

# The Depression Treatment Cascade: Disparities by Alcohol Use, Drug Use, and Panic Symptoms Among Patients in Routine HIV Care in the United States

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## Abstract

Little is known about disparities in depression prevalence, treatment, and remission by psychiatric comorbidities and substance use among persons living with HIV (PLWH). We conducted a cross-sectional analysis in a large cohort of PLWH in routine care and analyzed conditional probabilities of having an indication for depression treatment, receiving treatment, receiving indicated treatment adjustments, and achieving remission, stratified by alcohol use, illicit drug use, and panic symptoms. Overall, 34.7% (95% CI 33.9–35.5%) of participants had an indication for depression treatment and of these, 55.3% (53.8–56.8%) were receiving antidepressants. Among patients receiving antidepressants, 33.0% (31.1–34.9%) had evidence of remitted depression. In a subsample of sites with antidepressant dosage data, only 8.8% (6.7–11.5%) of patients received an indicated treatment adjustment. Current drug users (45.8%, 95% CI 43.6–48.1%) and patients reporting full symptoms of panic disorder (75.0%, 95% CI 72.9–77.1%) were most likely to have an indication for antidepressant treatment, least likely to receive treatment given an indication (current drug use: 47.6%, 95% CI 44.3–51.0%; full panic symptoms: 50.8%, 95% CI 48.0–53.6%), or have evidence of remitted depression when treated (22.3%, 95% CI 18.5–26.6%; and 7.3%, 95% CI 5.5–9.6%, respectively). In a multivariable model, drug use and panic symptoms were independently associated with poorer outcomes along the depression treatment cascade. Few differences were evident by alcohol use. Current drug users were most likely to have an indication for depression treatment, but were least likely to be receiving treatment or to have remitted depression. These same disparities were even more starkly evident among patients with co-occurring symptoms of panic disorder compared to those without. Achieving improvements in the depression treatment cascade will likely require attention to substance use and psychiatric comorbidities.

**Keywords** HIV infections · Depression · Drug users · Alcohol drinking · Anxiety disorders

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## Introduction

Depression is the most common psychiatric comorbidity among persons living with HIV (PLWH), affecting 20–30% of infected adults [1–6]. Depression in PLWH is associated with negative health behaviors and outcomes, including reduced antiretroviral (ART) adherence [7, 8], missed HIV primary care appointments [9], reduced viral suppression [8, 10], and higher rates of AIDS-related morbidity and mortality [11, 12]. Studies have shown that treatment for depression can improve outcomes among PLWH, including reduced depressive symptoms [5, 13, 14], and improved ART adherence and viral suppression [15–18], although the evidence remains mixed [14, 19, 20].

Despite its high burden and negative consequences, depression is often undiagnosed and untreated among PLWH [13, 21]. The “depression treatment cascade,” [13, 22] similar to the HIV treatment cascade, outlines steps in care that are critical for successfully addressing depression [23–25]. These steps include diagnosis, treatment initiation, and guideline-concordant treatment adjustment in order to achieve remission. Studies of the depression treatment cascade in PLWH have identified substantial gaps in treatment, treatment adjustment, and remission [13, 22], with approximately half of those with depression going unrecognized, about half of those recognized going untreated, and only a small minority of those treated receiving guideline-concordant treatment adjustments when indicated. As a result, successful clinical resolution of depression in this population is rare [13].

In addition to depression, other psychiatric comorbidities, including anxiety and panic disorder [1, 4, 21, 26], hazardous alcohol use [1, 21, 27], and illicit drug use [1, 2, 21] are common in PLWH. Anxiety, alcohol use, and drug use also tend to be associated with adverse health and behavioral HIV outcomes [2, 10, 27–30], although evidence is mixed regarding the association between drug use and ART adherence [31]. In depressed PLWH, studies have shown that the presence of co-occurring psychiatric disorders is the norm rather than the exception, with more than half of those with depression also having at least one other psychiatric disorder [1, 5, 6, 28, 32–34]. While evidence suggests that occurrence of drug use, panic disorder, or heavy alcohol use [27, 30] is associated with disparities in HIV treatment outcomes, less is known about the impact of such co-occurrence on disparities in depression treatment [32].

Given the high burden of psychiatric comorbidities among PLWH, understanding how they affect disparities in depression treatment is crucial for improving mental health treatment and achieving improved health outcomes

in this population. This paper seeks to characterize the association of (1) co-occurring alcohol use, (2) drug use, and (3) panic symptoms with the prevalence of depression and the likelihood of receiving treatment, including exploratory analyses of receiving evidence-based treatment adjustments and achieving depression remission, in a large multi-site sample of patients receiving HIV primary care.

