

# Survey of noncontrolled medication misuse patterns

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## Abstract

**Introduction:** The abuse potential of opioids and other controlled substances is well-known; however, reports of noncontrolled prescription medication (NCPM) misuse deserves further attention. Whereas several studies investigate patterns, motivations, and biochemical mechanisms underlying the misuse potential of NCPM, the clinical significance of NCPM misuse is not well-understood. The primary objectives of this project were to identify prescriber perceptions of NCPM misuse and evaluate patient reported patterns of misuse through survey responses.

**Methods:** Adult patients admitted to psychiatry services and prescribers working in psychiatry or on a general medicine service during the study time frame were invited to participate. Surveys were collected anonymously for both patients and prescribers.

**Results:** NCPM misuse was reported by 38.4% of patients. Trazodone (35%) and quetiapine (30%) were most commonly reported as being misused. Opioid (24.1% vs 4.3%;  $P=.023$ ) and cannabis use disorders (13.8% vs 0%;  $P=.019$ ) were reported more frequently in patients who misuse NCPM, whereas no difference was seen for other SUDs ( $P > .05$ ). There was no difference between psychiatric and general medicine prescribers regarding familiarity with NCPM misuse ( $n = 21$  [87.5%] vs  $n = 13$  [81.3%];  $P=.668$ ).

**Discussion:** High rates of NCPM misuse were seen in this patient population. Our findings confirm previous reports of quetiapine misuse and also reveal that trazodone is frequently misused. Based on the observations in this study, the misuse of NCPM is identified as prevalent and noteworthy at our institution, warranting provider education and future studies.

**Keywords:** medication misuse, substance use disorders, patient survey, prescriber survey

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## Introduction

The National Institute on Drug Abuse<sup>1</sup> defines medication misuse as “taking a medication in a manner or dose other

than prescribed; taking someone else’s prescription, even if for a legitimate medical complaint such as pain; or taking a medication to feel euphoria (ie, to get high).”<sup>(p.2)</sup> The misuse of controlled medications is an evolving epidemic that has continued to persist in the last decade.<sup>2</sup> The misuse of opioids, benzodiazepines, and stimulants is widely recognized by both prescribers and patients as it is a leading cause of hospitalizations, emergency room visits, and deaths.<sup>3</sup> Wide recognition of opioid misuse has resulted in increased provider awareness and subsequent decreased dispensing.<sup>4</sup> In 2018, the Centers for Disease Control released data showing a decrease in prescription opioid-involved deaths by 13.5% from 2017.<sup>5</sup> This reduction is thought to be due to increased awareness,



changes in prescribing habits, and decreased stigmas associated with receiving treatment for OUD.<sup>6</sup>

A less widely recognized yet related topic is medication misuse involving noncontrolled prescription medications (NCPM). It is demonstrated that patients with co-occurring mental health disorders are 3 times more likely to misuse NCPM.<sup>7</sup> It is also shown that individuals often misuse NCPM in combination with other prescriptions, non-prescriptions, or substances.<sup>8</sup> Documented motivations for misusing a NCPM are not well-studied, but some motivations for misuse of NCPM include to self-medicate for existing physical or mental health disorders, to achieve the *high* feeling associated with misuse, and because of perceived safety of abusing NCPM instead of substances.<sup>7</sup>

Federally, gabapentin is an NCPM; however, it has a moderate amount of evidence surrounding its misuse potential.<sup>9</sup> Due to this, several states have adjusted the scheduling of gabapentin making it a controlled substance. In the state of South Carolina, gabapentin remains classified as an NCPM. Historically, it was thought that gabapentin did not have misuse potential, and it was frequently prescribed for a variety of conditions, including seizure disorders, peripheral neuropathy, and insomnia.<sup>10</sup> Within the past decade, a misuse signal has emerged.<sup>10</sup> Gabapentin is thought to inhibit the release of excitatory neurotransmitters through its inhibition of voltage-gated calcium channels, resulting in central nervous system effects, including dizziness and fatigue.<sup>11</sup> Survey studies have been conducted looking at the rates of gabapentin misuse in the general population and found it to be as high as 1.1%.<sup>12</sup> Two studies looked at rates of gabapentin misuse in treatment facilities for substance use; rates of misuse were found to be 22% overall.<sup>12</sup> Patients with a history of OUD were found to be more likely to also misuse gabapentin.<sup>12</sup> The misuse of gabapentin is thought to be due in part to its ease of access, its affordability, and minimal adverse side effects associated with its use.<sup>10</sup> Notably, pregabalin, a medication with structural similarities to gabapentin, is a federally controlled substance due to its misuse potential.<sup>13</sup> Pregabalin and gabapentin differ in regard to some pharmacokinetic properties.<sup>14</sup> For example, pregabalin does not depend on active transport for absorption, whereas gabapentin does.<sup>14</sup> This property results in predictable, linear pharmacokinetics with pregabalin compared with gabapentin, exhibiting saturable, nonlinear pharmacokinetics.<sup>14</sup> These properties theoretically make gabapentin less desirable for misuse.

