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# Adjunctive psychosocial intervention following Hospital discharge for Patients with bipolar disorder and comorbid substance use: A pilot randomized controlled trial

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ABSTRACT

Bipolar disorder and substance use disorders are highly debilitating conditions, and especially when co-occurring, are associated with a variety of negative outcomes. Surprisingly, there is a relative lack of research on feasible and effective psychosocial treatments for individuals with comorbid bipolar and substance use disorder (BD-SUD), and a dearth of literature examining interventions designed specifically to improve outcomes such as symptoms, functioning, and treatment engagement/adherence following psychiatric hospitalization in this population. In the current paper, we report results of a pilot randomized controlled trial (n=30), comparing the recently developed Integrated Treatment Adherence Program, which includes individual and telephone sessions provided to patients and their significant others, versus Enhanced Assessment and Monitoring for those with BD-SUD. Participants who received the Integrated Treatment Adherence Program demonstrated significantly faster and greater improvements in depression, mania, functioning, and values-consistent living than participants randomized to Enhanced Assessment and Monitoring, and there was a trend for increased treatment adherence over time. Results are discussed in light of existing literature and study limitations, and suggestions for future research are proposed.



## 1. Introduction

Bipolar disorder (BD) and substance use disorders (SUDs) are highly debilitating and often comorbid conditions (Murray and Lopez, 1996; Degenhardt et al., 2013). Epidemiological research suggests that rates of comorbid SUDs are higher in BD than in any other psychiatric disorder (Tohen et al., 1998; Goldberg, 2001), and individuals with BD have also been shown to have the highest rates of *multiple* substance use disorders (Kessler et al., 1997). The Epidemiologic Catchment Area study reported that over 60% of those with BD had a comorbid SUD, with 46% meeting criteria for alcohol abuse or dependence and 41% meeting criteria for drug abuse or dependence (Regier et al., 1990). Conversely, individuals with SUDs also have a significantly elevated risk of BD, with rates estimated at 5–8 times greater than in the general population (Regier et al., 1990; Kessler et al., 1997).

BD with comorbid SUD (hereafter abbreviated "BD-SUD") is associated with many negative outcomes, including more frequent and severe mood episodes, greater persistence of clinically significant inter-episodic symptoms, longer time to recovery, shorter time to bipolar relapse, greater disability, higher mortality rates, poorer psychosocial outcomes, increased psychiatric hospitalizations, more suicide attempts, and poorer treatment adherence when compared to those with BD without a SUD (Aagaard et al., 1988; Brady et al., 1991; Brady and Sonne, 1995; Feinman and Dunner, 1996; Tondo et al., 1999; Potash et al., 2000; Salloum and Thase, 2000; Cassidy et al., 2001). Of note, research indicates that the period immediately following discharge from the hospital is associated with particularly poor outcomes in patients with BD (Miller et al., 2004; Gaudiano and Miller, 2006) and in those with SUDs (Merrall et al., 2013). Among individuals with BD-SUD, hospital discharge is similarly associated with a heightened risk of negative outcomes such as nonadherence, suicidality, mood and drug relapse, and rehospitalization (Keck et al., 1998; Strakowski et al., 1998a, 1998b; Gaudiano et al., 2008).

A number of psychosocial treatments have been developed as adjuncts to pharmacotherapy for BD. Cognitive-behavioral

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therapy, family therapy, interpersonal and social rhythm therapy, and psychoeducation have typically been shown to improve outcomes in at least some areas (Castle et al., 2009; Reinares et al., 2014). Reinares and colleagues (2014) note that one way to improve psychosocial treatment outcomes in BD is to tailor the treatment to the particular characteristics of the targeted population. However, most research to date on adjunctive treatments for BD has specifically excluded those with SUDs. In our earlier report of an open case series used to develop the current intervention (Gaudiano et al., 2011), we documented improvements in adherence, substance use, and mood symptoms in participants with BD and comorbid SUD. The 5 additional studies on BD-SUD also found positive effects on important clinical outcomes, such as reductions in substance use, increases functioning, and declines in mood symptoms (Weiss et al., 2000, 2007, 2009; Schmitz et al., 2002; Goldstein et al., 2014).

No previous clinical trials to our knowledge have focused on improving the often difficult transition from inpatient to outpatient treatment in acutely ill patients with BD-SUD. Furthermore, previous studies in BD-SUD samples have tested more traditional and intensive psychosocial interventions. There is an urgent need to develop and test adjunctive psychosocial interventions that are more feasible to deliver and can work in concert with patients' other community treatments, which may include pharmacotherapy, case management, support groups, and other substance abuse treatment programs. Given the previously-discussed challenges often encountered in the post-hospitalization period (Keck et al., 1998; Strakowski et al., 1998a, 1998b), as well as especially high rates of psychiatric hospitalizations among those with BD-SUD (Brady et al., 1991), this constitutes an important gap in the literature.

