Distinct Patterns of Intentional and Unintentional Overdose Among Psychiatric Patients With Bipolar and Substance Use Disorders

MADELINE B. BENZ, PhD; RITA ROSSI, MA; JIHOON CHOI, BS; ALANA DAVIS, BA; TONI M. AMARAL, BA; ANA RABASCO, PhD; MICHAEL D. STEIN, MD; LAUREN M. WEINSTOCK, PhD; IVAN MILLER, PhD; BRANDON A. GAUDIANO, PhD

ABSTRACT

BACKGROUND: Co-occurrence of Bipolar Disorder (BD) and Substance Use Disorder (SUD) increases the risk of negative mental health outcomes, including both intentional (i.e., suicide self-poisoning) and unintentional overdose (i.e., accidental). While it is clear that both forms of overdose are a relevant concern, less is understood about the differences in phenomenology between intentional and unintentional overdose among this high-risk group.

METHODS: Demographic and clinical characteristics were drawn from a sample of patients at a Rhode Island hospital during their baseline session of a larger psychosocial intervention clinical trial.

RESULTS: Among 171 participants with co-occurring BD-SUD, 77% reported a history of any type of overdose, 48% reported a history of unintentional overdose, 56% reported a lifetime suicide attempt via intentional overdose, and 28% reported experiencing both intentional and unintentional overdose. Collectively, antidepressant/antipsychotic/mood-stabilizing medications were the most frequently reported substances for intentional overdose, followed by sedating medications and alcohol. Opioids were the most frequently reported substance for accidental overdose, followed by alcohol and stimulants. Polysubstance use was indicated for 62% of intentional overdose events and 43% of accidental overdose events. Compared to participants with a history of intentional overdose only, those who have experienced both types of overdose were significantly younger and more likely to have co-occurring alcohol use disorder and drug use disorder.

CONCLUSIONS: Our findings suggest that psychotropic medications traditionally used to treat BD and other psychiatric disorders are often implicated in intentional overdose. Additionally, our results highlight the need for a focus on prevention of polysubstance overdose across the intentionality spectrum.

KEYWORDS: Bipolar Disorder; Substance Use Disorder; overdose; suicide

INTRODUCTION

Bipolar Disorder (BD), involving extreme fluctuations in mood, energy, and activity levels (known as manic/hypomanic and depressive episodes),[1] is characterized by a profoundly elevated risk of premature mortality, largely driven by high rates of suicide and intentional self-harm.[2,3] Individuals with BD face a suicide risk approximately 20–30x higher than the general population,[4] and estimates suggest up to 50% of individuals with the diagnosis attempt suicide at least once in their lifetime.[5] While suicide methods vary, intentional self-poisoning is a predominant mechanism of lethality for this group, particularly among women.[6] These intentional overdoses are often characterized by use of prescribed medications, rather than illicit substances,[6,7] possibly related to increased access to psychiatric medications in the context of complex treatment regimes.[8,9]

In parallel, people diagnosed with Substance Use Disorders (SUD) are at high risk of unintentional overdose death, fueling an epidemic in the United States (U.S.) that has claimed more than 800,000 lives over the past decade.[10] Unlike the intentional overdoses prevalent in BD, overdose deaths in the context of SUDs are overwhelmingly classified as accidental.[11] Mortality in this context is heavily predicted by the presence of opioids, along with the proliferation of illicitly manufactured fentanyl and physiological vulnerability following periods of abstinence.[12] Overdose deaths from substances other than opioids are also on the rise in the U.S.[13]

BD and SUDs are commonly co-occurring psychiatric disorders. In fact, the National Epidemiologic Survey on Alcohol and Related Conditions indicates that approximately 40–70% of U.S. adults with BD will experience a co-occurring SUD in their lifetime.[14] This comorbidity fosters an environment that elevates risk for both intentional and unintentional overdose.[15] Consequently, patients with co-occurring BD and SUD face a substantial increase in overdose death risk, such that the risk is significantly higher than for those with either disorder alone.

