VALIDITY OF THE BECK DEPRESSION INVENTORY AMONG WOMEN WITH HIV ENGAGED IN CARE: IMPLICATIONS FOR TRANSDIAGNOSTIC PSYCHIATRY IN HIV TREATMENT

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Abstract

Major depressive disorder is highly prevalent among women with HIV and is associated with decreased antiretroviral therapy adherence and increased risk of mortality. As major depressive disorder often goes undiagnosed among women with HIV, one proposed solution to this problem has been to establish routine depression screening and integrated psychiatric care as part of HIV treatment. However, the high prevalence of other psychiatric and substance use disorders among women with HIV complicates the accurate diagnosis of major depressive disorder, as depressive symptoms are common across these distinct disorders with varying treatment recommendations. While previous studies have validated screening tools, such as the Beck Depression Inventory, for major depressive disorder among women with HIV, none have addressed the extent to which the presence of these other conditions results in psychiatric misdiagnosis.

This thesis addresses this gap by examining the impact of psychiatric disorders and substance use behaviors on the validity of the Beck Depression Inventory in screening for major depressive disorder among women with HIV. Women in our sample were engaged in care at the Johns Hopkins HIV Clinic and were recruited between April 2006 and July 2010 to join a trial of a brief intervention for hazardous alcohol use. Using baseline trial data, we compare women's Beck Depression Inventory scores to their major depressive disorder diagnosis obtained from a structured clinical interview and calculate sensitivity and specificity in the full study population and stratified by post-traumatic stress disorder diagnosis, bipolar affective disorder diagnosis, and alcohol use risk classification.

Beck Depression Inventory sensitivity and specificity were 65% and 75% overall. Sensitivity was higher among women with current (79%) or lifetime (74%) PTSD compared to those without a current (55%) or lifetime (53%) diagnosis. Sensitivity did not vary by alcohol use risk classification. Specificity was higher among women without current (78%) or lifetime (81%) PTSD, without BPAD (78%), or with low-risk alcohol use (80%), and lower among women with these diagnoses (59%, 66%, 62%) or with hazardous alcohol use (68%). We discuss the implications of these results for transdiagnostic psychiatry in HIV care and highlight the need for evaluating major depressive disorder in the context of other psychiatric and behavioral factors prevalent among women with HIV.

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1. Introduction

Major depressive disorder (MDD) is the most common psychiatric comorbidity among people living with HIV (PLWH), with current prevalence estimates ranging from 30% to 40%.[1,2,3] Beyond its associations with decreased quality of life[4] and behaviors carrying increased risk for HIV transmission, [5,6] MDD is also linked to decreased retention in routine HIV care,[7,8] decreased antiretroviral therapy (ART) adherence,[9,10] increased viral load,[11,12,13] and increased risk of mortality.[14,15] Although several psychotherapeutic and pharmacologic interventions are effective in treating MDD among PLWH,[16,17,18,19] it remains a highly prevalent, modifiable risk factor for poor HIV treatment outcomes.

Substantial disparities in the prevalence of MDD and its association with worse HIV outcomes exist for women living with HIV (WLWH) compared to other populations. WLWH are nearly twice as likely to receive an MDD diagnosis as women in the general population[20,21] and are more likely to report depressive symptoms and be indicated for MDD treatment than men living with HIV.[22,23,24] Prospective studies have found that chronic MDD is associated with increased viral load and a nearly two-fold increase in the risk of death among WLWH in both the pre-ART and ART eras of HIV care.[15,25] This increase in all-cause mortality is even more striking among WLWH with MDD who have not yet initiated ART.[26] Identifying MDD among WLWH and connecting them to integrated behavioral and pharmacological care, both prior to and after initiation of ART, therefore represents a crucial point of intervention in optimizing HIV treatment outcomes.

However, the extremely high prevalence of other psychiatric disorders and substance use behaviors among WLWH complicates the accurate diagnosis of MDD and the referral of patients to appropriate evidence-based care. The prevalence of bipolar affective disorders,[8,20] post-traumatic stress disorder (PTSD),[20,27] substance use disorders,[20] and hazardous alcohol use[20,28] among WLWH each far exceed levels among women in the general population. Because symptoms of these conditions overlap with symptoms of MDD assessed using common screening tools, misdiagnosis of MDD can be common in populations with high prevalence of other psychiatric and substance use disorders.[29,30] Thus, while MDD is often underdiagnosed among WLWH,[31,32] another concern is that WLWH with depressive symptoms stemming from other disorders with unique treatment practices may be misdiagnosed with MDD when assessed using MDD-specific screening tools alone. Identifying groups of WLWH most likely to be underdiagnosed or overdiagnosed by these screening tools can have important downstream impacts on their HIV treatment outcomes.

