

#### **Screening for Mental Health Conditions**

This is a PDF version of the following document:

Module 2: Basic HIV Primary Care

Lesson 6: Screening for Mental Health Conditions

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#### **Background**

In the United States, people with HIV have a high prevalence of mental health conditions. This curriculum uses the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as the basis for screening for these conditions. In the DSM-5, all psychiatric conditions meeting the criteria for diagnosis are referred to as "mental disorders." For the purposes of this curriculum, screening for substance use disorders has been separated from screening for the other mental illnesses frequently seen among people with HIV, and we refer to this latter group of illnesses as mental health conditions.

People with HIV and mental health conditions often have comorbid substance use disorders.[1,2] Among the disorders described in the DSM-5, evidence suggests that major depression and substance use disorders have the strongest impact on the HIV care continuum, as they contribute to less safe sexual and injection drug-use practices, difficulty engaging in care along the entire HIV clinical care continuum, and problems with antiretroviral medication adherence.

People with mental health conditions are also overrepresented among those with poverty, homelessness, and incarceration. Mental health conditions, especially the most serious conditions (such as schizophrenia and bipolar disorder) and those combined with concomitant substance use disorders, often lead to a shortened lifespan in persons with HIV, even if they engage in HIV care and adhere to treatment.

#### Challenges in Evaluating Mental Health Conditions in Persons with HIV

Persons with HIV may also experience neurocognitive deficits. In particular, HIV-associated neuropsychiatric disorder (HAND) is an increasing concern for persons aging with HIV, and HAND often complicates the care of older persons (and some younger persons) with HIV. The aging of people with HIV and the neurocognitive problems associated with many of the comorbidities associated with HIV, such as substance use and chronic hepatitis C, contribute to the complexity of diagnosing and managing cognitive problems. In addition, severe depression and psychotic disorders are in and of themselves strongly associated with cognitive problems. Therefore, clinicians caring for individuals with HIV should be aware of the multitude of challenges implicit in the screening, diagnosis, and management of mental health conditions and neurocognitive deficits and should assist their patients in obtaining access to appropriate, integrated neuropsychiatric treatment. It is also important to bear in mind that persons with HIV may have more than one psychiatric or neuropsychiatric diagnosis.

#### **Overview**

This Topic Review will emphasize screening recommendations and tools for persons with HIV to identify

common mental health conditions, including depression, bipolar disorders, common anxiety disorders, and post-traumatic stress disorder (PTSD), as well as neurocognitive disorders. Delirium in persons with HIV will not be addressed in this review, but delirium should always be ruled out prior to making a psychiatric diagnosis. A detailed discussion of definitions, diagnostic criteria, and treatment for particular DSM-5 conditions is beyond the scope of this review. Screening tools for Alcohol/Substance Use Disorders are addressed in the topic <u>Substance Use Disorders</u>.



#### Estimates of Mental Health Conditions in Persons with HIV

Separate studies performed during different time periods have consistently shown that persons with HIV have relatively higher prevalence rates of various mental health conditions than are present among persons without HIV.[1,2,3,4,5] Several investigators have described a chronic neuroinflammatory state that exists in persons with HIV that may contribute to the high prevalence of depression among people with HIV.[6,7]

- Depression Symptoms Reported Medical Monitoring Project 2021 Cycle: This survey was conducted from June 2021 through May 2022, and it evaluated 3,995 persons with HIV for the presence of depression during the 2-week period prior to the interview.[8] Using DSM-IV criteria, 15.3% reported depression (8.6% had major depression and 6.7% had other depression); using criteria of a PHQ-8 score ≥10, 12.5% of participants had symptoms of moderate or severe depression (Figure 1).[8] In this same survey, 20.7% of persons with HIV reported anxiety, including 7.9% with severe anxiety (Figure 2).[8] Because the Medical Monitoring Project largely includes data only from persons with HIV who are receiving care, these data may not entirely reflect rates of depression and anxiety for all people with HIV.[8]
- PTSD Meta-Analysis in Women with HIV: In a meta-analysis of psychological trauma and post-traumatic stress disorder (PTSD) in women with HIV from the United States, investigators reported a PTSD rate of 30% among women with HIV, a rate approximately five times higher than among women without HIV.[9]

# Mental Health Conditions and Risk of HIV Acquisition and Transmission

#### **HIV Acquisition Risk**

An extensive body of medical literature has documented an increased risk of HIV acquisition among individuals with mental health conditions.[10,11] For example, bipolar disorder may be associated with increased sexual activity, impaired judgment, risk-taking, substance use, and lack of stable housing—all factors that may increase the likelihood of HIV acquisition or transmission.[12,13,14] Social impairments associated with serious mental illness also increase HIV acquisition risk by interfering with the ability of an individual to maintain adherence with HIV preexposure prophylaxis (PrEP) and to negotiate condom use with casual or anonymous partners.[15] The following studies, when taken together, provide indirect support that mental illness is associated with HIV acquisition.

