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Examining The Relationship Between Anxiety And Depression Symptoms, Protective Behavioral Strategies And Opioid Use Outcomes

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BY

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ABSTRACT

Protective behavioral strategies (PBS), behaviors individuals use to reduce negative consequences of substance use, have been shown to mediate and moderate the relationship between mental health and substance use outcomes. The present study aimed to examine the relationships between anxiety and depression symptoms and opioid PBS on risky opioid use and opioid-related consequences. Participants in this secondary data analysis were non-treatment seeking individuals who reported past-month opioid use (n=257). Structural equation modeling was used to examine 1) PBS as a mediator of the relationship between anxiety/depression symptoms and opioid use outcomes, and 2) anxiety/depression symptoms as a moderator of the relationship between PBS and opioid use outcomes. Despite significant correlations among many of the variables of interest, no statistically significant mediation or interaction effects were found. Given the statistically null findings, various methodological considerations are discussed, as well as future directions for this underexplored area of research.

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Introduction

The Opioid Epidemic in the US

Drug overdose deaths are at an all-time high in the United States. In 2020, 91,799 people in the US died of drug overdose and nearly 75% of these deaths involved an opioid (CDC, 2022). Although not a problem unique to the United States, overdose mortality rates in the US have been increasing rapidly in the past two decades (Ho, 2019). The US currently has the highest drug overdose mortality rate among high-income countries where painkillers and mortality data are accessible (Ho, 2019). In 2017, the CDC estimated the economic cost of opioid use disorder (OUD) and fatal opioid overdose in the US to be over $1,021 billion.

Myriad factors contribute to the magnitude of the current opioid epidemic, the first of which being a shift in the 1990's among the medical community to recognize pain as the "fifth vital sign" (Ostling et al., 2018). This shift resulted in the expansion of pain medicine as a field and encouraged physicians to prescribe painkillers for an increasingly long list of conditions (Conrad & Muñoz, 2010). Alongside this shift in the medical community, Purdue Pharma, the manufacturer of one of the most-prescribed opioids, spent hundreds of millions of dollars aggressively marketing OxyContin as a safe and effective form of pain management. In a 2002 US Senate hearing, it was estimated that Purdue Pharma spent over $200 million in marketing OxyContin in a single year (Goldenheim, 2002). Since that time, there have been three waves of opioid overdose deaths in the US, the first attributable to an increase in the prescription of opioids (CDC, 2011), the second to increased heroin overdoses (Rudd et al., 2014), and the third to synthetic opioids, such as fentanyl (CDC, 2022; Gladden et al., 2016).

In addition to overdose fatalities, individuals who use opioids in a risky manner are more likely to experience a range of adverse social, physical, and mental health issues. Individuals who use opioids are more likely to be incarcerated, exhibit violent behavior, and attempt suicide than the general population (Gholami et al., 2022). Risky opioid use is also associated with increased risk of premature death, accidental overdose, and infectious disease (Schukit, 2016). All these heightened adverse consequences make a compelling case for the need to identify those in the community at risk for OUD.

Relationship Between Opioid Use, Anxiety, and Depression

While much attention has been given to risky opioid use among individuals with chronic pain or pain-related health conditions, evidence also suggests that individuals with psychiatric issues are at high risk for hazardous opioid use and OUD. Several cross-sectional studies have displayed the correlation between depression and anxiety and opioid use in community samples (Becker et al., 2008; Huang et al., 2006; Sullivan et al., 2005). In one national sample of individuals with lifetime OUD, 52% also met criteria for major depression and 39% met criteria for at least one anxiety disorder in their lifetime (Grella et al., 2009). In another large nationally representative sample, it was found that 36% of individuals with OUD also had an anxiety disorder in their lifetime and 45% had major depression in their lifetime (Conway et al., 2006).

Only seven studies have been conducted examining the temporal relationship between anxiety and depression and opioid use/OUD, but it is thought to be a bi-directional relationship (Rogers et al., 2021). In one notable study with a large, nationally representative community sample, Martins and colleagues (2012) found support for a bi-directional pathway when testing the longitudinal correlations between mood and anxiety disorders and

non-medical prescription opioid use and OUD. The data suggested that non-medical prescription opioid use predicted future mood/anxiety disorders (a precipitational pathway), that mood/anxiety disorders predicted future non-medical prescription opioid use and OUD (self-medication pathway), and that due to the presence of both pathways, there is also the potential for shared vulnerability to mood/anxiety disorders and non-medical prescription opioid use and OUD. In a recent review of the literature, Roger and colleagues (2021) concluded that although the literature appears to suggest that the relationship between anxiety/depression and opioid use/OUD is bi-directional, greater attention to the temporal relationship between these variables is warranted. They went on to suggest that future research should focus on opioid-anxiety-depression relations and mediators of that relationship, which to date have been largely unexplored (Rogers et al., 2021). Among the many factors that may explain the co-occurrence of mood/anxiety disorders and risky opioid use, one potential explanation is the ways in which individuals protect themselves from harm.

