

**THE LONGITUDINAL IMPACT OF INTRINSIC MOTIVATION ON
SUBSTANCE USE SEVERITY IN SCHIZOPHRENIA AND ITS
PATTERNS IN MEN AND WOMEN**

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Abstract

Schizophrenia is a complex and disabling psychiatric disorder that results in significant burden and challenges to those who suffer from it, their families, and to our larger society. One of the most vexing problems facing individuals with schizophrenia today is the co-occurrence of substance use disorders (SUDs). Longitudinal evidence indicates that many individuals with schizophrenia and comorbid SUD exhibit severe patterns of substance use over the course of the disorder, such that few achieve sustained remission or recovery. Intrinsic motivation deficits are promising potential contributors to substance use severity in this population, and consequently might serve as effective treatment targets. There is also evidence to suggest that women show less deficit in intrinsic motivation than men. To date, measurement in this area has been limited, and no study has investigated the longitudinal relations between prospective changes in intrinsic motivation and changes in substance use severity among individuals with schizophrenia and comorbid SUD. This study makes use of baseline, 6-, and 12-month follow-up data from patients with schizophrenia and comorbid SUD ($n = 535$ at baseline; $n = 219$ at 6-months; $n = 150$ at 1-year) selected from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study to: (1) extend validation of a promising new measure of intrinsic motivation developed by

Nakagami, Xie, Hoe, and Brekke (2008) for schizophrenia to schizophrenia and comorbid SUD; (2) elucidate its longitudinal relations with substance use severity among this population; (3) and examine whether such relations vary across genders. A comprehensive psychometric analysis was used to examine the factor structure, reliability, and retest reliability of the instrument in this population; and hierarchical linear regression and hierarchical linear modeling were among the analytic methods used to examine the cross-sectional and longitudinal relations between intrinsic motivation and substance use severity. Psychometric results supported the reliability and retest reliability of the intrinsic motivation measure when applied to schizophrenia and comorbid SUD, but also revealed a potential shift in the latent factor structure of the instrument. Cross-sectional findings revealed a significant negative prediction of intrinsic motivation by alcohol and drug use severity after adjusting for demographic and clinical confounds, neurocognition and negative symptoms. Longitudinal results with intrinsic motivation strengthened the findings garnered in the cross-sectional analyses. Evidence was found suggesting longitudinal intrinsic motivation change is a salient incremental predictor of reductions in patient's alcohol/ drug use severity, above and beyond the effects of age, illness chronicity, overall psychopathology, comorbidity status, and phase 1 randomization medication effects. Analyses of relations with gender indicated little to no cross-sectional associations between intrinsic motivation and substance use severity, and gender did not moderate the longitudinal association between intrinsic motivation and substance use severity. These findings suggest that changes in intrinsic motivation may be uniquely associated with changes in substance use severity in schizophrenia and comorbid SUD. Future research will need to replicate these findings, while focusing on intervention efforts that seek to target the intrinsic motivation deficits of schizophrenia and comorbid SUD, to help offset the severe and destabilizing effects exacted by substance use severity in this population.

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PREFACE

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I. INTRODUCTION

A. OVERVIEW

Schizophrenia is a complex and disabling psychiatric disorder that poses significant challenges to those who suffer from it, their families, and to our larger society. The disorder affects about 1% of the population, is considered among the top 10 disease related disabilities in the world (Murray & Lopez, 1996), and is characterized by the presence of positive (thought disturbance, delusions, hallucinations) and negative symptoms (ahedonia, amotivation, anergia). One of the most vexing problems facing people with schizophrenia today is the co-occurrence of substance use disorders (SUDs), which affects about 50% of those with the disorder during a lifetime (Reiger et al., 1990; Volkow, 2009; see Chapter 2 for a more detailed description of SUD pathology in schizophrenia). Many people with co-occurring SUDs and schizophrenia experience severe and persistent patterns of substance use during the course of the disorder, such that few are clinically stable, gainfully employed, or adequately housed (Drake, O'Neal, & Wallach, 2008). Since few persons among this population are motivated to reduce their use of substances, many persist with their patterns of use for years in the face of significant disability (Horsfall, Cleary, Hunt, & Walter, 2009). Consequently, this comorbidity is associated with less favorable long-term outcomes in schizophrenia and represents a major, unsolved challenge for the clinical management and outcome of this population (Mueser et al., 1990; Green, Zimmet, Strous, & Schildraut, 1999; Green, 2005).

Recent evidence indicates that one of the most likely potential contributors to the pervasive patterns of substance use severity in persons with comorbid SUD and schizophrenia are deficits in intrinsic motivation. Intrinsic motivation concerns the inherent tendencies that all human beings have to seek out novelty and challenges, to extend and exercise capacities, and to

explore and to learn (Deci & Ryan, 2007). When people carry out behaviors in the absence of any extrinsic tangible reward (i.e., money or praise), and do not require any external support to sustain the behavior, the motivation for engaging in such a process is said to be intrinsic (Deci & Ryan, 2007). Recently, research among persons with dual disorders has begun to point to the importance of deficits in intrinsic motivation to substance use severity in schizophrenia (Martino, Carroll, Kostas, Perkins, & Rounsaville, 2002; Graber, Moyers, Griffith, Guajardo, & Tonigan, 2003; Kavanagh et al., 2004a; James et al., 2004; Edwards et al., 2006; Baker, Bucci, Lewin, Kay-Lambkin, Constable, & Carr, 2006; Martino, Carroll, Nich, & Rounsaville, 2006; Drapalski, Bennett, & Bellack, 2011), with emerging evidence suggesting that women exhibit a greater readiness to change their substance use behaviors than men (Drapalski et al., 2011), which may lead to greater reductions in substance use severity for women in this population. However, this research has been largely limited by modest sized samples of dual diagnosis participants selected from specialty populations (i.e., veterans, first episode psychosis) that has included few women and persons with comorbid SUD and schizophrenia. Consequently, there is a need for studies that seek to comprehensively examine intrinsic motivation among larger and more heterogeneous samples of persons with comorbid SUD and schizophrenia by investigating its impact on substance use severity, and whether such relations vary across genders.

For this dissertation, intrinsic motivation is conceptualized in terms of the behaviors people carry out because of the positive feelings that are associated with performing actions in the absence of extrinsic rewards (Deci & Ryan, 2007). These actions do not require for such persons to rely on external support to be initiated or sustained. This dissertation utilizes an operational definition of intrinsic motivation that is based on the sum of theoretically relevant items taken from the Quality of Life Scale (Heinrichs, Hanlon, & Carpenter, 1984), including

purpose, curiosity, and motivation. Using these conceptual and operational definitions, Nakagami, Xie, Hoe, and Brekke (2008) developed a promising new instrument for measuring intrinsic motivation in schizophrenia. Psychometric evaluations of the instrument have shown that it yields valid assessments of intrinsic motivation and demonstrates moderate levels of internal consistency ($\alpha = .74$) among community patients with the disorder (Nakagami et al., 2008). Subsequent investigations using this instrument have not only confirmed a long history of evidence indicating that persons with schizophrenia possess intrinsic motivation deficits (i.e., Barch, 2004), but have also shown that such deficits impede the ability of those with the disorder to generate internal drives to sustain behavior changes absent external support or reinforcement (Nakagami et al., 2008; Yamada, Lee, Dinh, Barrio, & Brekke, 2010; Nakagami, Xie, Hoe, & Brekke, 2010). Perhaps not surprisingly, evidence from the dual diagnosis field has also shown that such deficits can disengage intrinsic motivational processes when persons with comorbid SUD and schizophrenia try to generate their internal drives toward reducing substance use severity (i.e., Drake et al., 2008; Horsfall et al., 2009).

While various instruments have been used to measure intrinsic motivation in the dual diagnosis treatment research, such approaches largely focus on the degree to which such persons exhibit intrinsic motivation to change substance-specific behaviors (i.e., DiClemente, 2003; DiClemente, Nidecker, & Bellack, 2008). This research does not seek to take any of these more widely used substance-specific behavior approaches to the measurement of intrinsic motivation (i.e., DiClemente 2003), but rather seeks to extend validation of a more general measure of the construct developed by Nakagami and colleagues (2008) in schizophrenia to schizophrenia and comorbid SUD. This instrument may not only provide greater accuracy to estimating the base rates of intrinsic motivation deficits schizophrenia and comorbid SUD, but may also provide

greater insight into the longitudinal relationship between such deficits and substance use severity among this population. Further, it is also important to clarify that this research does not seek to estimate the relationship between intrinsic motivation and substance use severity via readiness-to-change measures in the context of a motivational rehabilitation program, but rather seeks to examine the prospective naturalistic changes in such relations in schizophrenia and comorbid SUD. Conducting such a study is important as extending validation of a diagnosis-specific instrument to schizophrenia and comorbid SUD may serve as a critical component in informing whether prospective naturalistic changes in intrinsic motivation can lead to reductions in substance use severity among this population.

Recently, Nakagami, Xie, Hoe, and Brekke (2010) showed that their intrinsic motivation instrument predicted change in functional outcomes in community patients with schizophrenia, suggesting that such deficits are important areas to target in intervention research. While this measure has yet to be validated in schizophrenia and comorbid SUD, there is evidence from the dual diagnosis treatment research to suggest that such deficits can be improved among this population via participation in motivation rehabilitation programs (i.e., which generally, though not always, target reductions in SUD pathology), and that improvements in intrinsic motivation may be linked with reductions in substance use severity (i.e., Hunt et al., 2013; for review). For example, compelling evidence from a motivational intervention study by Graber and colleagues (2003) demonstrated that non-treatment seeking (for SUD pathology) persons with co-occurring SUDs and schizophrenia can develop and/or build intrinsic motivation for carrying out and sustaining behavior changes to reduce their use of substances. More recently, evidence from a motivational intervention study by Drapalski and colleagues (2011) showed that treatment-seeking (for SUD pathology) women with dual disorders were more intrinsically motivated to

change their behaviors associated with SUD pathology than men. Indeed, these motivational rehabilitation studies suggest that persons with schizophrenia and comorbid SUD can reduce their substance use severity so long as they make gains in their intrinsic motivation. Compared to men, women may exhibit a greater ability to reduce such severities as they make gains in their intrinsic motivation. However, little is known about the relationship between changes in intrinsic motivation and changes in substance use severity as they naturally occur outside of these specialty intervention programs that very few in this population receive.

The contribution of this dissertation is to investigate the relationship between prospective naturalistic changes in intrinsic motivation and substance use severity in a large heterogeneous sample of participants with co-occurring SUDs and schizophrenia ($n = 535$ at baseline; $n = 219$ at 6-months; $n = 150$ at 1-year), after extending validation of the intrinsic motivation instrument developed by Nakagami and colleagues (2008) to this population. This will be accomplished by utilizing the QLS-derived measure of intrinsic motivation to examine whether people with schizophrenia and comorbid SUD exhibit less severe patterns of SUD pathology as they make gains in intrinsic motivation, and whether men and women differ in their patterns of severity as they make gains in intrinsic motivation. The present study is conducted within the context of a large-scale randomized-controlled trial of medication treatments for persons with schizophrenia (i.e., first and second generation antipsychotic medications); however, rather than focus on the effects of such treatments on SUD pathology or intrinsic motivation, this research uses its longitudinal context to conduct a robust examination of the link between prospective naturalistic changes in intrinsic motivation and changes in substance use severity, and then investigates whether such relationships vary across genders. This investigation is important because it seeks to test a potentially critical determinant (intrinsic motivation) by which substance use severity

can be reduced in comorbid SUD and schizophrenia, and may not only serve to extend treatment development efforts aimed at reducing such pathology in the larger dual diagnosis population to include a provision targeting the intrinsic motivational deficits of schizophrenia, but may also lead to findings that call for gender-specific care.

What follows is an overview to the importance of substance use severity in co-occurring SUDs and schizophrenia, as well as a summary of the current state of the evidence with regard to the factors that contribute to SUD pathology in this population that signal the need for further research on the relationship between intrinsic motivation and substance use severity among persons with co-occurring SUDs and schizophrenia. The following section is only intended to serve as a brief introduction to the topic, as a greatly expanded review of the research discussed herein is provided in Chapter 2.

B. THE PROBLEM OF SUBSTANCE USE SEVERITY IN SCHIZOPHRENIA

Persistent and pervasive patterns of substance use severity are highly problematic features of SUD pathology that often plague the lives of those who suffer from co-occurring SUDs and schizophrenia. Many reports have considered U.S. deinstitutionalization policies as a key contributor to the emergence of co-occurring SUDs in schizophrenia, which have worsened these conditions in terms of the persistent severities of substance use observed among this population. Such efforts had begun in the mid-1960s by shifting the locus of care from state hospitals to the community, thereby removing individuals with schizophrenia from the controlled conditions that had limited their access to substances of abuse. Consequently, the post-deinstitutionalization rates of SUDs among people with schizophrenia grew from 30% in 1970 to nearly 50% by 1990 (Westermeyer, 2006), with this effect on comorbidity becoming widely

acknowledged as a national public health issue in the mid-1980s (McHugo et al., 2006). In addition, while there was a lack of treatments and services available to accommodate the unique needs of this population at this time, such individuals became characterized as “difficult to serve” (Pepper, Krishner, & Ryglewicz, 1981; Bachrach, 1982), with their severe patterns of substance use being labeled as “treatment resistance” (Osher & Drake, 1996). Ever since deinstitutionalization, the problem of co-occurring SUDs in schizophrenia has proliferated, yet since no social policies, treatments, or services have been able to successfully address this issue, a large number of affected persons have sustained their substance use for years in despite facing significant disability. Today, such patterns characterize the severity of SUD pathology, and are defined within the context of the frequency, duration, consequences, and impairments associated with the long-term and recurrent use in schizophrenia and comorbid SUD (Drake et al., 2006).

Research on co-occurring SUDs in schizophrenia has shown that affected individuals tend to experience prolonged disability stemming from the significant severity that SUD pathology exacts on schizophrenia, although some improvements do occur over the long-term course of these conditions. For example, in a 10-year study of 130 people with co-occurring SUDs and schizophrenia, Drake and colleagues (2006) found that after at least 3 years of experiencing significant substance use severity, 50% of the sample had begun to show signs of recovery (as measured by achieving control over both disorders, attaining independent housing, or a better quality of life). While such findings are seemingly optimistic, research conducted over the past several decades has indicated that this comorbidity remains present in affected persons throughout the lifespan (Westermeyer, 2006), and thus recovery does not mean that those who achieve such a status are cured. Further, this comorbidity has been linked with a host of adverse clinical outcomes at relatively low substance use severity thresholds among

individuals with schizophrenia (Drake et al., 1990; Ziedonis et al., 2005). For example, studies of persons with co-occurring SUDs and schizophrenia have shown that the use of substances significantly contribute to missed general and medication appointments (Owen, Fischer, Booth, & Cuffel, 1996; Hipwell, Singh, & Clark, 2000; Coldham, Addington, & Addington, 2002), which lead to more positive symptom exacerbations (Pencer & Addington, 2003), more relapses, higher rates of emergency service utilization (Curran et al., 2003; Barnes, 2008), and greater rates of inpatient hospitalizations (Linszen, Dingemans, & Lenior, 1994; Swofford, Kasckow, Scheller-Gilkey, & Inderbitzin, 1996).

Research following people with co-occurring SUDs and schizophrenia throughout the long-term course of these conditions has documented just how problematic the severity of SUD pathology, can be for this population. Bartles, Drake, and Wallach (1995) followed a cohort of people with co-occurring SUDs and schizophrenia for 7-years and found that the prevalence of SUD increased by 1% per year. Notably, at the 7-year follow-up, there was no indication that any of the 148 participants had achieved sustained remission (i.e., after meeting criteria for alcohol use disorder, none of the criteria are met during a period of 12-months or longer; American Psychiatric Association [APA], 2013). Another study by Lambert and colleagues (2005) found that when following a cohort of 643 people for 18-months after their first episode, high baseline severities of substance use predicted poorer rates of remission over the study. While these data suggest that people with this comorbidity can sustain their use of substances for several years in the face of significant severity, other studies suggest that this population may adopt abstinence (Drake, McHugo & Noordsy, 1993; Dixon, McNary, & Lehman, 1998; Drake et al., 2006). Drake, McHugo, and Noordsy (1993) followed a cohort of 18 persons with co-occurring SUDs and schizophrenia for 4-years and found that 11 achieved at least one 6-month

remission. In addition, emerging research indicates that women with co-occurring SUDs and schizophrenia use substances less frequently than men (Leung & Chue, 2000), and that such women also exhibit less longitudinal severities of use than men (Køster, Lajer, Lindhardt, & Rosenbaum, 2008). As such, the weight of the evidence in this area of research supports observations that show co-occurring SUDs in schizophrenia are frequently characterized by persistent patterns of severe substance use. These patterns may be less severe for women; and when present, such pathology limits remission and recovery rates among this population.

Unfortunately, while the evidence is clear that SUD pathology is problematic in schizophrenia, previous attempts to understand the factors that may have an impact on substance use severity among those with the disorder has produced mixed results. Diversity in the extant research findings has resulted, at least in part, from variability in the measurement instruments used to assess the degree of severity associated with a SUD diagnosis in schizophrenia (Dixon, 1999; Carey, 2002; Ziedonis et al., 2005). Exposure to trauma has been a salient predictor of substance use severity among this population, as such factors tend to worsen SUD pathology in schizophrenia, perhaps due to the inherent difficulties such persons have in coping with and tolerating emotionally charged situations (Gearon, Bellack, Rachbeisel, & Dixon, 2001; Scheller-Gilkey, Moynes, Cooper, Kant, & Miller, 2003; Gearon, Kaltman, Brown, & Bellack, 2003). Symptoms of psychosis would also seem to be likely contributors to SUD pathology; however, investigations of these contributions have yielded mixed results, with a few studies showing modest relations between social anhedonia, delusions, hallucinations, and more frequent substance use (Gregg, 2012). Antisocial personality disorder (ASPD) and its childhood precursor, conduct disorder, are known predictors of increased substance use severity among this population (Mueser, Noordsy, Drake, & Fox, 2003; Mueser et al., 2006). This is perhaps due to

the serious challenges stemming from the poor treatment compliance associated with this combination of comorbidities. While gender has shown some potential as a salient predictor of SUD pathology, most studies of these relations have also produced mixed results, with some reporting significant differences between men and women (Køster et al., 2008; Koskien et al., 2009a), and others reporting no significant relationships (Brunette & Drake, 1997; Brunette & Drake, 1998; Koskien et al., 2009b). Taken together, such factors are far from accounting for all the variance in SUD pathology in co-occurring SUDs in schizophrenia, indicating that there are other important factors precluding the remission and recovery from the severe patterns of substance use among this population.

What follows is an overview of the importance of investigating the relevance of intrinsic motivation deficits as a potential contributor to the persistent patterns of substance use severity observed in persons with co-occurring SUDs and schizophrenia, and whether such a relationship varies across genders among this population. The following section is only intended to serve as a brief introduction to the potential relationship between intrinsic motivation deficits and substance use severity in schizophrenia, as a greatly expanded review of the research discussed herein is provided in Chapter 2.

C. INTRINSIC MOTIVATION AS A CONTRIBUTOR TO SUBSTANCE USE SEVERITY IN SCHIZOPHRENIA

One of the most promising potential contributors to the persistent patterns of substance use severity observed in individuals with schizophrenia is deficits in intrinsic motivation. Studies conducted over the past century have supported the conceptualization of schizophrenia as a disorder of motivational impairment, with some of the earliest descriptions of the illness

emphasizing a disturbance of volition as the fundamental process in its pathology (see Foussias & Remington, 2010, for review). In fact, psychiatrists as early as Emile Krapelin (1919) have described schizophrenia as an illness of early and progressive deterioration, attributing deficits in core motivational processes in dictating the changes characterizing this decline. Today's nosology of mental disorders considers the presence of prominent motivational deficits such as amotivation and ahedonia to be defining features of the disorder (APA, 2013). Such deficits are characterized by a diminished capacity in taking interest in activities (amotivation), and by an inability to experience pleasure from tasks that most people find enjoyable (ahedonia).

Over the past decade, evidence has begun to suggest that the intrinsic motivation deficits observed in schizophrenia impede the ability of those with the disorder to generate internal drives to sustain behavior changes absent external rewards (see Chapter 2, Section C.2 for an expanded discussion on intrinsic motivation deficits in schizophrenia). Regarding individuals with co-occurring SUDs and schizophrenia, evidence has also begun to suggest that such deficits can disengage persons with these conditions from generating internal drives to achieve reductions in substance use severity (see Chapter 2, Section C.3 for an expanded discussion on intrinsic motivation deficits in co-occurring SUDs and schizophrenia). Most of the evidence regarding this issue has emerged within the context of investigations of psychosocial approaches designed to enhance dual diagnosis clients' intrinsic motivation to reduce or cease their use of substances (see Hunt et al., 2013, for review). For example, compared to dual diagnosis clients without schizophrenia, the weight of the evidence indicates that persons with co-occurring schizophrenia and SUDs demonstrate less motivation to change the behaviors associated with their use of substances while participating in treatment programs, are more difficult to engage, make slower progress, and drop out of such programs at faster rates (see Drake et al, 2008;

Horsfall et al., 2009; Hunt et al., 2013, for reviews). While such patterns may actually implicate the problems associated with the intrinsic motivation deficits observed in schizophrenia rather than issues with compliance associated with the pathology of the SUD, this question has remained largely unexamined in the dual diagnosis treatment research to date.

Unfortunately, relatively little research has examined the actual contributions of intrinsic motivation deficits to substance use severity in co-occurring SUDs and schizophrenia, even within the context of relevant motivational rehabilitative approaches (see Dixon et al., 2009; Hunt et al., 2013; for reviews). Nonetheless, among the studies that have been conducted among this population, a compelling investigation by Graber and colleagues (2003) examined the relationships between intrinsic motivation and the substance use behavior of 30 non-treatment seeking (i.e., for SUD pathology) veterans with schizophrenia and co-occurring SUDs participating in a motivational rehabilitative treatment program. The investigators found that the ability to increase intrinsic motivation was stronger among the participants in the experimental condition (motivational interviewing), which was a significant predictor of reduced alcohol use disorder pathology (Graber et al., 2003). Subsequent studies of motivational rehabilitative programs for people with co-occurring SUDs and schizophrenia have shown that such persons can improve their substance use outcomes regardless of the treatment to which they were assigned (Martino et al., 2006; Edwards et al., 2006), perhaps suggesting both groups made comparable gains in intrinsic motivation. Finally, one recent study by Drapalski and colleagues (2011) examined gender differences between treatment seeking (i.e., for SUD pathology) and treatment non-seeking groups in their readiness to change substance use behaviors upon study enrollment. The investigators found that treatment-seeking women exhibited the highest motivation for changing their behaviors associated with substance use upon enrollment

compared to all other groups observed. Taken together, these findings highlight the significance of intrinsic motivation deficits to substance use severity in co-occurring SUDs in schizophrenia, and the potential for such relationships to vary by gender among this population.

D. LIMITATIONS OF PREVIOUS RESEARCH

1. Narrow focus on motivational rehabilitation

While studies have investigated the relationship between deficits in intrinsic motivation and substance use severity in persons with co-occurring SUDs and schizophrenia, this research suffers from several important limitations. First, to date investigations of intrinsic motivation in co-occurring SUDs and schizophrenia have exclusively been conducted within the context of motivational rehabilitation programs for the larger dual diagnosis population. Some of these programs have adapted their motivational modalities to accommodate the symptoms of psychosis (Martino et al., 2002; Martino et al., 2006), yet not one has modified a treatment protocol to account for the intrinsic motivation deficits unique to the pathophysiological processes of schizophrenia (see Chapter 2, Section C.2). Nevertheless, a limited number of such motivational rehabilitation studies conducted within the larger dual diagnosis population have shown that individuals with schizophrenia and comorbid SUD can reduce their substance use severity as they make gains in their intrinsic motivation (Graber et al., 2003; Kavanaugh et al., 2004; Edwards et al., 2006; Baker et al., 2006). It should be noted, however, that the positive effect of changes in intrinsic motivation in relation to changes in substance use severity has been obtained within the context of several limiting conditions. For example, not only have these studies made use of modest sized samples, but such investigations also selected their samples from specialty populations that included few women as well as small proportions of persons with co-occurring

SUDs and schizophrenia. Consequently, this narrow focus on examining such effects within the context of dual diagnosis motivational programs has raised several important questions about how such findings generalize to the larger population of persons with co-occurring SUDs and schizophrenia (McHugo et al., 2006). As such, elucidating the relationship between changes in intrinsic motivation and changes in substance use severity as they naturally occur outside of these specialty intervention programs that very few people in the population actually receive represents an important area of further investigation.

2. Lack of representativeness

Second, the majority of investigations examining the relationship between intrinsic motivation and substance use severity have largely lacked samples that are generalizable to the larger population of persons with co-occurring SUDs and schizophrenia. For example, the only study to observe relations between intrinsic motivation and substance use severity where 100% of the study sample consisted of schizophrenia participants was conducted with a modest number of veterans ($N = 30$) who were mostly male (1 woman participant) (Graber et al., 2003). Similar issues are readily discernable in studies conducted by Kavanaugh et al. (2004) and Edwards et al. (2006). Both investigations observed relations between intrinsic motivation and substance use severity using specialty samples of dual diagnosis clients, where only about 50% of their modest sized ($N = 25$; $N = 47$, respectively) samples consisted of first episode schizophrenia patients. In addition, Kavanaugh et al. (2004) recruited their study sample from an inpatient unit, and then followed such patients after they were (mostly) discharged to the care of their families. While Kavanaugh et al. (2004) has contributed to the evidence supporting significant relations between intrinsic motivation and substance use severity among this population, the findings may be less applicable to the vast majority of chronic patients with co-occurring SUDs and schizophrenia

who live in the community, have free access to drugs and alcohol, and rely on public rather than family support (Drake et al., 2008). As a consequence of the methodological issues inherent to these studies, most of dual diagnosis research that has considered the importance of intrinsic motivation to substance use severity may not generalize to the majority of individuals with co-occurring SUDs and schizophrenia. As such, research on larger and more heterogeneous samples of persons with these conditions is needed.

3. Inattention to confounding effects/extrinsic rewards

Third, the studies investigating the relations between intrinsic motivation and substance use severity in schizophrenia and comorbid SUD have also been limited by the potential confounding influence of extrinsic rewards. Relevant evidence from studies conducted with healthy individuals indicates that extrinsic rewards, such as money and praise, can undermine the development of intrinsic motivation unless the information is delivered in a context that supports the person's autonomy (Deci, Ryan, & Koestner, 1999, for review). A few motivational studies delivered extrinsic rewards in the form of remuneration payments to participants at the time that such persons received the motivational session targeting improvements in intrinsic motivation to reduce their SUD pathology (i.e., James et al., 2006; Martino et al., 2006). This makes it difficult to discern the actual mechanisms underlying the relations between improvements in intrinsic motivation and reductions in substance use severity that were documented in these investigations.

4. Limited use of intrinsic motivation measures

Finally, studies of the relations between intrinsic motivation and substance use severity in co-occurring SUDs and schizophrenia have primarily employed readiness-to-change assessments to measure the stage of change associated with the individual's current level of motivation to

improve specific target behaviors, such as reductions in substance use severity. Such a person's stage of change is based on one of 5 stages of change that coincide with the transtheoretical model (TTM) of intentional behavior change (precontemplation, contemplation, preparation, action, maintenance) (DiClemente, 2003). Motivation, according to the TTM perspective, requires for individuals to engage in enough cognitive/ experiential activities to move through the early stages and to engage in behavioral activities to initiate and sustain the change (DiClemente, Nidecker, & Bellack, 2008). While it can be assumed that targeted behaviors that are sustained over the long-term likely result from intrinsic goals, readiness-to-change measures do not actually account for whether the motivation for a person's engagement in change processes is intrinsic (i.e., motivated by internal desire to change) or extrinsic (i.e., motivated by money or other external factors). Given the potential for low intrinsic motivation base rates in co-occurring SUDs and schizophrenia to impede the recovery of such persons from severe and persistent patterns of substance use (see Chapter 2, Section C.1 for an expanded discussion of the base rates of intrinsic motivation deficits in schizophrenia), a measure that is more focused on intrinsic motivational processes among this population is needed to supplement the assessment.

Recently, a promising measure of intrinsic motivation has been developed, tested, and validated among individuals with schizophrenia by Nakagami et al. (2008). Such a measure is premised on a conceptualization of intrinsic motivation acknowledging that behaviors are carried out because of the positive feelings associated with an action in the absence of any tangible reward, or actions that are taken for their own sake that do not require any reinforcement or external supports to be initiated or sustained (Deci & Ryan, 2007). This measure utilizes an operational definition of intrinsic motivation that is based on the sum of theoretically pertinent items from the Quality of Life Scale (Heinrichs et al., 1984), including purpose, motivation, and

curiosity. These items show face validity in terms of their focus on cross-situational phenomena in life experience such as goals, plans, and in areas of interest/ drive (Nakagami et al., 2010). Thus, it stands to reason such items may also characterize the interest/ drive such persons with schizophrenia and comorbid SUD manifest in terms of reducing their substance use severity. This research uses these operational and conceptual definitions of the construct, yet prior schizophrenia research has conceptualized and operationalized intrinsic motivation in various ways (i.e., Yodkovik, Sypher-Locke, & Hanewinkel, 2008; Choi & Medalia, 2010). However, not only has Nakagami and colleagues' (2008) instrument shown reliable assessments of intrinsic motivation among persons with schizophrenia living in the community (Nakagami et al., 2008; Nakagami et al., 2010; Yamada, Lee, Dinh, Barrio, & Brekke, 2010), but it has also shown valid predictions of change in functional outcomes in comparative samples of those with the disorder (Nakagami et al., 2010). Unfortunately, the validity of this measure has yet to be confirmed among those with co-occurring SUDs and schizophrenia. Given the broad applicability of employing this measure for predicting changes across a host of functional outcome domains among those with the disorder, this study seeks to extend the research in this area by examining prospective naturalistic changes in the relationship between intrinsic motivation and substance use severity for a large sample of persons with co-occurring SUDs and schizophrenia. This study also seeks to examine the degree to which such a relationship varies across genders, after extending the validation of this instrument to persons with comorbid schizophrenia and SUD.

E. STUDY AIMS

This study aims to conduct a longitudinal investigation examining the impact of intrinsic motivation on substance use severity among persons with schizophrenia and comorbid SUD and

its patterns in men and women, after extending validation of a promising new measure of intrinsic motivation to this population. Such analytic aims will be carried out using secondary data that were collected as part of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study (Lieberman et al., 2005). The CATIE study evaluated a broad array of functional, clinical, and substance use outcomes in persons with schizophrenia who were participating in a randomized clinical trial of the effectiveness of first and second generation antipsychotic medications (i.e., Stroup, McEvoy, & Lieberman, 2010). This research is not focused on elucidating the pharmacological treatment effects of the CATIE trial, but rather seeks to make use of its longitudinal context to follow the 535 participants who had schizophrenia and comorbid SUD at baseline for up to 1-year of treatment. This was done in order to examine naturalistic the prospective relationship between changes in intrinsic motivation and changes in substance use severity among the sample, and to then investigate whether such a relationship varies across genders. The CATIE study sought to include adults with schizophrenia who would be representative of those seen in typical clinical settings across the U.S. by recruiting “real-world” patients, including those with comorbid substance use disorders (an exclusion of many clinical trials), and thus provides a unique dataset for examining whether improvements in intrinsic motivation are related to improvements in substance use severity among this population. Using data from the CATIE study, this research aims to:

Aim #1: Extend the validation of a promising measure of intrinsic motivation to persons with schizophrenia and comorbid SUD. Intrinsic motivation is assessed using an inventive technique recently developed by Nakgami, Xie, Hoe, and Brekke (2008), which gauges intrinsic motivation by taking the sum of theoretically pertinent intrapsychic deficit items from the Quality of Life

Scale (Heinrichs et al., 1984), probing purpose, motivation, and curiosity. This measure of intrinsic motivation has not been previously applied to persons with comorbid SUD and schizophrenia. Thus, this analytic aim will be addressed by subjecting the total pool of 7-items from the intrapsychic deficit subscale to an exploratory factor analysis.

Aim #2: Examine the cross-sectional relationships between intrinsic motivation, gender, and substance use severity. This analytic aim will be carried out using baseline data ($n = 535$) to employ independent sample t -tests (two-tailed) for examining the bivariate relationships between gender and intrinsic motivation and gender and substance use severity. Baseline data will also be used to compute correlation matrices and hierarchical linear regression analyses to examine the zero-order and unique associations (adjusting for negative symptoms and neurocognition) between intrinsic motivation and substance use severity.

Aim #3: Investigate the longitudinal contribution of changes in intrinsic motivation to changes in substance use severity, and then examine whether gender moderates this relationship. This analytic aim will be carried out by employing a series of growth curve models. Unconditional models will first be fit to examine whether or not there is variability in the initial status and the rates of change in the 1-year trajectories of substance use severity among the sample. Analysis will proceed by then expanding unconditional models to conditional models to examine the longitudinal contribution of changes in intrinsic motivation to changes in substance use severity. Conditional growth curve models will then be expanded to examine the moderating effects of gender on these relations.

Taken together, the results of these aims will be used to derive implications for future intervention development efforts for persons with co-occurring SUDs and schizophrenia. The analytic aims and associated hypotheses proposed above seek to take an important step in

establishing empirical support for targeting deficits in intrinsic motivation within specialized dual diagnosis treatment programs for persons with co-occurring SUDs and schizophrenia, and in identifying the significance of intrinsic motivation deficits as a potential gender-specific treatment target among this population. In observing significant relationships between intrinsic motivation deficits and substance use severity, such findings can be directed toward existing interventions to enhance their effects on intrinsic motivation deficits in an effort to reduce the pervasive patterns of substance use severity among this population. In the presence of significant variability across genders with regard to these relationships, findings from this research can be directed toward novel treatments that not only enhance their effects on intrinsic motivation deficits but also attend to their unique impact on men and women among this population.

F. RELEVANCE TO SOCIAL WORK

Patterns of severe and persistent substance use are pervasive among persons with co-occurring SUDs and schizophrenia and are refractory to many of the currently available medication and psychosocial treatments for dual disorders (Westermeyer, 2006). Taking a multi-systemic social work approach to this social problem emphasizes how the U.S. social policies that closed mental hospitals for humanitarian reasons exposed vulnerable individuals with schizophrenia to substances in the community. This has resulted in significant SUD pathology being observed among those with the disorder. Such a counterbalance to an overly medical perspective is important because it necessarily considers the psychosocial factors that create and sustain an environment in which persons with co-occurring SUDs and schizophrenia persist in their patterns of severe substance use over the long-term course of these conditions. Since the problem of co-occurring SUDs in schizophrenia largely resulted as an unintended psychosocial

effect of U.S. deinstitutionalization policies (i.e., what failed with respect to hospitals, housing, and community-based services)—it stands to reason that a potential solution to this problem may be largely a matter of developing psychosocial remedies that lie within the grasp of social work investigators to undertake. Social work investigations are needed that seek to understand the factors that contribute to SUD pathology in schizophrenia, to gain insights for developing treatments to offset the destabilizing effects of the persistent and severe patterns of substance use that continue to plague the lives of those who suffer from these conditions. Intrinsic motivation deficits have been identified as potential contributors to substance use severity in this population, and women may exhibit more intrinsic motivation toward changing their behaviors associated with substance use than men. Persons with co-occurring SUDs and schizophrenia comprise a vulnerable group of individuals who are in desperate need of better treatments and services to improve their quality of life and to lessen the impact of the psychosocial consequences of substance use. Social work has long been concerned with helping vulnerable populations in need by applying multi-systemic approaches to psychosocial phenomena, and thus a study proposing to examine the relationship between intrinsic motivation and substance use severity among persons with co-occurring SUDs and schizophrenia, and then investigate whether such a relationship varies across genders is important and relevant to the field.

II. LITERATURE REVIEW

A study proposing to investigate the impact of intrinsic motivation deficits on outcomes of substance use severity and its patterns in men and women among persons with co-occurring SUDs and schizophrenia brings together a diverse array of literature from the disciplines of social work, addictions, psychiatry, psychology, and public health. This chapter provides a review of this literature within and across these disciplines to denote the importance of substance use severity to persons with co-occurring SUDs and schizophrenia and larger society, as well as evidence pointing to the construct of intrinsic motivation for understanding the profound degree of substance use severity experienced by this population. The review begins by providing initial information regarding the nature and socio-political trends in the disorder, and then examines the literature surrounding the patterns of substance use severity within and across genders. The review then proceeds with an examination of the intrinsic motivation construct that highlights its potential for understanding the degree of substance use severity persons with schizophrenia and comorbid SUD experience. This review does so by first providing a general overview of the intrinsic motivation construct. What follows is a critical analysis of the evidence surrounding intrinsic motivation deficits in schizophrenia and comorbid SUD and the relationships between these deficits and substance use severity among this population and its patterns in men and women. Finally, this review concludes by providing a brief discussion of the current issues surrounding the measurement of intrinsic motivation in schizophrenia, which underscores the importance of a study on the impact of intrinsic motivation on outcomes of substance use severity among persons with co-occurring SUDs and schizophrenia and its patterns in men and women.

A. OVERVIEW OF CO-OCCURRING SUBSTANCE USE DISORDERS AND SCHIZOPHRENIA

Schizophrenia is a complex and disabling psychiatric disorder that poses significant challenges to those who suffer from it, their families, and to our larger society. One of the most vexing problems among adults with schizophrenia today is the co-occurrence of SUDs, often called dual diagnosis or dual disorders. These individuals are diagnostically complex, clinically unstable, difficult to recruit to studies, difficult to engage in treatment, and especially difficult to retain in treatment. Such challenges and motivational issues have led to the exclusion of people with schizophrenia and comorbid SUD from controlled research studies and to difficulties with completing studies aimed at this population. Within the U.S. healthcare system, the historical separation between mental health and addiction systems of care has led to a lack of cooperation concerning the treatment of these disorders, and to date, no social policies have specifically addressed the unique needs of this population. As such, people with schizophrenia and comorbid SUD are vulnerable to a host of adverse consequences, including high rates of hospitalization, relapse, legal problems, homelessness, family difficulties, and serious infectious diseases such as HIV and hepatitis C. Today both schizophrenia and SUDs are conceptualized as biologically-based disorders of the brain such that symptom relapse and remission are common over the life-course, and there is no known cure for either condition. The problem of co-occurring SUDs in schizophrenia is now considered a major public health issue due to its destabilizing effects and considerable cost to families and societies. This section will first provide a brief discussion of schizophrenia, and will then move into a more focused discussion of co-occurring SUDs among those with the disorder and its significance as a major public health issue in both the U.S. and

abroad to highlight the relative importance of this problem to both science and society.

1. Description and Social Significance

Burden of disease. Schizophrenia is a chronic and persistent psychiatric disorder that affects approximately 1% of the population worldwide, and comparatively equal prevalence rates have been observed between genders (American Psychiatric Association [APA], 2013). Despite its relatively low lifetime prevalence rate, schizophrenia is among the top ten leading causes of disease-related disability in the world (Murray & Lopez, 1996; World Health Organization [WHO], 2001). Within the U.S. alone, it is estimated that approximately 30.3 billion dollars are spent on the treatment and the cost of living for people with schizophrenia annually (Wu et al., 2005). In addition to the high direct cost of caring for people with schizophrenia, it is estimated that other factors among those with the disorder, such as unemployment and reduced workplace productivity, cost the U.S. 23.4 billion dollars annually (Wu et al., 2005), making this condition one of the most costly psychiatric disorders in the world (Knapp, Mangalore, & Simon, 2004).

These direct care and other societal costs are not the only financial burdens associated with schizophrenia. There are also costs of the disorder that are frequently incurred by families or caregivers (Magliano et al., 1998; Clark, Xie, Adarhi-Meija, & Sergupta, 2001). For example, research has documented that up to 83% of the friends and family members of people with schizophrenia experience practical, emotional, and financial burdens (Magliano et al., 2002). They report time lost from work, unreimbursed medical expenses, limited time for leisure, elevated symptoms of psychological distress, and disturbed sleep (Schene, Van Wijngaarden, & Koeter, 1998; Angermeyer, Liebelt, & Matschinger, 2001; Ohaeri, 2001; Magliano et al., 2002; McDonell, Short, Berry, & Dyck, 2003). This additional source of economic or caregiver burden has also been linked to the high mortality rates observed among those with schizophrenia (Knapp

et al., 2004). For example, long-term follow-up studies of schizophrenia patients post-psychiatric hospital discharge have shown an approximately two fold increase in all causes of mortality compared to the general population (Tsuang & Woolson, 1978; Allebeck & Wistedt, 1986; Anderson, Connelly, Johnstone, & Owens, 1991), with suicide as the leading reason for the excess mortality (Allebeck, Varla, & Wistedt, 1986; Newman, & Bland, 1991; Brown, 1997). Further, about 10% of all people with schizophrenia will eventually have a completed suicide (Siris, 2001), and of those who survive, many will experience persistent functional disability throughout their lives. Those who have these severe and enduring needs often require long term multi-disciplinary input to help them reach an optimal state of functioning (Huxley & Fonseca, 2013). Although this entails a comprehensive approach to treatment including medication, psychosocial interventions, and assistance with housing and financial sustenance, many individuals with schizophrenia remain significantly disabled despite these efforts, often being unable to maintain gainful employment, complete schooling, or marry and have families (Andreasen, 1995; Huxley & Fonsca, 2013).

Psychopathology. The severe degree of disability that schizophrenia has on individuals with the disorder, their families, and broader society stems from its clinical features, which are commonly expressed in terms of positive and negative symptom clusters (Davies, 2007). The first symptom cluster present in schizophrenia is positive symptoms. Such symptoms include delusions (i.e., erroneous beliefs based upon false perceptions that persist despite indisputable evidence to the contrary), hallucinations (i.e., experiencing a perception in the absence of an apparent stimulus that has qualities of a real perception), and/or thought disturbance (i.e., disorganized thinking and speech). The second symptom cluster consists of negative symptoms. These symptoms include alogia (i.e., a general lack of additional, unprompted content seen in

normal speech), affective flattening (i.e., reduced range and/or intensity of emotional expression), avolition/ amotivation (i.e., general lack of drive, or motivation to pursue meaningful goals), and anhedonia (i.e., diminished capacity to experience intrinsic pleasure from activity). While individuals with schizophrenia experience both negative and positive symptoms, negative symptoms tend to persist even when positive symptoms are controlled with medication (Tandon, Nasrallah, & Keshavan, 2010). According to the most recent Diagnostic and Statistical Manual of Mental Disorders (APA, 2013), the continuous presence of any two signs of positive and/or negative symptoms for at least one month, in combination with significant functional impairment for the past six months, permits the consideration of a diagnosis of schizophrenia.

Nature and course. Although schizophrenia has been studied as a major disease entity for the past century, to date, its nature and pathogenesis have continued to remain elusive. The disorder has been shown to be associated with a host of neurobiological deviations (Shenton, Dickey, Frumin, & McCarley, 2001; Keshavan, Tandon, Butros, & Nasrallah, 2008), and to have a strong genetic component (Sullivan, Kendler, & Neale, 2003; Sullivan, 2008), with gene-environment interactions contributing to over 80% of the liability for developing the disorder (Tandon, Keshavan, & Nasrallah, 2008). However, despite recent advances that have been made in neurobiology and molecular biology, no single gene variation or neurobiological marker has been consistently associated with a greater likelihood of developing schizophrenia (Tandon et al., 2008). Nevertheless, a host of environmental factors have been linked to a greater likelihood of developing the disorder some of which include, cannabis use (Semple, McIntosh, & Lawrie, 2005; Løberg & Hugdahl, 2009), prenatal infection (influenza) or malnutrition (Meyer, Yee, & Feldon, 2007; St Clair et al., 2005), perinatal (fetal hypoxia) problems (Byrne, Agerbo, Bennedsen, Eaton, & Mortensen, 2007), and early life stress (Norman & Malla, 1993; Harrison,

2004; Allardayce & Boydell, 2006). While any of these factors may increase a person's risk for developing the disorder, none are sufficient to precipitate symptom onset, and the actual cause of schizophrenia is not currently known.