- NYC Psychiatric Inpatient Study (I): In a study conducted from December 1989 through July 1990, HIV testing was performed on all persons admitted to an acute psychiatric unit in Manhattan and a large state hospital in Queens, and investigators identified an HIV prevalence of 5.5% (25 of 451) with an HIV prevalence of 11.1% among black individuals.[16]
- NYC Psychiatric Inpatient HIV Prevalence Study (II): A second larger study from New York City reported HIV testing data from persons aged 19-59 years who were admitted at two public psychiatric hospitals from November 1989 through July 1991.[17] The HIV prevalence was 5.2% (50 of 962), and the prevalence rates were similar among women (5.3%) and men (5.2%).[17]
- Four-State Psychiatry Care HIV Prevalence Study: In this 4-state study, testing for HIV, hepatitis C, and hepatitis B was performed on adults aged 18 to 60 years undergoing inpatient or outpatient treatment in Connecticut, Maryland, New Hampshire, or North Carolina between June 1997 and December 1998.[14] The overall HIV seroprevalence rate was 2.7% (25 of 931), a rate at least 8 times the rate of the general United States population.[14]
- Global HIV Prevalence in Persons with Serious Mental Illness: This was a large meta-analysis of articles published between January 1, 1980, and January 1, 2015, related to HIV prevalence in persons with psychiatric conditions. This analysis included multiple global regions, but when analyzing the subset of 21 studies from North America, investigators found an HIV prevalence of 6.0% in this patient population.[10]
- Multisite HIV Prevalence Study in Mental Health Care Settings: A separate multisite crosssectional study conducted in Philadelphia and Baltimore from January 2009 to August 2011 found an HIV prevalence of 4.8% (51 of 1061) among persons seen in different types of mental health care settings (university-based inpatient psychiatric units, intensive case-management programs, and community mental health centers).[18]
- **Duke Psychiatric Outpatient HIV Prevalence Study**: In a retrospective review at Duke University, HIV was present in 1.2% of the psychiatric patients seen in the outpatient setting, a prevalence rate approximately 4 times the rate of HIV in the general population in the United States (Figure 3).[19]

#### **HIV Transmission Risk**

Mental health conditions may increase HIV transmission risk through less medication adherence and increased sexual activity, often in the context of substance use.[20] Since persons with HIV who regularly take antiretroviral therapy and consistently maintain suppressed HIV RNA levels do not transmit HIV to sex partners, any factor that negatively influences antiretroviral adherence can interfere with this antiretroviral medication-related transmission benefit.[21] Major depression has been linked to increased rates of nonadherence to antiretroviral therapy, thus raising the likelihood of HIV transmission to partners.[22,23,24] In addition, anxiety, depression, and bipolar disorder have all been linked to increased sexual activity.[25,26,27] Treatment for mental health conditions, including treatment of substance use disorders, should be part of the overall efforts to reduce HIV transmission.[28,29,30] A Duke University psychiatry group has generated a conceptual model outlining the impact of mental health treatment on HIV transmission risk



behavior in persons with HIV (Figure 4).[29]



#### Impact of Mental Health Conditions on HIV Outcomes

#### Impact of Mental Health Conditions on the HIV Continuum of Care

The presence of untreated mental health conditions in persons with HIV correlates with decreased initiation of antiretroviral therapy, reduced medication adherence, and lower rates of viral suppression, all of which have significant implications for individual health.[31] Studies have established a relationship between reduced adherence with antiretroviral therapy and symptoms of depression, post-traumatic stress disorder (especially in those patients with concomitant depression), and bipolar disorder.[23,27,32,33] Post-traumatic stress disorder has also been shown to predict increased HIV symptomatology among both men and women with HIV, high rates of emergency room utilization, and increased HIV-related morbidity.[34,35]

#### impact of Mental Health Conditions on Morbidity and Survival

Mental health conditions have been shown to predict adverse outcomes in some groups of individuals with HIV who have a psychiatric condition. In particular, untreated depression significantly worsens adherence to antiretroviral medication, decreases the likelihood of full virologic suppression or CD4 cell recovery, and appears to increase the risk of disease progression and death.[36] Among individuals with HIV, those with mental health conditions experience increased morbidity and mortality when compared to comparable people who do not have these conditions.[37] Certain health problems are inherently increased in general with mental health conditions, such as the well-established association of major depression with heart disease. In addition, some psychotropic medications have the unfortunate side effect of weight gain, contributing to obesity and metabolic syndrome. Further, several studies have shown that anxiety and depression in people with HIV are associated with a decline in cognitive functioning, particularly in learning and memory.[38,39]

#### **Benefit of Mental Health Care on HIV Outcomes**

Among persons with HIV who have mental health conditions, treatment can improve psychiatric symptoms as well as improve adherence to antiretroviral therapy and overall HIV outcomes.[40] In some patients, the diagnosis of a mental health condition may facilitate closer monitoring and medical scrutiny, which fosters engagement in care and improved adherence rates. The following studies highlight evidence that shows addressing mental health care can have a major favorable impact on HIV outcomes.