## Methods

### Data Source

Data for this analysis come from the Center for AIDS Research (CFAR) Network of Integrated Clinical Systems (CNICS) observational clinical cohort. To date, over 32,000 patients who are routinely seen for HIV clinical care across eight large academically-affiliated sites in the United States (US) have entered the CNICS cohort. Data from administrative and medical records at each site are de-identified and uploaded to a central CNICS repository on a quarterly basis. Nearly all patients consent to have their data captured. CNICS gathers information on demographics, medications, health care utilization, clinical diagnoses, laboratory values and vital signs, ART resistance, biologic specimens, and mortality. Beginning between 2005 and 2011, most CNICS sites integrated patient-reported outcomes (PROs) into routine clinical care to assess depression, panic symptoms, and drug and alcohol use among other domains. PROs are collected every 4–6 months at routine clinical visits and are self-administered on electronic touch-screen devices. Information on mental health counseling is not systematically available in the CNICS database. Data quality procedures have been previously described [35]. Data collection procedures are approved by institutional review boards (IRBs) at each site, and participants provide written informed consent. Ethical approval for these analyses was provided by the IRB at the University of North Carolina at Chapel Hill.

### Analysis Sample

The present analysis included all CNICS participants from seven sites who had completed at least one PRO. We completed a cross-sectional assessment of depression treatment and remission status by psychiatric comorbidity, defining all measures at the time of the most recent PRO. A sub-analysis was restricted to participants from three sites located in southern, western, and northeastern US with reliable medication dosing data to evaluate guideline-concordant dose adjustments.

## Measures

Depression was measured via the Patient Health Questionnaire-9 (PHQ-9) [36], included as part of the PRO administration. The PHQ-9 assesses presence of the nine DSM-IV criteria symptoms for depression in the past 2 weeks and is well-validated among PLWH [37]. A score  $\geq 10$  (on a scale of 0–27) is indicative of probable major depressive disorder [36, 38] and a score  $< 5$  among individuals receiving depression treatment is indicative of remission.

The PROs additionally included validated measures for alcohol use (The Alcohol Use Disorders Identification Test-Consumption (AUDIT-C)) [39], illicit drug use (The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST)) [40, 41], and panic symptoms (Patient Health Questionnaire-5 (PHQ-5)) [42]. Patients with AUDIT scores  $\geq 4$  (male sex at birth) or  $\geq 3$  (female sex at birth) were characterized as having “high-risk alcohol use.” Illicit drug use was defined as “Never used,” “Past use,” or “Current use.” Drugs of interest were illicit opiate use, methamphetamine, cocaine or crack, and illicit amphetamine use, but marijuana use was excluded. Patients were classified based on their PHQ-5 total panic symptom score as having no evidence of panic symptoms (PHQ-5=0), some panic symptoms (PHQ-5=1–4), or full panic symptoms (PHQ-5=5).

For this analysis, we analyzed disparities in depression prevalence and depression treatment, with further exploratory analyses of evidence of remitted depression. We defined an indication for depression treatment as a PHQ-9 score  $\geq 10$  or a current antidepressant prescription at the time of the most recent PHQ-9. We defined antidepressant treatment as a current antidepressant prescription. A patient with a current antidepressant prescription and a PHQ-9 score  $< 5$  was considered to be in remission. We additionally conducted a secondary exploratory analysis of treatment adjustments in this dataset. Patients were characterized as having an indication for antidepressant treatment adjustment if they were already receiving antidepressants and had a score  $\geq 10$  on their most recent PHQ-9. Patients were classified as having received an indicated treatment adjustment if they had an indication for an adjustment on their most recent PHQ-9 and their antidepressant dose was increased or their antidepressant was augmented or switched within 30 days of that elevated PHQ-9 score [22].

## Data Analysis

In the primary analysis including all CNICS sites with PRO data, we examined the conditional probability of (1) having an indication for depression treatment, (2) receiving antidepressant treatment, and (3) achieving remission, stratified by alcohol use, drug use, and panic symptoms. The conditional

probability of being in each step along the continuum was determined by dividing the number of patients in each step of the cascade by those in the previous step. Conditional probabilities are reported as percentages. In order to estimate the association of alcohol use, drug use, and panic symptoms with each step of the treatment cascade, we then used a multivariable Poisson regression model with cluster-robust standard errors to account for fixed effects by treatment site, adjusting for sex, race/ethnicity, and age.