Other agents, such as quetiapine, bupropion, trazodone, clonidine, and venlafaxine, are associated with reports of misuse.<sup>15-23</sup> These medications have varying pharmacodynamic properties that may underlie their potential misuse. Some medications are misused along with other medications or substances for greater effect, whereas

others are used to recover from or mitigate the adverse effects of medications or substances.<sup>18,23</sup> As an example, clonidine is a centrally acting alpha agonist and is hypothesized to *boost* the effects of methadone and cocaine by minimizing withdrawal symptoms, enhancing sedation, and *optimizing* a patient's high.<sup>17</sup> Whereas several studies review the theoretical explanations behind misusing these agents, few studies determine the clinical significance of this misuse.

An estimated 38% of patients admitted to a psychiatric hospital have co-occurring mental health and SUDs.<sup>24</sup> It is largely known that opioids and other controlled medications are being misused, but NCPM misuse is less consistently reported. Due to the gap in literature regarding the clinical significance or frequency of NCPM misuse, this study aims to identify prescriber perceptions of NCPM misuse and to evaluate patient reported patterns of misuse at this academic medical center.

## Methods

### Design

This was a prospective, observational, cross-sectional survey studying patient reports and prescriber perceptions of NCPM misuse. Data for this analysis was obtained through anonymous survey responses from patients and prescribers at a large academic medical center. Data was stored in REDCap. Medications with a potential for misuse were identified through a literature search on PubMed. Eight medications were identified, including quetiapine, bupropion, venlafaxine, trazodone, clonidine, dextromethorphan, gabapentin, and loperamide.

### Study Population

Adult patients hospitalized from November 1, 2020 to March 31, 2021, who were under the care of psychiatry services on either the general psychiatry or addictions unit were eligible to participate. Psychiatric and general medicine prescribers at this institution from November 1, 2020 to March 31, 2021, were eligible to participate. IRB approval was obtained.

### Patient Survey

The following baseline demographic information was collected for patients: hospital unit, age, sex, medical diagnoses, and admission reasons. The anonymous patient surveys focused on questions regarding medication misuse patterns, including patient-reported definitions for medication misuse, identification of medications misused if any, and intent behind misuse if applicable. Survey participation was voluntary, and surveys were

distributed by nursing staff with other paperwork at the time of discharge. The surveys were contained in sealed envelopes and picked up regularly by the primary investigator. Patient surveys were distributed via paper and data was subsequently entered into REDCap.

## Prescriber Survey

The following baseline demographic information was collected for prescribers: age, year of graduation, degree, additional training completed, classification (attending, resident, or other), primary practice site, and practice site setting. The anonymous prescriber surveys focused on questions regarding medication misuse perceptions, including awareness of NCPM misuse and whether prescribing patterns differ based on medication misuse perceptions. Prescriber surveys were distributed via email and input directly into REDCap.

## Outcome Measures

### Primary Endpoints

The primary endpoints of the study were to identify rates of misuse of individual NCPMs, to identify rates of misuse among patients, to assess the familiarity of NCPM misuse among prescribers (including analysis of familiarity based on type of prescriber: psychiatric vs general medicine), and to determine rates of individual NCPMs considered to have the highest likelihood for misuse by prescribers.

### Patient-Specific Secondary Endpoints

Patient-specific secondary endpoints included identifying rates of NCPM misuse in patients with various types of patient-reported SUDs, for example, AUD, OUD, etc, along with other patient-reported comorbid medical conditions. Additional endpoints included assessing the most common definition, route of administration, intent, and adverse effect of misuse.

