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Subtypes of patients with opioid use disorder in methadone maintenance treatment: A pathways model analysis

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ABSTRACT

This study applied constructs from a widely-utilized subtyping model in the field of gambling studies, the Pathways Model, to a sample of 118 patients with opioid use disorder receiving methadone-maintenance-treatment. Surveys were analyzed using latent class analysis (LCA) to examine whether the Pathways Model indicators distinguished class membership, with confidence band interpretation used to compare class scores, and multinomial logistic regression conducted to examine associations with other correlates. LCA fit indices supported a three-class solution: (1) 'opioid-related only' (55.9%), (2) 'personal trauma/emotionally vulnerable' (15.3%), and (3) 'impulsive/current psychopathology' (28.8%). Class 1 was characterized by lower scores on nearly all indicators. Class 2 was characterized by the highest scores for personal experiences with sexual, physical, and emotional abuse during childhood and interpersonal trauma, and high impulsivity scores. Class 3 was characterized by the highest scores on stress, depression, loneliness, and impulsivity. Classes 2 and 3 both had higher scores for witnessing community violence, opioid-related coping motives, and impulsivity than Class 1. Gender, age, opioid-related consequences, and social network substance misuse were associated with membership. Our findings generally demonstrate trans-diagnostic overlap with the Pathways Model, offering support for the model's translation to other addictions.

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Introduction

People living with opioid use disorder (OUD) are at high risk for a variety of negative consequences, including overdose-related death (Mattson et al., 2021), blood-borne illnesses and physical health problems that contribute to mortality risk (Degenhardt et al., 2011), and co-occurring substance use and emotional disorders (Jones &

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McCance-Katz, 2019). The gold-standard approach for OUD is medication treatment (Crotty et al., 2020; Volkow et al., 2014), with comparative effectiveness for opioid agonist medications, methadone and buprenorphine, to reduce opioid-related overdose and morbidity compared to other medications, behavioral treatment, and self-help approaches (Wakeman et al., 2020). Despite the effectiveness of methadone maintenance treatment (MMT) and buprenorphine maintenance treatment (BMT), treatment drop-out, relapse, and future overdose are still common (Bell & Strang, 2020). Thus, projects that examine patient characteristics that can be used to tailor assessment and treatment protocols in settings that deliver MMT have the potential to improve treatment outcomes.

To date, subtyping studies among OUD patient samples have primarily been conducted in Italian clinics providing MMT and/or BMT. The most influential study to date, by I. Maremmani et al. (2010) generated an OUD subtyping classification by assigning patients (N = 1,055) to one of five factors using an exploratory factor analysis (EFA) and classifying patients on the basis of their highest z-score factor. The study's EFA used the Symptom-Checklist 90 (Derogatis et al., 1974), which resulted in the item count being trimmed from 90 to 77 items (I. Maremmani et al., 2010). Their analysis yielded five subtypes: (1) worthlessness-being trapped; (2) somatization; (3) sensitivity and psychoticism; (4) panic anxiety; and (5) violence-suicide. Subsequently, the authors have analyzed differences in clinical, demographic, and treatment outcome variables within a cohort from the larger sample (Maremmani et al., 2012) and extended their OUD-specific subtype focus to a general substance use disorder (SUD) sample (Maremmani et al., 2016). More recently, the authors compared the factors and correlates for OUD and gambling disorder patients. OUD patients demonstrated greater severity of psychopathology across factors, whereas patients with gambling disorder were characterized by subtypes reflecting a lower propensity for somatization and violence-suicide measures, and a higher propensity for symptoms of worthlessness and feeling trapped (Maremmani et al., 2018).

These studies generated a greater understanding of OUD patient subtypes, however, the I. Maremmani et al. (2010) subtyping model has some limitations. First, it relied on a single measure (SCL-90) that was not grounded in theory to ascertain OUD subtypes. Second, a psychometric analysis of the SCL-90 supported a different factor structure and item exclusion (Prunas et al., 2012). Third, these studies have generally combined OUD patients receiving MMT or BMT in their sampling, most likely to increase statistical power, though this has the potential in the United States (US) context to cause challenges, because MMT and BMT patients often differ on demographic and treatment-seeking characteristics (Gryczynski et al., 2013; Hansen et al., 2013). Other attempts at subtyping in OUD have been generally limited to non-treatment samples of people who misuse opioids (Afshar et al., 2019) and subtypes of non-opioid substance use among MMT patients (Fong et al., 2015).

