significant functional impairments that may not only drive them to seek treatment, but also put them at higher risk for suicidal behavior (Yuodelis-Flores et al., 2015).

The feasibility of suicide screening has been demonstrated in different healthcare settings, including emergency departments (EDs) and primary care settings (Boudreaux et al., 2013; Boudreaux et al., 2016; King et al., 2009; Lish et al., 1996). Standardized suicide screening improves identification of at-risk individuals previously not identified (King et al., 2009; Boudreaux et al., 2016). The Emergency Department-Safety Assessment and Follow-up Evaluation (ED-SAFE), a quasi-experimental multisite clinical trial, found that standardized suicide screening resulted in a nearly two-fold increase in patient endorsement of any past or present intentional self-harm ideation or behavior (i.e. suicide risk detection) (Boudreaux et al., 2016). While presumably suicide screening is occurring in addiction treatment programs, there are no psychometrically validated overdose screening assessments, and it is unlikely that overdose history documentation specifies intentionality. Given the magnitude of the opioid and suicide epidemics (Rockett et al., 2019; Hedegaard et al., 2020), and due to evidence that prevention interventions can reduce the risk of suicide (Zalsman et al., 2016) and overdose (Irvine et al., 2019), integrated screening and risk evaluation are warranted. The objective of this study is to evaluate the feasibility of an integrated overdose and suicide standardized screen, in the context of inpatient treatment for individuals with OUD. This feasibility study includes assessment of screen acceptability for patients and clinical staff.

3.3 Methods

Study Design

A cross-sectional study was conducted, and patient data was collected using a structured in-person interview, a web-based survey (screening acceptability), and extraction of data from administrative clinical records. Clinician data was collected using a web-based survey on screen acceptability. Both participating patients and clinical staff provided written informed consent.

Study Setting

Patients with an OUD were recruited from two treatment programs associated with a university-based health care system. One site was an acute inpatient dual-diagnosis unit that treats individuals who: 1) need medically managed detoxification and 2) are a danger to themselves or others (i.e. suicidal ideation/suicide attempt and/or homicidal ideation or actions). The second site was an inpatient treatment program that offered detoxification services and a 28-day residential program; subjects were only recruited from the residential unit.

Data Collection

Study Sample.

A convenience sample of patients were recruited from the acute inpatient unit starting in February 2019, and recruitment at the residential unit began in August 2019. Recruitment concluded at both sites in October 2019. Patients were included in the study if they were currently being treated at a recruitment site, had a confirmed diagnosis of OUD (communicated the attending physician or electronic medical record (EMR) documentation of OUD), and were willing to provide written informed consent. Patients were excluded if they were: 1) unable to read and write in English, 2) deemed not psychiatrically stable (i.e. no medical decision making capacity, active hallucinations, or homicidal ideation as determined by the attending physician),

3) met the definition of incarceration (i.e. known to have a current warrant for their arrest, pending criminal charges, currently wearing an electronic ankle monitoring device, and/or mandated to treatment by law enforcement), 4) under the age of 18 years, or 5) were pregnant. Participation was completely voluntary, and compensation was not provided for study participation.

Clinical staff, who were actively employed during the study period, were recruited from the two sites. Staff recruitment occurred from December 2019 through February 2020. Staff were eligible for study participation if they: 1) provided treatment (i.e. conducted therapy groups, distributed medications, conducted therapeutic interventions, or were a treatment provider) to patients enrolled in the study, 2) attended treatment team meetings, and 3) were willing and able to provide written informed consent. Administrative staff without patient contact were ineligible to participate.

Measures

Administrative Clinical Database.

Administrative clinical data was extracted from a patient reported outcomes monitoring system used at both recruitment sites, details of which are provided elsewhere (Winstanley et al. 2020). Variables extracted included sex, race (white/non-white), ethnicity, education (less than high school, high school graduate/GED, or some college+), employment (employed full/part-time or unemployed), number of times arrested (lifetime), substance use history, and the adverse childhood experiences (ACEs) instrument. Substance use history included lifetime use (yes/no), age of first use, and route of administration for tobacco, alcohol, cocaine, marijuana, heroin, prescription opioids (illicit use), buprenorphine (illicit use), methamphetamines, and benzodiazepines. Other clinical characteristics extracted included lifetime injection drug use

(yes/no), number of overdoses (lifetime), and age of first overdose. The 17 ACE items were categorized as mental health problems (2 items); alcohol or drug use (2 items); emotional, physical or sexual abuse (6 items); neglect (3 items); physical or emotional abuse by a significant other (1 item), and family dissolution (3 items). These categories were summed to generate a total score.

Modified Patient Safety Screener.

Subjects were administered a modified version of the Patient Safety Screener (PSS), developed by Boudreaux and colleagues (2013, 2015). A positive PSS is defined as suicidal ideation in the past two weeks or a suicide attempt in the past six months. The modified PSS (mPSS) included a sixth (new) question on previous drug overdose. The first question assesses depressed mood, and this item is not included in screen scoring. The second question was “over the past two-weeks, have you had thoughts of killing yourself?” and the response options are 1) yes, 2) no, 3) patient unable to complete, or 4) patient refused. The third question asked, “In your lifetime, have you ever attempted to kill yourself?” Subject responses included: 1) yes, 2) no, 3) patient unable to complete, or 4) patient refused. If the subject responded in the affirmative, a follow-up question asked, “when did this happen?” There were six possible responses: 1) within the past 24 hours (including today), 2) within the past month (not including today), 3) between one and six months ago, 4) more than six months ago, 5) patient was unable to complete, or 6) patient refused. The overdose question, added for this study, was modeled to match the suicide question just described. However, the words “attempted to kill yourself” were replaced with “overdose.” The mPSS took approximately five minutes to administer, and a positive mPSS was defined as suicidal ideation in the past two weeks, a suicide attempt in the past six months, and/or overdose in the past six months. The ‘in the past 24-hours and ‘past month’ response

options were combined because subjects were not interviewed within the first 24 hours of their admission. For a subject with a positive mPSS screen, the attending physician and the subject's primary therapist were notified of the result via encrypted e-mail with a PDF of the subject's mPSS attached. If subject told a study team member that they were an immediate danger to themselves or others, the unit lead (i.e. charge nurse or lead therapist) was notified immediately and the attending physician was paged.

Patient Acceptability Survey.

Subjects who completed the mPSS were asked to complete a web-based patient acceptability survey. Subjects were asked to rate the extent to which they agreed or disagreed with six statements about comprehension, time burden, relevance of the screen to treatment, invasiveness of the screening questions, willingness to complete the screen questions in the future, and usefulness of the screening. The responses used a five-point Likert scale ranging from strongly disagree to strongly agree. Due to the distribution of responses, they were recoded as: 1) disagree, 2) neither disagree nor agree, or 3) agree. The survey took approximately ten minutes to complete.

Staff Acceptability Survey.

The staff acceptability survey comprised ten closed-ended and five open-ended questions. Twenty-four staff were eligible to participate in the study. Four were unable to be contacted because they were no longer employed at either site and their contact information was inaccessible. A web-based survey was sent via e-mail to 20 staff who had provided written informed consent. Staff who were unresponsive to the email request to complete the online survey, were provided a hard copy of the survey. The staff survey comprised questions on respondent age, job title, number of years working in current position, and number of years

working in addiction treatment. Staff responded to four statements using a five-point Likert scale ranging from strongly disagree to strongly agree: 1) information provided by the safety screen is useful in clinical practice, 2) information provided on the safety screen changed how I treated the patient, 3) the safety screen placed an unnecessary burden on the clinical staff, and 4) the safety screen placed an unnecessary burden on the patient. Responses were recoded as agree, neither agree nor disagree, or disagree. The survey included a question on which patients should receive the mPSS, also referred to as the “safety screen” (all patients/high risk patients only/done at physician discretion/none). The open-ended questions included whether the screening information changed how patients were treated, improvements that would make the screen more useful, aspects of the screen that were most useful, potential barriers to implementing the screen into routine clinical practice and whether the screen should be integrated into clinical practice.

Statistical Analysis

Descriptive statistics were used to summarize the sociodemographic and clinical characteristics of the sample, as well as the acceptability surveys. Medians were reported for variables that were not normally distributed, with the exception of age. Statistics were reported for the overall sample, as well as by recruitment site to determine whether important clinical differences were associated with recruitment site. Recruitment site differences were determined using Pearson’s chi-square tests for categorical variables, t-test for means, and the Mann-Whitney U (Wilcoxon Ranksum) test to compare medians. Quantitative data analysis was conducted using Stata/SE 15.0 analytical software (StataCorp, 2017). Statistical significance was defined as $p \leq 0.05$.

The open-ended questions in the staff acceptability survey were analyzed using a thematic analysis approach (Biggerstaff & Thompson, 2008; Vaismoradi et al., 2013; Wagstaff

& Williams, 2014). The open-ended responses were coded and then combined into two overarching themes of advantages and disadvantages of the screen. These themes were used to subcategorize responses from clinical staff and were based on procedures outlined for previous qualitative methods (Vaismoradi et al., 2013). The qualitative analysis was hand coded by two members of the study team (ANS and ELW), and the study protocol was approved by the West Virginia University Institutional Review Board (IRB).

3.4 Results

Two hundred and eight patients were pre-screened for study eligibility. Ninety-five patients were excluded, and 113 provided written informed consent. The primary reasons for exclusion included inability to provide informed consent for mental health reasons (29.5%, n=28), patient discharge or leaving treatment before screening (25.3%, n=24), pregnancy among female clients (15.9%, n=15), declining to participate (13.7%, n=13), legal issues/current arrest warrant (8.4%, n=8), failure to comply with study procedures (4.2%, n=4), and complications due to detoxification (3.2%, n=3). Seventy-two patients (63.7%) were recruited from the acute inpatient unit and 41 (36.3%) were recruited from the residential treatment facility (Figure 3.1).

The overall sample was predominantly non-Hispanic (95.6%), white (95.6%) and male (64.3%). The majority of the sample had at least a high school diploma or GED (46.9%), and 23.9% of participants were employed in the past 30 days (Table 3.1). Clinical characteristics of the sample are reported in Table 3.1. There were no statistically significant differences in demographic or clinical characteristics by recruitment site, except subjects at the acute inpatient program were, on average, 3.3 years older than those recruited from the residential program (Table 3.1).

Overall, 58.4% of the subjects screened positive on the mPSS, 38.1% had suicidal ideation in the past two weeks, 46.3% had a suicide attempt(s) in the past six months and 39.7% had overdosed in the past six months. Subjects recruited from the acute inpatient program were significantly more likely to report suicidal ideation in the past two weeks (50.0% versus 17.1%; $p<0.01$) and a suicide attempt in the past six months (29.7% vs 5.9% or 11.8%, $p=0.02$) than subjects recruited from the residential program.