### Prescriber-Specific Secondary Endpoints

Prescriber-specific secondary endpoints included identifying the most common definition of misuse, analysis of awareness of NCPM misuse based on level of training (ie, resident or attending) or primary practice site (ie, outpatient or inpatient), and identifying clinical characteristics influencing prescribers to change prescribing habits.

## Statistical Analysis

Continuous variables are reported as medians with IQRs, and categorical variables are reported as counts with percentages. Age, the only continuous variable, was found to have non-normal distribution and was, therefore, compared between cohorts using Mann-Whitney *U* tests, whereas categorical variables were compared with  $\chi^2$  or Fisher exact tests when appropriate. IBM SPSS version 25 was used for statistical analysis. *P*-values  $<.05$  were considered statistically significant.

**TABLE 1: Baseline demographics for included patients (N = 76) and prescribers (N = 46)**

	n (%) <sup>a</sup>
<b>Patients</b>	
Age, y	34.5 (29-49)
Male	40 (53.3)
SUD	25 (32.9)
Anxiety	45 (59.2)
Suicidal ideation	39 (51.3)
Depression	45 (59.2)
Mania	13 (17.1)
Psychosis	9 (11.8)
<b>Prescribers</b>	
Age, y	34 (29-40)
MD degree	43 (93.5)
Residency completed	26 (57.8)
Fellowship completed	10 (22.2)
Attending physician	26 (56.5)
Resident	17 (37)
Psychiatry practice site	24 (52.2)
Medicine practice site	17 (36.9)
Inpatient prescriber	32 (69.6)
Outpatient prescriber	14 (30.4)

<sup>a</sup>Values shown as n (%) except for age, which is denoted as median (IQR).

## Results

### Characteristics of Patients

In total, 79 patients completed the survey between November 2020 and March 2021; 3 patient surveys were excluded due to missing data. Missing data is defined as patients not answering any questions regarding medication misuse but only baseline demographic information. As a result, 76 patient surveys were included in the final analysis. Demographics are included in Table 1. The median age of patients was 34.5 years (IQR 29-49), and patients were predominantly male (n = 40; 53.3%). Depression (n = 45; 59.2%) and anxiety (n = 45; 59.2%) were the most commonly reported admission reasons. To note, of the patient surveys included, not all surveys had all medication misuse questions fully answered, leading to differing sample sizes for each endpoint based on response rates of individual questions.

### Characteristics of Prescribers

Demographics are included in Table 1. In total, 46 prescribers completed the survey between November 2020 and March 2021. The median age of prescribers was 34 years (IQR 29-40), prescribers predominantly held an

**TABLE 2:** Demographics among respondents with noncontrolled prescription medication (NCPM) misuse (N = 29) versus without (N = 47)

	NCPM Misuse, n (%) <sup>a</sup>	No NCPM Misuse, n (%) <sup>a</sup>	P Value
<b>Demographic</b>			
Age, y	30 (23-44)	40 (32-51)	.007
Male	15 (53.6)	25 (53.2)	.738
<b>Reasons for Hospitalization</b>			
SUD	9 (31.0)	16 (34.0)	.786
Anxiety	14 (48.3)	31 (66.0)	.128
Suicidal ideation	18 (62.1)	21 (44.7)	.141
Depression	17 (58.6)	28 (59.6)	.934
Mania	6 (20.7)	7 (14.9)	.544
Psychosis	5 (17.2)	4 (8.5)	.290

<sup>a</sup>Values shown as n (%) except for age, which is denoted as median (IQR).

MD degree (including current residents and those who had completed a residency; n=43; 93.5%), 57.8% had completed a residency (n=26), and 22.2% a fellowship (n=10). Notably, the remaining prescribers (n=3; 6.5%) held a DO degree. Additionally, 56.5% of prescribers were currently classified as an attending (n=26), 52.2% practice primarily in the area of psychiatry (n=24), and 69.6% practice in the inpatient setting (n=32).