Harm Reduction Efforts in the US

The harm reduction movement began in Europe in the 1970's and has been gaining traction globally (Marlatt, 1996; Marlatt & Witkiewitz, 2010). Harm reduction is a term that encompasses policy and program efforts designed to reduce adverse impacts associated with drug use at both the individual and community levels. Harm reduction does not necessarily focus on eliminating drug consumption (i.e., abstinence), but rather centers on ways to make it safer for individuals who use drugs through the provision of protection, treatment, and resources (Single, 1995; SAMHSA, 2022). As part of a compensatory model of addiction, harm reduction is designed to address various biopsychosocial risk factors for addiction and

is intended to be tailored toward what may be most useful to the individual (Brickman et al., 1982; Marlatt & Witkiewitz, 2010). This is an alternative to two predominant models seen in the US: the moral model (i.e., the War on Drugs, incarceration for drug use) and the disease model (i.e., biological causes and genetic underpinnings) of addiction. A core principle of harm reduction is "meeting individuals where they're at" to assist in reducing negative consequences associated with risky behaviors (Marlatt, 1996; Marlatt & Witkiewitz, 2010). Harm reduction approaches acknowledge that not all individuals want to abstain from substance use and that many individuals can live happy, productive lives with moderate use. Instead, the focus of harm reduction is to attend to the consequences that come from risky substance use and to provide skills and resources for individuals to prevent undesirable consequences.

Various harm-reduction efforts and policies have been initiated in the U.S. to address the opioid epidemic. Some of the most successful evidence-based strategies that have been implemented to reduce opioid-related harm include syringe services programs, targeted naloxone distribution, medication-assisted treatment, the elimination of prior-authorization requirements for the prescribing of medications for opioid use disorder, the distribution of fentanyl test strips, and good Samaritan laws (Centers for Disease Control and Prevention, 2018).

While these efforts have shown efficacy in reducing mortality from OUD, they are largely legislative- and practitioner-focused and may overlook individuals who are not accessing treatment. This is especially concerning given many individuals in the US experience barriers to accessing treatment for OUD. Among those with OUD, only about a quarter (26.2%) utilize any alcohol or drug treatment and less than a fifth (19.4%) receive

opioid-specific treatment (Wu, Zhu & Swartz, 2016). In particular, those in rural areas (Grimm, 2020) may have difficulty accessing treatment. Additionally, there is recent evidence during the COVID-19 pandemic of racial and ethnic disparities in ability to access harm reduction services (Rosales et al., 2022). For these and many other reasons, most individuals with OUD do not receive any treatment, and therefore are not benefitting from many of the widely studied harm-reduction efforts. Additionally, these legislative and practitioner-focused efforts do not address strategies individuals use on a daily basis to prevent harm when using opioids. By not attending to how individuals in the community who use opioids keep themselves safe, we may be missing a key aspect of harm reduction that is particularly salient to individual users.

Protective Behavioral Strategies

Protective behavioral strategies (PBS) are specific behaviors individuals can use to reduce the negative consequences of engaging in substance use. PBS can be conceptualized as an individual-level harm-reduction approach and have been most extensively studied in relation to alcohol use, where use of PBS has been shown to be consistently negatively correlated with alcohol-related problems (Pearson, 2013). Multiple scales have been published to measure the use of alcohol PBS (e.g., Protective Behavioral Strategies Survey [PBSS; Martens et al., 2005], Protective Behavioral Strategies Measure [PBSM; Novik & Boekeloo, 2011], Strategy Questionnaire [SQ; Sugarman & Carey, 2007]), which differ in length and rigor of psychometric testing. These scales measure constructs such as reducing the quantity of alcohol consumed (e.g., “determine not to exceed a set number of drinks”; PBSS) and reducing the number or severity of consequences resulting from use (e.g., “use a designated driver”; PBSS).

Several studies have examined PBS as a mediator in the relationship between mental health symptoms and alcohol use. Depressive symptoms have been shown to be associated with less use of PBS, and in turn, greater alcohol consumption (Linden-Carmichael et al., 2015; Martens et al., 2008). The same relationship has been found among individuals who experience anxiety symptoms and consume alcohol (Litt et al., 2013; Linden et al., 2013). PBS use has also been shown to mediate the relationship between depressive (Martens et al., 2008) and anxiety (Linden et al., 2013) symptomology and alcohol-related consequences in college student samples.