There has been significantly more research into subtyping individuals with gambling problems. These studies may be especially important as OUD shares etiological mechanisms, symptom presentation, and co-occurring disorder risk with gambling disorder (Carr et al., 2021), and as a result, the disorders often co-occur in MMT samples (Himelhoch et al., 2016). This body of literature has principally been examined using the Pathways Model (Blaszczynski & Nower, 2002), which recently underwent empirical

validation (Nower & Blaszczynski, 2017). The model proposes there are common factors across all people with gambling disorder – ecological factors, erroneous cognitions, and conditioning effects. However, there are also distinct sub-groups of etiological factors that differentially predispose individuals to develop problems with gambling. People in Pathway 1, the 'behaviorally conditioned' group, are distinguished by a lack of psychopathology before their development of gambling problems. It is theorized they develop gambling problems as a result of the interplay of ecological factors such as availability, accessibility, and acceptability of gambling; develop erroneous cognitions about the ability to control the outcome of chance; and fall into a habitual pattern of gambling that increases in frequency and intensity until problems develop. People in Pathway 2, the 'emotionally vulnerable' group, experience the same factors, cognitions, and conditioning effects as Pathway 1, but they also present with evidence of childhood maltreatment in the form of neglect, trauma, or abuse as well as pre-morbid anxiety and/or depression. The original Pathways Model characterized the 'antisocial impulsivist' group, Pathway 3, as a subgroup of Pathway 2, with the addition of antisocial and impulsive traits. However, a subsequent empirical investigation of the model clarified that Pathways 2 and 3 are distinct, with some shared motivation for gambling to cope with stress and supplement meaning-in-life deficits (Nower & Blaszczynski, 2017).

Studies have found general support for the Pathways Model across treatment- and nontreatment-seeking samples (Bonnaire et al., 2009; Ledgerwood & Petry, 2010; Moon et al., 2017), purposive samples of at-risk age cohorts (Gupta et al., 2013; Tirachaimongkol et al., 2010), and large-scale representative samples (Mader et al., 2019; Nower et al., 2013). While studies have found general support (Hum & Carr, 2018; Mader et al., 2019; Moon et al., 2017; Valleur et al., 2016), few investigations have tapped all facets proposed by the model and only one tested the model in a representative sample (Nower et al., 2013). Though other models have been used to subtype individuals with other SUDs (Cloninger et al., 1996), the etiological factors in the Pathways Model may be more optimal when examining treatment-level data since the factors were designed to guide individualized care and don't rely on factors (genetics) that cannot be addressed in treatment. Furthermore, with the inclusion of gambling disorder alongside substance use disorders in the DSM-5, it is notable that few studies have explored the possibility of parallel etiological processes among individuals with other types of substance and behavioral addictions. Thus, an analysis adapting the Pathways Model for OUD patients receiving MMT has the potential to identify whether the subtypes translate to another addictive disorder, OUD, while offering both novel and theoretically-informed findings to the broader field of addictions.

The current study

Collectively, the literature on OUD patient subtypes is underdeveloped and in need of greater attention. By contrast, the gambling literature has used the Pathways Model (Blaszczynski & Nower, 2002) to guide a range of subtype investigations. Accordingly, our objectives in this study were three-fold. First, we analyzed survey data using latent class analysis (LCA) to examine whether select indicators in the Pathways Model categories (emotional vulnerability, antisocial impulsivist) translate to a sample of patients with OUD. Second, we conducted multinomial logistic regressions to account

for associations of demographic and clinical factors to class membership. Third, we compared these findings to those identified in gambling and OUD samples to identify directions for future research and clinical implications for OUD patients receiving MMT, as well as to generate knowledge about subtyping for the broader field of addictions. We hypothesized that using the Pathways Model indicator categories would generate a three-class solution with similar subtypes in our OUD patient sample (i.e. support a trans-diagnostic model of addiction), though some disorder-specific differences would be observed. We predicted that some demographic and clinical factors would be associated with class membership based on the considerable heterogeneity of OUD patient age, race, gender, age of opioid use onset, injection opioid use, and co-occurring addiction symptoms. Specifically, we hypothesized that emotional vulnerability scores would be higher among patients who preferred injection and were female. We predicted antisocial impulsivist scores would be higher among patients with co-occurring addiction, a greater accumulation of opioid-related consequences, and were male. Last, we hypothesized patients with lower scores on emotional vulnerability and antisocial impulsivist measures would have lower risk for prior MMT, greater opioid-related consequences, and earlier opioid use onset.