For those who develop schizophrenia, the onset of symptoms usually occurs during late adolescence or early adulthood, and once present, the disorder often takes on a recurrent pattern of acute positive symptom exacerbation that is accompanied by persistent cognitive, social, and vocational dysfunction (APA, 2013). These functional deficits tend to persist even when other symptoms are in remission or controlled with medication (Tandon et al., 2010). As the course of the disorder progresses, the acute exacerbations of positive symptoms usually remit, such that around 50% of people with schizophrenia meet criteria for recovery (defined as remission of positive symptoms, participation in work or school, and increased social functioning [Lieberman, Kopelowicz, Ventura, & Gutkind, 2002; Lieberman & Kopelowicz, 2002]) for periods of time during their lives, with such periods increasing in frequency and duration once such persons are past middle age (Bellack, 2006). As many who are in recovery continue to experience negative symptoms and functional disability across several domains, even the most optimistic views on the course of the disorder do not consider those who have achieved this status as being cured of schizophrenia (Bellack, 2006). Although there are few reliable predictors of symptom remission and recovery in schizophrenia (Lieberman et al., 2002), persons who have the disorder and live in developing countries tend to have better long-term outcomes than those who live in developed countries (Harding, 2003). Further, persons with an earlier age of onset generally have poorer outcomes than those who are diagnosed with schizophrenia later in life (APA, 2013; Leung & Chue, 2000), though the effect of age at onset is likely related to gender. For example, men have an earlier onset of the disorder, poorer premorbid functioning, lower educational achievement,

greater structural brain abnormalities, and more prominent negative symptoms and cognitive impairment than women (APA, 2013; Leung & Chue, 2000). While there are no clear differences in family history by gender, women generally display more prominent affective symptoms and respond better to medications than men (Leung & Chue, 2000).

Contributors to functional disability. The past decade of research evidence has identified neurocognition as one of the strongest long-term predictors of recovery in schizophrenia (Green, Kern, & Heaton, 2004), with cognitive deficits accounting for much of the functional disability that is exacted by the disorder (Keefe, 2010). These deficits are already present at symptom onset across a host of information processing domains, including diverse aspects of attention and memory and in the executive functions that are critical for initiating and carrying out higher order reasoning and problem solving processes (Addington, Saeedi, & Addington, 2005). According to the current state of the field evidence, up to 75% of people with schizophrenia experience profound cognitive deficits (Green, 1996; Tandon et al., 2009), and those with such impairments often have difficulties with being able to identify salient environmental cues, which are necessary to avoid problematic situations that lead to adverse outcomes (Gearon & Bellack, 1999). As such, perhaps it is not surprising then that these deficits have been linked with the high rates of criminal justice system involvement, substance use, homelessness, and joblessness, observed in schizophrenia (Cook, & Razzano, 2000; Folsom & Jeste, 2002; Dickerson et al., 2007; Bell, Greig, Zito, & Wexler, 2007; Brekke, Hoe, Long, & Green, 2007; Løberg & Hugdahl, 2009; Ascher-Svanum, Nyhuis, Faries, Ball, & Kinon, 2010).

Relevant estimates indicate that up to 80% of people with schizophrenia are unable to work (Bond & Drake, 2008), that about 50% of those with the disorder experience comorbid SUDs during their lifetime (Reiger et al., 1990), and that up to 45% of people who are homeless

also have schizophrenia (Folsom & Jeste, 2002). Indeed, all of these factors significantly add to the disability that people with schizophrenia experience, and within the past several decades, SUDs have come to be seen as the most common and clinically significant comorbidity affecting the management and outcome of those with the disorder worldwide (Ziedonis et al., 2005; Buckley, Miller, Leher, & Castle, 2009; O'Hare, 2008). Additionally, homelessness has been linked to both criminal activity and to being a victim among those with the disorder (Lam & Rosenheck, 1998), and a study of the correlates of victimization among 962 people with schizophrenia by Chapple and colleagues (2004) found that over the course of 1 year, about 18% (over 1 in 6) reported being the victim of violence (Chapple et al., 2004). These rates are well above the annual rates of violent victimization in the U.S. general population (Hiday, Swanson, Swartz, Borum, & Wagner, 1999; Brekke, Prindle, Bae, & Long, 2001), and studies have consistently shown that substance use (Hiday et al., 1999; Brekke, Prindle, Bae, & Long, 2001), more severe cognitive deficits (Lehman & Linn, 1984; Brekke et al., 2001; Hiday, Swartz, Swanson, Borum, & Wagner, 2002), as well as homelessness or criminal behaviors (Lehman & Linn, 1984; Honkonen, Henriksson, Kovisto, Stengard, & Salokangas, 2004), are all associated with the higher rates of violent victimization observed in schizophrenia. Further, high unemployment rates in schizophrenia make this population vulnerable to low income levels, which may lead to poverty and then into illegal behaviors and associations with potentially violent situations (Hiday et al., 2002).

In summary, schizophrenia is a devastating psychiatric disorder affecting approximately 1% of the population worldwide during a lifetime. The onset of the disorder usually occurs early in life, and most people who develop schizophrenia experience lasting functional disability even when positive symptoms are in remission or controlled with medication. The co-occurrence of

SUDs with schizophrenia has been widely acknowledged as the most common and clinically significant comorbidity affecting the management and outcome of those with the disorder throughout the world. Although schizophrenia has been studied as a major disease entity for at least the past century, only within the past several decades has attention been paid to those with co-occurring schizophrenia and SUDs as a subgroup with unique treatment needs. Nevertheless, this comorbidity portends a particularly severe course of the disorder, and thus investigators have recently begun to turn to the pervasive problem of co-occurring SUDs in schizophrenia as a salient factor that may explain the profound degree of observed disability in this population.

Co-occurring substance use disorders. Co-occurring or dual disorders are broad terms used interchangeably in the literature to refer to the simultaneous presentation of one or more psychiatric disorder with one or more SUD (Ziedonis et al., 2005; O'Hare, 2008). Although there is no consensus on how to diagnose a SUD in the presence of a psychiatric disorder or vice versa (Ziedonis et al., 2005; Buckley, 2006; O'Hare, 2008), definitions of comorbidity often (though not always) include people who acquire a SUD subsequent to a psychiatric disorder commonly characterized as severe and persistent, such as bipolar disorder, major depressive disorder, or schizophrenia (Mueser et al., 2003; Ziedonis et al., 2005). Within the U.S., the reason for this distinction is premised on the rationale that a person's psychiatric disorder determines his/her eligibility for treatment and services. This eligibility is defined by most states on the basis of the primary psychiatric diagnosis, the degree of disability, and the duration of illness (New Freedom Commission on Mental Health, 2003). From this service eligibility perspective, a diagnosis of schizophrenia often precedes the SUD diagnosis in persons who develop co-occurring disorders, even if the SUD pathology presented first (Drake et al., 2008).

Because even infrequent use of relatively minimal quantities of substances can cause

clinically relevant symptoms in individuals with schizophrenia, accurately detecting substance-related problems among those with the disorder is important (Ziedonis et al., 2005). This can be accomplished by using a series of brief tools to screen for substance-related problems. These tools often include clinician rated scales, self-reports, collateral sources, and biological indicators (analysis of blood, breath, urine, or hair), which are evaluated in terms of their sensitivity (i.e., ability to detect substance-related problems if present) and their specificity (i.e., the ability to accurately identify persons who do not have substance-related problems) (Ziedonis et al., 2005).

While many of these tools are suitable for evaluating substance-related problems in the general population, some may unreliably estimate such problems in schizophrenia (Safer, 1987; De Beurpaire et al., 2007; Bahorik, Newhill, Queen, & Eack, 2014). Challenges have included a high rate of under-detected substance use despite abundant evidence to suggest otherwise (Safer, 1987; De Beurpaire et al., 2007; Bahorik et al., 2014). Further, people with schizophrenia often lack collaterals that can attest to their substance use, perhaps due to social isolation, compliance issues, or estrangement from family members (Ziedonis et al., 2005).

While biological indicators can reliably confirm the presence of use, accurate detection depends on many factors such as the frequency and type of substance used (Ziedonis et al., 2005). Given the potential problems that may arise with any single screening modality tool, the most reliable and valid way to assess for substance-related problems in schizophrenia is to gather information from many sources, using multiple methods, and to bring those measures into a rule-based process for mounting consensus ratings (McHugo et al., 2006). Finally, a positive screen signals a need to determine whether an actual diagnosis of SUD in schizophrenia is present.

As mentioned, there is currently no consensus on how to define a SUD in the context of schizophrenia (Ziedonis et al., 2005), although to date, most studies conducted within the U.S.

have employed DSM-III, DSM-III-R, and DSM-IV diagnoses (Westermeyer, 2006), yet few have used the most recent DSM-V criteria. While there is relatively little variation across these different versions of the DSM in their criteria for a diagnosis of schizophrenia, differences in SUD diagnoses do occur, especially regarding abuse (i.e., a pattern of substance use that does not result in tolerance [when increased amounts of the substance are needed to achieve the desired effect] or withdrawal [when blood or tissue concentrations of a substance decline in an individual who had maintained prolonged heavy use], but it is manifested by recurrent and significant adverse consequences) (APA, 2000), versus dependence (i.e., a pattern of substance use that can result in tolerance and/or withdrawal) (APA, 2000), with such distinctions being omitted from the most recent DSM-V (APA, 2013). Nevertheless, across all versions of the DSM, SUDs are broadly defined within the context of substance-specific pathological behaviors. This signifies that that that the person has developed maladaptive patterns of clinically significant substance use resulting in physical, psychological, and/or social impairment.

Such disorders comprise ten substance-specific classes (i.e., alcohol; caffeine; cannabis; hallucinogen; inhalant; opioid; sedative, hypnotic, and anxiolytics; stimulant [amphetamine, cocaine, and other stimulants], and tobacco), and when any are used (except for caffeine), they can produce such an intense activation of the brain reward system that the resulting effects may manifest as more frequent and longer periods of using such substances; cravings or stronger urges to use such substances; unsuccessful efforts to reduce the use of such substances; failure to fulfill role obligations due to the use of such substances; and/or failure to reduce or abstain from substance use (APA, 2013; McLellan, Lewis, O'Brian & Kleber, 2000).

According to the DSM-V, any two of these substance-specific patterns of pathological behaviors occurring within a 12-month period, in combination with significant functional

impairment, permits the consideration of a SUD diagnosis (APA, 2013). The DSM-V describes several levels of SUD remission, useful for determining lifetime (i.e., the person met diagnostic criteria for SUD at some point during their lifetime) and current (i.e., the person currently meets diagnostic criteria for a SUD) prevalence, and the severity of the disorder. In *early remission*, persons meet no criteria for a SUD for at least three months, but for less than 12-month except that such persons can experience cravings or urges to use substances. In *sustained remission*, no criteria for an SUD are met at any time for 12-months, but such persons may have cravings or urges to use substances. In a *controlled environment*, refers to persons who are in a setting where the use of substances is restricted. Lastly, the DSM-V has specifiers to denote the severity of the SUD diagnosis (i.e., mild = 2-3 symptoms; moderate = 4-5 symptoms; severe > 6 symptoms). In the context of a schizophrenia diagnosis, distinguishing between current and lifetime diagnoses is not necessarily clinically meaningful, as even the minimal use of substances infrequently (i.e. low substance use severity) can result in symptom exacerbation and adverse consequences (i.e., hospitalization) (Drake et al., 2006).

Substance use prevalence. Research indicates that large numbers of people with schizophrenia use drugs or alcohol, and as a result, many of these individuals develop co-occurring SUDs during their lifetime (Gregg, 2012). Estimates of prevalence vary between settings and across geographical location (McLellan & Druley, 1977; Chouljian et al., 1995; Cuffel, 1996; Bell, Greig, Gill, Whelahan, & Bryson, 2002), but the majority of studies have found that SUDs are more prevalent among people with schizophrenia than in the general population (Reiger et al., 1990; Westermeyer, 2006; Volkow, 2009). The largest U.S. population prevalence study, the Epidemiologic Catchment Area study (Reiger et al., 1990), involved comprehensive assessments of both psychiatric and SUDs via structured interviews with 20, 291

randomly selected people from the general population and institutional settings (psychiatric hospitals, nursing homes, jails and/or prisons). The data revealed that that 27% of those with schizophrenia experienced a drug use disorder in comparison to 6% of the general population, and 34% experienced an alcohol use disorder in comparison to 13% of the general population. Overall, 47% of people with schizophrenia were found to have experienced a SUD during their lifetime (Reiger et al., 1990). Similar lifetime comorbidity rates (45%) were reported in the National Comorbidity Survey for people with non-affective psychosis (Kessler et al., 1997).

Clinical studies have shown significant variations (~20% to 70%) in the prevalence of SUDs in schizophrenia from one sample to the next (McLellan & Druley, 1977; Chouljian et al., 1995; Cuffel, 1996; Bell et al., 2002), which generally result from sample differences between treatment settings and across geographic locations (Mueser et al., 2003). For example, alcohol is the most commonly used substance followed by cannabis, and cocaine among people with schizophrenia and co-occurring SUDs in the U.S. and the United Kingdom, but studies that have been conducted in the U.K. generally report lower rates of use than those that have been conducted in the United States (Volkow, 2009; Gregg, 2012). Further, a review of relevant treatments and services estimated that 38% to 50% of people with schizophrenia and co-occurring SUDs received primary inpatient services, 20% to 37% received primary mental health services, and 6% to 15% received primary addiction services (Carra & Johnson, 2008). Given these differences, it is not surprising that variations in the prevalence of SUDs in schizophrenia have been observed across the treatment settings where such persons receive services. However, regardless of the type of treatment setting or amount of services received, many studies have reported variations in the prevalence of co-occurring SUDs and schizophrenia across Australian, European, Canadian, and South American samples (Soyka et al., 1993; Jablensky et al., 2000;

Korkeila et al., 2005; Margolese, Malchy, Negrete, Tempier, & Gill, 2004; Rossi Menezes, & Ratto, 2004). Such evidence suggests that this comorbidity may depend on environmental and cultural changes including alcohol and drug availability in social environments (Gregg, 2012), which supports the commonly held view that people with schizophrenia and co-occurring SUDs use substances that are readily available and accessible in the community in which they live (Mueser et al., 2003; Gregg, 2012).

The types of substances used by people with schizophrenia and co-occurring SUDs vary widely. As mentioned, alcohol tends to be the most commonly used substance, followed by cannabis, and cocaine within the United States (Volkow, 2009). Corresponding estimates of lifetime prevalence have revealed that between 43% and 65% of people with schizophrenia have co-occurring alcohol use disorders, 51% have cannabis use disorders, and 23% have cocaine use disorders (Volkow, 2009). Further, multiple drug and alcohol use is common, and many people with co-occurring schizophrenia and SUDs are diagnosed with more than one substance-related disorder (Gregg, 2012). One recent investigation of 122 outpatients with schizophrenia found that 70% of the study sample met DSM diagnostic criteria for both alcohol and drug use disorder diagnoses (Sheller-Gilkey et al., 2003). Other substances used by people with schizophrenia and co-occurring SUDs include hallucinogens, hypnotics, opiates, and prescription medications, though the patterns of use tend to vary widely across studies (Roncero et al., 2011).

Risk of substance use. Approximately 8.5% of the U.S. population aged 12 or older met criteria for a SUD in 2012 (Hughes, Muhuri, Sathe, & Spagnola, 2012), with biological features such as heredity and the reinforcing properties of substances of abuse in relation to neurological mechanisms being important determinants of addiction (Donovan et al., 2012). Clinical and social aspects of addiction, such as the expectancies of drug effect, social networks, dysphoria,

poverty, and unemployment are also critical (Drake et al., 2002). Regarding schizophrenia, the substance-related problems that contribute to a SUD diagnosis necessarily are biopsychosocial phenomena, with multiple contributing risk factors (Drake, Wallach, Alvenson, & Mueser, 2002).

People with schizophrenia are more likely to be diagnosed with a SUD than the general population, and as a result, many studies have sought to gain a better understanding of the correlates that contribute to the increased risk of substance-related problems in this population. To date, a number of demographic correlates of SUDs have been documented for people with schizophrenia. While there is some variation in terms of the type of SUD (i.e., cannabis or alcohol use disorder), there is also some consistency in terms of the correlates that have been identified among those with the disorder (Mueser et al., 2003; Koskien et al., 2009a; Koskien et al., 2009b). Like people in the general population with SUDs, people with schizophrenia who develop co-occurring SUDs are more likely to be male (Koskien et al., 2009b; Roncero et al., 2011; Mueser et al., 2003; Gregg et al., 2007). They tend to be younger (with the exception of those with alcohol use disorders) (Koskien et al., 2009a; Koskien et al., 2009b), less educated (Dixon, Haas, Weiden, Sweeny, & Frances, 1991), and are more likely to have a family history of substance use problems (Mueser, Bennet, & Kushner, 1995; Menezes et al., 1996; Cantwell, 2003; Barnes, Mutsatsa, Hutton, Watt, & Joyce, 2006; Kavanagh et al., 2004b). People with schizophrenia who develop co-occurring SUDs also experience many of the known social and psychological risk factors for substance-related problems in the general population, such as poverty, living in high-risk neighborhoods, having deviant peer groups, and unemployment (Drake et al., 2002).

Although relatively few studies have examined the relationship between SUD pathology and psychiatric history, there is some evidence to suggest that substance-related problems are

associated with an earlier onset of schizophrenia (Kovaszny, Fleischer, & Tanenberg-Karant, 1997), and with an earlier age at first hospitalization (Salyers & Mueser, 2001). Further, this comorbidity has also been associated with better premorbid social functioning (defined as the quantity and quality of society relationships attained prior to symptom onset) as well as superior cognitive functioning (defined as the cognitive functioning level a person with schizophrenia achieved before symptom onset) (Salyers & Mueser, 2001; Løberg, & Hugdahl, 2009). People who are more socially active and have greater cognitive capacities have resources to procure substances through their environments and social networks, and thus are at an increased risk to develop a SUD (Salyers & Mueser, 2001; Løberg, & Hugdahl, 2009). However, it is important to mention that these correlates are not always reliable, and certainly some people with poor premorbid cognitive function and poor premorbid social function go on to develop schizophrenia and co-occurring SUDs (Mueser et al., 2003).

The only reliable clinical correlate of SUD comorbidity in schizophrenia is antisocial personality disorder (ASPD), and its childhood precursor, conduct disorder (Kavanagh et al., 2004; Mueser et al., 2003). A host of studies have shown that individuals with schizophrenia and ASPD are more likely to have a co-occurring SUD than individuals without ASPD (Caton, Shrout, Eagle, Opler, & Felix, 1994; Mueser et al., 2000). Among people who develop these conditions, ASPD has been associated with a more severe course of SUD, including an earlier age of onset and larger quantities of use (Mueser et al., 2003). Further, a recent study uncovered a late-onset subtype of ASPD in persons with schizophrenia. These persons tended to have the most severe SUD pathology, the most homelessness and criminal justice system involvement (Mueser et al., 2006). Due to their vulnerability to numerous adverse consequences, people with co-occurring schizophrenia, ASPD, and SUDs represent a high-need subgroup that require

intensive monitoring and treatment in order to optimize outcomes.

Models of comorbidity. There are a host of risk factors that place individuals with schizophrenia at much greater risk for SUD than the general population. However, despite more than twenty years of research there is still no consensus on the aetiology of the increased rates of SUD among people with schizophrenia. In the absence of confirmatory scientific evidence to explain such phenomena, Kushner and Mueser (1993) have put forward four types of models: (1) secondary psychosis models (i.e., substance use causes psychosis), (2) secondary substance use models (i.e., substance use is a consequence of psychosis), (3) common origin models (i.e., substance use and psychosis share a common origin), and (4) bidirectional models (i.e., substance use and psychosis are bidirectional; interacting and maintaining each other). While Gregg, Barrowclough, & Haddock (2007) revealed that the support for these models is modest, they do provide some useful clues into the etiopathogenic relationship between these conditions.

Secondary psychosis models are premised on the idea that substance use causes the onset of schizophrenia. While many of the substances people with schizophrenia use are known to use have acute psychotic effects (alcohol, cannabis, hallucinogens, and stimulants [D'Souza et al., 2004; Gregg et al., 2007]), and studies have shown that some of these substances (alcohol and amphetamines [Roncero et al., 2011, Gregg, 2012]) worsen symptoms, there is little evidence to suggest that such substances actually cause the onset of the disorder (Gregg et al., 2007; Gregg, 2012). However, a number of large-scale prospective longitudinal cohort studies have shown that cannabis users are more likely to develop schizophrenia than non-cannabis users (Andreasson, Allebeck, Engstrom, & Rydlberg, 1987; van Os et al., 2002; Arseneault et al., 2002; Weiser, Knobler, Noy, & Kaplan, 2002; Zammit, Allebeck, Andreasson, Lundberg, & Lewis, 2002; Ferdinand et al., 2005; Henquet et al., 2005; Fergusson, Horwood, & Ridder, 2005;

Foti, Kotov, Guey, & Bromet, 2010). Nevertheless, many people who use cannabis do not go on to develop schizophrenia (Gregg, 2012), which signals a need for future research to investigate the reasons for why some people may be more vulnerable to its (cannabis) effects than others.

Secondary substance use models posit that schizophrenia leads to substance use. The most widely-documented of these is the self-medication hypothesis (Khantzian, 1985, 1997), which suggests that substance use is an attempt to self-medicate symptoms such as depression, anxiety, and hallucinations (Gregg et al., 2007). There is some data to suggest that people with schizophrenia use substances to help them cope with problems or decrease the symptoms of the disorder (i.e., [Addington & Duchak, 1997; Gearon, Bellack, Rachbeisel, & Dixon, 2001; Goswami, Mattoo, Basu, & Singh, 2004; Spencer, Castle, & Michie, 2002; Gregg, Haddock & Barrowclough, 2009]), with the majority of this evidence being obtained from self-report studies (Gregg et al., 2007). Such studies have indicated that people with schizophrenia reportedly prefer drugs such as cocaine, cannabis, amphetamine, and hallucinogens (Lieberman et al., 1987; Van Kammen & Baronow, 1988; Dixon et al., 1991; Green et al., 1999, 2005), and that these substances may be used to alleviate insomnia, psychomotor disturbances, anxiety, social deficits, feelings of loss of vitality, dysphoria, or hopelessness—all of which have been associated with SUD among individuals with the disorder (Sommers, 1985; Dixon et al., 1991; Addington & Duchak, 1997; Fowler, Carr, Carter, & Lewin, 1998; Scheller-Gilkey et al., 2003). However, it is important to note that investigations of the self-medication hypothesis have been largely mixed, and thus this hypothesis remains unsupported by the available empirical evidence (see Gregg et al., 2007, for review).

Common origin models of substance use and schizophrenia have been proposed emphasizing biological, individual, and societal factors. Although most of these factors have

already been addressed in the previous section on risk factors a few points are highlighted here. While there is evidence to suggest that genetic factors uniquely contribute to schizophrenia and to SUD (Gottesman & Shields, 1976; Tsuang, Bar, Harley & Lyons, 2001), the extent to which the two disorders share a common genetic vulnerability is not currently known (Gregg et al., 2007). However, some authors have suggested the possible role of reward circuitry dysfunction and dopamine opioid neurotransmission systems (Chambers, Krystal, & Self, 2001; Volkow, 2009). It has been suggested that this relationship implies a common underlying vulnerability for both disorders in which the pathology of the cannabinoid system in schizophrenia is associated with both increased rates of cannabis use and increased rates of schizophrenia (Volkow, 2009). Nevertheless, further research is needed to determine the relevant underlying neuropathological processes before confirmatory conclusions can be made.

Bidirectional models are premised on the idea that schizophrenia and SUD trigger and maintain each other. For example, substance use may serve as a stressor precipitating the onset of schizophrenia in vulnerable persons and then such problems are subsequently maintained by continued use (Mueser, Drake, & Wallach, 1998). Consequently, bidirectional models tend to involve multiple risk factors (Mueser et al., 2003), as delineated in the previous section. For example, trauma precedes the onset of substance use in some people with schizophrenia, but also put some people at increased risk of subsequent substance-related problems, re-traumatization, and relapse of positive symptomatology (Gregg, 2012). Although there is significant literature to support that certain situations and experiences trigger SUD pathology and maintain substance use problems in people with schizophrenia (Gregg et al., 2009), there has not yet been a direct empirical test of this model (Gregg, 2012).

While the four types of models help clarify our understanding of the increased rates of

SUDs among persons with schizophrenia, it is clear that no single model can adequately explain this problem in its entirety. As a result of the risk conferred by substance use, people with co-occurring SUDs and schizophrenia are vulnerable to a host of adverse consequences.

Consequences of substance use. For people with schizophrenia, the consequences of SUD pathology diverge from what is seen in the general population in several important ways. Rather than facing job loss, marital problems, and driving violations, people with schizophrenia have difficulties managing entitlement funds, participating in treatment and rehabilitation, maintaining stable housing, and avoiding victimization (Drake et al., 2002). As a product of these substance-related challenges, people with schizophrenia are at greater risk than the general population for suffering illness and injury caused by risky behaviors like unprotected sex and needle sharing (Gearon & Bellack, 1999), and serious infectious diseases like HIV and hepatitis C (Cournos, McKinnon, & Sullivan, 2005). People with co-occurring SUDs and schizophrenia also present a host of challenges to the clinical management and long-term outcome of their conditions that diverge from what is seen in the larger dual diagnosis population. For instance, after inpatient treatment, individuals with co-occurring SUDs and schizophrenia are less likely to present for outpatient follow-up (Olfson, Marcus, & Doshi, 2010), and compared to dual diagnosis clients without schizophrenia, this population is less motivated to change their substance use, are more difficult to engage in treatment, display slower progress, and drop out of long-term programs more easily (Horsfall et al., 2009). As a product of these challenges, people with co-occurring SUDs and schizophrenia are also at greater risk than the larger dual diagnosis population for incurring a host of adverse outcomes that are uniquely associated with these conditions.

Further, there is also evidence to suggest that people with schizophrenia and co-occurring SUDs have poorer long-term outcomes than their counter-parts with schizophrenia without SUDs

(Menezes et al., 1996; Margolese, Malchy, Negrete, Tempier, & Gill, 2004). For example, in an 18-month longitudinal study of 100 outpatients with schizophrenia, those who had co-occurring SUDs showed a deteriorating functional status over time whereas those with schizophrenia only tended to remain functionally stable (Chouljian et al., 1995). Such outcomes largely result from treatment non-compliance among persons with schizophrenia and co-occurring SUDs (Owen et al., 1996; Cuffel, 1996; Hipwell et al., 2000; Coldham et al., 2002), such that both medication and general appointment attendance are poorer, leading to more positive symptoms (Pencer & Addington, 2003), more relapses, higher rates of emergency services use (Barnes, 2008; Curran et al., 2003), and greater rates of inpatient hospitalization (Linszen et al., 1994; Swofford et al., 1996; Schmidt, Hesse, & Lykke, 2011). Studies have also shown that, compared to individuals with schizophrenia only, those with co-occurring SUDs and schizophrenia have an elevated risk of suicide (Suokas et al., 2010), and are otherwise at risk of experiencing higher rates of mortality (mean age at time of death SZ/ SUD = 50; mean age at the time of death SZ = 62) (Schmidt et al., 2011).

Since even the infrequent use of substances in small amounts can have a significant adverse impact on these clinical outcomes (Drake, Osher, & Wallach, 1989; Mueser, Drake, & Wallach, 1998; Gonzales, Bradizza, Vincent, Stasiewicz, & Paas, 2007), people with co-occurring SUDs and schizophrenia are less likely than other substances users to develop the physiological stigmata of addiction (Drake et al., 1990), and thus the consequences of SUD pathology are largely psychosocial (i.e., the psychological and social impact of SUD pathology is generally more severe than the biological impact of SUD pathology) in this population (Drake et al., 2002). Substance use appears to produce greater psychological morbidity by undermining specific psychological functions in schizophrenia, thereby reducing an affected person's ability

to cope with chronic or recurrent manifestations of the disorder (Westermeyer, 2006). Further, several studies have documented reduced attention and memory function among persons with co-occurring schizophrenia and SUDs (Sevy, Kay, & Opler; 1990; Oepen, Levy, & Saemann, 1993; Tracy, Josiassen, & Bellack, 1995), demonstrating an interruption of specific cognitive and psychological processes. Chronic cocaine use largely produced these deficits in combination with impaired nonverbal problem solving and abstracting ability in one study (O'Malley, Adamse, & Heaton, 1992). Research has also suggested that cocaine users with co-occurring schizophrenia and SUDs may be at risk to more severe forms of tardive dyskinesia (Brady, Anton, & Ballenger, 1990), and there is also evidence to suggest that chronic cannabis use may increase the risk of tardive dyskinesia in this population (Zaretsky, Rector, & Seeman, 1993).

Aside from the clinical manifestations of substance use, this population suffers from a host of adverse social consequences. For example, people with schizophrenia and co-occurring SUDs are more prone to violent victimization than their counterparts without SUDs (Scheller-Gilkey et al., 2003; Gearon et al., 2003; Compton, Furman, & Kaslow 2004; Swartz et al., 2006). Such individuals are more likely to be exposed to people who may take advantage of them both financially and sexually (Goodman et al., 2001). This is particularly true for women with these conditions, who are more prone to have experienced childhood sexual and physical abuse (Gearon & Bellack, 1999; Alexander, 1996), and who are more vulnerable to subsequent violent victimization in adulthood (Gearon et al., 2003). Relevant research has also reported findings to suggest that childhood abuse in African Americans with schizophrenia may increase the risk of co-occurring SUDs for this subgroup (Compton et al., 2004).

Compared to their counter-parts with schizophrenia and without SUDs, people with co-occurring SUDs and schizophrenia are vulnerable to a range of other substance-related adverse

outcomes including increased rates of suicidal ideation (Bartels, Drake, & McHugo, 1992), more severe aggression and violence (Cuffel, Shumway, Chouljian, & MacDonald, 1994; Fulwiler, Grossman, Forbes, & Ruthazer, 1997), as well as increased criminal activity and incarceration (Abram & Teplin, 1991; Abram, Teplin, & McClelland, 2003). These consequences lead to greater degrees of interpersonal conflict and stress, which contribute to increased rates of family conflict and contentious interactions with service providers (Kashner et al., 1991; Salyers & Mueser, 2001; Barrowclough, Ward, Wearden, & Gregg, 2005). Such behaviors coupled with the pervasive patterns of substance use observed among this population result in a host of negative consequences such that people with co-occurring SUDs and schizophrenia are more prone to social exclusion (Todd et al., 2004), housing instability, and homelessness (Drake et al., 1991; Caton et al., 1994). Despite these severe consequences, studies have shown people with schizophrenia and co-occurring SUDs have little incentive to change their substance-related behaviors, with one study showing that up to 77% of their sample manifested low motivations to cease their use of substances (Ziedonis & Trudaeu, 1997).

Longitudinal severity of substance use. There is overwhelming evidence to suggest that alcohol and other drug use can lead to a host of negative consequences for people who suffer from co-occurring schizophrenia and SUDs. The strong associations between the presence of a comorbid substance use disorder and adverse outcomes in schizophrenia has led to increased pessimism with regard to the course and severity (i.e., the patterns, frequency, duration, impairment, and consequences of substance use) of substance use problems in this population (Drake et al., 2006). This pessimistic outlook has been in part confirmed by Bartles, Drake, and Wallach (1995) in a 7-year study of 148 persons with schizophrenia and co-occurring SUDs. At the 7-year follow-up, results revealed that the lifetime prevalence of alcohol use disorders

increased by 1% per year (7% overall). This study, which began in the 1980s, did not show any propensity for remission of alcohol use severity for these participants with schizophrenia (Bartles et al., 1995). Another study by Wade and colleagues (2006) found that when following 103 persons for 15-months after their first episode of schizophrenia, high severities of substance use was associated with an increased risk of inpatient admission, relapse and shorter time to relapse.

While these data suggest that persons with such conditions can sustain their use for years in the face of significant disability (Drake et al., 1996), there is also data to suggest that this population may adopt abstinence (Drake & Wallach, 1993; Dixon et al., 1998; Drake et al., 2006). For example, one 4-year study of 18 persons with co-occurring schizophrenia and SUDs by Drake, McHugo, and Noordsy (1993) found that 11 had at least one six-month remission at 4-year follow-up, and of the three who failed to achieve any remission, all were cannabis users. Of the 11 who had achieved one 6-month remission, the average duration of the remission was 26.5 months ($SD = 13.5$). Overall, this study suggested a high rate of sustained remission, lasting up to a few years on average once the remission was sustained for six-months or longer (Drake et al., 1993).

In general, alcohol use disorders have been associated with higher remission rates, and thus less substance use severity, than other SUDs (i.e., cocaine use disorders or cannabis use disorders) that co-occur with schizophrenia (Westermeyer, 2006). For example, one study reported sustained remission rates of up to 90% in a sample of persons with schizophrenia and co-occurring alcohol use disorders (Bell et al., 2002). This study by Bell and colleagues (2002) confirmed the earlier findings by Drake and colleagues (1993), whereby those with co-occurring alcohol use disorders and schizophrenia achieved higher remission rates than those with cannabis use disorders. Evidence also suggests high cocaine use severity and poor remission from cocaine

use disorders. For example, the study by Bell and colleagues (2002) found that the rate of one-month remission was 58% ($n = 37$) for persons with schizophrenia and cocaine use disorders compared to 90% ($n = 35$) for persons with schizophrenia and alcohol use disorders. Further, the results of a longitudinal study of 100 persons with schizophrenia and co-occurring SUDs showed cocaine users significantly increased the quantity and frequency of their use, whereas other substance users maintained stable patterns (Chouljian et al., 1995).

Recovery from substance use. As an attempt to conceptualize severity, course, and outcome, the concept of recovery has emerged as a central theme in the mental health and behavioral addiction treatment literature (Drake et al., 2006). Although the concept has been defined in numerous ways in the fields of both mental health and addictions, most definitions include some notion that people need to feel hopeful of a future that contains the essentials for working, learning, and participating fully in the community (Vaillant, 1995; New Freedom Commission Report on Mental Health, 2003; Jacobson, 2004), with achieving sustained remission being particularly important in the field of addictions (Drake et al., 2006). In the general population, people with SUDs achieve recovery, and they consistently cite psychosocial factors such as hope, new beliefs, relationships, and activities, as key to their recoveries (Vaillant, 1995).

Recovery from substance-related problems among persons with schizophrenia and SUDs involves similar changes. In an ethnographic study of the longitudinal course of persons with co-occurring schizophrenia and SUDs, Alverson, Alverson, and Drake (2000) identified four factors that were strongly correlated with such persons' efforts to achieve sustained abstinence. These factors included (1) habitual engagement in an enjoyable activity; (2) decent, stable housing; (3) a caring relationship with someone who accepts mental illness and does not abuse substances;

and (4) a positive, valued relationship with a mental health professional. Quantitative survey research generally supports the ethnographic work of Alverson and colleagues (2000) (i.e., Bebout et al., 1997; Sengupta, Drake, & McHugo, 1998; Trumbetta et al., 1999), and a recent 10-year recovery outcome study of 130 people with co-occurring schizophrenia and SUDs showed that many were able to achieve control over (63%) both disorders, to live independently (57%), to achieve competitive employment (40%), and to attain what they perceived as a (58%) better quality of life (Drake et al., 2006). Most notably, the results of this study documented severe and prolonged disability during years 1 to 3, and then steady improvement from years 3 to 10. At the 3-year follow-up, the majority were still at sub-threshold recovery levels, which suggests that recovery from substance-related problems in this population improves and progresses over many years, not just during the early phase of integrated dual diagnosis treatment (Drake et al., 2006).

In summary, substance-related problems and co-occurring SUDs are common and problematic for persons with schizophrenia. These conditions are more prevalent in persons with schizophrenia than in the general population of adults, although these estimates may vary by treatment setting and geographic location. Taken together, the various manifestations of substance-related problems in schizophrenia suggest that biological vulnerability reacts with psychosocial vulnerability, to produce extraordinarily negative outcomes for this population. Already disadvantaged by the stigma of having a serious mental illness these individuals are drawn to use substances that are accessible and available to them in the communities in which they live. As substance-related problems increase in severity, such persons often cannot manage the few resources society affords them, and as a result they may become victims of abuse, socially isolated, unemployed, or homeless. While these consequences may represent the failures of the social welfare, addiction, and mental health service delivery systems in the U.S., emerging

evidence suggests that many people with co-occurring schizophrenia and SUDs meet broad definitions for recovery, and achieve what they perceive as a good quality of life.

2. Socio-Political Trends in Co-Occurring Substance Use Disorders and Schizophrenia

The co-occurrence of SUDs with schizophrenia is associated with a number of negative consequences that make this comorbidity a major public health issue in both the U.S. and abroad. As such, any investigation that attempts to improve our understanding of those who suffer from these conditions must be grounded not only in the scientific evidence-base, but also in the socio-political context that drives society's response to this comorbidity and its treatment. Within the U.S., the co-occurrence of SUDs with schizophrenia is not only an issue of psychiatric diagnosis but a sociological phenomenon reflecting our broader society's extrusion of people with schizophrenia from protected living arrangements that limit access to substances of abuse. Such an assertion is generally supported by published reports indicating that comorbid SUDs occurred infrequently in schizophrenia prior to 1960. Before then, such persons were treated in state hospitals, where their use of substances was largely restricted—suggesting that the problem of comorbid SUDs in schizophrenia proliferated as the result of the deinstitutionalization policies for those with severe mental illness in the United States. By the 1980s the co-occurrence of SUDs with schizophrenia had become widely acknowledged as a major public health issue, but available treatments were delivered in different settings. This disconnect in services, coupled with the need for both addiction and mental health treatment for persons who would have notable difficulty negotiating two separate systems of care, led to the subsequent development of integrated treatment strategies. To date, these efforts have not been widely implemented across the U.S., and no social policies specifically address the unique needs of this population. Such factors have led to an unfortunate lack of responsibility and cooperation within addiction and

mental health systems of care regarding the treatment of persons with co-occurring SUDs and schizophrenia. These unfortunate outcomes largely stem from the fact that addiction and mental health services emerged via separate historical movements, with the treatment of addictive disorders being both shunned and alternatively embraced by mental health providers. This section briefly reviews the progression of socio-political trends that drive society's response to the treatment of persons with co-occurring SUDs and schizophrenia, via the lens of the historical separation of mental health and addiction services in the United States. As such, the purpose of this review is to provide an overview of the relevant social policies and current federal initiatives attempting to address the treatment and services available to those who suffer from this comorbidity, in order to delineate the significance of a study of substance use severity in co-occurring SUDs and schizophrenia to current social policy.

Over the centuries, the treatment of addictive disorders has been alternatively embraced and shunned by the U.S. health care system in general, and by the providers of mental services in particular (Osher & Drake, 1996). Addictive disorders were first treated in medical settings in the nineteenth century, after Benjamin Rush advocated for a disease-based theory of addiction and Samuel Woodward successfully argued for their treatment in the asylum (Baumohl & Jaffe, 1995). Such asylums were the byproduct of the moral treatment movement of mental illness, where the absence of effective treatments led to a palliative social welfare response to disorders like schizophrenia via institutional reform (Morrissey & Goldman, 1986). Dorothea Dix, a social worker who was attracted to the cause of the “insane poor” in the 1840s, was the key lobbyist for the construction of moral public asylums in the United States (Dix, 1975). While this movement was premised on the idea that mental illnesses could be cured by treating afflicted persons with dignity and respect, such principles became expendable by the mid-1850s under the pressures of

increasing rates of mental illness due to immigration to the U.S., poverty, and industrialization (Trattner, 1999). Absent federal support, state legislatures had to respond to these pressures, and initially did so by expanding asylum capacity or by erecting larger facilities (Morrissey & Goldman, 1986). Such asylums became filled with chronic patients that overcrowded these facilities and undermined any attempts at therapeutic practice. Under these circumstances, psychiatrists could not produce medical “cures” for patients with addictions or schizophrenia, and such disorders soon became associated with incurability (Deutsch, 1949). These challenges coupled with the mounting costs that became associated with such institutions eroded public support and asylums began to vanish across the United States (Trattner, 1999). Such events occurred at the turn of twentieth century, just as a budding mental hygiene movement posited that inexpensive, community-based care could treat acute schizophrenia, as well as engage patients in early stages of addiction and arrest the development of addictive conditions.

The pessimism associated with the asylums gave way to a new found optimism for the mental hygiene movement, a national wave of reform leading to community-based care for persons with schizophrenia and addictive disorders. At the turn of the twentieth century, society was outraged by exposés of the conditions in asylums, which included a personal account by Clifford Beers (Dain, 1980). Beers, who had recovered from schizophrenia himself, documented his experiences within the deteriorating conditions of the asylum in 1908, and then went on to found the National Committee for Mental Hygiene in 1909 (Morrissey & Goldman, 1986). Since the National Committee for Mental Hygiene was premised on principles of early prevention and detection of mental illness, the mental hygienists could do little for the treatment of chronic schizophrenia or alcoholism (the dominant substance-related disorder) (Morrissey & Goldman, 1986). However, this reform spawned the development of new mental health

agencies such as psychiatric dispensaries and child guidance clinics, and had a large impact on educating the public on the potential causes and early diagnosis of mental illnesses (Trattner, 1999). All of these factors suggest that the mental hygiene movement not only exposed the ineffective asylum treatments, but also provided support for community-based services. Additionally, while largely focused on mental health, this movement also carried with it the trend of medically treating addictive disorders, and extended such practice to include prevention (Osher & Drake, 1996).

During the 1930s, Alcoholics Anonymous (AA) provided a mechanism for transferring the treatment of alcohol-related problems from institutions to the community (Osher & Drake, 1996). Narcotics Anonymous (NA) similarly facilitated non-institutional treatment for persons with drug addictions. However, these “non-medical” approaches diverted addictions treatment away from psychiatry and established parallel systems of care. Further, the health care system largely shunned the treatment of addictive disorders for at least the next twenty years, and it was not until new theories posited biologic underpinnings to addictions that the traditional system reluctantly reconsidered its role in providing treatment. Most notably, in 1960 E.M. Jellinek posited a model that was substantiated by science and justified the re-medicalization of addictive disorders. It should be noted that Mary Richmond, a social worker most commonly credited for her work with the Charity Organization Society, actually posited a model of alcoholism nearly a half-century earlier in *Social Diagnosis* (1917, 1944). Richmond specifically documented that “inebriety is a disease”, and went on to provide a description of this “disability” that mirrored Jellinek’s model, yet her model of alcoholism was largely ignored for decades until it could be substantiated by science (Straussner, 2008).

Between 1930 and 1960, the federal response to mental health and addictive disorders

reinforced the separation of these systems. Via the Mental Health Act of 1946, the National Institute of Mental Health (NIMH) was charged with the responsibility for developing mental health, alcohol and drug initiatives, and policy (Osher & Drake, 1996). However, the NIMH remained silent on the issue of addictive disorders until their re-medicalization in the 1960s, and then the institute had begun to actively advocate for more community-based alcohol treatment clinics. When Congress subsequently enacted the Narcotic Addict Rehabilitation Act in 1966, NIMH was authorized to make grants to establish community-based drug treatment programs and had begun to support the development of numerous therapeutic communities. A few years later, decriminalization laws were passed such that interventions for persons with drug addictions were diverted from the criminal justice system to the health sector (Osher & Drake, 1996). While these socio-political trends in the treatment of addictions show that such disorders were widely acknowledged as medically-based problems by the 1960s, affected persons had still received their treatment in settings separate from those with mental disorders.

Unlike people with primary substance-related disorders, a considerable proportion of people with schizophrenia continued to receive treatment for the disorder in institutional settings up through the mid-1960s. However, by the mid-1960s, the emergence of aftercare clinics, acute inpatient facilities, phenothiazines, and brief psychosocial modalities, had established considerable advocacy support for community mental health care (Morrissey & Goldman, 1986). Further, via the promise of early intervention, and especially with the discovery of new drug therapies, public advocacy groups championed that the long-term disability of schizophrenia could be offset, which would render the need for institutional treatment obsolete (Lyons, 1984). Such advocacy support combined with the results of several federal studies that were conducted during the late-1950s on the needs of the mentally ill, promoted a strong case for a community

care (Morrissey & Goldman, 1986). As a result, in 1963 Congress passed the Community Mental Health Centers Act to allow states to deinstitutionalize persons with schizophrenia by providing federal funding to build an elaborate system of community mental health treatment centers (Rochefort, 1984).

Although the resulting effect of the Community Mental Health Centers Act cut the state hospital census by two-thirds (~6,000) by 1970 (Rochefort, 1984), this shift in the locus of care did little to solve the problem of chronic mental illness (Morrissey & Goldman, 1986). By the 1970s it became clear that many with schizophrenia were in need of services well beyond what the meagerly funded community centers could provide (Grob, 1994). Consequently, existing state hospitals continued to provide back up for these untried community programs, which were able, in turn, to focus on less disabled persons (Rochefort, 1984). Nevertheless, state hospitals continued to be used as last ditch efforts for treatment refractory patients while a growing recognition that socioeconomic factors are critical to community well-being stimulated a host of social policies to help sustain mentally ill people in the community (Rochefort, 1984). Most notably, in the 1960s and early 1970s Social Security amendments were made to Medicaid and Supplemental Security Income to provide cash and in-kind benefits to people with schizophrenia living in the community (Frank, Goldman, & Hogan, 2003). Unfortunately, and despite these efforts, the community offered very little to no material supports or protection, which inevitably raised this population's vulnerability to an array of adverse consequences (Drake et al., 2002).