Several studies have investigated the validity of the Beck Depression Inventory-II (BDI-II) among PLWH, with sensitivities between 74% and 95% and specificities between 68% and 74%.[33,34,35] While these findings align with estimates of BDI-II sensitivity and specificity in general population samples across several countries,[36,37] they do not address diagnostic accuracy among WLWH specifically. These studies also have substantial limitations, such as the use of another self-reported screening tool as a gold standard assessment for an MDD diagnosis, and none of these studies assess the extent to which the prevalence of other psychiatric conditions or substance use behaviors may lead to differential accuracy in screening for MDD.

Our study aims to address these gaps by examining psychiatric disorders and substance use behaviors that impact validity of the BDI-II in screening for MDD among WLWH. Using data from a study of WLWH engaged in HIV care in Baltimore, MD, we first examine whether the accuracy of the BDI-II among these women aligns with previous estimates obtained in general populations of PLWH. We then assess whether the accuracy of the BDI-II varies across women with PTSD, bipolar affective disorder, and hazardous alcohol use. Finally, we discuss the implications of these findings on the evaluation of MDD among WLWH in the context of comorbidity and the non-specificity of depressive symptoms in this population.

2. Methods

2.1 Study population

Women in our sample were recruited from the Johns Hopkins HIV Clinic. One group that consumed alcohol at heavy or hazardous levels were recruited as part of a randomized controlled trial of a brief intervention for hazardous drinking among WLWH. Study investigators used two concurrent recruitment approaches based on potential participants' drinking behaviors, as assessed by the first three items (i.e., quantity and frequency) of the Alcohol Use Disorders Identification Test (AUDIT)[38] and the full Tolerance, Worried, Eye-opener, Amnesia, Cut Down (TWEAK)[39] test at screening. Women met criteria for heavy or hazardous alcohol use if they reported consuming eight or more alcoholic drinks per week, reported two or more binge drinking episodes (four or more drinks per occasion) in the prior six months, or had a score of two or

higher on the TWEAK. Women who met at least one of these criteria were then randomized to either the brief intervention or to the usual standard of care. A comparison group of low-risk or non-drinkers consisted of women who reported either no alcohol consumption or drinking behaviors that did not meet the study criteria for heavy or hazardous alcohol use. All women were 18 years of age or older and were receiving care in the Johns Hopkins HIV Clinic between April 2006 and July 2010. Women were deemed ineligible if they were experiencing an active psychotic episode, were pregnant, or were currently enrolled in a treatment program for alcohol use.

Complete descriptions of the larger study design and protocol have been published previously.[40,41,42] The Johns Hopkins University School of Medicine Institutional Review Board reviewed and approved both the intervention study and this secondary analysis.

2.2 Data sources

Women completed the 21-item BDI-II[43] using an audio computer-assisted self-interview (ACASI) at the time of study enrollment. The BDI-II has empirically demonstrated high internal consistency and test-retest reliability and has been shown to capture both mood and somatic factors contributing to MDD.[44,45]

We obtained diagnoses of MDD, bipolar affective disorders, and PTSD from the non-patient version of the Structured Clinical Diagnostic Interview (SCID), a series of standardized modules considered a gold standard for the diagnosis of Axis-I psychiatric disorders outlined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV).[46] Two trained master's level therapists administered and scored the SCID within one month after study enrollment. Two research assistants then

independently reviewed diagnostic coding for accuracy, with lingering discrepancies adjudicated by two study investigators (HH and GC) to obtain a final diagnosis.

Women completed the first three items of the AUDIT and the 5-item TWEAK scale at study screening. The AUDIT has proven to be a highly reliable and valid assessment of hazardous alcohol use across a range of populations with varying comorbidities.[47,48,49] The TWEAK was originally developed for use with pregnant women, but it has subsequently been shown to capture alcohol-related problems indicative of disordered use or dependence in the general population and in outpatient care facilities.[50] Additionally, women provided information on past 90-day illicit drug use, including cocaine and heroin use, at study enrollment using a Timeline Followback (TLFB) interview.[51]

2.3 Analytic approach

We first examined the validity of the BDI-II with respect to a SCID diagnosis of current MDD in the full sample, which includes all women regardless of PTSD or bipolar affective disorder diagnosis or alcohol use classification. Congruent with official scoring guidelines for the BDI-II,[40] we summed item ratings to create a total scale score for each participant, which we dichotomized to define MDD at a cutoff score of ≥20 to indicate moderate or severe depressive symptoms. We then calculated sensitivity and specificity for the BDI-II using this criterion.

