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Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep



Use of item response theory and latent class analysis to link poly-substance use disorders with addiction severity, HIV risk, and quality of life among opioid-dependent patients in the Clinical Trials Network*

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ARTICLE INFO

Article history: Received 9 November 2010 Received in revised form 18 March 2011 Accepted 23 March 2011 Available online 17 April 2011

Keywords:
Clinical Trials Network
Comorbidity
Item response theory
Latent class analysis
Multiple indicators—multiple causes model
Opioid dependence
Polysubstance use
Substance use disorders

ABSTRACT

Background: This study applied item response theory (IRT) and latent class analysis (LCA) procedures to examine the dimensionality and heterogeneity of comorbid substance use disorders (SUDs) and explored their utility for standard clinical assessments, including the Addiction Severity Index (ASI), HIV Risk Behavior Scale (HRBS), and SF-36 quality-of-life measures.

Methods: The sample included 343 opioid-dependent patients enrolled in two national multisite studies of the U.S. National Drug Abuse Treatment Clinical Trials Network (CTN001–002). Patients were recruited from inpatient and outpatient addiction treatment settings at 12 programs. Data were analyzed by factor analysis, IRT, LCA, and latent regression procedures.

Results: A two-class LCA model fit dichotomous SUD data empirically better than one-parameter and two-parameter IRT models. LCA distinguished 10% of severe comorbid opioid-dependent individuals who had high rates of all SUDs examined—especially amphetamine and sedative abuse/dependence—from the remaining 90% who had SUDs other than amphetamine and sedative abuse/dependence (entropy = 0.99). Item-level results from both one-parameter and two-parameter IRT models also found that amphetamine and sedative abuse/dependence tapped the more severe end of the latent poly-SUD trait. Regardless of whether SUDs were defined as a continuous trait or categorically, individuals characterized by a high level of poly-SUD demonstrated more psychiatric problems and HIV risk behaviors.

Conclusions: A combined application of categorical and dimensional latent approaches may improve the understanding of comorbid SUDs and their associations with other clinical indicators. Abuse of sedatives and methamphetamine may serve as a useful marker for identifying subsets of opioid-dependent individuals with needs for more intensive interventions.

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1. Introduction

Opioid use disorders are among the most prevalent substance use disorders (SUDs) in addiction treatment programs, and comorbid SUDs are widespread among patients with opioid addiction (Strain, 2002; Substance Abuse and Mental Health Services Administration [SAMHSA], 2009). Due to a significant increase in prescription opioid abuse, opioid use disorders now comprise the

second most prevalent drug use disorder in the United States (following marijuana), and opioids are associated with the highest rate of increase in addiction treatment use (SAMHSA, 2010). Evidence from the National Epidemiologic Survey on Alcohol and Related Conditions confirms a higher lifetime rate of SUDs (alcohol, nicotine, any drug) among heroin users (63–85%), other opioid users (53–76%), and heroin–other opioid users (72–94%) than among non-opioid drug users (34–63%) (Wu et al., 2011).

Comorbid SUDs complicate clinical courses and treatment designs (Strain, 2002; Veilleux et al., 2010). Although researchers have highlighted the significance of incorporating full diagnostic configurations into treatment and research designs (Carroll and Rounsaville, 2002; Rounsaville et al., 2003), little is known about

A Supplementary figure for this article can be found by accessing the online.

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how to conceptualize and classify co-occurrences of multiple SUDs and how to link this information with other clinical indicators to inform research and the forthcoming fifth edition of the *Diagnostic* and *Statistical Manual of Mental Disorders* (DSM-5) (Saunders et al., 2007). Here, we apply item response theory (IRT) and latent class analyses (LCAs) to examine co-occurring SUDs, employing regression procedures to link empirically defined latent variables with standard assessments of clinical severity indicators.

The IRT approach to SUDs recognizes variability in the risk and manifestations of the addiction severity continuum (Kirisci et al., 2006; Vanyukov et al., 2009). It assumes that a latent severity trait underlies response patterns of SUDs; severity refers to various degrees of maladaptive substance use behaviors and consequences measured by DSM-IV SUD criteria. This approach suggests that SUDs are a continuous condition and that the severity level increases as greater numbers of SUDs are present. In particular, IRT can evaluate how items perform (e.g., item difficulty) along the underlying latent liability. IRT studies of DSM-IV SUD criteria for individual SUD have found a unidimensional latent trait underlying diagnostic symptoms for each disorder (Gillespie et al., 2007; Langenbucher et al., 2004; Saha et al., 2006; Wu et al., 2009a,b, 2010a).

These IRT studies focus mainly on an individual substance class. Because polysubstance use is common among drug abusers, and the risk for addiction generally is accounted for by shared, multiple familial and environmental factors (Kendler et al., 2003; Leri et al., 2003; Rounsaville et al., 2003; Tsuang et al., 1998), it is likely that various SUDs indicate a unifying dimensional severity trait (Kirisci et al., 2006). Very few studies have examined polysubstance use as reflecting a single latent trait. Kirisci et al. (2002) examined lifetime use of 10 substance classes and found that the 10 binary substance use variables were scalable as an index for a continuous latent trait score, which was positively associated with the level of other drug use-related problems. Kirisci et al. (2006) further applied IRT analysis to examine dichotomous indicators (abuse/dependence vs. no) of nine lifetime SUDs (alcohol, cannabis, amphetamines, inhalants, hallucinogens, cocaine, opioids, phencyclidine, sedatives) in a sample of family studies of SUDs. They found that various binary variables of SUDs formed a unidimensional trait and that the trait score correlates with risky sexual behavior and treatment use. These findings suggest the feasibility of linking the latent factor score with other measures to better understand patients' severity profiles and inform nosological research (American Psychiatric Association [APA], 2010).