- Women's Interagency HIV Study (WIHS): In the Women's Interagency HIV Study (WIHS), researchers analyzed the impact of depression on utilization of antiretroviral therapy in a total of 1,668 women with HIV who were enrolled in the WIHS at 6 sites nationwide between April 1, 1996, and September 30, 1998.[41] The analysis demonstrated that individuals who used mental health services had a 20% increase in the adjusted odds of utilizing antiretroviral therapy compared to those who did not access mental health services.[41]
- Kaiser/Group Health HMO Study: In a retrospective cohort study of 3,559 persons with HIV and depression who were enrolled in the Kaiser Permanente and Group Health Cooperative Health Maintenance Organizations (HMOs) in an 8-state region in the period January 2000 through December 2003, investigators analyzed the impact of depression and treatment of depression on HIV outcomes.[42] Among individuals with depression, rates of virologic suppression were lower, but those treated with selective serotonin reuptake inhibitors (SSRIs) had better adherence to antiretroviral therapy, improved virologic suppression, and a greater rise in CD4 cell count compared to their counterparts who did not receive SSRI treatment.[42]
- HIV Research Network (HIVRN): In a large, retrospective analysis of 4,989 persons with HIV who
  were receiving outpatient treatment during 2000 through 2005 at 5 sites affiliated with the HIV
  Research Network, investigators reported individuals with a psychiatric diagnosis who had six or more
  mental health visits in a year were significantly less likely to discontinue antiretroviral therapy
  compared with individuals with no mental health visits.[43]
- Atlanta Metropolitan Study: In this study, investigators followed 324 persons with HIV (on antiretroviral therapy) across 3 months time within during the study period of March 2005 to October 2008, with the goal of analyzing the impact of adherence to psychotropic medications on both depressive symptoms and antiretroviral adherence.[40] Overall, 33% (106 of 324) of those followed were also prescribed at least one psychiatric medication.[40] The investigators reported depression was associated with lower antiretroviral adherence, but adherence to psychiatric medications, regardless of medication class, increased antiretroviral adherence.[40]
- **UAB Project CONNECT**: In a retrospective analysis of 743 people with HIV who were seen at the University of Alabama at Birmingham (UAB) and enrolled in the Client-Oriented New Patient Navigation to Encourage Connection to Treatment (CONNECT) project between January 1, 2007, and December 31, 2013, investigators reported persons who received mental health services were more likely to be retained in primary care at 12 months relative to those who did not receive mental health services during their first year of care.[44]



#### **Neurocognitive Disorders in Persons Living with HIV**

#### **Estimates of Neurocognitive Disorders in Persons with HIV**

Cognitive disorders are widespread in the general population, with prevalence estimated to be 5 to 7% in most parts of the world; age is the major predictive factor for the development of dementia, and the prevalence of dementia nearly doubles every 10 years after age 60.[45] Overall, adults with HIV have poorer cognitive performance compared with those without HIV.[3,46,47] The prevalence of HIV-associated neurocognitive disorders (HAND) is estimated to be in the range of 25 to 50%.[46,48,49]

#### Factors Associated with Neurocognitive Decline in Persons with HIV

In persons with HIV, older age has been identified as a strong predictor of neurocognitive decline; other factors associated with neurocognitive decline include low nadir CD4 count, detectable plasma HIV RNA levels, previous central nervous system (CNS) injury, and comorbid conditions, such as hypertension, insulin resistance, viral hepatitis, and substance use disorder.[3,46,50] In addition, major depression, another common comorbid condition in persons with HIV, carries a significant burden of cognitive impairment that is reversible in part with the treatment of depression.[51,52] Among individuals with cognitive impairment and suppressed HIV RNA levels, intensification of antiretroviral therapy does not improve the cognitive impairment.[53]

#### **HIV-Associated Neurocognitive Disorder (HAND)**

The term HIV-associated neurocognitive disorder (HAND) is used to describe the spectrum of neurocognitive dysfunction that includes (1) asymptomatic neurocognitive impairment, (2) mild neurocognitive disorder, and (3) HIV-associated dementia.[54] These three conditions have been classified based on criteria established by consensus research definitions, referred to as the Frascati Criteria, and are not readily applied to clinical settings.[55]

- **Asymptomatic Neurocognitive Impairment**: This refers to mild neuropsychological impairment established by testing (rather than patient symptoms) in at least two ability domains that is not attributable to comorbid conditions.
- **HIV-Associated Mild Neurocognitive Disorder**: This disorder is defined by mild neuropsychological impairment in at least two domains not attributable to comorbid conditions plus at least mild interference in activities in daily functioning.
- **HIV-Associated Dementia**: This type of dementia is characterized by neuropsychological impairment of at least moderate severity and major functional decline in day-to-day functioning.