Material and methods

Setting and procedure

Patients in the study were receiving MMT for OUD at a university-affiliated clinic situated in a large urban and medically underserved community of a Midwestern state. Patients were recruited using a 'consent to contact' flyer, distributed by clinic staff during the patient intake, which were then subsequently gathered by research staff. When patients were interested, research staff coordinated a time for participation on another floor of the building. All patients completed research participation within two weeks of their intake and induction to methadone. Recruitment took place from September 2016 – February 2019. Study participation involved an informed consent and survey battery (45–60 minutes total). Patients were remunerated with a $25 gift card and round-trip bus tickets after completing the study. All research procedures were approved by reviewing and relying Institutional Review Boards.

Demographic and clinical factor measures

Four demographic characteristics were assessed. These included age at the time of the survey, race (recoded as Black/African American race, other race), education (recoded as high school degree or more, less than high school degree), and gender (male, female).

Nine clinical factors were assessed. Two items from the Drug History and Use Questionnaire (DHUQ: Greenwald et al., 2013) assessed route of opioid administration (recoded as lifetime history of opioid injection use, no history) and the age when the patient's regular opioid use onset (3+ times per week). We used 17 of the 20 items (deleting the three-item factor about school-related consequences due to the age range in this sample) of the Heroin Use Consequences scale (HUC, Moses et al., 2018), which assessed lifetime experiences with a variety of consequences experienced from opioid use

(e.g. arrest or legal problems, overdose) and demonstrated good internal consistency (α = .81). While items in the original scale were written specific to heroin use, patients were instructed to answer the question about consequences related to their preferred opioid type. Patients also reported whether they had been in MMT before (yes, no), if anyone in their social network (parent, sibling, partner, close friend) had a problem in their lifetime with substance misuse, and whether they had ever lived with someone while they were misusing substances; items similar to those commonly gathered in MMT chart review data (Kumar et al., 2021; Lister et al., 2017). Last, brief screeners (and established cut-scores) assessed positive screens for co-occurring problems with alcohol (Alcohol Use Disorders Identification Test, AUDIT-C: Bush et al., 1998), cocaine (Severity of Dependence Scale, SDS: Gossop et al., 1995; Kaye & Darke, 2002), and gambling (NORC Diagnostic Screen for Gambling Disorders-Control, Lying, and Preoccupation, NODS-CliP: Toce-Gerstein et al., 2009). Internal consistency was acceptable for the AUDIT-C (α = .76), good for the NODS-CLiP (α = .83), and excellent for the SDS (α = .96) screening measures. These three measures were re-coded (any/no positive screen for co-occurring addiction) for inferential analyses.

Emotional vulnerability measures

Nine emotional vulnerability measures were assessed as continuous variables. A three-item scale assessing loneliness demonstrated good internal consistency (α = .89) (UCLA Loneliness Scale-Version 3, Hughes et al., 2004). Two subscales of the DASS-21 (Antony et al., 1998) assessed past-week depression (α = .90) and stress (α = .90), demonstrating excellent internal consistency for both seven-item sub-scales. The Childhood Trauma Questionnaire-Short Form (CTQ-SF: Bernstein et al., 2003) assessed personal experiences with physical (α = .92), emotional (α = .90), and sexual abuse (α = .97) during childhood, with each five-item sub-scale demonstrating excellent internal consistency. The Revised Conflict Tactics Scale (CTS2: Straus et al., 1996) assessed eight items about personal experiences with interpersonal violence enacted upon the patient in their lifetime and demonstrated excellent internal consistency (α = .90). The Things I Have Seen and Heard scale (Richters & Martinez, 1992) assessed fifteen items about witnessing community violence in their lifetime, demonstrating good internal consistency (α = .81). Opioid-related coping motives were measured by adapting three items of the Drinking Motives Questionnaire (DMQ: Cooper et al., 1992) for opioid use, which demonstrated good internal consistency (α = .81).