The patient acceptability survey had a 95.6% response rate ($n=108$). Overall, 18.5% of respondents found the screen time consuming. Additionally, 4.6% found it difficult to understand and 6.4 % would not want to complete another screening. Furthermore, 5.6% were uncomfortable with the questions on the mPSS. Finally, 4.6% of subjects did not find the mPSS useful and 6.5% did not understand how the screening related to their treatment. Across all of the items in acceptability survey, 14-23% endorsed ‘neither agree nor disagree.’ Screen acceptability did not vary by recruitment site (see Table 3.3).

Twenty staff completed the acceptability survey, with a response rate of 83.3%. The mean age of staff respondents was 35.0 years ($SD=10.1$). A quarter of the staff was physicians, another quarter drug and alcohol technicians, 20.0% were clinical therapists or counselors, 20.0% were social workers, 5.0% were nurses, and 5.0% were clinical coordinators. Ninety-five percent of staff agreed the mPSS provided useful information, 45.0% found it provided information that changed how they treated the patient, 70.0% reported it did not place an unnecessary burden on the patients, 85.0% thought all patients should receive the mPSS, 100% of staff thought the assessment was useful in clinical practice, and 95.0% thought the mPSS should be integrated into standard clinical practice.

Open-ended items in the staff acceptability survey were categorized as follows: 1) treatment change, 2) improvements to increase usefulness in clinical practice, 3) aspects of the safety screen found most useful, 4) extant barriers to clinical implementation, and 5) integration into clinical practice. Overall analysis of the open-ended response data found that respondents reported 12 advantages and 9 disadvantages. Most respondents found the results of the mPSS to be informative (n=17) and stated that “It allows for clinicians to make more educated, evaluated decisions,” and “I think it is a good tool to measure where the patient is mentally when they arrive to the facility.”

Other advantages of the mPSS included the ability to convey risk (n=8), assess the patient (n=7), evaluate safety (n=7), the completeness of the assessment (n=5), its usefulness (n=4) in clinical practice, and informing patient history (n=3; Figure 3.2). For instance, the clinical therapists and social workers conveyed:

“This helps better understand this person's past coping mechanisms.”

“The safety of the guest is the utmost importance. This is another tool to ensure that the most is being done to keep them safe.”

“It provides more detail about the patients history so we can tailor treatment to the individual and reduce risk.”

Other advantages mentioned by respondents included reporting comorbidities (n=2), clinical management (n=1), efficiency (n=1), individual care (n=1), and relatability (n=1).

The most frequently reported disadvantage of the mPSS was time to complete (n=7). This problem was compounded by other issues, such as workflow (n=6), communication (n=4), patient resistance (n=2), and concerns about patient re-traumatization (n=2). For example:

“While some of these questions may be asked/answered in the admissions process, it would be

nice to have them definitely in their chart and always in one spot.” While, other staff members provided the following feedback: “Takes a long time to administer, was sometimes triggering to the patients.” A complete list of themes is depicted in Figure 3.2.

3.5 Discussion

This study found that nearly 60% of subjects receiving inpatient OUD treatment had suicidal ideation, suicide attempts and/or overdose. A fifth of the subjects had a history of only overdose(s), whereas a third had current suicidal ideation and a history of overdose(s) and suicide attempt(s). Lifetime suicide attempt(s) (46.3%) in this study was consistent with existing research (Roy, 2010; Roy, 2002; Ravndal & Vaglum 1999); however, the prevalence of a lifetime overdose (60.2%) was still higher than reported in previous research of patients seeking addiction treatment (Ross et al., 2005). This difference speaks to the point that, while suicide history is important to address in addiction treatment, screening for overdose plays an equally important role in understanding patient history as a whole.

The most positive feedback received was for comprehension of screening questions. Given that more than half of subjects had a high school education or less, it is important that 83.3% of subjects reported that the mPSS questions were easy to understand. Furthermore, although patients in both clinical settings were required to be psychiatrically cleared by the attending physician, some patients were receiving various pharmaceutical interventions to treat their addiction or psychiatric conditions. Particularly for patients in the acute inpatient settings, some patients may have experienced the effects of detoxification and possibly were still adjusting to their new environment (Rapeli et al., 2006). Thus, it is essential to have a screening tool with easily comprehended questions. A minority of respondents (18.5%) reported that the screen was

time consuming; while the survey question was in reference to administration time for the mPSS only, subjects might interpret it as the time to complete the entire research interview.

Despite clinical concerns that patients may be uncomfortable completing a standardized screen on suicide and overdose, 94.4% of patients were comfortable with the screen. A previous literature review found most studies reported that only a small minority of patients, who participated in trauma-focused research, experienced distress (Legerski & Bunnell, 2010). Moreover, most studies reported that negative feelings dissipate quickly, and that the great preponderance of patients participating in research feel rewarded (Legerski & Bunnell, 2010). A study by Biddle and colleagues measured the emotional state of adult and adolescent participants, with a history of self-harm or suicidality, before and after interviews on their personal experiences (Biddle et al., 2013). They reported that over 50% of participants found talking about their experiences beneficial. Affirming previous findings, 73.2% of patients in our study reported the mPSS was useful and 78.7% understood how the questions pertained to their current treatment. Nevertheless, it is important to consider that the screening questions on potentially traumatic events may cause patient distress (LeFevre, 2014). In these instances, it is important to address patient concerns, provide them with the appropriate resources, and allow them time to process their emotions before ending the interview (Espisto, 2019; LeFevre, 2014)

All staff reported that the mPSS was useful in clinical practice and was a minimal burden to patients. All but one agreed that the instrument should be integrated into standard clinical procedures. However, the clinical staff did not administer the screen, and it was not administered upon treatment entry. If clinicians had to administer the screen, overall acceptability may have been lower. Conversely, if the screen was administered at intake and integrated into the standard workflow, then it may have had higher clinical utility. There was disagreement on whether the

screening results changed how the patient was treated, and this variation may be partially explained by the respondent's clinical role and involvement in treatment planning.

The staff acceptability survey also included six open-ended response questions. Several disadvantages were frequently reported by the staff. Seven reported administration time as a disadvantage. This involvement may actually reflect disruption to clinical workflow and indicate a barrier in terms of the division of labor regarding which staff members would be tasked with administering the mPSS in the future. Furthermore, workflow could be impacted by several features of the screen, such as when the mPSS is administered and how the results are communicated. For the current study, mPSS was administered during intake or the patient's unstructured free time; however, the results were often not communicated to the therapist prior to interview. Although results were provided to the clinical staff, results were not recorded in the EMR or communicated at the same point in treatment. This knowledge gap resulted in potential duplication of work and redundancy. It bolsters the case for having the mPSS incorporated directly into the patient's EMR and readily accessible for care team review. Conversely, another common theme was that staff treat all patients uniformly irrespective of background. This could partially be due to the large number of staff members completing the survey, who did not have one-on-one patient contact, but rather interacted with patients in group settings. One such group was drug and alcohol technicians, who comprised 25.0% of survey respondents. Regarding barriers to implementation, time was the biggest disadvantage reported by staff members. Overall, the mPSS was thought to be efficient in providing a concise reporting tool for conveying safety risk. However, patients who screened positive would ultimately require longer assessments. This means a longer time commitment for the patient and for the staff member administering the detailed suicidal ideation, suicide attempt, and/or overdose assessment—

depending on the initial mPSS result. However, despite these barriers and concerns, 95.0% of staff reported the mPSS should be integrated into standard clinical practice.

Limitations

As the study sample was recruited from an inpatient population, the results may not generalize to other treatment modalities. Likewise, the majority of the subjects recruited for this study was predominantly white and non-Hispanic, and results might not generalize to more diverse patient populations. In order to integrate this instrument into clinical practice, members of the clinical team would need to administer the screening to patients or have the screen self-administered by patients. Integration may require more time from the staff to debrief with patients that become distressed. Although it is ideal to administer the mPSS at intake to help inform treatment planning, the accuracy of the results may be compromised if the patient arrives intoxicated or has not established rapport with the treatment team.

Future Directions

Overall, additional research is needed to determine the optimal timing of mPSS administration and to establish the test-retest validity of the instrument. Furthermore, additional research needs to be conducted to establish the prospective validity of the tool and if the tool changes clinical practice and/or the provision of prevention services. Stricter criteria for when to administer the mPSS should be established to obtain consistent results, and/or criteria set for re-screening at various points throughout the inpatient stay to address fluctuations in suicidality. The next step would be to test the mPSS among patients enrolled in outpatient treatment programs, so as to assess overdose and suicide in patients at varying stages of recovery.

3.6 Conclusions

Based on the current findings from this study, concurrent screening for overdose and screening is acceptable and warranted. Through a dual screening procedure, this may increase the clinical awareness of the overlap between overdose and suicide among patients with OUD. For this reason, suicidal behaviors warrant more clinical and research attention in the addiction field (Yuodelis-Flores et al., 2015), and support the need to for all clients receiving addiction treatment services to also be screened and monitored for suicidality and overdose. This finding indicates screening for both suicide and overdose is an important clinical contributor to overall patient safety assessment and provides crucial information for treatment and discharge planning. Both patients and staff found the mPSS informative and appropriate for assessment and approved of the application of instrument to the clinical setting. In general, the greater the burden of risk factors, the higher the likelihood for suicide attempt or death by suicide. The information gathered in this study shows that the mPSS is an appropriate screening tool to address these issues. Additional research is necessary to determine whether screening improves provision of services and reduces self-injurious behavior.