In our secondary exploratory analysis examining indicated treatment adjustments, we restricted our sample to three CNICS sites with sufficient antidepressant dosage data to identify dose escalations. In this sample, we examined the conditional probabilities of (1) having an indication for depression treatment, (2) receiving antidepressant treatment, (3) having an indication for treatment adjustment, (4) receiving an indicated treatment adjustment, and (5) having evidence of remission. The conditional probability of remission was calculated as the probability of remitted depression given receipt of antidepressant treatment. All analyses were completed in Stata 14 (College Station, TX).

## Results

Our primary analysis sample included 12,776 patients who completed at least one PRO. The sample was largely male (84%) and identified as white non-Hispanic (49%) (Table 1). The majority of patients were currently taking ART (89%), had a CD4 count  $> 500$  (55%), and had an undetectable viral load (72%) within 6 months prior to their most recent PRO completion. Twenty-three percent of the sample had PHQ-9 scores  $\geq 10$  indicating probable major depression, and 19% were taking antidepressants at the time of PRO completion. Full panic symptoms were evident in 13% of patients, 17% were classified as having high-risk alcohol use, and 16% percent of patients reported current illicit drug use. Among patients with a PHQ-9 score  $\geq 10$  and/or taking antidepressants, 29% had evidence of full panic symptoms, 18% had high-risk alcohol use, and 21% reported current drug use (data not shown).

Across all sites, 34.7% (95% CI 33.9–35.5%) of patients had an indication for depression treatment, only 55.3% (53.8–56.8%) of whom were receiving antidepressant treatment. Of those receiving antidepressant treatment, only 33.0% (31.1–34.9%) had evidence of remitted depression based on PHQ-9 score (Table 2a). When restricted to the subsample of three sites with dosing data ( $n = 5484$ ), a higher proportion of patients had an indication for depression treatment (40.8%, 95% CI 39.6–42.2%) and received antidepressant treatment (66.3%, 95% CI 64.3–68.2%), but the proportion of those receiving antidepressant treatment who had evidence of remitted depression was similar to the

**Table 1** Characteristics of the study sample (n=12,776)

Characteristic	N (%) or median (IQR)
Age	47 (38, 53)
<i>Gender</i>	
Male	10,678 (83.6)
Female	2097 (16.4)
Intersexed	1 (0.0)
<i>Race/ethnicity</i>	
White, non-Hispanic	6210 (49.0)
Black, non-Hispanic	4139 (32.7)
Hispanic	1798 (14.2)
Other	518 (4.1)
<i>On ART</i>	11,250 (89.1)
<i>CD4 count, cells/mm<sup>3</sup></i>	
≤ 200	1255 (10.7)
201–500	3975 (33.9)
> 500	6502 (55.4)
<i>Viral load</i>	
Undetectable, < 50 copies/mL	8165 (72.2)
Detectable, ≥ 50 copies/mL	3146 (27.8)
<i>PHQ9≥10</i>	2943 (23.0)
<i>Antidepressant use</i>	
Not on antidepressants	10,326 (80.8)
On antidepressants	2450 (19.2)
<i>Panic disorder</i>	
No panic symptoms	8784 (73.2)
Some panic symptoms	1626 (13.6)
Panic disorder	1587 (13.2)
<i>Alcohol use risk</i>	
No risky use	8595 (73.7)
Low-risk use	1057 (9.1)
High-risk use	2008 (17.2)
<i>Drug use (excluding marijuana)</i>	
No use	5677 (46.7)
Past use	4600 (37.8)
Current use	1891 (15.5)

Missing data: race/ethnicity 0.9%, ART 1.1%, CD4 8.2%, viral load 11.5%, Anxiety 6.1%, Alcohol use, 8.7%, Drug use (no marijuana) 4.8%

overall sample (34.1%, 95% CI 31.7–36.6%) (Table 2b). Of those receiving antidepressant treatment who had an indication for a treatment adjustment based on PHQ-9 score (37.5%, 95% CI 35.1–40.0%), only 8.8% (95% CI 6.7–11.5%) received a treatment adjustment within 30 days.

Figure 1 shows depression severity and treatment status stratified by substance use and panic symptoms. Prevalence of depression and treatment status varied little across categories of alcohol use (Fig. 1a). When stratified by drug use status, disparities along the treatment cascade were apparent (Fig. 1b). Significantly more patients reporting current drug

use (21.8%, 95% CI 20.0–23.8%) or past use (21.6, 95% CI 20.4–22.8%) were taking antidepressants than patients who never used drugs (16.8%, 95% CI 15.9–17.8%). However, the percentage of patients with untreated depression was highest among current drug users (24.0%, 95% CI 22.1–26.0%). Differences were even more evident by level of panic symptoms (Fig. 1c). The percentage of patients on antidepressants (38.1%, 95% CI 35.8–40.5%) as well as the percentage with untreated depression (36.9%, 95% CI 34.6–39.3%) was highest among those reporting full symptoms of panic disorder. The percentage of patients who had evidence of remitted depression was lowest in this group (2.8%, 95% CI 2.1–3.7%).