Antisocial impulsivist measures

Three antisocial impulsivist measures were assessed. These included a summed score of trait impulsivity using the brief Barratt Impulsiveness Scale (BIS-15: Spinella, 2007), which measures broad impulsivity and includes risk-taking items, and demonstrated good internal consistency (α = .84). Two meaning-in-life domains, searching for meaning-in-life (α = .79) and presence of meaning-in-life (α = .92),

were assessed using three-item subscales of the Meaning in Life Questionnaire (MLQ: Steger et al., 2006), which demonstrated acceptable and excellent internal consistency, respectively.

Data analysis

First, data were screened for normality and missingness. Some scales contained a very small amount of missing data (1–3 cases); continuous data were imputed using expectation maximization (Musil et al., 2002) and binary missing data were estimated by substituting missing values with Bernoulli-distributed random values (Bernaards et al., 2007). Latent class analysis (LCA) was performed to examine whether the Pathways Model indicator categories (emotional vulnerability, antisocial impulsivist) were observed in a sample of patients with OUD. The number of classes was determined by model fit statistics including Akaike Information Criteria (AIC), Bayesian Information Criteria (BIC), adjusted BIC (ABIC), entropy, and bootstrapped likelihood ratio test (BLRT). Three-step LCA using the R3step procedure (Asparouhov & Muthén, 2013) was employed to examine associations of demographic and clinical factors with class membership. Analyses were conducted using Mplus v8.6. We determined class differences for indicators when 95% confidence interval bands did not overlap (Du Prel et al., 2009). In the multinomial logistic regression, significant associations for class membership to demographic and clinical factors was met when confidence intervals did not contain 1.

Results

Sample characteristics

Table 1 provides information describing the study sample (N = 118)[1] across demographic, clinical, emotional vulnerability, and antisocial impulsivist measures.

Latent class analyses

Table 2 shows model fit statistics for each latent class model. Although the five-class model showed the lowest AIC and ABIC, the smallest class of this model was 3.4%, which is too small given our sample size of 118. Additionally, the three-class model showed the lowest BIC, and the smallest class of this model was 15.3%, which is greater than the smallest class (5.9%) of the four-class model. Further, model nonconvergence occurred after three classes, suggesting four or five class models were not appropriate for our data. Thus, a three-class model was identified as the best fitting model. The identified groups were similar to the subtypes of the Pathways Model. Table 3 presents these groups, which we conceptualized as (1) 'opioid-related only' (55.9%), (2) 'personal trauma/emotionally vulnerable' (15.3%), and (3) 'impulsive/current psychopathology' (28.8%). Class 1 was characterized by lower scores on all indicators compared to Class 2 and Class 3, with the exception of comparable scores for meaning-in-life measures. Class 2 was characterized by higher scores than Class 1 and Class 3 for experiencing sexual abuse and interpersonal violence, and higher scores for depression, stress, experiencing physical and emotional

Table 1. Sample characteristics (N = 118).

	n (%)	M (SD)	Range
Demographic and Clinical Factors			
Black/African American Race	75 (63.6)		
Male Gender	69 (58.5)		
High School Education	83 (70.3)		
Age at Survey		52.65 (13.63)	25–73
Age of Regular Opioid Use Onset (DHUQ)		27.11 (9.67)	14–59
Prior MMT	92 (78.0)		
Lifetime Opioid-Related Consequences (HUC)		9.72 (3.90)	1–16
Injection Opioid Use in Lifetime (DHUQ)	52 (44.1)		
Substance Misuse History in Social Network	84 (72.4)		
Lived with Someone Misusing Substances	87 (73.7)		
Positive Screen, Co-Occurring Addiction	75 (63.0)		
Past-Year Cocaine (SDS)	46 (39.0)		
Past-Year Alcohol (AUDIT-C)	30 (25.4)		
Lifetime Gambling (NODS-CLiP)	34 (28.8)		
Emotional Vulnerability			
Loneliness (UCLA-3)		5.84 (2.04)	3–9
Depression (DASS-21)		13.36 (8.83)	0–40
Stress (DASS-21)		16.34 (9.14)	2–42
Physical Abuse (CTQ-SF)		9.54 (5.12)	5–25
Emotional Abuse (CTQ-SF)		10.37 (5.34)	5–25
Sexual Abuse (CTQ-SF)		7.79 (5.95)	5–25
Interpersonal Violence (CTS2)		2.93 (2.84)	0–8
Community Violence (TISH)		9.06 (3.38)	0–15
Opioid-Related Coping Motives (DMQ)		16.29 (4.11)	3–21
Antisocial Impulsivist			
Trait-based Impulsivity (BIS-15)		36.58 (7.33)	16–60
Meaning-in-life Search (MLQ)		15.53 (4.30)	3–21
Meaning-in-life Presence (MLQ)		14.07 (4.78)	3–21