The interaction between mental health symptoms, protective behavioral strategies and alcohol use has also been explored in recent years through moderation analyses. One study examining this interaction found that undergraduate students who reported poorer mental health and greater PBS use displayed a larger reduction in negative alcohol-related consequences than students reporting better mental health (LaBrie et al., 2010). Another study examining the role of mental health, gender, and race in the relationship between the use of alcohol PBS and alcohol consequences in undergraduate students found that greater use of PBS was associated with fewer alcohol-related consequences for students who reported anxiety and depression symptoms (Kenney & LaBrie, 2013). These studies underscore the multifaceted nature of substance use and highlight the need to utilize multiple methodologies to examine the relationship between mental health, PBS, and substance use.

Further examination is needed to determine the role of PBS in the relationship between depression/anxiety symptoms and opioid use behaviors. Given the demonstrated efficacy of PBS in reducing substance use-related problems and the high addiction potential of opioids, it is surprising that until recently no such PBS measure existed for opioid use. To

fill this gap, Hurlocker and Pearson developed and performed preliminary analyses of the Opioid Protective Behavioral Strategies Survey (OPBSS; Hurlocker & Pearson, 2022).

Items for the OPBSS were selected based on a thorough examination of the opioid use literature, other validated PBS scales, such as those for alcohol and cannabis, and qualitative feedback from opioid use researchers. The items were then administered at two timepoints approximately four weeks apart to a community sample of 257 individuals who endorsed past-month use of prescription opioids, heroin, and/or fentanyl. From the 60 items tested in this sample, 48 items were retained following item level and construct validity analyses. The resulting OPBSS was found to have good construct validity, criterion-related validity, and test-retest reliability. Items included ways that individuals prevent opioid-related harm by manner of use (e.g., “Only use one time during a day/night”, “Limit use to weekends”), socially responsible use (e.g., “Use opioids only among trusted peers”, “Avoid using opioids alone”), psychologically responsible use (e.g., “Avoid situations that you anticipate being pressured to use opioids”, “Avoid using opioids out of boredom”), and serious harm reduction (e.g., “Only purchase opioids from a trusted source”, “Avoid using injectable opioids”). The OPBSS was found to account for a significant amount of variance in risky opioid use and opioid-related consequences in this community sample. Further examination of this measure to determine its potential role in mitigating harm among particularly at-risk groups is warranted.

Current Study

To date, most harm reduction research on opioid use has focused on overdose prevention efforts among individuals accessing treatment. While these efforts have been helpful and integral to reducing opioid-related harm, they have largely overlooked the

strategies non-treatment seeking individuals in the community use to keep themselves safe. The use of these strategies may be particularly important for individuals with mood or anxiety disorders who use opioids, as they are among those at greatest risk for problematic use. The present study aims to address this gap through the examination of opioid protective behavioral strategies among individuals reporting symptoms of anxiety and depression. This aim will be accomplished by exploring the relationships among anxiety and depression symptomology, PBS use, and risky opioid use and opioid-related consequences.

Hypotheses

As the use of PBS has been shown to mediate the relationship between anxiety/mood disorders and alcohol use and problems, we hypothesized a similar mediation pathway with risky opioid use and consequences. Specifically, we hypothesized that anxiety and depression symptoms would be associated with less frequent use of opioid protective behavioral strategies, which would in turn be associated with greater risky opioid use and opioid-related consequences.

Additionally, as anxiety and depression have been shown to moderate the relationship between PBS and substance use outcomes, we hypothesized that anxiety and depression symptoms would moderate the relationship between PBS and risky opioid use and consequences, such that those reporting more symptoms of anxiety and depression would experience greater benefit from PBS use than those reporting fewer mental health symptoms.

Method

Participants and Procedures

The present study was a secondary analysis of data gathered in a pilot study that aimed to develop and evaluate the psychometric properties of a measure of opioid protective

behavioral strategies. Participants (*n*=257) for this secondary data analysis were recruited through multiple recruitment platforms, including the anonymous online crowdsourcing platform Prolific and online forums (e.g., Reddit). A brief screener survey was posted on these platforms, and adults aged 18 or older residing in the United States who reported past-month opioid use and who were not currently in treatment for opioid use disorder were deemed eligible to participate. Eligible participants were invited to review a brief overview of the study and an IRB-approved electronic consent form before completing the first of two 45-minute surveys on substance use and related behaviors. Approximately four weeks later, participants were invited to complete a second 45-minute survey. For a full description of the parent study, see Hurlocker and Pearson (2022). Of the 257 participants included in this study, 196 completed both the Time 1 and Time 2 surveys.