3.7 Acknowledgements

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Table 3.1: Study Sample Demographics				
Characteristics	Overall Sample (n=113)	Acute Inpatient (n=72)	Residential Program (n=41)	p-value
Mean Age (years), (SD)*	35.2 (9.2)	36.4 (9.0)	33.1 (9.3)	0.02
Sex (% Male)	72 (63.7)	47 (65.3)	25 (61.0)	0.65
White (%)	108 (95.6)	68 (94.4)	40 (97.6)	0.65
Non-Hispanic (%)	108 (95.6)	68 (94.4)	40 (97.6)	0.65
Employed (%)	27 (23.9)	21 (29.2)	6 (14.6)	0.08
Education (%)				0.42
Less than High School	18 (15.9)	9 (12.5)	9 (22.0)	
High School Grad/GED	53 (46.9)	35 (48.6)	18 (43.9)	
Some College/College Grad	42 (37.2)	28 (38.9)	14 (34.1)	
Lifetime Arrests (Median)	5.0	5.0	4.0	0.23
Ever Used, Lifetime (% Yes)				
Tobacco	112 (99.1)	71 (98.6)	41 (100.0)	1.00
Alcohol	112 (99.1)	71 (98.6)	41 (100.0)	1.00
Cocaine	102 (90.3)	63 (87.5)	39 (95.1)	0.32
Marijuana	111 (98.2)	70 (97.2)	41 (100.0)	0.53
Heroin	100 (88.5)	62 (86.1)	38 (92.7)	0.37
Prescription Opioids	104 (92.0)	68 (94.4)	36 (87.8)	0.28
Illicit/Non-Medical Buprenorphine Use	49 (43.4)	29 (40.3)	20 (48.8)	0.38
Methamphetamines/Amphetamines	98 (86.7)	61 (84.7)	37 (90.2)	0.57
Benzodiazepines	74 (65.5)	61 (84.7)	37 (90.2)	0.64
Mean age of First Use (Years), (SD)				
Tobacco*	13.1 (5.0)	12.9 (5.2)	13.6 (4.7)	0.62
Alcohol*	13.8 (6.9)	13.9 (8.4)	13.7 (3.1)	0.71
Cocaine*	19.0 (4.9)	18.8 (5.0)	19.4 (4.7)	0.69
Marijuana*	14.3 (3.9)	14.7 (4.5)	13.6 (2.4)	0.18
Heroin*	24.8 (9.3)	24.4 (9.1)	25.4 (9.6)	0.61
Prescription Opioids*	18.3 (6.4)	18.6 (7.0)	17.6 (5.3)	0.56
Illicit/Non-Medical Buprenorphine Use*	25.6 (9.1)	25.9 (10.2)	25.2 (7.5)	0.71
Methamphetamines/Amphetamines*	27.4 (8.6)	27.5 (8.3)	27.3 (9.2)	0.71
Benzodiazepines*	20.4 (8.2)	21.4 (8.6)	18.9 (7.3)	0.27
Ever Inject Drugs (%Yes, Lifetime)	88 (77.9)	58 (80.6)	30 (73.2)	0.36
Mean Age First Injection Drug Use (SD)*	25.1 (8.4)	25.6 (8.9)	24.1 (7.4)	0.68
Median Number of Lifetime Overdoses	1.0	1.0	1.0	-
Median Number of Overdoses (Past Six-Months)	3.0	3.0	2.5	0.64
Mean Age First Overdose (Years) (SD)*	26.5 (10.3)	27.1 (9.9)	25.4 (11.2)	0.33
ACE Total Domain Score	4.8 (1.8)	4.8 (1.7)	4.8 (1.9)	0.91
Table 3.1: For ease of comparison ages were reported as means. However, variables designated with an “*” did not follow a normal distribution therefore medians were compared using Wilcoxon rank-sum tests. Unless otherwise noted variables were compared using chi-squared, Fisher’s exact, or t-tests where appropriate. Additional details are described in the methods section. Statistical significance was set at $p \leq 0.05$.				

Table 3.2: Modified Patient Safety Screen (mPSS) Responses							
2A) Modified Patient Safety Screener (mPSS) Items	Overall Sample (n=113)		Acute Inpatient (n=72)		Residential Program (n=41)		p-Value
	n	%	n	%	n	%	
Depression in past two-weeks (Yes)	101	89.4	64	88.9	37	90.2	1.00
Suicidal Ideation in past-two weeks (Yes)	43	38.1	36	50.0	7	17.1	<0.01
Lifetime Suicide Attempt (Yes)	54	47.8	37	51.4	17	41.5	0.31
Most Recent Suicide Attempt							0.02
Within the last month	12	22.2	11	29.7	1	5.9	
Between 1-6 months ago	13	24.1	11	29.7	2	11.8	
More than 6 months ago	29	53.7	15	40.6	14	82.4	
Ever Overdose (Yes)	68	60.2	43	59.7	25	61.0	1.00
Most Recent Overdose							0.15
Within the last month	14.0	20.6	12	27.9	2	8.0	
Between 1-6 months ago	13.0	19.1	8	18.6	5	20.0	
More than 6 months ago	41.0	60.3	23	53.5	18	72.0	
2B) Positive mPSS Response Combinations	Overall Sample (n=66)		Acute Inpatient (n=52)		Residential Program (n=14)		p-Value
Suicidal Ideation Only	5	7.58	5	9.62	0	0.0	0.57
Suicide Attempt Only	4	6.1	3	5.8	1	7.1	1.00
Overdose Only	13	19.7	8	15.4	6	35.7	0.09
Suicidal Ideation + Suicide Attempt	11	16.7	10	19.2	1	7.1	0.43
Suicidal Ideation + Overdose	7	10.6	6	11.5	1	7.1	1.00
Suicide Attempt + Overdose	6	9.1	5	9.6	1	7.1	1.00
Suicidal Ideation + Suicide Attempt + Overdose	20	30.3	15	28.9	5	35.7	0.62
Table 3.2: Comparisons were made using chi-squared or Fisher's exact tests where appropriate. Statistical significance was set at $p \leq 0.05$. Additional details are described in the methods section.							

Table 3.3: Patient Acceptability Questionnaire Responses				
Patient Acceptability Questions (Frequency), (%)	Overall Sample (n=108)[†]	Acute Inpatient (n=69)	Residential Program (n=39)	p-Value
The self-harm screen was time consuming.				0.99
Disagree	63 (58.3)	40 (58.0)	23 (59.0)	
Neither disagree nor agree	25 (23.2)	16 (23.2)	9 (23.1)	
Agree	20 (18.5)	13 (18.8)	7 (18.0)	
The questions in the screening questionnaire were hard to understand.				0.78
Disagree	90 (83.3)	56 (81.2)	34 (87.2)	
Neither disagree nor agree	13 (12.0)	9 (13.0)	4 (10.3)	
Agree	5 (4.6)	4 (5.8)	1 (2.5)	
In the future I would not want to complete another self-harm screen.				0.29
Disagree	83 (76.9)	56 (81.2)	27 (69.2)	
Neither disagree nor agree	18 (16.7)	9 (13.0)	9 (23.1)	
Agree	7 (6.4)	4 (5.8)	3 (7.7)	
The questions on the self-harm screen made me uncomfortable.				0.35
Disagree	85 (78.7)	51 (73.9)	34 (87.2)	
Neither disagree nor agree	17 (15.7)	13 (18.8)	4 (10.3)	
Agree	6 (5.6)	5 (7.3)	1 (2.5)	
The questions asked in the self-harm screen were not useful.				0.71
Disagree	79 (73.2)	49 (71.0)	30 (76.9)	
Neither disagree nor agree	24 (22.2)	17 (24.6)	7 (18.0)	
Agree	5 (4.6)	3 (4.4)	2 (5.1)	
I do not understand how the self-harm screen relates to my treatment.				0.57
Disagree	85 (78.7)	53 (76.8)	32 (82.1)	
Neither disagree nor agree	16 (14.8)	10 (14.5)	6 (15.4)	
Agree	7 (6.5)	6 (8.7)	1 (2.5)	
Table 3.3: Comparisons were made using chi-squared or Fisher's exact tests where appropriate. Statistical significance was set at $p \leq 0.05$. Additional details are described in the methods section. [†] Five study participants did not complete the survey, two interviews were discontinued before the patient acceptability survey by the interviewer for safety reasons and three patients could not complete the patients acceptability survey due to time constraints.				

Table 3.4: Staff Characteristics and Acceptability Questionnaire Responses	
3.4A) Staff Characteristics (n=20)	
Age (Mean (years)), (SD)	35.0 (10.1)
Job Title (%), (n)	
Drug & Alcohol Technician	25.0 (5.0)
Physician	25.0 (5.0)
Social Worker	20.0 (4.0)
Clinical Therapist/Counselor	20.0 (4.0)
Nurse	5.0 (1.0)
Clinical Coordinator	5.0 (1.0)
Years Worked in Current Position (mean), (SD)	3.4 (4.8)
Total Years in AOD* Field (mean), (SD)	9.2 (8.0)
3.4B) Acceptability Questionnaire Responses (Frequency) (%)	
The information provided by the safety screen is useful to clinical practice.	
Disagree	1 (5.0)
Neither disagree nor agree	0 (0.0)
Agree	19 (95.0)
Information provided on the safety screen changed how I treated the patient.	
Disagree	3 (15.0)
Neither disagree nor agree	8 (40.0)
Agree	9 (45.0)
The safety screen places unnecessary burden on the clinical staff.	
Disagree	16 (80.0)
Neither disagree nor agree	4 (20.0)
Agree	0 (0.0)
The safety screen places unnecessary burden on the patient.	
Disagree	14 (70.0)
Neither disagree nor agree	6 (30.0)
Agree	0 (0.0)
Which patients should receive safety screening?	
All patients	17 (85.0)
High risk patients only	1 (5.0)
Done at the discretion of the physician	2 (10.0)
None	0 (0.0)
Is the self-harm assessment useful for clinical practices (% Yes)	20 (100.0)
Should the patient safety screen become part of clinical practice? (% Yes)	19 (95.0)
4C) Staff Acceptability Open-Ended Questions (Frequency) (%)	
Please explain how the information did or did not change how you treated the patient.	10 (50.0)
What improvements could be made to the safety screen to make it more useful in clinical practice?	7 (35.0)
What aspects of the safety screen did you find the most useful?	13 (65.0)
What barriers might prevent the patient safety screen from being implemented into routine clinical practice?	11 (55.0)
Should the patient safety screen become part of clinical practice?	12 (60.0)
Table 4: Comparisons were not made between treatment facilities due to small sample size recruited for this portion of the study. Open-ended question responses are reported in Figure 2. Additional details are provided in the methods section. *AOD=Alcohol or Drug	

Figure 3.1: Recruitment Diagram

Figure 3.2: Open-ended Response Summary from Staff Acceptability Questionnaire

Chapter 4

4 Distinguishing Clinical Factors Associated with Unintentional Overdose, Suicidal Ideation, Suicide Attempt, and Opioid Use Disorder

4.1 Abstract

Background: Both suicide and opioid use disorder (OUD) represent significant threats to public health. Premature mortality due to opioid-related overdose and suicide continues to rise in the United States. *Objective:* The objective of this study is to examine the clinical factors that may distinguish three patient groups: 1) unintentional overdose(s) (OD), 2) suicidal ideation or suicide attempt(s) (SI/SA), and 3) suicidal ideation or suicide attempt and unintentional overdose (SI/SA/OD). *Design:* This was a cross-sectional study conducted in a subset of subjects recruited from two inpatient addiction treatment facilities (n=66). *Methods:* Subjects were categorized as having a history of unintentional OD (n=13); SI/SA (n=33); or SI/SA/OD (n=20). Multinomial logistic regression models were used to determine whether adverse childhood experiences, self-injurious behaviors, substance use history, overdose history, and past year stressful life events were differentially associated with history of SI/SA/OD. *Results:* Overall, 19.7% of the study sample reported an overdose, while 50.0% reported SI/SA, and 30.3% reported SI/SA/OD. Subjects in the overdose group were more likely to have used heroin in the 24-hours preceding their most recent overdose compared to either the SI/SA or SI/SA/OD groups. In the multivariable model, subjects with history of SI/SA had higher adverse childhood experience scores and more subjects with history of SI/SA endorsed childhood physical abuse and teen dating violence. *Conclusions:* Overall, history of overdose is distinct from suicidal ideation and attempt. However, patients with SI/SA/OD appear to have greater clinical severity. More thorough evaluation of drugs involved in overdose and history of self-injury may help distinguish future risk and better inform treatment planning. More thorough evaluation of drugs

involved in overdose and history of self-injury may help distinguish future risk and better inform treatment planning.