Figure 2 demonstrates the conditional probability (%) of having an indication for treatment, receiving treatment, and achieving remission. Patients in each category of alcohol use had similar conditional probabilities of having an indication for antidepressant treatment and receiving treatment given a treatment indication, although patients with high-risk use were least likely to achieve remission given treatment (26.5%, 95% CI 22.3–31.2%) compared to those with low-risk use or no risky alcohol use (33.5%, 95% CI 27.0–40.7%; and 35.2%, 95% CI 33.0–37.5%, respectively) (Fig. 2a).

Disparities were apparent by drug use and panic symptoms at each step of the cascade. Patients who reported current drug use were most likely to have an indication for depression treatment (45.8%, 95% CI 43.6–48.1%) compared to patients who reported past use (37.5%, 95% CI 36.1–38.9%) or patients who reported never using drugs (27.6%, 95% CI 26.5–28.8) (Fig. 2b). Given an indication for antidepressant treatment, patients who reported current drug use were least likely to receive depression treatment (47.6%, 95% CI 44.3–51.0%), and were least likely to have evidence of remitted depression given treatment (22.3%, 95% CI 18.5–26.6%).

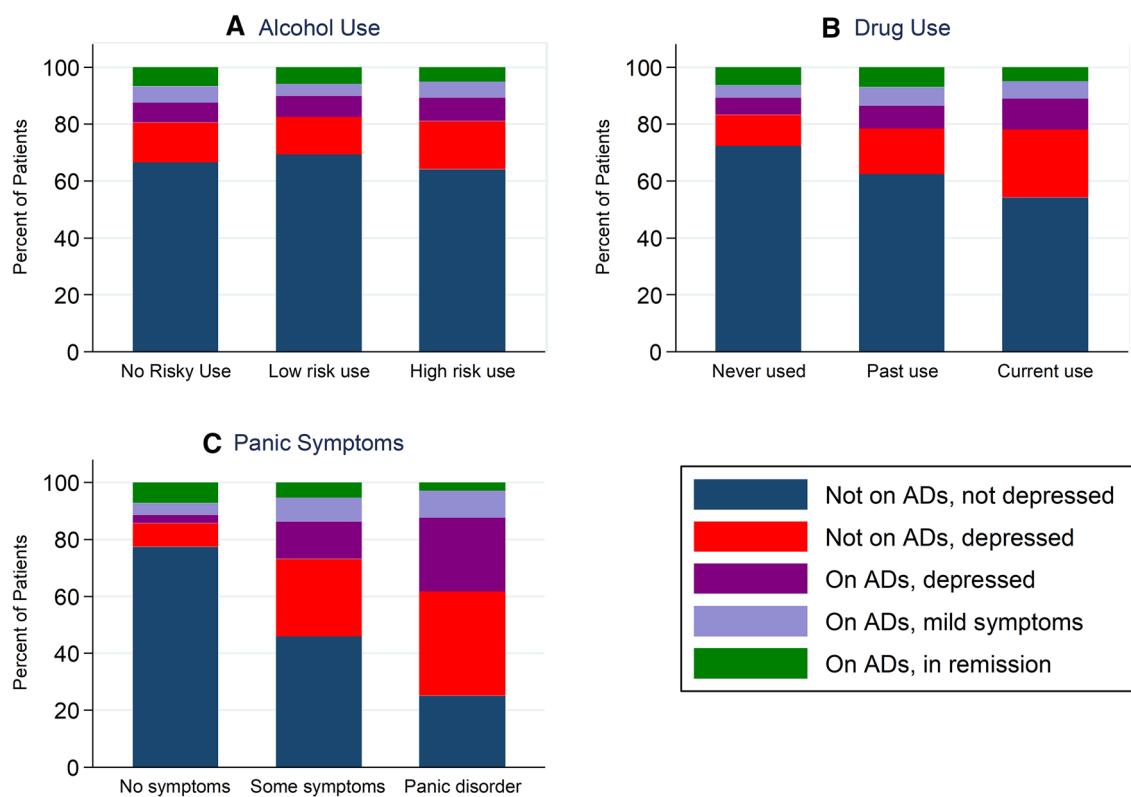
Seventy-five percent (95% CI 72.9–77.1%) of patients with full panic symptoms had an indication for depression treatment compared to 54.0% (95% CI 51.6–56.4%) of patients with some panic symptoms and 22.7% (95% CI 21.8–23.6%) of patients with no symptoms (Fig. 2c). Given an indication for treatment, patients with full panic symptoms or some panic symptoms (50.8%, 95% CI 48.0–53.6%; and 49.8%, 95% CI 46.5–53.1%, respectively) were less likely to receive treatment than patients with no panic symptoms (63.8%, 95% CI 61.6–65.8%). Patients with full panic symptoms had the lowest conditional probability of having evidence of remitted depression (7.3%, 95% CI 5.5–9.6%).