Measures

Sociodemographics

Sociodemographic measures included age, birth sex, race, ethnicity, marital status, employment status, living situation, type of opioid use (e.g., prescription opioids, heroin), current/past opioid prescription for pain, and route of opioid administration (e.g., oral, injection, intranasal).

Opioid Use

Quantity and frequency of weekly opioid use was measured using the Timeline Followback (TLFB) (Sobell & Sobell, 1992). Prior to responding, participants were provided with an example of how to report opioid quantity, (“For example, if you consumed a 10mg Percocet pill in a single day, then please enter 10 pills for that day”), and participants reported prescription opioid use (measured in milligrams) separately from heroin (measured

in grams) and fentanyl use (measured in micrograms). Participants reported the quantity of each substance they used on all days of a typical week in the past month.

Opioid-Related Consequences

A modified version of the 50-item Inventory of Drug Use Consequences (i.e., InDUC-Opioids) was used to assess past-month opioid-related consequences. The original scale, the InDUC-2R (Blanchard et al., 2003), has previously demonstrated strong psychometric properties and is an adaptation from the Drinker Inventory of Consequences (DrInC; Miller et al., 1995). The modifications made for the present study included adapting the instructions and item wording of the InDUC-2R to reflect consequences specific to the use of opioids (e.g., "I have felt bad about myself because of my opioid use" and "I have been sick and vomited after using opioids"). Participants reported past-month consequences on a four-point Likert scale ranging from 0 (never) to 3 (Daily or almost daily) and a summary score was created by summing all responses. The InDUC-opioids displayed excellent internal consistency in the present sample (αs = .971 and .970).

Risky Opioid Use

The eight-item Rapid Opioid Dependence Screen (RODS) was used to assess risky opioid use (Wickersham et al., 2015). Participants indicated any type of opioid they have used in the past year (e.g., heroin, morphine, methadone) and responded to seven dichotomous (yes/no) measures assessing severity of use (e.g., "Did you find it difficult to stop or not use opioids?"). The RODS has demonstrated strong internal consistency and inter-item correlations (Wickersham et al., 2015). In the present study, a summary score was created to capture risky opioid use at each time point. The RODS demonstrated good internal consistency at both time points in the present sample (αs = .862 and .880).

Opioid Protective Behavioral Strategies

The Opioid Protective Behavioral Strategies Scale (OPBSS) was used to assess past-month use of cognitive-behavioral strategies to reduce opioid-related harm (e.g., "Determine not to exceed a set amount/dose of opioids", and "Avoid mixing opioids with other drugs"). Participants responded to the prompt, "Please indicate how often you have used each of the following strategies in the past 30 days" using seven response options: 1 – *never*, 2 – *rarely*, 3 – *occasionally*, 4 – *sometimes*, 5 – *usually*, 6 – *always* and 7 – *not applicable* (i.e., response option for items that did not apply based on their method of opioid use). The scale also evidenced good convergent validity with validated alcohol and cannabis PBS measures, good criterion-related validity, and test-retest intraclass correlations ranging from fair to excellent (.50<ICCs<.83) (Hurlocker & Pearson, 2022). Preliminary factor analyses suggested a four-factor solution, however, for the present study, a single average score of the 48 items was used to quantify PBS use. The OPBSS demonstrated excellent internal consistency at both time points in the present study (αs = .972 and .973).

Mental Health

Depression and anxiety symptoms were assessed using domains I and IV of the Adult version of the DSM-5 Self-Rated Level 1 Cross-Cutting Symptom Measure (American Psychiatric Association, 2013). This measure uses a five-point scale (0- None/Not at all to 4-Severe/Nearly every day) to measure severity/frequency of mental health symptoms in the past two weeks. Depression symptoms (Domain I) are measured using two items ("Little interest or pleasure in doing things" and "feeling down, depressed, or hopeless") and anxiety symptoms (Domain IV) are measured with three items ("Feeling nervous, anxious, frightened, worried, or on edge", "Feeling panic or being frightened", and "Avoiding

situations that make you anxious"). The DSM-5 Self-Rated Level 1 Cross-Cutting Symptom has good to excellent test-retest reliability for Domains I and IV and has demonstrated convergent validity with longer, validated measures of depression and anxiety (Bravo et al., 2018). This heightens confidence that this brief scale captured severity of anxiety and depression symptoms in this sample. The DSM-5 Self-Rated Level 1 Cross-Cutting Symptom Measure demonstrated acceptable internal consistency at both time points for Domain I (αs = .793 and .733) and Domain IV (αs = .768 and .753).