The Rhode Island (RI) population experiences increased risk for negative outcomes at the intersection of BD and SUD. Recently, the state ranked 16th in the nation for rates of illicit drug use and opioid-related fatalities,[16] creating a high-risk context for individuals with mood disorders. While overdose death rates have been declining since 2022, 329 Rhode Islanders died from accidental drug overdose in

2024.[17] Similarly, the latest confirmed data from the Centers for Disease Control and Prevention found 126 suicide deaths in RI in 2022,[18] and provisional estimates of suicide-related emergency department visits in 2025 suggest increasing rates since 2024.[19]

The overdose crisis in RI has traditionally been segmented into intentional suicide vs. accidental overdose fatalities; however, local data suggest a different picture for these dual-diagnosis individuals (i.e., those who meet diagnostic criteria for a SUD and co-occurring psychiatric disorder). A recent analysis of state overdose deaths revealed that while individuals with a history of intentional overdose were significantly more likely to have a known mental health diagnosis (77.9%), about 15% of unintentional overdose victims also had a documented diagnosis of BD.[20] This finding underscores a critical vulnerability in that RI patients with BD are not only at heightened risk for intentional self-poisoning, but they are also disproportionately represented in accidental drug-related deaths.[20,21]

The Current Study

While overdoses are clearly a serious public health concern in RI, less is understood about the differences in phenomenology between intentional and unintentional overdose for dual-diagnosis individuals. The current study sought to address gaps in the literature by characterizing intentional and unintentional overdose patterns among BD-SUD patients in a hospital in RI. While the general RI population has an accidental overdose event rate of <1% annually, we hypothesized that (1) our hospital sample would report rates exceeding 40%. This estimate is based on recent literature indicating 36–49% of individuals with severe SUDs experience a lifetime non-fatal accidental overdose.[22,23] Similarly, given estimates that 32–36% of individuals with BD attempt suicide (with self-poisoning a predominant method),[24] we hypothesized that (2) rates of intentional overdose in our sample would exceed 20%. We also hypothesized that (3) antidepressant/antipsychotic/mood-stabilizing medications would be more frequently implicated in intentional self-poisoning events, while opioids would be more frequently reported for unintentional overdoses. Lastly, we sought to explore how participants who report a history of both types of overdose compare on demographic variables to those with intentional overdose alone and accidental overdose alone.

METHODS

Data for this analysis were drawn from the baseline assessment of a larger randomized controlled trial designed to evaluate the efficacy of a specialized psychosocial intervention for English-speaking adults with co-occurring bipolar and substance use disorders taking at least one mood-stabilizing medication (ClinicalTrials.gov Identifier: NCT04202393). The parent study recruited adult hospital patients meeting DSM-5 criteria for BD (I, II, or unspecified) and a current co-occurring SUD (alcohol and/or drug). Following recruitment during acute hospitalization, participants were randomized to receive either a multicomponent psychosocial intervention involving individual and family sessions, or an enhanced treatment as usual condition with additional assessment and care coordination. Only baseline overdose history and sample characteristics were analyzed in the current report. Patients were recruited from 2020–2025.

Measures

All participants completed a brief demographics questionnaire at baseline.

Eligibility Criteria: BD and SUD diagnoses were determined using the Mini-International Neuropsychiatric Interview (MINI),[25] which is a brief, structured diagnostic interview for DSM-5 disorders, designed for use in clinical practice and research settings. Extensive validation studies have demonstrated that the MINI possesses high reliability and validity when compared to established gold-standard measures.[26] Medication use was measured through the Brief Adherence Rating Scale (BARS),[27] which is a clinician-administered instrument consisting of questions regarding the patient's knowledge of their medication regimen and missed doses. The BARS has demonstrated reliability and validity.[28]

Intentional Overdose: The Columbia Suicide Severity Rating Scale (C-SSRS)[29] is a well-validated measure of suicidal ideation and behavior in clinical samples.[30] After assessing for a history of suicide attempt, the C-SSRS interviewer obtains information regarding the suicide method. If a participant endorsed lifetime history of intentional overdose on the C-SSRS, they were asked to identify and answer descriptive questions (including which substances were involved) about their most recent intentional overdose on the Overdose Interview (see below).

Accidental Overdose: The Overdose Interview (ODI) was developed by the authors and used in prior studies (e.g., Johnson et al., 2020). Participants were asked if they had ever in their lifetime experienced an accidental overdose, described as, "…taking too much of a substance or a combination (including medications, alcohol, and/or drugs) that causes immediate negative health effects without ANY intention to die or wish to die." Participants provided descriptive details regarding their most recent accidental overdose event, including which substances were involved.

Substance Categorization: Substances were categorized according to their primary central nervous system effects, with an emphasis on pharmacologic mechanisms and behavioral outcomes relevant to acute risk states (e.g., disinhibition, perceptual alteration, or sedation). This approach is consistent with established frameworks (e.g., DSM-5[31]) that group substances based on shared neurobiological effects rather than legal status or route of administration. See **Table 1** for additional details regarding substances included in each category.