In multivariable models adjusting for race/ethnicity, sex, and age, and controlling for fixed effects by treatment site, we examined associations between alcohol use, drug use, and panic symptoms with each step in the treatment cascade (Table 3). Consistent with results reported above, alcohol use was not associated with depression or receipt

**Table 2** Depression treatment cascade

	N (%)	95% CI
<i>a. Depression treatment cascade across all sites (n = 12,776)</i>		
Indication for depression treatment	4430 (34.7)	33.9–35.5
Of those with an indication: On AD treatment	2450 (55.3)	53.8–56.8
Of those receiving AD treatment: Depression remitted	808 (33.0)	31.1–34.9
<i>b. Depression treatment cascade across sites with AD dosing data (n = 5484)</i>		
Indication for depression treatment	2240 (40.8)	39.6–42.2
Of those with an indication: On antidepressant treatment	1484 (66.3)	64.3–68.2
Of those receiving AD treatment: Indication for treatment adjustment	557 (37.5)	35.1–40.0
Of those with indication for treatment adjustment: Adjustment received	49 (8.8)	6.7–11.5
Of those receiving AD treatment: Depression remitted	506 (34.1)	31.7–36.6

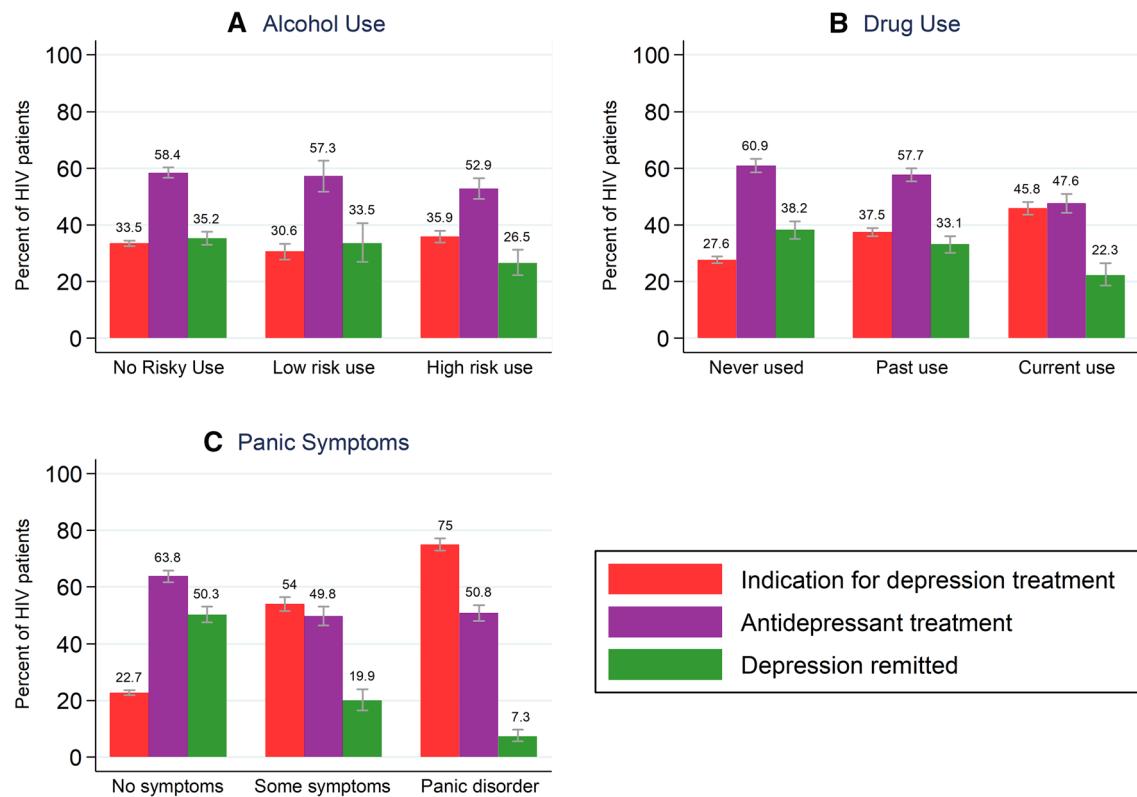
AD Antidepressant

**Fig. 1** Depression severity and depression treatment stratified by psychiatric comorbidity across all sites. AD Antidepressant