Consequently, by the mid-1970s recently deinstitutionalized schizophrenia patients accounted for nearly 30% of the urban homeless population (Bassuk, 1985). Related to the vulnerabilities conferred by being homeless (Kogel, Burnam, & Farr, 1988), a new subgroup of "difficult to serve" patients emerged (Pepper et al., 1981; Bachrach, 1982), and substance abuse

was associated with their “treatment resistance” (Osher & Drake, 1996). Public concerns about this subgroup and about the treatment of addictive disorders led to the 1975 amendment of the Community Mental Health Center Act, which expanded the scope of community treatment to include drug and alcohol services (Drake & Osher, 1996). However, such provisions did little to assuage the stark increase in the post-deinstitutionalization rates of SUDs among people with schizophrenia, which grew from 30% in 1970 to nearly 50% by 1990 (Westermeyer, 2006). Further, as a result of greater access to addiction treatment, the costs of providing community addiction and mental health care soared, and the states quickly began to experience declining support (Baumohl & Jaffe, 1995). Consequently, the community mental health infrastructure soon proved to be grossly inadequate for fulfilling the needs of this newly identified population of persons with co-occurring SUDs and schizophrenia.

Although funding for the community mental health centers was insufficient from the start, the enactment of the Omnibus Budget Reconciliation Act in the 1980s and the repeal of the Mental Health Systems Act depleted what meager funds remained (Rocheffort, 1984). As a result, states could no longer sustain these programs, and the community centers began to vanish across the United States. With the dissolution of these centers came the advent of the 1987 Alcohol, Drug Abuse, and Mental Health Administration Reorganization Act (Osher & Drake, 1996), which formed the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA). While this policy sought to improve community outcomes in people with addictive and mental health disorders, it did so by firming the separation of these systems (Osher & Drake, 1996). The Act introduced a state-managed block grant mechanism such that federal alcohol, drug, and mental health grants were joined into a single block grant, allowing for the states to develop separate and corresponding structures for alcohol, drug, and mental health services. Then,

between 1970 and 1990, a notable shift had been reported with regard to the delivery of addiction services via settings separate from mental health services (Schnibble & Manderville, 1993). During this time, such systems had become more exclusive via seeking to provide treatment and services within the context of narrowly defined populations (Osher & Drake, 1996). As such, the results of a series of federally funded studies beginning in 1985 showed people with co-occurring disorders had worse outcomes than those with one disorder, and that such findings were due to numerous administrative barriers, resistances, and gaps between the addiction and mental health service delivery systems (Minkoff & Drake, 1991). Consequently, during a time of waning resources, and when addiction and mental health services were both in high demand, persons with co-occurring SUDs and schizophrenia often did not receive any treatment for their conditions.

In yet another federal reorganization in 1992, ADAMHA was split into a services agency – the Substance Abuse and Mental Health Services Administration (SAMHSA), which had been officially authorized to oversee strategies to serve persons with co-occurring disorders (Osher & Drake, 1996). This reorganization occurred just as new approaches began to underscore the importance of integrated strategies for persons co-occurring disorders (Ziedonis, 2004). Such a model is premised on the idea that the treatment system bears the burden of ensuring that the client’s needs are met by linking addiction and mental health approaches in a coherent fashion within the same setting (Mueser et al., 2003). Basic elements include an assertive engagement style, close monitoring, comprehensive care, supportive living, step-wise treatment, and a long-term perspective (Mueser et al., 2003). Despite all of the optimism surrounding integrated treatment models, diverse licensing agreements between addiction and mental health service delivery systems largely precluded any opportunity to co-mingle funds (Ridgley & Dixon, 1995),

which created a mismatch of these structures to clinical need (Osher & Drake, 1996). As such, many agencies struggled with making integrated services available for persons with co-occurring disorders, and had to resort to providing sequential treatment (stabilized in one system and then referred to the other), or treatment in parallel (treatment in separate systems, absent stabilization) systems with little coordination (Minkoff & Drake, 1991). Consequently, the mismatch of these structures to clinical need promoted an inappropriate use of services and raised the level of suffering in persons with co-occurring SUDs and schizophrenia (Bachrach, 1982).

Ever since deinstitutionalization, the problem of co-occurring SUDs in schizophrenia has proliferated, and many of the social policies that were enacted during this time largely worked against this population. As the complex needs of this population had both exposed the separation of mental health and addiction services, they also signaled a convergence of treatment principles and a plan for service integration. Such integrated systems had begun (as available) to be applied to this population as early as the 1980s, with the hope that such models of service delivery would improve the treatment and long-term recovery outcomes for those with co-occurring disorders. At the same time, a powerful consumer movement had begun to grow such that the traditional perspective on the course of schizophrenia and the associated assumptions about the potential of those with the disorder to live a productive and satisfying life were challenged (Bellack, 2006). These consumer voices were backed by evidence from a series of long-term outcome studies, demonstrating that the course of schizophrenia is variable across and within individuals and that many people with the disorder who meet strict diagnostic criteria can achieve good outcomes (Bellack, 2006). These 2 forces—new data and consumer voices— contributed to a political change that has recently begun to have an impact on public attitudes, patterns of service delivery, and the relationships between providers and consumers.

A central focus in this recent political change is the concept of recovery. Although definitions of the recovery concept have varied over the past decade, most include some notion that people with schizophrenia need to feel hopeful of a future that contains the essentials for living, working, learning, and participating fully in the community (New Freedom Commission Report on Mental Health, 2003). Notably, recovery has a different set of meanings in the field of addictions (Vaillant, 1995). These definitions also variously address processes and outcome, subjective and objective status, but a consistent feature of recovery in the field of addictions is sustained abstinence (Drake et al., 2006). For people with schizophrenia and co-occurring SUDs, achieving sustained abstinence and/or active remission from substance use is critical, with one recent study observing 10-year recovery rates of over 50% such that participants had achieved what they perceived as a better quality of life, and over 60% were actively attaining remissions from substance use (Drake et al., 2006). While these findings are hopeful, it is noteworthy to mention that the total 130 participants of this study do not represent the large majority of persons with co-occurring SUDs and schizophrenia who would have challenges negotiating comparable integrated treatment outside of the context of a structured research program.

Recent attention on the recovery outcomes of persons with co-occurring disorders has stemmed in part from the findings of federally funded studies on the systems of service delivery in the United States. Most notably, findings of the 2003 President's New Freedom Commission on Mental Health recently concluded that the most significant barrier precluding persons with co-occurring disorders from being able to accomplish a productive and fulfilling life is poor service integration (Executive Order No. 13263). Such results spurred a flurry of initiatives sponsored by SAMHSA, including a National Co-Occurring Center for Excellence that provides cross-

training on-site to support state and community-based program efforts to better address the problem of co-occurring disorders (Ziedonis, 2004). Regardless of these efforts, challenges have persisted with regard to launching system-level integrated services that seek to bridge federal and state agencies, modify reimbursement, and establish networks of integrated programs (Ziedonis, 2004). The resulting effects have produced a fragmented service delivery system, with addiction and mental services being largely unaccountable to the consumer (Ziedonis et al., 2005). Consequently, poor service-level integration has been identified as the largest current problem in addressing the problem of co-occurring SUDs in schizophrenia today (Ziedonis, 2004).

Consistent with the recovery model, the New Freedom Commission report stated, “consumers, along with service providers, will actively participate in designing and developing the systems of care in which they are involved...consumers and their families will play a larger role in managing the funding for their services” (New Freedom Commission Report on Mental Health, 2003, p. 8). However, programmatic challenges to implementing integrated treatment modalities within addiction and mental health settings largely preclude the likelihood of such partnerships at the clinical level. First, co-occurring disorders are conceptualized differently in mental health versus addiction treatment settings, with clinical staff having different perspectives on treatment, in part because of the different presentations encountered in each setting (Ziedonis, 2004). Second, it is often the case that no single entity or agency takes responsibility for case management services and service coordination. Third, there is a need for greater availability of improved communication between treatment providers, and enhanced access to a wide range of medical, psychiatric, and addiction services (Ziedonis et al., 2005). With no social policies or regulatory agencies mandating improved service coordination, the existing settings cannot support collaborative design and treatment development efforts for people with co-occurring

SUDs and schizophrenia at the clinical level.

As a consequence of these systemic and clinical barriers to integrated treatment, current federal initiatives and social policies have had a limited impact on improving the outcomes of substance use severity and recovery for persons with co-occurring SUDs and schizophrenia. Unfortunately, such efforts will continue to have a limited impact on improving the clinical management and outcome of people with co-occurring SUDs and schizophrenia until the issues undergirding a unified framework are effectively addressed. While very recent efforts to improve service quality have achieved great importance and permeated health care generally with the passage of the Affordable Care Act of 2010, such concepts do not appear to have penetrated very far into improving the quality of service integration for persons with co-occurring mental health and substance use disorders (Pincus, Spaeth-Rublee, & Watkins, 2011). In fact, rather disturbing results from a recent study by the Institute of Medicine revealed that, despite gains that have been made in the quality of care in general medical/surgical sector, the quality of care for Americans with mental health and substance use problems remains as poor today as it was several years ago (Institute of Medicine, 2006). The contentious history between mental health versus addiction service delivery systems in the U.S. has undoubtedly had a negative impact on launching and subsequently delivering requisite integrated approaches designed to improve outcomes of substance use severity and maximize recovery among people with co-occurring SUDs and schizophrenia (Ziedonis et al., 2005). As such, this investigation has the potential to make important contributions to highlight these limitations in current policies by building an evidence-base that supports a potentially important determinant of disability in schizophrenia (intrinsic motivation), and by deriving practice implications for addressing this determinant to facilitate the recovery of persons with co-occurring SUDs and schizophrenia by

improving substance use severity outcomes in this population.

B. ROLE OF GENDER IN THE PATTERNS OF SUBSTANCE USE SEVERITY IN MEN AND WOMEN WITH SCHIZOPHRENIA

Over the past century, gender differences in schizophrenia have been consistently reported in the research literature (Krapelin, 1909, 1919; Kretschmer, 1921; Leung & Chue, 2000; Goldstein & Lewine, 2000); with the weight of the evidence largely indicating that women experience a better longitudinal course and outcome in the disorder than men (Angermeyer, Kuhn, & Goldstein, 1990; Leung & Chue, 2000). The areas of outcome in which women with schizophrenia have been found to exhibit a better prognosis than men include education (Goldstein & Link, 1988), vocational functioning (Angermeyer, Kuhn, & Goldstein, 1990; McGlashan & Bardenstein, 1990; Salokangas & Stengard, 1990; Andia et al., 1995), social functioning (Wattie & Kedward, 1985; Mueser, Bellack, Morrision, & Wixted, 1990; Andia et al., 1995; Murray & Van Os, 1998), fewer and shorter hospitalizations (Angermeyer et al., 1990; Eaton et al., 1995), lower suicide rates (Test, Burke, & Wallisch, 1990; Heila et al., 1997), and less frequent use of alcohol and illicit drugs (McGlashan & Bardenstein, 1990; Test et al., 1990; Cuffel & Chase, 1994).

While differences between the genders have long been studied in schizophrenia research, only recently has attention begun to be paid to variations in the severity of substance use in co-occurring SUDs and schizophrenia. Thus, the consistently better outcomes observed among women with the disorder would seem to suggest the potential for women with co-occurring SUDs and schizophrenia to exhibit less severe patterns of substance use severity than men with these conditions. However, the weight of the limited evidence suggest mixed results, with some

studies showing that women exhibit less severe SUD pathology than men, and others showing no significant relations with regard to the severity of substance use between the genders. As such, not only is a study that proposes to examine differences in the longitudinal patterns of SUD pathology in schizophrenia greatly needed, but the results of such a study may lead to important implications for gender-specific interventions, which could inform the treatment and recovery of this population in a unique way. This section reviews the limited gender-specific literature in co-occurring SUDs and schizophrenia, to substantiate a hypothesis that tests whether women demonstrate better outcomes of substance use severity than men among this population.

During the course of the disorder, people with co-occurring SUDs and schizophrenia experience recurrent patterns of substance use severity, which pertains to the frequency, duration, and impairments (symptom and functional) associated with long-term use (Drake et al., 2006). Regarding these indicators, prior investigations have shown that women with co-occurring SUDs tend to use fewer substances less frequently and in smaller amounts than men (Drake, et al., 1989; Mueser et al., 1990; Test et al., 1990; Køster et al., 2008). Consequently, these women tend to exhibit less impairment as a result of their substance use over the course of the disorder than men (Køster et al., 2008; Roncero et al., 2011). For example, Køster, Lajer, Lindhardt, and Rosenbaum (2008) followed 62 patients with co-occurring schizophrenia and SUDs for 2-years from symptom onset. Upon enrollment, more men used alcohol and cannabis in significantly greater quantities compared to women, and these men persisted in using these substances in significantly greater frequencies (3 times the rate of women) and quantities over the follow-up than women (Køster et al., 2008). However, despite these differences, both genders exhibited marked improvements on indicators of severity (i.e., drug consumption and abuse) during the 2-year follow-up (Køster et al., 2008). Results showed that the overall sample improved in terms of

their substance use severity over the follow-up, with women exhibiting greater propensities toward remission than men, which supports a hypothesis that seeks to test whether women exhibit faster gains in substance use severity improvement than men among this population.

Other studies (mostly cross-sectional) that have examined the severities of substance use in relation to gender among persons with co-occurring SUDs and schizophrenia report similar findings (Koskien et al., 2009a; Brunette & Drake, 1998), with some variability being observed depending on whether the primary substance of abuse is alcohol or cannabis. For example, Koskien and colleagues (2009a) conducted a meta-analysis on the rates of cannabis use disorders in schizophrenia, and reported significantly higher severities among men for all studies (3 of 28, studies) comparing cannabis use in relation to gender. For a sample of homeless men ($n = 42$) and women ($n = 66$) with co-occurring SUDs and schizophrenia, Brunette and Drake (1998) found that men had significantly greater cannabis severity than women; the only exception to similar severities being observed between the genders. For a sample of outpatients with co-occurring SUDs and schizophrenia, Brunette and Drake (1997) reported similar results such that men were found to abuse cannabis for longer periods of time than women prior to enrollment (Brunette & Drake, 1997). However, results revealed no significant differences between the genders with regard to the severities of alcohol, cannabis, or poly-drug use, as indicated by comparable frequencies and durations of use (Brunette & Drake, 1997). Taken together, the results of these studies suggest a high potential for comparable severities of alcohol use to be observed between the genders with men having greater severities of cannabis use than women.

Such mixed findings observed among these mostly cross-sectional studies of gender differences in the severities of substance use among persons with co-occurring SUDs and schizophrenia signal a need for further longitudinal research to examine these effects. The

proposed study seeks to take an important step in advancing field knowledge by identifying whether there is significant variability in the longitudinal patterns of substance use severity between men and women with co-occurring SUDs and schizophrenia, and potentially deriving gender-based treatment implications from such findings, which may lead to optimal long-term recovery outcomes of substance use severity among this population.

C. INTRINSIC MOTIVATION AND SUBSTANCE USE SEVERITY IN SCHIZOPHRENIA

Intrinsic motivation concerns the inherent tendencies that all human beings have to seek out novelty and challenges, to extend and exercise capacities, and to explore and to learn. For this dissertation study, intrinsic motivation is conceptualized in terms of behaviors people carry out because of the positive feelings that are associated with performing an action in the absence of extrinsic rewards. These actions do not require for such persons to rely on external support or reinforcement to be initiated or sustained. This research uses an operational definition of intrinsic motivation based on the sum of QLS-derived items; purpose, curiosity, and motivation. Reports using these conceptual and operational definitions of the construct have shown persons with schizophrenia possess intrinsic motivation deficits that impede their ability to generate internal drives to sustain behavior changes absent external support. Evidence from the dual diagnosis literature suggests that such deficits can disengage intrinsic motivational processes when persons with co-occurring SUDs and schizophrenia try to generate their internal drives toward achieving reductions in substance use severity. Although various motivational rehabilitative programs are available to the larger dual diagnosis population, such interventions may not address the deficits in intrinsic motivation that are potentially unique to schizophrenia. Consequently, this research

seeks to extend validation of Nakagami and colleague's (2008) measure of intrinsic motivation deficits for schizophrenia to schizophrenia and comorbid SUD. This approach is taken because methodological limitations inherent to the dual diagnosis treatment research call for extending validation of an intrinsic motivation measure that can provide further research into the relevance of intrinsic motivation deficits to substance use severity among this population. This section first provides an introduction to the construct of intrinsic motivation by broadly describing its relevance to behavior change processes, and then provides an overview of the application of intrinsic motivation to schizophrenia and comorbid schizophrenia and SUD. Relevant literature on the measurement of intrinsic motivation in schizophrenia is then reviewed. Lastly, research supporting the validity of using the intrinsic motivation measure developed by Nakagami and colleagues (2008) to predict prospective naturalistic changes in substance use severity among persons with co-occurring SUD and schizophrenia is provided.

1. Overview and Relevance of Intrinsic Motivation

The study of intrinsic motivation has been a broad area of adaptive behavior change investigation for several decades. Much of the early research on intrinsic motivation stemmed from the behavioral neuroscience literature, which focused on the concept of homeostatic drives or the idea that organisms may be driven to maintain a stable internal state in regard to variables such as thirst, hunger, or other injunctive behaviors (see Berridge, 2004, for review). Beginning with Hull's (1943) theory of drives, intrinsically motivated behaviors were posited as those that emerged from psychological needs (and their derivatives) to restore system balance. Such a view on intrinsic motivation focused on the fact that a deficit or error signal in these systems (i.e., lack of water, hunger, low blood glucose) triggers behaviors designed to return the system to a set point or stable state (see Berridge, 2004, for a discussion of alternative points of view).

While views of motivation and intrinsic motivation that rely on homeostatic mechanisms have powerful explanatory force in many domains, subsequent social psychological researchers had argued that other types of mechanisms that do not rely on explicit deficit signals are needed to explain the full range of intrinsically motivated behaviors seen in animals and humans. Such a focus gave rise to the appetitive approach to motivation, which posited that animals and human beings may be intrinsically motivated to seek stimuli that are reinforcing in some sense, even if these stimuli do not serve to remediate some internal deficit state (Berridge, 2004). Compared to homeostatic views, the appetitive motivational system was seemingly more appealing, as it could explain domains in which intrinsic behaviors may be removed from basic needs and potentially emerge from abstract concepts such as tendencies, desires, or interpersonal needs.

Subsequent focus on appetitive motivation systems in experimental animal research led to the contemporary conceptualization of intrinsic motivation, as it was discovered that many organisms engage in exploratory, playful, and curiosity-driven behaviors even in the absence of reinforcement or reward (White, 1959). Over the years, a unique set of inherent tendencies have come to be seen as the mechanisms potentially underlying intrinsically motivated outcome behaviors in humans (Deci et al., 1999, for review). Such tendencies include (1) the tendency to seek out novelty and challenges, or *curiosity tendencies*; (2) the tendency to extend and exercise capacities, or *purpose tendencies*; and (3) the tendency to explore and to learn, or *performance tendencies* (Ryan & Deci, 2000; Deci et al., 1999). According to Ryan and Deci (2000), human beings can use intrinsic motivation to change their behaviors by catalyzing any of these inherent tendencies when they are engaged in an activity that satisfies their needs for being autonomous, self-determined, or competent. Such a process is described in more detail in Figure 1, and has become widely acknowledged as the way in which human beings carry out a range of activities

to change their behaviors in the absence of reinforcement or reward (Deci & Ryan, 2007). This model can be used to understand the processes that go awry in schizophrenia when deficits in intrinsic motivation impede the ability of those with the disorder to generate internal drives to sustain behavior changes absent external rewards, and are discussed in further detail in Section C.2. Aspects of this model can also be used to understand how such processes become even more disengaged when persons with co-occurring SUDs and schizophrenia try to generate internal drives toward achieving and actually sustaining reductions in substance use severity, and are discussed in further detail in Section C.3.

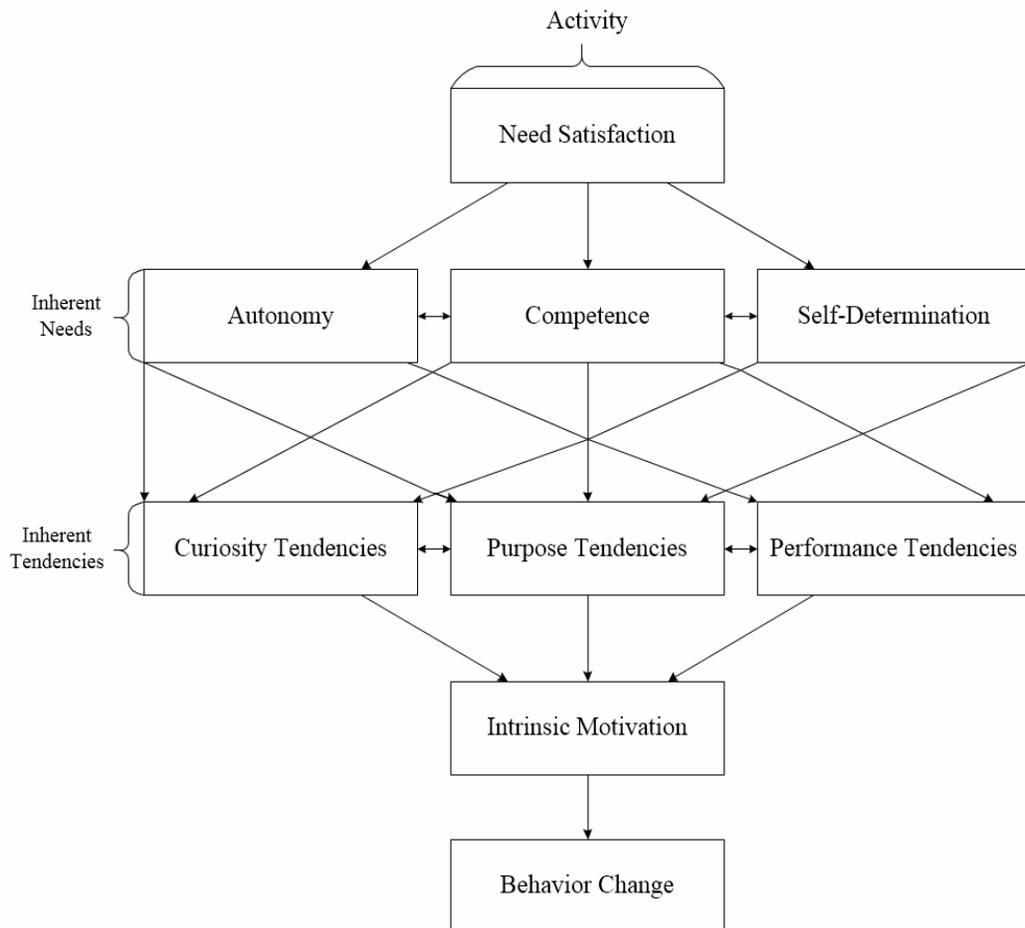


Figure 1. Processes by which a person's needs direct the inherent tendencies of human behavior toward intrinsically motivated outcome behaviors

Psychological processes underlying intrinsic motivation. One important area of work concerning the significance of intrinsic motivation to adaptive behavior change has stemmed from studies of curiosity tendencies of human behavior. Early work by Berlyne (1960) on the curiosity tendencies of human behavior documented their growth promoting properties, and the developmental characteristics such tendencies provide for facilitating novelty seeking behaviors. Specifically, such properties have been found to promote cognitive, social, and physical growth among both children and adults (Deci et al., 1999; LaGuardia, Ryan, Couchman, & Ryan, 2000). Other studies have shown that the degree to which such curiosity tendencies become catalyzed toward intrinsically motivated outcome behaviors varies as a function of the degree to which people perceive that the activity they are engaged in satisfies their needs for feeling competent, autonomous, or self-determined (Deci et al., 1999; Deci et al., 1981). Such findings not only signal the importance of these curious tendencies to behavior change processes by highlighting their growth promoting effects, but also suggest that when people are engaged in an activity that supports their needs for feeling competent, autonomous, or self-determined, then such a person's curious tendencies may become catalyzed toward intrinsically motivated outcomes.

Research on the purpose tendencies of intrinsic motivation has also focused on how need satisfaction is a critical component to catalyzing these tendencies toward intrinsically motivated outcomes. Many investigations have found consistent correlations between service providers who supported their patient's autonomous decision making and their patient's intrinsically motivated behaviors that resulted in more healthy lifestyles (see Deci & Ryan, 2007, for review). For example, such studies have focused on how a person's need for feeling autonomous and self-determined was critical to catalyzing such tendencies toward facilitating intrinsically motivated

outcomes in smoking cessation (Williams et al., 2006), depression reduction (Zuroff et al., 2007), and exercise/health promotion (Fortier, Sweet, O'Sullivan, & Williams, 2007; William, Grow, Freedman, Ryan, & Deci, 1996) intervention programs. Taken together, these findings suggest that whether any particular intervention can catalyze these purpose tendencies toward adaptive behavior change varies as a function of the person's level of interest in the intervention itself, and if such an intervention promotes autonomous decision making.

Finally, the performance tendencies of human behavior are another important area of work concerning the significance of intrinsic motivation to adaptive behavior change (Deci et al., 1989; Baard, Deci & Ryan, 2004). For example, studies on the performance tendencies of intrinsic motivation have focused on how autonomous decision making in a learning environment is a critical component to catalyzing these tendencies toward intrinsically motivated outcome behaviors among high school students (Chirkov & Ryan, 2001), medical students (Williams & Deci, 1998), and law students (Sheldon & Krieger, 2007). For example, Sheldon and Krieger (2007) found that mentors promoting autonomous decision making in law schools had an important influence on catalyzing performance tendencies among their students toward intrinsically motivated outcomes, which manifested as higher grade point averages and bar passages rates. Such findings suggest that not only do people have inherent tendencies to explore and to learn, but that one's perception of his/her autonomous academic performance is critical to promoting intrinsically motivated outcome behaviors in learning environments.

Social contextual variables, extrinsic rewards, and intrinsic motivation. In addition to studying the ways in which people can build intrinsic motivation to facilitate behavior change, researchers have also examined a host of factors that can undermine its expression, including the presence of extrinsic rewards. Extrinsic motivation is the motivation to do something because a

tangible reward will occur (Deci & Ryan, 2007). The clearest examples of extrinsically motivated behaviors are those performed to obtain a tangible reward or to avoid a punishment. Further, results of a meta-analysis of over 100 studies revealed that extrinsic rewards decreased intrinsic motivation across a range of activities, ages, rewards, and reward contingencies (Deci et al., 1999). In other words, when people were given extrinsic rewards such as money for doing an intrinsically interesting activity, their intrinsic motivation for the activity tended to become undermined. That is, the presence of the reward led them to lose their intrinsic interest in the activity. There were, however, limiting conditions to these findings. For example, such results largely indicated the rewards that were not dependent on activities conducted to achieve some standard or goal tended not to undermine intrinsic motivation, perhaps because they were not perceived as controlling one's behavior (Deci et al., 1999). In fact, subsequent research has shown that the provision of choice increases intrinsic motivation, despite the presence of extrinsic rewards (Zuckerman, Porac, Lathin, Smith & Deci, 1978). For example, Ryan, Mims, and Kostner (1983) found that when extrinsic rewards were delivered in an environment that supported participants' autonomy, intrinsically motivated outcomes persisted. However, Ryan (1982) found that when extrinsic rewards were delivered in a controlling context, participants' propensity toward intrinsically motivated outcome behaviors decreased. Taken together, such findings suggest that the presence of extrinsic rewards may undermine intrinsic motivation; however, this potential is greatly reduced when one's needs for competence, self-determination, or autonomy are satisfied within the social context of the activity or by the target activity itself.

In summary, intrinsic motivation is a unique social psychological construct that holds particular relevance to adaptive behavior change. The components of the construct include the tendency to seek out novelty and challenges (i.e., curiosity tendencies), the tendency to extend

and exercise capacities (i.e., purpose tendencies), and the tendency to explore and to learn (i.e., performance tendencies) (Ryan & Deci, 2000; Deci et al., 1999). When individuals are intrinsically motivated to pursue a goal, they engage in targeted behaviors because of the interest, enjoyment, and satisfaction derived from their engagement in the activity, rather than due to external rewards. Thus, intrinsically motivated behaviors are repeated without external rewards or constraints and, therefore, more likely to be maintained. This is particularly relevant to developing treatments for co-occurring SUDs and schizophrenia, as such persons demonstrate deficits in increasing intrinsic motivation to change the behaviors associated with their patterns of substance use to achieve remission or recovery. As suggested by the literature pursued in this section, research in social psychology has progressed over the past several decades pointing to the significance of the construct of intrinsic motivation and its relevance as a key motivational component in behavior change processes, signaling the potential promise of the construct for understanding recovery from substance use severity in schizophrenia. What follows is a review of the research examining the presence of intrinsic motivation deficits in schizophrenia. Such a discussion focuses on how the motivational processes that go awry in schizophrenia impair the ability of those with the disorder to generate internal drives to sustain behavior changes absent external rewards, and provides a basis for understanding how such processes can become even more disengaged when persons with co-occurring SUDs and schizophrenia try to generate internal drives toward achieving reductions in substance use severity.

2. Intrinsic Motivation Deficits in Schizophrenia

Research over the past century has supported the conceptualization of schizophrenia as a disorder of motivational impairment, with the earliest descriptions of the disorder emphasizing a disturbance of volition (avolition/ amotivation) as the underlying process in its pathology (see

Foussias & Remington, 2010, for review). Today's nosology of mental disorders considers the presence of motivational deficits such as amotivation and anhedonia to be among the defining features of schizophrenia (APA, 2013). Such deficits are characterized by a diminished capacity to take interest in activities (amotivation), and an inability to experience pleasure from activities that most people find enjoyable (anhedonia). There is no consensus on how to define intrinsic motivation deficits in the context of schizophrenia (Foussias & Remington, 2010). Therefore, this dissertation study conceptualizes the construct in terms of the behaviors people carry out because of the positive feelings associated with performing an action in the absence of extrinsic rewards, and operationally defines the construct based on the sum of pertinent intrapsychic deficit items of the Quality of Life Scale, including purpose, curiosity, and motivation. Since such an approach is premised on the idea that intrinsically motivated outcomes arise from behaviors that people with schizophrenia engage in for their own sake or for the satisfaction they get from working towards a goal, perhaps it is not surprising that other studies utilizing such an approach have begun to turn to negative symptoms such as amotivation and anhedonia in schizophrenia to potentially explain the marked difficulties those with the disorder have in developing intrinsically motivated outcome behaviors (Harvey & Strassnig, 2012).

Psychopathology impairing intrinsic motivational processes. Work by Gard, Kring, Gard, Horan, and Green (2007) has provided some clues into these relations by showing that anhedonia in schizophrenia is linked to deficits in the hedonic experience of anticipatory pleasure (enjoyment related to the anticipation of future activities), which impairs intrinsic motivational processes, and leads to decrements in goal-directed behaviors among those with the disorder. However, individuals with schizophrenia tend to have intact pleasure responses (consummatory anhedonia) when exposed to present stimuli (Berenbaum & Oltmanns, 1992;

Kring, Kerr, Smith, & Neale, 1993; Kring & Neale, 1996; Burbridge & Barch, 2007; Heerey & Gold, 2007; Der-Avakian & Markou, 2011). Previous work by Heerey and Gold (2007) has provided some insight into this issue by comparing the ratings of pleasure and arousal from control and schizophrenia participants. Results of their investigation showed that participants with schizophrenia tended to experience a reduced capacity to anticipate that future goal pursuits will be pleasurable (anticipatory anhedonia), in addition to lacking an ability to translate their subjective experiences into action, which consequently led to a decrease in the initiation of goal-directed behaviors (amotivation) (Heerey & Gold, 2007). Taken together, such results suggest that the interrelationship between anhedonia (i.e., anticipatory anhedonia) and amotivation in schizophrenia may contribute to the intrinsic motivational deficits observed in the disorder. Such deficits could preclude persons with schizophrenia from achieving intrinsically motivated outcomes including the ability to achieve remission and recovery from substance use.

Social contextual variables, extrinsic rewards, and intrinsic motivation in schizophrenia.

In addition to studying the ways in which amotivation and anhedonia are linked to the nature and causes of intrinsic motivational deficits in schizophrenia, relevant work has considered the impact social contextual variables may have on its expression. For example, recent work by Silverstein (2010) has highlighted the challenges of engaging highly symptomatic individuals with schizophrenia into treatment who have low base rates of a desired behavior. He has suggested that by using tangible rewards with this subset of patients, it may be possible to change the value such patients attach to a behavior. Specifically, tokens, money, and other rewards may increase task value sufficiently to enhance the performance of desired behaviors (Silverstein, 2010). Silverstein (2010) further argues that if this activation of extrinsic motivation is done properly (i.e., in an environment that promotes autonomy or self-

competence), it may turn out to be a first step in promoting the internalization of task goals that is sometimes necessary for the development of intrinsic motivation (Deci & Ryan, 2007). In addition, Nakagami and colleagues (2010) have provided causal data to suggest that when both intrinsic motivation and daily functioning are low among individuals with schizophrenia, initial functional improvement might be required to trigger increased levels of intrinsic motivation. Such a finding expands upon Silverstein's (2010) notions to suggest that extrinsic properties could be used to stimulate initial behavior change as well as functional improvement and thereby trigger higher levels of intrinsic motivation in schizophrenia, contrary to the previous description of the intrinsic/extrinsic relationship in healthy individuals.

However, there are data to suggest that positive behavior changes initiated through the use of monetary compensation during activities is not sustained in schizophrenia after rewards are withdrawn (Dickerson, Tenhula, & Green-Paden, 2005). The degree to which extrinsic rewards generalize to everyday task performance is also limited. In addition, further research is needed to support the argument by Silverstein (2010), suggesting that low base rates of intrinsic motivation among highly symptomatic persons with schizophrenia is a justification for employing extrinsic rewards to promote behavior change. While there is evidence to suggest that the most impaired inpatients with schizophrenia exhibit improvements when exposed to cognitive remediation that includes manipulations of both extrinsic (Silverstein, 2010), and intrinsic motivation (Medalia, Revheim, & Casey, 2002), the comparative advantages of these manipulations for subsamples of community patients with schizophrenia, which comprise the vast majority of those who are affected by the disorder today, requires further investigation. Taken together, the weight of the limited evidence supports the use of extrinsic goals to potentially enhance the low base rates of intrinsic motivation among individuals with

schizophrenia, yet further research is needed to more fully understand the clinical circumstances in which extrinsic and intrinsic goals are best used.

Physiological processes underlying intrinsic motivation in schizophrenia. Over the past decade, the physiological processes involved in motivation have become a focus of investigation in schizophrenia research (Barch, 2004), and behavioral neuroscientists have begun to gain a better understanding of how abnormalities in the dopamine system can lower drive- and goal-directed behaviors via animal experiments (Berridge & Kringelbach, 2008). Recent work by Barch and Dowd (2010) identified four operative components to motivation in schizophrenia, and then reviewed the physiological processes that have been linked to each component. The one component that appears to be intact in schizophrenia, which is hedonics or liking a received reward, seems to be mediated by activation of the opioid and gamma butyric acid-ergic systems in the nucleus accumbens shell and its projections to the ventral pallidum, as well as in the orbitofrontal cortex (Pecina, Smith, & Berridge, 2006; Burgdorf & Panksepp, 2006; Smith & Berridge, 2007). The other three components, which include wanting, assessing value, and goal-directed action, may be mediated by the mid-brain dopamine system, orbitofrontal cortex and anterior cingulate cortex, and dorsolateral prefrontal cortex, respectively (Barch & Dowd, 2010). Further, another report by Silverstein (2010) considered a functional disconnectivity between the dorsolateral prefrontal cortex and the subcortical mesolimbic dopamine system in accounting for the marked difficulties people with schizophrenia display in wanting and valuing what they like. Taken together, an important implication of these findings is that the dopaminergic system may be a physiological mechanism underlying regulatory function of intrinsic motivational processes among persons with schizophrenia.

Recent investigations have also examined the physiological processes underlying

intrinsic motivation in schizophrenia by questioning if cognition is a rate-limiting factor for change (Nakagami et al., 2010). Indeed, cognitive deficits have long been thought to reflect disruption in the pathophysiological processes involved in schizophrenia (Green et al., 2004), and as such could potentially represent a physiologically-based rate-limiting factor (Nakagami et al., 2010). Notably, however, Nakagami and colleagues (2010), in their longitudinal study of 130 outpatients with schizophrenia and schizoaffective disorder, found that baseline cognition did not predict change in intrinsic motivation over a 12-month period. Further, longitudinal changes in cognition were not associated with longitudinal changes in intrinsic motivation (Nakagami et al., 2010). Nevertheless, an important implication of these findings is that the study participants who had high and low baseline cognitive function increased their intrinsic motivation, regardless of whether they had improved in their cognition over the 1-year study. Another noteworthy implication of the study conducted by Nakagami et al. (2010) is that the physiological mechanisms that mediate aspects of cognition that they measured did not appear to be a rate-limiting factor for change in intrinsic motivation. Perhaps the most important implications of the naturalistic longitudinal study conducted by Nakagami et al. (2010) were the findings that intrinsic motivation is in fact dynamic over time in schizophrenia; and that study participants' social disability improved as they made gains in intrinsic motivation. Taken together, such findings suggest that while persons with schizophrenia do have deficits in intrinsic motivational processes, intrinsic motivation is malleable among those with the disorder, and thus can be improved.

In another study of 57 outpatients with schizophrenia, Choi and Medalia (2010) used the Intrinsic Motivation Inventory for Schizophrenia Research (IMI-SR), a self-report measure for assessing intrinsic motivation, and reported on changes in intrinsic motivation in relation to a 4-

week cognitive training program. Results supported the dynamic nature of intrinsic motivation in schizophrenia, although the change in intrinsic motivation was significant only in a subgroup that received a motivationally enhanced version of the training task (Choi & Medalia, 2010). Such results elaborate on those previously reported by Nakagami and colleagues (2010), by showing that changes in intrinsic motivation can be detected relative to participation in a learning program and that such changes are sensitive to the motivational properties of the context in which the learning tasks are embedded (Choi & Medalia, 2010). Taken together, these two studies provide strong preliminary support for the malleability of intrinsic motivation in schizophrenia and give a basis for future studies to replicate and extend the findings by varying the social context and sample characteristics, and investigating the validity of methods of assessing intrinsic motivation.

In summary, the weight of the limited evidence in this area of research suggests that persons with schizophrenia have significant deficits in intrinsic motivation, which likely stem from symptoms such as anhedonia and amotivation as well as other pathophysiological processes affecting dopaminergic systems in the disorder. However, while recent investigations have begun to take interest in examining intrinsic motivational processes in schizophrenia, many of these studies have been limited in scope, with only one longitudinal investigation focusing on the relationships between social disability, cognition, and intrinsic motivation among this population. Furthermore, not one of the aforementioned studies have been conducted in a sample of individuals with schizophrenia and comorbid SUD. Unfortunately, while intrinsic motivation deficits are clearly present in schizophrenia, the way in which such deficits impair behavioral change processes in the disorder by interfering with the development of intrinsically motivated goals has not been clearly established. Nevertheless, since intrinsic motivation deficits in

schizophrenia have been shown to impair the ability of those with the disorder to generate internal drives for sustaining behavior changes in the absence of receiving extrinsic rewards (Nakagami et al., 2008; Yamada et al., 2010; Nakagami et al., 2010), it seems likely that individuals with co-occurring SUDs and schizophrenia would be prone to experience considerable challenges with developing internal drives to change their addictive behaviors and reduce their substance use severity. What follows is a review of the limited evidence examining the significance of deficits in intrinsic motivation to substance use severity among persons with schizophrenia and co-occurring SUDs, as well as investigations that have studied differences between the genders with regard to this relationship.

3. Intrinsic Motivation as a Contributor to Substance Use Severity in Schizophrenia

While considerable research supports the relevance of the construct of intrinsic motivation to behavior change processes and evidence within schizophrenia research has documented intrinsic motivation deficits in the disorder, not one of these studies has included persons with co-occurring SUDs and schizophrenia in their study sample. Despite the apparent lack of available evidence on such persons within schizophrenia research, evidence has begun to emerge within the dual diagnosis treatment literature suggesting that the pervasive patterns of substance use observed among those with co-occurring SUDs and schizophrenia may be linked to deficits in intrinsic motivation among this population. However, dual diagnosis programs are often premised on the assumption that people with co-occurring conditions have intact intrinsic motivational processes, which may not be the case for those with comorbid schizophrenia and SUD. Thus, examining the relevant literature in this area may provide insight into the reason for which persons with comorbid schizophrenia and SUD are often unsuccessful with reducing the severity of use in treatment. Within the dual diagnosis treatment research, various instruments

have been used to measure intrinsic motivation, with the majority of approaches focusing on the degree to which persons with co-occurring conditions are intrinsically motivated to change substance-specific behaviors (see DiClemente, 2003; DiClemente et al., 2008). However, few, if any studies have used more general measures of the construct to gauge the intrinsic motivation deficits that are potentially unique to comorbid schizophrenia and SUD. While this dissertation does not seek to take any of the more widely employed substance-specific behavior approaches to the measurement of intrinsic motivation reviewed in this section (this dissertation takes a general approach to the measurement of intrinsic motivation, which is discussed in greater detail in Section C.4), it is still important to review the evidence that has emerged within the context of dual diagnosis motivational programs. This evidence not only signals the importance of intrinsic motivation deficits to SUD pathology among this population, but also signals the potential for the relationship between intrinsic motivation and substance use severity to vary across genders.

Such evidence suggesting that intrinsic motivation deficits may impede persons with schizophrenia and comorbid SUD from their ability to recover from severe substance use has largely stemmed from studies of psychosocial approaches designed to enhance dual diagnosis clients' motivation to change their substance use behaviors (see Hunt et al., 2013, for review). The weight of the evidence indicates that, compared to dual diagnosis clients without schizophrenia, individuals with co-occurring SUDs and schizophrenia are less motivated to change the behaviors associated with their substance use while participating in such programs, are more difficult to engage, make slower progress, and drop out of such programs at faster rates (Drake et al., 2008; Horsfall et al., 2009). While such patterns may be in part due to problems stemming from the intrinsic motivation deficits of schizophrenia rather than treatment compliance issues stemming from the pathology of the SUD, this question has remained largely

unexamined within the dual diagnosis research to date. As such, there is a current need for investigations that seek to understand how these intrinsic motivational processes are actually linked among this population, as well as further research on the contributions of intrinsic motivation to substance use severity in co-occurring SUDs in schizophrenia.

Relatively little research has examined the actual contributions of intrinsic motivation to substance use severity in co-occurring SUDs and schizophrenia (Hunt et al., 2013, for review). In one of the few studies to examine the relationship between intrinsic motivation and substance use severity, Graber and colleagues (2003) observed such relations in 30 non-treatment seeking veterans with co-occurring alcohol use disorders and schizophrenia in an outpatient motivational rehabilitative program. They found participants' ability to increase intrinsic motivation was stronger among those in the experimental condition (motivational interviewing), and that such a modality significantly predicted decreased drinking days and increased rates of abstinence over the 24-week follow-up. Another study by James and colleagues (2004) examined substance use behavior outcomes in 63 treatment seeking dual diagnosis outpatients (63% schizophrenia) in a motivational rehabilitative program. Similar to Graber and colleagues (2003), they also found that the ability to increase intrinsic motivation was stronger among those in the experimental condition (motivational enhancement), and that building intrinsic motivation via such a modality significantly predicted improved alcohol and drug dependence severity at the 3-month follow-up (James et al., 2003). A study by Kavanagh and colleagues (2004a) also observed the relations between intrinsic motivation and substance use outcomes in a sample of 25 first episode patients with dual disorders (48% schizophrenia) in a motivational rehabilitative program. Here too, these investigators found that the ability to increase intrinsic motivation was stronger among those in the experimental condition (start over and survive), and that the gains in intrinsic

motivation that were made through participating in such a modality significantly predicted less substance use at the 12-month follow-up. Subsequent motivational rehabilitation studies of dual diagnosis clients have revealed that participants reduced their use of substances, regardless of the modality to which they were assigned (Martino et al., 2006; Edwards et al., 2006; Baker et al., 2006), perhaps because both groups developed similar improvements in intrinsic motivation over the follow-up periods. Such studies of persons with dual disorders in motivational rehabilitative programs provide evidence of the relationship between intrinsic motivation and substance use severity in this population. It should be noted, however, such positive effects of changes in intrinsic motivation on changes in substance use severity have been obtained within the context of studies employing modest sized samples of dual diagnosis participants selected from specialty populations that have included few women and individuals with co-occurring SUDs and schizophrenia.

In fact, the study by Graber and colleagues (2003) only included 1 woman in their modest sized sample of 37 non-treatment seeking veterans with co-occurring alcohol use disorders and schizophrenia. Such a small proportion of women studied by these investigators highlights the potential for this subgroup to be underrepresented within the relevant research in this area and thus signals a need for further study. In the only investigation to examine gender differences in the relationship between intrinsic motivation and outcomes of substance use severity among persons with dual disorders, Drapalski and colleagues (2011) examined such relations in samples of treatment non-seeking ($N = 175$) and treatment seeking ($N = 134$) men and women with dual disorders. Specifically, the investigators of this cross-sectional study sought to examine gender differences in the patterns and consequences of substance use, treatment-seeking patterns, and participants' motivation to change for the two samples of study participants. The investigators

found that, in both groups, men and women exhibited more similar patterns and severities of substance use than differences (retrospectively rated). However, the findings also showed that treatment-seeking women demonstrated greater readiness to change their substance use patterns and severities than men among this population. Such a finding may be indicative of higher levels of intrinsic motivation being present among these women, which could potentially lead to greater longitudinal improvements of substance use severity being observed among women than men in this population.