4.2 Introduction

Premature mortality due to opioid-related overdose and suicide represent a significant threat to public health in the United States (U.S.) across all age groups; both of which are leading causes of injury death that have continued to rise over the past decade (Connery et al., 2019; Bohnert & Ilgen, 2019; Oquendo and Volkow, 2018). However, since drug overdose is the third most frequently used method of suicide the overlap between unintentional overdose and suicide is often murky (Centers for Disease Control and Prevention, 2017). Large population studies confirm that individuals with OUD, who survive an opioid-related overdose, remain at significantly elevated risk for repeat, fatal overdose (Olfson et al., 2018b) and death by suicide (Bogdanowicz et al., 2016; Olfson et al., 2018a). Multiple clinical factors are associated with opioid-related overdose and/or suicidal behavior among individuals with OUD, including use of heroin (Dai et al., 2019; Darke et al., 2015; Hakansson et al., 2008; Park et al., 2018), history of injection drug use (IDU) (Bohnert et al., 2011; Hakansson et al., 2008), polysubstance use (Bohnert et al., 2011; Bradvik et al., 2009; Darke et al., 2004; Jonsson et al., 2007), benzodiazepine use (Bohnert et al., 2017; Darke, 1996; Hakansson et al., 2008; Jones and McAninch, 2015), co-occurring psychiatric disorder (Bohnert et al., 2017; Darke et al., 2004, 2015; Maloney et al., 2007), history of sexual/physical trauma (Bohnert et al., 2011; Darke et al., 2004; Stein et al., 2017), violence directed toward others (Bohnert et al., 2011; Hakansson et al., 2008), and history of suicide attempt or persistent suicidal ideation (Darke et al., 2004, 2007; Hakansson et al., 2008; Maloney et al., 2007; Pan et al., 2014).

A 2010 review by Bohnert and colleagues reported that overdose and suicide are distinct, yet potentially related events. This review cited that the primary association between overdose and suicidal behaviors was based upon a single study by Darke and Ross in 2001, which found that individuals who had overdosed were also more likely to have attempted suicide, compared to those who had never overdosed. However, this association was largely explained by overdose as a method of suicide attempt, and when intentional overdose cases were removed from the analysis, it was no longer statistically significant (Darke & Ross, 2001). Furthermore, when examining individuals with non-fatal overdoses and suicide attempts separately, both groups had worse psychological and social functioning as well as more severe drug-related problems (Bohnert et al., 2010). Patients with a history of both overdose and suicide attempt have significantly impaired functioning and increased severity in substance use, which necessitates delivery of higher intensity services compared to their peers without either previous suicide attempt(s) or overdose (Bohnert et al., 2010). Individuals with OUD who attempt suicide by drug overdose are more likely to use prescription medications, cocaine, alcohol, and sedatives; whereas, heroin is more likely to be used in unintentional overdoses (Bohnert et al., 2010; Pfab et al., 2006; Ravndal and Vaglum, 1999; Schifano et al., 2006). Existing research has not adequately accounted for precursory events and behaviors, such as trauma and self-injury, which may contribute to the intersection between overdose and suicide. Poor social functioning, psychiatric decline, and higher severity of substance use are overlapping risk factors for overdose and suicide that require further investigation.

Nonfatal overdoses are associated with increased acute care utilization and elevated risk of subsequent mortality. Between 2005 and 2014, opioid-related emergency department visits in the U.S. nearly doubled, while hospital admissions related to opioid use increased by nearly two-

thirds (Weiss et al., 2016). This has resulted in increased clinical interest in characterizing the subsequent risk of overdose and non-overdose related causes of death (Olfson et al., 2018). Previous research has shown that OUD is associated with an elevated risk of premature mortality (Pierce et al., 2015). In the year after a nonfatal opioid overdose, patients died at approximately 24 times the rate of the general population (Olfson et al., 2018). Beyond stabilizing patients after nonfatal opioid overdoses, clinicians in acute care settings have opportunities to initiate medications for treatment of opioid use disorder and engage patients in ongoing treatment, harm reduction, or specialty addiction services (D’Onofrio et al., 2017). After a nonfatal overdose, men, but especially women, were at exceptionally high risk of suicide. In a recent study of veterans, the association between OUD and suicide was significantly stronger among women (Bohnert et al., 2017). The rate of suicide during the first-year post overdose, for women (29.3 per 10 000 person-years), resembled the rate of suicide following the year after SIB (30.9 per 10 000 person-years) (Olfson et al., 2017). Although SIB and nonfatal overdose are distinct behaviors that utilize different prevention strategies, they can co-occur within an individual, and careful clinical assessment may be necessary to delineate them. A high risk of suicide after nonfatal opioid overdose underscores the importance of careful mental health assessment with appropriate follow-up for selected patients (Oqueno et al., 2017). Understanding these risks could inform efforts to provide preventive and potentially lifesaving medical care after a nonfatal opioid overdose and better integrate mental health care with the treatment of OUDs.

The objective of this study is to examine the clinical profiles of three patient groups: 1) unintentional overdose (OD), 2) suicidal ideation and suicide attempt (SI/SA), and 3) suicidal ideation, suicide attempt, and unintentional overdose (SI/SA/OD). These objectives were accomplished by examining the age of onset of substance use, age of initiation of SIB, last

episode of self-injury, ACE domain scores, and past year stressful life experiences for each of the three groups. Previous research has found an association between higher ACE scores and younger age of onset of opioid use, recent injection drug use, and lifetime overdose (Stein et al., 2017). Likewise, studies have reported that higher ACE scores are associated with increased risk of suicidal ideation and a suicide attempt (Dube et al., 2001; Thompson et al., 2019). Based on previous research, it is hypothesized that perceived stressful life events will be associated with SI/SA while ACE domain scores will be an overlapping factor in both SI/SA (Chen et al., 2010) and the unintentional overdose groups (Stein et al., 2017). Furthermore, subjects with more recent episodes of SIB will represent the group with a more severe behavioral profile (i.e., SI/SA/OD) who engage in more high-risk behaviors and require higher levels of care.

4.3 Methods

Study Design

This was a cross-sectional study conducted in a subset of subjects recruited as part of a larger inpatient study. The original study recruited inpatients with OUD to test the acceptability of an integrated suicide and overdose screen.

Setting

A convenience sample of patients with an OUD was recruited from two treatment programs associated with a university-based health care system in West Virginia. One facility is an 18-bed acute inpatient dual-diagnosis unit that treats individuals who: 1) need medically managed detoxification and 2) are a danger to themselves or others (i.e., suicidal ideation/suicide attempt and/or homicidal ideation or actions). The second site is a 28-day residential addiction treatment program.

Data Collection

Study Sample.

The parent study recruited subjects (n=113) between February 2019 and October 2019. Patients were included in the study if they had an opioid use disorder, were psychiatrically stable, and were over the age of 18 years old.

Participation was voluntary, and subjects were not compensated for study participation. Only subjects that self-reported suicidal ideation in the past two weeks, an overdose in the past six months, and/or a suicide attempt in the past six months, were included in this study (n=66).

Measures

Administrative Clinical Data

Demographic (sex, race, ethnicity, education, and number of lifetime arrests), clinical characteristics, substance use history, ACE sub-scores, and ACE total score were extracted from an administrative clinical database (Winstanley et al., 2020). Race was recoded into a dichotomous variable (white/non-white); because the sample was predominantly white and had little variability. Employment was also recoded into a dichotomous variable (employed full/part-time or unemployed). Education was recoded into a categorical variable (less than high school education, high school graduate/GED, or some college/college graduate). Substance use history was recoded as lifetime use (yes/no) for tobacco, alcohol, cocaine, marijuana, heroin, prescription opioids, illicit/non-medical use of buprenorphine, methamphetamines, and benzodiazepines. This history also included age of first use for each substance endorsed by the subject, and lifetime injection drug use.

Adverse Childhood Experiences.

The clinical administrative database included a modified version of the adverse childhood experiences (ACEs) questionnaire (Winstanley et al. 2020). ACEs measure different types of childhood adversities experienced before age 18 and higher scores are associated with overdose and suicidal behaviors (Chen et al., 2010; Stein et al., 2017; Thompson et al., 2019). The modified ACE has 17 items that were grouped into the following categories of adverse experiences: mental health problems; alcohol or drug use; emotional, physical or sexual abuse; neglect; physical or emotional abuse by a significant other (teen dating abuse), and family dissolution. A total ACE score was generated by summing the number of categories endorsed.

Self-Harm Assessment

This assessment was a 30-minute face-to-face interview, which included information on drugs used prior to last overdose, past year stressful life events, self-harm behaviors, suicidal ideation, and suicide attempts. Global mental health was assessed using the Patient Reported Outcomes Measurement Information System (PROMIS) item, “In general, how would you rate your mental health, including your mood and ability to think?” This was rated on a 5-point Likert scale from poor to excellent (Cella et al., 2010). Due to the distribution of responses, “excellent,” “very good,” and “good were collapsed into one category to create the following three categories: 1) “good,” 2) “fair,” and 3) “poor.” Two items from the Beck scale for suicidal ideation (Beck et al., 1979). The first item was “how you have been feeling over the past week, including today” and the response options were 1) “I have a moderate to strong wish to live,” 2) “I have a weak wish to live,” or 3) “I have no wish to live” and it was recoded as moderate/strong wish to live or weak/no wish to live. For the second item asked how he or she was feeling in the past week and the response options were 1) “I would try to save my life if I

found myself in a life-threatening situation,” 2) “I would take a chance on life or death,” or 3) “I would not take the steps necessary to avoid death if I found myself in a life-threatening situation.”

Overdose Assessment

For this study, an opioid overdose was defined as “when you cannot breathe and cannot wake up without medical help.” Irrespective of when the overdose occurred, subjects who endorsed ever having an overdose, were asked 10 questions that queried details about their most recent overdose. They were asked to report their age of first overdose and the number of overdoses they have experienced in their lifetime. Subjects were asked for the date of their most recent overdose, the location where the overdose occurred and, if it was the first time they experienced an overdose (yes/no). Subjects were also asked if their most recent overdose was an accident (yes/no). They were further asked if they used alcohol (yes/no), prescription drugs (yes/no), street drugs (yes/no), and/or over the counter medications (yes/no) in the 24-hours prior to their overdose. For each category that the subject reported “yes,” he/she was asked to specify the name of the substance used. Drugs and medications used were categorized as antidepressants, antipsychotics, benzodiazepines, cocaine, prescription opioids, heroin, methamphetamines, and sedatives. Subjects were asked if naloxone was used to revive them (yes/no); did anyone do anything to help you when you last overdosed (yes/no); if measures were taken to help you during your last overdose, what were these helpful measures (open-ended); if counseling or overdose education was provided after the overdose (yes/no); and if the patient would like any additional services (yes/no).