Data Analysis Plan

Analyses were conducted using SPSS version 31. Prevalence estimates were obtained to identify the percentage of the sample reporting a history of intentional overdose, accidental overdose, and both types of overdose. These groups were then compared on demographics and the participant reported substance types using independent-samples *t* tests and χ^2 tests, as appropriate. Among the 176 participants with baseline data, 5 were missing the full ODI measure and were therefore excluded from analyses, leaving a final sample of $n = 171$.

RESULTS

Hypotheses 1 & 2

We hypothesized that our hospital sample would report (1) rates of accidental overdose exceeding 40% and (2) rates of intentional overdose exceeding 20%.

Among 171 participants with co-occurring BD-SUD, 77% ($n = 131$) reported a history of any type of overdose, 48% ($n = 82$) reported a history of unintentional overdose, 56% ($n = 96$) reported a lifetime suicide attempt via intentional overdose, and 28% ($n = 47$) reported experiencing *both* intentional and unintentional overdose.

Hypothesis 3

We hypothesized that antidepressant/antipsychotic/mood-stabilizing medications would be more frequently implicated in intentional self-poisoning events, while opioids would be more frequently reported for unintentional overdoses.

Among those who reported an intentional overdose ($n = 96$), antidepressant/antipsychotic/mood-stabilizing medications were the most frequently reported substance (42%), followed by sedating medications (38%) and alcohol (34%). A majority of participants (62%) noted their intentional overdose event involved use of more than one substance (i.e., polysubstance overdose). For participants who reported an accidental overdose ($n = 82$), opioids were the most frequently reported substance (59%), followed by alcohol (33%), and stimulants (24%). Just under half of the participants (43%) indicated polysubstance use during their accidental overdose event. See **Table 1** for additional substance frequencies.

Table 1. Substances Involved in Overdose Events

Substance	Intentional Overdose ($n = 96$)	Accidental Overdose ($n = 82$)
Alcohol	33 (34%)	27 (33%)
Opioid	23 (24%)	48 (59%)
Sedative	36 (38%)	12 (15%)
Stimulant	13 (14%)	20 (24%)
Antidepressant/Antipsychotic/ Mood-stabilizing medications	40 (42%)	6 (7%)
Over-the-counter medication	13 (14%)	3 (4%)
Cannabis and related plant-based psychoactives	6 (6%)	8 (10%)
Perceptual-altering substances	2 (2%)	4 (5%)
Polysubstance	59 (62%)	35 (43%)

Note: Opioid category is inclusive of both prescribed (e.g., Percocet) and illicit (e.g., heroin) opioids; Sedative category is inclusive of medications that are primarily sedating (e.g., benzodiazepines, sedative-hypnotics); Stimulant category is inclusive of primary stimulant agent, both prescribed (e.g., Adderall) and illicit (e.g., cocaine); Antidepressant/Antipsychotic/Mood-stabilizing medications category is inclusive of the listed traditional therapeutic psychiatric medications; Over-the-counter medications category is inclusive of non-prescription medications (e.g., Benadryl); Cannabis and related plant-based psychoactives category is inclusive of THC, CBD, and Kratom; Perceptual-altering substances category is inclusive of recreational drugs with hallucinogenic qualities (e.g., ecstasy, LSD); Polysubstance category is inclusive of any overdose event that involved more than 1 substance (e.g., alcohol + opioids, sedative + antidepressant medication, etc.).

Exploratory Analyses

How do participants who report history of both types of overdose compare on demographic variables to those with intentional overdose alone or accidental overdose alone?

When compared to participants in the intentional overdose only group, those who reported both types of overdose were significantly younger (36.9 years vs. 41.4 years, $p = .02$) and significantly more likely to have co-occurring alcohol and drug use disorder (rather than either disorder alone; 87.9% vs. 65.6%, adjusted residual = 2.1). There were no significant differences in demographic characteristics between participants in the accidental overdose-only group and those who reported both types of overdose.

DISCUSSION

In support of Hypotheses 1 and 2, baseline data from a larger clinical trial indicate a concerning prevalence of overdose history among patients admitted to a psychiatric hospital with co-occurring bipolar and substance use disorders, with 77% reporting at least one lifetime overdose event. The fact that 28% of this sample reported a history of both intentional and unintentional overdose is notable. This overlap suggests that for many dual-diagnosis patients, the distinction between a "suicide attempt" and an "accidental overdose" may be fluid or possess similar underlying pathology, such as mood instability and tendency to self-medicate (i.e., using non-prescribed substances with the intent to alleviate psychological distress or manage symptoms of a mental health condition). While we can theorize that these rates may be driven by the convergence of mood instability, acute distress, and intoxication-related impairment, it is important to recognize the other ways in which mental health comorbidities increase overdose risk.