Note: Reference categories include Other Race, Female Gender, Less Than High School Degree, and the absence of all remaining dichotomous measures. The HUC scale excluded the three-item factor assessing school-related consequences due to the age range in this sample.

Table 2. Model fit indices.

Number of Classes	AIC	BIC	ABIC	Entropy	BLRT p-value	Smallest class, %
1	8511.149	8577.645	8501.775	N/A	N/A	N/A
2	8255.922	8358.437	8241.471	.869	<.001	39.5
3	8088.346	8226.881	8068.818	.932	<.001	15.3
4	8018.594	8193.147	7993.989	.951	<.001	5.9
5	7991.747	8202.319	7962.064	.941	<.001	3.4

Note. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; ABIC = Adjusted Bayesian Information Criterion; BLRT = Bootstrap Likelihood Ratio Test. Models 4 and 5 did not converge.

abuse, witnessing community violence, opioid-related coping motives, and trait-based impulsivity than Class 1. Class 3 was characterized by higher scores for loneliness than Class 1 and Class 2, and higher scores for depression, stress, experiencing physical, emotional, and sexual abuse, interpersonal violence, witnessing community violence, opioid-related coping motives, and trait-based impulsivity than Class 1. Scores for depression, stress, and physical abuse measures were observably different for Classes 2 and 3, though confidence bands overlapped [see Figure 1].

Table 3. Three-latent-class model of the Pathways Model indicators in patients initiating methadone maintenance treatment for opioid use disorder.

	Class 1: Opioid-Related Only (55.9%)	Class 2: Personal Trauma/ Emotionally Vulnerable (15.3%)	Class 3: Impulsive/Current Psychopathology (28.8%)
Indicators	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)
Emotional Vulnerablility			
Loneliness	4.88 (4.24, 5.42)	6.02 (2.21, 6.87)	7.55 (6.97, 8.13)[c, d]
Depression	8.86 (7.39, 10.32)	15.18 (11.23, 19.88)[a]	20.82 (16.77, 24.87)[c]
Stress	11.22 (9.42, 13.02)	20.28 (16.28, 25.06)[a]	23.87 (20.60, 27.15)[c]
Physical Abuse	7.15 (6.46, 7.84)	14.93 (12.53, 17.78)[a]	11.26 (9.03, 13.49)[c]
Emotional Abuse	7.22 (6.19, 8.24)	14.50 (12.36, 17.05)[a]	14.16 (11.88, 16.44)[c]
Sexual Abuse	5.04 (4.95, 5.13)	20.95 (18.87, 23.43)[a, b]	6.18 (5.43, 7.08)[c]
Interpersonal Violence	1.58 (1.02, 2.14)	5.95 (5.02, 7.06)[a, b]	3.91 (2.82, 5.00)[c]
Community Violence	7.69 (6.89, 8.49)	10.60 (9.57, 11.82)[a]	10.84 (9.62, 12.06)[c]
Opioid-Related Coping Motives	14.43 (13.26, 15.61)	18.46 (17.40, 19.73)[a]	18.64 (17.80, 19.48)[c]
Antisocial Impulsivist			
Trait-based Impulsivity	33.43 (31.68, 35.17)	39.62 (36.79, 43.00)[a]	40.90 (38.62, 43.18)[c]
Meaning-in-life Search	15.29 (14.19, 16.39)	17.12 (15.52, 19.02)	15.19 (13.68, 16.69)
Meaning-in-life Presence*	14.90 (13.82, 15.98)	14.93 (12.83, 17.44)	12.07 (10.05, 14.10)

Note. CI = Confidence Interval. All indicators are continuous. *Higher scores for Meaning-in-Life Presence is a protective measure for OUD risk. Superscripts indicate confidence bands that do not overlap, for the following group comparisons: [a] Class 2 higher than Class 1; [b] Class 2 higher than Class 3; [c] Class 3 higher than Class 1; [d] Class 3 higher than Class 2.