The Multicohort AIDS Study (a prospective study with gay and bisexual men) found that asymptomatic neurocognitive impairment doubles the risk of developing symptomatic HAND compared to a diagnosis of normal cognition.[48] In this study, only 2% of participants met the criteria for HIV-associated dementia, which is a significant drop from the 10 to 15% prevalence of HIV-associated dementia prior to the availability of effective antiretroviral therapy.[46] By contrast, the prevalence of milder forms of HAND has not declined despite effective antiretroviral therapy, though the study results are complicated by a CD4 nadir below 200 cells/mm³ in 70% of the participants. In addition to low nadir CD4 count, other risk factors linked to poor neurocognitive performance include increasing age, previous CNS injury, detectable HIV RNA, and comorbidities such as hypertension, viral hepatitis, substance use disorder, and depression.[46,50]

#### **Differential Diagnosis of Neurocognitive Impairment**

Although HAND describes a spectrum of neurocognitive impairment from mild to severe, it is important to recognize that persons with HIV continue to be at risk for other causes of neurocognitive decline, including cerebrovascular disease, severe psychiatric disorders, Alzheimer's disease, metabolic disorders (such as

hypothyroidism), alcohol and drug use disorders, side effects of psychotropic drugs, neurotoxicity related to certain antiretroviral medications, previous or current central nervous system opportunistic infections (and their sequelae), or other neurological diseases.[3,56,57,58,59] Treatable causes of neurocognitive disorders, such as depression, thyroid disease, B12 deficiency, syphilis, an opportunistic infection, and tumors should be identified and addressed.

#### **HIV-Associated Brain Injury (HABI)**

In 2023, an International HIV-Cognition Working Group issued a Consensus Statement that outlined recommendations for a new approach to cognitive impairment and causes of brain injury in people with HIV.[60] This working group has proposed a shift from using the HAND concept to an emphasis on conceptualizing brain injury in people with HIV as either (1) injury directly caused by HIV (HIV-associated brain injury [HABI]) or (2) injury from causes that are not directly caused by HIV (e.g., cerebrovascular disease, traumatic brain injury, neurodegenerative disorders).[60] In this context, HABI is subdivided based on whether plasma HIV RNA levels are suppressed or not suppressed.[60] Further, for individuals with suppressed plasma HIV RNA levels and evidence of brain injury, the working group characterized the brain injury as legacy (inactive brain injury from pretreatment damage) or active (ongoing brain injury leading to clinical and/or radiological progression).[60] The HIV-Cognition Working Group provided six main recommendations that summarize a new diagnostic approach to cognitive impairment in people with HIV (Table 1).[60]

# Overview of Screening Tools for Common Mental Health Conditions History of Mental Health Screening Tools

In the early 1990s, Drs. Robert Spitzer, Janet B.W. Williams, Kurt Kroenke, and coworkers developed the 26-item Primary Care Evaluation of Mental Disorders (PRIME-MD) patient questionnaire as a screening tool for five of the most common psychiatric disorders: (1) depression, (2) anxiety, (3) somatoform disorders, (4) alcohol use disorder, and (5) eating disorders.[61] Although the PRIME-MD emerged as a groundbreaking mental health screening tool, its utility in clinical practice settings has been limited by the long administration time required by the clinician to complete the 26-item survey. These same investigators subsequently developed and validated a self-administered form of the PRIME-MD known as the Patent Health Questionnaire (PHQ).[62] The development of the PHQ led to shorter, more practical screening tools, such as the PHQ-9 screening tool for depression and the Generalized Anxiety Disorder 7 (GAD-7) screening tool. See the screening tools for Mental Disorders Screening category in the Tools & Calculators section of this website.

#### **Barriers to Usefulness of Screening Tools**

The primary limitation of screening tools for mental health conditions is the low rates of further diagnostic evaluation and linkage to and retention in mental health care that follows the initial screening. This problem has been well demonstrated with depression screening tools.[63,64] Barriers to treatment have led to a number of new team-based models for delivering mental health services within primary care; studies of these new models are promising, but they are not often conducted in settings where HIV care is delivered.[65] Although people with schizophrenia and other psychotic disorders have an increased risk of acquiring HIV, simple and reliable screening tools for these conditions are not available. Asking patients about prior psychiatric diagnoses, the use of psychotropic medications, and a history of psychiatric hospitalization is helpful in detecting these serious mental health conditions.

#### **Ideal Aspects of Screening Tools in Primary Care**

Practical screening tools for use in the primary care setting should be brief, easily scored, free, evidence-based, and accessible to a range of providers without specific training. In addition, screening tests should be limited to conditions for which there is an available, effective treatment that can directly target the disease and improve prognosis and outcomes.[66] Most of the common mental health conditions seen among people with HIV have effective treatments. An ideal screening test for a mental health condition will accurately identify individuals with the clinical condition of interest without diagnosing individuals who do not have the condition. This is referred to as the sensitivity (probability of a test being positive when illness is present) and specificity (the probability of a test being negative when illness is absent) of a screening test. In addition, the test should ideally identify persons with the condition and simultaneously not falsely categorize people without the condition as having the condition; this is referred to as the positive predictive value.