Data Analysis

SPSS version 28 was used to prepare the data, identify potential outliers, test for normality and multi-collinearity issues and run descriptive statistics. Extreme outliers (greater than three standard deviations from the mean) were Winsorized (Dixon, 1960). Primary analyses were conducted using M*plus* Version 8.1 (Muthén & Muthén, 2017). Structural equation modeling (SEM) was used to determine whether PBS mediated the relationship between depression and anxiety symptoms and risky opioid use and consequences. Anxiety and depression symptoms were then examined as a moderator in the relationship between PBS use and risky opioid use and consequences.

The temporal associations between anxiety and depression symptoms and risky opioid use and consequences were conducted using a path model. Anxiety and depression symptoms were examined at Time 1 and risky opioid use and consequences were examined at Time 2, while accounting for risky opioid use and consequences at Time 1.

In the mediation models, the predictor variables were anxiety and depression symptoms at Time 1, the mediator variable was OPBSS scores at Time 2 and the outcome variables were risky opioid use and opioid-related consequences at Time 2. Weekly opioid,

heroin, and fentanyl use and OPBSS scores at Time 1 were included as covariates in the models.

In the moderation analyses, the predictor variable was OPBSS scores at Time 1, the moderator variables were anxiety and depression symptoms at Time 1 and the outcome variables were risky opioid use and opioid-related consequences at Time 2. The predictor and moderator variables were centered prior to conducting the moderation analyses. Weekly opioid, heroin and fentanyl use, risky opioid use and opioid-related consequences at Time 1 were included as covariates in the models.

For the mediation and moderation analyses, a χ^2 test was used to indicate model fit, with non-significant statistics indicating good model fit. Given the χ^2 is sensitive to sample size, additional estimates of model fit included Comparative Fit Index (CFI), which is less affected by sample size, Root Mean Square Error of Approximation (RMSEA), and Tucker-Lewis Index (TLI) (Chen et al., 2008; Curran et al., 1996; Hu & Bentler, 1999). An indicator of good (adequate) model fit based on CFI or TLI is .95 (.90-.94) and a further indicator of good (adequate) model fit based on RMSEA is less than .05 and SRMR less than .08 (Browne & Cudeck, 1993; Hu & Bentler, 1999; MacCallum et al., 1996). For mediation, a bootstrapping technique of 10,000 resamples (with replacement from the original sample) was used to determine confidence interval (CI) effect-size estimations (Preacher & Hayes, 2004; Preacher & Kelley, 2011). Significant mediation and moderation were indicated if bootstrap CIs did not include zero.

Results

Descriptive Statistics

The sample (*n*=257) was comprised of individuals who endorsed using prescription opioids, heroin, and/or fentanyl in the past 30 days. Sample characteristics at baseline are listed in Table 1. Means, standard deviations and correlations for all study variables are reported in Table 2. At baseline, in an average week in the past month, participants reported using 59.56 (SD = 147.01) milligrams of opioids, 2.23 (SD= 6.93) grams of heroin, and 5.01 (SD = 13.18) micrograms of fentanyl. For past month opioid use, values greater than three standard deviations from the mean were winsorized (Dixon, 1960). Participants scored an average of 3.90 (SD = 2.25) on the depression subscale and 5.19 (SD = 3.04) on the anxiety subscale. On average, participants scored a 3.76 (SD = 1.06) on the OPBSS, 4.22 (SD=2.57) on the RODS and 38.45 (SD=28.52) on the InDUC.

Temporal Associations

The temporal associations between anxiety and depression symptoms and risky opioid use and consequences were conducted using a path model, with anxiety and depression symptoms examined at Time 1 and risky opioid use and consequences examined at Time 2, while accounting for risky opioid use and consequences at Time 1. The resulting model was just-identified. There was a significant effect of depression on risky opioid use (β= 0.172, p=0.026, CI [0.027, 0.329]). However, there was no significant effect depression on consequences (β= 0.004, p=0.929) or of anxiety on risky opioid use (β= -0.097, p=0.144) or consequences (β= -0.034, p=0.488). Results of the temporal analyses are presented in Table 3. Because there is no need for a significant zero-order effect of X on Y to establish mediation (Zhao et al., 2010), we proceeded with the mediation analyses next.

Mediation Models

Model Fit

Two mediation models were conducted to examine OPBS use as a mediator of the relationship between anxiety and depression symptoms and risky opioid use and consequences. Opioid, fentanyl, heroin and OPBS use at Time 1, as well as the criterion variable at Time 1, were entered as covariates. The resulting mediation models contained the same number of free parameters and known values, resulting in zero degrees of freedom and a just-identified model. Global fit indices cannot be computed for just-identified models, therefore only the parameter estimates are provided. There were no inadmissible solutions based on the residual variances. Total, direct, and indirect parameter estimates for both mediation models are provided in Table 4.