As can be seen by this review of the literature examining the relationship between intrinsic motivation deficits and SUD pathology in co-occurring SUDs and schizophrenia, and the potential for this relationship to vary across the genders, some evidence exists to suggest that such deficits may be important contributors to the severe and persistent patterns of substance use severity observed in this population. Specifically, people with schizophrenia do exhibit deficits in intrinsic motivational processes, which considerably impair the ability of those with the disorder to generate internal drives to sustain behavior changes absent external rewards. With regard to persons with co-occurring SUDs and schizophrenia, such deficits may disengage intrinsic motivational processes when persons with these conditions try to generate internal drives to achieve reductions in substance use severity. Consequently, deficits in intrinsic motivational processes among persons with co-occurring SUDs in schizophrenia appear to be an important contributor to the severe and persistent patterns of substance use severity observed among this population.

4. Limitations of the Research on Intrinsic Motivation and Substance Use Severity in Schizophrenia

Confirmatory evidence has yet to be established regarding the significance of deficits in

motivational processes to substance use severity in schizophrenia, as work in this area has suffered from several important limitations that are readily discernable from this review of the literature. In particular, to date investigations of intrinsic motivation in co-occurring SUDs and schizophrenia have largely been conducted within the context of motivational rehabilitation programs for the larger population of dual diagnosis clients. While some of these programs have adapted their modalities to accommodate the symptoms of psychosis (Martino et al., 2002; Martino et al., 2006), not one has modified their treatment protocol to account for the intrinsic motivation deficits of schizophrenia (see Section C.2). In addition, not only have these studies made use of modest sized samples, but such investigations have also selected their samples from specialty populations that have included few women as well as small proportions of persons with co-occurring SUDs and schizophrenia. This narrow focus on examining such effects within the context of dual diagnosis motivational programs has raised several important questions about how such findings generalize to the larger population of persons with co-occurring SUDs and schizophrenia who are not participating in motivational interviewing programs that are generally not widely available (McHugo et al., 2006). As such, elucidating the prospective longitudinal significance of such deficits in motivational processes to SUD pathology in this population represents an important area of further investigation.

In terms of whether the findings of motivational rehabilitation studies showing reductions in patient's substance use severity reviewed in Section C.2 generalize to the larger population of those with schizophrenia and comorbid SUD, a few areas of concern should be mentioned. The only study that observed the relationship between intrinsic motivation and substance use severity where 100% of the study sample consisted of persons with schizophrenia was conducted with a modest number of veterans ($N = 30$) who were mostly male (1 woman participant) (Graber et al.,

2003). Further, the investigations conducted by Kavanaugh et al. (2004a) and Edwards et al. (2006) also observed such effects using specialty samples of dual diagnosis clients, where only about 50% of their modest sized ($N = 25$; $N = 47$, respectively) samples consisted of persons in their first episode of schizophrenia. In addition, Kavanaugh et al. (2004a) recruited their sample from an inpatient unit, and subsequently followed such patients after they were (mostly) discharged to the care of a family member. Further, the positive effect of the experimental condition on developing intrinsic motivation to change the behaviors that were associated with participants' substance use severity could not be explained beyond positive interaction with such family members (Kavanaugh et al., 2004a). While Kavanaugh et al. (2004a) has contributed to the evidence supporting significant relations between motivation and substance use severity among this population, the findings may be less applicable to the majority of chronic patients with co-occurring SUDs and schizophrenia who live in the community, have free access to drugs and alcohol, and rely on public rather than family support (Drake et al., 2008). As a consequence of the methodological limitations and issues inherent to these studies, most of the dual diagnosis research that has considered the importance of intrinsic motivation to substance use severity may not generalize to the vast majority of individuals with co-occurring SUDs and schizophrenia, and thus research on larger and more heterogeneous samples of persons with these conditions is needed.

In the context of the limitations discussed, the findings of such studies may be limited by the potential confounding influence of extrinsic rewards on intrinsically motivated substance use outcomes. Some of the motivational rehabilitation studies reviewed in Section C.3 delivered extrinsic rewards (i.e., participant remuneration payments) to participants at the same time that such persons received the motivational session targeting improvements in intrinsic motivation to

reduce their SUD pathology (i.e., James et al., 2006; Martino et al., 2006). While many of the approaches that have been adapted to co-occurring disorders to date do foster environments such that the persons' choice and responsibility are valued (see Hunt et al., 2013), without assessing change in intrinsic motivation after removing the extrinsic reward, it is difficult to discern the actual motivation underlying improvements in substance use severity. As such, these studies highlight the potential for extrinsic rewards, such as participant payments, to confound the relationship between changes in intrinsic motivation and changes in substance use severity among persons with co-occurring SUDs and schizophrenia. Clearly future investigations are needed that can account for these important potential confounding effects and directly examine the contributions of intrinsic motivation deficits to substance use severity among this population.

Another important limitation to the studies reviewed above is the limited use of intrinsic motivation measures. Each investigation used readiness-to-change assessments to measure the stage of change associated with the person's current level of motivation to improve their target outcome behavior (i.e., reduction in use, cessation of use, or improvements in the severity of use). Although not all of these studies consistently employed the same readiness-to-change assessment, such measures generally base the person's stage of change on one of the 5 stages of change that coincide with the TTM of intentional behavior change (i.e., precontemplation, contemplation, preparation, action, maintenance) (DiClemente, 2003). Motivation, according to the TTM perspective, requires for individuals to engage in enough cognitive and experimental activities to move through early stages and to engage in behavioral activities to initiate and sustain the change (DiClemente et al., 2008). However, because persons with co-occurring SUDs and schizophrenia are disadvantaged in cognitive areas, assessing motivation and its role in behavior change is more challenging than assessing persons who abuse substances without

schizophrenia (DiClemente et al., 2008). For example, schizophrenia research clearly indicates that the cognitive impairments individuals with schizophrenia (without SUD) possess make it difficult for them to benefit from rehabilitation programs (Silverstein, Schenkel, Valone, & Nuernberger, 1998; Bellack, Gold, & Buchanan, 1999), and it would stand to reason that these same deficits interfere with the ability of those with co-occurring SUDs and schizophrenia to benefit from such programs. Perhaps not surprisingly, there have been questions as to whether the same cognitive impairments (perception, attention, memory, and reasoning deficits) and the psychotic symptoms that accompany schizophrenia impact the way in which these persons go about changing their substance use behavior (DiClemente et al., 2008). Further, investigators have speculated that negative symptoms could make readiness-to-change measures difficult to use in schizophrenia because such individuals may be unable to exert the thought and effort required to validly complete the assessments (Carey, Maisto, Carey, & Purnine, 2001). Since negative symptoms such as anhedonia and amotivation have been implicated in deficits in intrinsic motivational processes among persons with schizophrenia, the utility of these measures among this population remains questionable. Finally, although it is probably safe to assume that the targeted behaviors participants' sustained over the long-term in the studies reviewed above likely resulted from intrinsic goals, readiness-to-change measures do not actually account for whether the motivation for a person's engagement in change processes is intrinsic (motivated for the desire to change) or extrinsic (motivated for money or external factors). Given the potential for low intrinsic motivation base rates in co-occurring SUDs and schizophrenia to impede the recovery of such persons from severe patterns of substance use, a measure that is more focused on the deficits specific to the intrinsic motivational processes of this population is needed to supplement the assessment.

In summary, there is evidence to suggest that deficits in intrinsic motivation may be related to substance use severity among persons with co-occurring SUDs and schizophrenia. However, a review of the investigations that have been conducted in this area of research signal several important limitations, including (1) narrow focus on motivational rehabilitation, (2) lack of samples that represent the larger population of individuals with co-occurring SUDs and schizophrenia, (3) inattention to the potential confounding influence of extrinsic rewards, (4) limited use of intrinsic motivation measures. Such limitations highlight the need for further investigations that seek to comprehensively examine intrinsic motivation in larger and more heterogeneous samples of persons with co-occurring SUDs and schizophrenia by investigating its impact on outcomes of substance use severity among this population. What follows is a brief overview of the measures currently used to assess intrinsic motivation deficits in persons with schizophrenia, which offers insight into how difficulties experienced in the measurement of this construct have contributed to the limited investigation of the relevance of intrinsic motivation to substance use severity among persons with co-occurring SUDs and schizophrenia.

5. Intrinsic Motivation Measurement in Schizophrenia

Intrinsic motivation has been a widely studied construct in behavioral neuroscience and social psychology for the past several decades, and recently has been recognized as a potential key construct for understanding the pervasive patterns of substance use severity among persons with co-occurring SUDs and schizophrenia. Unfortunately, many of the assessments used in dual diagnosis research do not provide direct measures the construct of intrinsic motivation, and only recently have investigators begun to develop ways of measuring intrinsic motivation deficits in schizophrenia. This section presents a brief overview of intrinsic motivation measurement as applied to schizophrenia, which both identifies the few existing measurement techniques for

persons with schizophrenia and points to the potential for using a cross-situational measure of intrinsic motivation that has been validated among those with the disorder to persons with co-occurring SUDs and schizophrenia. This intrinsic motivation measure may provide a promising supplement to the readiness-to-change assessments used in dual diagnosis treatment.

To date, the majority of the measures attempting to assess intrinsic motivation in schizophrenia have made use of self-report measurement strategies. For example, Barch, Yodkovik, Sypher-Locke, and Hanewinkel (2008) recently examined the integrity of intrinsic motivation among persons with schizophrenia using a reliable and valid self-report measure of intrinsic motivation for healthy individuals, the Motivational Trait Questionnaire (MTQ; Heggestad & Kanfer, 2000; Kanfer & Ackerman, 2000; Hinsz & Jundt, 2005). Prior to Barch and colleagues' (2008) application of the MTQ to schizophrenia, it was used to assess the intrinsic motivation of business professionals for carrying out competitive mastery goals in the workplace. Since up to 80% of individuals with schizophrenia are unable to work (Bond & Drake, 2008), it is unclear whether this measure can capture the motivational processes by which people with schizophrenia adapt and change their behaviors. Consequently, the MTQ may not capture the aspects of intrinsic motivation relevant to understanding intrinsic motivation in schizophrenia. In addition, even if the MTQ can assess motivation for (putatively) pleasurable tasks, such activities are limited in scope to learning and work-related behavior dimensions of intrinsic motivation (performance), and do not account for the curiosity and purpose dimensions of the construct. Within the context of these considerations, such researchers found that work statements from the MTQ tapped aspects of intrinsic motivation relevant to work function in the disorder—personal mastery self-reports in the disorder were related to work behavior, with higher personal mastery being associated with being gainfully employed (Barch et al., 2008).

Although the MTQ is limited in its scope and application to persons with schizophrenia, the constructs tapped by this measure assess at least one relevant domain of intrinsic motivation.

Another self-report, the Intrinsic Motivation Inventory for Schizophrenia Research (IMI-SR) was designed to gauge the central motivational structures as pertinent to cognitive task engagement, skill acquisition, treatment compliance, and remediation outcome (Choi & Medalia, 2010). The instrument was developed from the original IMI (Ryan, 1982), comprising 6-subscales and 54 total items that gauge subjective experiences of interest/enjoyment, effort, value/usefulness, pressure/tension, relatedness, and perceived choice (“I enjoy doing this very much,” “I think I am pretty good at this activity”) (Choi et al., 2009). Although the original scale has been tailored for a wide range of tasks in nonpsychiatric samples (college students, athletes, etc.), this was the first psychometric adaptation to a neuropsychiatric population. Results revealed a final 21-item questionnaire with 3 domains relevant to motivation for treatment (interest/ enjoyment, perceived choice, value/ usefulness). Additionally, the IMI-SR possessed good internal consistency ($\alpha = .92$) and test-retest reliability (interclass correlation coefficient = .77). Although the IMI-SR seems to be a viable measure for assessing intrinsic motivation among persons with schizophrenia, its utility is limited to studies of cognitive remediation or social disability among those with the disorder, and its cross-situational applicability has yet to be determined. Unfortunately, here too, the IMI-SR appears to be primarily focused on one to two (performance and purpose) dimensions of intrinsic motivation, yielding little information about the curiosity dimensions of the construct.

Recently, Nakagami and colleagues (2008) developed a promising new instrument to gauge intrinsic motivation deficits in schizophrenia. This measure is premised on a conceptual definition of intrinsic motivation that accounts for the behaviors that people that carry out

because of the positive feelings associated with performing actions in the absence of extrinsic rewards (Deci & Ryan, 2007). Such a measure operationalizes the intrinsic motivation construct by taking the sum of theoretically pertinent intrapsychic deficit items (i.e., purpose, motivation, and curiosity) from the clinician-rated Quality of Life Scale (QLS; Heinrichs et al., 1984). Since this measure is not dependent on (predetermined) treatment specific goals or targeted outcomes (Nakagami et al., 2008), it is particularly ideal for observing naturalistic prospective changes in the relationship between intrinsic motivation and substance use severity among persons with comorbid SUD and schizophrenia in this dissertation. Psychometric evaluations of this intrinsic motivation instrument have shown that it demonstrates ($\alpha = .74$) moderate levels of internal consistency in community patients with schizophrenia (Nakagami et al., 2008). Subsequent investigations employing this instrument have not only confirmed a long history of evidence indicating that persons with schizophrenia possess deficits in intrinsic motivation (i.e., Barch, 2004), but have also shown that such deficits impede the ability of those with the disorder to generate internal drives to sustain behavior changes absent external support (Nakagami et al., 2008; Yamada et al., 2010; Nakagami 2010). In addition, evidence from the dual diagnosis field has shown that such deficits can disengage intrinsic motivational processes when persons with comorbid SUD and schizophrenia try to generate their internal drives toward reducing substance use severity (i.e., Drake et al., 2008; Horsfall et al., 2009). Unfortunately, to date, no studies have extended validation of this measure to persons with schizophrenia and comorbid SUD or sought to apply it for examining the relationship between prospective naturalistic changes in intrinsic motivation and changes in substance use severity among this population. Consequently, extending validation of this instrument may not only provide greater accuracy to estimating the base rates of intrinsic motivation deficits that are potentially unique to comorbid SUD and

schizophrenia, but may also provide greater insight into the relationship between intrinsic motivation deficits and substance use severity among this population.

6. Evidence to the Validity of the Intrinsic Motivation Measure Developed by Nakagami and Colleagues (2008) in Schizophrenia

While the previous section highlighted the few measures that have been used to estimate deficits in intrinsic motivation among persons with schizophrenia, not one of these instruments has been validated in schizophrenia and comorbid SUD. This section puts forth evidence to the validity of the instrument developed by Nakagami and colleagues (2008) to assess intrinsic motivation deficits in schizophrenia, and then advances the reasons for which such an instrument is appropriate to utilize for predicting change in substance use severity among persons with schizophrenia and comorbid SUD.

Two recent investigations by Nakagami and colleagues (2008, 2010) support the validity of using this intrinsic motivation instrument among community patients with schizophrenia, as well as using the instrument to predict prospective naturalistic changes in functioning in this population. This instrument is premised on a conceptual definition of intrinsic motivation acknowledging that behaviors are carried out because of the positive feelings that are associated with an action in the absence of any tangible reward (Deci & Ryan, 2007), and an operational definition of intrinsic motivation that is based on the sum of theoretically relevant items (i.e., purpose, motivation and curiosity) from the QLS (Heinrichs et al., 1984). These conceptual and operational definitions of the construct are consistent with the deficits in intrinsic motivation that are potentially unique to persons with schizophrenia, which tend to impede the ability of such persons to carry out their goals and plans, particularly in the areas of interest and drive across various life domains, including social and occupational role functioning (Nakagami et al., 2010).

These life domains are also profoundly and negatively affected by the pervasive patterns of substance use among persons with comorbid SUD and schizophrenia (Drake et al., 2008). Since this dissertation examines whether prospective naturalistic changes in the intrinsic motivation deficits unique to schizophrenia predict changes in substance use severity, rather than whether the readiness such persons have to change their substance use behaviors predict changes in substance use severity, it is relevant to extend validation of the instrument developed by Nakagami and colleagues (2008) to this sample of schizophrenia and comorbid SUD patients.

As mentioned previously, prior psychometric evaluations of the intrinsic motivation measure developed by Nakagami and colleagues (2008) showed that the instrument demonstrates moderate levels of internal consistency ($\alpha = .74$) among community patients with schizophrenia. These investigators then used this instrument to estimate intrinsic motivation in a cross-sectional examination, which provided the first data on the relationships between neurocognition and intrinsic motivation, and between intrinsic motivation and psychosocial functioning in a sample of community patients with schizophrenia. Results revealed that both of these associations reflected a large effect size (Pearson $r > .5$, using Cohen's [1998] criterion), such that intrinsic motivation had a strong and positive association with both neurocognition and psychosocial functioning. Since the results of this cross-sectional study suggest that relations exist among these variables, but cannot provide an indication of how such variables are related or change over time, Nakagami and colleagues (2010) subsequently sought to examine the prospective relationships among intrinsic motivation, neurocognition, and psychosocial functioning in schizophrenia. Results showed that intrinsic motivation is dynamic over time in community patients with schizophrenia, and also showed that prospective changes in intrinsic motivation were a salient predictor of changes in psychosocial functioning (functional disability) among

community patients with schizophrenia over the 1-year study. Such studies show that the intrinsic motivation instrument developed by Nakagami and colleagues (2008) provides valid estimates of intrinsic motivation deficits in schizophrenia, and is a valid longitudinal predictor of change in functional disability as well as other theoretically relevant outcomes among this population. Given this evidence in addition to the broad cross-situational applicability of this instrument, this measure is likely to be valid in schizophrenia and comorbid SUD may provide greater accuracy in estimating the base rates of such deficits among those with these conditions, and could provide greater insight into whether prospective changes in intrinsic motivation (improvement) predict changes in substance use severity (reduction) among this population. This dissertation study seeks to confirm previous evidence regarding the psychometric properties of this measure in sample of persons with comorbid SUD and schizophrenia, followed by conducting a longitudinal study of the relationship between prospective changes in intrinsic motivation to substance use severity among this population.

D. PROPOSED STUDY AND HYPOTHESES

This study proposes to conduct a longitudinal investigation of the relationship between prospective naturalistic changes in intrinsic motivation and changes in substance use severity among persons with co-occurring SUDs and schizophrenia ($n = 535$ at baseline; $n = 219$ at 6-months; $n = 150$ at 1-year), and then seeks to examine whether this relationship varies across genders. Such an examination will be carried out by using secondary data that was collected as part of the CATIE study (Lieberman et al., 2005), and begins with extending the validation of a promising new measure of intrinsic motivation to this population.

1. Study Context

This research is embedded within the context of the CATIE study, a multi-site multi-phase randomized controlled trial comparing the effectiveness of first and second generation antipsychotic medications (as measured by the discontinuation of an assigned study treatment at any time, for any reason) among persons with schizophrenia (Lieberman et al., 2005). The rationale, design, and methods of the CATIE trial have been extensively described in prior reports (Stroup et al., 2003; Swartz et al., 2003; Rosenheck, Doyle, Leslie, & Fontana, 2003; Davis, Koch, Davis, & LaVange, 2003). Thus, this section briefly discusses the way in which the study sample for this research was recruited, enrolled, and selected for the purpose of conducting a secondary analysis of the CATIE data. Data were collected for the CATIE study from January 2001 to December 2004, with 1894 potential participants being screened for the trial from 57 clinical sites across the United States (Lieberman et al., 2005). As CATIE sought to recruit a sample that would broadly represent those with schizophrenia that are seen across various clinical settings, few exclusion criteria were employed. These efforts resulted in a total of 1493 persons with schizophrenia being initially randomly assigned to different study medications at Phase 1, which is shown in further detail in Figure 2, and treated for up to 18-months (Lieberman et al., 2005). This trial was designed such that those who discontinued the medication to which they were assigned in Phase 1 for any reason moved to the next phase to receive a new treatment (i.e., Phase 2, followed by Phase 3). The focus on this study is on Phase 1, which contains the largest sample size and least amount of attrition. While such participants were being followed on these treatments, a broad array of assessments were administered at baseline, 6-, 12-, and 18-month follow-up periods to capture meaningful information with regard to their cognitive and functional status; symptoms and quality of life; service utilization and use of substances.

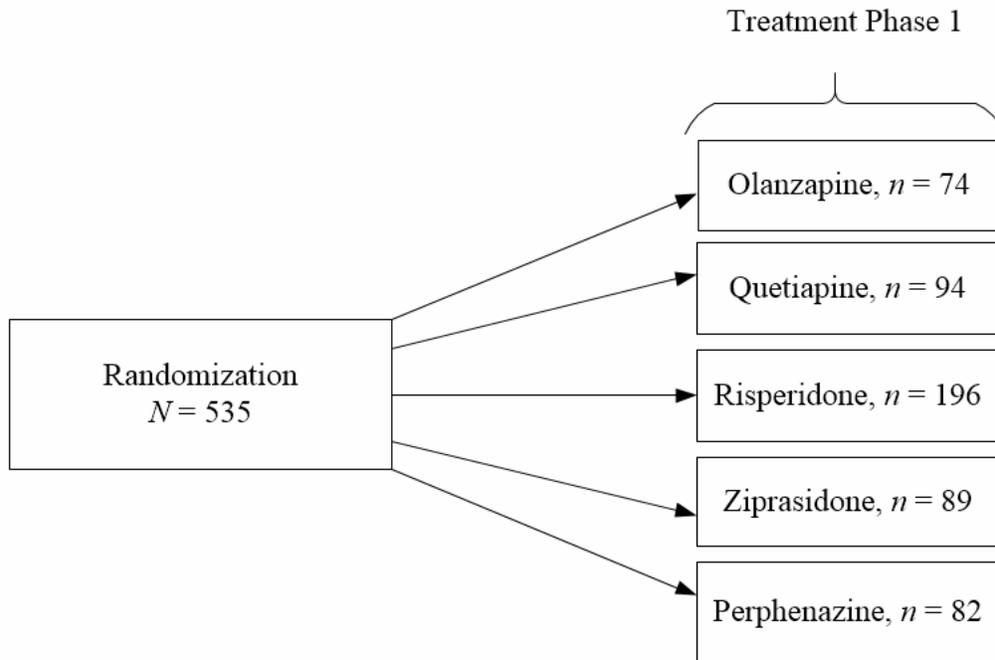


Figure 2. Treatment Phase 1 of the CATIE Trial

The present study reports data on 535 persons with co-occurring SUDs and schizophrenia who enrolled in the CATIE study at baseline, subsequently underwent Phase 1 randomization, and were followed for up to 1-year of treatment. Of the 535 individuals with co-occurring SUD and schizophrenia who enrolled in CATIE at baseline, 219 were available at the 6-month follow-up, and 150 were available at the 1-year follow-up. Using cross-sectional and longitudinal data collected on these individuals during their participation in CATIE, this study seeks to investigate the impact of intrinsic motivation on substance use severity in schizophrenia and its patterns in men and women. While most of the research that has been conducted in this area has examined such effects among this population within the context of a motivational rehabilitation program, this study investigates the impact of naturalistic prospective changes in intrinsic motivation on substance use severity in a sample of persons with schizophrenia and comorbid SUD, who were

not seeking treatment for substance use or substance use severity. In this regard, this research makes use of the longitudinal context of the CATIE study to first conduct a robust examination of the link between changes in intrinsic motivation and changes in substance use severity, and to then examine whether such a relationship varies across genders. The selections that were used to derive the sample for carrying out the aims, hypotheses, and analytic techniques for conducting this secondary analysis of the CATIE data is presented in Figure 3.

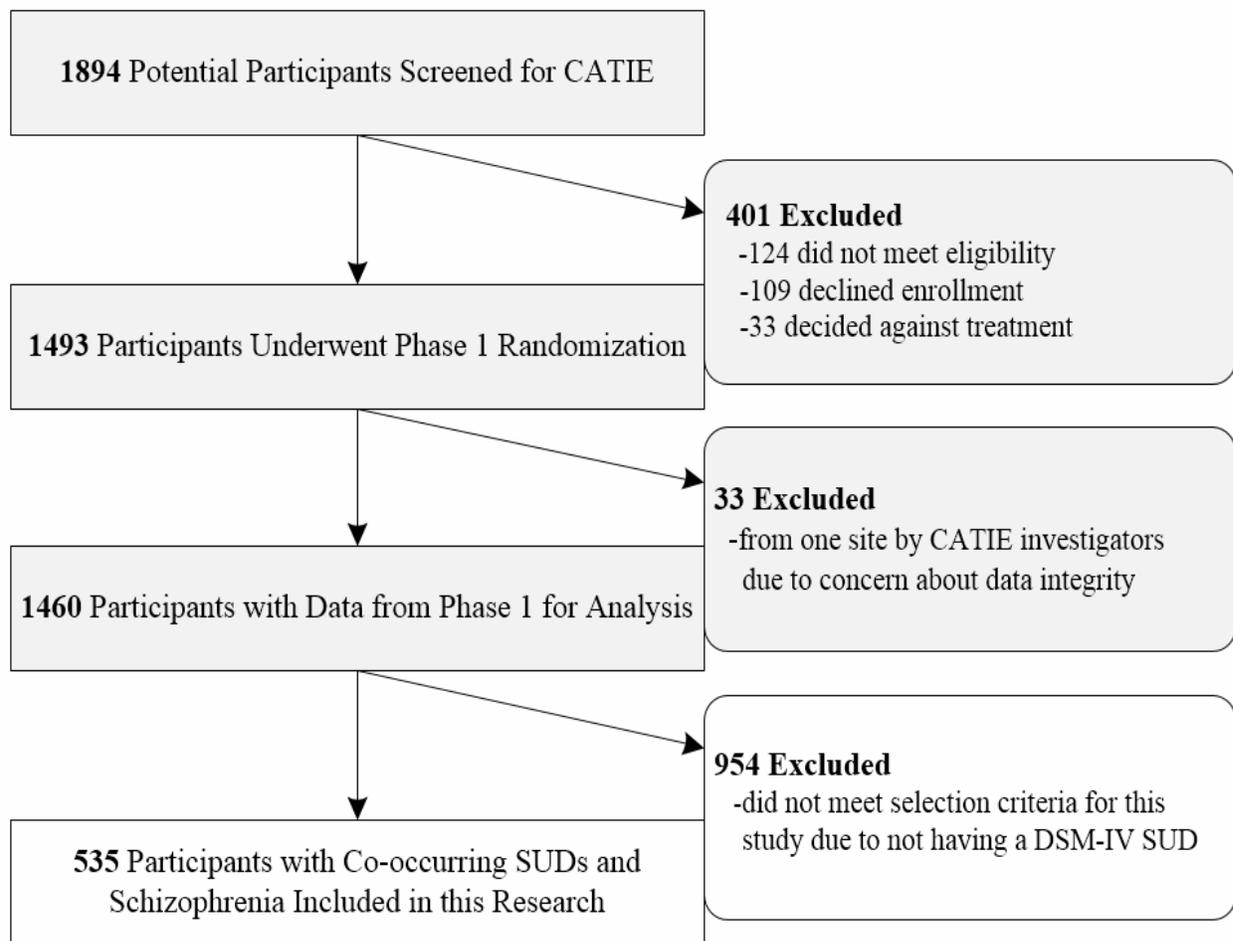


Figure 3. Selection of participants with co-occurring SUDs and schizophrenia from the CATIE study to derive the sample for the present investigation

2. Aims and Hypotheses

Using data from the CATIE trial, this research aims to examine the longitudinal impact of intrinsic motivation on substance use severity outcomes among persons with co-occurring SUDs and schizophrenia and its patterns in men and women, after extending validation of a promising measure of intrinsic motivation to this population. The specific aims and associated hypotheses include:

Aim #1: Validate the factor structure of the intrinsic motivation measure. Intrinsic motivation is conceptualized in this research as behavior change processes that are carried out because of the positive feelings associated with an action in the absence of any tangible reward, or actions that are taken for their own sake that do not require any external supports or reinforcement to be initiated or sustained. Recently, Nakagami, Xie, Hoe, and Brekke (2008) used a novel cross-situational method to validate the construct in community patients with schizophrenia (Nakagami et al., 2008; Yamada, Dinh, Barrio, & Brekke, 2010; Nakagami et al., 2010), which gauges intrinsic motivation by summing theoretically pertinent intrapsychic deficit items from the Quality of Life Scale (Heinrichs et al., 1984), probing purpose, motivation, and curiosity. This measure of intrinsic motivation has not yet been applied to comorbid SUD and schizophrenia. As such, this analytic aim will be addressed by subjecting the total pool of 7-items from the intrapsychic deficit subscale to an exploratory factor analysis. It is expected that the results of this analysis will show that the 3-items of purpose, motivation, and curiosity load together on one factor and form a distinct factor apart from the other 4-items of the intrapsychic deficit subscale. This intrinsic motivation measure is also expected to yield estimates considered to be indicative of a minimally adequate internally consistent scale ($\alpha \geq .70$), and demonstrate at least minimally sufficient levels of retest reliability across study assessment periods ($r \geq .40$)

(Nunnally, 1978), when applied to this sample of individuals with schizophrenia and comorbid SUD.

Hypotheses include:

H_{1a}: The 3-items of purpose, motivation, and curiosity (intrinsic motivation) form a distinct and coherent factor apart from the other 4-items of the intrapsychic deficit subscale.

H_{1b}: The 3-item intrinsic motivation measure demonstrates acceptable levels of internal consistency ($\alpha \geq .70$) when applied to persons with schizophrenia who have comorbid SUDs.

H_{1c}: The 3-item measure of intrinsic motivation demonstrates at least minimally sufficient levels of retest reliability ($r \geq .40$) across study assessment periods.

Aim #2: Examine the cross-sectional relationships between intrinsic motivation, gender, and substance use severity. Baseline data ($n = 535$) will be used to compute correlation matrices and hierarchical linear regression analyses will examine the zero-order and unique associations (adjusting for negative symptoms and neurocognition) between intrinsic motivation and substance use severity. Baseline data will also be used to compute independent sample *t*-tests (two-tailed) for examining the bivariate relationships between gender and intrinsic motivation and gender and substance use severity.

Hypotheses include:

H_{2a}: Intrinsic motivation is significantly, negatively correlated with substance use severity at baseline.

H_{2b}: Intrinsic motivation is significantly, negatively correlated with substance use severity at baseline, after adjusting for the potentially confounding effects of

neurocognition and negative symptoms.

H_{2c}: Men demonstrate significantly greater degrees of substance use severity compared to women at baseline.

H_{2d}: Men exhibit significantly greater deficits in intrinsic motivation compared to women at baseline.

Aim #3: Examine the impact of intrinsic motivation on the 1-year outcomes of substance use severity, and then investigate the impact of gender on the longitudinal association between intrinsic motivation and substance use severity. This analytic aim will be carried out using a series of individual growth curve models. Unconditional models will first be fit to test whether or not there is variability in the initial status and the rates of change in the 1-year trajectories of substance use severity among participants. Analysis will proceed by expanding these unconditional models to conditional growth curve models to examine the longitudinal contribution of changes in intrinsic motivation to changes in substance use severity over the 1-year study. Conditional models will then be expanded to investigate the moderating effects of gender on these relations such that an interaction between intrinsic motivation and gender predicts the initial level and the rates of change in the 1-year trajectories of substance use severity among participants. All growth curve models will control for relevant demographic and clinical confounders.

Hypotheses include:

H_{3a}: Participants exhibit, on average, significant improvement in substance use severity over the 1-year study period.

H_{3b}: Improvement in intrinsic motivation is associated with significant reductions in substance use severity over the 1-year study period.

H_{3c}: Women demonstrate a stronger association between improvement in intrinsic motivation and greater reductions in substance use severity than men over the 1-year study period.

III. METHOD

This research makes use of a secondary analysis of data that were collected as part of the CATIE trial. To carry out the aims and hypotheses proposed in this dissertation study, a unique dataset is created to answer several cross-sectional and longitudinal research questions regarding the significance of intrinsic motivation deficits to substance use severity in a large heterogeneous sample ($n = 535$ at baseline; $n = 219$ at 6-months; $n = 150$ at 1-year) of persons with comorbid SUD and schizophrenia. Such a dataset will first be used to examine the psychometric properties of a promising new measure of intrinsic motivation that has yet to be validated among persons with comorbid SUD and schizophrenia. This data set will then be used to conduct rigorous, cross-sectional, and longitudinal examinations of the relationship between deficits in intrinsic motivation and substance use severity among participants with comorbid SUD and schizophrenia. Finally, this dataset will be used to conduct cross-sectional and longitudinal examinations of the moderating impact of gender on the relationships between intrinsic motivation and substance use severity. The contents of this chapter provide a detailed description of the participants, design, and measures that were used as part of the CATIE trial that not only help address such questions, but also comprise the proposed analytic methods for carrying out the aims of this research.

A. PREVIOUS WORK SUPPORTING THE RATIONALE FOR THE PROPOSED DISSERTATION STUDY

My previous work supports various decisional aspects, as well as the rationale for a study proposing to examine the impact of intrinsic motivation on substance use severity and its patterns across genders in adults with schizophrenia and comorbid SUD. Since I previously found that a

considerable proportion (44%) of CATIE participants did not accurately self-report their drug use compared to biological assays (Bahorik et al., 2013), the clinician-rated alcohol use scale and drug use scale will be used to measure current substance use severity status and change (as a scaled variable) in substance use severity for this dissertation. Of note, the most consistent predictor of under-reported drug use in the aforementioned study was cognitive impairment, which I thought may help explain the puzzling results of studies demonstrating improved cognitive function in schizophrenia patients using drugs, or at least those who self-report using drugs (see Yücel et al., 2010). Perhaps not surprisingly, when biological assays were used to confirm drug use status in a subsequent investigation, few cognitive differences emerged between CATIE participants using and not-using drugs (Bahorik et al., 2014). Since such results largely suggested that substance misusing schizophrenia patients (SMS) do not exhibit superior cognition compared to their non-substance misusing counterparts, I then sought to determine the degree to which substance use severity impacts cognition in an SMS sample (selected with at least moderate levels of alcohol or cannabis severity). This study revealed that moderate levels of alcohol severity were associated with worse emotion processing than high levels of alcohol severity, and no significant associations were observed with regard to moderate or high levels of cannabis severity (Bahorik et al., 2014). Despite the fact that such findings showed few differences between SMS patients with high or moderate levels of alcohol or cannabis severity, the deficits observed are known to create difficulties when such patients try to form social relationships, negotiate out of dangerous situations, and build intrinsic motivation to reduce the severity of substance use (Drake et al., 2008). Furthermore, in another investigation, I found noteworthy differences in the patterns of alcohol and cannabis between men and women with schizophrenia (i.e., Bahorik, Newhill & Eack, 2013). The outcomes of this study suggest the

potential for the mentioned difficulties to vary across genders among this population. All of these factors may have an impact on the severe and pervasive substance use patterns observed in schizophrenia; therefore studies are needed that build from this work by investigating the role factors other than cognition may have in precluding this population from achieving abstinence and recovery. The study proposed in this dissertation seeks to build from my previous work by examining relations between prospective changes in intrinsic motivation to changes in substance use severity and the degree to which such a relationship varies across genders in a larger and more heterogeneous sample of participants with comorbid SUD and schizophrenia.

B. STUDY DESIGN AND PARTICIPANTS

This research is conducted within the context of the CATIE study (Lieberman et al., 2005), which evaluated various functional, clinical, and substance use outcomes among persons with chronic and recurrent forms of schizophrenia participating in a clinical trial comparing the effectiveness of first and second generation antipsychotic medications (Stroup et al., 2003; Lieberman et al., 2005; Stroup et al., 2010). This study made use of a longitudinal, randomized-controlled design where participants were randomly assigned to antipsychotic treatment under double-blind conditions, and followed for up to 18-months. Patients were recruited from 57 settings across the U.S., including 16 university clinics, 10 state mental health agencies, 7 Veterans Affairs medical centers, 6 private nonprofit agencies, 4 private-practice sites, and 14 mixed-system sites to participate in the CATIE study (Stroup et al., 2003; Stroup et al., 2010). Individuals were eligible for enrollment if they had a diagnosis of schizophrenia, as confirmed by the Structured Clinical Interview (SCID; First, Spitzer, Gibbon, & Williams, 1996) for DSM-IV disorders, and were between the ages of 18 and 65 (Lieberman et al., 2005). Persons older

than 65 were excluded from the CATIE study to avoid potential confounds in physical and cognitive decline that can occur in aging patients with schizophrenia (Stroup et al., 2010). Persons in their first episode of schizophrenia (i.e., those who first began antipsychotic drug treatment for psychosis within the previous 12-months and had psychotic symptoms for less than 3 years) were also excluded, in order to avoid the potential bias of high antipsychotic medication responsiveness that occurs in these patients at relatively low dosages. Persons with refractory illness were excluded (i.e., resistant to treatment), because their severe illness was thought to preclude the detection of treatment effectiveness. Women who were pregnant or breastfeeding; those who had known contraindications to study medications assignments; and/or those with acutely unstable medical conditions were also excluded. No further exclusion criteria were employed as part of the CATIE study to make the results generalizable to the broad group of persons with chronic and recurrent forms of schizophrenia for whom a change in medications was appropriate due to incomplete symptom remission or adverse effects (Stroup et al., 2003; Stroup et al., 2010). Finally, this research selected CATIE study participants who met DSM-IV criteria for a co-occurring SUD and schizophrenia, as confirmed by the SCID to carry out the aims, hypotheses, and methods proposed herein. As indicated in Figure 2 (see Section 2.D.1), such selection procedures resulted in a 535 participants with co-occurring disorders at baseline, 219 at 6-months, and 150 at 1-year who comprised the baseline and follow-up samples for this research.

C. MEASUREMENTS

To achieve the aims of this research and *examine the longitudinal impact of intrinsic motivation on substance use severity and its patterns in men and women*, a combination of self-report and clinician-rated instruments were used to assess intrinsic motivation (independent

variable), substance use severity (dependent variable), and gender (moderator variable). The moderator variable in Aim 3, gender, was recorded as part of a demographic questionnaire that was administered during the screening procedures of the CATIE study. The instruments used to assess these variables included the Drug Use Scale; the Alcohol Use Scale; and the Quality of Life Scale (intrinsic motivation). A summary of the measures employed for assessing the relationship between the independent (intrinsic motivation) and dependent variables (alcohol use severity and drug use severity, respectively) as part of the research conducted herein as well as the variables that may potentially confound this relationship (negative symptoms and neurocognition) are provided in Table 1. The psychometric properties and use of these measures among individuals with co-occurring SUDs and schizophrenia are discussed in further detail in the following sections.

Table 1. *Study Variables and Measurement Sources*

Variable	Source (Items)	Calculation
Substance Use Severity	AUS ^a (1 item) DUS ^c (1 item)	NA ^b
Total Psychopathology	PANSS ^d total (30 items)	Sum of items P1 – P7; N1 – N7; G1 – G16
Negative Symptomatology	PANSS negative (7 items)	Sum of items N1 – N7
Total Neurocognitive Function ^e	Reasoning: based on the 64 card version of the WCST (perseverative error [reverse scored] and categories completed) and WAIS-R Mazes (2 items) Working Memory: based on visuospatial computerized tests of memory and the LNS test (2 items) Processing Speed: based on the Grooved Pegboard (dominant hand), the WAIS-R Digit-span test; and COWAT/category instances test scores (3 items) Vigilance: based on d' averages from the CPT (3 items) Verbal Memory: based on scores from the HVLТ (3 items)	Mean of scaled items 1– 13
Intrinsic Motivation	QLS ^f intrapsychic deficit subscale items of purpose, motivation, and curiosity (3 items)	Sum of items 14, 15, 16
Gender	Demographic questionnaire (1item)	Male = 1, Female = 2

^a AUS = Alcohol Use Scale (Drake, Mueser, & McHugo, 1996).

^b AUS/DUS scores were computed by research project clinicians during the CATIE trial; final scores are available for use in this research.

^c DUS = Drug Use Scale (Drake et al., 1996).

^d PANSS = Positive and Negative Symptom Scale (Kay, Fiszbein, & Opler, 1987).

^e Total Neurocognitive Function = overall neurocognition composite. (WCST = Wisconsin Card Sorting Test [Heaton Chelune, Taley, Kay, & Kurtiss, 1993]; WAIS-R Mazes = Wechsler Intelligence Scale Mazes [Wechsler, 1991]; LNS = Letter Number Sequencing Test [Gold, Carpenter, Randolph, Goldberg, & Weinberger, 1997]; WAIS-R Digit-span test = Wechsler Adult Intelligence Scale-Revised, Digit Span Test [Wechsler, 1981]; COWAT = Controlled Oral Word Association Test [Benton & Hamscher, 1978]; CPT = Continuous Performance Test [Cornblatt et al., 1988]; HVLT = Hopkins Verbal Learning Test [Brandt, 1991]).

^f QLS = Quality of Life Scale (Heinrichs et al., 1984).

1. Independent Variable: Intrinsic Motivation

Intrinsic motivation is conceptualized in this research as behavior change processes that are carried out because of the positive feelings associated with an action in the absence of any tangible reward, or actions that are taken for their own sake that do not require any external supports or reinforcement to be initiated or sustained (Deci & Ryan, 2007). To examine the cross-sectional (Aim #2) and longitudinal (Aim #3) relationship between intrinsic motivation and substance use severity and its patterns in men and women, an approach will be used to measure intrinsic motivation that was recently developed by Nakagami and colleagues (2008). Such a technique utilizes an operational definition of intrinsic motivation that is based on the sum of theoretically relevant intrapsychic deficit items from the Quality of Life Scale (QLS; Heinrichs et al., 1984), including purpose, motivation, and curiosity. The selection of these three items show face validity in terms of their focus on cross-situational phenomena in life experience such as goals, plans, and in areas of interest and drive (see Table 2).

The QLS was originally developed to assess deficit syndrome in schizophrenia (i.e., the presence of high negative symptoms and an absence of dysphoria), but is now widely used as a

proxy measure of major role functioning in clinical outcome studies in schizophrenia research (Swartz, 2010). The instrument is a structured interview-based, clinician-rated measure that gathers information on the patient's symptoms and functioning for the preceding 4-weeks in the areas of work (4-items), interpersonal relationships (8-items), community functioning (2-items), and intrapsychic deficits (7-items) (Heinrichs et al., 1984). The QLS consists of 21-items covering the previous mentioned domains, each of which is rated on a 7-point scale (0 to 6) and then summed, with lower scores reflecting more severe impairment of the function in question. The model on which the QLS is based had conceptualized the intrapsychic domain as being at the core of the deficit syndrome in schizophrenia. In this regard, these 7-items are intended to elicit clinical judgments in the dimensions of cognition, conation, and affectivity such that the patient's sense of purpose, motivation, curiosity, ability to experience pleasure, and emotional interactions are assessed. Given this context, recent studies have put forth theoretically driven and empirically supported evidence showing that particular aspects of these intrapsychic deficits lie at the core of another feature of schizophrenia—deficits in intrinsic motivation (Nakagami et al., 2008).

Such investigations have assessed deficits in intrinsic motivation among community samples of patients with schizophrenia by using the sum of 3-items (purpose, curiosity, and motivation) from the intrapsychic deficit subscale of the QLS (Nakagami et al., 2008; Yamada et al., 2010; Nakagami et al., 2010). Recent psychometric evaluations of this inventive technique indicate that the 3-items of purpose, curiosity, and motivation load together on one factor, and that the measure demonstrates acceptable levels of internal consistency ($\alpha = .74$) in community schizophrenia patients without comorbid SUD (Nakagami et al., 2008; Yamada et al., 2010). Further, this measure of intrinsic motivation has previously shown good discriminant construct

validity by demonstrating little overlap with the negative symptom items of the Brief Psychiatric Rating Scale (BPRS; range of $r = .12$ to $.19$) (Nakagami et al., 2008). Taken together, such findings suggest that the intrinsic motivation construct assessed by this measure is a construct unique from negative symptoms, that such a construct is premised on a theoretically driven and empirically supported factor structure, and is predictive of theoretically relevant outcomes in community patients with schizophrenia. However, despite the potential of using this measure for assessing intrinsic motivation deficits in schizophrenia, it has not yet been examined among a sample of persons with co-occurring SUDs and schizophrenia.