### NCPM Misuse

Of the 76 patient responses, 29 (38.4%) reported either historic or current misuse of NCPM. Twenty patients answered questions regarding specific medications they had previously misused. Trazodone (n=7; 35%), quetiapine (n=6; 30%), gabapentin (n=5; 25%), and dextromethorphan (n=5; 25%) were most commonly reported as being misused. Of the 45 prescriber responses, 39 (86.7%) reported familiarity with NCPM misuse. There was no difference regarding familiarity of NCPM misuse when comparing psychiatric and general medicine prescribers (n=21; 87.5% vs n=13; 81.3%;  $P=.668$ ). Prescribers perceived that dextromethorphan (n=40; 88.9%), gabapentin (n=34; 75.6%), and quetiapine (n=30; 66.7%) had the highest risk for misuse in the list of medications provided.

### Secondary Outcomes

#### Rates of NCPM Misuse Among Various Comorbid Conditions

As shown in Table 2, there was no difference in the rate of NCPM misuse in patients admitted secondary to SUD (n=9; 31% vs n=16; 34%;  $P=.786$ ), anxiety (n=14; 48.3% vs n=31; 66%;  $P=.128$ ), suicidal ideation (n=18; 62.1% vs n=21; 44.7%;  $P=.141$ ), or depression (n=17;

**TABLE 3:** SUDs among respondents with noncontrolled prescription medication (NCPM) misuse (N = 29) versus without (N = 47)

Disorder	NCPM Misuse, n (%)	No NCPM Misuse, n (%)	P Value
Any substance use	11 (37.9)	13 (27.7)	.349
Alcohol use	6 (20.7)	11 (23.4)	.783
Opioid use	7 (24.1)	2 (4.3)	.023
Cannabis use	4 (13.8)	0 (0)	.019
Hallucinogen use	0 (0)	1 (2.1)	>.99
Stimulant use	1 (3.4)	3 (6.4)	>.99

58.6% vs n=28; 59.6%;  $P=.934$ ). Opioid and cannabis use disorders were reported more frequently in patients who misuse NCPM vs those who do not (opioid: n=7; 24.1% vs n=2; 4.3%,  $P=.023$ ; cannabis: n=4; 13.8% vs n=0; 0%;  $P=.019$ ; Table 3). No differences in misuse rates were seen among patients with AUD, hallucinogen use disorder, or stimulant use disorder ( $P >.05$ ). Additionally, there was no difference in the rate of NCPM misuse in patients with any of the comorbidities analyzed. Notably, this included ADHD, chronic pain, or hepatitis C virus ( $P >.99$ ; Table 4).

#### Patient-Specific Outcomes

Oral (n=25; 86.2%) misuse of NCPM was most common, whereas the intranasal route was rare (n=3; 10.3%). Misuse of NCPM to get high was the most commonly reported reason for misuse (n=10; 38.5%). The most

**TABLE 4:** Comorbidities among respondents with (N = 29) versus without (N = 47) noncontrolled prescription medication (NCPM) misuse

Comorbidity	NCPM Misuse, n (%)	No NCPM Misuse, n (%)	P Value
Diabetic neuropathy	0 (0)	1 (2.1)	>.99
Anxiety	17 (58.6)	33 (70.2)	.301
Bipolar	8 (27.6)	13 (27.7)	.994
Chronic pain	5 (17.2)	8 (17.0)	>.99
OCD	3 (10.3)	3 (6.4)	.669
ADHD	3 (10.3)	6 (12.8)	>.99
PTSD	9 (31.0)	16 (34.0)	.786
Hypertension	1 (3.4)	7 (14.9)	.145
Personality disorder	1 (3.4)	2 (4.3)	>.99
Eating disorder	1 (3.4)	5 (10.6)	.398
Schizophrenia	4 (13.8)	8 (17.0)	>.99
Sleep disorder	3 (10.3)	10 (21.3)	.348
Hepatitis C virus	0 (0)	1 (2.1)	>.99
Depression	18 (62.1)	33 (70.2)	.463



commonly reported definition of medication misuse was taking more medication than prescribed (n = 58; 85.3%).  
*Prescriber-Specific Outcomes*

The most common definition of medication misuse was taking medication that is not prescribed solely for the purpose of getting high (n = 44; 95.7%). Prescribers reported utilizing different prescribing habits in patients with a history of substance use (n = 42; 91.3%), for those with multiple controlled substance prescriptions in the prescription drug monitoring database (n = 36; 78.3%), and in patients with a history of nonadherence (n = 28; 60.9%).