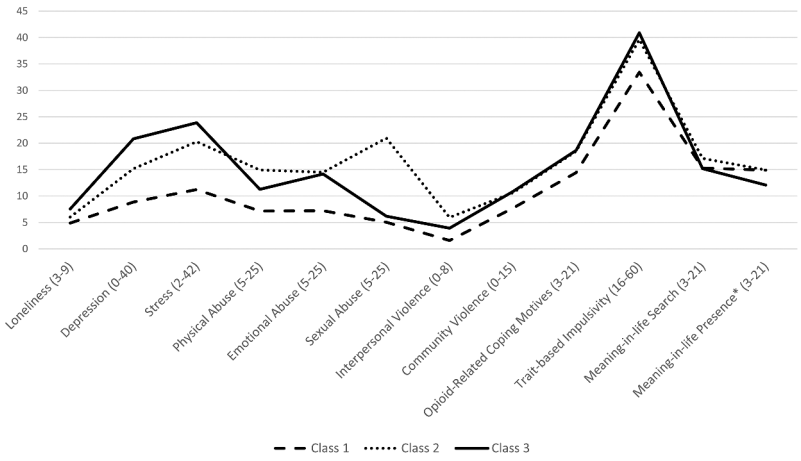

Figure 1. Plot of the three-latent-class model of the pathways model indicators in patients receiving methadone maintenance treatment for OUD. *Higher scores for meaning-in-life presence is a protective measure for OUD risk. Score range in sample in parentheses.

Characteristics associated with class membership

Table 4 presents the associations of demographic and clinical factor measures with latent class membership. Male patients (OR = 0.14) and older patients (OR = 0.91) had lower odds of being in Class 2 compared to Class 1. Patients with greater opioid-related consequences had higher odds of being in Class 2 than Class 1 (OR = 1.26) and Class 3 compared to Class 1 (OR = 1.30). Patients with a substance misuse history in their social network had higher odds of being in Class 2 compared to Class 1 (OR = 12.25). Class 2

Table 4. Multinomial logistic regression results predicting latent class membership.

	Class 1 vs.				Class 2 vs.	
	Class 2		Class 3		Class 3	
Reference Group	OR	95% CI	OR	95% CI	OR	95% CI
Black/African American Race	0.75	0.11–5.04	3.72	0.21–65.83	4.95	0.41–60.33
Male Gender	0.14*	0.03–0.76	0.49	0.15–1.66	3.47	0.63–19.09
High School Education	0.60	0.12–2.94	0.90	0.20–4.10	1.50	0.35–6.45
Age at Survey	0.91*	0.84–0.99	0.90	0.81–1.01	0.99	0.91–1.09
Age of Regular Opioid Use Onset	1.03	0.94–1.13	1.00	0.94–1.05	0.96	0.88–1.06
Prior MMT	1.30	0.23–7.23	0.49	0.09–2.62	0.38	0.07–1.90
Lifetime Opioid-Related Consequences	1.26*	1.01–1.58	1.30*	1.09–1.55	1.03	0.85–1.25
Injection Opioid Use in Lifetime	0.41	0.06–2.70	0.43	0.12–1.51	1.05	0.19–5.84
Substance Misuse History in Social Network	12.25*	1.63–91.98	2.48	0.47–13.14	0.20	0.02–1.73
Lived with Someone Misusing Substances	0.30	0.07–1.40	0.44	0.09–2.22	1.45	0.34–6.18
Positive Screen, Co-Occurring Addiction	1.13	0.28–4.58	4.08	0.73–22.88	3.62	0.86–15.28

Note. OR = Odds Ratio; CI = Confidence Interval. Positive screens for addiction was defined as having one or more positive screen on co-occurring addiction measures for alcohol, cocaine, and gambling.
* denotes that confidence interval does not contain 1.

did not differ from Class 3 on any measures. Race, education, prior MMT, age of regular opioid use onset, injection opioid use in lifetime, living with someone misusing substances, and having a positive screen for co-occurring addiction were not associated with latent class membership.