Second, we stratified participants based on the presence or absence of SCID diagnoses of current and lifetime PTSD and lifetime bipolar affective disorder and used the previously defined BDI-II cutoff criterion to calculate sensitivity and specificity of the BDI-II given these psychiatric conditions. As bipolar affective disorders are lifelong,

episodic conditions,[52] we limited our analysis to lifetime diagnosis of bipolar affective disorder-I or bipolar affective disorder-II assessed via the SCID. Additionally, because DSM-IV guidelines preclude an MDD diagnosis if a depressive episode is determined to be the product of bipolar affective disorder,[53] we did not calculate BDI-II sensitivity among women with a bipolar affective disorder diagnosis.

Finally, we stratified participants based on self-reported recent alcohol use and alcohol-related problems. Participants were classified as low-risk drinkers or hazardous drinkers based on the first three items of the AUDIT (≥8 drinks per week or ≥2 binge drinking episodes in the prior six months) and their total TWEAK score (≥2). We calculated sensitivity and specificity for the BDI-II conditional on these alcohol use criteria.

We completed all statistical analyses in Stata 16.[54]

3. Results

3.1 Participant Characteristics

Our study sample consisted of 372 WLWH who had complete BDI-II data at their baseline study visit and completed the SCID within one month of ACASI completion. Our sample excluded 13 women with missing baseline ACASI data and three women with missing SCID data. The median age was 46 years old (41, 52), and women identified predominantly as non-Hispanic Black (86%) and heterosexual (90%). Only 10% of women were employed full-time (and only 7% employed part-time), explaining the median income of $7,968 ($5,160, $9,048). Reflecting a study population currently

engaged in HIV care, women had a median CD4 count of 433 cells/mm^3 (268, 647), and most were on ART at the time of assessment (79%) and had HIV-1 RNA levels of fewer than 50 copies/mL (55%). Participant characteristics can be found in Table 3.1.

Table 3.1. Participant characteristics

Variable	Study Sample (N = 372)
Demographics	
Age, years [median (Q1, Q3)]	46 (41, 52)
Education (#, %)	
<12 years	168 (45%)
≥12 years	204 (54%)
Race (#, %)	
Non-Hispanic Black	319 (86%)
Non-Hispanic white	43 (12%)
Hispanic	4 (1%)
American Indian	5 (1%)
Refused to answer	1 (<1%)
Sexual orientation (#, %)	
Heterosexual	333 (90%)
Homosexual	11 (3%)
Bisexual	26 (7%)
Other	2 (<1%)
Employment status (#, %)	
Working full-time	36 (10%)
Working part-time	27 (7%)
Looking for work	72 (19%)
Not looking for work	237 (64%)
Income, dollars [median, (Q1, Q3)]	7,968 (5,160, 9,048)
HIV Characteristics	
Undetectable HIV-1 RNA (<50 copies/mL) (#, %)	205 (55%)
CD4 count, cells/mm^3 [median, (Q1, Q3)]	433 (268, 647)
On ART (#, %)	293 (79%)
Substance Use	
Classified as hazardous drinker (HD) in original study (#, %)	143 (38%)
Past 90-day cocaine use (#, %)	77 (20.7%)
Past 90-day heroin use (#, %)	37 (9.9%)

In the full sample, the SCID-based prevalence of current MDD was 9% (95% CI: 6%, 13%). Approximately 13% of women in our sample had a SCID-confirmed lifetime diagnosis of bipolar affective disorder. PTSD was highly prevalent, with 36% of women having a lifetime diagnosis and 17% of women having a current diagnosis, and MDD-PTSD comorbidity was common. The prevalence of MDD was 14% among women with a lifetime PTSD diagnosis (compared to 6% among women without a lifetime diagnosis) and 22% among women with a current PTSD diagnosis (compared to 7% among women without a current diagnosis). MDD prevalence among women classified as having high-risk drinking under the original study criteria was 12% (95% CI: 7%, 18%), whereas only 7% (95% CI: 4%, 12%) of women who reported low-risk drinking had an MDD diagnosis.