Life Events Checklist

Stressful life events were measured using a modified Life Events Checklist (LEC), which measures life events that adults often find difficult or stressful in the past year. These events included experiencing a natural disaster, fire or explosion, transportation accident, serious accident, exposure to a toxic substance, physical assault, assault with a weapon, sexual assault, unwanted sexual experience, combat exposure, captivity, severe human suffering, sudden violent death, sudden accidental death, serious injury or harm the person inflicted on another person, and/or any other very stressful event or experience (Weathers et al., 2013). The original 17-item LEC was modified by the inclusion of an additional item on dissolution of a romantic relationship in the past year. This item was added because research has found that ending of a romantic relationship is a stressful event that is associated with suicide attempt (Dragisic et al., 2015; Heale et al., 2003). The LEC has five response items and subjects were instructed to select all options that applied for each event over the course of their lifetime. For this study, subjects were instructed to only consider these events for the past year instead of over the course of their lifetime and to only choose one response instead of choosing all responses that apply (Weathers et al., 2013). For the purposes of this study, a total score was generated to reflect the number of stressful life events in the past year. Each response was assigned a numeric value: (a) it happened to you personally=3, (b) you witnessed it happen to someone else=2, (c) you learned about it happening to someone close to you=1, (d) you're not sure if it fits (coded as missing), or (e) it doesn't apply to you=0. For the questions on sudden violent death (for example, a homicide or suicide) and sudden accident death, witnessing it happen to someone else was scored as 3 and learning about it as 2, since these events could not directly happen to the subject or participant. The LEC items were summed to generate a total score, which ranged from 0-54.

Self-Injurious Behaviors Assessment

The non-suicidal self-injury section of the *Self-Injurious Thoughts and Behaviors Interview* (SITBI-SF) (Nock et al., 2007) was used to measure SIB and evaluate lifetime suicidal ideation. Lifetime suicidal ideation was measured using the first three questions from the SITBI-SF suicidal ideation section. Self-injurious behaviors were measured using all questions from the SITBI-SF included in the non-suicidal self-injury portion of the interview. The questions related to suicide plan, attempt, and gesture were omitted for the purposes of this research study.

Suicidal Behaviors Assessment

Additional suicidal behaviors were evaluated using the suicide behaviors questionnaire-revised form (SBQ-R) (Osman et al, 2001). This tool uses four questions that ask patients if they have ever thought about or attempted suicide, how often they have thought about suicide in the past year, if they ever told another person they might attempt suicide, and how likely is it they would attempt suicide in the future. For the last question, the response options are never, no chance at all, rather unlikely, unlikely, likely, rather likely, and very likely. For analytic purposes, the categories of never/no chance at all, rather unlikely/unlikely, and likely/rather likely were collapsed into four response options. SBR-Q scoring is calculated using the original responses, without alteration of the response categories. This tool is used to identify suicide risk and risk behaviors, yielding a score ranging from 3-18, among inpatients (Osman et al., 2001), A score of greater than or equal to eight classified inpatients as having increased suicide risk with 80% sensitivity (true-positivity) and 91% specificity (true-negativity).

Data obtained during the patient interview was entered into a REDCap (Remote Electronic Data Capture) database, using an encrypted tablet computer. If an immediate crisis was identified (i.e., patient discloses intent to harm themselves, others, or discloses current

suicidal ideation/plan), the attending physician and charge nurse were notified immediately. The duration of the total screening and interview time was approximately 40-50 minutes.

Data Analysis

The outcome variable was based on patient self-report of suicidal ideation in the past two weeks, overdose in the past six months, and/or suicide attempt in the past six months. This information was used to create the following mutually exclusive categories: 1) unintentional overdose(s) only (no suicidal ideation in the past two weeks or attempt in the past six months); 2) suicidal ideation (past two weeks), suicide attempt (past six months) (SI/SA); and 3) unintentional overdose, suicidal ideation, and suicide attempt(s) including intentional overdose (SI/SA/OD). Descriptive statistics were used to summarize the sociodemographic and clinical characteristics of the sample. Medians were reported for variables that were not normally distributed, except for age. Statistical analysis employed using Pearson's chi-square tests for categorical variables, ANOVAs for means, and Kurskal-Wallis H-test to compare medians with Dunn's test post-hoc analysis.

Bivariable analysis was conducted with 47 variables, including ACE category scores, total ACE domain score, each item of the LEC, LEC-total score, SIB behavior measures, lifetime overdose(s), substances used 24-hours prior to overdose, suicidal behaviors, hopelessness, and social support. Two multinomial logistic regression models were built (adjusted and unadjusted) with the SI/SA group as the base outcome. The unadjusted multinomial logistic regression examined ace total category score, past year work accident, past year sexual assault, past year combat exposure, hitting, depression in the past two weeks, and hopelessness in the past two weeks. The second model was an adjusted model that controlled for age and sex while examining ACE total category score, past year work accident, past year sexual assault, past year combat

exposure, hitting, depression in the past two weeks, hopelessness in the past two weeks, and global social support score. Data analysis was conducted using Stata/SE 15.0 analytical software (StataCorp, 2017).

4.4 Results

The sample included 66 subjects that endorsed suicidal ideation in the past two weeks, an overdose in the past six months, and/or a suicide attempt in the past six month; 19.7% (n=13) reported unintentional OD, 50.0% (n=33) SI/SA and 30.0% (n=20) SI/SA/OD. The overall sample was predominantly male (65.2%), white (93.4%), non-Hispanic (93.4%), unemployed (74.2%), and had a high school education (50.0%). There were no statistically significant group differences in the demographic characteristics (data not shown).

With respect to lifetime substance use, the only statistically significant differences were for cocaine and prescription opioid use. The OD group more likely to have used lifetime cocaine use during their lifetime (100.0%) compared to either of the other two groups (SI/SA=72.7%, SI/SA/OD=95.0%, $p=0.02$). For the overall sample, the mean age of initiation of prescription opioids was 18.4 years ($SD=7.4$). The mean age of initiation of heroin use was 24.7 years ($SD=9.8$). The SI/SA group was more likely to have used prescription opioids during their lifetime (97.0%) compared to the unintentional OD group (69.2%) or the SI/SA/OD group (90.0%, $p=0.03$). There were no statistically significant group differences in age of onset of drug use (see Table 4.1). Age of first prescription opioid use preceded onset of heroin use for all groups (Table 4.1). There groups did not differ in terms of recent (past month) drug use, injection drug use, age of first overdose or number of overdoses. With respect to substances used in the 24-hours prior to the most recent overdose, the five most commonly used substances were

heroin (67.4%), benzodiazepines (21.7%), alcohol (20.0%), prescription opioids (19.6%), and methamphetamine (15.2%).

Only two substances reported in the 24-hours prior to overdose were found to be statistically significantly different between groups: antipsychotics and heroin. In the 24-hours prior to their most recent overdose, 30.7% of the SI/SA group reported using an anti-psychotic medication compared to 7.7% in the OD group and no one in the SI/SA/OD group reported using anti-psychotic medications prior to their last overdose ($p=0.02$). For the OD group, 92.3% reported using heroin prior to their most recent overdose compared to 30.7% of subjects in the SI/SA and 75.0% in the SI/SA/OD group ($p<0.01$) (see Table 4.1).

The SI/SA group were more likely to report physical abuse (93.9%), than either the OD group (46.2%) or the SI/SA/OD group (85.0%; $p<0.01$). Teen dating violence was reported more frequently by subjects in the SI/SA (93.9%), than either the unintentional OD group (46.2%), or the SI/SA/OD group (85.0%; $p<0.01$). Overall, the SI/SSA group had a higher mean ACE score (mean=5.5) compared to either the OD group (mean=4.0) or the SI/SA/OD group (mean=5.0, $p=0.04$). No statistically significant differences were observed with respect to cumulative mean past year stressful life event (LEC score) scores or individual LEC items (Table 4.2).

The overall sample had a median number of lifetime SIBs of 15. The OD group reported more lifetime SIBs (median=20) compared to the SI/SA group (median=45, $p=0.05$) (Table 4.3). No statistically significant difference was observed for mean age of first SIB, last occurrence of SIB, or type of SIB. with 40.6% of subjects in the SI/SA group reporting hitting themselves on purpose compared to 30.0% of the SI/SA/OD group and 7.7% of subjects in the unintentional OD group.

The unintentional OD group was more likely to report a moderate/strong wish to live (100.0%), compared to either the SI/SA (63.6%) or SI/SA/OD group (65.0%, $p=0.02$) (Table 4.4). Last occurrence of suicidal ideation more frequently occurred in the past month for the SI/SA (90.9%) and SI/SA/OD groups (68.4%) whereas more of the unintentional OD group reported suicidal ideation more than a year ago (50.0%, $p=0.02$). There was no statistically significant difference in terms of mean age of first suicidal ideation or median lifetime episodes of suicidal ideation. There was however, a statistically significant difference between groups for last occurrence of suicidal ideation ($p<0.01$; Table 4.4). In the past month 75.8% of subjects reported suicidal ideation in the past month. The largest portion of subjects reporting past month suicidal ideation were those in the SI/SA group (90.9%), followed by the SI/SA/OD group (68.4%), and the unintentional OD group (16.7%; Table 4.4). Results of suicidal behaviors are reported in Table 4.4 and the OD group never attempted suicide; 69.7% of the SI/SA group and 45.0% of SI/SA/OD group reported lifetime suicide attempt with hope to die ($p<0.01$; Table 4.4).

The following covariates were statistically significant in the bivariable regression models: ACE score, work accidents (past year), sexual assault (past year), past year combat exposure, (past year), hitting (lifetime), depression (past two weeks), hopelessness (past two weeks), and global social support measures (data not shown). ACE score ($p=0.05$), work accident ($p<0.01$), sexual assault ($p<0.01$), combat exposure ($p<0.01$), and hopelessness ($p=0.03$) remained statistically significant in the unadjusted regression model between the OD and SI/SA groups. For subjects with SI/SA/OD there was a statistically significant difference for past year work accidents ($p=0.02$) and combat exposure ($p<0.01$) when compared to subjects with SI/SA (see Table 4.5).

In the adjusted (adjusting for age and sex) multivariable model past year work accidents ($p=0.02$) and combat exposure ($p<0.01$) for subjects in the SI/SA/OD group compared to the SI/SA group (see Table 4.5). The OD group compared to the SI/SA group for ACE score ($p=0.03$), work accident ($p<0.01$), sexual assault ($p<0.01$), and combat exposure ($p<0.01$).