Specifically, there is a paradox in that the multiple medications sometimes used to treat co-occurring BD and SUD can introduce significant risks by complicating medication regimens, which increases the likelihood of treatment

non-adherence, and by providing increased access to lethal means via medications. Because these dual-diagnosis patients are often prescribed complex polypharmacy medication regimens (e.g., a combination of mood stabilizers and adjunctive anxiolytics to manage symptom severity),[32] they are routinely in possession of large quantities of medication that carry significant risk of toxicity.[33] Agents used in standard care, such as lithium, possess narrow therapeutic indices, meaning that a standard quantity prescribed can easily constitute a fatal dose if ingested impulsively as an intentional overdose during a crisis.[34] Furthermore, the risk of unintentional toxicity is amplified when sedating medications like benzodiazepines or sedating antipsychotics are combined with use of alcohol or opioids, which can significantly lower the threshold for accidental overdose death through synergistic depression of the central nervous system.[35] Consequently, clinicians must weigh the stabilization benefits of pharmacotherapy against the reality that the very medications prescribed to prevent clinical deterioration may, without rigorous safeguards, facilitate overdose events.

Historically, many overdose prevention efforts have prioritized addressing opioid use to mitigate accidental overdose; however, in line with Hypothesis 3, we found that collectively antidepressant/antipsychotic/mood-stabilizing medications were the substances most frequently identified in intentional self-poisoning events, followed by alcohol and sedating medications. Furthermore, 62% of intentional overdoses involved polysubstance use, often combining medications with alcohol, which highlights a critical area for clinical intervention. Conversely, opioids remained the primary driver of unintentional overdoses, followed by alcohol and stimulants. This reflects broader national and local trends, where the proliferation of illicit substances, including fentanyl, increases mortality. However, the high prevalence of alcohol consumption across both overdose categories suggests that alcohol remains a ubiquitous catalyst for overdose, possibly by exacerbating the impulsivity and cognitive disinhibition inherent in both BD and SUD. Therefore, it is important to focus on preventing psychiatric medication overdoses among individuals at higher risk of suicide in this community, as well as reducing the practice of mixing medications with alcohol.

Regarding exploratory analyses of group comparisons [**Table 2**], we found that participants in the group reporting both types of overdose were significantly younger and more likely to have co-occurring alcohol and drug use disorder than those reporting only intentional overdose. This finding highlights an important group to be targeting in overdose prevention efforts across the full intentionality spectrum. Mainly, it appears that the BD-SUD overlap is compounded even further when considering polysubstance use and co-occurring SUDs. As providers assess for comorbid conditions, it may be helpful to flag those with multiple SUDs as potential beneficiaries of additional overdose risk management.

Table 2. Between Group Comparisons

	Both Types of OD (n = 47)	Intentional OD only (n = 49)	Comparison Both vs. Intentional only	Accidental OD only (n = 35)	Comparison Both vs. Accidental only
Variable	**m (SD)**	**m (SD)**	**p-value (t)**	**m (SD)**	**p-value (t)**
Age	36.9 (*9.4*)	41.4 (*12.0*)	.02	39.0 (*12.1*)	ns
Variable	**n (%)**	**n (%)**	**p-value (χ^2)**	**n (%)**	**p-value (χ^2)**
Birth Sex			ns		ns
Male	24 (*51.1*)	22 (*44.9*)		24 (*68.6*)	
Female	23 (*48.9*)	27 (55.1)		11 (*31.4*)	
Race/Ethnicity			ns		ns
White	34 (*72.3*)	40 (*81.6*)		28 (*80.0*)	
Black	4 (*8.5*)	3 (*6.1*)		0 (*0.0*)	
Multiracial	6 (*12.8*)	4 (*8.2*)		5 (*14.3*)	
Hispanic	8 (*17.0*)	3 (*6.1*)		2 (*5.9*)	
Marital Status			ns		ns
Single	36 (*76.6*)	28 (*57.1*)		24 (*68.6*)	
Married/ Domestic partner	3 (*6.4*)	4 (*8.2*)		8 (*22.9*)	
Separated/Divorced/ Widowed	8 (*17.0*)	17 (*34.7*)		3 (*8.6*)	
Household Income			ns		ns
Under $20,000	27 (*60.0*)	32 (*65.3*)		22 (*64.7*)	
Over $20,000	18 (*40.0*)	12 (*34.7*)		12 (*35.3*)	
Employment Status			ns		ns
Full or part time	20 (*42.6*)	26 (*53.1*)		13 (*37.1*)	
Unemployed	11 (*23.4*)	7 (*14.3*)		9 (*25.7*)	
Disabled	12 (*25.5*)	15 (*30.6*)		13 (*37.1*)	
Substance Use Disorder			.03		ns
Alcohol Use	2 (*6.1*)	10 (*31.3*)	*	3 (*11.1*)	
Non-alcohol	2 (*6.1*)	1 (*3.1*)		2 (*7.4*)	
Both alcohol and non-alcohol	29 (*87.9*)	21 (*65.6*)	*	22 (*81.5*)	