Table 2. *Pertinent Intrapsychic Deficit items from the Quality of Life Scale that comprise the proposed Measure of Intrinsic Motivation*

Item	Suggested Probes	Rating	Rating Anchors
<u>Sense of Purpose:</u> To rate the degree to which the person posits realistic, integrated goals for his/her life.	<i>What makes life worth living for you?</i>	0	No plans or plans are bizarre, delusional or grossly unrealistic.
	<i>Do you think much about the future?</i>	1	
	<i>Have you set any goals for yourself?</i>		
	<i>What plans do you have for your life over the next year?</i>	2	Has plans, but they are vague, not integrated, with the person's life.
		3	
		4	
	5		
		6	Realistic plans, short/long range.
<u>Degree of Motivation:</u>	<i>How motivated have you been?</i>	0	Lack of motivation significantly interferes with basic routine.
To rate the extent to	<i>Have you had much enthusiasm,</i>	1	

<p>which the person is unable to initiate or sustain goal directed activity due to inadequate drive.</p>	<i>energy, and drive?</i>		
	<i>Have you tended to get into a rut?</i>		
	<i>Have you tended to put things off?</i>		
		2	Able to meet basic maintenance demands of life, but lacks motivation to make accomplishments.
		3	
		4	Able to meet routine demands of life, but lack of motivation results under-achievement in some areas.
	5		
	6		
<u>Curiosity:</u>	<i>How often have you seen or heard about something that you wanted to know more about or understand better?</i>	0	Very little curiosity or interest in new topics or events.
<p>To rate the degree to which the person is interested in his/her surroundings and questions those things he/she doesn't understand.</p>	<i>What sorts of things?</i>	1	
	<i>How curious about things have you been?</i>		
		2	Some sporadic curiosity, but not pursued in thought or action.
		3	
		4	Some curiosity and time spent thinking about topics or interest and some actual effort to learn about them.
		5	
	6	Curiosity about a number of topics and effort to learn more about some of them.	

Note. The QLS consists of 21-items, each of which is clinician rated on a 7-point scale. Lower scores reflect more severe impairment of the function in question.

2. Dependent Variable: Substance Use Severity

Substance use severity is conceptualized in this research as pervasive patterns of drug and/or alcohol use that can profoundly and negatively impact symptom and functional outcomes. To examine the relationships among intrinsic motivation, gender, and substance use severity (Aim #2 and #3), these indicators of substance use severity are assessed using the clinician-rated Alcohol Use Scale and the Drug Use Scale (AUS, DUS; Drake et al., 1990; Mueser et al., 1995; Drake, Mueser, & McHugo, 1996; Mueser et al., 2003). The AUS and DUS are parallel 5-point (1-item) behaviorally anchored scales, where each rating anchor corresponds with DSM criteria for substance abuse/ dependence (see Table 3), and higher scores indicate greater degrees of substance use severity (Mueser et al., 2003). For example, a rating of 1 corresponds to no use (i.e., abstinence); a rating of 2 parallels substance use without evidence of abuse or dependence (i.e., use of drug or alcohol, but no evidence of persistent or recurrent problems in psychosocial domains of functioning stemming from such use); a rating of 3 corresponds to meeting criteria for abuse, but not dependence (i.e., use resulting in problems with social relationships, role functioning, and/or legal problems); a rating of 4 indicates that the patient meets criteria for dependence (i.e., either non-physiological or psychological); and a rating of 5 suggests that in addition to meeting criteria for dependence, the patient's use has been so severe that it has resulted in institutionalization (i.e., repeated hospitalizations, emergency room visits, or time spent incarcerated). Clinicians complete the AUS and DUS during brief (15 to 45 minutes) face-to-face interviews with patients by rating the worst period of drug (DUS) and/ or alcohol (AUS) severity over the past 6-months (Mueser et al., 2003). During the process of rating the AUS and

DUS, clinicians assess the functional impact (or lack thereof) drug and/or alcohol use has across patients' social (i.e., family problems, housing instability, social isolation, difficulty budgeting funds, and legal status), physical (i.e., hygiene problems, change in physical appearance, health problems, and injuries), and psychiatric (i.e., treatment non-adherence, suicidal thoughts, cognitive impairment, symptom relapses, sudden mood shifts, and appearance of new symptoms) domains of functioning. If the patient is in an institution, then the reporting period for drug (DUS) and/ or alcohol (AUS) severity for the time period considered is that (time) preceding institutionalization. Following the patient interview, clinicians then garner information about the patient's drug and/or alcohol use from collateral contacts, group home staff, and family members (if available and per the patient's consent). While patient responses (i.e., self-report) provide the basis of the 1-5 rating on the AUS and DUS, clinicians consider any existing records (i.e., medical release, psychiatric hospitalization records) and available collateral information in the final rating for the 6-month reporting period (Mueser et al., 2003).

The AUS and DUS have been widely used among persons with co-occurring SUDs and schizophrenia for several decades (Drake et al., 1990), and have accumulated a considerable amount of psychometric validation (Carey, Cocco, & Simons, 1996). Drake and colleagues found excellent sensitivity (95%) and specificity (100 %) for ratings of alcohol use for the previous 12-months among outpatients with schizophrenia, compared with diagnoses of alcohol abuse or dependence made in clinical consensus (Drake et al., 1990). Notably, the AUS was the most accurate single instrument used in their study, which also included a self-report and a diagnostic interview (Drake et al., 1990). Ratings covering 6-month periods have shown good inter-rater reliability (range of ICC = .80 to .94 for AUS; range of ICC = .93 to .95 for DUS) and retest reliability (ICC = .92) among outpatient samples of persons with schizophrenia and

comorbid SUD (Drake et al., 2006; Drake, et al., 1990).

Table 3. Alcohol Use Scale and Drug Use Scale Probes, Ratings, and Anchors

Rating Scale	AUS/ DUS Probes ^a	Rating	Rating Anchors
<u>Abstinence:</u>	<i>Have you used alcohol/ drugs over the past 6-months?</i>	1	Client has not used alcohol (AUS)/ drugs (DUS) over the past 6 months.
<u>Use without Impairment:</u>	<i>Have you had family problems stemming from alcohol/ drug use?</i> <i>Have you encountered physical injury stemming from alcohol/ drug use?</i>	2	Client has used alcohol (AUS)/ drugs (DUS) over the past 6-months, but there is no evidence of persistent or recurrent problems in social functioning, legal status, role functioning, psychiatric status, or physical problems related to use, and no evidence or recurrent dangerous use.
<u>Abuse:</u>	<i>Has recurrent alcohol/ drug use led to patterns of disruptive behavior and housing problems?</i> <i>Have serious problems stemming from alcohol/ drug use persisted for at least 1 month?</i>	3	Client has used alcohol (AUS)/ drugs (DUS) over the past 6-months, and there is evidence of persistent problems in social functioning, legal status, role functioning, psychiatric status, or physical problems related to use, or evidence of recurrent dangerous use.
<u>Dependence:</u>	<i>Has drinking/ drug use caused you to stop partaking in non-drinking/ non-drug related social activities?</i> <i>Have you experienced needing to drink/ use a lot more drugs to get high (marked tolerance)?</i> <i>Do you have problems with sweating, hands shaking, racing heart, agitation (withdrawal symptoms)?</i> <i>Do these problems go away when you drink or use drugs?</i>	4	Client meets criteria for abuse, plus at least three of the following: (1) greater amounts of use than intended; (2) much of time spent obtaining or using alcohol (AUS)/ drugs (DUS); (3) frequent intoxication or withdrawal interferes with other activities; (4) important activities given up because of alcohol/ drug use; (5) continued use despite knowledge of alcohol (AUS)/ (DUS) drug-related problems; marked tolerance; (6) withdrawal symptoms; (7) or alcohol (AUS)/ drug (DUS) taken to relieve or avoid withdrawal symptoms.

<u>Dependence with Institutionalization:</u>	<i>Have you been hospitalized or incarcerated in the past 6-months?</i>	5	Client meets criteria for alcohol (AUS)/ drug (DUS) dependence, plus related problems are so severe that they make noninstitutionalized living difficult.
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Note. AUS = Alcohol Use Scale; DUS = Drug Use Scale. The AUS and DUS are 1-item parallel 5-point behaviorally anchored scales that correspond to the patient’s most severe use of alcohol or drugs over a 6-month period from direct observation of behavior, patients self-report, and collateral sources. Drug Use Scale substances include: cannabis, cocaine, amphetamine, hallucinogens, and/or phencyclidine. Nicotine/ Tobacco products are not included in the DUS composite rating.

^aTo reduce visual clutter and redundant information, only select AUS/ DUS probes are presented.

3. Moderator Variable: Gender

To examine gender differences in the cross-sectional relationship between intrinsic motivation and substance use severity (Aim #2), and whether gender moderates the longitudinal relationship between intrinsic motivation and substance use severity (Aim #3), data on gender are garnered from a demographic form that was administered during the screening procedures of the CATIE study. This screening form is a questionnaire that queries information about the patient’s age, gender, race, ethnicity, illness severity, chart diagnosis, and probable comorbidity status (Stroup et al., 2010). The questionnaire consists of 11-items covering the aforementioned areas, with the patient’s gender being categorized as male or female by the clinician administering the form (Stroup et al., 2010).

D. PROCEDURES

Upon recruitment and study enrollment, the 535 individuals with co-occurring SUDs and schizophrenia selected for this research were randomly assigned to receive up to 18-months of antipsychotic treatment (Figure 1; Figure2). Prior to the initiation of treatment, demographic

information was initially garnered from these participants, and then such participants were assessed using the previously described measure of intrinsic motivation (as assessed via the QLS) and substance use severity. Participants then began the medication to which they were randomly assigned in treatment Phase 1, and were assessed every 6-months for up to 18-months using the same instruments. Medication compliance, dosage, and side-effects were closely monitored for all participants throughout the course of the study. This research only makes use of baseline, 6-month follow-up, and 12-month follow-up data from the CATIE study, as the most data are available for the first year of the study. For this secondary analysis of these data, only assessment information on the sample of 535 participants who remained in Phase 1 for the 12-month duration of the study is reported. This decision was made to avoid introducing new treatment effects (i.e., treatment phase 2 and phase 3), which could considerably affect the primary outcomes of this research, as well as to maximize the sample of available participants for this study, the largest set of whom came from Phase 1. All participants provided written, informed consent prior to participation in this research, and this study was monitored and reviewed annually by local University Institutional Review Boards.

E. DATA ANALYSIS

The data analysis plan for this research proposes to test the hypotheses delineated within the specific aims above to (1) validate the factor structure of the intrinsic motivation measure developed by Nakgami and colleagues (2008) when applied to persons with schizophrenia and co-occurring SUDs; (2) examine the cross-sectional relationships among intrinsic motivation, gender, and substance use severity; and (3) examine the longitudinal relationship between changes in intrinsic motivation and changes in substance use severity, and whether gender

moderates this relationship. This section will provide a detailed description of the analyses proposed to carry out these aims and associated hypotheses.

1. Preliminary Analysis

Prior to investigating the primary analytic aims of this research, four preliminary analyses are conducted to verify internal consistency among study measures, check assumptions associated with the statistical tests proposed for this research, and inform subsequent analyses about the potential effects of demographic heterogeneity and patient attrition on estimates obtained from subsequent analyses. First, the internal consistency of the neurocognitive composite and the PANSS (the PANSS will be used to measure negative symptoms [negative symptom subscale] and overall psychopathology [PANSS total score]) will be checked to ensure measurement reliability (the internal consistency of the intrinsic motivation measure will be examined separately in Aim #1). Second, the distributions the continuous variables will be examined for skewness and transformed using non-linear transformations and outliers will be winsorized as appropriate, to meet the assumptions of parametric testing.

Third, to examine the effects of patient attrition on longitudinal relationship estimates, baseline differences in demographics, illness chronicity, medication (i.e., pre-randomization medications and self-reported side-effects), neurocognitive function, overall psychopathology, and legal status will be examined between completer ($n = 145$: patients with complete observations across the 12-month study period) and attrited ($n = 390$: patients with missing follow-up data due to attrition) samples using independent t tests or χ^2 tests, as appropriate. Any significant differences uncovered between the 145 completers and 390 patients who dropped out of the study before 1-year will be noted as potential limitations to the generalizability of the sample.

Finally, since previous research has indicated that intrinsic motivation may be related to negative symptoms and neurocognition (Nakagami et al., 2010; Yamada et al., 2010; Choi & Medalia, 2010; Gard, Fisher, Garrett, Genevsky, & Vinogradov, 2009; Medalia et al., 2002; Nakagami et al., 2008), preliminary analyses will be conducted to determine whether such variables need to be controlled in subsequent analyses. In addition, previous research has suggested the potential for demographic characteristics such as race and education (Yamada et al., 2010), as well as clinical characteristics such as chronicity (schizophrenia), overall psychopathology, medication dosage, and self-reported medication side effects (i.e., whether antipsychotic medications produce somnolence effects) to confound the relationship between intrinsic motivation and substance use severity (Choi & Medalia, 2010; Yamada et al., 2010; Barch, 2004). As such, Pearson, point-biserial, tetrachoric, or polychoric correlation matrices will be computed to determine whether these variables need adjusted in the analyses used to carry out the analytic aims of this research. Any significant relationships that are detected between these demographic and clinical characteristics and two or more of the primary study variables will be adjusted using partial correlation and multiple regression in subsequent analyses. Further, this research tested and adjusted for potential variation across the 57 sites included in CATIE by treating study site as a covariate in relevant analyses.

2. Approach to Missing Data

The majority of missing data in this research come from those participants who dropped out of the study before completing 1-year of treatment (see Table 4). Recent research suggests that when large proportions of attrition are present in longitudinal investigations, the current best approach for handling such missing data is to employ an intent-to-study analysis (Georguieva & Krystal, 2004; Chakraoty & Gu, 2009; Graham, 2009), using the expectation maximization (EM)

algorithm (Shafer & Graham, 2002; Graham, 2009). EM takes a maximum likelihood approach to missing values at the time of analysis (Dempster, Larid, & Rubin, 1997; McCulloch, 1977), meaning that the growth curve model parameters in Aim #3 are estimated using all of the data gathered on participants over 1-year (i.e., measurement occasions for participants, overall sample parameter estimates, and model covariates adjusted in the analysis). Prior studies have shown that intent-to-study growth curve approaches not only provide more powerful tests than other analytic options commonly used in longitudinal studies with large proportions of attrition (i.e., complete case analysis or last observation carried forward) (Shafer & Graham, 2002; Lachin, 2002; Chakraborty & Gu, 2009), but can also be safely used with the EM algorithm even when missing completely at random assumptions are not met (Graham, 2009). Since such an approach to missing data is the current standard in longitudinal research (Gueorguieva & Krystal, 2004; Hamer & Simpson, 2009), the primary longitudinal analyses in Aim #3 of this research are conducted on the intent-to-study sample. However, due to the large proportion of missing data observed in the intent-to-study sample over 1-year, complete case ($n = 145$) sensitivity analyses are conducted (presented in Appendix A) to observe variance in the findings between complete and intent-to-study ($n = 535$, at baseline) samples. As can be seen in Table 4, overall missing data in the intent-to-study sample is estimated to be 43% across the study duration, with the largest proportion of missing observations at 1-year.

Table 4. *Participants Lost to Attrition over 1-year*

Sample	Baseline	6-Month	1-Year	Overall
<i>N</i> - Intent to Study	535	535	535	1605
<i>N</i> - Complete	535	219	150	906
<i>N</i> - Missing	0	316	385	701
% - Missing	0	59	71	43
Women				
<i>N</i> - Intent to Study	86	86	86	258
<i>N</i> - Complete	86	32	24	142
<i>N</i> - Missing	0	54	62	116
% - Missing	0	62	72	44
Men				
<i>N</i> - Intent to Study	449	449	449	1347
<i>N</i> - Complete	449	187	126	762
<i>N</i> - Missing	0	262	323	585
% - Missing	0	58	71	43

Note. Baseline = Pre-treatment data. 6-month/1-Year = Phase 1 data.

The remaining missing data in this research comes from 34 participants who were missing neurocognitive data at baseline. These participants are not missing any other data on the primary study variables at baseline, and therefore their scores on the neurocognition total scores are assumed to be missing at random. Recent research suggests that when data are missing at random, the current best approach for handling missing data is to impute using the expectation-maximization algorithm (Schafer & Graham, 2002), as described previously. Consequently, for these 34 cases of missing data, the expectation-maximization approach was used to estimate the neurocognition total scores of these participants from available data on the other primary study variables, as well as demographic and clinical characteristics.

3. Aim #1: Extend Validation of the Intrinsic Motivation Measure developed by Nakagami and colleagues (2008) to Co-occurring SUDs and Schizophrenia

Hypothesis 1a. The 3-items of purpose, motivation, and curiosity form a distinct and coherent factor apart from the other 4-items of the intrapsychic deficit subscale.

A preliminary examination of the factor structure for this intrinsic motivation measure will be conducted using a varimax rotated, exploratory factor analysis on the 7-items from the intrapsychic deficit subscale of the QLS (Heinrichs et al., 1984), specifying two fixed factors for extraction. Using this approach, previous research has shown support for the 3-items of purpose, motivation, and curiosity loading together on one factor and forming a distinct factor apart from the other 4-items of the intrapsychic deficit subscale when applied to community patients with schizophrenia (Nakagami et al., 2008). Consequently, demonstrating the 3-items of purpose, motivation, and curiosity from the 7-item intrapsychic deficit subscale of the QLS load together on one factor, using exploratory factor analysis of baseline data ($n = 535$), with varimax rotation, and specifying two fixed factors for extraction, would provide preliminary support for the validation of this measure of intrinsic motivation when applied to persons with co-occurring SUDs and schizophrenia. Since the QLS items of interest (i.e., purpose, motivation, and curiosity) are hypothesized to be correlated, alternative factor-analytic solutions will also be explored to examine the best fit to the observed data structure.

Hypothesis 1b. The 3-item intrinsic motivation measure demonstrates acceptable levels of internal consistency ($\alpha \geq .70$) when applied to persons with co-occurring SUDs and schizophrenia.

To evaluate the internal consistency of this intrinsic motivation measure, baseline data on participants with co-occurring SUDs and schizophrenia will be used to calculate the Cronbach's

α coefficient for the instrument. Previous research has shown that this measure of intrinsic motivation demonstrated acceptable levels of internal consistency ($\alpha = .74$) when applied to a sample of community patients with schizophrenia. As such, showing that this measure of intrinsic motivation yields estimates of $\alpha \geq .70$, which are considered to be indicative of a minimally adequate internally consistent scale (Nunnally, 1978), would suggest that the reliabilities of the instrument are comparable between persons with schizophrenia and persons with co-occurring SUDs and schizophrenia.

Hypothesis 1c. The 3-item measure of intrinsic motivation demonstrates adequate levels of retest reliability ($r \geq .40$) across study assessment periods.

The retest reliability of the intrinsic motivation measure will be evaluated by calculating pairwise lagged Pearson correlation coefficients of participants intrinsic motivation scores across the study (i.e., baseline to 6-month; 6-month to 12-month). Results showing that this measure of intrinsic motivation meets at least minimally sufficient levels of retest reliability ($r \geq .40$) when examined across the 3 assessment observation periods of the study, would provide adequate retest reliability support for this measure of intrinsic motivation among persons with co-occurring schizophrenia and SUDs.

4. Aim#2: Examine the Cross-sectional Relationships Between Intrinsic Motivation, Gender, and Substance Use Severity

Hypothesis 2a. Intrinsic motivation is significantly, negatively correlated with substance use severity at baseline.

The zero-order, cross-sectional relationship between intrinsic motivation and substance use severity at baseline will be examined by computing Pearson correlation coefficients between baseline total intrinsic motivation measure scores and baseline AUS and DUS total scores. The

presence of significant, negative relationships between these measures would indicate that intrinsic motivation is negatively associated with substance use severity.

Hypothesis 2b. Intrinsic motivation is significantly, negatively correlated with substance use severity at baseline, after adjusting for neurocognition and negative symptoms.

The relationship between intrinsic motivation and substance use severity, after adjusting for neurocognition and negative symptoms will be investigated by employing a series of hierarchical linear regression analyses. These analyses will predict baseline AUS/ DUS scores from intrinsic motivation scores, and adjust for the potentially confounding effects of baseline neurocognition composite and negative symptom total scores from the PANSS. The presence of significant increments in variance explained in AUS/ DUS scores by intrinsic motivation scores after entering neurocognitive composite and negative symptom scores into the model would indicate that intrinsic motivation is significantly associated with substance use severity, independent of neurocognitive function and negative symptomatology.

Hypothesis 2c. Men demonstrate significantly greater degrees of substance use severity compared to women at baseline.

The bivariate, cross-sectional relationship between men and women and substance use severity at baseline will be examined by computing independent sample *t*-tests (two-tailed) between a dichotomously coded gender (male = 1; female = 2) variable and baseline AUS/ DUS scores. The presence of relationships showing that men have significantly higher mean scores on the AUS or the DUS than women at baseline, would indicate that men demonstrate significantly greater degrees of substance use severity compared to women at baseline.

Hypothesis 2d. Men exhibit significantly greater deficits in intrinsic motivation compared to women at baseline.

The bivariate, cross-sectional relationship between the genders and intrinsic motivation deficits at baseline will be investigated by computing independent sample *t*-tests (two-tailed) using a dichotomously coded gender (male = 1; female = 2) variable and baseline intrinsic motivation scores. The presence of relationships showing that men have significantly lower intrinsic motivation means than women at baseline, would indicate that men demonstrate significantly greater deficits in intrinsic motivation compared to women at baseline.

5. Aim #3: Investigate the Longitudinal Association Between Changes in Intrinsic Motivation and Changes in Substance Use Severity, and then Examine the Impact of Gender on these Relationships

This analytic aim will be addressed by employing a series of linear growth curve models. Growth curve modeling involves examining the way in which individuals change over time and whether there are differences in patterns of change (Bliese & Ployhart, 2002). Such data can be analyzed using a structural equation modeling framework (see Bollen & Curran, 2006) or using a random coefficient modeling (i.e., hierarchical/mixed model) framework (see Singer & Willet, 2003; Bliese & Polyhart, 2002; Raudenbush & Bryk, 2009). According to Raudenbush and Bryk (2009), investigations that seek to capture systematic change in individual phenomena, such as relations between changes in intrinsic motivation and changes in substance use severity, can be robustly examined by fitting a two-level random coefficients model to the longitudinal data structure. This approach to longitudinal data analysis is a form of hierarchical linear modeling for repeated measures data, where multiple measurement occasions are nested within individuals (Raudenbush & Bryk, 2009). Such an approach to longitudinal data analysis will be used to carry out this analytic aim and its associated hypotheses.

H3a. Participants exhibit, on average, significant improvement in substance use severity over the 1-year study period.

Analysis will begin by fitting two unconditional linear growth curve models to the substance use severity outcomes of interest, where the outcomes of alcohol use severity (AUS scores) and drug use severity (DUS scores) will each be predicted from time. The multilevel unconditional growth curve model that will be used to fit these data is presented in eq. 1-3.

Level 1:

$$Y_{ti} = \pi_{0i} + \pi_{1i}(\text{Time})_{ti} + e_{ti} \quad (1)$$

Level 2:

$$\pi_{0i} = \beta_{00} + r_{0i} \quad (2)$$

$$\pi_{1i} = \beta_{10} + r_{1i} \quad (3)$$

As shown in the unconditional growth curve model above, the level-1 equation (eq. 1) represents scores on the substance use severity outcome Y for an individual i at time t as a function of his/her intercept, π_{0i} , and rate of change, π_{1i} , plus error, e_{ti} . The subscript i ($i = 1 \dots 535$) indicates that the model estimates a separate intercept (π_{0i}) and a separate growth rate (π_{1i}) for each person in the sample. The set of two level-2 equations (eq. 2 & 3) characterize the initial status (π_{0i}) and the rate of change (π_{1i}) for each substance use severity outcome of interest, Y , as a function of the average initial status, β_{00} , and the rates of change, β_{10} , for the sample plus individual variation in these parameters (that is, r_{0i} and r_{1i}). For this study, the growth covariate (Time) will be coded such that: 0 = baseline, 0.5 = follow-up at 6-months, 1 = follow-up at 12-months in order to interpret the intercept for each of these unconditional models in terms of each

participant's initial status (study baseline) on outcome Y (AUS/ DUS scores). Since time is coded so that initial status = 0/baseline, the between-person variance in the intercept (τ_{00}) is interpreted as the between-person variability in each participant's initial status. As such, this parameter, τ_{00} , captures how much between-person variability exists in terms of where participants start the study. The variance parameter, τ_{11} , for the time slope captures the variability between participants in terms of their linear growth rates, and the covariance parameter, τ_{01} , represents the correlation between participant's initial scores (or intercepts) and their growth rates.

These unconditional growth curve models are premised on the assumption that the AUS and DUS data collected on participants over the 1-year study period display significant non-independence. While researchers have cautioned that it is unlikely longitudinal data will be independent (Bliese & Ployhart, 2002), it is often valuable to estimate the interclass correlation coefficient (ICC) to determine the strength of the non-independence (Raudenbush & Bryk, 2009; Hox, 2002). As such, the ICC for AUS/ DUS unconditional models will be assessed to ascertain the magnitude of non-independence in the sample, which represents the proportion of between-individual variance to the sum of between- and within individual variances [i.e. $(\tau_{00} / (\tau_{00} + \sigma^2))$].

In addition, these unconditional growth curve models are premised on the assumption that the level-1 within-individual errors are independently and identically distributed with a mean of 0 and homogeneous variance σ^2 across the sample (Raudenbush & Bryk, 2009). According to Campbell and Kenny (1999), the correlation structure of longitudinal data often has proximally autocorrelated errors (i.e., adjacent waves of measurement correlate more highly than non-adjacent waves), and therefore cannot meet these basic error distribution assumptions. Such a problem has been widely acknowledged by methodologists, who have recommended that fitting a first-order autoregressive (AR(1)) error structure to the level-1 within-individual covariance

matrix often provides the best solution in longitudinal growth curve analysis (Kenny & Campbell, 1989; Campbell & Reichardt, 1991; Singer, 1998; Campbell & Kenny, 1999; Singer & Willet, 2003). As such, this research will make use of time-structured data such that participant measurement occasions are identically spaced over the 12-month study period (T = 3 occasions), and an AR(1) error structure will be fit to the level-1 within-individual covariance matrix for the unconditional models. The error structures used at level-1 and level-2 for both unconditional models are presented in eq. 4-5.

$$\text{Level 1: } \Sigma\epsilon = \begin{bmatrix} \sigma^2 & \sigma^2\rho & \sigma^2\rho^2 \\ \sigma^2\rho & \sigma^2 & \sigma^2\rho \\ \sigma^2\rho^2 & \sigma^2\rho & \sigma^2 \end{bmatrix} \quad (4)$$

$$\text{Level 2: } \begin{bmatrix} r_{01j} \\ r_{11j} \end{bmatrix} \sim N \left[\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \tau_{\pi00} & \tau_{\pi01} \\ \tau_{\pi10} & \tau_{\pi11} \end{pmatrix} \right] \quad (5)$$

While checking the aforementioned assumptions for the AUS and DUS unconditional models, competing models in terms of complexity [i.e., models fit with AR(1) versus models fit without AR(1)] will be compared using the χ^2 of difference test based on the deviance statistic (log likelihood ratios) (Lou & Kwok, 2006; Meyers & Beretvas, 2006; Raudenbush & Bryk, 2009; McCoach & Kaniskan, 2010). The final AUS/ DUS unconditional models selected will be estimated using either full maximum likelihood (FIML) or restricted maximum likelihood (REML) estimation methods as appropriate. For example, current best practice is to use FIML estimation by default for hierarchically nested models derived from the same sample (Hox, 2000; McCoach & Black, 2008; Raudenbush & Bryk, 2009). However, when two hierarchically nested models differ only in terms of their random effects (not fixed-effects), then such models can be compared using deviances derived using REML estimation (McCoach & Black, 2008). Finally,

the presence of fixed effects showing that participants exhibit, on average, significant reductions in their AUS/ DUS scores over 1-year, would signal improvements in substance use severity.

H3b. Improvement in intrinsic motivation is associated with significant reductions in substance use severity over the 1-year study period.

Analysis will proceed by expanding the unconditional models to conditional growth curve models, where the outcomes of alcohol use severity (AUS scores) and drug use severity (DUS scores) will each be predicted from time and a time-varying intrinsic motivation variable. The conditional growth curve model that will be used to fit these data is presented in eq. 6-9.

Level 1:

$$Y_{ti} = \pi_{0i} + \pi_{1i}(\text{Time})_{ti} + \pi_{2i}(\text{Intrinsic Motivation})_{ti} + e_{ti} \quad (6)$$

Level 2:

$$\pi_{0i} = \beta_{00} + r_{0i} \quad (7)$$

$$\pi_{1i} = \beta_{10} + r_{1i} \quad (8)$$

$$\pi_{2i} = \beta_{20} \quad (9)$$

As shown in the conditional growth curve model above, the coefficient for the time-varying intrinsic motivation slope (β_{20}) represents the relationship between changes in intrinsic motivation to changes in substance use severity for patients over the 1-year study period. As defined, time-varying variables are those whose values change across time. Notably, however, the parameter value estimating the effect of the time-varying variable (intrinsic motivation) on the dependent variable (AUS/ DUS scores) is assumed to be constant across time (McCoach & Kaniskan, 2010). In the context of this study, this means that the rate of improvement in intrinsic

motivation may change at each data collection point (i.e., baseline, 6-, 12-month), but the estimated relationship between changes in intrinsic motivation to changes in substance use severity remains constant over time.

Since this study includes three time points (i.e., baseline, 6-, 12-months), random effects can be estimated for the intercept (β_{00}), the linear trajectory (β_{10}), and for the slope of time-varying intrinsic motivation (β_{20}). While allowing time-varying intrinsic motivation's slope to randomly vary (i.e., intrinsic motivation would take on a different value for every patient in the sample) across patients may seem preferable to fixing the slope (i.e., every patient would have the same average estimate of intrinsic motivation improvements), methodologists have cautioned against estimating such slopes as random effects by default to avoid estimation and convergence issues in subsequent models (Raudenbush & Bryk, 2009). Others have indicated that the temptation to automatically allow the effects of time-varying predictors to randomly vary at level-2 should be avoided unless there is good reason, and sufficient data (i.e., measurement occasions) to do so (Lou & Kwok, 2006; Meyers & Beretvas, 2006; Raudenbush & Bryk, 2009; McCoach & Kaniskan, 2010). Since there is no consensus on whether to fit the slopes of time-varying variables as fixed or random (McCoach & Kaniskan, 2010), and only three-measurement occasions are utilized in this present study, analysis will proceed by fitting time-varying intrinsic motivation's slope as fixed in the AUS/ DUS conditional growth models.

The conditional models will then be expanded to include person-level characteristics at level-2, which include baseline covariates that may confound the relationship between intrinsic motivation and substance use severity. As such, previously conducted cross-sectional analyses will be used to inform whether it is necessary to adjust for study site effects, patient comorbidity status, age, race, education, negative symptoms, neurocognition, psychopathology, self-reported

medication side-effects, and illness chronicity in this series of growth curve analyses. Any potential confounders will be included in these conditional models as time-invariant covariates in the level-2 model (eq. 7 & 8), as they may account for differences in the growth parameters on the AUS/ DUS outcomes. In addition, phase1 randomization treatment assignment will be adjusted at level-2. After determining potential confounders, the conditional growth curve models will be estimated using either FIML or REML as appropriate (see Hox, 2000; McCoach & Black; Raudenbush & Bryk, 2009), and an AR(1) error structure that is suitable for longitudinal data structures will be employed at level-1 for each of these models (Singer, 1998). The presence of relationships indicating that patients show significant reductions in substance use severity as they make gains in intrinsic motivation over 1-year, would demonstrate that improvements in intrinsic motivation are associated with reductions in substance use severity.

H3c. Women demonstrate a stronger association between improvement in intrinsic motivation and reductions in substance use severity than men over 1-year.

To test whether women demonstrate stronger associations between improvements in intrinsic motivation and reductions in substance use severity over the study, two gender moderated growth curve models will be constructed such that an interaction between intrinsic motivation and gender predicts the initial levels and the 1-year rates of change on the outcomes of alcohol use severity and drug use severity for the sample. The gender moderated conditional growth curve model that will be used to fit these data is presented in eq. 10-13.

Level 1:

$$Y_{ti} = \pi_{0i} + \pi_{1i}(\text{Time})_{ti} + \pi_{2i}(\text{Intrinsic Motivation})_{ti} + e_{ti} \quad (10)$$

Level 2:

$$\pi_{0i} = \beta_{00} + r_{0i} \quad (11)$$

$$\pi_{1i} = \beta_{10} + r_{1i} \quad (12)$$

$$\pi_{2i} = \beta_{20} + \beta_{21} (\text{Gender}) \quad (13)$$

As shown in the conditional gender moderated growth curve model in eq. 10-13, a dichotomously coded variable representing gender (1= male; 2 = female) is now a predictor of both the level-2 intercept (π_{0i}), growth rate/slope (π_{1i}), and time-varying intrinsic motivation slope (π_{2i}). The coefficient for the cross-level interaction Gender \times Intrinsic Motivation (time-varying) slope (β_{21}) represents the impact of gender on the longitudinal association between changes in intrinsic motivation and changes in substance use severity (AUS/ DUS scores, respectively). The presence of a significant Gender \times Intrinsic Motivation (time-varying) would signal a need to further decompose this conditional effect to evaluate the pattern of significance reflected in this relationship (Aiken & West, 1991). According to Preacher, Curran, & Bauer (2006), a simple slopes test provides a robust method to evaluate the pattern of significant interaction effects detected as part of a linear growth curve analysis. Specifically, simple slopes denote the regression of an outcome Y (AUS/ DUS) on the predictor (intrinsic motivation) at a specific value of the moderator z (gender). The simple slope equation that will be used to fit these data is presented in eq. 14.

$$\hat{\omega}_1 = \hat{\beta}_{20} + \hat{\beta}_{21} (\text{Gender}) \quad (14)$$

The simple slope ($\hat{\omega}_1$) will then be evaluated using the simple slope technique and test of

significance. Such a technique indicates that the first step in deriving the significance of $\hat{\omega}_1$ is to determine the variance of the simple slope, which can be computed for any conditional value (gender coded: 1=male; 2=female) of the moderator (Preacher et al., 2006). The equation that will be used to compute the variance of $\hat{\omega}_1$ is shown in eq. 15.

$$\begin{aligned} \text{var}(\hat{\omega}_1|\text{Gender}) = & \text{var}(\hat{\beta}_{20}) + 2(\text{Gender})\text{cov}(\hat{\beta}_{20}, \hat{\beta}_{21}) \\ & + (\text{Gender})^2 \text{var}(\hat{\beta}_{21}) \end{aligned} \quad (15)$$

The requisite values for computing the variance of $\hat{\omega}_1$ will be taken from the parameter estimates of the gender moderated growth curve models. Then, the square root of the quantity derived in eq. 15 will be used to compute the standard error of $\hat{\omega}_1$, $SE_{\hat{\omega}_1}$. This value ($SE_{\hat{\omega}_1}$) will then be used to form the critical ratio to perform a significance test for determining the difference between $\hat{\omega}_1$ and 0. The critical ratio equation is presented in eq. 16.

$$t = \frac{\hat{\omega}_1}{SE_{\hat{\omega}_1}} \quad (16)$$

The simple slope significance test can then be computed by taking the t obtained in eq. 16 to a t distribution at an $\alpha = .05$ level, using an equation such that $(df) = N - p - 1$, where N will be substituted with the sample size, 535, and p will be substituted with the number of predictors in these gender moderated growth curve models. Because methodologists increasingly recommend the use of confidence intervals in addition to hypothesis tests whenever possible (Wilkinson, 1999; Preacher et al., 2006), confidence bands will be computed to supplement the simple slope

tests of significance. The general formula for a $100 \times (1 - \alpha) \%$ *CI* for a simple slope (Cohen, Cohen, West, & Aiken, 2003) is presented in eq. 17.

$$CI_{\hat{\omega}_1} = \hat{\omega}_1 \pm t_{crit} SE_{\hat{\omega}_1} \quad (17)$$

Such an analysis will conclude by plotting and examining the results of the simple slopes analysis and the confidence bands ($CI_{\hat{\omega}_1}$). The presence of a significant Gender \times Intrinsic Motivation (time-varying) interaction, followed by confirmatory simple slope test results reflecting a pattern of significance such that women exhibit a stronger association between change in intrinsic motivation and change in substance use severity over the 1-year study than men, would provide sufficient support to substantiate this hypothesis.

6. Power Analysis

Statistical power to detect cross-sectional relationships among the constructs discussed above is based upon the 535 participants with co-occurring SUDs and schizophrenia who have completed baseline assessments. Statistical power to detect longitudinal relationships among the constructs above is based upon those participants who were available at baseline ($n = 535$) 6-months ($n = 219$) and 1-year ($n = 150$) follow-up periods. All power analyses were conducted *a priori* using G*Power statistical software (Faul, Erdfelder, Lang, & Buchner, 2007).

Psychometric analyses proposed in Aim #1 will depend on examining the factor structure of the intrinsic motivation measure. Although guidelines for sample sizes required to estimate a reliable factor structure remain controversial and dependent on a number of different parameters (Fabrigar, Wegener, MacCallum, & Strahan, 1999), more conservative approaches suggest that reliable factor structures can be estimated with participant to item ratios of 10:1 (Everitt, 1975;

Nunnally, 1978). As such, with 535 participants and 8 intrapsychic deficit items, this analytic aim will be able to meet these more conservative requirements for examining the factor structure of the intrinsic motivation measure developed by Nakagami and colleagues (2008) among this sample of persons with co-occurring SUDs and schizophrenia.

Investigating the cross-sectional relationship between intrinsic motivation and substance use severity in Aim #2 hypothesis 2b, relies on a series of hierarchical linear regression analyses with 3 predictors. As can be seen in Figure 4, using power analytic methods outlined by Cohen (1988), with 535 participants, given power = .80, $\alpha = .05$, and $k = 3$, adequate power will be available to detect medium to large relationship sizes in variance explained in AUS/ DUS scores by intrinsic motivation scores, after adjusting for the potentially confounding effects of negative symptoms and neurocognition. Examining the cross-sectional relationship between gender and intrinsic motivation and gender and substance use severity in hypothesis 2c and hypothesis 2d will rely upon a series of independent sample *t*-test (two-tailed). Using power analytic methods outlined by Cohen (1988), with $n = 86$ women and $n = 449$ men at baseline, power = .80, and $\alpha = .05$, adequate power will be available to detect medium to large relationship sizes ($d = .50$ and greater) between gender and intrinsic motivation and gender and substance use severity.

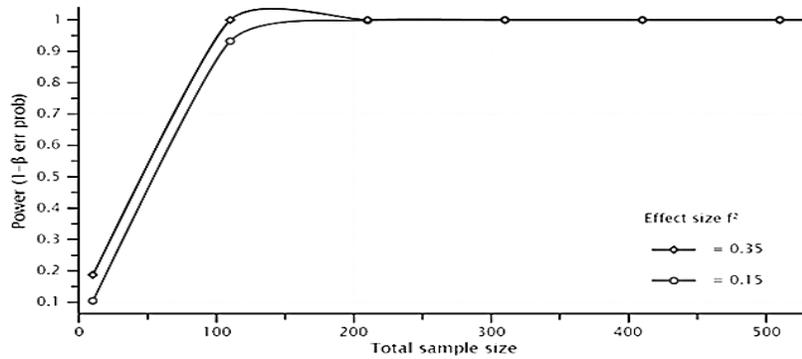


Figure 4. Power as a function of total sample size ($n = 535$) for the hierarchical regression analysis $k = 3$, $\alpha = .05$, in study Aim #2, hypothesis 2b

The relationship between longitudinal changes in intrinsic motivation and changes in substance use severity examined in Aim #3 hypothesis 3b will rely upon a linear growth curve analysis with a single time-varying predictor (intrinsic motivation). As can be seen in Figure 5, using data from the intent-to-treat sample ($n = 535$ at baseline; $n = 219$ at 6-months; $n = 150$ at 1-year), given power = .80, $\alpha = .05$, $k = 2$ (intrinsic motivation and time), measurement occasions = 3 (every 6-months for 1-year), and 1 group of participants, adequate power will be available to detect medium to large relationship sizes between changes in intrinsic motivation and changes in substance use severity over the 1-year study period.

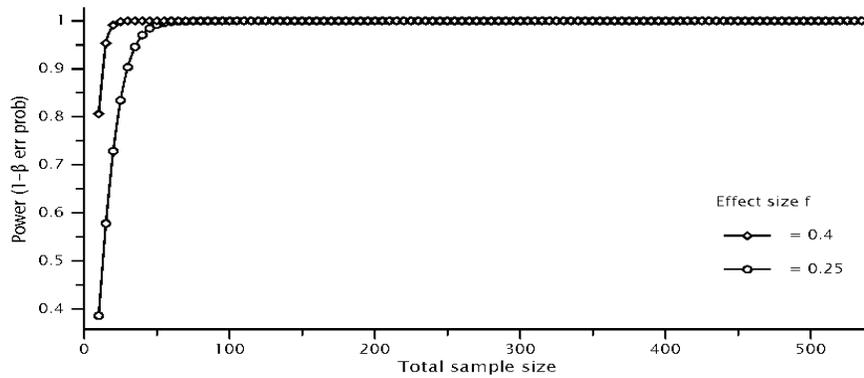


Figure 5. Power as a function of total sample size ($n = 535$) for the linear growth curve analysis (groups = 1, repeated measurement occasions = 3, $k = 2$, $\alpha = .05$), in study Aim #3, hypothesis 3b.

The relationship testing the impact of gender on the longitudinal association between intrinsic motivation and substance use severity in hypothesis 3b will rely on a gender moderated linear growth curve analysis such that an interaction between change in intrinsic motivation and gender predicts the outcomes of changes in alcohol use severity and drug use severity for the sample. As can be seen in Figure 6, using data from the $n = 449$ men and $n = 86$ women from the intent-to-treat sample ($n = 535$ at baseline; $n = 219$ at 6-months; $n = 150$ at 1-year), given power = .80, $\alpha = .05$, $k = 3$, and 2 participant groups, adequate power will be available to detect medium to large relationship sizes with regard to the impact of gender on the relationship between intrinsic motivation and substance use severity over the 1-year study.

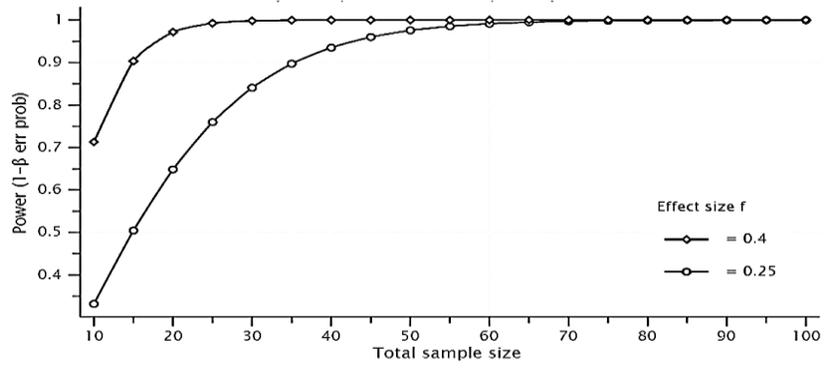


Figure 6. Power as a function of total sample size ($n = 535$) for the gender moderated growth curve analysis (groups = 2 [$n = 86$ women; $n = 449$ men], repeated measurement occasions = 3, $k = 3$, $\alpha = .05$), in study Aim #3, hypothesis 3c

IV. RESULTS

This chapter presents a series of statistical analyses designed to answer the primary analytic questions of this research. These analyses were carried out to answer questions focused on (1) extending the intrinsic motivation instrument developed by Nakagami and colleagues (2008) for schizophrenia to schizophrenia and comorbid SUD, (2) examining the cross-sectional relationships between intrinsic motivation, gender, and substance use severity, (3) investigating the association between longitudinal changes in intrinsic motivation and changes in substance use severity, and (4) examining whether gender moderates the longitudinal association between changes in intrinsic motivation and changes in substance use severity. This chapter begins with a presentation of the demographic and clinical characteristics ascertained for this research, and then proceeds by presenting the results of a series of preliminary analyses designed to check the internal consistency of the study measures, verify that the study data meets criteria for parametric statistical testing, examine potential differences between study completers and those lost to attrition, and investigate potential demographic and clinical confounds with primary study variables. Subsequent to these preliminary analyses, the results from the primary study aims are presented. The statistical analyses presented in this chapter will be carried out using R version 2.14.2 (R Development Core Team, 2014).

A. SAMPLE CHARACTERISTICS

A total of 535 persons with comorbid SUD and schizophrenia were included in this research, 220 were available at the 6-month follow-up, and 151 completed 1-year follow-up. At baseline, most participants were male (83.9%), white (56.4%), and in their late thirties ($M =$

37.98; $SD = 10.62$). Few patients were married (8.4%), completed a college degree (including a community college or a trade school) (10.3%), and were employed (6.2%). Further, while most patients were taking an antipsychotic medication at baseline (78.1%), such patients had been ill (schizophrenia) for 15 years on average ($SD = 10.43$) and presented for treatment with moderate degrees of illness chronicity ($M = 4.00$; $SD = 0.95$). As can be seen in Table 4, many patients with schizophrenia and comorbid SUD reported that they had used substances within 90-days of enrollment, with alcohol, cannabis and cocaine being among the most frequent recently used substances reported. In addition, 86.0% of patients with schizophrenia and comorbid SUD reported using tobacco products within 90-days of enrollment. Notably, there was a considerable degree of overlap in SUD diagnoses (comorbidity status) observed among these schizophrenia patients at baseline. For example, 65.8% were diagnosed with any alcohol use disorder, 62.2% were diagnosed with any cannabis use disorder, and 41.7% were diagnosed with any cocaine use disorder (see Table 5).