On the other hand, LCA can elucidate the presence of heterogeneity of poly-substance use or disorders by using the information from response patterns of various SUDs to classify individuals into a few mutually exclusive classes (Muthén and Muthén, 2000). For example, Wu et al. (2009c) found three LCA-defined groups of ecstasy users distinguished by level of drug use (primary marijuana, marijuana/cocaine, polysubstance); the most severe group was most likely to use addiction treatment. Agrawal et al. (2007) performed LCA on 10 binary indicators of lifetime drug use disorders and identified five groups (none, marijuana, stimulants/hallucinogens, prescription drugs, pervasive polysubstance) that differed in other psychiatric disorders. These results and others have shown that LCA-defined classes often vary from lessto-more-severe profiles in family history and multiple health indicators, suggesting LCA's utility in distinguishing less from more severe groups to inform research and differential intervention (e.g., Bucholz et al., 1996).

To date, studies often have focused on a single SUD and relied exclusively on either IRT or LCA. Here, we consider all available SUDs and compare IRT and LCA results to evaluate latent factor and class structures that may explain comorbid SUDs. While IRT analysis provides empirical information on item-level function-

ing along the latent liability, LCA may complement IRT results by differentiating less from more severe groups (heterogeneity). The utility of IRT-defined latent poly-SUD score and LCA-defined poly-SUD groups then is examined by regression procedures to assess their association with other standard assessments of clinical severity, including the Addiction Severity Index (ASI), HIV Risk Behavior Scale (HRBS), and SF-36 quality of life (Veilleux et al., 2010).

Due to high rates of comorbid SUDs in treatment-seeking patients and the need for empirical data to inform treatment research and classification of SUDs, we examined a geographically diverse sample of opioid-dependent adults to: (a) determine whether various SUDs relate to a latent poly-SUD trait or latent groups (poly-SUD vs. severe poly-SUD); (b) identify demographic characteristics of opioid-dependent adults with increased odds of poly-SUD to inform subgroup disparities; and, as suggested by the DSM-5 workgroup (Saunders et al., 2007), (c) explore the utility of the latent poly-SUD by determining its associations with subscales from ASI, HRBS, and SF-36. We extend from prior research by examining study participants recruited from inpatient and outpatient addiction treatment settings at 12 programs across the U.S., focusing on current SUDs and other clinical measures to better reflect clinical indicators of severity, including nicotine use disorders, and using both continuous and categorical approaches to improve understanding of heterogeneity among individuals with SUDs.

2. Methods

2.1. Data source

Analyses were performed on the data from two multisite Clinical Trials Network (CTN) studies that evaluated the effectiveness of buprenorphine–naloxone and clonidine for opioid detoxification in inpatient (N = 113) and outpatient (N = 230) community-based treatment programs (Ling et al., 2005). Inpatients were recruited from six programs located in eastern, southeastern, midwestern, or western regions of the U.S.; outpatients were recruited from six programs located in eastern, midwestern, or western regions. Eligible patients included adults aged \geq 18 years who met DSM-IV criteria for opioid dependence and were in need of medical management for opioid withdrawal.

Patients were excluded if they had a serious psychiatric/medical condition that would make participation medically hazardous; had a known allergy or sensitivity to buprenorphine, naloxone, or clonidine; were receiving medications contraindicated with clonidine or had a systolic blood pressure <100 mm Hg or pulse <56 beats/min; had been enrolled in a methadone treatment program or had participated in another investigational drug study within 30 days of study enrollment; or could not remain in the area for the duration of active treatment. To enhance the study's generalizability, dependence on other drugs did not exclude individuals from participation unless immediate medical attention was required to manage these disorders. Female participants were excluded if pregnant or lactating and were required to have a negative pregnancy test prior to randomization.

2.2. Study variables

Demographics included age, gender, race/ethnicity, education, and employment status. Past-year SUDs (abuse or dependence: tobacco/nicotine, alcohol, cannabis, cocaine, inhalants, amphetamines/methamphetamine, sedatives, hallucinogens) were assessed by the DSM-IV checklist (Hudziak et al., 1993). Substance-specific dependence criteria were assessed, and endorsing ≥ 3 of the seven DSM-IV dependence criteria resulted in a dependence diagnosis (tolerance, withdrawal, substance often taken in large amounts/for longer periods of time, persistent desire or unsuccessful attempt to cut down, a great deal of time spent in activities necessary to get the substance, important activities given up, continued substance use despite knowledge of having recurrent physical/psychological problems). Substance-specific abuse criteria were assessed, and endorsing ≥ 1 of the four DSM-IV abuse criteria resulted in an abuse diagnosis (role interference, hazardous use, problems with the law, relationship problems).

Addiction severity at intake was assessed by the ASI—a standardized clinical interview widely used to assess substance use-related problems in alcohol use, drug use, medical, psychiatric, legal, family/social, and employment domains (McGahan et al., 1982; McLellan et al., 1985). Each ASI composite score (range 0–1) is mathematically derived to summarize responses to several questions within a problem area, with higher scores indicating greater problem severity.

HIV risk was assessed by the HRBS, an instrument with demonstrated reliability and construct validity in drug users (Darke et al., 1991; Petry, 2001). It assesses injection drug use (needle sharing, use of unclean needles) and unprotected sexual behaviors (multiple sexual partners, lack of condom use) in the past 30 days.

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