#### Follow-Up for a Positive Screen

A positive screen for a mental health condition usually needs to be followed by a further clinical diagnostic evaluation to clarify that the condition crosses the threshold for a true mental health condition. Unfortunately, there are no biological tests that can be conducted in clinical care settings to clarify the presence of the vast majority of mental health conditions. The diagnostic accuracy of the screening test can be improved by testing for medical conditions that can cause delirium and dementia and screening for the presence of substance use disorder with alcohol and/or other drugs. Several screening tools for the most common mental health conditions encountered in primary care are described below, with links provided to the screening tool.



#### **Depression Screening Tools**

In June 2023, the United States Preventive Services Task Force (USPSTF) updated the screening recommendation for Depression and Suicide Risk in Adults (including women who are pregnant or postpartum), providing a Grade B recommendation for screening for major depression and a Grade I recommendation for suicide risk screening.[67] The USPSTF recommendations state, "It is important that persons who screen positive are evaluated further for diagnosis and, if appropriate, are provided or referred for evidence-based care."[67] The HIVMA/IDSA Primary Care Guidance recommends screening people with HIV for depression at least annually and more frequently if needed.[68]

#### Patient Health Questionnaire-9 (PHQ-9)

The <u>Patient Health Questionnaire-9 (PHQ-9)</u> can be self-administered or administered by a health professional. The questionnaire scores each of the 9 DSM-5 criteria in the range of 0 (not at all) to 3 (nearly every day) for items in the survey during the most recent 2 weeks. The PHQ-9 was designed to serve as a multipurpose instrument tool for screening, diagnosing, monitoring, and measuring the severity of depression.[69] The PHQ-9 has also been validated across diverse patient populations, including African Americans, Chinese Americans, Latinos, and non-Hispanic whites.[70]

- Interpretation: The PHQ-9 score ranges from 0 to 27, with higher scores correlating with a greater likelihood of major depression (Figure 5).[69] In addition, a cumulative score of 10 points or higher has 88% sensitivity and specificity for major depression. The following PHQ-9 score ranges have been shown to correlate with different degrees of depression: 5 to 9 (mild), 10 to 14 (moderate), 15 to 19 (moderately severe), and 20 to 27 (severe).[69] For persons who have a score of 1 or higher on any question, an additional tenth question is asked that evaluates how these problems impact function at home, at work, and with others. Based on both clinical practice and a review of the literature, a PHQ-9 score of 10 or higher is often used as the basis for referring individuals for further assessment of depression.[71] This further evaluation is essential because a PHQ-9 score of 10 or greater substantially overestimates the prevalence of major depression.[72]
- **Recommendation**: Individuals who reach the threshold for a positive screen (a score of 10 or higher) should ideally be offered a full diagnostic interview using standard diagnostic criteria from the DSM-5.[73] If prompt further diagnostic evaluation is not available, the primary care clinician should use good clinical judgment, taking into account the duration and severity of the depression, its impact on functioning, and the individual's treatment preferences. Moderately severe depression or severe depression warrants treatment using antidepressants, psychotherapy, and/or a combination of both. In addition, any positive response to question 9 (presence and duration of suicide ideation) warrants immediate further evaluation to determine if there is an imminent risk of self-harm. Suicide screening instruments, including the PHQ-9, have not been shown to significantly predict near-term outcomes, so additional risk stratification may be necessary.[74]

#### Patient Health Questionnaire-2 (PHQ-2)

The <u>Patient Health Questionnaire-2 (PHQ-2)</u> is a 2-item, validated screening tool that uses the first two questions of the PHQ-9 that ask about the frequency of depressed mood and anhedonia (the first two DSM-5 criteria for diagnosing major depression).[75] The PHQ-2 focuses the time frame to the past 2 weeks and grades answers on a 4-point scale.

- **Interpretation**: The PHQ-2 score ranges from 0 to 6. Using a cutoff score of 3, the PHQ-2 has a sensitivity of 83% and specificity of 90% for major depressive disorder. In one study, investigators concluded a cutoff score of 3 was the optimal cut point for screening purposes, with the qualification that moving the cut point to 2 would enhance sensitivity and moving to 4 would increase specificity (Figure 6).[75]
- Recommendation: The PHQ-2 functions as a brief, practical, first-step screening tool intended to



identify individuals who require additional evaluation with another instrument, such as the PHQ-9, or a direct diagnostic psychiatric interview.[76] The PHQ-2 should not be used as a final diagnostic tool for depression.