3.2 Diagnostic Accuracy of the BDI-II

BDI-II test validity is presented in Table 3.2. Under the recommended scoring cutoff of 20, the BDI-II had a sensitivity of 65% (95% CI: 47%, 80%) and a specificity of 75% (95% CI: 71%, 80%).

Table 3.2. Major depressive disorder prevalence and BDI-II sensitivity and specificity

	MDD Prevalence (95% CI)	**BDI-II Sensitivity (95% CI)**	**BDI-II Specificity (95% CI)**
Overall (N = 372)	9% (6%, 13%)	65% (47%, 80%)	75% (71%, 80%)
Lifetime PTSD (N = 371)			
Positive diagnosis (N = 135)	14% (9%, 21%)	74% (49%, 91%)	66% (56%, 74%)
No diagnosis (N = 236)	6% (4%, 10%)	53% (27%, 79%)	81% (75%, 86%)
Current PTSD (N = 372)			
Positive diagnosis (N = 63)	22% (13%, 35%)	79% (49%, 95%)	59% (44%, 73%)
No diagnosis (N = 309)	7% (4%, 10%)	55% (32%, 77%)	78% (73%, 83%)
Lifetime BPAD (N = 372)			
Positive diagnosis (N = 47)	---	---	62% (46%, 75%)
No diagnosis (N = 325)	10% (7%, 14%)	65% (46%, 80%)	78% (72%, 82%)
Alcohol use (N = 372)			
Low-risk alcohol use (N = 229)	7% (4%, 12%)	65% (38%, 86%)	80% (74%, 85%)
Hazardous alcohol use (N = 143)	12% (7%, 18%)	65% (38%, 86%)	68% (59%, 86%)

Note: BPAD = bipolar affective disorder. MDD prevalence and BDI-II sensitivity are not calculated, as DSM-IV guidelines preclude a major depressive disorder diagnosis given a diagnosis of bipolar affective disorder.

BDI-II accuracy varied based on both lifetime and current diagnoses of PTSD. BDI-II sensitivity and specificity were 74% (95% CI: 49%, 91%) and 66% (95% CI: 56%, 74%), respectively, among women with a lifetime PTSD diagnosis compared to 53% (95% CI: 27%, 79%) and 81% (95% CI: 75%, 86%) among women without a lifetime diagnosis. When we stratified women by current PTSD diagnosis, BDI-II sensitivity was 79% (95% CI: 49%, 95%) and specificity was 59% (95% CI: 44%, 73%) among women with a current diagnosis compared to 55% (95% CI: 32%, 77%) and 78% (95% CI: 73%, 83%) among women without a current diagnosis.

BDI-II specificity in people without bipolar affective disorder (78%, 95% CI: 72%, 82%) was higher than that obtained using the full sample of all women. BDI-II specificity among those with a bipolar affective disorder diagnosis was only 62% (95% CI: 46%, 75%), indicating that the BDI-II inaccurately classified 38% of women with bipolar affective disorder as having unipolar major depressive disorder.

Finally, BDI-II sensitivity was 65% (95% CI: 38%, 86%) in both the HD and ND alcohol use groups, but specificity was higher among ND women (80%, 95% CI: 74%, 85%) compared to HD women (68%, 95% CI: 59%, 86%).

4. Discussion

In a sample of women engaged in HIV care in Baltimore, MD, we found that diagnostic accuracy of the BDI-II was influenced by the presence of comorbid psychiatric disorders and hazardous alcohol use. Specifically, BDI-II sensitivity was higher among women with a lifetime or current diagnosis of PTSD, but it did not vary when stratified by alcohol use. Specificity was higher among women without a lifetime or current diagnosis of PTSD, without a bipolar affective disorder diagnosis, and low-risk alcohol use, and lower among women with these diagnoses or with hazardous alcohol use.

Our findings highlight the importance of evaluating MDD among WLWH within the context of other psychiatric disorders that have overlapping symptom dimensions, particularly given the high degree of comorbidity in this population. For example, we found that PTSD increased the overall likelihood that women would screen positively for MDD on the BDI-II, resulting in a higher likelihood of both correctly classifying those with comorbid disorders and incorrectly classifying those with PTSD alone. One solution to this imprecision in symptom classification may involve balancing a lower BDI-II screening threshold with the removal of items with high overlap between MDD and PTSD, but such an approach may exacerbate the issue of assigning those with bipolar

affective disorders an improper diagnosis of MDD. The crossover of depressive symptoms between these prevalent disorders among WLWH should instead underscore the need for comprehensive psychiatric screening for MDD in HIV care settings rather than relying upon unidimensional screening measures in isolation. Adopting a transdiagnostic approach, which focuses on the common etiologic roots across psychiatric disorders and emphasizes flexible nosology over prescriptive categorical approaches,[55] can improve the diagnosis and treatment of these conditions among WLWH by situating depressive symptoms within the broader psychiatric context of this population.