4.5 Discussion

This study found that clinical characteristics and life event differences do exist between treatment-seeking adults with OUD with history of SI/SA/OD. While the national focus is on unintentional overdoses among individuals with OUD, this study found 50% had a history of suicidal ideation or attempts and 19.7% had a history of only unintentional overdose. This indicates that greater attention be paid to factors contributing to co-morbid OUD and suicidal behaviors. Specifically, as it applies to substances used prior to overdose, adverse childhood experiences (ACEs), history of stressful life events, and self-injurious behaviors.

Consistent with previous research (Vingoe et al., 1999; Maloney et al., 2007; Neale, 2000), heroin is infrequently used as a method of suicide or in self-reported intentional overdoses. Even in samples where heroin was reported in the overdose, it was significantly more likely to be used in an accidental overdose than a deliberate overdose (Maloney et al., 2007; Neale, 2000).

Another finding, consistent with previous research, is that subjects with SI/SA/OD and SI/SA reported a higher prevalence of lifetime prescription opioid use than subjects with unintentional overdose (Hakansson et al. 2010; Roy 2002). However, rates of antipsychotic use could in part be explained by the large number of subjects recruited from an acute inpatient setting. Contrary to previous studies (Ilgen et al, 2009; Roy 2002; Roy 2010), this study found that subjects with unintentional overdose more frequently reported lifetime use of cocaine compared to subjects in the group with SI/SA. However, use of cocaine among individuals in the unintentional OD group

contradicts previous studies which found significant associations between cocaine use among individuals with OUD who attempted suicide (Ilgen et al, 2009; Roy 2002; Roy 2010). In our sample, the lack of association between cocaine and suicide attempt may be explained by lack of racial heterogeneity. Additionally, the SI/SA group reports overall less use of methamphetamine, cocaine, and heroin compared to the unintentional OD group, but higher use of antidepressants, antipsychotics, and benzodiazepines. Among subjects in the current study, in addition to heroin, the most frequently reported drug taken in the 24-hours prior to overdose among subjects with SI/SA was antipsychotics. Overall patterns of substance use may be indicative of time in treatment, more utilization of mental and/or behavioral healthcare services, which may limit access to other illicit substances. However, length of stay and healthcare utilization were not measured in the current study. Although specific mental health diagnoses were not recorded as part of the current study, considering the recruitment setting (acute inpatient treatment and 28-day residential treatment programs), it is possible that participants may receive psychiatric medication interventions where the medication can be used in a suicide attempt (Bohnert & Ilgen, 2019).

Individuals in the SI/SA group had higher ACE scores and were more likely to have experienced physical abuse or teen dating violence before the age of 18, which is consistent with previous research (Hakansson et al., 2006; Roy, 2002; Darke et al, 2012). While previous research has demonstrated a connection between childhood sexual abuse and the risk of overdose among individuals with OUD (Molnar et al., 2001; Roy, 2002), interestingly our study found that sexual abuse in the past year more strongly associated with unintentional overdose. These patterns of abuse both inside and outside the home could be associated with low levels of family

support, high levels of hopelessness, and perpetuating cycles of depression and hopelessness that contribute to resulting suicidal behaviors (Bradvik et al., 2007; Chen et al., 2009).

Moreover, self-injurious behaviors are one of the most important risk factors for future suicide and are often even more predictive than a history of suicidal ideation (Cavanagh et al., 2003). As seen with previous research (Darke et al., 2012), this study found that the mean age of onset for SIB (14 years old) preceded the mean age of onset of suicidal ideation (21 years old). Most research reports first SIB in early adolescence (Maloney et al., 2010) while this was true for the unintentional overdose group, the SI/SA and SI/SA/OD groups had mean age of onset of SIB occurring later at age 16.7 and 16.9 respectively. Furthermore, more individuals in the SI/SA group engaged in SIBs in the past month compared to either the SI/SA/OD group or the unintentional OD group where no participants reported any SIBs in the past month. While these results were not statistically significant, they are clinically meaningful in that participants engaging in SIB also reported suicidal behaviors more frequently than those without any SIBs in the prior month.

Limitations

We acknowledge this study has several limitations. First, despite specification of opioid overdose as “decreased respiratory depression,” subjects reported non-opioid related overdoses. Lifetime suicidal ideation was assessed using retrospective self-reporting and recall bias may be problematic. Recall bias could have also influenced reporting of substances used in the 24-hours prior to the most recent overdose, since the time period between interview and date of the subject’s last overdose was variable. Additionally, length of stay and healthcare utilization were not measured in the current study. This limited our ability to examine or extrapolate any causal relationships between past 30-day substance use with outcome behaviors such as overdose,

suicide attempt, suicidal ideation, and self-injurious behaviors. Likewise, the sample size was small limiting this study to be conducted as exploratory research and hence the power to detect group differences was not calculated. Our sample was predominantly white and included residents residing in a non-urban Appalachian area, which may limit generalizability regarding different demographic groups and subjects receiving outpatient OUD treatment.

Future Research

There are several future directions suggested by this research. First, the results such more in-depth investigation of overdose typologies that differentiate overdose intentionality and specification of substances used. Prospective studies are needed to understand causality and model the dynamics of intentionality, as well as account for how impulsivity may moderate the association. Moreover, unintentional overdoses and suicidal behaviors were found to be associated with wish to live and SIB. These results have the potential to inform clinical interventions and harm reduction strategies as it may help identify intentionality. These patients may utilize multiple methods for suicide attempts further complicating the determination of overdose intentionality. This issue warrants further investigation not only from an intentionality perspective, but also to develop more effective harm reduction strategies.

4.6 Conclusions

Results from this study partially elucidated differences clinical and behavioral differences between OUD patients with a history of unintentional overdose versus suicidal ideation/attempt. Whereas, subjects with a history of SI/SA/OD represent a diverse group with potentially greater severity that would likely benefit from multimodal intervention. Despite, differences in substance use that distinguish intentional from unintentional overdoses, future research needs to focus on systematically addressing overdose typologies. Overall, this study highlights the

importance of addressing the contribution of history of self-injury, types of substances used the day of overdose, recent life stressors, and adverse childhood experiences for both overdose and suicide among patients with opioid use disorders.

4.7 Acknowledgements

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Table 4.1: Overdose History and Substance Use Associated with Recent Overdose					
	Overall Sample (n=66)	Unintentional OD ¹ (n=13)	SISA ² (n=33)	SI/SA/OD ³ (n=20)	p-value
Characteristics					
Mean number substances used (Past 30 days), (SD) [†]	2.5 (1.5)	2.2 (2.0)	2.5 (1.2)	2.7 (1.7)	0.64
Ever Inject Drugs (%Yes, Lifetime)	75.8	84.6	66.7	85.0	0.26
Mean Age First IDU (SD) [†]	24.9 (9.2)	23.5 (8.5)	24.5 (9.0)	26.3 (10.1)	0.72
Median Number Overdoses	3.0	3.0	3.0	1.5	0.71
Mean Age First Overdose (SD) [†]	27.4 (11.0)	29.9 (11.8)	25.7 (9.9)	26.7 (11.5)	0.54
Substances Used 24 hours Prior to OD (% Yes)					
Alcohol	20.0	23.1	18.8	20.0	0.92
Antidepressants	10.9	7.7	23.1	5.0	0.36
Antipsychotics	10.9	7.7	30.7	0.0	0.02
Benzodiazepines	21.7	23.1	15.4	25.0	0.90
Cocaine	13.0	7.7	0.0	25.0	0.15
Prescription Opioids	19.6	15.4	23.1	20.0	1.00
Heroin	67.4	92.3	30.7	75.0	<0.01
Methamphetamine	15.2	23.1	7.7	15.0	0.69
Sedatives	2.2	0.0	0.0	5.0	1.00
Naloxone to reverse (% Yes)	52.4	76.9	41.7	41.2	0.11
¹ Unintentional Overdose= patients who self-reported only unintentional overdoses. ² SI/SA= patients who self-reported any of the following: 1) suicide attempt only, 2) intentional overdose only, 3) suicidal ideation and suicide attempt, 4) suicidal ideation and intentional overdose, 5) suicide attempt and intentional overdose, or 6) intentional overdose, suicidal ideation, and suicide attempt. ³ SI/SA/OD= patients who self-reported any of the following: 1) suicidal ideation, 2) suicidal ideation and intentional overdose, 3) suicide attempt and unintentional overdose, or unintentional overdose, suicidal ideation, and suicide attempt. Abbreviations: IDU=Injection drug use; OD=overdose; SA= suicide attempt; SD= standard deviation; SI= suicidal ideation [†] All ages noted with “+” were noted as means for ease of comparison, but nonparametric statistics were used for comparison as these samples did not follow a normal distribution. [†] This value does not include alcohol or tobacco. These values were excluded due to high rates of use. (alcohol, n=66 and tobacco, n=65).					

Table 4.2: Adverse Childhood Experiences (ACE) and Life Events Checklist (LEC) Scores					
	Overall Sample (n=66)	Unintentional OD¹ (n=13)	SISA² (n=33)	SI/SA/OD³ (n=20)	p-value
ACE Domains (% Yes)					
Mental Health Problems	63.6	38.5	75.8	60.0	0.06
Alcohol or Drug Use	77.3	61.5	81.8	80.0	0.37
Emotional Abuse	71.2	46.2	75.8	80.0	0.09
Physical Abuse	81.8	46.2	93.9	85.0	<0.01
Teen Dating Violence*	81.8	46.2	93.9	85.0	<0.01
Sexual Abuse	51.5	38.5	63.6	40.0	0.17
Neglect	93.9	100.0	97.0	85.0	0.12
Family Dissolution	65.2	69.2	69.7	55.0	0.52
Total mean ACE domain score (SD)	5.0 (1.7)	4.0 (1.7)	5.5 (1.4)	5.0 (1.9)	0.04
Total mean LEC score (SD)	11.7 (8.5)	10.8 (6.9)	11.7 (8.3)	12.1 (10.0)	0.90
¹ Unintentional Overdose = patients who self-reported only unintentional overdoses. ² SI/SA = patients who self-reported any of the following: 1) suicide attempt only, 2) intentional overdose only, 3) suicidal ideation and suicide attempt, 4) suicidal ideation and intentional overdose, 5) suicide attempt and intentional overdose, or 6) intentional overdose, suicidal ideation, and suicide attempt. ³ SI/SA/OD = patients who self-reported any of the following: 1) suicidal ideation, 2) suicidal ideation and intentional overdose, 3) suicide attempt and unintentional overdose, or unintentional overdose, suicidal ideation, and suicide attempt. *Define as physical or emotional abuse experienced by a significant other before the age of 18 years old. Abbreviations: ACE= adverse childhood experiences; LEC=life events checklist; OD=overdose; SA= suicide attempt; SD= standard deviation; SI= suicidal ideation					