#### 2-Item PRIME-MD

The 2-item PRIME-MD, based on the 27-item PRIME-MD, is less commonly used but remains an option for screening for depression.[77,78] A positive screening result, answering *yes* to either one or both of the screening questions, requires additional evaluation with the PHQ-9 or a direct psychiatric interview that uses diagnostic criteria from the DSM-5.[73]

#### **Hospital Anxiety and Depression Scale (HADS)**

The Hospital Anxiety and Depression Scale (HADS), which was developed in 1983 to assess anxiety disorders and depression among patients attending hospital-associated clinics that were not psychiatric clinics, is another option for anxiety and depression screening.[79,80] Individuals who screen positive with a score of at least 8 points should be referred for a full diagnostic interview that uses diagnostic criteria from the DSM-5. Compared to several other screening tools, the HADS is not as useful in primary care settings.[81] People who reach the threshold for a positive score should be referred for a full diagnostic interview that uses diagnostic criteria from the DSM-5.



#### **Anxiety Disorder Screening Tools**

Generalized anxiety disorder (GAD) and panic disorder are two of the most common anxiety disorders in the United States. In people with HIV, treatment of these disorders has been shown to improve patient outcomes.[82] In June 2023, the United States Preventive Services Task Force (USPSTF) issued screening recommendations for Anxiety Disorders in Adults (including pregnant and postpartum women), providing a Grade B recommendation for those younger than 65 years of age and an I recommendation for those 65 years of age and older.[83] The USPSTF recommendations state, "It is important that persons who screen positive are evaluated further for diagnosis and, if appropriate, are provided or referred for evidence-based care."[83] The HIVMA/IDSA Primary Care Guidance does not have any recommendations regarding screening for anxiety in persons with HIV[68]

#### **Generalized Anxiety Disorder-7 (GAD-7)**

The 7-item <u>Generalized Anxiety Disorder-7 (GAD-7)</u> anxiety scale is a brief, self-administered questionnaire that has been validated in the general population to identify patients with probable generalized anxiety disorder.[84,85,86] The questionnaire includes questions about anxiety symptoms occurring in the past 2 weeks.

- Interpretation: The GAD-7 scores can range from 0 to 21. A major study identified a cut-point score of 10 as having the optimized sensitivity (89%) and specificity (82%) for diagnosing generalized anxiety disorder (Figure 7).[86] Score categories correlate with different levels of anxiety: 0-4 (minimal), 5 to 9 (mild), 10 to 14 (moderate), and 15 to 19 (severe). A more recent meta-analysis suggested using a cutoff score of 8 to optimize sensitivity without compromising specificity.[87]
- **Recommendation**: Individuals who meet the threshold for a positive GAD-7 screen (a score of 8 or above) should ideally have a complete diagnostic evaluation.

#### Patient Health Questionnaire for Panic Disorder (PHQ-PD)

This 5-item screening instrument is one subset of questions (questions 3a-d and questions 4a-k) derived from the longer Patient Health Questionnaire (PHQ), which itself is a short, self-reported instrument derived from a physician-administered PRIME-MD interview. The PHQ-PD (also called the panic module of the PHQ) has been found to be a valid screening instrument with a sensitivity of 44 to 66% and a specificity of 87 to 95%, depending on the scoring algorithm that is applied.[88] Using a single screening question taken from the PHQ-PD module (e.g., question 3a: "In the last 4 weeks, have you had an anxiety attack—suddenly feeling fear or panic?") improves sensitivity to 71% but drops specificity to 84%.

- Interpretation: A positive score on the original panic module is indicated with a positive (yes) answer on all four questions 3a-d plus a positive (yes) answer on at least four items from questions 4a-k. Modified versions of the test improve sensitivity by requiring only 2 or 3 positive answers for questions 3a-d. The most sensitive version of the panic module screener is the single screening question 3a; a yes answer to this single question is considered a positive screen.
- **Recommendation**: Many experts recommend using the single screening question (question 3a) since it has better psychometric properties than the full PHQ-PD algorithm.[88] Moreover, because primary care settings do not usually screen for panic disorder, adding only one question minimizes any additional burden to screening procedures already in place. Individuals who screen positive require follow-up with a formal diagnostic procedure.



#### Post-Traumatic Stress Disorder (PTSD) Screening Tools

There is limited evidence to support screening the civilian primary care population for post-traumatic stress disorder, and the United States Preventive Services Task Force does not address PTSD screening. In contrast, other organizations, including the National Institute of Health Care and Excellence in the United Kingdom (NICE-UK), recommend screening for PTSD when there is known exposure to a traumatic stressor.[89] Multiple PTSD screening instruments are available, including the 5-item Primary Care PTSD Screen from DSM-5 (PC-PTSD-5), the 17-item PTSD Checklist, the 4-item Startle-Physiologic Arousal-Anger-Numbness (SPAN), the 7-item Breslau's scale, the 10-item Trauma Screening Questionnaire, and the Single-Item PTSD Screener.[89,90,91] Among these screening tools, the PC-PTSD-5 test (five items) appears to be the best single screening test for PTSD for use in primary care.[90]