## Discussion

To our knowledge, this is the first prospective study evaluating both patient patterns and prescriber perceptions of NCPM misuse. Our study was designed most similarly to a self-report questionnaire published by Wilens et al<sup>22</sup> investigating the concomitant use of prescription medications among opioid- and/or alcohol-dependent patients seeking inpatient detoxification. In our study, 38.4% of patients surveyed reported NCPM misuse. This finding matches the findings from Wilens et al<sup>22</sup> as 30% of their surveyed population reported prescription medication misuse. The findings in our study specifically emphasize the potential for increased rates of NCPM misuse within the past several years. The aforementioned study analyzes both noncontrolled and controlled medication misuse, whereas this study only reviews NCPM misuse but finds comparable rates of misuse. Additionally, all patients reporting misuse in the Wilens et al<sup>22</sup> study were a part of the OUD subsample with none from the AUD subsample. The findings of our study align with the findings of Wilens et al<sup>22</sup> because it was more common for patients with OUD to report NCPM misuse.

Additionally, results suggest that perceptions of NCPM misuse by prescribers do not necessarily align with patient-reported patterns of NCPM misuse. Despite previous literature signaling a potential for misuse, we were surprised to discover that trazodone was the most common patient-reported medication of misuse in our sample. Trazodone is generally considered a *safe* medication to prescribe as an adjunct to other medications for insomnia.<sup>23,25</sup> This is exemplified by trazodone being a frequently utilized medication at our institution and only 28.9% of prescribers identifying trazodone as a *high-risk* medication for misuse. The format of our survey and the small sample size did not allow us to delineate the pattern and intent behind its misuse. Published literature<sup>23,25</sup> determines trazodone to have low misuse potential, but given our results, more research is needed.

Similar to trazodone, quetiapine is frequently prescribed at this institution, even for off-label indications, such as

delirium and insomnia despite 66.7% of prescribers identifying quetiapine as a high-risk medication. Both trazodone and quetiapine are theorized to have misuse potential due to having sedative and anxiolytic properties, but again, the exact mechanism is not fully elucidated.<sup>16,25</sup> These results highlight the need for enhanced education to prescribers. Additionally, all health care providers should keep these findings in mind when caring for patients. Everyone can play an active role in optimizing prescribing of these medications and minimizing polypharmacy.

The finding of OUD and cannabis use disorders being reported more frequently in patients who misuse NCPM is consistent with previously conducted literature.<sup>22</sup> Additionally, the finding that other SUDs, including alcohol, hallucinogen, and stimulant use disorders, were not associated with NCPM misuse is important and reassuring. In a previously conducted study,<sup>22</sup> no significantly higher rates of medication misuse are seen in patients misusing alcohol.

Several limitations exist in our study with most being directly related to the inherent limitations of the survey study design. Due to the data being a direct result of surveys, there is an inherent risk for reporting bias, and thus, results could be impacted. Overall, there were low participation rates for both patients and prescribers resulting in a smaller sample size than initially expected. This small sample size could impact the overall generalizability, so caution should be used when interpreting the results. Also, due to varying levels of education typically represented within this population, there may have been a lack of understanding for some of the survey questions within the patient survey that could influence the results. When analyzing the patient surveys, 3 surveys were not completed in their entirety and had to be excluded. More extensive education to patients and team members distributing surveys could provide a solution to this limitation. The utilization of paper surveys for patients resulted in issues with coordinating survey distribution and collection. This process required several individuals to work together as a team to ensure surveys were completed and returned for analysis. Last, this study was not designed to assess misuse pattern/intent based on individual medications. A much larger sample size would be needed to assess that endpoint.

After completion of this study, several steps can be taken to optimize clinical practice. To start, wide dissemination of the study findings to prescribers will be completed at our institution to raise awareness of NCPM misuse and promote safe prescribing. Also, education sessions will be provided to prescribers regularly to assess current prescribing patterns and ensure polypharmacy is avoided when possible.

Our study determined that NCPM misuse is prevalent and occurs frequently within our institution. Prescribers were generally aware of NCPM misuse as a whole; however, psychiatric prescribers were more familiar than general medicine prescribers. NCPM misuse is a prevalent and important topic that warrants more attention in the literature. Future studies should be aimed at determining the most likely mechanism of misuse for trazodone based on the findings of this study. Future studies aimed at analyzing the intent of NCPM misuse would help to fill a gap that still exists in the literature.

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