With this background in mind, we sought to develop and test an adjunctive psychosocial intervention for BD-SUD that was designed to improve a range of clinical outcomes in the transition from acute to maintenance treatment. We were also interested in establishing the acceptability, feasibility, and credibility of such an intervention with this challenging and high-risk population. Details of the rationale for and initial development of the intervention are described in our report of the previous open trial (Gaudiano et al., 2011). In the current paper, we report results of a small, pilot, randomized controlled trial, comparing our intervention to an enhanced assessment and monitoring only condition to further assess its acceptability and potential efficacy in preparation for a future full-scale clinical trial.

## 2. Method

### 2.1. Participants

Participants (n=30) were recruited at a private psychiatric hospital from inpatient units (n=27, 90%), with supplemental recruitment of at-risk outpatients (n=3, 10%)[1]. Participants met the following criteria: 1) DSM-IV diagnosis of Bipolar I or II Disorder or Bipolar Disorder NOS (BD), as determined by the Structured Clinical Interview for DSM-IV (SCID; First et al., 2002); 2) DSM-IV drug and/or alcohol use disorder (abuse and/or dependence) also based on the SCID; 3) current prescription for at least one mood-stabilizing medication; 4) at least 18 years of age; 5) ability to speak and read English sufficiently well to complete study procedures; and 6) regular access to a telephone. Exclusion criteria were: 1) borderline or antisocial personality disorder with therapy-interfering behaviors (e.g., chronic suicidality and self-harm), based on the SCID-II (First et al., 1997); 2) nicotine dependence as the only substance use disorder; 3) a medical illness that contraindicated the use of mood-stabilizing medication; 4) pregnancy (due to the potential adverse effects of mood stabilizing medications for this population); 5) current homelessness; or 6) discharge to long-term residential substance abuse treatment. Whenever possible, participants identified a significant other (SO; spouse/partner, sibling, child, parent, or close friend), who also participated in the study (n=22; see Procedure section). SOs were: 1) 18 years or older; 2) able to speak and read English; and 3) in weekly contact with the participant.

### 2.2. Procedure

The Butler Hospital Institutional Review Board approved all study procedures. Newly-admitted patients' hospital charts were screened based on inclusion and exclusion criteria using a Protected Health Information waiver. After obtaining permission from the treating psychiatrist, patients who appeared to meet study criteria were approached, given a brief verbal overview of the study, including the nature, purpose, risks, and benefits, and invited to participate. Informed consent was obtained from those who expressed interest. A Certificate of Confidentiality (issued by the National Institutes of Health), which permits refusal to comply with requests for identifying information from participants engaged in civil or criminal proceedings, was also obtained to further protect privacy.

Assessments were conducted at pre-treatment (baseline), mid-treatment (3 months), and post-treatment (6 months), and administered by trained interviewers (bachelor's or master's-level research assistants) who were blind to treatment condition. Training consisted of a formal didactic workshop followed by several weeks of: a) trainee review and practice scoring of gold standard assessment recordings, b) supervised role plays, c) trainee observation of assessments in real time, and d) supervisor observation of trainee-conducted assessments in real time. All raters were required to achieve acceptable inter-rater reliability (kappas > 0.80) with expert faculty ratings prior to conducting independent assessments with ongoing monitoring of assessment recordings to prevent rater "drift." Participants were compensated with gift cards for completing assessments.

Study participants were allocated to Enhanced Assessment and Monitoring or the Integrated Treatment Adherence Program using urn randomization procedures (Wei, 1978). Urn randomization is a stratified randomization technique, which randomly assigns patients of a given subgroup to treatment conditions, but systematically biases the randomization in favor of balance among the treatment conditions on the stratification variables (in this case, sex and polarity of mood episode at intake). During baseline assessments or early in treatment, participants identified an SO who was informed and consented in a similar fashion to participants. SOs participated in treatment (if the participant was randomized to the Integrated Treatment Adherence Program) as described below. Given the adjunctive nature of the intervention and its focus on increasing treatment engagement/adherence, treatment as usual was not restricted in this study. However, for

[1] Outpatients were recruited based on clinical judgment regarding severity of mood symptoms, substance use, functional impairment, and/or treatment non-adherence. Two outpatients were in a manic/mixed episode and 1 was in a depressed episode. One had a diagnosis of Bipolar I Disorder, 1 had a diagnosis of Bipolar II Disorder, and 1 had a diagnosis of Bipolar Disorder NOS. All 3 had a lifetime diagnosis of alcohol dependence, and 2 also had a lifetime substance use disorder diagnosis. Outpatients did not differ from inpatients on any baseline clinical or demographic variables (all $p$'s > 0.05) except for lifetime suicide attempts; inpatients had a higher number of attempts ($t(26)=4.73$, $p < 0.001$). We re-ran all analyses using baseline treatment status (inpatient versus outpatient) as a covariate at level 2. Results were similar (i.e., betas were comparable and significance levels did not change) for all but 2 analyses: the effect of treatment condition on suicidal ideation and on number of days using drugs was no longer marginally significant.