#### **Primary Care Post-Traumatic Stress Disorder (PC-PTSD)**

The <u>Primary Care PTSD for DSM-5 (PC-PTSD-5)</u> screening test is a 5-item scale that includes questions about symptoms unique to PTSD (re-experiencing, avoidance, numbness, hyperarousal, and feelings of guilt or blame).[91] One study found that the previously used 4-item PC-PTSD was more effective when used in combination with the General Health Questionnaire-12 (GHQ-12), which is a set of 12 questions used to screen for nonpsychotic psychiatric disorders and graded on a 4-point response scale.[92]

- **Interpretation**: Different studies recommend different cutoff scores for a positive screen. A study involving 398 Veterans patients at a primary care clinic found a score of 3 correlated with 95% sensitivity and 85% specificity for the diagnosis of PTSD (Figure 8).[90,91] Another large study that used data extracted from clinical databases for Veterans Affairs primary care patients used a score of 2 or greater as the cutoff for a positive PC-PTSD screen.
- **Recommendation**: Individuals who screen positive on the PC-PTSD screening test qualify for additional evaluation from the primary care provider or a mental health practitioner that includes an interview evaluating PTSD criteria from the DSM-5.



#### **Bipolar Disorder Screening Tool**

Bipolar disorder encompasses a spectrum of clinical disorders (bipolar I disorder, bipolar II disorder, and cyclothymic disorder) consisting of episodes of manic, hypomanic, and depressive symptoms. The heterogeneous presentation of bipolar disorder can make it difficult to detect this disorder through screening, and lifetime prevalence estimates of bipolar disorder vary widely across studies.[93] The National Comorbidity Survey estimates that the lifetime and 12-month prevalence for bipolar I disorder is 1.0% and 0.6%, respectively; for bipolar II disorder, these numbers are 1.1% and 0.8%.[94] There are no formal recommendations for screening for bipolar disorder; however, some experts recommend that primary care physicians implement selective screening for bipolar disorder in patients with known depression, anxiety, or substance use disorders.[93]

#### **Mood Disorders Questionnaire (MDQ)**

The Mood Disorders Questionnaire (MDQ) can be used to screen for a lifetime history of mania or hypomania. The MDQ consists of 13 yes or no questions based on DSM-5 criteria for bipolar disorder with two additional items to assess the frequency and severity of yes responses. In primary care, evaluation of whether a person has bipolar disorder arises most frequently in the context of beginning an antidepressant medication, since these medications can precipitate mania in vulnerable individuals. The MDQ is not a practical screening tool for most primary care clinicians, primarily because of the need to ask so many questions. Accordingly, some clinicians may find that asking a few pointed questions during history taking can be useful in ruling out a history of mania: (1) "Have you ever been told that you have manic-depressive illness or bipolar disorder?" and (2) "Has there ever been a period of time when you were not your usual self, and you had much more energy than usual?" These questions parallel two of the items on the MDQ. Any yes answer would then lead to further inquiry.[95,96]

- **Interpretation**: In the primary care setting, a score of 7 on the MDQ has a sensitivity of 43% and a specificity of 95% for detecting any type of bipolar disorder. In the mental health setting, diagnostic characteristics are better overall: for a score of 7, sensitivity is 81% and specificity is 85% (Figure 9).[ 96]
- **Recommendation**: Based on data showing low sensitivity but high specificity (and high negative predictive value), bipolar disorder screening tools, such as the MDQ, may be utilized most appropriately to rule out bipolar disorder in patients presenting with depression, rather than as a general screening tool.[97,98]

#### **Neurocognitive Screening Tools**

#### **Recommendations to Screen for Neurocognitive Disorders**

The United States Preventive Services Task Force (USPSTF) has found insufficient evidence to recommend for or against screening for cognitive impairment in older adults in the general population in the absence of known impairments.[99] Considering that as many as 50% of persons with HIV have some form of HIV-associated neurocognitive disorder, most experts recommend that persons with HIV should ideally have a baseline neurocognitive assessment, with follow-up screening every 6 to 12 months for individuals at high risk for HAND and every 12 to 24 months in persons at lower risk.[100] From a practical standpoint, however, this recommendation is often not implemented because existing clinical screens do not perform well in identifying milder forms of HAND. Therefore, identifying and developing practical screening tools for individuals with HIV that can detect milder forms of HAND and distinguish among the different HAND disorders is essential.