Table 4.3: Measures of Ambivalence and Self-Injurious Behavior (SIB)					
	Overall Sample (n=66)	Unintentional OD¹ (n=13)	SISA² (n=33)	SI/SA/OD³ (n=20)	p-value
Wish to live					0.02
Moderate/Strong	71.2	100.0	63.6	65.0	
Weak/None	28.3	0.0	36.4	35.0	
Life Threatening Situation					0.71
Would try to save my life	60.6	76.9	54.6	60.0	
Would take a chance on life/death	30.3	23.1	33.3	30.0	
Would not avoid death	9.1	0.0	12.1	10.0	
History of SIB (% Yes)	37.9	23.1	42.4	40.0	0.56
Mean age first SIB+	16.4 (6.8)	14.0 (1.0)	16.7 (8.3)	16.9 (5.4)	0.66
Median lifetime episodes SIB	15.0	20.0	45.0	5.0	0.05
Last occurrence of SIB					0.73
In past month	28.0	0.0	35.7	25.0	
Past 2-12 months	40.0	33.3	42.9	37.5	
More than a year ago	32.0	66.7	21.4	37.5	
SIB Behaviors (% Yes)					
Cutting	33.9	15.4	40.6	35.0	0.30
Hitting oneself on purpose	30.8	7.7	40.6	30.0	0.08
Hair pulling	18.5	7.7	28.1	10.0	0.22
Self-tattooing	13.9	7.7	15.6	15.0	0.90
Picked a wound	21.5	7.7	31.3	15.0	0.20
Burning	15.4	7.7	21.9	10.0	0.48
Inserted objects under nails or skin	4.6	0.0	9.4	0.0	0.30
Biting	9.2	0.0	15.6	5.0	0.32
Picked areas of body to point of drawing blood	13.9	0.0	18.8	15.0	0.32
Scraped skin	10.8	0.0	15.6	10.0	0.38
“Erased” skin to the point of drawing blood	6.2	0.0	6.3	10.0	0.66
Received medical treatment for SIB (% Yes)	40.0	33.3	42.9	37.5	1.00
¹ Unintentional Overdose = patients who self-reported only unintentional overdoses. ² SI/SA = patients who self-reported any of the following: 1) suicide attempt only, 2) intentional overdose only, 3) suicidal ideation and suicide attempt, 4) suicidal ideation and intentional overdose, 5) suicide attempt and intentional overdose, or 6) intentional overdose, suicidal ideation, and suicide attempt. ³ SI/SA/OD = patients who self-reported any of the following: 1) suicidal ideation, 2) suicidal ideation and intentional overdose, 3) suicide attempt and unintentional overdose, or unintentional overdose, suicidal ideation, and suicide attempt. Abbreviations: IDU=Injection drug use; OD=overdose; SA= suicide attempt; SD= standard deviation; SI= suicidal ideation <i>All ages noted with “+” were noted as means for ease of comparison, but nonparametric statistics were used for comparison as these samples did not follow a normal distribution.</i>					

Table 4.4: Measures Suicidal Behaviors (Suicidal Ideation and Attempt)					
	Overall Sample (n=66)	Unintentional OD¹ (n=13)	SISA² (n=33)	SI/SA/OD³ (n=20)	p-value
Mean Age first suicidal ideation (SD)+	21.0 (12.2)	23.3 (11.9)	20.6 (13.5)	20.8 (10.1)	0.64
Median episodes suicidal ideation	10.0	7.0	15.0	10.0	0.45
Last occurrence of suicidal ideation					0.02
In the past month	82.7	16.7	90.9	68.4	
Past 2-12 months	9.6	33.3	9.1	10.5	
More than one year ago	7.7	50.0	0.0	21.1	
Suicide Attempt(s) (% Yes)					<0.01
Never	28.8	100.0	9.1	15.0	
Brief, passing thought	10.6		12.1	15.0	
I had a plan once, but did not try	6.1		6.1	10.0	
I had a plan once, and really wanted to die	0.0		0.0	0.0	
I have attempted to kill myself, but did not want to die	6.1		3.0	15.0	
I have attempted to kill myself, and really hoped to die	48.5		69.7	45.0	
Frequency of Suicidal Ideation (% Yes)					0.55
Never/Rarely	7.5		3.9	14.3	
Sometimes	7.5		3.9	7.1	
Often/Very Often	85.0		88.5	78.6	
Disclosure of Suicide Attempt (% Yes)					0.91
No	50.0		53.9	42.9	
Yes, at one time, but did not want to die	5.0		3.9	7.1	
Yes, at one time, and really wanted to die	12.5		11.5	14.3	
Yes, more than once, but did not want to die	2.5		3.9	0.0	
Yes, more than once, and really wanted to die	30.0		26.9	35.7	
Likelihood of future suicide attempt (% Yes)					0.23
Never/No Chance	32.5		30.8	35.7	
Unlikely	37.5		30.8	50.0	
Likely	15.0		15.4	14.3	
Very Likely	15.0		23.1	0.0	
Mean Suicide Behaviors Questionnaire (SBQ-R) Total Score ⁺	8.2 (6.1)		10.8 (5.5)	8.7 (5.5)	0.15
¹ Unintentional Overdose = patients who self-reported only unintentional overdoses. ² SI/SA = patients who self-reported any of the following: 1) suicide attempt only, 2) intentional overdose only, 3) suicidal ideation and suicide attempt, 4) suicidal ideation and intentional overdose, 5) suicide attempt and intentional overdose, or 6) intentional overdose, suicidal ideation, and suicide attempt. ³ SI/SA/OD = patients who self-reported any of the following: 1) suicidal ideation, 2) suicidal ideation and intentional overdose, 3) suicide attempt and unintentional overdose, or unintentional overdose, suicidal ideation, and suicide attempt. Abbreviations: IDU=Injection drug use; OD=overdose; SA= suicide attempt; SD= standard deviation; SI= suicidal ideation <i>All ages noted with “+” were noted as means for ease of comparison, but nonparametric statistics were used for comparison as these samples did not follow a normal distribution.</i>					

Table 4.5: Multivariable Regression Model						
	Unadjusted Analyses					
	Unintentional OD			SI/SA/OD		
Variable	Coefficient	95 % CI	p-value	Coefficient	95 % CI	p-value
ACE total domain score	-0.5	-1.1, -0.01	0.05	-0.4	-0.9, 0.1	0.15
Work accident (past year)	-15.1	-18.3, -17.2	<0.01	2.1	0.3, 3.9	0.02
Sexual assault (past year)	-19.2	-21.2, -17.2	<0.01	-0.9	-2.9, 1.1	0.38
Combat exposure (past year)	-18.2	-21.6, -14.9	<0.01	-18.2	-21.1, -15.3	<0.01
Hitting	0.4	-2.1, 2.9	0.74	-0.2	-2.0, 1.6	0.9
Depression (past two weeks)	-0.4	-3.4, 2.5	0.78	-0.8	-4.0, 2.4	0.6
Hopelessness (past two weeks)	-3.0	-5.9, -0.2	0.03	-0.2	-2.6, 2.3	0.9
	Adjusted Analyses					
	Unintentional OD			SI/SA/OD		
Variable	Coefficient	95 % CI	p-value	Coefficient	95 % CI	p-value
Age	-0.1	-0.2, 0.03	0.15	-0.1	-0.2, -0.01	0.02
Sex	-0.7	-2.5, 1.1	0.43	-0.1	-1.6, 1.3	0.87
ACE total domain score	-0.6	-1.2, -0.1	0.03	-0.5	-1.03, 0.06	0.08
Work accident (past year)	-13.8	-17.0, -10.7	<0.01	2.1	0.3, 3.9	0.02
Sexual assault (past year)	-17.0	-19.6, -14.5	<0.01	-0.7	-2.6, 1.2	0.45
Combat exposure (past year)	-15.1	-20.3, -9.9	<0.01	-16.7	-19.2, -14.1	<0.01
Hitting	-1.2	-5.3, 2.8	0.56	-0.5	-2.2, 1.2	0.54
Depression (past two weeks)	-1.3	-4.5, 1.9	0.43	-1.5	-5.4, 2.5	0.47
Hopelessness (past two weeks)	-1.6	-4.4, 1.2	0.27	-0.6	-3.7, 2.4	0.69
Global social support score	-0.2	-1.7, 1.2	0.75	-0.6	-2.2, 0.9	0.42
Base Outcome: SI/SA= Suicidal Ideation & Suicide Attempt Abbreviations: ACE= adverse childhood experiences; CI=confidence interval; LEC=life events checklist; OD= overdose; SA=suicide attempt; SIB=self-injurious behavior; SI=suicidal ideation; SI/SA/OD= patients who self-reported any of the following: 1) suicidal ideation, 2) suicidal ideation and intentional overdose, 3) suicide attempt and unintentional overdose, or unintentional overdose, suicidal ideation, and suicide attempt.						

Chapter 5

5 Discussion of Findings and Research Implications

5.1 Summary

The literature review presented in this study is the first to include self-injurious behaviors to evaluate the relationship between suicide, overdose, and OUD. Results from this review provided the foundation for implementation of patient safety screening for overdose and suicide history in addiction treatment facilities. The mPSS is potentially the first screening tool to simultaneously assess suicide risk and overdose in these setting. Additionally, the brevity of the mPSS increases the probability of integration in routine clinical practice. Results from initial implementation of these screening procedures indicates that persistence of non-fatal SIB needs continued assessment over the course of the lifespan, paying attention to how these behaviors may evolve in adulthood. Furthermore, traumatic childhood events and past year stressful experiences are important in SIB assessment. Future research needs to address comprehensive discharge planning and risk management for both suicide and overdose. This includes provision of global social support, acute and long-term crisis management, and trauma informed care.

5.2 Strengths and Limitations

5.2.1 Strengths

Strengths of this study are that it includes the first systematic review to focus on self-injurious behavior, overdose, and suicidal behaviors. While several systematic reviews have studied these relationships to varying degrees in the past, this review is the first to examine literature that reports on overdose and SIB simultaneously. Additionally, this review examines precursory behaviors to suicide and overdose among individuals with a specific focus on OUD. This literature review was further used to inform a feasibility and acceptability study of the first

standardized tool for universal suicide and overdose screening for patients receiving addiction treatment services. Although, suicide screening and assessment is usually a part of standard mental healthcare procedures, behavioral health practices do not consistently evaluate additional self-harm and overdose behaviors. This study provided a standardized tool that could be integrated into clinical framework and address these aspects with one instrument. Finally, through examination of subjects who screened positive on the mPSS, patients could be separated into three distinct clinical groups: 1) unintentional overdose only, 2) suicidal ideation/suicide attempt, and 3) unintentional overdose/suicidal ideation/suicide attempt. This allowed for preliminary investigation of clinical and behavioral characteristics that may provide more insight for distinguish intentional and unintentional overdose. Elucidating these factors would ultimately have implications for treatment planning and risk reduction.