The non-specificity of depressive symptoms among WLWH has key implications for adequate and relevant treatment of MDD. Mirroring the treatment cascade seen along the HIV care continuum,[56,57] an estimated 45% of prevalent MDD cases among PLWH are recognized clinically, with only 40% of these recognized cases currently receiving treatment and less than one-third of these treated PLWH achieving remission.[58] While these measures indicate a need for integration of routine MDD screening and referral to psychiatric care in HIV treatment settings, the extent to which this rapid decline along the care continuum may be attributable to diagnostic misclassification and improper treatment stemming from screen-then-treat approaches remains unclear. Several studies using screening-based criteria for MDD have demonstrated the effectiveness of antidepressant treatment in reducing depressive symptoms among PLWH, but high variation in these estimates could be explained by a lack of attention to psychiatric comorbidity or alternative diagnoses.[59] For instance, people with comorbid MDD and PTSD may respond more poorly to antidepressant

treatment compared to those with MDD alone, a pattern also seen in trials involving cognitive behavioral therapies.[60,61] Among people with BPAD, antidepressant treatment can trigger the exacerbation of depressive symptoms or the induction of rapid cycling between depressive and manic states.[62,63] The disproportionately high rates of these disorders among WLWH[64] therefore favor screen-then-interview approaches for MDD over screen-then-treat strategies that ignore the non-specificity of depressive symptoms in this population and may preclude referral to adequate MDD care or appropriate care for other diagnoses.

Our findings are consistent with previous studies showing that WLWH who report hazardous alcohol use are more likely than those reporting no or low-risk alcohol use to have MDD.[65,66,67] However, women reporting hazardous alcohol use were also more likely to falsely screen positive for MDD on the BDI-II, which may explain why our prevalence estimate of this comorbidity using SCID-confirmed MDD diagnoses is lower than those found in these studies using screening tool criteria. Notably, using a structured clinical interview to identify MDD can exclude cases in which depressive symptoms are the product of alcohol withdrawal or acute intoxication, which lead to a separate categorical diagnosis of substance-induced mood disorder.[68] This context provides further support for multidimensional behavioral health screening combined with clinical interviews that can inform appropriate combinations of pharmacologic and behavioral interventions to reduce both depressive symptoms and hazardous drinking among WLWH.

Our study has two notable limitations. First, our study population was limited to WLWH engaged in HIV care who were able and willing to participate in a research study

including intensive questionnaires and interviews. As women with severe MDD may be more likely to abstain from study participation[69] and less likely to be engaged in HIV treatment,[7,8] selection into our study could be conditional upon having fewer or less severe depressive symptoms, potentially explaining why our prevalence estimate of current MDD is lower than other epidemiologic studies involving WLWH.[20,21,22] However, this lower estimate is also likely related to our use of SCID-confirmed MDD diagnoses, which use more specific diagnostic criteria than screening tools and can rule out depressive symptoms attributable to PTSD, bipolar affective disorder, or alcohol use. Finally, illicit substance use disorders are highly prevalent among WLWH[20] and may further complicate the screening-based diagnosis of MDD. In our sample, 21% of women reported cocaine use and 10% reported heroin use in the 90 days prior to their baseline study visit using the TLFB. With only these prevalence data, we were unable to reliably determine whether these women met criteria for an associated substance use disorder. Future studies should investigate the impact of drug use on MDD screening accuracy using assessment methods that account for both the quantity and frequency of drug use and the behavioral factors and consequences that characterize substance use disorders.

Overall, our study highlights the issues in trading efficiency for accuracy when using screening-based approaches for identifying MDD among WLWH and provides empirical evidence for transdiagnostic psychiatry as part of routine HIV care. Diagnostic approaches informed by the non-specificity of depressive symptoms in this population are critical to ensuring referral to adequate psychiatric treatment and therefore

minimizing the detrimental impact of MDD, other psychiatric disorders, and substance use on retention in HIV treatment.

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