of treatment, but high-risk users were least likely to have remitted depression (Prevalence Ratio (PR) 0.81, 95% CI 0.67–0.98). Current drug users (PR 1.35, 95% CI 1.21–1.51) and past users (PR 1.18, 95% CI 1.08–1.28) were more likely than non-users to have an indication for depression treatment. Current drug users were least likely to receive antidepressant treatment given treatment indication (PR 0.81, 95% CI 0.69–0.96) and to have evidence of remitted depression (PR 0.70, 95% CI 0.58–0.84). Patients with full panic symptoms were most likely to have an indication for depression

treatment (PR 3.09, 95% CI 2.67–3.57) and were least likely to have evidence of remission given treatment (PR 0.15, 95% CI 0.12–0.20). Patients with full panic symptoms (PR 0.81, 95% CI 0.66–0.99) and those with some symptoms of panic disorder (PR 0.79, 95% CI 0.70–0.90) were less likely to receive antidepressant treatment given treatment indication than patients with no symptoms.

Next, we examined patients at three sites with sufficient antidepressant dosage data to explore whether comorbidity influenced antidepressant treatment adjustments. In this



**Fig. 2** Depression treatment cascade across all sites, stratified by alcohol use, drug use, and panic disorder

**Table 3** Results from a multivariable Poisson model of the association between alcohol use, drug use, and panic symptoms with depression, antidepressant treatment, and remission, adjusted for race/ethnicity, sex, and age

Characteristic	Indication for AD treatment PR, 95% CI	On AD treatment <sup>a</sup> PR, 95% CI	Depression remitted <sup>b</sup> PR, 95% CI
No risky alcohol use	1.00	1.00	1.00
Low-risk alcohol use	0.89 (0.82–0.97)	0.99 (0.92–1.07)	0.97 (0.83–1.12)
High-risk alcohol use	0.99 (0.94–1.06)	0.96 (0.87–1.05)	0.81 (0.67–0.98)
Never used drugs	1.00	1.00	1.00
Past drug use	1.18 (1.08–1.28)	0.94 (0.85–1.04)	0.92 (0.83–1.02)
Current drug use	1.35 (1.21–1.51)	0.81 (0.69–0.96)	0.70 (0.58–0.84)
No panic symptoms	1.00	1.00	1.00
Some panic symptoms	2.28 (1.99–2.60)	0.79 (0.70–0.90)	0.42 (0.34–0.52)
Full panic symptoms	3.09 (2.67–3.57)	0.81 (0.66–0.99)	0.15 (0.12–0.20)