5.2.2 Limitations

This study has some potential limitations. In conducting the systematic review, the majority of studies was cross-sectional. Thus, temporal conclusions could not be drawn that linked onset of OUD with SIB, suicidal ideation, and/or attempted suicide. A large portion of the available data relied on self-report measures for attempted suicide history, overdose history, and some clinical data. Therefore, recall bias was a predominant research limitation. Furthermore, there is limited generalizability of the studies conducted among inpatient or outpatient treatment samples. Unknown is whether treatment seeking individuals have more functional impairments or experience more symptom severity than non-treatment seeking individuals.

Additionally, several limitations are associated with the studies conducted among patients receiving addiction treatment services. Recruiting subjects from an inpatient population may limit whether these results can be generalized to patients seeking treatment services in other

settings. The majority of the subjects recruited for this study was predominantly white and non-Hispanic, which may not generalize to other ethnic and demographic groups. All assessments were administered by members of the study team. However, in order to integrate these tools into clinical practice, members of the clinical team would need to administer the screening to patients or have patients self-administer the tool. This may require more individualized time from the staff, and increased cooperation from patients that could increase the burden on both patients and staff. To avoid the confounding effects of acute intoxication on our results, patients were not interviewed for at least 24-hours after admission. However, this cautionary measure may not be practical in all treatment settings. Likewise, despite specification of overdose as “decreased respiratory depression,” subjects reported non-opioid related overdoses. Lifetime suicidal ideation, overdose(s), and suicide attempt(s) were retrospectively self-reported, and thus recall bias may be a potential limitation.

5.6 Conclusions and Implications

The relationship between self-injurious behaviors, suicidal ideation, suicide planning, and suicide attempt has been investigated to varying degrees throughout the published literature. Individuals with these behaviors demonstrate decreased social function, psychiatric decline, and more severe substance. This finding provides crucial information for potential clinical intervention, treatment, and crisis management. However, there is still a lack of prospective longitudinal data that provide adequate temporal information between onset of OUD, SIB and/or suicide outcomes. Previous literature has found that patients with OUD at highest risk of attempted suicide and SIB tended to have more severe psychiatric profiles, be female, have increased rates of poly-drug use, and experienced significant life stressors and childhood maltreatment. In this study, 60% of patients screened positive on the mPSS, with 86% of subjects

screening positive on more than one factor. Further assessment found that approximately 20% of subjects experienced an unintentional overdose with no suicidal ideation, and 30% of the sample experienced all three events: an unintentional overdose, suicidal ideation, and at least one suicide attempt during their lifetime. Results from this study appear to be the most compelling between the unintentional overdose and suicidal ideation/suicide attempt group. Differences most commonly related to a history of lifetime substance use, substances used in the 24-hours prior to overdose, physical or emotional abuse during childhood, and frequency of lifetime SIB.

Overall, this study highlights the importance of addressing the contribution of history of self-injury, types of substances used the day of overdose, and ACEs for both overdose and suicide among patients with OUD. These patients may engage in a range of high-risk behaviors that further complicate developing effective risk reduction strategies and effective discharge planning. While there are distinctive characteristics between individuals that have unintentional overdoses only and individuals with suicidal ideation/suicide attempts without history of overdose; patients with a history of all three events may complicate the overall picture and require more complex clinical interventions. Despite, differences in substance use that distinguish intentional from unintentional overdoses, future research needs to focus on systematically addressing substance typologies in overdose. However, additional research is needed to determine whether screening improves the provision of services and reduces future associated self-injurious behavior. In general, the greater the burden of risk factors, the higher the risk for potential self-injury and attempted suicide.

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7. Appendices

7.1 Supplemental Figure (Chapter 2): Systematic Review Themes

7.2 Supplemental Figure (Chapter 3): Modified Patient Safety Screen

Modified Patient Safety Screener	
1. Over the past 2 weeks, have you felt down, depressed, or hopeless?	
☐ Yes ☐ No ☐ Patient unable to complete ☐ Patient refused	
2. Over the past 2 weeks, have you have you had thoughts of killing yourself?	
☐ Yes ☐ No ☐ Patient unable to complete ☐ Patient refused	
3. In your lifetime, have you attempted to kill yourself?	
☐ Yes ☐ No ☐ Patient unable to complete ☐ Patient refused	
3a. When did his happen?	
☐ Within the past 24 hours ☐ Within the past month (not including today) ☐ In the past 1-6 months ☐ More than 6 months ago ☐ Patient unable to complete ☐ Patient refused	
4. In your lifetime, have you ever overdosed?	
☐ Yes ☐ No ☐ Patient unable to complete ☐ Patient refused	
4a. When did this happen?	
☐ Within the past 24 hours ☐ Within the past month (not including today) ☐ In the past 1-6 months ☐ More than 6 months ago ☐ Patient unable to complete ☐ Patient refused	

7.3 Supplemental Figure (Chapter 3)

Visualization of Positive mPSS Screening Responses

7.4 Supplemental Table (Chapter 4)

Table 4.1.1 Expanded Demographic Characteristics of mPSS Positive Sample					
	Overall Sample (n=66)	Unintentional OD ¹ (n=13)	SISA ² (n=33)	SI/SA/OD ³ (n=20)	p-Value
Characteristics					
Mean Age (years), (SD)	36.1 (9.5)	36.1 (9.3)	37.3 (9.6)	34.1 (9.7)	0.47
Sex (Male)	65.2	69.2	63.6	65.0	1.00
White	93.4	100.0	93.9	90.0	0.66
Non-Hispanic	93.4	100.0	90.9	95.0	0.81
Employed	25.8	23.1	21.2	35.0	0.57
Education					0.68
Less than High School	19.7	23.1	24.2	10.0	
High School Grad/GED	50.0	46.2	51.5	50.0	
Some College/College Grad	30.3	30.8	24.2	40.0	
Lifetime Arrests (Median)	5	3	3	6	0.88
Lifetime Substance Use (% Yes)					
Tobacco	98.5	100.0	97.0	100.00	1.00
Alcohol	100.0	100.0	100.0	100.0	-
Cocaine	84.9	100.0	72.3	95.0	0.02
Marijuana	97.0	100.0	97.0	95.0	1.00
Heroin	87.9	92.3	81.8	95.00	0.43
Prescription Opioids	89.4	69.2	97.0	90.0	0.03
Buprenorphine to get high	39.4	38.5	39.5	40.0	1.00
Methamphetamines/Amphetamines	87.9	84.6	87.9	90.0	1.00
Benzodiazepines	69.7	69.2	69.7	70.0	1.00
Mean age of Initiation of Substance Use (Years), (SD)					
Tobacco ⁺	13.1 (5.5)	13.4 (4.0)	13.2 (6.7)	12.8 (4.1)	0.92
Alcohol ⁺	13.8 (8.7)	12.5 (3.9)	15.1 (11.4)	12.7 (4.6)	0.55
Cocaine ⁺	18.7 (5.4)	20.7 (6.1)	18.0 (6.1)	18.2 (3.8)	0.42
Marijuana ⁺	14.5 (4.5)	14.5 (3.0)	15.1 (5.5)	13.4 (3.4)	0.47
Heroin ⁺	24.7 (9.8)	26.4 (12.6)	25.0 (9.2)	23.2 (9.1)	0.74
Prescription Opioids ⁺	18.4 (7.4)	17.3 (5.5)	19.1 (7.7)	17.8 (7.9)	0.41
Illicit use of Buprenorphine	25.6 (10.6)	23.6 (10.7)	25.5 (9.6)	26.9 (13.1)	0.87
Methamphetamines/Amphetamines ⁺	26.6 (8.9)	29.5 (9.4)	24.9 (8.3)	27.8 (9.4)	0.31
Benzodiazepines	21.4 (9.3)	19.8 (7.9)	22.5 (10.4)	20.5 (8.6)	0.79
Mean number substances used (Past 30 days), (SD)	2.5 (1.5)	2.2 (2.0)	2.5 (1.2)	2.7 (1.7)	0.64
Ever Inject Drugs (%Yes, Lifetime)	75.8	84.6	66.7	85.0	0.26
Mean Age First IDU (SD) ⁺	24.9 (9.2)	23.5 (8.5)	24.5 (9.0)	26.3 (10.1)	0.72
¹ Unintentional Overdose= patients who self-reported only unintentional overdoses. ² SI/SA= patients who self-reported any of the following: 1) suicide attempt only, 2) intentional overdose only, 3) suicidal ideation and suicide attempt, 4) suicidal ideation and intentional overdose, 5) suicide attempt and intentional overdose, or 6) intentional overdose, suicidal ideation, and suicide attempt. ³ SI/SA/OD= patients who self-reported any of the following: 1) suicidal ideation, 2) suicidal ideation and intentional overdose, 3) suicide attempt and unintentional overdose, or unintentional overdose, suicidal ideation, and suicide attempt. Abbreviations: IDU=Injection drug use; OD=overdose; OTC=over the counter; SA= suicide attempt; SD= standard deviation; SI= suicidal ideation ⁺ All ages noted with “+” were noted as means for ease of comparison, but nonparametric statistics were used for comparison as these samples did not follow a normal distribution.					

7.5 Supplemental Table Chapter 4: Not Included in Analysis

Supplemental Table: Life Events Checklist Item Analysis (Chapter 4)					
	Overall (n=66)	Unintentional OD (n=13)	SI/SA (n=33)	SI/SA/OD (n=20)	p-value
<i>Past Year Event (% Yes)</i>					
Relationship Dissolution	59.1	86.6	60.6	40.0	0.04
Natural Disaster	4.6	0.0	6.1	5.0	1.0
Fire	7.6	7.7	3.0	15.0	0.27
Work Accident	4.6	0.0	6.1	5.0	1.0
Car Accident	13.6	7.7	9.1	25.0	0.23
Exposure to Toxic Substance	18.2	15.4	18.2	20.0	1.0
Physical Assault	37.9	30.8	36.4	45.0	0.75
Assault with a Weapon	13.6	7.7	15.2	15.0	0.90
Sexual Assault	10.6	0.0	15.2	10.0	0.38
Unwanted Sexual Experiences	15.2	7.7	18.2	15.0	0.90
Combat Exposure	-	-	-	-	-
Captivity	15.2	7.7	12.1	25.0	0.42
Severe Suffering	34.9	30.8	27.3	50.0	0.26
Violent Death (witnessed)	4.6	0.0	6.1	5.0	1.0
Unexpected Death (witnessed)	15.2	15.4	21.1	5.0	0.35
Caused Harm or Death	7.6	0.0	9.1	10.0	0.70
Illness	34.9	38.5	27.3	45.0	0.38
Misc. Stressful Experiences	50.0	69.2	48.5	40.0	0.28
Supplemental Table: Response variables were recoded to yes or no. "Yes," was defined as having experienced or witnessed any of the events listed on the life events check list. All other responses were coded as "No." This was done due to small sample size and overall distribution of response rates.					