Table 5. *Comorbid Substance Use Disorder Diagnoses and Self-Reported Substance Use among Schizophrenia Patients at Baseline*

Variable	Substance Use ^a	DSM Diagnosis ^b
	<i>n</i> (%)	<i>n</i> (%)
Alcohol	300 (56.1%)	352 (65.8%)
Cannabis	197 (36.8%)	333 (62.2%)
Cocaine	106 (19.8%)	223 (41.7%)
Amphetamine	27 (5.0%)	62 (11.6%)
Opiate	15 (2.8%)	34 (6.4%)
Phencyclidine	3 (0.6%)	19 (3.6%)

^aPatient's were asked to report their use of any substance (alcohol, cannabis, cocaine, amphetamine, opiates, or phencyclidine) within 90-days of baseline. Responses were recorded as "yes=1" indicating use or "no=0" indicating no use.

^bPatient's were assessed at baseline by research project clinicians trained in administering the DSM-IV SCID (First et al., 1996) for the presence of a substance use disorder.

In order to obtain a greater understanding of the heterogeneity of the sample regarding SUD diagnoses, an analysis was conducted to examine demographic characteristics across three mutually exclusive groups distinguished by comorbidity status (i.e., comorbid schizophrenia and alcohol use disorders [*n* = 119]; comorbid schizophrenia and SUD other than an alcohol use disorder [*n* = 183], and comorbid schizophrenia and poly disorders [*n* = 233]). As can be seen in Table 6, overall differences were observed across 5 of the 17 baseline characteristics among these mutually exclusive groups. Planned follow-up pairwise comparisons showed that patients with comorbid schizophrenia and alcohol use disorder were significantly older and in more chronic stages of schizophrenia illness. Patients with comorbid schizophrenia and alcohol use disorders also demonstrated greater neurocognitive deficits than the other groups. A greater proportion of patients with alcohol use disorders were white; polysubstance disordered patients

were significantly more likely to have encountered the legal system within 30-days of study enrollment compared to schizophrenia patients with comorbid alcohol use disorder.

Table 6. *Participant Baseline Characteristics*

Variable	A (<i>n</i> = 119)		D (<i>n</i> = 183)		A/D (<i>n</i> = 233)		Analysis ^a	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>p</i>	Direction ^b
Age	43.19	9.21	37.41	10.90	35.76	10.91	<.001	D < A > AD
Education ^c	12.07	2.05	11.92	1.94	11.63	1.92	.108	-
Chronicity ^d	17.89	10.98	13.94	10.90	14.30	10.45	.002	D < A > AD
PANSS Total ^e	77.80	17.24	75.60	18.16	76.83	16.30	.538	-
Negative ^f	20.50	6.09	19.64	6.70	19.53	6.30	.375	-
Neurocognition ^g	-0.16	1.03	0.12	0.89	0.23	0.92	.001	D > A < AD
CPZ ^h	423.48	10.98	387.23	405.38	297.85	225.85	.090	-
	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	<i>p</i>	Direction
Male	97	81.5	150	82.0	202	86.7	.307	-
White	87	73.1	95	51.9	120	51.5	<.001	A < D, AD
Employed ⁱ	22	18.5	21	11.5	41	17.6	.177	-
Married	15	12.6	14	7.7	16	6.9	.307	-
Legal ^j	10	8.4	22	12.0	41	17.6	.043	AD > A, D
Antipsychotic	84	70.6	130	71.0	154	66.1	.815	-
Antidepressant	40	33.6	51	27.9	75	32.2	.525	-
Anxiolytic	22	18.5	28	15.3	34	14.6	.752	-
Antiepileptic	84	70.6	28	15.3	35	15.0	.855	-
No Medication	97	81.5	12	6.6	13	5.6	.471	-
SE-1 ^k	32	26.8	63	34.4	55	23.6	.682	-
SE-2 ^l	69	57.9	124	67.7	104	44.6	.643	-

Note. A = alcohol use disorder; D = substance use disorder other than an alcohol use disorder (i.e., cannabis, cocaine, amphetamine, opiate, or phencyclidine [PCP]); A/D = concurrent alcohol

use disorder and other substance use disorder diagnoses. All SUD diagnoses are combined current (present within 30-days), or lifetime (present within 5 years).

^a χ^2 test or analysis of variance test, two tailed, for significant differences between mutually exclusive A, D, or A/D groups with comorbid SUD and schizophrenia at baseline.

^b *p*-values of analysis of variance tests are adjusted using Hochberg's (1988) correction.

^c Based on years of education.

^d Based on years of treatment for schizophrenia.

^e Positive and Negative Syndrome Scale Total Scores; higher scores indicate more symptoms.

^f Positive and Negative Syndrome Scale Negative subscale scores; higher scores indicate greater negative symptoms.

^g Neurocognition composite; higher scores indicate better neurocognitive performance.

^h Chlorpromazine equivalent dose; pre-treatment antipsychotic medications were converted to CPZ equivalent dose for all participants. CPZ data are available for 358 participants.

ⁱ Based on any paid employment.

^j Legal is based on any parole, probation, or incarceration within 30 days of enrollment.

^k Based on patient reported somnolence effects of taking antipsychotic medications; response of "true" indicated that such medications have zombie-like effects.

^l Based on patient reported somnolence effects of taking antipsychotic medications; response of "true" indicated that such medications were associated with tired/sluggish effects.

B. PRELIMINARY ANALYSES

1. Internal Consistency of the PANSS and Neurocognitive Composite

Preliminary analysis of study data began by performing a series of analyses to check the internal consistency of the primary baseline covariates (PANSS Total, PANSS Negative subscale, Neurocognition Composite). The internal consistency of the independent intrinsic motivation measure is examined separately in Aim #1; the internal consistency of the dependent substance use severity measures are not computed as only 1-item composite scores for AUS/DUS scales are available. Using baseline data, these analyses provided reliability estimates of

the study measures, but did not serve as the sole basis for including and excluding items within measures. Cronbach's α was utilized as the internal consistency measure for these analyses. Estimates of $\alpha \geq .80$ were considered indicative of a highly internally consistent scale (Nunnally, 1978). Estimates of $\alpha \geq .70$ were considered indicative of minimally adequate internally consistent scale (Nunnally, 1978). Internal consistency estimates for scales with missing data were calculated using the EM algorithm, which has been shown to be more accurate than listwise or pairwise deletion when computing Cronbach's α (Enders, 2003).

PANSS. Table 7 presents internal consistency estimates of the total scale and three subscales of the PANSS at baseline. This study only considers total scale and negative subscales; other subscales were considered insofar that they comprise part of the total scale. The internal consistencies of the PANSS total, negative symptomatology, and general psychopathology subscales were all within acceptable ranges.

Table 7. *Positive and Negative Symptom Scale Internal Consistency*

Item	Alpha	
	Total	Without
Total	.86	-
Positive	.70	-
Delusions (P1)	.57	.61
Conceptual Disorganization (P2)	.35	.67
Hallucinatory Behavior (P3)	.41	.66
Excitement (P4)	.36	.67
Grandiosity (P5)	.45	.64
Suspiciousness (P6)	.38	.65
Hostility (P7)	.29	.68
Negative	.81	-

Blunted Affect (N1)	.62	.77
Emotional Withdrawal (N2)	.63	.77
Poor Rapport (N3)	.70	.76
Passive/Apathetic Social Withdrawal (N4)	.58	.78
Difficulty in Abstract Thinking (N5)	.34	.83
Lack of Spontaneity and Flow of Conversation (N6)	.63	.77
Stereotyped Thinking (N7)	.39	.81
General Psychopathology	.78	-
Somatic Concerns (G1)	.37	.77
Anxiety (G2)	.43	.76
Guilt Feelings (G3)	.28	.78
Tension (G4)	.45	.76
Mannerisms and Posturing (G5)	.38	.77
Depression (G6)	.27	.77
Motor Retardation (G7)	.40	.76
Uncooperativeness (G8)	.41	.76
Unusual Thought Content (G9)	.41	.76
Disorientation (G10)	.26	.77
Poor Attention (G11)	.43	.76
Lack of Judgment and Insight (G12)	.32	.77
Disturbance of Volition (G13)	.50	.76
Poor Impulse Control (G14)	.29	.77
Preoccupation (G15)	.51	.76
Active Social Avoidance (G16)	.35	.77

Neurocognitive composite. Table 8 presents internal consistency estimates of the neurocognitive composite measure at baseline. The internal consistency of the neurocognitive composite was within acceptable ranges. Since this study is only focused on accounting for the potentially confounding effects of neurocognitive total scores in primary analyses, the internal consistency of the neurocognitive subdomains (i.e., processing speed, reasoning/problem solving, verbal/working memory, and vigilance) are not reported or discussed herein.

Table 8. *Neurocognitive Composite Internal Consistency*

Item	Alpha	Item Total	Alpha Without
Total	.88	-	-
WAIS-R Mazes: 9 timed mazes		.42	.88
WCST: Number of categories complete/perseverative errors		.36	.88
LNS: Repeat clusters of letters combined with numbers		.66	.86
Computerized Test of Visuospatial WM: Variable Inter-stimulus interval (no delay, 5 second delay, 15 second delay)		.49	.87
WAIS-R: Digit-span test		.72	.86
COWAT/category instances: Generate words beginning with F, A, and S. Name animals, fruits, vegetables within 60 seconds.		.56	.87
Grooved Pegboard: choice reaction time; dominant hand		.50	.87
CPT 1: Vigilance response to identical 2-digit paired numbers		.63	.87
CPT 2: Vigilance response to identical 3-digit paired numbers		.64	.86
CPT 3: Vigilance response to identical 4-digit paired numbers		.60	.87
HVLT 1: List A; Recall 12 words read aloud by the tester		.52	.87
HVLT 2: List B; Recall 12 words read aloud by the tester		.59	.87
HVLT 3: List C; Recall 12 words read aloud by the tester		.59	.87

Note. Scores are standardized. WAIS-R = Wechsler Adult Intelligence Scale-Revised Mazes; WCST = Wisconsin Card Sorting Test; LNS = Letter Number Sequencing Test; WMS-R = Wechsler Memory Scale-Revised; COWAT = Controlled Word Association Test; CPT = Continuous Performance Test; HVLT = Hopkins Verbal Learning Test.

2. Verifying Parametric Assumptions

After checking the internal consistency of these covariates, a series of analyses was conducted to examine the distributions of these measures as well as the independent/dependent measures to ensure they met the assumptions of parametric testing. These analyses were conducted by visually inspecting Box and Whisker plots for each of these measures to identify potential outliers, calculating skewness statistics to quantify skewed data distributions, and inspecting histograms of data distributions to identify potentially non-normal distributions. Skewness statistics greater than .75 were considered to be indicative of moderately skewed distributions (McAweeney & Klockars, 1998), and for those distributions that exceeded this threshold, non-linear transformation procedures were used to reduce the skewness. Cases were identified as outliers if their score on a single measure was 2 times the interquartile range of the distribution of scores in the sample (Hoaglin, Iglewicz, & Tukey, 1986). Outliers were handled by employing a winsorization procedure to bring such cases within 2 times the interquartile range of the data distribution, by setting the score value of the outlier to that of the next closest number within 2 times the interquartile range (Dixon & Tukey, 1968). In order to preserve comparability between baseline and follow-up measures for the primary study variables (intrinsic motivation, and drug/alcohol use severity), baseline, 6-, and, 12-month data were stacked and simultaneously transformed across study periods. Further, baseline covariates were only transformed at baseline.

As can be seen by the descriptive statistics and skewness information for the primary study variables and baseline covariates presented in Table 9, slightly over half of these variables required a non-linear transformation or winsorization procedure to reduce skewness or remove outliers. Nevertheless, once transformed or winsorized, all study variables demonstrated

acceptable ranges of skewness and contained no significant outliers. The two substance use severity dependent variables (AUS/ DUS) demonstrated significant skewness across study periods. After applying logarithmic transformations to these two dependent measures, skewness was substantially reduced. Only the neurocognitive composite covariate required a winsorization procedure to remove outliers and reduce skewness. All subsequent analyses will make use of these transformed and winsorized variables, and any transformation applied to them will not be considered or discussed hereafter.

Table 9. *Descriptive and Skewness Statistics of Primary Study Variables*

Variable	N^a	N^b	M	SD	Min	Max	Skew (pre)	Transform	Skew (post)
Baseline Covariates									
PANSS Total	0	535	76.63	17.16	33	140	.26	-	-
Negative	0	535	19.79	6.40	7	41	.29	-	-
Neurocognitive Composite	0	535	0.11	0.94	-2.48	2.51	.05	win(5)	.03
Stacked Longitudinal Data									
Intrinsic Motivation	609	904	5.02	0.91	0	12	.36	-	-
AUS	609	904	0.97	0.29	0	1.79	1.05	log1p	.47
DUS	609	904	0.95	0.31	0	1.79	1.00	log1p	.63

Note. Skew (pre) refers to skewness before non-linear transformation. Skew (post) refers to skewness after non-linear transformation. win(n) = winsorization procedure performed on n outliers.

^a N = missing data at baseline for covariates; N = missing data for stacked longitudinal data.

^b N = baseline sample for covariates; N = combined observations across study periods for stacked longitudinal data.

3. Examining Potential Attrition Bias

Having winsorized outliers and transformed variables to reduce skewness, a series of analyses were then conducted to examine the possibility of systematic differences between those participants for whom complete observations were available across all study time points (i.e. completer sample: $n = 145$) and those participants who had any missing follow-up data due to study attrition (i.e., dropped out—attrited sample: $n = 390$). These analyses were conducted by calculating descriptive statistics for the primary study variables, and demographic and clinical characteristics between these two groups at baseline, and then conducting independent t tests or χ^2 tests to identify significant between-group differences at baseline on these variables.

As can be seen in Table 10, the only statistically significant baseline difference between completer and attrited samples was with regard to participant comorbidity status. A significantly greater proportion of participants with alcohol use disorders completed the study than dropped out of the study. However, a significantly greater proportion of participants with substance use disorders other than an alcohol use disorder dropped out of the study than completed the study. Overall, these results suggest that the completer and attrited samples were generally comparable on most of the primary study variables at baseline; however, systematic differences do exist with regard to pre-randomization comorbidity status.

Table 10. Comparison of Baseline Characteristics of Patints in Completer and Attrited Samples

Variable	Completer	Dropped Out ^a	<i>p</i> ^b
	(<i>n</i> = 147)	(<i>n</i> = 390)	
	<i>M</i> (<i>SD</i>) / <i>N</i> (%)	<i>M</i> (<i>SD</i>) / <i>N</i> (%)	
Age	38.70 (10.54)	37.71 (10.65)	.335
Education (years)	11.91 (1.73)	11.80 (2.04)	.533
Chronicity	14.89 (10.92)	14.99 (10.26)	.924
White	85 (58.6%)	217 (55.6%)	.302
Employed	22 (14.9%)	62 (15.8%)	.458
Married	9 (6.2%)	36 (9.2%)	.173
Legal ^c	22 (15.2%)	51 (13.1%)	.309
Antipsychotic	110 (75.9%)	258 (66.2%)	.064
Antidepressant	50 (30.1%)	116 (29.7%)	.096
Anxiolytic	27 (18.6%)	57 (14.6%)	.080
Antiepileptic	21 (14.5%)	58 (14.9%)	.092
No Medication	6 (4.1%)	22 (5.6%)	.069
CPZ	302.41 (331.43)	381.34 (498.31)	.132
SE-1 ^d	38 (25.8%)	117 (30.0%)	.431
SE-2 ^e	82 (56.5%)	215 (55.1%)	.890
Study Site ^f	128.67 (15.32)	127.82 (15.97)	.579
Comorbidity Status			
Alcohol/SZ	42 (29.0%)	77 (19.7%)	<.001
Drug/SZ	39 (26.9%)	144 (36.9%)	<.001
Poly/SZ	64 (44.1%)	169 (43.3%)	.945
PANSS Total	74.99 (17.26)	77.24 (17.10)	.178
Negative	20.18 (6.49)	19.64 (6.36)	.385
Neurocognition	0.09 (0.86)	0.11 (0.97)	.728
Intrinsic Motivation	4.98 (2.75)	4.86 (2.72)	.658
Male	123 (84.8%)	326 (83.6%)	.420
AUS (log)	0.99 (0.29)	0.99 (0.29)	.990
DUS (log)	0.94 (0.28)	0.99 (0.32)	.087

Note. PANSS = Positive and Negative Syndrome Scale; Negative = Negative Symptom subscale of the PANSS; CPZ = Chlorpromazine equivalent dose. Comorbidity Status = mutually exclusive groups based on DSM-IV SCID diagnoses [SZ = schizophrenia; Alcohol = alcohol use disorder; drug = disorder other than an alcohol use disorder; Poly = alcohol and drug use disorder]. AUS = Alcohol Use Scale; DUS = Drug Use Scale.

^a Dropped out = attrited sample.

^b χ^2 or independent *t*-test, two-tailed, for differences between completer and attrited samples.

^c Legal is based on any parole, probation, or incarceration within 30 days of enrollment.

^d Patient reported somnolence effects of taking antipsychotic medications; response of “true” indicated that such medications have zombie-like effects.

^e Patient reported somnolence effects of taking antipsychotic medications; response of “true” indicated that such medications were associated with tired/sluggish effects.

^f Study Site = 57 study sites included in the CATIE trial.

4. Identifying Potential Demographic and Clinical Confounds with Study Variables

After examining potential systematic differences between participants with complete observations across the study time points, and those participants with missing follow-up data due to study attrition, a series of correlation analyses was conducted to examine the associations between the primary study variables (i.e. drug/alcohol use severity, intrinsic motivation, gender), and potential clinical and demographic confounders at baseline. Based on previous research, these potential confounders included the demographic characteristics of age, education, and race, as well as the clinical characteristics of illness chronicity, medication dosage, self-reported medication side effects (i.e., somnolence effects), neurocognition, negative symptoms, and overall psychopathology.

As can be seen by the correlation matrix presented in Table 11, age, race, illness chronicity, and overall psychopathology showed significant and moderate associations with a number of the primary study variables. In particular, age, illness chronicity, and overall

psychopathology exhibited significant and moderate associations with components of both intrinsic motivation and one of the substance use severity dependent variables (DUS, log), suggesting their potential confounding influence on estimates between these constructs. As a consequence, subsequent cross-sectional and longitudinal analyses examining the relations among intrinsic motivation and substance use severity adjusted for age, illness chronicity, and overall psychopathology. In addition to adjusting for these variables, subsequent cross-sectional analyses (Section 4.D.2) examining such relations adjusted for study site effects, comorbidity status, neurocognition, and negative symptoms; longitudinal analyses (Section 4.E.2.) examining such relations adjusted for phase 1 randomization, comorbidity status, neurocognition, and negative symptoms.

Table 11. Association Between Primary Study Variables and Potential Confounders at Baseline

Variable	Age	Race ^a	ED ^b	IC ^c	CPZ ^d	P-tot ^e	P-neg ^f	Neuro ^g	SE-1 ^h	SE-2 ⁱ
IM ^j	-.13**	-.05	.08	-.13**	-.05	-.33**	-.34**	.28**	-.09*	-.05
Gender ^k	.01	.16**	.04	-.04	-.04	-.03	-.07	.06	.07	.18**
AUS (log) ^l	.01	-.07	.01	.02	-.02	.05	-.01	.04	-.02	.01
DUS (log) ^m	-.16**	.10**	.02	-.10*	-.07	.13**	.04	.05	-.01	-.01

Note. Pearson, point-biserial, polychoric, or tetrachoric correlations between primary study variables and potential confounders at baseline ($n = 535$). IM = Intrinsic Motivation; ED = Years of Education. IC= Illness Chronicity; P-tot = Positive and Negative Syndrome Scale. P-neg = Negative Symptom Subscale of the Positive and Negative Symptom Scale; Neuro = Neurocognition; SE-1 = Patient reported somnolence effects of taking antipsychotic medications (response of “true” indicate such medications have zombie-like effects); SE-2 = Patient reported somnolence effects of taking antipsychotic medications (response of “true” suggests such medications are associated with tired/sluggish effects); AUS = Alcohol Use Scale; DUS = Drug Use Scale.

^a1 = White; 2 = Non-White.

^b Higher values indicate more years of education.

^c Higher values indicate more years of schizophrenia treatment.

^d Chlorpromazine equivalent dose; higher numbers indicate higher medication dosages.

^e Higher scores indicate greater degrees of psychopathology.

^f Higher scores indicate greater degrees of negative symptomatology.

^g Higher scores indicate better neurocognitive performance.

^h 1 = True; 0 = False

ⁱ 1 = True; 0 = False

^j Higher scores indicate greater degrees of intrinsic motivation.

^k 1 = Men; 2 = Women.

^l Higher scores indicate greater alcohol use severity.

^m Higher scores indicate greater drug use severity.

** $p < .01$, * $p < .05$, 2-tailed.

C. AIM #1 EXTEND VALIDATION OF NAKAGAMI AND COLLEAGUES INTRINSIC MOTIVATION MEASURE TO COMORBID SUD AND SCHIZOPHRENIA

1. Factor Structure

Analysis proceeded by conducting the first ever examination of the intrinsic motivation measure's factor structure among patients with schizophrenia and comorbid SUD. As such, a series of exploratory factor analyses were conducted, and began using principal axis factoring with varimax rotation, on a correlation matrix of the QLS's 7 intrapsychic deficit subscale scores among ($n = 535$) the baseline sample (see Table 12). Support for taking this initial approach was garnered from a recent investigation by Nakagami and colleagues (2008), which showed that the 3 items of purpose, motivation, and curiosity form a distinct intrinsic motivation factor in schizophrenia, when two fixed factors are specified for extraction using varimax rotation. While similar results were hypothesized in this study (Aim #1; Chapter 3, Section E.3), it is important

to mention that exploratory techniques are critical for examining alternative solutions that may better represent the construct in schizophrenia and comorbid SUD, which could be overlooked using confirmatory models (Kelloway, 1995; Hurley et al., 1997; Tomarken & Waller, 2003). In addition, methodologists caution against using confirmatory models in the early stages of scale validation and development, as such factor-analytic methods do not show how well items load on non-hypothesized factors (Kelloway, 1995). Given the fact that Nakagami and colleagues (2008) intrinsic motivation scale has yet to be validated in schizophrenia and comorbid SUD, an exploratory approach was taken in this research to avoid prematurely settling on a model that may only adequately describe the construct among this population.

Table 12. *Correlations Among Quality of Life Scale Intrapsychic Deficit Subscale Items*

Item	1	2	3	4	5	6	7
1. Purpose	-						
2. Motivation	.60**	-					
3. Curiosity	.40**	.48**	-				
4. Anhedonia	.40**	.52**	.45**	-			
5. Time Utilization	.40**	.55**	.40**	.50**	-		
6. Empathy	.34**	.37**	.42**	.45**	.31**	-	
7. Engagement	.38**	.43**	.43**	.49**	.36**	.57**	-

Note. Analyses were conducted on the baseline sample ($n = 535$).

** $p < .01$, 2-tailed.

As can be seen in Figure 7, the scree plot of the intrapsychic deficit subscale components suggested a 2-factor solution. Nonetheless, a 3-factor solution was also examined from principal axis analyses, in addition to a 2-factor solution, to explore the degree to which intrapsychic

deficit subscale items fit intrinsic motivation factor solutions (curiosity, purpose, and motivation) previously identified in schizophrenia patients (see Nakagami et al., 2008).

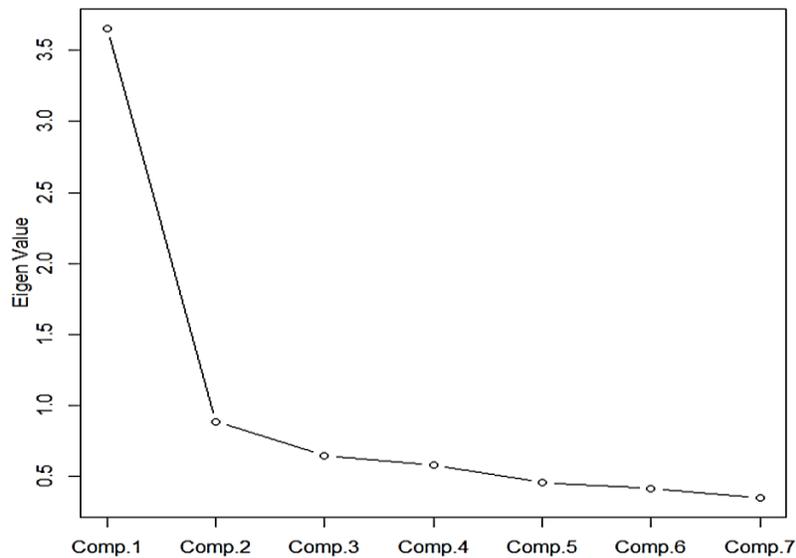


Figure 7. Screeplot of Eigen Values for the QLS Intrapyschic Deficit Subscale Components

As can be seen in Table 13, both 2 and 3-factor solutions with varimax rotation produced numerous split loadings and generally indefinite factor solutions that raised serious concern about prematurely settling on an intrinsic motivation factor without exploring alternative solutions. Therefore, this series of exploratory analyses proceeded by investigating other solutions that may better fit the data structure.

Table 13. *Factor Structure of the Intrapsychic Deficit Subscale with Varimax Rotation*

Variable	2-Factor Solution ^a		3-Factor Solution ^b		
	Factor 1	Factor 2	Factor 1	Factor 2	Factor 3
	Standardized Loadings				
Purpose	.60	.27	.21	.26	.64
Motivation	.84	.24	.45	.23	.69
Curiosity	.46	.43	.34	.40	.34
Anhedonia	.51	.48	.56	.43	.25
Time Utilization	.60	.43	.59	.20	.35
Empathy	.21	.72	.18	.71	.19
Engagement	.31	.70	.24	.68	.24

Note. Factor loadings greater than .40 appear in boldface.

^a $\chi^2(8, n = 535) = 19.75, p = .011$

^b $\chi^2(3, n = 535) = 0.27, p = .966$

Given the high degree of significant correlations among QLS intrapsychic deficit subscale items (see Table 12), subsequent exploratory analyses proceeded using principal axis factoring, with oblique oblimin rotation instead of the orthogonal varimax rotation used by Nakagami and colleagues (2008) (see Table 13). As methodologists have cautioned (Fabrigar, MacCallum, Wegener, & Strahan, 1999; Preacher, Zhang, Kim, & Mels, 2013), solely relying on an orthogonal rotation (varimax) forfeits any knowledge of the existing correlations among factors, which signals the importance of exploring whether using an oblique rotation improves the degree to which intrinsic deficit subscale items fit the intrinsic motivation factor solutions previously identified in schizophrenia (see Nakagami et al., 2008). An oblique solution is also more appropriate and likely given that the items identifying different factors come from the same subscale, and thus are factors hypothesized to be correlated. As can be seen in Table 14, both 2

and 3-factor solutions with oblique oblimin rotation provided a good fit to the observed data, with a 3-factor solution providing a better fit than the 2-factor solution.

Table 14. *Factor Structure of the Intrapsychic Deficit Subscale with Oblique Oblimin Rotation*

Variable	2-Factor Solution ^a		3-Factor Solution ^b		
	Factor 1	Factor 2	Factor 1	Factor 2	Factor 3
Standardized Loadings					
Purpose	.60	.07	.75	.07	-.12
Motivation	.91	-.06	.75	-.03	.16
Curiosity	.37	.33	.24	.32	.17
Anhedonia	.40	.37	.04	.33	.49
Time Utilization	.60	.08	.24	.01	.52
Empathy	-.50	.78	-.02	.78	-.02
Engagement	.05	.73	.05	.71	.04
Factor Correlations					
	Factor	1	2	3	
3-Factor Solution					
	Factor 1	-			
	Factor 2	.60	-		
	Factor 3	.68	.53	-	

Note. Factor loadings greater than .40 appear in boldface.

^a $\chi^2(8, n = 535) = 19.75, p = .011$

^b $\chi^2(3, n = 535) = 0.27, p = .966$

Although a 3-factor oblique solution appeared to best represent the observed data, the pattern of results obtained was not congruent with the 2-factor orthogonal solution previously found among community patients with schizophrenia by Nakagami and colleagues (2008). As such, the hypothesis (Hypothesis 1a) that a 2-factor orthogonal solution would yield an intrinsic

motivation factor consisting of the QLS's intrapsychic deficit items of purpose, motivation, and curiosity was not supported. This current research found that the items of purpose and motivation load together on the same factor; as expected; however, the curiosity item did not load with these items or on any other factor in any of the solutions examined. Consequently, 1 of the 3 items (curiosity) will not be retained as part of the intrinsic motivation factor, as this exploratory investigation suggests that curiosity does not strongly represent part of the intrinsic motivation construct in comorbid SUD and schizophrenia. Subsequent analyses proceeded using this empirically-derived 2-item scale, which consists of the QLS items of purpose and motivation, to measure intrinsic motivation deficits in comorbid schizophrenia and SUD.

2. Internal Consistency of the Intrinsic Motivation Measure

Having found preliminary evidence of an intrinsic motivation factor that consists of 2-items (purpose and motivation) from the QLS in comorbid SUD and schizophrenia, the internal consistency of this scale was then examined. This 2-item measure showed surprisingly strong levels of internal consistency, given the small number of items (see Table 15). These results support the hypothesis (Hypothesis 1b) that the intrinsic motivation measure would demonstrate at least adequate levels of internal consistency ($\alpha \geq .70$) in comorbid SUD and schizophrenia.

Table 15. *Intrinsic Motivation Measure Internal Consistency*

Item	Item		Alpha
	Alpha	Total	Without
Total	.75	-	-
Purpose		.59	-
Motivation		.59	-

Note. Analyses were conducted on the baseline sample ($n = 535$).

3. Re-test Reliability of the Intrinsic Motivation Measure

After demonstrating that the 2-item intrinsic motivation measure possesses at least adequate levels of internal consistency among persons with comorbid SUD and schizophrenia, the re-test reliability of this intrinsic motivation measure was evaluated. As can be seen in Table 16, this intrinsic motivation measure satisfied re-test reliability criteria of 0.40 or greater across study assessment periods (baseline to 6-month; 6-month to 12-month). As such, the hypothesis (Hypothesis 1c) that the intrinsic motivation measure would demonstrate at least minimally sufficient levels of re-test reliability ($r \geq .40$) when examined across the 3 multi-month assessment observation periods of the study was supported.

Table 16. *Correlations Among Participant Intrinsic Motivation Scores Across Study Periods*

Period	0	6	12
0 - Intrinsic Motivation	-		
6 - Intrinsic Motivation	.50**	-	
12 - Intrinsic Motivation	.50**	.60**	-

Note. Analyses were conducted on the intent-to-study sample (baseline, $n = 535$; 6-month, $n = 219$; 1-year, $n = 150$). 0 = Baseline; 6 = 6-month; 12 = 12-month are presented in boldface

** $p < .01$, 2-tailed.

In summary, factor-analytic findings provided strong support for a 3-factor oblique solution with an intrinsic motivation factor consisting of the QLS items purpose and motivation; as expected; however, the curiosity item did not load with these items or on any other factor in any of the solutions examined. Psychometric analyses provided robust support for the reliability of this 2-item intrinsic motivation measure and its re-test reliability in this sample of individuals

with schizophrenia and comorbid SUD. Taken together, such results were persuasive enough to use this 2-item intrinsic motivation measure for informing the subsequent analytic approaches employed for examining the cross-sectional and longitudinal relationships between intrinsic motivation and substance use severity, and whether such relations vary across genders.

D. AIM#2 EXAMINE THE CROSS-SECTIONAL RELATIONSHIPS BETWEEN INTRINSIC MOTIVATION, GENDER, AND SUBSTANCE USE SEVERITY

1. Bivariate Relationship between Intrinsic Motivation and Substance Use Severity

After validating an intrinsic motivation measure consisting of 2-items (purpose and motivation) taken from the QLS in comorbid SUD and schizophrenia, the first step was taken in elucidating the relations between intrinsic motivation and substance use severity by examining the bivariate, cross-sectional relationship between intrinsic motivation and AUS (log)/ DUS (log) scores at baseline. As can be seen in Table 17, small but significant or trend-level relationships were observed between intrinsic motivation scores and AUS (log)/ DUS (log) scores at baseline. Relationship estimates were the largest and only statistically significant for the relationship between intrinsic motivation scores and AUS (log) scores, although a trend toward significance was observed for the association between intrinsic motivation and DUS (log) scores. The direction of these relationships indicated the hypothesis (Hypothesis 2a) that statistically significant negative relations would exist between intrinsic motivation and substance use severity in a bivariate context at baseline was partially supported.

Table 17. *Bivariate Associations Between Intrinsic Motivation and Substance Use Severity at Baseline*

Variable	AUS (log) ^a	DUS (log) ^b
Intrinsic Motivation ^c	-.09*	-.07†

Note. Zero-order correlation analyses were conducted on the baseline sample ($n = 535$). AUS = Alcohol Use Scale; DUS = Drug Use Scale.

^a Higher scores indicate greater alcohol use severity.

^b Higher scores indicate greater drug use severity.

^c Higher scores indicate greater degrees of intrinsic motivation.

† $p < .15$, * $p < .05$, two-tailed.

2. Multivariable Relationship between Intrinsic Motivation and Substance Use Severity, Adjusting for Demographic and Clinical Confounds, Neurocognition and Negative Symptoms

Having found partial support for significant negative relations between intrinsic motivation and substance use severity in a bivariate context, such relationships were further examined in a multivariable context, after adjusting for age, illness chronicity, and total psychopathology. Table 18 presents the results of partial correlation analyses investigating the relations between intrinsic motivation scores and AUS (log)/ DUS (log) scores at baseline, after adjusting for the effects of these potential demographic and clinical confounds. As can be seen in this table, only small and statistically non-significant relations were observed between intrinsic motivation scores and AUS (log)/ DUS (log) scores in this multivariable context, adjusting for age, illness chronicity, and overall psychopathology. Such findings surprisingly suggest no cross-sectional relationship between intrinsic motivation and substance use severity

among persons with comorbid SUD and schizophrenia after adjusting for these clinical and demographic and clinical confounds.

Table 18. *Multivariable Associations Between Intrinsic Motivation and Substance Use Severity at Baseline*

Variable	AUS (log) ^a	DUS (log) ^b
Intrinsic Motivation ^c	-.06	-.05

Note. Partial correlation analyses adjusting for age, illness chronicity, and psychopathology were conducted on the baseline sample ($n = 535$). AUS = Alcohol Use Scale; DUS = Drug Use Scale.

^a Higher scores indicate greater alcohol use severity.

^b Higher scores indicate greater drug use severity.

^c Higher scores indicate greater degrees of intrinsic motivation.

Upon finding little to no support for significant cross-sectional relations between intrinsic motivation and substance use severity after controlling for age, illness chronicity, and overall psychopathology, such relations were further investigated using hierarchical regression analyses. This approach examines the relationship between intrinsic motivation scores and AUS (log)/DUS (log) scores, adjusting for these demographic and clinical confounds, neurocognition and negative symptoms. While this series of analyses may seem excessive, given the null results garnered from the partial correlation analyses, such an approach affords benefits beyond the previous analyses. For example, the potential for a suppression effect of negative symptoms and neurocognition should not be overlooked, given that the aspects of intrinsic motivation that are most strongly associated with substance use severity may only be those that are independent of negative symptoms and neurocognition (see Paulhus, Robins, Trzesniewski, & Tracy, 2004, for

review). In addition, this approach allows for the examination of the effects of study site variability and participant comorbidity status on the relationship between intrinsic motivation and substance use severity.

Table 19 presents the results of a series of hierarchical linear regression models examining the relationship between intrinsic motivation scores and AUS (log)/ DUS (log) scores at baseline, after adjusting for demographic and clinical confounds, negative symptoms and neurocognition. As can be seen in this table, a significant negative prediction of AUS (log) scores was observed by intrinsic motivation scores, after adjusting for the effects of demographic and clinical confounds, negative symptoms and neurocognition, $B = -0.03$, $t(457) = -2.02$, $p = .043$. In addition, a significant prediction of DUS (log) scores was observed by intrinsic motivation scores, after adjusting for these potential confounds, $B = -0.03$, $t(457) = -2.36$, $p = .018$. Further, patient comorbidity status and total psychopathology scores were also found to significantly predict DUS scores (all $p < .001$). No other clinical or demographic confounders were observed to significantly predict AUS (log) or DUS (log) scores (all $p > .415$).

Overall, results garnered from such hierarchical regression analyses showed significant negative relations exist between intrinsic motivation scores and AUS (log)/ DUS (log) scores at baseline, after adjusting for demographic and clinical confounds, neurocognition and negative symptoms. While such results are inconsistent with those observed in the partial correlation analyses (see Table 18), methodologists have indicated that this paradoxical pattern occurs when variables (i.e., neurocognition and negative symptoms) improve the prediction of the criterion independent variable (i.e., intrinsic motivation) by suppressing criterion irrelevant variance (see Paulhus et al., 2004, for review). Consequently, results of this series of multivariable analyses appear to suggest a suppression effect of neurocognition and negative symptoms on relations

between intrinsic motivation and substance use severity at baseline.

In summary, results garnered from the hierarchical regression analyses support the hypothesis (Hypothesis 2b) that significant negative relations would exist between intrinsic motivation scores and substance use severity scores in a multivariable context, adjusting for demographic and clinical confounds, negative symptoms and neurocognition.

Table 19. *Associations Between Intrinsic Motivation and Substance Use Severity after Adjusting for Neurocognition and Negative Symptoms*

Variable/Step	AUS (log) ^a			DUS (log) ^b		
	<i>B</i>	<i>SE</i>	<i>p</i>	<i>B</i>	<i>SE</i>	<i>p</i>
Step 1	Demographic and Clinical Characteristics					
Age	0.00	0.01	.732	0.00	0.02	.824
Comorbidity Status ^c	0.00	0.02	.923	0.20	0.02	<.001
Study Site ^d	0.11	0.13	.403	0.03	0.13	.818
Illness Chronicity ^e	0.01	0.02	.744	-0.00	0.02	.869
PANSS Total ^f	0.00	0.02	.762	0.04	0.15	<.001
	Negative Symptoms and Neurocognition					
Step 2	$\Delta R^2 = .00$			$\Delta R^2 = .00$		
PANSS Negative ^g	-0.01	0.02	.565	-0.03	0.02	.300
Neurocognition Total ^h	0.01	0.16	.742	-0.00	0.01	.704
	Intrinsic Motivation					
Step 3	$\Delta R^2 = .01$			$\Delta R^2 = .01$		
Intrinsic Motivation ⁱ	-0.03	0.01	.043	-0.03	0.01	.018

Note. Analyses were conducted on the baseline sample ($n = 535$). AUS = Alcohol Use Scale; DUS = Drug Use Scale; PANSS = Positive and Negative Syndrome Scale. Step 1 and Step 2 are only presented once to reduce visual clutter and to avoid redundancy.

^a Higher scores indicate greater alcohol use severity.

^b Higher scores indicate greater drug use severity.

^c Comorbidity Status = 3 mutually exclusive groups based on DSM-IV SCID diagnoses. *B* represents the average effect of participant comorbidity status.

^d Study Site = 57 study sites for the CATIE trial. *B* represents the average effect of study site.

^e Higher values indicate greater years of schizophrenia treatment.

^f Higher scores indicate greater psychopathology.

^g Higher scores indicate greater degrees of negative symptomatology

^h Higher scores indicate better neurocognitive function.

ⁱ Higher scores indicate greater degrees of intrinsic motivation.

3. Bivariate Relationship between Gender and Substance Use Severity

Having found that intrinsic motivation scores were statistically related to AUS (log)/DUS (log) scores after adjusting for demographic and clinical confounds, neurocognition and negative symptoms, the relations between gender and substance use severity were investigated. Comparable degrees of substance use severity were observed for men and women with comorbid SUD and schizophrenia at baseline (see Table 20). Such findings suggest no cross-sectional relations between gender and substance use severity among persons with comorbid SUD and schizophrenia. The hypothesis that men would demonstrate significantly higher mean scores on the AUS (log) or the DUS (log) than women at baseline (Hypothesis 2c) was not supported.

Table 20. *Comparisons of Substance Use Severity Between Men and Women at Baseline*

Variable	Men	Women	Analysis ^a	
	<i>n</i> = 449	<i>n</i> = 86	<i>t</i>	<i>p</i>
	<i>M</i> (<i>SD</i>)	<i>M</i> (<i>SD</i>)		
AUS (log) ^b	1.00 (0.29)	0.93 (0.28)	1.25	.210
DUS (log) ^c	0.31 (0.14)	0.35 (0.04)	0.17	.865

Note. Analyses were conducted on the baseline sample (*n* = 535). AUS = Alcohol Use Scale; DUS = Drug Use Scale.

^a Independent sample *t*-test (two-tailed).

^b Higher mean scores indicate greater alcohol use severity.

^c Higher mean scores indicate greater drug use severity.

4. Bivariate Relationship between Gender and Intrinsic Motivation

After observing comparable degrees of substance use severity between the genders at baseline, the cross-sectional relationship between men and women and intrinsic motivation was investigated. Women demonstrated significantly higher intrinsic motivation scores than men at baseline (Table 21). This finding supports the hypothesis (Hypothesis 2d) that men would demonstrate significantly greater deficits in intrinsic motivation compared to women at baseline.

Table 21. *Comparisons of Intrinsic Motivation Between Men and Women at Baseline*

Variable	Men	Women	Analysis ^a	
	<i>n</i> = 449	<i>n</i> = 86	<i>t</i>	<i>p</i>
	<i>M</i> (<i>SD</i>)	<i>M</i> (<i>SD</i>)		
Intrinsic Motivation ^b	4.71 (2.66)	5.84 (2.89)	3.53	<.001

Note. Analyses were conducted on the baseline sample (*n* = 535).

^a Independent sample *t*-test (two-tailed).

^b Higher mean scores indicate greater degrees of intrinsic motivation.

E. AIM#3 EXAMINE THE LONGITUDINAL CONTRIBUTION OF CHANGES IN INTRINSIC MOTIVATION TO CHANGES IN SUBSTANCE USE SEVERITY, AND THEN INVESTIGATE THE IMPACT OF GENDER ON THESE RELATIONSHIPS

1. Longitudinal Change in Substance Use Severity

To begin examining the longitudinal contribution of changes in intrinsic motivation to changes in substance use severity, and the impact of gender on such relations, the 1-year rates of

change in AUS (log)/ DUS (log) scores were investigated. This was accomplished by fitting two linear unconditional growth curve models to the longitudinal data structure, where AUS (log) and DUS (log) scores were each predicted from time (0 = baseline, 0.5 = follow-up at 6-months, and 1 = follow-up at 1-year). Such an approach provides useful empirical evidence for determining a proper specification of individual growth over time (i.e., 1-year rates of change in AUS [log]/ DUS [log] scores) and baseline statistics (i.e., initial status in AUS [log]/ DUS [log] scores) for expanding to subsequent conditional models. Consistent with guidelines for the appropriateness of using linear growth curve models to capture systematic change in individual substance use severity phenomena over time, sufficient between-patient dependence was achieved for both AUS (log) (ICC = 0.56) and DUS (log) (ICC = 0.59) unconditional models (Hox, 2000; Raudenbush & Bryk, 2009). As can be seen in Table 22, the χ^2 of difference test favored the AUS (log)/ DUS (log) unconditional models fit with level-1 AR(1) error covariance structures. Consequently, final AUS (log)/ DUS (log) unconditional models were fit with level-1 AR(1) error covariance structures and were estimated using REML methods (Bliese & Ployhart, 2002; Raudenbush & Bryk, 2009).

Table 22. Comparisons of Deviance Statistics Across Alternative Models (Unconditional Models)

AUS (log) Model Summary	Deviance	df	
1- Unrestricted Model	-80.91	6	
2- AR(1)	-124.84	7	
AUS (log) Model Comparison	Deviance Difference	χ^2 ^a	p
Model 1 vs. Model 2	43.93	87.86	<.001
DUS (log) Model Summary	Deviance	df	
1- Unrestricted Model	-142.31	6	
2- AR(1)	-174.07	7	
DUS (log) Model Comparison	Deviance Difference	χ^2 ^b	p
Model 1 vs. Model 2	31.76	63.51	<.001

Note. Analyses were conducted on the intent-to-study sample (baseline, $n = 535$; 6-month, $n = 219$; 1-year, $n = 150$). AUS = Alcohol Use Scale; DUS = Drug Use Scale. AR(1) = first order autoregressive error structure. FIML estimation was used for comparing model1 with model2.