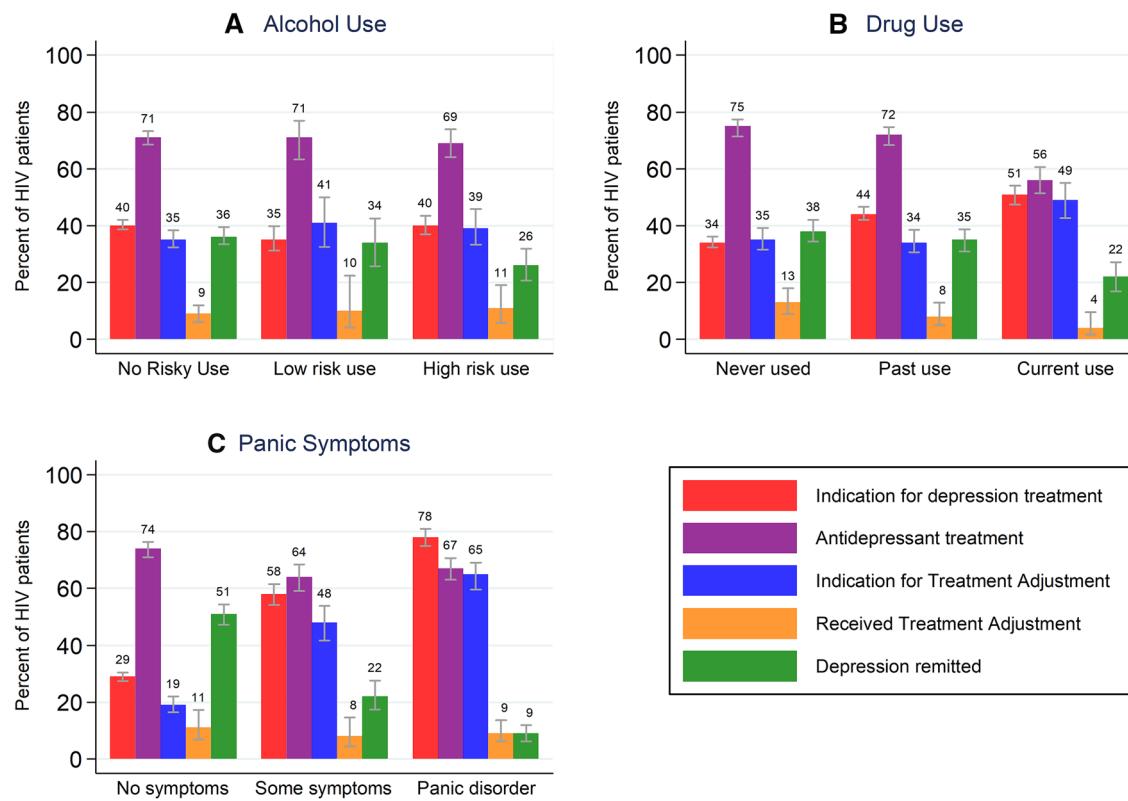
AD Antidepressant, PR prevalence ratio

<sup>a</sup>Among those with an indication for antidepressant treatment

<sup>b</sup>Among those receiving antidepressant treatment

subgroup, the pattern of gaps between indication for treatment, receipt of antidepressant treatment, and remission was similar to that observed across all sites for each stratification. Few differences in the conditional probability of having an indication for a treatment adjustment and of receiving a treatment adjustment were seen when stratified by alcohol use (Fig. 3a).

When stratified by drug use, current drug users had the highest conditional probability of having an indication for treatment adjustment (48.8%, 95% CI 42.6–55.0%), but the conditional probability of these patients receiving a treatment adjustment was lowest (4.1%, 95% CI 1.7–9.6%), although not significantly (Fig. 3b). Stratified by panic symptom severity, patients with full panic symptoms had



**Fig. 3** Depression treatment cascade among sites with antidepressant dosage data

the highest conditional probability of having an indication for treatment adjustment given antidepressant treatment (64.5%, 95% CI 59.6–69.1%), but the conditional probability of receiving a treatment adjustment was similar across each level of symptom severity, ranging from 8 to 11% (Fig. 3c).

## Discussion

In this large sample of PLWH seen for routine HIV primary care, 35% of patients had an indication for depression treatment at their most recent PHQ-9 assessment, which is consistent with previous estimates of depression in patients receiving HIV primary care in the US [1, 2, 4, 43]. Large gaps in treatment were present along the depression treatment cascade, confirming results from previous studies conducted in similar settings [13, 22, 43, 44]. Among patients with an indication for depression treatment in our total sample, just over half were receiving treatment and of those, one-third had achieved remission. Of patients receiving antidepressant treatment with an indication for treatment adjustment, only 9% received a dose escalation or medication change within 30 days.

Prevalence of co-occurring depression and severe panic symptoms, illicit drug use, or high-risk alcohol use in our

sample were high, consistent with previous studies in HIV-positive populations in the US [1, 2, 5, 26, 27]. While alcohol use was not associated with gaps in depression treatment, there were differences in response to treatment by alcohol use status. Large gaps in depression treatment and response were evident by drug use and panic symptom status. Current drug users were most likely to have an indication for depression treatment, least likely to be receiving treatment, and least likely to have evidence of remitted depression compared to past drug users or patients who reported never using drugs. Even starker disadvantages were observed for patients with full panic symptoms compared to those with partial or no panic symptoms. Of note, among those receiving antidepressants, patients with current drug use and with full panic symptoms were most likely to need a treatment adjustment. Patients with full panic symptoms were similarly likely to receive an indicated adjustment compared to those with partial symptoms or no symptoms, but current drug users were least likely to receive a treatment adjustment despite having an indication. In multivariable models, drug use and panic symptoms remained independently associated with higher burden of depression and larger gaps in treatment and remission.