Risky Opioid Use

The first set of parameters examined the mediating effect of OPBS use on the relationship between anxiety symptoms and risky opioid use, controlling for opioid, fentanyl, heroin and OPBS use and risky opioid use at Time 1. Results demonstrated no direct or indirect effects of anxiety and opioid PBS on risky opioid use. The second set of parameters examined the mediating effect of OPBS use on the relationship between depression symptoms and risky opioid use, controlling for opioid, fentanyl, heroin and OPBS use and risky opioid use at Time 1. These results demonstrated no direct or indirect effects of depression and opioid PBS on risky opioid use.

Opioid-Related Consequences

The first set of parameters examined the mediating effect of OPBS use on the relationship between anxiety symptoms and opioid-related consequences, controlling for opioid, fentanyl, heroin and OPBS use and opioid-related consequences Time 1. Results demonstrated no direct or indirect effects of anxiety and opioid PBS on opioid-related

consequences. The second set of parameters examined the mediating effect of OPBS use on the relationship between depression symptoms and opioid-related consequences, controlling for opioid, fentanyl, heroin and OPBS use and opioid-related consequences Time 1. These results also demonstrated no direct or indirect effects of depression and opioid PBS on opioid-related consequences.

Moderation Tests

Both moderation tests conducted had zero degrees of freedom, resulting in a just-identified model. Therefore, parameter estimates are provided but global fit statistics are not reported. The predictor and moderator variables were centered prior to conducting the moderation analyses. Results of the moderation tests are provided in Table 5.

Risky Opioid Use

The first moderation model examined included OPBS use as the predictor variable, anxiety and depression symptoms as the moderator variables, and risky opioid use as the criterion variable. Opioid, fentanyl, heroin, and risky opioid use at Time 1 were entered as covariates. There was a significant main effect of depression symptoms at Time 1 on risky opioid use at Time 2 (β= 0.23, p=0.027) and risky opioid use at Time 1 on risky opioid use at Time 2 (β= 0.666, p<0.001). However, there was no main effect of OPBS use on risky opioid use (β= 0.038, p=0.649) and there was no significant interaction between OPBS and depression on risky opioid use (β= -0.051, p=0.611). Additionally, there was no significant main effect of anxiety symptoms at Time 1 on risky opioid use (β= -0.160, p=0.122) and there was no significant interaction between OPBS and anxiety symptoms on risky opioid use (β= 0.108, p=0.272).

Opioid-Related Consequences

The second moderation model examined OPBS use as the predictor variable, anxiety and depression symptoms as the moderator variables, and opioid-related consequences as the criterion variable. Opioid, fentanyl, heroin use and opioid-related consequences at Time 1 were entered as covariates. There was a significant main effect of prescription opioid use at Time 1 on opioid-related consequences at Time 2 (β= 0.106, $p<0.02$) and opioid-related consequences at Time 1 on opioid-related consequences at Time 2 (β= 0.799, $p<0.001$). However, there was no main effect of OPBS use (β= -0.051, p=0.425), anxiety symptoms (β= -0.072, p=0.380) or depression symptoms (β= 0.042, p=0.607) on opioid-related consequences. Additionally, there was no significant interaction between OPBS use and depression symptoms at Time 1 (β= -0.025, p=0.747) or OPBS and anxiety symptoms at Time 1 (β= 0.047, p=0.538) on opioid-related consequences at Time 2.

Discussion

This study aimed to explore the relationship between anxiety and depression symptoms, opioid protective behavioral strategies, and risky opioid use and consequences. Previous research suggests that mental health symptoms and the use of protective behavioral strategies both play an important role in substance use outcomes (Linden-Carmichael et al., 2015; Linden et al., 2013; Litt et al., 2013; Martens et al., 2008). Given that this is the first study to examine the relationship between mental health, opioid PBS and risky opioid use and consequences, it is notable that there were significant correlations between many of these variables. Although the present study did not demonstrate support for our hypotheses regarding mediation and moderation pathways, the positive main effect of depression on risky opioid use is consistent with previous research (Martins et al., 2012).

The relationship between mental health symptoms and opioid use is multifaceted and merits further consideration. One potential explanation for why PBS did not mediate the relationship between anxiety and depression symptoms and risky opioid use and consequences is that compared to individuals with fewer symptoms of anxiety and depression, individuals with more anxiety and depression symptoms may engage in different types of PBS that are less effective and therefore are less likely to reduce harm. To this end, the four factors identified in the recent factor analysis of the OPBSS merit further exploration (Hurlocker & Pearson, in preparation).