Discussion

The aim of this study was to examine OUD subtypes in a sample of patients receiving MMT at a university-affiliated clinic. To date, the OUD subtyping literature has largely relied on a subtyping classification developed using the Symptom-Checklist 90 (Derogatis et al., 1974; I. Maremmani et al., 2010), a self-report symptom inventory of psychological distress, and not a measure designed for the purposes of OUD subtyping analyses. By comparison, subtyping in the field of gambling studies has relied on the Pathways Model, a theoretically-informed (Blaszczynski & Nower, 2002) and empirically-validated subtyping framework (Nower & Blaszczynski, 2017). To address this gap, our objective was to adapt the Pathways Model to an OUD patient sample to see whether the model translates to another addictive disorder.

Our LCA findings generally demonstrated overlap with the three Pathways Model subtypes (Nower & Blaszczynski, 2017), with some noteworthy differences. Our Class 1 'opioid-related only' subtype was characterized by lower scores on nearly all indicators, similar to the Pathways Model's 'behaviorally conditioned' subtype (Pathway 1). Our Class 2 'personal trauma/emotionally vulnerable' subtype is similar to the model's 'emotionally vulnerable' subtype (Pathway 2) in that both have high levels of childhood trauma, stress, coping, and mood impairments (Nower & Blaszczynski, 2017). Our Class 2 also demonstrated higher scores for experiencing interpersonal violence than other classes. Our Class 3 'impulsive/current psychopathology' subtype is similar to the Pathways Model's 'antisocial impulsivist' subtype, though it differs in some respects. Most notably, our Class 3 had the highest scores for all current psychopathology

measures and didn't differ in meaning-in-life measures. Similar to Pathway 3, our Class 3 also had the highest levels of impulsivity and higher trauma scores than Class 1. In contrast, impulsivity scores for Class 2 were only marginally lower than Class 3 scores, whereas impulsivity scores for Pathway 2 were intermediate relative to Pathways 1 and 3. These findings likely reflect preliminary evidence that some pathways (trauma, emotional vulnerability) between OUD and gambling disorder samples may be trans-diagnostic and represent processes that generally underlie addictions, while others (e.g. meaning-in-life domains) may be disorder-specific. One pathway, impulsivity, had a key role in characterizing OUD subtypes, as it has with gambling samples, though its role in our study was nuanced and supports trans-diagnostic and disorder-specific interpretations. Similar to the findings demonstrated by Maremmani et al. (2018), which demonstrated that the OUD sample generally experienced greater levels of psychological severity than the gambling disorder sample, this analysis of OUD patients revealed high levels of opioid-related and psychological severity in two of the three classes.

Although our subtyping findings generally overlapped with the Pathways Model, it is possible some of the differences are due to measurement discrepancies. Compared to the Pathways Model validation study (Nower & Blaszczynski, 2017), we included a wider array of trauma measures (e.g. personal trauma experiences in interpersonal relationships, witnessing of community violence) and a less comprehensive assessment of antisocial traits and risk-taking. In addition, this study did not differentiate depression or anxiety pre- and post-initiation of opioid use, included additional emotional vulnerability variables (e.g. loneliness) that were not prescribed by the Pathways Model, and involved a broader conceptualization of impulsivity than the narrow impulsivity prescribed by the model.

Compared to the foundational OUD subtyping study led by I. Maremmani et al. (2010), our framework reveals a few key differences. Our analysis yielded fewer subtypes, and some aspects of our subtyping model utilized indicators not captured by the psychological distress symptoms of the Symptom-Checklist 90. For example, our analysis included external events (personal experiences with interpersonal violence, witnessing community violence) reported by patients and meaning-in-life measures that can correlate with both psychological distress and psychological growth (Davis et al., 2007). Furthermore, our model allowed subtypes such as the 'opioid-related only' class to emerge based on low scores that distinguish membership, whereas participants with low scores would be classified in the model developed by I. Maremmani et al. (2010) on the basis of their highest z-score risk factor, potentially merging patients with pervasive and narrow severity levels to the same subtype.

The multinomial regression revealed correlations between class membership and demographic and clinical factors. Most notably, we found that male and younger patients were more likely to be in Class 2 than Class 1. By comparison, gender distinguished each class in Nower and Blaszczynski's (2017) analysis, and the original Pathways Model hypothesized that the youngest group would be in Pathway 3. We also found that a greater accumulation of lifetime opioid-related consequences distinguished Classes 2 and 3 from Class 1, offering support for interpreting Class 1 as having lower opioid-related severity. Similarly, Class 1 had lower scores for having someone misuse substances in their social network than Class 2. Other studies have found that women were more likely to report substance misuse in their social network (Brown et al., 2015; Lister

et al., 2019), similar to what we found in this analysis, where Class 2 was distinguished from Class 1 by female gender and social network substance misuse. From a generalizability perspective, the lack of associations for the remaining demographic and clinical factors suggests that our subtyping framework was not unduly influenced by our sampling idiosyncrasies.