The present study suggests that patients with depression and psychiatric comorbidities relating to illicit drug use or

panic disorder are even less likely to receive and respond to antidepressant treatment relative to depressed PLWH who do not have these comorbidities. This may be because clinicians choose to prioritize treatment of the comorbid condition over depression treatment or because the comorbid condition is a barrier to depression remission. Additionally, patients with psychiatric comorbidity may be more likely to receive individual or group psychotherapy as opposed to medication-based treatment. However, it is important for physicians and mental health professionals to recognize disparities along the depression treatment cascade to more effectively target patients with psychiatric comorbidities in addition to depression. Antidepressant therapy is effective for depression and panic disorder [45], and clinical trial evidence supports the use of antidepressants in PLWH with depressive disorders and active alcohol and/or drug use [46].

An important strength of this study is its size and inclusion of multiple large academic medical centers throughout the US. The overall study sample included patients seen for routine HIV primary care in the northeastern, southern, mid-Atlantic, and western US. Prevalence of depression in this sample was similar to previous estimates of depression among PLWH [1, 5, 28], and the present study confirms gaps in the depression treatment cascade reported in other multi-site populations of patients with depression and substance use in the US [13, 22]. Additionally, overall prevalence of panic disorder, alcohol use, and drug use, as well as comorbid psychiatric conditions were seen at levels comparable to estimates from similar study settings [5, 28, 32]. Therefore, the results from this study are likely generalizable to populations of PLWH similar to those in the CNICS cohort. However, these results may be less generalizable to the overall population of PLWH in the US.

This study has several limitations that should be considered when interpreting these results. Data for this analysis are a cross-sectional snapshot of patients captured at their last PRO. Therefore, inferences cannot be made about movement through the depression treatment cascade over time. Second, classification of depression is completed using the PHQ-9, a depressive severity assessment tool that is well validated and widely used but not diagnostic [36, 37]. Additionally, analyses of treatment adjustment and treatment remission are exploratory and based on PHQ-9 scores and antidepressant medication data. Patients with a history of depression who have successfully achieved remission and have ended antidepressants are not captured as having remission in this analysis, though the majority of depression among PLWH in the US is chronic and unlikely to remain in remission in the absence of treatment [32]. Patients may be receiving antidepressant treatment for an indication other than depression, and thus may be misclassified as having remitted depression. Several clinical factors may be considered in addition to PHQ-9 score and current antidepressant

dosage when a clinician is determining whether a treatment adjustment is appropriate that may not be captured in the current available data.

Further, data on mental health counseling were not available for this analysis. Patients may have had their depression care augmented by mental health counseling or may have received depression treatment in the form of counseling without antidepressants. However, recent validation work has demonstrated that the proportion of patients in the CNICS cohort who are receiving mental health counseling without also receiving antidepressants is small [47]. Fourth, classification of depression and other psychiatric comorbidities was based on self-report. Patients may choose not to disclose their drug use status or may underreport alcohol consumption, which may result in exposure misclassification in these patients. Among drug users, there may be differences between patients based on the type of illicit drugs that they use. Additionally, dosage data to assess treatment adjustments was available for less than half of the overall study sample and may not be representative of the larger CNICS cohort. Finally, patients in this cohort were largely male, almost half identified as white, and all are seen for HIV primary care at large academically-affiliated treatment centers across the US. Thus, the results of this study may not be generalizable to other patient populations or to areas with smaller medical centers.

## Conclusions

We found important treatment gaps among PLWH with co-occurring psychiatric comorbidities at each step of the depression treatment cascade. This study is among the first to characterize disparities in depression treatment by psychiatric comorbidity. Specifically, current drug users were most likely to have an indication for depression treatment and, among those treated, to have an indication for treatment adjustment, but they were less likely to be receiving treatment or to have remitted depression. These same disparities in depression treatment indication and response were even more starkly evident among patients with co-occurring symptoms of panic disorder compared to those without. These disparities are concerning since co-occurring psychiatric comorbidities in PLWH have been shown to be the norm rather than the exception and antidepressant treatment has utility in this population irrespective of these comorbidities. Efforts to address the gaps in the depression treatment cascade in HIV primary care should carefully consider psychiatric comorbidities to be maximally effective.

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the manuscript. BWP, AMB, RDM, DJG, RM, CMO, and BNG assisted with the interpretation of the data and critically revised the manuscript for important intellectual content. All authors take responsibility for and approve the final version of the manuscript. We thank the National Institutes of Mental Health (Grant Number R01MH100970) and the National Institute of Allergy and Infectious Diseases (Grant Numbers R24AI067039 and P30 AI50410) for their support of this work.

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## Compliance with Ethical Standards

**Conflict of interest** BWP has received a speaking honorarium from MSD. No other conflicts of interest are declared.

**Ethical Approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed Consent** Informed consent was obtained from all individual participants included in the study.

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