There are several methodological considerations that may contribute to these null findings. Though the internal consistency was excellent in the current sample, the InDUC, used to assess opioid-related consequences, was developed for drug use broadly and was adapted for opioid use in this study. Future research with a larger sample of opioid users would allow us to evaluate the psychometric properties of the InDUC for opioid use, as well as to test these hypotheses using the five InDUC consequence subscales (physical, social, intrapersonal, impulse control and interpersonal) rather than a total summary score. Furthermore, it may be that some of the current items included in the InDUC are not applicable to opioid use and that certain opioid-specific consequences may not be captured with this scale. For example, accidental overdose, one of the most severe potential consequences of opioid use, is not directly measured by the InDUC. Given the recent rise of overdoses in the US (CDC 2022; Ho, 2019), the addition of items evaluating for this, and other serious opioid-related harm may be needed to assess the full scope of opioid-related consequences. Additionally, the Risky Opioid Dependence Screen (RODS) was developed based on the DSM-IV criteria for opioid use disorder, which may be a limitation in a non-

treatment seeking community sample. Variables that are important to consider in a healthcare setting in regard to risky opioid use (e.g., withdrawal) may be different than factors that should be considered in a community sample (e.g., safety).

Although the DSM-5 Self-Rated Level 1 Cross-Cutting Symptom Measure (American Psychiatric Association, 2013) used in this study to assess anxiety and depression symptoms has demonstrated convergent validity with longer, validated measures of anxiety and depression (Bravo et al., 2018), it is an abbreviated measure of mental health symptoms and was validated with a population of college students, which may not generalize to a broader, community-based sample. It is also possible that the two items used to assess depression and three items assessing anxiety did not accurately capture the range of mood/anxiety symptoms in this non-clinical sample.

In one study examining the DSM-5 Self-Rated Level 1 Cross-Cutting Symptom Measure as a screening tool, it was found to result in a large number of false positives (Bastiaens & Galus, 2018). The authors suggested that it functioned well in negative prediction, but due to low positive predictive values, it should not be used to identify positive findings (Bastiaens and Galus, 2018). In their 2021 systematic review, Rogers and colleagues reported that past studies examining the association between opioid use, anxiety and depression have used a range of longer measures to assess for mood and anxiety symptoms, including the Structured Clinical Interview for DSM-III/IV (American Psychiatric Association 1980, 2000), the 28-item Beck Depression Inventory (Beck et al., 1988) and the 7-item Generalized Anxiety Disorder -7 (GAD-7; Spitzer et al., 2006). Future research examining the relationship between mental health symptoms and opioid PBS may benefit

from the use of one of these longer measures which may be more sensitive to differences among a non-treatment-seeking sample.

A final methodological consideration is that the OPBSS is a newly developed measure designed to capture a broad range of strategies that individuals may use to reduce opioid-related harm, and takes into consideration both type of opioid used and route of administration (e.g., oral, syringe). A four-factor structure was recently identified in a factor analysis, yet due to small sample size, a summary score was used in the present study. Future research focusing on the psychometric properties of this measure with a larger sample is needed. Additionally, it may be that there are significantly different PBS use patterns based on route of administration or opioid type, and separate measures specific to these dimensions may more accurately capture use patterns.

Limitations

This study must be viewed in light of its limitations. First, the present study was a secondary analysis using data from two timepoints. Therefore, the mediator and outcome variables were measured concurrently. Mediation is typically not recommended for datasets with only two time points, and this may have diminished the reliability of these findings. Ideally, three time points would be used to test mediation, with the predictor variables measured at time one, the mediator variable measured at time two and the outcome variables at time three. Inferences from cross-sectional models have been shown to result in different findings from longitudinal mediation models (O'Laughlin et al., 2018).

Secondly, this study included a relatively small, heterogeneous sample of individuals who reported various types of opioid use (n=257; see Tables 1 & 2). While a strength of this study was the forethought given to the assessment of opioid quantity, the small sample size

prevented the ability to account for the variability in type of opioid used and route of administration. Both factors likely contribute to an individuals' patterns of opioid use. Another consideration is that there is no current consensus on the best way to assess opioid use quantity, particularly when comparing the various types of opioids (e.g., prescription opioids, heroin, fentanyl) that individuals in this sample reported using.

Conclusion

In conclusion, although we did not find support for our hypotheses regarding mediation or moderation, many of the variables examined were correlated with one another. Given the sample and measurement limitations described above, it is notable that OPBS and depression symptoms at Time 1 were both correlated with risky opioid use and related consequences at Time 2, and that anxiety at Time 1 was correlated with opioid-related consequences. These findings are consistent with previous literature, and additional research with these constructs may be warranted. There is the need to bolster our response to the opioid epidemic in the United States through harm reduction efforts that keep people safe. Further examination of how individuals who use opioids reduce personal harm could provide important information to strengthen these efforts, particularly for individuals who do not have access to opioid use disorder treatment.