^a χ^2 of difference test based on the deviance statistic indicated that adding an AR(1) error covariance structure to the unrestricted model improved the AUS unconditional model fit.

^b χ^2 of difference test based on the deviance statistic indicated that adding an AR(1) error covariance structure to the unrestricted model improved the DUS unconditional model fit.

Table 23 presents the results for the AUS (log) and DUS (log) unconditional growth curve models. As can be seen in this table, the estimated average AUS (log) score at baseline was 1.00 (log), with patients showing significant reductions in alcohol use severity by -0.07 (log) every six months over 1-year, $t(367) = -3.72, p < .001$. The estimated average DUS (log) score at baseline was 0.98 (log), with patients exhibiting significant reductions in drug use severity by -0.09 (log) every six months over 1-year, $t(367) = -4.22, p < .001$. In addition, significant variability was observed among patients in terms of their mean baseline AUS scores, [$\tau_{01} = 0.04$ (95% $CI = 0.18$ to 0.24)]; and with regard to the mean rates of reduction in alcohol use severity

observed over 1-year, [$\tau_{11} = 0.01$ (95% *CI* = 0.01 to 1.64)]. Patients also demonstrated significant variability with regard to their mean baseline DUS scores, [$\tau_{01} = 0.05$ (95% *CI* = 0.18 to 0.26)], but not in terms of the mean rates of reduction in drug use severity observed over 1-year, [$\tau_{11} = 0.04$ (95% *CI* = 0.14 to -0.20)]. While significant variability was not observed in terms of the mean rates of reduction in drug use severity observed over 1-year, subgroups may exist for whom there are differences in such longitudinal trajectories (i.e., women, patients with low intrinsic motivation), and thus the moderators of these slopes are still tested in subsequent conditional growth models (Hoffman, 1997). Taken together, results garnered from these unconditional models support the hypothesis (Hypothesis H3a) that patients would demonstrate, on average, significant reductions in AUS (log) and DUS (log) scores over 1-year, suggesting significant longitudinal improvement in substance use severity.

Table 23. 1-Year Trajectories of Substance Use Severity (Unconditional Models)

Parameter	AUS (log) Unconditional Model ^a			
	Coefficient	SE	t	p
Fixed Effect				
Mean Initial Status, β_{00}	1.00	0.01	80.15	<.001
Mean Growth Rate, β_{10}	-0.07	0.02	-3.72	<.001
Random Effect	Variance Component	95% CI		
Initial Status, $\text{Var}(r_{0i}) = \tau_{01}$	0.04	0.18 to 0.24		
Growth Rate, $\text{Var}(r_{1i}) = \tau_{11}$	0.01	0.01 to 1.64		
Level-1 error, $\text{Var}(e_{1i}) = \sigma^2$	0.04	-		
Parameter	DUS (log) Unconditional Model ^b			
	Coefficient	SE	t	p
Fixed Effect				
Mean Initial Status, β_{00}	0.98	0.01	69.98	<.001
Mean Growth Rate, β_{10}	-0.09	0.02	-4.22	<.001
Random Effect	Variance Component	95% CI		
Initial Status, $\text{Var}(r_{0i}) = \tau_{01}$	0.05	0.18 to 0.26		
Growth Rate, $\text{Var}(r_{1i}) = \tau_{11}$	0.04	0.14 to -0.20		
Level-1 error, $\text{Var}(e_{1i}) = \sigma^2$	0.05	-		

Note. Analyses were conducted on the intent-to-study sample (baseline, $n = 535$; 6-month, $n = 219$; 1-year, $n = 150$). AUS = Alcohol Use Scale; DUS = Drug Use Scale.

^a Only the final AUS unconditional model is presented to reduce visual clutter, which was fit using AR(1) and REML estimation.

^b Only the final DUS unconditional model is presented to reduce visual clutter, which was fit using AR(1) and REML estimation.

2. Longitudinal Relationship between Changes in Intrinsic Motivation and Changes in Substance Use Severity

After finding that patients demonstrated significant reductions in substance use severity over the 1-year study, the longitudinal contribution of changes in intrinsic motivation to changes

in substance use severity was investigated. This was accomplished by expanding the previously fit unconditional models to conditional models such that AUS (log)/ DUS (log) scores were each predicted from time and a time-varying intrinsic motivation variable. Notably, there is no consensus on whether to fit the slopes of time-varying variables as fixed or random (McCoach & Kaniskan, 2010), and methodologists have cautioned against fitting such slopes as randomly varying by default particularly when individual phenomena are observed over few measurement occasions (i.e., < 5) (Lou & Kwok, 2006; Meyers & Beretvas, 2006; Raudenbush & Bryk, 2009; McCoach & Kaniskan, 2010). As such, given that only three measurement occasions (baseline, 6-months, and 1-year) were used to test this hypothesis, time-varying intrinsic motivation's slope was fit as a fixed effect only in the final AUS (log)/ DUS (log) conditional growth models, which provides estimates of the average relationship between changes in intrinsic motivation and changes in substance use severity for patients in the overall sample.

Table 24 presents the results of the final conditional growth curve models where AUS (log)/ DUS (log) scores were each predicted from time and time-varying intrinsic motivation. As can be seen in this table, the average effect of intrinsic motivation on AUS (log) scores was highly statistically significant ($\beta_{20} = -0.01, p < .001$). Such results indicate that average improvements in intrinsic motivation were associated with significant reductions in patient's alcohol use severity over the 1-year study. In addition, the average effect of intrinsic motivation on DUS (log) scores was also statistically different from 0 ($\beta_{20} = -0.01, p = .024$). These findings indicate that average improvements in intrinsic motivation were associated with significant reductions in patient's drug use severity over 1-year. Consequently, it appears that the results garnered from these conditional growth curve analyses lend support to the Hypothesis (Hypothesis 3b) that patients would exhibit significant reductions in substance use severity as

they make improvements in intrinsic motivation over the 1-year study period.

Table 24. *1-Year Relationship Between Changes in Intrinsic Motivation and Changes in Substance Use Severity (Conditional Growth Models)*

Parameter		AUS (log) Conditional Model ^a			
Fixed Effect		Coefficient	SE	t	p
	Mean Initial Status, β_{00}	1.06	0.02	50.45	<.001
	Mean Growth Rate, β_{10}	-0.08	0.02	-4.11	<.001
	Time-Varying IM, β_{20}	-0.01	0.01	-3.79	<.001
Parameter		DUS (log) Conditional Model ^b			
Fixed Effect		Coefficient	SE	t	p
	Mean Initial Status, β_{00}	1.02	0.02	45.07	<.001
	Mean Growth Rate, β_{10}	-0.09	0.02	-4.15	<.001
	Time-Varying IM, β_{20}	-0.01	0.01	-2.25	.024

Note. Analyses were conducted on the intent-to-study sample (baseline, $n = 535$; 6-month, $n = 219$; 1-year, $n = 150$). AUS = Alcohol Use Scale; DUS = Drug Use Scale; IM = Intrinsic Motivation.

^a Only the final AUS conditional model is presented to reduce visual clutter, which was fit with AR(1) and accounted for heteroscedasticity of level-1 errors. REML estimation was used.

^b Only the final DUS conditional model is presented to reduce visual clutter, which was fit using AR(1) and REML estimation.

Previous preliminary (Section 4.B.4) and cross-sectional (Section 4.D.2) analyses signaled age, illness chronicity, overall psychopathology, and comorbidity status as potential confounds to the relationship between intrinsic motivation and substance use severity. As such, analysis proceeded by including these potential confounds as time-invariant covariates at level-2, as they may account for differences in estimating the longitudinal relationships between changes in intrinsic motivation and changes in substance use severity. In addition, AUS (log)/ DUS (log)

conditional models adjusted for phase1 randomization medication effects at level-2.

Table 25 presents the results of the AUS (log) conditional growth curve model where such scores were predicted from time and time-varying intrinsic motivation, adjusting for age, illness chronicity, overall psychopathology, comorbidity status, and phase1 randomization. As can be seen in this table, the average effect of intrinsic motivation on AUS (log) scores was statistically different from 0 ($\beta_{20} = -0.01, p < .001$). Therefore, after adjusting for these potential demographic and clinical confounds, the results continued to suggest that average improvements in intrinsic motivation were associated with significant reductions in patient's alcohol use severity over 1-year. Consequently, these findings indicate that intrinsic motivation change is an important incremental predictor of reductions in patient's alcohol use severity above and beyond the effects of age, illness chronicity, overall psychopathology, comorbidity status, and phase1 randomization.

Table 25. 1-Year Relationship Between Changes in Intrinsic Motivation and Changes in Alcohol Use Severity, Adjusting for Demographic and Clinical Confounds

Fixed Effect	Parameter	Coefficient	SE	<i>t</i>	<i>p</i>
Initial Status	β_{00}	1.06	0.04	24.03	<.001
AUD/ SUD ^a	β_{01}	0.05	0.03	1.69	.090
SUD ^a	β_{02}	-0.68	0.03	-1.96	.049
AUD ^b	β_{03}	0.06	0.03	1.96	.050
Quetiapine ^c	β_{04}	-0.01	0.04	-0.41	.681
Perphenazine ^c	β_{05}	-0.01	0.04	-0.25	.801
Ziprasidone ^c	β_{06}	-0.01	0.05	-0.28	.778
Risperidone ^c	β_{07}	-0.01	0.04	-0.15	.876
Olanzapine ^d	β_{08}	0.01	0.04	0.41	.681
Age	β_{09}	-0.00	0.00	-0.07	.940
Chronicity	β_{010}	0.00	0.00	0.17	.863
PANSS Total	β_{011}	0.00	0.01	0.13	.893
Growth Rate	β_{10}	-0.07	0.05	-1.26	.205
Time x AUD/ SUD ^a	β_{11}	0.01	0.05	-0.23	.813
Time x SUD ^a	β_{12}	-0.02	0.06	0.29	.765
Time x AUD ^b	β_{13}	0.01	0.05	0.29	.770
Time x Quetiapine ^c	β_{14}	-0.05	0.06	-0.82	.412
Time x Perphenazine ^c	β_{15}	0.03	0.06	0.65	.513
Time x Ziprasidone ^c	β_{16}	0.03	0.07	0.45	.652
Time x Risperidone ^c	β_{17}	0.02	0.05	0.43	.666
Time x Olanzapine ^d	β_{18}	0.05	0.06	0.82	.412
Time x Age	β_{19}	-0.00	0.00	-1.45	.147
Time x Chronicity	β_{120}	0.00	0.00	0.96	.333
Time x PANSS Total	β_{121}	0.00	0.00	0.24	.805
Time-Varying IM	β_{20}	-0.01	0.01	-3.61	<.001

Note. Analyses were conducted on the intent-to-study sample (baseline, *n* = 535; 6-month, *n* = 219; 1-year, *n* = 150). IM = Intrinsic Motivation. AUD/ SUD = alcohol use disorder and other substance use disorder; SUD = substance use disorder other than alcohol use disorder; AUD =

alcohol use disorder; PANSS = Positive and Negative Syndrome Scale. Only the final AUS (log) model is presented to reduce visual clutter, which was fit using AR(1) and accounted for heteroscedasticity of level-1 errors. REML estimation was used. Age, Chronicity, and PANSS Total were grand mean centered.

^aReference category is AUD.

^bReference category is SUD.

^cReference category is Olanzapine.

^dReference category is Quetiapine.

Table 26 presents the results of the DUS (log) conditional growth curve model where such scores were predicted from time and time-varying intrinsic motivation, adjusting for age, illness chronicity, overall psychopathology, comorbidity status, and phase1 randomization. As can be seen in this table, the average effect of intrinsic motivation on DUS (log) scores was statistically significant ($\beta_{20} = -0.01, p = .039$). Therefore, after adjusting for such confounds, the findings continued to suggest that average improvements in intrinsic motivation were associated with significant reductions in patient's drug use severity over 1-year. These findings also signal that intrinsic motivation change is a key incremental predictor to reductions in patient's drug use severity above and beyond the effects of age, illness chronicity, overall psychopathology, comorbidity status, and phase1 randomization.

Table 26. *1-Year Relationship Between Changes in Intrinsic Motivation and Changes in Drug Use Severity, Adjusting for Demographic and Clinical Confounds*

Fixed Effect	Parameter	Coefficient	SE	<i>t</i>	<i>p</i>
Initial Status	β_{00}	0.85	0.04	17.98	<.001
AUD/ SUD ^a	β_{01}	0.29	0.03	8.31	<.001
SUD ^a	β_{02}	0.27	0.03	7.36	<.001
AUD ^b	β_{03}	0.06	0.03	1.96	.050
Quetiapine ^c	β_{04}	-0.06	0.04	-1.29	.196
Perphenazine ^c	β_{05}	-0.05	0.05	-1.14	.252
Ziprasidone ^c	β_{06}	-0.09	0.04	-1.99	.046
Risperidone ^c	β_{07}	-0.07	0.04	-1.72	.085
Olanzapine ^d	β_{08}	0.01	0.04	0.41	.681
Age	β_{09}	-0.00	0.00	-0.09	.927
Chronicity	β_{010}	-0.00	0.00	-0.92	.357
PANSS Total	β_{011}	0.00	0.00	2.70	.007
Growth Rate	β_{10}	-0.07	0.06	-1.20	.229
Time x AUD/ SUD ^a	β_{11}	-0.12	0.06	-2.11	.035
Time x SUD ^a	β_{12}	-0.11	0.06	-1.82	.068
Time x AUD ^b	β_{13}	0.01	0.05	0.29	.770
Time x Quetiapine ^c	β_{14}	0.74	0.07	0.97	.332
Time x Perphenazine ^c	β_{15}	0.09	0.07	1.29	.197
Time x Ziprasidone ^c	β_{16}	0.22	0.08	2.60	.009
Time x Risperidone ^c	β_{17}	0.10	0.06	1.51	.131
Time x Olanzapine ^d	β_{18}	0.05	0.06	0.82	.412
Time x Age	β_{19}	0.00	0.00	0.50	.612
Time x Chronicity	β_{120}	0.00	0.00	0.08	.932
Time x PANSS Total	β_{121}	-0.00	0.00	-0.27	.783
Time-Varying IM	β_{20}	-0.01	0.00	-2.06	.039

Note. Analyses were conducted on the intent-to-study sample (baseline, $n = 535$; 6-month, $n = 219$; 1-year, $n = 150$). IM = Intrinsic Motivation. AUD/ SUD = alcohol use disorder and other

substance use disorder; SUD = substance use disorder other than alcohol use disorder; AUD = alcohol use disorder. PANSS = Positive and Negative Syndrome Scale. Only the final DUS (log) model is presented to reduce visual clutter, which was fit using AR(1) and REML estimation. Age, Chronicity, and PANSS Total were grand mean centered.

^aReference category is AUD.

^bReference category is SUD.

^cReference category is Olanzapine.

^dReference category is Quetiapine.

Having found evidence that intrinsic motivation change is an important incremental predictor of reductions in patient's alcohol/ drug use severity above and beyond the effects of several key demographic and clinical confounders, the consistency of these findings were further examined, adjusting for neurocognition and negative symptoms. Even after adjusting for key demographic and clinical confounds, neurocognition and negative symptoms, the findings continued to suggest that average improvements in intrinsic motivation were associated with significant reductions in patient's substance use severity over 1-year (see Table 26).

Taken together, results garnered from the AUS (log)/ DUS (log) conditional models highlight the importance of longitudinal changes in intrinsic motivation to changes in substance use severity among individuals with schizophrenia and comorbid substance use disorders. This series of conditional growth curve analyses support the study hypothesis (Hypothesis 3b) that improvements in intrinsic motivation would be associated with significant reductions in substance use severity over the 1-year study.

Table 27. 1-Year Relationship Between Changes in Intrinsic Motivation and Changes in Substance Use Severity, Adjusting for Demographic and Clinical Confounds, Neurocognition and Negative Symptoms

Fixed Effect	Parameter	Coefficient	SE	<i>t</i>	<i>p</i>
AUS (log) Conditional Growth Model ^a					
Initial Status	β_{00}	1.07	0.04	24.20	<.001
PANSS Negative	β_{012}	-0.01	0.00	-1.48	.137
Neurocognition	β_{013}	-0.01	0.02	-0.03	.979
Growth Rate	β_{10}	-0.08	0.05	-1.50	.134
Time x PANSS Negative	β_{122}	0.01	0.00	1.64	.101
Time x Neurocognition	β_{123}	-0.00	0.02	-0.02	.279
Time-Varying IM	β_{20}	-0.01	0.01	-3.95	<.001
DUS (log) Conditional Growth Model ^b					
Initial Status	β_{00}	0.87	0.04	19.20	<.001
PANSS Negative	β_{012}	-0.01	0.00	-2.08	.037
Neurocognition	β_{013}	-0.01	0.01	-0.01	.984
Growth Rate	β_{10}	-0.07	0.06	-1.16	.244
Time x PANSS Negative	β_{122}	0.01	0.00	0.45	.652
Time x Neurocognition	β_{123}	0.02	0.02	0.93	.352
Time-Varying IM	β_{20}	-0.01	0.01	-2.69	.007

Note. Analyses were conducted on the intent-to-study sample (baseline, $n = 535$; 6-month, $n = 219$; 1-year, $n = 150$). AUS = Alcohol Use Scale; DUS = Drug Use Scale; IM = Intrinsic Motivation. PANSS = Positive and Negative Syndrome Scale.

^a Only the final AUS conditional growth model with effects of interest are presented to reduce visual clutter. Age, chronicity, overall psychopathology, comorbidity status, phase 1 randomization, negative symptoms, and neurocognition were adjusted at level-2. Age, Chronicity, PANSS Total, PANSS Negative, and neurocognition were grand mean centered. This model was fit using AR(1) and accounted for heteroscedasticity of level-1 errors. REML estimation was used.

^b Only the final DUS conditional growth model with effects of interest are presented to reduce visual clutter. Age, chronicity, overall psychopathology, comorbidity status, phase 1

randomization, negative symptoms, and neurocognition were adjusted at level-2. Age, Chronicity, PANSS Total, PANSS Negative, and neurocognition were grand mean centered. This model was fit using AR(1) and REML estimation.

Finally, to understand the magnitude of the aforementioned results from a threshold perspective, raw metric conversions were computed from log transformations to discern expected reductions in AUS (raw)/ DUS (raw) scores for one, two, and three unit increases in intrinsic motivation. As can be seen in Table 28, patients AUS (raw)/ DUS (raw) scores reduced by approximately 1 point for a 1 unit increase in IM scores every 6-months over the 1-year study period.

Table 28. Raw metric and threshold conversions for expected increases in AUS/ DUS scores for one, two, and three unit increases in intrinsic motivation

	1x (raw)		2x (raw)		3x (raw)	
	Coefficient	SE	Coefficient	SE	Coefficient	SE
AUS Conditional Model						
Time-Varying IM, β_{20}	0.99	1.01	1.98	2.02	2.97	3.03
	1x (raw)		2x (raw)		3x (raw)	
DUS Conditional Model	Coefficient	SE	Coefficient	SE	Coefficient	SE
Time-Varying IM, β_{20}	0.99	1.01	1.98	2.02	2.97	3.03

Note. Analyses were conducted on the intent-to-study sample (baseline, $n = 535$; 6-month, $n = 219$; 1-year, $n = 150$). AUS = Alcohol Use Scale; DUS = Drug Use Scale; IM = Intrinsic Motivation. 1x = expected decrease in AUS/ DUS for 1 unit increase in IM; 2x = expected decrease in AUS/ DUS for a 2 unit increase in IM; 3x = expected decrease in AUS/ DUS for a 3 unit increase in IM.

3. Moderating Effect of Gender on the Longitudinal Association between Changes in Intrinsic Motivation and Changes in Substance Use Severity

Having demonstrated average longitudinal improvements in intrinsic motivation were associated with significant reductions in substance use severity, the impact of gender on these relationships estimates was investigated through the use of gender moderated conditional growth curve models. As can be seen in Table 29, no significant gender interactions were found for estimates of the relationship between changes in intrinsic motivation and changes in alcohol or drug use severity. Consequently, such findings do not support the study hypothesis (Hypothesis 3c) that women would demonstrate a stronger association between improvements in intrinsic motivation and reductions in substance use severity than men over the 1-year study.

Table 29. 1-Year Relationship Between Changes in Intrinsic Motivation and Changes in Substance Use Severity (Gender Moderated Conditional Growth Models)

Fixed Effect	Parameter	Coefficient	SE	T	p
AUS (log) Gender Moderated Conditional Growth Model ^a					
Initial Status	β_{00}	1.07	0.07	14.53	<.001
Male	β_{01}	-0.04	0.06	0.72	.469
Growth Rate	β_{10}	-0.04	0.06	-0.78	.433
Time-Varying IM	β_{20}	-0.02	0.01	-2.61	.009
Time-Varying IM x Male	β_{21}	0.01	0.01	1.19	.232
DUS (log) Gender Moderated Conditional Growth Model ^b					
Initial Status	β_{00}	0.86	0.07	11.40	<.001
Male	β_{01}	0.02	0.06	0.37	.708
Growth Rate	β_{10}	-0.09	0.06	-1.46	.144
Time-Varying IM	β_{20}	-0.01	0.01	-0.50	.613
Time-Varying IM x Male	β_{21}	-0.01	0.01	-0.61	.536

Note. Analyses were conducted on the intent-to-study sample (baseline, $n = 535$; 6-month, $n = 219$; 1-year, $n = 150$). AUS = Alcohol Use Scale; DUS = Drug Use Scale; IM = Intrinsic Motivation.

^a Only the final AUS gender moderated conditional growth model with effects of interest are presented to reduce visual clutter. Age, chronicity, psychopathology, comorbidity status, phase I randomization, and race were adjusted at level-2. Age, Chronicity, and PANSS Total were grand mean centered. This model was fit using AR(1) and accounted for heteroscedasticity of level-1 errors. REML estimation was used.

^b Only the final DUS gender moderated conditional growth model with effects of interest are presented to reduce visual clutter. Age, chronicity, psychopathology, comorbidity status, phase I randomization, and race were adjusted at level-2. Age, Chronicity, and PANSS Total were grand mean centered. This model was fit using AR(1) and accounted for heteroscedasticity of level-1 errors. REML estimation was used.

After finding no significant gender interactions, follow-up analyses were computed within subsamples of men and women using conditional growth models for estimates of the relations between changes in intrinsic motivation and changes in substance use severity. As can be seen in Table 30, average improvements in intrinsic motivation was associated with significant reductions in drug/ alcohol use severity within the subsample of men. Within the subsample of women, average improvements in intrinsic motivation was only associated with a non-significant trend in alcohol use severity reductions, and no significant or marginal associations were observed with regard to the relationship between intrinsic motivation and drug use severity over 1-year (Table 30). Such findings were unexpected and seemingly contradict the study hypothesis (Hypothesis 3c) that women would show stronger associations between improvements in intrinsic motivation and greater reductions in substance use severity than men over 1-year.

Table 30. 1-Year Relationship Between Changes in Intrinsic Motivation and Changes in Substance Use Severity (Subsamples of Men and Women)

Fixed Effect	Parameter	Coefficient	SE	<i>t</i>	<i>p</i>
Men ^a					
AUS (log) Conditional Growth Model					
Initial Status	β_{00}	1.04	0.05	19.47	<.001
Growth Rate	β_{10}	-0.04	0.07	-0.63	.528
Time-Varying IM	β_{20}	-0.01	0.00	-2.69	.007
Women ^b					
Initial Status	β_{00}	0.98	0.10	9.03	<.001
Growth Rate	β_{10}	-0.06	0.08	-0.71	.478
Time-Varying IM	β_{20}	-0.01	0.01	-1.97	.054
Men ^a					
DUS (log) Conditional Growth Model					
Initial Status	β_{00}	0.89	0.05	16.77	<.001
Growth Rate	β_{10}	-0.05	0.07	-0.67	.497
Time-Varying IM	β_{20}	-0.01	0.00	-2.73	.006
Women ^b					
Initial Status	β_{00}	0.77	0.13	5.73	<.001
Growth Rate	β_{10}	-0.24	0.17	-1.35	.183
Time-Varying IM	β_{20}	0.01	0.01	0.10	.914

Note. AUS = Alcohol Use Scale; DUS = Drug Use Scale; IM = Intrinsic Motivation. Only final AUS/ DUS conditional growth models with effects of interest are presented to reduce visual clutter. Models adjusted for the effects of age, chronicity, psychopathology, comorbidity status, phase1 randomization, and race at level-2. Age, Chronicity, and PANSS Total were grand mean centered. Models were fit using AR(1) and accounted for heteroscedasticity of level-1 errors. REML estimation was used.

^a Analyses were conducted on the subsample of Men (baseline, *n* = 449; 6-month, *n* = 187; 12-month, *n* = 126).

^b Analyses were conducted on the subsample of Women (baseline, *n* = 86; 6-month, *n* = 32; 12-month, *n* = 24).

Having found that investigating gender differences in the relationship between intrinsic motivation and substance use severity yielded results that were weaker and somewhat contrary to expectations, a series of analyses were conducted to explore subsamples for which substance use and SUD diagnosis may have a greater impact on the relationship between intrinsic motivation and substance use severity. For example, variations in smoking, drinking, and other substance use behavior patterns are frequently associated with different clinical outcomes and potentials for achieving remission and recovery among individuals with schizophrenia and comorbid SUD (i.e., Volkow, 2009). Consequently, it stands to reason that the relationship between intrinsic motivation and substance use severity may differ in strength depending on the patient's use of substances (i.e., reported within 90-days of enrollment) and/or specific SUD diagnosis (i.e., SCID DSM-IV [First et al., 1996] diagnosis determined by a project clinician at study baseline). As such, a series of post-hoc exploratory moderator models were carried out to examine the longitudinal association between intrinsic motivation and substance use severity by the substances patient's most frequently reported using within 90-days of enrollment (i.e., tobacco, alcohol, cannabis, and cocaine), as well as the most commonly diagnosed SUDs (i.e., alcohol use disorder, cannabis use disorder, and cocaine use disorder) represented among the sample.

Results revealed no significant interactions between intrinsic motivation and tobacco use ($\beta_{21} = 0.01, p = .590$), alcohol use ($\beta_{21} = 0.01, p = .524$), cannabis use ($\beta_{21} = -0.00, p = .968$), or cocaine use ($\beta_{21} = -0.01, p = .330$) on alcohol use severity. Given this pattern of results, perhaps it is not surprising that no significant interactions were found between intrinsic motivation and tobacco use ($\beta_{21} = -0.00, p = .831$), alcohol use ($\beta_{21} = -0.01, p = .418$), cannabis use ($\beta_{21} = 0.01, p = .191$), or cocaine use ($\beta_{21} = 0.01, p = .425$) on drug use severity either. Having found patient's use of substances within 90-days of enrollment did not moderate the relationship

between intrinsic motivation and substance use severity, potential variations in such relations were then examined by patient's SUD diagnosis. Such results revealed no significant interactions between intrinsic motivation and any of the most commonly diagnosed SUDs (i.e., alcohol use disorder, cannabis use disorder, and cocaine use disorder) on alcohol use severity (all $p > .095$) or on drug use severity (all $p > .426$). Such results do not suggest that subsamples of substance users or patients with specific SUD diagnoses exist for which intrinsic motivation has a greater impact on the relationship between intrinsic motivation and substance use severity among individuals with schizophrenia and comorbid SUD. Consequently, such findings lend support to the previously garnered results suggesting that average improvement changes in intrinsic motivation lead to broad and significant reductions in substance use severity among those who suffer from schizophrenia and comorbid SUD.

V. DISCUSSION

Persistent and pervasive patterns of substance use severity are highly problematic features of SUD pathology that often plague the lives of those who suffer from schizophrenia and comorbid SUD. Despite the introduction of novel rehabilitation programs designed to offset the destabilizing patterns of substance use severity observed among this population, individuals with schizophrenia and SUD remain difficult to engage, demonstrate low motivation to change their substance use behaviors, make slow progress, and drop out of such programs at high rates (see Drake et al., 2008; Horsfall et al., 2009; Hunt et al., 2013, for reviews). Consequently, this comorbidity continues to be associated with less favorable long-term outcomes in schizophrenia and represents a major, unsolved challenge for the clinical management and outcome of this population (Mueser et al., 1990; Green et al., 1999; Green, 2005). Research has increasingly pointed to the importance of intrinsic motivation deficits, particularly those stemming from the negative symptoms of amotivation and anticipatory anhedonia (Heerey & Gold, 2007; Foussias & Remington, 2010; Harvey & Strassnig, 2012), as potential overlooked or unexamined contributors to substance use severity in comorbid schizophrenia and SUD and novel areas for therapeutic intervention (Martino et al., 2002; Graber et al., 2003; Kavanagh et al., 2004a; James et al., 2004; Edwards et al., 2006; Baker et al., 2006), with evidence suggesting that women may demonstrate lower deficits in intrinsic motivation than men (Drapalski et al., 2011). Recently, exciting research on the presence of deficits in intrinsic motivation, or the ability to carry out goal directed behaviors (i.e. reducing substance use severity) in the absence of extrinsic reward (i.e., money or praise) (Deci & Ryan, 2007) has documented pervasive deficits in this domain among individuals with schizophrenia (Nakagami et al., 2008; Yamada et al., 2010; Nakagami et

al., 2010), and linked such deficits to prospective change in psychosocial functioning in a 1-year study of community patients with the disorder (Nakagami et al., 2010). Notably, however, the study of intrinsic motivation in comorbid schizophrenia and SUD and its contribution to substance use severity has been profoundly limited by measures that do not estimate the way such deficits may impede this population's ability to carry out goals, particularly in the areas of interest and drive. As such, the longitudinal role of naturalistic change in intrinsic motivation to change in substance use severity among individuals with schizophrenia and comorbid SUD and the degree to which such relations vary across genders has largely remained unexamined.

This research sought to begin to elucidate the role of prospective naturalistic changes in intrinsic motivation to changes in substance use severity among persons with schizophrenia and comorbid SUD, and the degree to which such relations varied across genders. Secondary data were garnered from 535 community patients with schizophrenia and comorbid SUD who were randomized (first or second generation antipsychotic medication) to phase 1 of the CATIE (see Liberman et al., 2005) study and were treated for up to 1-year to (1) extend validation of a promising measure of intrinsic motivation to persons with schizophrenia and comorbid SUD; (2) examine the cross-sectional relationships between intrinsic motivation, gender, and substance use severity; and (3) investigate the longitudinal contribution of changes in intrinsic motivation to changes in substance use severity, and whether gender moderates this relationship. This chapter provides a summary of the results of this research designed to address these aims, as well as a discussion of the study limitations and implications for future research and social work practice.

A. SUMMARY OF FINDINGS

This investigation provided three important advances to substance use comorbidity in

schizophrenia research. First, psychometric examination of a promising measure of intrinsic motivation deficits in schizophrenia developed by Nakagami et al. (2008), has now been extended to individuals with comorbid SUD and schizophrenia. Of particular importance, results garnered from a series of exploratory factor analyses revealed compelling reasons to question the prevailing 2-factor orthogonal solution of the intrinsic motivation measure in this population, which is considered to be a significant contribution of this research. The resulting 3-factor oblique solution found in this research showed an intrinsic motivation factor consisting of the QLS items purpose and motivation. This solution is inconsistent with the 2-factor orthogonal solution previously found in community schizophrenia samples by Nakagami et al. (2008), which showed an intrinsic motivation factor consisting of QLS items purpose, motivation, and curiosity. Nevertheless, such results were persuasive enough to inform the subsequent analytic approaches used for examining the cross-sectional and longitudinal relations between intrinsic motivation and substance use severity in this sample of patients with schizophrenia and comorbid SUD. Psychometric analyses also provided robust support for the reliability of the intrinsic motivation measure and its re-test reliability among this population.

The second major contribution of this research comes from parsing the relations between intrinsic motivation and substance use severity in schizophrenia and comorbid SUD. Cross-sectional bivariate relationship estimates were significant for the relationship between intrinsic motivation and alcohol use severity, and marginal support was found regarding the association between intrinsic motivation and drug use severity. In addition, cross-sectional multivariate relationship estimates revealed a significant negative prediction of alcohol/ drug use severity by intrinsic motivation, after adjusting for demographic and clinical confounds, neurocognition and negative symptoms. Results of the longitudinal analyses with intrinsic motivation strengthened

the findings garnered in the cross-sectional analyses. Evidence was found suggesting that longitudinal intrinsic motivation improvement is a salient incremental predictor of reductions in patient's alcohol/ drug use severity, above and beyond the effects of age, illness chronicity, overall psychopathology, comorbidity status, and phase 1 randomization medication effects. Such results suggest that changes in intrinsic motivation may be uniquely associated with changes in substance use severity in schizophrenia and comorbid SUD. While future research will need to replicate these findings, it seems promising that interventions seeking to target change in intrinsic motivation deficits as a method of reducing substance use severity in this population, may help offset the long-term disability exacted by chronic and pervasive use.

The third contribution of this study comes from the elucidation of relations between intrinsic motivation, substance use severity, and gender, which were contrary to hypotheses. Analyses of relationships with gender indicated little to no cross-sectional associations between intrinsic motivation and substance use severity, and gender did not moderate the longitudinal association between changes in intrinsic motivation and changes in substance use severity. Specifically, while cross-sectional analyses with gender showed that women had significantly less intrinsic motivation deficits than men at baseline, these women did not maintain a stronger association with intrinsic motivation improvements leading to faster reductions in substance use severity than men over 1-year. Exploratory longitudinal analyses within the subsamples of men and women supported average improvements in intrinsic motivation to significant reductions in substance use severity within the subsample of men, which was unexpected and contrary to expectations. In addition, average improvements in intrinsic motivation were associated with trend-level reductions in alcohol use severity within the subsample of women. Consequently, while gender may play some important role in the relationship between intrinsic motivation and

substance use severity among those with schizophrenia and comorbid SUD, the outcomes of this research suggest that future investigations of these relationships will be needed before deriving firm conclusions.

The broader implications of the three major contributions of this research will be discussed below in detail within the study context in which they were conducted. In addition, a number of important study limitations will also be addressed, which require replication of these results before confirmatory conclusions can be made regarding the factor structure of the 2-item intrinsic motivation instrument and its relations to substance use severity in individuals with schizophrenia and comorbid SUD. First, however, a detailed discussion of the findings of this investigation are provided.

1. Psychometric Properties of the Intrinsic Motivation Measure

One of the major aims of this research, beyond investigating the relationship between intrinsic motivation deficits and substance use severity in schizophrenia and comorbid SUD, was to first extend validation of a promising measure of intrinsic motivation deficits in schizophrenia to schizophrenia and comorbid SUD. This research sought to measure intrinsic motivation by employing a novel cross-situational technique developed by Nakagami et al. (2008), which gauges intrinsic motivation by taking the sum of theoretically pertinent intrapsychic deficit items from the QLS (Heinrichs et al., 1984), probing purpose, motivation, and curiosity (Nakagami et al., 2008). The psychometric findings of this dissertation study signaled a number of strengths and limitations with regard to using the intrinsic motivation measure as developed by Nakagami et al. (2008) to assess intrinsic motivation deficits among individuals with schizophrenia and comorbid SUD. Most notably, a series of exploratory factor analyses provided compelling reasons to challenge the validity of Nakagami and colleague's (2008) 2-factor 3-item (purpose,

motivation, curiosity) orthogonal solution to their intrinsic motivation instrument when applied to individuals with schizophrenia and comorbid SUD. Rather, this current research found clear evidence supporting an alternative factor structure in schizophrenia and comorbid SUD to the 2-factor orthogonal solution previously found in community patients with schizophrenia.

Quite surprisingly, factor analytic results of both 2 and 3-factor solutions with orthogonal rotation were generally uninterpretable due to numerous split loadings and indefinite solutions. Since this series of analyses were being conducted via an exploratory framework, the degree to which oblique rotated solutions improved the model fit were investigated. Of note, no evidence was found from the screeplots of eigenvalues for additional factors extending beyond a 3-factor solution. While factor-analytic results using oblique rotation pointed to the possibility of a 2-factor solution, a moderately correlated 3-factor solution provided a significantly better fit to the observed data. The resulting 3-factor solution found in this research demonstrated an intrinsic motivation factor consisting of the QLS items purpose and motivation; the item of curiosity did not load to together with these items or on any other factor. Consequently, the curiosity item was not retained as part of the intrinsic motivation factor, as the item does not seemingly represent part of the construct in schizophrenia and comorbid SUD. While this factor-analytic solution is at variance with the 2-factor orthogonal solution previously reported in community patients with schizophrenia (Nakagami et al., 2008), it does make some conceptual sense as purpose (i.e., degree to which the person posits realistic, integrated goals for his/her life) and motivation (i.e., extent to which a person is able to initiate or sustain goal directed activity due to adequate drive) both largely rely upon intrinsic processes related to interest and drive, whereas curiosity (i.e., degree to which the person is interested in his/her surroundings) in this sample may be linked with novelty seeking behaviors associated with procuring substances of abuse and less relevant

to intrapsychic deficits (Dervaux et al., 2001).

That previous factor-analytic studies of the intrinsic motivation instrument developed by Nakagami et al. (2008) have yet to demonstrate the 3-factor solution derived in this research may indicate a true difference in the construct among individuals with schizophrenia and comorbid SUD, compared to those with schizophrenia. Another likely alternative, is that the intrinsic motivation construct in schizophrenia and comorbid SUD extends well beyond this 2-item scale, which is of course limited in this study to theoretically relevant items derived from the QLS. It is important to highlight the fact that while deficits in intrinsic motivation are thought to emerge from negative symptoms such as anhedonia and avolition (Barch, 2004; Nakagami et al., 2010), the QLS's anhedonia item was not hypothesized to comprise part of the intrinsic motivation construct in schizophrenia and comorbid SUD. Such a decision was largely influenced by the fact that the QLS's anhedonia item does not measure anticipatory anhedonia or deficits in an individual's ability to formulate goals that are premised on anticipating pleasurable/ desirable outcomes (i.e., such as achieving remission or recovery from substance use severity), but rather estimates a person's present ability to experience pleasure or consummatory anhedonia (Harvey & Strassnig, 2012), which has not been previously identified or linked with intrinsic motivational processes in schizophrenia (Nakagami et al., 2010; Harvey & Strassnig, 2012). Consequently, it remains unclear whether the factor structure found for the intrinsic motivation measure in this research fully represents such deficits in schizophrenia and comorbid SUD, as the QLS does not estimate anticipatory anhedonia, which may comprise part of the intrinsic motivation construct among this population. Nevertheless, it is important to note that this is the first factor analytic study that sought to extend validation of Nakagami and colleagues (2008) intrinsic motivation instrument for schizophrenia to individuals with schizophrenia and comorbid SUD. As such, all

subsequent analyses of the relationship between intrinsic motivation and substance use severity were conducted based upon the 3-factor solution demonstrating an intrinsic motivation factor with purpose and motivation, as this solution provided the best fit to the sample.

While psychometric results pointed to an alternative factor-analytic solution for the intrinsic motivation measure developed by Nakagami et al. (2008) among persons with schizophrenia and comorbid SUD, analyses of the internal consistency and re-test reliability provided strong evidence regarding the reliability and validity of the instrument in this population. Estimates of internal consistency for the intrinsic motivation measure were found to be indicative of at least a minimally adequate internally consistent scale (i.e., $\alpha \geq .70$) as hypothesized (Nunnally, 1978), and satisfied re-test reliability criteria of 0.40 or greater across all study assessment periods (baseline to 6-month; 6-month to 12-month). Reliability estimates mirrored that of Nakagami and colleagues (2008), who found that the internal consistency of their intrinsic motivation measure was $\alpha = .74$ among community patients with schizophrenia.

2. Relationship between Intrinsic Motivation and Substance Use Severity

The first aim of this investigation guided subsequent aims toward an appropriate factor-analytic solution for this sample of individuals with schizophrenia and comorbid SUD, and provided some confidence in the reliable and valid use of such an intrinsic motivation measure's use in substance use comorbidity in schizophrenia research. While garnering such psychometric evidence is critical to employing this intrinsic motivation measure among individuals with schizophrenia and comorbid SUD, the primary focus of this study was on parsing the relations between intrinsic motivation and substance use severity among this population. The critical findings from the analyses of these relations in the second and third aims of this research pointed to a host of interesting cross-sectional and longitudinal relationships between intrinsic motivation

and substance use severity. The bivariate analyses conducted on relations between intrinsic motivation and substance use severity were nonetheless mixed, where such results were only statistically significant for the relationship between intrinsic motivation scores and AUS (log) scores, though a trend was observed indicating an association between intrinsic motivation and DUS (log) scores. As such, some support was found for Hypothesis 2a, indicating intrinsic motivation was significantly and negatively correlated with alcohol use severity at baseline. These results signaled the need to examine the consistency of such results in a multivariable context, adjusting for the confounding effects of age, illness chronicity, and psychopathology.

The patterns of significant and marginal findings observed in the bivariate relationship between intrinsic motivation and substance use severity were not maintained in a multivariable context, after adjusting for age, illness chronicity, and overall psychopathology. While such results seemed to suggest the potential for no cross-sectional relations to exist between intrinsic motivation and substance use severity among the sample, that these effects were null indicates the fact that potential suppression effects of negative symptoms and neurocognition on such relationship estimates should not be overlooked, and a series of hierarchical linear regression analyses were then employed to test Hypothesis 2b. Results of the hierarchical linear regression models revealed a significant negative prediction of AUS (log) scores and DUS (log) scores by intrinsic motivation scores after adjusting for demographic and clinical confounds, negative symptoms and neurocognition. Given these results were at variance with the previous findings conducted in a multivariable context, and such relations were not significant until neurocognition and negative symptoms were entered into the model, a suppression effect of neurocognition and negative symptoms on the relationship between intrinsic motivation and substance use severity seems to explain such phenomena. While there is not an exact statistical test for suppression

effects, this interesting, yet paradoxical pattern of results can occur when variables, such as neurocognition and negative symptoms, improve the prediction of the criterion independent variable (intrinsic motivation) after they are added to the regression model, by suppressing criterion-irrelevant variance (see Paulhaus et al., 2004, for review). Such an explanation is plausible given this pattern of results, and supports Hypothesis 2b, that significant negative relations exist between intrinsic motivation and substance use severity in a multivariable context, adjusting for demographic and clinical confounds, negative symptoms and neurocognition. Consequently, cross-sectional findings suggesting a significant negative relationship between intrinsic motivation and substance use severity laid the foundation for the possibility of such effects to persist over time in this sample of individuals with schizophrenia and comorbid SUD.

Over the course of the 1-year study, patients with schizophrenia and comorbid SUD demonstrated significant average reductions in substance use severity (Hypothesis 3a). Results garnered from the conditional models suggested that intrinsic motivation may accelerate the rate of reduction from substance use severity among patients with schizophrenia and comorbid SUD over 1-year. Longitudinal analyses with intrinsic motivation not only significantly accelerated the rate of reduction from substance use severity recovery for the sample over 1-year, but also strengthened the findings observed with intrinsic motivation in the cross-sectional analyses. For example, evidence was found indicating intrinsic motivation change is an important incremental predictor of reduction in patient's substance use severity above and beyond the effects of age, illness chronicity, overall psychopathology, comorbidity status, and phase1 randomization. Consequently, sufficient support was found for Hypothesis 3b, that improvement in intrinsic motivation would be significantly associated with reductions in substance use severity over 1-year. Further, the consistency of such findings were confirmed for the relationship between

intrinsic motivation and alcohol use severity using a complete case sensitivity analysis (see Appendix A), and trend-level support was observed for the relationship between intrinsic motivation and drug use severity (see Appendix A). While this relatively high degree of consistency observed between primary intent-to-study and completer findings suggests that the statistical conclusions derived from this research are accurate, the high proportion of attrition observed over 1-year signals a need for replication studies. Nevertheless, longitudinal analyses with intrinsic motivation signal promising support for interventions seeking to target change in intrinsic motivation deficits as a method of reducing substance use severity among individuals with schizophrenia and comorbid SUD. These efforts are desperately needed, and could considerably help offset the long-term disability that is exacted by the chronic and pervasive patterns of substance use severity observed among this population.