Note: m (*SD*) indicates variables for which means and standard deviations are depicted; n (%) indicates number and percentage. OD = overdose. Comparisons were not made between intentional and accidental overdose. *Adjusted residual > ±1.96.

CLINICAL AND PUBLIC HEALTH IMPLICATIONS

In light of these results, several clinical shifts are recommended:

Integrated Prevention: Providers should avoid siloing intentional and unintentional overdose interventions into mutually exclusive categories; rather, we recommend that for patients with co-occurring BD and SUD, screening for suicide risk be paired with harm reduction strategies (e.g., naloxone distribution), even for patients who outwardly appear to be low risk for intentional or unintentional overdose.

Medication Management: Given the role of psychiatric medications in intentional overdose, clinicians should emphasize lethal means counseling and consider the safety of prescribing patterns for high-risk individuals. Through de-prescribing (i.e., discontinuing inappropriate or excessive medications), prescribers can reduce overdose rates by mitigating access to medications with higher risk profiles.[36]

Polysubstance Awareness: Public health campaigns in RI and beyond should focus on the high rates of polysubstance use, particularly the combination of medications with alcohol, which was prevalent across the intentionality spectrum in our sample. There is a need to increase education regarding the ways in which the chemical effects of one substance can compound the effects of another. For example, the depressant effects of alcohol may exacerbate the depressant effects of benzodiazepines, leading to higher overdose risk. Alternatively, the mood-altering effects of alcohol may lead to impulsive decisions to take higher doses of a medication, also increasing overdose risk. Similar to public health campaigns that have educated consumers about the impact of fentanyl in the RI drug supply (e.g., the *Assume Fentanyl* campaign and the *No Matter Why You Use* campaign), we hope to reduce both intentional and unintentional overdose rates by highlighting dangers of mixing substances.

CONCLUSION

This study highlights a critical vulnerability among psychiatric patients with dual diagnoses. While accidental opioid overdose is understandably a major public health priority, this study identifies intentional self-poisoning with antidepressants, antipsychotics, and mood-stabilizing medications as another prominent area of concern among patients with BD and SUD. Our data highlight a need to integrate the management of psychiatric medications with efforts to reduce the risks associated with illicit substance use, as well as the need for a focus on prevention of polysubstance overdose across the intentionality spectrum.

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Authors

Madeline B. Benz, PhD, Brown University, Warren Alpert Medical School; Butler Hospital, Psychosocial Research Department, Providence, RI.

Rita Rossi, MA, Butler Hospital, Psychosocial Research Department, Providence, RI.

Jihoon Choi, BS, Butler Hospital, Psychosocial Research Department, Providence, RI.

Alana Davis, BA, Butler Hospital, Psychosocial Research Department, Providence, RI.

Toni M. Amaral, BA, Butler Hospital, Psychosocial Research Department, Providence, RI.

Ana Rabasco, PhD, Brown University, Warren Alpert Medical School; Butler Hospital, Psychosocial Research Department, Providence, RI.

Michael D. Stein, MD, Boston University School of Public Health, Boston, MA.

Lauren M. Weinstock, PhD, Brown University, Warren Alpert Medical School; Butler Hospital, Psychosocial Research Department, Providence, RI.

Ivan Miller, PhD, Brown University, Warren Alpert Medical School; Butler Hospital, Psychosocial Research Department, Providence, RI.

Brandon A. Gaudiano, PhD, Brown University, Warren Alpert Medical School; Butler Hospital, Psychosocial Research Department, Providence, RI.

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Correspondence

Madeline B. Benz, PhD
Butler Hospital
345 Blackstone Blvd., Providence, RI 02906
madeline_benz@brown.edu