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Table 1

Sociodemographic Characteristics of Total Sample at Baseline (N=257)

Sociodemographic characteristic	M (SD) or % (n)
Age	35.98 (9.94)
Sex assigned at birth	
Female	43.2% (111)
Male	56.4% (145)
Race	
African American/Black	12.5% (32)
Asian American/Asian	5.4% (14)
European American/White	74.3% (191)
American Indian/Alaskan Native	4.7% (12)
Pacific Islander	0.4% (1)
Other	1.9% (5)
Hispanic	17.1% (44)
Employment	
Full-time employment	49.6% (127)
Part-time employment	19.9% (51)
Unemployed	30.5% (78)

Note. Some participants declined to respond to demographic questions. This was the case in all instances where the category percentiles provided do not add up to 100%.

Table 2

Descriptive Statistics and Correlations for Study Variables

Variable	*n*	*M*	*SD*	1	2	3	4	5	6	7	8
1. Opioid use	243	59.56	147.01	—							
2. Fentanyl use	238	5.01	13.18	.06	—						
3. Heroin use	239	2.23	6.93	< .001	.30**	—					
4. OPBSS	188	3.76	1.06	-.21**	-.03	.03	—				
5. RODS	168	4.22	2.57	.16*	.30**	.14	-.49**	—			
6. InDUC	196	38.45	28.52	-.03	.25**	.12	-.31**	.60**	—		
7. Depression	250	3.90	2.25	.07	.01	.04	-.22**	.26**	.14*	—	
8. Anxiety	250	5.19	3.04	-.03	-.06	.03	-.09	.13	.18*	.70**	—

Note. OPBSS = Opioid Protective Behavioral Strategies Scale at Time 2; RODS = Rapid Opioid Dependence Screen at Time 2; InDUC = Inventory of Drug Use Consequences (Opioids) at Time 2; all other variables measured at Time 1

*$p < .05$. **$p < .01$.

Table 3
Standardized coefficients of temporal analyses

Dependent variable:	β	*p*	95% CI	
			LL	UL
RODS				
Anxiety	-0.097	0.144	-0.234	0.027
Depression	**0.172**	**0.026**	**0.027**	**0.329**
InDUC				
Anxiety	-0.034	0.488	-0.133	0.062
Depression	0.004	0.929	-0.089	0.098

Note. All parameter estimates and significance test are based on 10,000 bootstrapped samples. Significant effects ($p<.05$) are bolded. RODS = Rapid Opioid Dependence Screen at Time 2; InDUC = Inventory of Drug Use Consequences (Opioids) at Time 2. CI=Confidence Interval; LL=lower limit; UL=upper limit.

Table 4

Standardized Total, Direct and Indirect Effects of Anxiety and Depression at Time 1 on Opioid-Related Outcomes at Time 2

Dependent variable:	RODS		InDUC	
	β	*p*	β	*p*
Independent Variable:				
Depression symptoms				
Total effect	0.145	0.073	0.019	0.719
Direct effect	0.117	0.152	0.032	0.558
Total indirect	0.028	0.185	-0.013	0.411
Anxiety symptoms				
Total effect	-0.044	0.547	-0.036	0.528
Direct effect	-0.015	0.845	-0.044	0.452
Total indirect	-0.030	0.246	0.008	0.515

Note. All parameter estimates and significance test are based on 10,000 bootstrapped samples. Significant effects ($p<.05$) are bolded. RODS = Rapid Opioid Dependence Screen; InDUC-Opioids = Inventory of Drug Use Consequences (Opioids)

Table 5
PBS and Mental Health Interactions

Criterion variable:	RODS T2		InDUC T2	
	β	*p*	β	*p*
Predictor				
OPBSS	0.04	0.65	-0.05	0.43
Covariates				
Opioid use	0.10	0.13	**0.12**	**0.02**
Fentanyl use	0.05	0.57	0.06	0.35
Heroin use	-0.10	0.07	-0.01	0.83
RODS T1	**0.67**	**< 0.001**	—	—
InDUC T1	—	—	**0.80**	**< 0.001**
Moderator variables				
Anxiety	-0.16	0.12	-0.07	0.38
Depression	**0.23**	**0.03**	0.04	0.61
Interactions				
OPBS*Depression	-0.05	0.61	-0.03	0.75
OPBS*Anxiety	0.12	0.27	0.05	0.54

Note. All parameter estimates and significance test are based on 1,000 bootstrapped samples. Standardized effects are reported. Significant effects (p<.05) are bolded. RODS = Rapid Opioid Dependence Screen; InDUC = Inventory of Drug Use Consequences (Opioids)