3. Gender Differences in the Relationship between Intrinsic Motivation and Substance Use Severity

The second aim of this research elucidated the cross-sectional and longitudinal relationships between intrinsic motivation and substance use severity among individuals with comorbid SUD and schizophrenia, and informed subsequent analyses to examine whether such relations varied across genders among this population. First, cross-sectional evidence garnered from this sample of patients with schizophrenia and comorbid SUD suggested that men and women demonstrated comparable degrees of substance use severity. While such results did not support Hypothesis 2c that women would demonstrate lower mean substance use severity scores compared to men, the literature in this area is mixed, with some studies suggesting comparable degrees of substance use severity across genders (Køster et al., 2008; Brunette & Drake, 1997), and others suggesting men exhibit higher mean substance use severity scores compared to

women (Brunette & Drake, 1998). Consistent with one study that examined and found evidence indicating that women in this population demonstrate less intrinsic motivation deficits than men (Drapalski et al., 2011), the cross-sectional evidence garnered from this sample revealed that women exhibited significantly less intrinsic motivation deficits than men at baseline (Hypothesis 2d). While these cross-sectional results seem to suggest the potential for women to continue to improve such deficits in intrinsic motivation at faster rates over 1-year than men, particularly because such women demonstrate better long-term outcomes on several domains (Angermeyer, Kuhn, & Goldstein, 1990; Leung & Chue, 2000), intrinsic motivation was not associated with faster reductions in substance use severity for women in this sample (Hypothesis 3c). Such unexpected findings led to an exploratory investigation of the longitudinal relationship between intrinsic motivation and substance use severity within subsamples of men and women. These analyses led to further unexpected results, as evidence was found supporting improvements in intrinsic motivation to significant reductions in substance use severity within the subsample of men. However, within the subsample of women, improvements in intrinsic motivation were associated with trend-level reductions in alcohol use severity over 1-year. Taken together, such results signal the potential for important differences to exist between men and women regarding the relationship between intrinsic motivation and substance use severity. However, the null and otherwise unexpected outcomes of this research call for replication before firm conclusions can be derived toward initiating gender-based models of care among this population.

B. LIMITATIONS

Prior to addressing the implications of this research, it is critical to discuss a number of limitations, which should both highlight the need for future research in this area as well as serve

to temper substantive interpretations of this work and its implications for research and social work practice. While specific hypotheses were developed based on previous evidence, this research, which is the first to examine the use of the intrinsic motivation measure developed by Nakagami et al. (2008) among individuals with schizophrenia and comorbid SUD, was largely exploratory in nature. Hypotheses proposed a general relationship between intrinsic motivation and substance use severity, but the degree to which differences in these relations may vary across genders and substances of abuse remained largely unknown. Given the somewhat exploratory nature of this research and the considerable proportion of study attrition observed over 1-year, a robust analytic approach (i.e., intent-to-study) was adopted favoring power to detect significant relations among the primary study variables of interest (i.e., Chakraborty & Gu, 2009). Such an approach is suitable for exploratory work, and is the current field standard to use in longitudinal studies with large proportions of attrition (i.e., Georgieva & Krystal, 2004; Hamer & Simpson, 2009). Given the increased likelihood of deriving false positive results from the biased parameter estimates that can result from high proportions of attrition (Chakraborty & Gu, 2009, Graham, 2009), this study conducted a series of complete case sensitivity analyses (see Appendix A) to maximize the potential for deriving accurate statistical conclusions (Chakraborty & Gu, 2009). In fact, the consistency of significant results garnered from the primary intent-to-treat analyses were maintained for AUS (log) models under complete case analyses, and marginal support was largely observed for the DUS (log) models. While this relatively high degree of consistency between intent-to-study and complete findings suggests that the statistical conclusions derived from this research are accurate, the considerable proportion of attrition observed over 1-year signals a need for replication studies. Further, while the attrition observed over 1-year in this research was considerable, it is similar to that reported in comparable studies (see Bellack et al.,

2006; Mueser et al., 2013). In summary, although the key longitudinal analyses (i.e., intent-to-treat) of this research largely revealed statistically significant relations between changes in intrinsic motivation and changes in substance use severity, the attrition observed in this research renders such results tentative until confirmatory evidence is available from future studies.

Another limitation of study attrition is the potential bias stemming from the baseline heterogeneity observed between patients who dropped out of the study before 1-year ($n = 390$, attrited sample) and the patients who completed the study ($n = 145$, completer sample). Cross-sectional analyses were conducted across 24 study variables between these groups (see Chapter 4, Section B.3., Table 9); a greater proportion of completers were diagnosed with alcohol use disorder compared to those patients who dropped out of the study. Further, a greater proportion of those who dropped out of the study were diagnosed with other substance use disorders (i.e., cannabis or cocaine use disorder) compared to those who completed the study. Recall that of the 535 patients with schizophrenia and comorbid SUD, the majority were diagnosed with poly-disorders (43.5%), followed by other substance use disorders (34.3%), and alcohol use disorders (22.2%). While other substance use disordered patients did not comprise the majority of the sample, the presence of systematic differences between completer and attrited samples with regard to comorbidity status signal some concern about the generalizability of the significant relations found between intrinsic motivation and substance use severity. Regardless of this limitation, however, the overall results of these analyses suggested that completer and attrited samples were largely comparable across all other study variables observed at baseline.

In addition to problems of study attrition, this research is limited by its unbalanced sample of men and women. This limitation could have precluded the detection of significant gender differences in the longitudinal relationship between changes in intrinsic motivation and

changes in substance use severity. While adequate power was seemingly available in this research to detect medium to large-sized estimates between these constructs, others have cautioned that it is difficult to obtain specific guidelines on sample size requirements for hierarchical linear models (Bassiri, 1988; VanDerLeeden & Busing, 1994), and many commonly used software packages may underestimate sample estimates needed for detecting significant cross-level interactions (Hoffman, 1997). With regard to specific numbers, at least two studies have indicated that to have adequate power (i.e., .80) to detect cross-level interactions, a sample of 30 groups with 30 individuals is necessary (Bassiri, 1988; VanDerLeeden & Busing, 1994), although unbalanced designs require more individuals per group to obtain sufficient power (Hoffman, 1997). Given such challenges, estimates of whether gender moderated the longitudinal association between changes in intrinsic motivation and changes in substance use severity, which were largely null, could have been undetected due to power limitations from the unbalanced sample (Hypothesis 3c). Currently, because of the unbalanced sample of men and women employed in this research coupled with the challenges of estimating power for cross-level interactions, it is difficult to draw firm conclusions from such results. Although some unexpected significant relations were found supporting average improvements in intrinsic motivation to reductions in substance use severity within the subsample of men, more pervasive moderator effects could also exist indicating that such relations vary across genders but were overlooked due to sample size limitations resulting from the unbalanced sample.

Another limitation of this research stems from the nature of the sample employed, in that such study participants were not enrolled in a motivational rehabilitation program targeting reductions in substance use severity, but were rather selected from a randomized controlled trial of antipsychotic medications. This may potentially explain the low base rates (initial status) of

alcohol use severity ($M = 2.71$; $SE = 1.01$, AUS raw score) and drug use severity ($M = 2.66$; $SE = 1.01$; DUS raw score) observed among the sample. While such scores suggest that this sample of patients with schizophrenia and comorbid SUD started the study at sub-threshold levels of drug/alcohol abuse, it is important to mention that severity levels are generally low in community samples of patients with these conditions (see Drake et al., 2006). This is usually the case as community patients with schizophrenia and comorbid SUD often become destabilized and hospitalized at moderate/ high severity levels (Drake et al., 2006). Indeed, participants in this current research demonstrated low/moderate substance use severity at baseline, and while subsequent findings did signal intrinsic motivation change is a key incremental predictor to naturalistic reductions in substance use severity beyond demographic and clinical confounds, these effects may be more modest than that observed in motivational rehabilitation programs.

Further, this research is also limited to some degree by the cross-situational nature of Nakagami and colleague's (2008) intrinsic motivation measure. This cross-sectional approach signaled compelling reason to question the prevailing 2-factor orthogonal solution of the intrinsic motivation measure in schizophrenia and comorbid SUD (i.e., Nakagami et al., 2008), while at the same yielded notable and unexpected limitations to its implementation. Such limitations are plausible given prior evidence suggests high levels of sensation seeking and curiosity-driven behaviors are associated with substance use in schizophrenia and comorbid SUD (i.e., Dervaux et al., 2001), which may explain the reason for why the QLS curiosity item did not load with purpose and motivation as hypothesized. As such, while this study presented strong evidence to question the application of Nakagami and colleague's (2008) 2-factor solution in this population, results based on the intrinsic motivation measure used in this research must be made with caution until confirmatory evidence is available from future studies.

Finally, this research is limited by its modest 1-year follow-up of participants. While the longitudinal nature of this research is a considerable strength, the longitudinal design employed is also limited in terms of answering some critical questions regarding the relationship between changes in intrinsic motivation and changes in substance use severity. Improvements in intrinsic motivation did lead to significant reductions in substance use severity over 1-year (Hypothesis 3b), yet the observed duration was not sufficient to determine whether this sample of patients actually achieved sustained remission. Consequently, the negative linear trajectory found in this research only suggests that improvements in intrinsic motivation were associated with significant reductions in substance use severity for the duration of 1-year. Unfortunately, what this research is unable to answer with a 1-year follow-up is whether such improvements in intrinsic motivation are significantly associated with sustained remission among this population. As such, additional studies will be needed to examine whether the impact of intrinsic motivation on individuals with schizophrenia and comorbid SUD leads to sustained remission among this population when such relations are observed over longer periods of time.

C. IMPLICATIONS

The results of this investigation have a number of notable implications for new research and social work practice, despite the existing limitations of this study. Consistent with the dual diagnosis treatment literature and hypotheses of this investigation, the deficits assessed by the 2-item intrinsic motivation measure were, for the most part, highly significant with substance use severity. Intrinsic motivation held the strongest relations to alcohol use severity; evidenced by the number of significant relations that were observed both cross-sectionally and longitudinally. In addition, the primary longitudinal analyses (i.e., intent-to-study) examining the relationship

between changes in intrinsic motivation and changes in alcohol use severity were maintained under complete case analysis (see Appendix A). In addition, a number of significant relations were also observed between intrinsic motivation and drug use severity; however, such findings were more robust in the longitudinal analyses, and the consistency of such results maintained trend-level thresholds of statistical significance under complete case analysis (see Appendix A). Further, few significant cross-sectional relations were observed between intrinsic motivation, gender, and substance use severity, and gender appeared to have no significant impact on the longitudinal relations observed between changes in intrinsic motivation and changes in substance use severity. While the limitations discussed above may account for the discrepancies noted between intent-to-study and complete analyses as well as the sparse gender differences found, it also seems clear from the results of this research that there is a need to further examine the intrinsic motivation construct among this population.

To date, schizophrenia researchers have shown individuals with the disorder exhibit profound deficits in intrinsic motivation (i.e., Nakagami et al., 2008; Barch et al., 2008; Yamada et al., 2010; Nakagami et al., 2010), however a consensus has yet to be achieved with regard to how to best measure such deficits among this population. Furthermore, this issue has become compounded by disagreement with regard to whether intrinsic motivation is a negative symptom dimension, or emerges from existing negative symptoms (i.e., amotivation and anticipatory anhedonia) in schizophrenia (i.e., Blanchard & Cohen, 2006; Nakagami et al., 2010). While some evidence suggests that such deficits may stem from the negative symptoms of anticipatory anhedonia (i.e., deficits in the ability to perceive pleasure, which preclude the formation of goal directed activities) and amotivation (i.e., decreases in goal directed activity and goal-directed cognition) (Heerey & Gold, 2007; Harvey & Strassnig, 2012), the relation of such deficits to

intrinsic motivation in schizophrenia and comorbid SUD have yet to be fully examined in this population. Consequently, given the limited scope of the 2-item intrinsic motivation measure used in this research, there is an urgent need to further examine, and potentially further develop the construct in schizophrenia and comorbid SUD. This should be done by carefully constructing and validating additional instruments that may capture the fundamental role of the key intrinsic motivational deficits in this population. Recently, discrete negative symptom subdomains have been investigated in individuals with schizophrenia and comorbid SUD, with findings showing a central role of motivational deficits in anticipatory pleasure (Foussias & Remington, 2010, for review). Consequently, future research may profitably focus measurement development efforts on incorporating deficits in anticipatory anhedonia as a step in further examining the intrinsic motivation construct in this population.

In addition to this research signaling the need to further examine the intrinsic motivation construct among this population in future studies, the results of this investigation pertaining to intrinsic motivation also call for additional studies of this probable negative symptom dimension among individuals with schizophrenia and comorbid SUD. While not all hypotheses in this research were supported, some cross-sectional and all primary (i.e., intent-to-study) longitudinal analyses did show significant relations between intrinsic motivation and substance use severity, signaling the potential importance of the tested construct to substance use severity among this sample of individuals with schizophrenia and comorbid SUD. Considerable study attrition, the unbalanced sample of men and women, and the somewhat exploratory nature of this research preclude drawing firm conclusions from this investigation, but these findings may provide some encouraging leads for future studies.

First, it will be important for subsequent studies to replicate the factor analytic findings of

this investigation, to examine whether these results might actually point to an alternative factor structure for Nakagami and colleague's (2008) intrinsic motivation measure among individuals with schizophrenia and comorbid SUD. This will be important for future studies employing this measure that seek to make valid cross-group comparisons between those with schizophrenia and those with schizophrenia and comorbid SUD. Such comparisons will only yield meaningful results if there is a consistent latent factor structure to intrinsic motivation observed across these groups, and the findings of this dissertation study call this point into question. As such, whether individuals with schizophrenia and comorbid SUD exhibit intrinsic motivation deficits by this 2-item measure will remain uncertain until future investigations resolve these factor-analytic questions. Consequently, studies of Nakagami and colleague's (2008) measure in individuals with schizophrenia and matched samples of individuals with schizophrenia and comorbid SUD are particularly important avenues for future research, given the findings of this investigation.

Second, future research will also need to replicate the findings examining potential gender differences in the longitudinal relationship between intrinsic motivation and substance use severity. While largely no significant relations were found in this regard, it is possible that relations did exist that were beyond the statistical power of this study to detect (Hoffman, 1997). Cross-sectional findings of this research showed that women did exhibit less intrinsic motivation deficits than men at baseline, yet such women did not continue to show stronger associations with intrinsic motivation leading to faster reductions in substance use severity than men over 1-year. This may suggest a limit to the prospective gains such women can make with regard to intrinsic motivation, yet another plausible explanation is that such findings stem from estimating growth parameters for the cross-level interaction using an unbalanced sample of men and women (Hoffman, 1997). Consequently, these limitations render such findings tentative, and clearly

indicate a need for future studies using adequately powered and balanced samples of men and women among this population.

Further, given the somewhat exploratory nature of this work, even the largely significant longitudinal findings of the relationship between changes in intrinsic motivation and changes in substance use severity need to be interpreted with caution and call for replication. As mentioned, the attrition observed in this research was considerable, such that missing data in the intent-to-study sample was estimated to be 43% across the study duration, with the largest proportion of missing observations at 1-year. This undoubtedly raises the possibility that some of the findings garnered from the primary intent-to-study sample reflected false positive results stemming from biased parameter estimates. In fact, such an issue may even explain the reason for which the significant relations observed between intrinsic motivation and drug use severity in the intent-to-study primary analyses were not maintained under complete case analysis in this research. As such, the outcomes of this dissertation study should be seen as providing a foundation for future investigations, rather than supplying definitive answers to the longitudinal relations between changes in intrinsic motivation and changes in substance use severity among individuals with schizophrenia and comorbid SUD. Based on the results on this investigation, studies focusing on intrinsic motivation deficits, alcohol use severity, and the severity of various other psychoactive substances of abuse are needed to replicate these findings among this population.

In addition, if the longitudinal relationships observed between changes in intrinsic motivation and changes in substance use severity demonstrated in this research are with merit, and improvement in intrinsic motivation deficits do in fact lead to reductions in substance use severity, subsequent studies might consider providing clarification to the long-term nature of this relationship. Similar to previous studies (i.e., Drake et al., 2006), evidence was found in this

research demonstrating low/ moderate substance use severity in this sample of patients with schizophrenia and comorbid SUD. As mentioned above, while improvements in intrinsic motivation did lead to significant reductions in substance use severity over the 1-year study period, the modest duration observed was not sufficient to determine whether this sample of patients actually achieved sustained remission. Given that substance use severity levels can either increase or decrease over time as a consequence of SUD pathology (Drake et al., 2006), long-term prospective studies with multiple follow-up periods will be needed to determine the nature and extent to which intrinsic motivation in schizophrenia and comorbid SUD may be associated with sustained remission and recovery in this population.

Notably, some critical implications of this research for social work practice are apparent from the findings of this investigation. Perhaps the most directly related to the primary focus of this research is the implication that intrinsic motivation deficits are salient factors by which substance use severity can be reduced among individuals with schizophrenia and comorbid SUD. Not only does this research confirm evidence garnered from long-term longitudinal studies that individuals with schizophrenia and comorbid SUD show prospective reductions in substance use severity (i.e., Drake et al., 2006), but it suggests that improvements in intrinsic motivation in this population are among the salient factors driving this effect. The limitations of this research notwithstanding, evidence provided by this investigation suggest that intrinsic motivation deficits may serve as one salient factor for which psychosocial interventions could target to produce faster reductions in substance use severity. Evidence garnered from this study also provides critical support for targeting intrinsic motivation deficits using diverse treatment approaches, particularly given the known challenges of conducting intervention studies in schizophrenia and comorbid SUD—as such individuals are difficult to engage in treatment and are especially

difficult to retain in treatment (Horsfall et al., 2009). If substance use severity can indeed be reduced by improving intrinsic motivation deficits, this could provide social work practitioners and treatment developers with critical insights into how to best help people with this comorbidity recover from the long-term disability exacted by persistent and pervasive use. To date, salient factors that contribute to the persistent patterns of substance use severity in schizophrenia and comorbid SUD have remained largely elusive, and refractory to psychosocial and medication treatment (Westermeyer, 2006). The elucidation of such relations provides a solid foundation for initiating future treatment development that could have a substantial impact on social work practice with this population, and ultimately serve to improve the lives of the many individuals with schizophrenia and comorbid SUD. That intrinsic motivation deficits indeed appear to be one salient factor by which substance use severity can be reduced suggest that interventions focusing on targeting such deficits could be effective for this population. Consequently, social work practitioners and researchers will need to collaborate to begin applying these findings in order to identify the utility and feasibility of initiating intrinsic motivation treatment approaches for schizophrenia and comorbid SUD.

Finally, not only does this research have broad treatment implications directly for those with schizophrenia and comorbid SUD, but these results provide some early support for initiating gender-based models of care within this population. To date, despite the growing interest in the study of substance use comorbidity in schizophrenia, little attention has been paid to subgroups of men and women with these conditions as potentially demonstrating different substance use severity patterns, which may necessitate unique treatment needs (Drapalski et al., 2011). Given the cross-sectional evidence garnered from this research suggested that men showed significantly greater deficits in intrinsic motivation compared to women at baseline, interventions initiated

within subsamples of men may benefit from using extrinsic rewards to boost (initially) low base-rates. Silverstein (2010) recently showed that extrinsic rewards (i.e., tokens/ money) increased the low base-rates of intrinsic motivation in schizophrenia patients upon treatment enrollment, which set the foundation for continued intrinsic motivation improvement in treatment. Recall that exploratory longitudinal evidence from this study showed that men exhibited significant reductions in substance use severity as they made improvements in intrinsic motivation over 1-year. While it is promising that exploratory results showed that men did exhibit improvement in intrinsic motivation leading to significant reduction in substance use severity, the fact that men had significantly lower levels of intrinsic motivation compared to women at baseline should not be overlooked. These results provide preliminary support for extending brief extrinsic reward-based interventions to improve the low base-rates of intrinsic motivation observed in men with schizophrenia and SUD. This could provide social workers with a critical understanding on how to initiate and continue to sustain the performance of intrinsically motivated behaviors (i.e., reductions in substance use severity) within subsamples of men, and ultimately serve to initiate gender-based models of care within this population. As such, the findings of this research have some important implications and applications for potentially leading the field toward developing gender-based models of care for individuals with schizophrenia and comorbid SUD.

In summary, the findings of this study provide a number of promising directions for future research and social work practice. Such directions include: (1) further developing the intrinsic motivation construct in schizophrenia and comorbid SUD; (2) replication of prospective longitudinal associations between intrinsic motivation and substance use severity in carefully conducted studies; (3) replication of findings examining the impact of gender on the longitudinal association between intrinsic motivation and substance use severity with balanced samples of

men and women; (4) develop and disseminate evidence-based multi-systemic interventions that address intrinsic motivation deficits in schizophrenia and comorbid SUD to accelerate the rate of substance use severity reduction; (5) explore the feasibility of using extrinsic rewards to improve the low-base rates of intrinsic motivation in subsamples of men with schizophrenia and comorbid SUD. With such research, it is anticipated that studies will lead to a better understanding of the longitudinal impact of intrinsic motivation on substance use severity among this population and its patterns in men and women, and begin to inform promising targets for future treatment development efforts.

D. CONCLUSIONS

This dissertation study sought to extend validation of a promising intrinsic motivation measure developed by Nakagami et al. (2008) for schizophrenia to schizophrenia and comorbid SUD, examine the unique contribution of change in intrinsic motivation to change in substance use severity, and then investigate the degree to which such relations vary across genders in a large heterogeneous sample of patients with schizophrenia and comorbid SUD. Psychometric findings revealed a potential shift in the latent factor structure of Nakagami and colleague's (2008) intrinsic motivation instrument when applied to schizophrenia and comorbid SUD, but at the same time pointed to the reliability and re-test reliability of the instrument. Evidence was found suggesting longitudinal intrinsic motivation change is a salient incremental predictor of reductions in patient's alcohol and drug use severity, above and beyond the effects of age, illness chronicity, psychopathology, comorbidity status, and phase 1 randomization medication effects. Given that the overall proportion of attrition in this research was considerable, the potential for deriving false positive results due to biased parameter estimates could not be ruled out. Future

research will need to replicate these findings with less attrition, while focusing on intervention efforts that seek to target the intrinsic motivation deficits of schizophrenia and comorbid SUD, which may help offset the destabilizing effects exacted by severe and persistent use. Relations with gender indicated little to no cross-sectional associations between intrinsic motivation and substance use severity, and gender did not moderate the longitudinal association between change in intrinsic motivation and change in substance use severity. Consequently, future research will need to replicate these findings with balanced samples of men and women, as little evidence can be garnered from this research to support developing and disseminating gender-based models of care among this population. The results of this investigation make three important contributions to the field by providing empirically-based information on the strengths and limitations of Nakagami and colleague's (2008) intrinsic motivation measure and its factor structure as applied to schizophrenia and comorbid SUD, parsing relatively robust relationship estimates between intrinsic motivation and substance use severity, and elucidating much more limited relationship estimates among gender, intrinsic motivation, and substance use severity. By identifying these strengths and limitations of Nakagami and colleague's (2008) intrinsic motivation measure and relations between intrinsic motivation and substance use severity, it is hoped that progress will be made by social workers and practitioners to identify additional salient contributors to the pervasive patterns of substance use severity among this population, and ultimately develop effective psychosocial treatments to improve the lives of those who suffer from this comorbidity.

APPENDIX A - RESULTS WITH COMPLETER SAMPLE ($N = 145$)

Primary longitudinal analyses (Aim #1, Hypothesis 1c; Aim #3) in this research were conducted by taking an intent-to-study approach to missing data, which used all relevant observations collected on participants over the 1-year study, regardless of whether the participant completed the study (see Shafter & Graham, 2002; Graham, 2009). This approach to handling missing data is the current field standard (see Georgieva & Krystal, 2004; Hamer & Simpson, 2009), as it provides more powerful tests than other analytic options used in longitudinal studies with attrition (Shafter & Graham, 2002; Lachin, 2002; Chakraborty & Gu, 2009), and can be safely employed with the EM algorithm even when missing completely at random assumptions are not met (Graham, 2009). Given the increased likelihood to obtain false positive results due to biased parameter estimates in longitudinal studies with high proportions of attrition, it is usually recommended that additional approaches be used and compared (Chakraborty & Gu, 2009). This appendix presents an examination of the key longitudinal analyses of this research (Aim #1, Hypothesis 1c; Aim #3) under complete case analysis. Results using the completer sample ($n = 145$) are compared to the primary analyses using the intent-to-study sample ($n = 535$). Findings are presented in identical tables to those that appear in the primary longitudinal analyses, and a *Change Note* is provided in each table outlining the differences between the results in the completer sample and those in the primary intent-to-study analyses.

A. AIM #1 EXTEND VALIDATION OF NAKAGAMI AND COLLEAGUES' INTRINSIC MOTIVATION MEASURE TO COMORBID SUD AND SCHIZOPHRENIA

1. Re-test Reliability of the Intrinsic Motivation Measure

As can be seen in Table A1.1, the intrinsic motivation measure satisfied re-test reliability criteria of 0.40 or greater across study assessment periods) baseline to 6-month; 6-month to 12-month). Similar to that observed in the intent-to-study sample, the hypothesis (Hypothesis 1c) that the intrinsic motivation measure would demonstrate at least minimally sufficient levels of re-test reliability ($r \geq .40$) when examined across the 3 multi-month assessment observation periods was also supported in the completer sample.

Table A1.1. *Correlations Among Participant Intrinsic Motivation Scores Across Study Periods*

Period	0	6	12
0 - Intrinsic Motivation	-		
6 - Intrinsic Motivation	.47**	-	
12 - Intrinsic Motivation	.48**	.61**	-

Note. Analyses were conducted on the completer sample ($n = 145$). 0 = Baseline; 6 = 6-month; 12= 12-month are presented in boldface.

Change Note. No significant changes.

** $p < .01$, 2-tailed.

B. AIM#3 EXAMINE THE LONGITUDINAL CONTRIBUTION OF CHANGES IN INTRINSIC MOTIVATION TO CHANGES IN SUBSTANCE USE SEVERITY, AND THEN INVESTIGATE THE IMPACT OF GENDER ON THESE RELATIONSHIPS.

1. Longitudinal Change in Substance Use Severity

Growth curve analyses in the completer sample began by computing the ICC for both AUS (log) and DUS (log) unconditional models. Consistent with guidelines for the appropriateness of using growth curve models to capture systematic change in individual substance use severity phenomena over time, sufficient between-patient dependence was achieved for both AUS (log) (ICC = 0.54) and DUS (log) (ICC = 0.52) unconditional models in the completer sample (Hox, 2000; Raudenbush & Bryk, 2009).

Table A1.2 presents the results for the AUS (log) and DUS (log) unconditional growth curve models in the completer sample. Similar to that observed in the intent-to-study sample, those patients with complete observations demonstrated, on average, significant reductions in alcohol and drug use severity over the 1-year study period. Also similar to that observed in the intent-to-study sample, patients with complete observations exhibited variability in terms of their mean baseline AUS (log)/ DUS (log) scores, and similar variability was observed with regard to the reduction of substance use severity observed over 1-year. Consequently, the study hypothesis (Hypothesis H3a) that patients would demonstrate, on average, significant reductions in AUS (log) / DUS (log) scores over 1-year, was also supported in the completer sample.

Table A1.2. 1-Year Trajectories of Substance Use Severity (Unconditional Growth Models)

Parameter		AUS (log) Unconditional Model ^a			
Fixed Effect		Coefficient	SE	t	p
Mean Initial Status, β_{00}		1.00	0.02	37.76	<.001
Mean Growth Rate, β_{10}		-0.08	0.02	-3.32	<.001
Random Effect		Variance Component	95% CI		
Initial Status, $\text{Var}(r_{0i}) = \tau_{01}$		0.02	0.07 to 0.27		
Growth Rate, $\text{Var}(r_{1i}) = \tau_{11}$		0.03	0.10 to 0.25		
Level-1 error, $\text{Var}(e_{1i}) = \sigma^2$		0.06	-		
Parameter		DUS (log) Unconditional Model ^b			
Fixed Effect		Coefficient	SE	t	p
Mean Initial Status, β_{00}		0.95	0.02	36.09	<.001
Mean Growth Rate, β_{10}		-0.07	0.02	-2.55	.011
Random Effect		Variance Component	95% CI		
Initial Status, $\text{Var}(r_{0i}) = \tau_{01}$		0.02	0.11 to 0.26		
Growth Rate, $\text{Var}(r_{1i}) = \tau_{11}$		0.03	0.12 to 0.28		
Level-1 error, $\text{Var}(e_{1i}) = \sigma^2$		0.05	-		

Note. Analyses were conducted on the completer ($n = 145$). AUS = Alcohol Use Scale; DUS = Drug Use Scale.

^a Only the final AUS unconditional model is presented here to reduce visual clutter, which was fit using AR(1) and REML estimation.

^b Only the final DUS unconditional model is presented here to reduce visual clutter, which was fit using AR(1) and REML estimation.

Change Note. No significant changes.

2. Longitudinal Relationship between Changes in Intrinsic Motivation and Changes in Substance Use Severity

Upon determining that patients showed significant reductions in substance use severity over 1-year in the completer sample, a series of conditional linear growth curve models were

then computed to examine the longitudinal contribution of changes in intrinsic motivation to changes in substance use severity. As can be seen in Table A1.3, the average effect of intrinsic motivation continued to be associated with significant reductions in patient’s alcohol use severity over 1-year in the completer sample. Such initial analyses also seemingly suggested that the average effect of intrinsic motivation on DUS scores was not statistically different from 0 in the completer sample.

Table A1.3. *1-Year Relationship Between Changes in Intrinsic Motivation and Changes in Substance Use Severity (Conditional Growth Models)*

Parameter	AUS (log) Conditional Model ^a			
Fixed Effect	Coefficient	SE	t	p
Mean Initial Status, β_{00}	1.08	0.03	30.12	<.001
Mean Growth Rate, β_{10}	-0.08	0.02	-3.31	<.001
Time-Varying IM, β_{20}	-0.01	0.01	-3.49	<.001
Parameter	DUS (log) Conditional Model ^b			
Fixed Effect	Coefficient	SE	t	p
Mean Initial Status, β_{00}	0.98	0.03	27.10	<.001
Mean Growth Rate, β_{10}	-0.09	0.02	-4.15	.012
Time-Varying IM, β_{20}	-0.01	0.01	-1.27	.204

Note. Analyses were conducted on the completer sample ($n = 145$). AUS = Alcohol Use Scale; DUS = Drug Use Scale; IM = Intrinsic Motivation.

^a Only the final AUS conditional model is presented here to reduce visual clutter, which was fit using AR(1) and REML estimation.

^b Only the final DUS conditional model is presented here to reduce visual clutter, which was fit using AR(1) and REML estimation.

Change Note. The effect of intrinsic motivation on DUS scores was not statistically different from 0 in the completer sample.

Completer sample analyses proceeded by expanding the AUS (log) / DUS (log) conditional models with such scores being predicted from time and time-varying intrinsic motivation, adjusting for age, illness chronicity, overall psychopathology, comorbidity status, and phase1 randomization. Such analyses continued to suggest that the average effect of intrinsic motivation was associated with significant reductions in patient's alcohol use severity over 1-year in the completer sample, after adjusting for age, chronicity, overall psychopathology, comorbidity status, and phase 1 randomization (Table A1.4). The findings of such analyses also continued to suggest that the average effect of intrinsic motivation on patient's DUS scores were not statistically different from 0 in the completer sample, after adjusting for these demographic and clinical confounds (Table A1.5).

Table A1.4. *1-Year Relationship Between Changes in Intrinsic Motivation and Changes in Alcohol Use Severity, Adjusting for Demographic and Clinical Confounds*

Fixed Effect	Parameter	Coefficient	SE	<i>t</i>	<i>p</i>
Initial Status	β_{00}	1.09	0.06	16.47	<.001
AUD/ SUD ^a	β_{01}	-0.03	0.06	-0.58	.558
SUD ^a	β_{02}	-0.09	0.07	-1.38	.167
AUD ^b	β_{03}	0.09	0.07	1.38	.167
Quetiapine ^c	β_{04}	0.06	0.07	0.82	.413
Perphenazine ^c	β_{05}	-0.01	0.06	-0.13	.893
Ziprasidone ^c	β_{06}	0.01	0.09	0.13	.889
Risperidone ^c	β_{07}	-0.01	0.06	-0.18	.852
Olanzapine ^d	β_{08}	-0.06	0.07	-0.82	.413
Age	β_{09}	0.00	0.00	0.24	.809
Chronicity	β_{010}	-0.00	0.00	-0.29	.771
PANSS Total	β_{011}	-0.00	0.01	-0.20	.840
Growth Rate	β_{10}	-0.09	0.06	-1.49	.137
Time x AUD/ SUD ^a	β_{11}	0.01	0.05	1.14	.252
Time x SUD ^a	β_{12}	0.02	0.07	0.31	.750
Time x AUD ^b	β_{13}	-0.02	0.07	-0.31	.750
Time x Quetiapine ^c	β_{14}	-0.09	0.07	-1.20	.227
Time x Perphenazine ^c	β_{15}	0.04	0.06	0.60	.542
Time x Ziprasidone ^c	β_{16}	0.01	0.09	0.08	.933
Time x Risperidone ^c	β_{17}	-0.00	0.06	-0.05	.959
Time x Olanzapine ^d	β_{18}	0.09	0.07	1.20	.227
Time x Age	β_{19}	-0.00	0.00	-1.22	.220
Time x Chronicity	β_{120}	0.00	0.01	1.11	.264
Time x PANSS Total	β_{121}	0.00	0.00	0.59	.553
Time-Varying IM	β_{20}	-0.01	0.01	-3.05	<.001

Note. Analyses were conducted on the completer sample ($n = 145$). IM = Intrinsic Motivation.

AUD/SUD = alcohol use disorder and other substance use disorder; SUD = substance use

disorder other than alcohol use disorder; AUD = alcohol use disorder; PANSS = Positive and Negative Syndrome Scale. Only the final AUS (log) model is presented to reduce visual clutter, which was fit using AR(1) and accounted for heteroscedasticity of level-1 errors. REML estimation was used. Age, Chronicity, and PANSS Total were grand mean centered.

^aReference category is AUD.

^bReference category is SUD.

^cReference category is Olanzapine.

^dReference category is Quetiapine.

Change Note. No significant changes.

Table A1.5. *1-Year Relationship Between Changes in Intrinsic Motivation and Changes in Drug Use Severity, Adjusting for Demographic and Clinical Confounds*

Fixed Effect	Parameter	Coefficient	SE	<i>t</i>	<i>p</i>
Initial Status	β_{00}	0.88	0.07	12.36	<.001
AUD/ SUD ^a	β_{01}	0.17	0.06	2.77	.006
SUD ^a	β_{02}	0.23	0.07	3.14	.002
AUD ^b	β_{03}	-0.23	0.07	-3.14	.002
Quetiapine ^c	β_{04}	-0.06	0.08	-0.82	.410
Perphenazine ^c	β_{05}	-0.03	0.07	-0.42	.671
Ziprasidone ^c	β_{06}	-0.06	0.10	-0.64	.519
Risperidone ^c	β_{07}	-0.09	0.07	-1.27	.206
Olanzapine ^d	β_{08}	0.06	0.08	0.82	.410
Age	β_{09}	-0.00	0.00	-0.55	.578
Chronicity	β_{010}	-0.00	0.00	-0.29	.771
PANSS Total	β_{011}	0.00	0.00	1.02	.305
Growth Rate	β_{10}	-0.09	0.06	-1.49	.137
Time x AUD/ SUD ^a	β_{11}	-0.04	0.07	-0.56	.574
Time x SUD ^a	β_{12}	-0.10	0.08	-1.27	.205
Time x AUD ^b	β_{13}	0.10	0.08	1.27	.205
Time x Quetiapine ^c	β_{14}	0.07	0.09	0.84	.398
Time x Perphenazine ^c	β_{15}	0.08	0.08	0.99	.323
Time x Ziprasidone ^c	β_{16}	0.31	0.11	2.74	.006
Time x Risperidone ^c	β_{17}	0.13	0.08	1.65	.099
Time x Olanzapine ^d	β_{18}	-0.07	0.09	-0.84	.398
Time x Age	β_{19}	-0.00	0.00	-1.22	.220
Time x Chronicity	β_{120}	0.00	0.01	0.27	.786
Time x PANSS Total	β_{121}	0.00	0.00	0.84	.399
Time-Varying IM	β_{20}	-0.01	0.01	-1.10	.271

Note. Analyses were conducted on the completer sample ($n = 145$). IM = Intrinsic Motivation.

AUD/SUD = alcohol use disorder and other substance use disorder; SUD = substance use

disorder other than alcohol use disorder; AUD = alcohol use disorder; PANSS = Positive and Negative Syndrome Scale. Only the final DUS (log) model is presented to reduce visual clutter, which was fit using AR(1) and REML estimation. Age, Chronicity, and PANSS Total were grand mean centered.

^aReference category is AUD.

^bReference category is SUD.

^cReference category is Olanzapine.

^dReference category is Quetiapine.

Change Note. The effect of intrinsic motivation on DUS scores was not statistically different from 0 in the completer sample, adjusting for demographic and clinical confounds.

Finally, this series of conditional growth curve models in the completer sample examined longitudinal relations between intrinsic motivation and substance use severity, after adjusting for demographic and clinical confounds, negative symptoms and neurocognition. Such analyses continued to suggest the average effect of intrinsic motivation was associated with significant reductions in patient's alcohol use severity over 1-year in the completer sample, after adjusting for age, illness chronicity, overall psychology, phase 1 randomization, neurocognition, and negative symptoms (Table A1.6). Notably, improvements in patient's intrinsic motivation were associated with trend-level reductions in patient's drug use severity over 1-year, after adjusting for these demographic and clinical confounds, neurocognition and negative symptoms.

The hypothesis (Hypothesis 3b) that improvements in intrinsic motivation would be associated with significant reductions over 1-year was only partially supported in the completer sample. However, the trend observed between intrinsic motivation and drug use severity, after adjusting for demographic and clinical confounds, neurocognition and negative symptoms in the completer sample increases the potential that primary intent-to-study results are derived from accurate statistical conclusions rather than false positives (Chakraborty & Gu, 2009).

Table A1.6. *1-Year Relationship Between Changes in Intrinsic Motivation and Changes in Substance Use Severity, Adjusting for Demographic and Clinical Confounds, Neurocognition and Negative Symptoms*

Fixed Effect	Parameter	Coefficient	SE	<i>t</i>	<i>p</i>
AUS (log) Conditional Growth Model ^a					
Initial Status	β_{00}	1.17	0.07	14.87	<.001
PANSS Negative	β_{012}	-0.00	0.01	-0.61	.536
Neurocognition	β_{013}	0.01	0.03	0.46	.536
Growth Rate	β_{10}	-0.16	0.07	-2.36	.018
Time x PANSS Negative	β_{122}	0.00	0.01	0.48	.626
Time x Neurocognition	β_{123}	-0.01	0.03	-0.55	.580
Time-Varying IM	β_{20}	-0.01	0.00	-3.08	.002
DUS (log) Conditional Growth Model ^a					
Initial Status	β_{00}	0.91	0.06	14.07	<.001
PANSS Negative	β_{012}	-0.01	0.00	-0.50	.615
Neurocognition	β_{013}	0.04	0.02	1.68	.093
Growth Rate	β_{10}	-0.09	0.07	-1.29	.194
Time x PANSS Negative	β_{122}	-0.00	0.00	-0.27	.652
Time x Neurocognition	β_{123}	0.02	0.02	-0.03	.972
Time-Varying IM	β_{20}	-0.01	0.01	-1.89	.059

Note. Analyses were conducted on the completer sample ($n = 145$). AUS = Alcohol Use Scale; DUS = Drug Use Scale; IM = Intrinsic Motivation. PANSS = Positive and Negative Syndrome Scale.

^a Only the final AUS conditional growth model with effects of interest are presented to reduce visual clutter. Age, chronicity, overall psychopathology, comorbidity status, phase1 randomization, negative symptoms, and neurocognition were adjusted at level-2. Age, chronicity, PANSS Total, PANSS Negative, and neurocognition were grand mean centered. This model was fit using AR(1) and REML estimation.

^b Only the final DUS conditional growth model with effects of interest are presented to reduce visual clutter. Age, chronicity, overall psychopathology, comorbidity status, phase1 randomization, negative symptoms, and neurocognition were adjusted at level-2. Age,

chronicity, PANSS Total, PANSS Negative, and neurocognition were grand mean centered.

This model was fit using AR(1) and accounted for heteroscedasticity of level-1 errors. REML estimation was used.

Change Note. A non-significant trend was observed for the relationship between intrinsic motivation and DUS scores, adjusting for demographic and clinical confounds, neurocognition and negative symptoms.

3. Moderating Effect of Gender on the Longitudinal Association between Changes in Intrinsic Motivation and Changes in Substance Use Severity

Completer sample analyses proceeded by examining the impact of gender on relationship estimates between changes in intrinsic motivation and changes in substance use severity through the use of gender moderated growth curve models. Similar to that observed in the intent-to-study sample, no significant interactions were found regarding estimates of the relationship between changes in intrinsic motivation and changes in alcohol or drug use severity in the completer sample (Table A1.7).

Table A1.7. 1-Year Relationship Between Changes in Intrinsic Motivation and Changes in Substance Use Severity (Gender Moderated Conditional Growth Models)

Fixed Effect	Parameter	Coefficient	SE	<i>t</i>	<i>p</i>
AUS (log) Gender Moderated Conditional Growth Model ^a					
Initial Status	β_{00}	1.21	0.12	9.66	<.001
Male	β_{01}	-0.11	0.10	-1.03	.302
Growth Rate	β_{10}	-0.12	0.07	-1.56	.119
Time-Varying IM	β_{20}	-0.02	0.01	-2.20	.028
Time-Varying IM x Male	β_{21}	0.01	0.01	1.02	.307
DUS (log) Gender Moderated Conditional Growth Model ^b					
Initial Status	β_{00}	0.85	0.10	7.89	<.001
Male	β_{01}	0.06	0.09	0.64	.517
Growth Rate	β_{10}	-0.13	0.07	-1.70	.089
Time-Varying IM	β_{20}	-0.01	0.01	-0.50	.613
Time-Varying IM x Male	β_{21}	-0.01	0.01	-0.32	.742

Note. Analyses were conducted on the completer sample ($n = 145$). AUS = Alcohol Use Scale; DUS = Drug Use Scale; IM = Intrinsic Motivation.

^a Only the final AUS gender moderated conditional growth model with effects of interest are presented to reduce visual clutter. Age, chronicity, psychopathology, comorbidity status, phase I randomization, and race were adjusted at level-2. Age, Chronicity, and PANSS Total were grand mean centered. This model was fit using AR(1). REML estimation was used.

^b Only the final DUS gender moderated conditional growth model with effects of interest are presented to reduce visual clutter. Age, chronicity, psychopathology, comorbidity status, phase I randomization, and race were adjusted at level-2. Age, Chronicity, and PANSS Total were grand mean centered. This model was fit using AR(1) and accounted for heteroscedasticity of level-1 errors. REML estimation was used.

Change Note. No significant changes.

Upon finding no significant gender interactions in the completer sample, follow-up analyses were computed within completer subsamples of men and women using conditional growth models for estimates of relations between changes in intrinsic motivation and changes in substance use severity. Within the completer subsample of men, the average effect of intrinsic motivation was associated with significant reductions in alcohol use severity over 1-year, but no significant associations were observed for the relationship between intrinsic motivation and drug use severity (Table A1.8). Within the completer subsample of women, average improvements in intrinsic motivation were only associated with a non-significant trend in alcohol use severity reductions; no significant or marginal associations were observed with regard to the relationship between intrinsic motivation and drug use severity over 1-year.

Table A1.8. 1-Year Relationship Between Changes in Intrinsic Motivation and Changes in Substance Use Severity (Subsamples of Men and Women)

Fixed Effect	Parameter	Coefficient	SE	<i>t</i>	<i>p</i>
Men ^a					
AUS (log) Conditional Growth Model					
Initial Status	β_{00}	1.06	0.08	12.99	<.001
Growth Rate	β_{10}	-0.08	0.08	-0.98	.323
Time-Varying IM	β_{20}	-0.01	0.00	-2.13	.033
Women ^b					
Initial Status	β_{00}	0.88	0.19	4.63	<.001
Growth Rate	β_{10}	-0.06	0.06	-0.95	.347
Time-Varying IM	β_{20}	-0.01	0.01	-1.95	.059
Men ^a					
DUS (log) Conditional Growth Model					
Initial Status	β_{00}	0.95	0.07	12.30	<.001
Growth Rate	β_{10}	-0.12	0.08	-1.40	.160
Time-Varying IM	β_{20}	-0.00	0.00	-1.41	.157
Women ^b					
Initial Status	β_{00}	0.54	0.13	4.04	<.001
Growth Rate	β_{10}	-0.08	0.18	-0.45	.651
Time-Varying IM	β_{20}	0.01	0.01	0.71	.479

Note. AUS = Alcohol Use Scale; DUS = Drug Use Scale; IM = Intrinsic Motivation. Only final AUS/ DUS conditional growth models with effects of interest are presented to reduce visual clutter. Models adjusted for the effects of age, chronicity, psychopathology, comorbidity status, phase1 randomization, and race at level-2. Age, Chronicity, and PANSS Total were grand mean centered. Subsample of men was fit using AR(1) and REML estimation was used. Subsample of women was fit using AR(1) and accounted for heteroscedasticity of level-1 errors. REML estimation was used.

^a Analyses were conducted on the subsample of Men ($n = 123$).

^b Analyses were conducted on the subsample of Women ($n = 22$).

Change note. The effect of intrinsic motivation on DUS scores was not statistically different from 0 within the subsample of men. No other significant changes were observed.

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