Implications

The findings from this analysis reveal directions for future research and clinical strategies to improve treatment protocols for OUD patients in MMT. With regard to future investigations, we encourage etiological researchers in addictions to see our findings as additional support for both a trans-diagnostic approach in the conceptualization of addictive disorders (Jacobs, 1986; Shaffer et al., 2004) and preliminary evidence of disorder-specific differences between addiction types (Kim et al., 2020). To find a balance between these approaches, we recommend addiction researchers include a variety of principal addiction types within their sampling strategy. When each subsample is sufficiently represented, we suggest research questions that examine whether study findings are trans-diagnostic, disorder-specific, or some combination thereof. Second, we believe these findings highlight the value of adapting established hypotheses and frameworks from one addictive disorder field to others where gaps in knowledge exist.

From a clinical strategy perspective, these findings show a considerable psychosocial burden experienced by most OUD patients in MMT, especially Classes 2 and 3. However, few of the measures we administered are routinely collected at MMT clinics, which often rely on intake data from non-validated measures. MMT clinics are encouraged to integrate validated screening tools, when feasible, to intake materials required by local, state, and/or federal regulations. As few investigations exist on how the characteristics we used as indicators predict MMT outcomes, future research examining treatment outcome patterns by OUD subtypes can demonstrate important information about treatment trajectories and help establish assessment and treatment protocols tailored to the needs of OUD subtypes.

Limitations

This study was not without limitations. First, all patients were recruited from one clinical setting in a large urban area with high poverty rates. Although these findings do not generalize to all OUD treatment settings, many MMT clinics are located in areas with similar sociodemographic characteristics. Second, our sample size may have influenced findings. Though large samples are ideal for correct identification of the number of classes, the LCA fit indices supported a three-class solution. Lower statistical power may have contributed to false negative interpretation (Type II error) of results in the multinomial regression analyses. Third, we did not collect the measures used in this study for the purpose of adapting the Pathways Model for an OUD patient sample. To address these limitations, future research should examine OUD patient subtypes with larger samples, drawn from multiple sites to allow for a greater number of indicators and/or wider range of principal addictive

disorders, conduct subpopulation analyses (e.g. OUD patients with and without co-occurring gambling disorder), and evaluate if our subtyping model improves after refining indicators.

Conclusion

There has been limited attention to subtyping in OUD patient samples drawing on theoretically-informed frameworks. The existing studies have occurred largely in Europe, where OUD patient and treatment-seeking characteristics differ from those in the US context. To address these issues, we adapted a widely-utilized subtyping framework in the field of gambling studies, the Pathways Model, for an OUD patient sample, to see whether the model translates to a different addictive disorder. Our findings generally demonstrate trans-diagnostic overlap with the Pathways Model subtypes in gambling disorder samples, with some differences that may reflect OUD-specific factors. We encourage etiological and clinical researchers in behavioral and substance-based addictions to consider our findings in future subtyping analyses.

Endnote

1. Three cases were removed from the dataset (n = 1, left before completing the study; n = 1, participated a second time; n = 1 enrolled 15 days after intake). After removals, the data set included a final sample of 118 patients.

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Preregistration statement

The authors declare that there is no pre-registration in relation to this study.

Data availability

Due to the nature of this research, participants of this study did not agree for their data to be shared publicly, so supporting data is not available.

Author Contributions

JJL led writing, conceptualization, methods, findings interpretation, and data collection; acquired funding as Principal Investigator; provided supervision to MY and JDE for data curation and statistical analyses. MY co-led statistical analyses; contributed to writing, conceptualization, methods, and findings interpretation. LN contributed to writing, conceptualization, methods, and findings interpretation. JDE led data curation; co-led statistical analyses; contributed to writing, conceptualization, methods, and findings interpretation. DML contributed to writing, conceptualization, methods, and findings interpretation; provided expertise on data collection strategies.

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