#### **Screening Tools for Neurocognitive Disorders**

Among the tools that are currently available, no consensus exists on which screening tool to use. The primary care literature offers four brief screening tools that are not specific to the diagnosis of HAND but are validated for general use in the primary care setting (Mini-Mental State Examination, General Practitioner Assessment of Cognition, Memory Impairment Screen, and Mini-Cognitive Assessment Instrument). The American Academy of Neurology acknowledged in its 2001 report on early detection of neurocognitive impairment that more research is needed to help clinicians differentiate among available screening instruments.[101,102,103] Several HIV-specific neurocognitive screening tools have been developed, but a consensus panel of experts on HIV neurocognitive disorders has concluded no single screening test is appropriate in all clinical situations—the choice of test may vary with patient population, provider experience and preference, cost, and time—and further acknowledges that all the available tools are less sensitive for detecting milder forms of cognitive impairment.[100] At the present time, a comprehensive neuropsychological assessment remains the gold standard for diagnosing HIV-associated neurocognitive disorders.

#### **General Population Neurocognitive Screening Tools**

#### Mini-Mental State Exam (MMSE)

The MMSE is among the oldest screening tools for cognitive impairment. The MMSE, which takes approximately 5 to 10 minutes to administer, includes a series of questions that cover 7 cognitive domains: orientation, registration, attention and calculation, recall, language, and construction.[104,105] A score of 24 points or lower (out of a total of 30 points) represents cognitive impairment. Most experts agree the MMSE is a weak tool for diagnosing HAND.[106,107] Despite free available versions of the MMSE, Psychological Assessment Resources (PAR) now holds exclusive rights to the MMSE and claims that any use of the MMSE requires their permission and ordering through them. Due to poor performance in evaluating HAND in persons with HIV (and the logistical problems obtaining this test), we do not recommend using MMSE as a neurocognitive screening tool for HAND.

#### Mini-Cognitive Assessment Instrument (Mini-Cog)

The Mini-Cog is a test consisting of a three-word registration, followed by a clock-drawing test, and then followed by three-word recall.[108] Patients receive 0 to 3 points based on the number of items recalled, and 0 or 2 points for clock drawing (a correct clock should have all the numbers placed appropriately, with the hands pointing to the time designated by the examiner). A total score of 0 to 2 indicates dementia. The test has sensitivity ranging from 76 to 99% and specificity ranging from 73 to 93% across studies.[101,109] Because of its speed, accuracy, and the fact it does not require patient fluency in English, some primary care providers suggest using this test as the initial screen.[101] Again, the Mini-Cog is not specific to HAND.

#### The General Practitioner Assessment of Cognition (GPCOG)

The GPCOG consists of 6 initial questions involving registration and recall, time orientation, clock drawing, and historical questions.[110] A two-part version of the GPCOG with an additional 6 questions can be used if the examiner knows the patient well enough to validate the historical questions. A score of 9 or above is considered normal, and a score of 4 or lower indicates cognitive impairment. For patients scoring in the 5 to 8 range who have a longstanding relationship with their provider, the second part of the GPCOG asks providers questions about the patient's current functional status compared to 5 years ago. Using a cutoff of 7 points for dementia, the sensitivity and specificity for the GPCOG is 82% and 70%, respectively; the two-part GPCOG increases the specificity to 83%.[101]

#### Memory Impairment Screen (MIS)

The MIS is a 4-minute, 4-item delayed, free, and cued recall test.[111] The patient is given a piece of paper with the names of four different items (an animal, vegetable, city, and musical instrument). The patient then counts from 1 to 20 and then back to 1; they are then asked to recall the names of the four items. A total of 2 points are given for items recalled without cueing, and 1 point is given for items recalled with cueing. As a screening tool for dementia, based on a cutoff score of 5, the sensitivity of the MIS is 86%, and the specificity is 91%.[101]

#### **Montreal Cognitive Assessment (MOCA)**

The MOCA is a free, online, validated instrument that is available in many languages to screen for mild cognitive impairments. The MOCA takes approximately 10 to 15 minutes to administer and consists of 30 items that measure function in 8 cognitive domains.[112] A score of 26 points or lower (out of a maximum of 30) indicates cognitive impairment. The MOCA has been found to be more sensitive than the Mini-Mental Status Exam (MMSE) at detecting mild cognitive impairment in the general population.[102,113] Among individuals with HIV, the MOCA has only moderate sensitivity and poor specificity for detecting mild cognitive impairment.[112]

#### **HIV-Specific Neurocognitive Screening Tools**

#### HIV Dementia Scale (HDS) and Modified HIV Dementia Scale (M-HDS)

The HIV Dementia Scale (HDS) is a test consisting of 4 items that address 4 cognitive domains: memory/recall, attention/learning, psychomotor functioning, and eye movements (visuoconstruction); the maximum score on the HDS is 16.[112,114,115] The HDS was originally developed in 1995 and found to be superior to the Mini-Mental Status Exam for identifying HIV-associated dementia. In one study, using an HDS cutoff score of 10 or less for identifying HIV dementia, the HDS performed with a sensitivity of 80%, specificity of 91%, and positive predictive value of 78%.[114] The HDS has been found to have inadequate sensitivity and specificity for detecting milder forms of cognitive impairment.[112,116] A modified version of the HDS (M-HDS) is a more practical screening tool for clinicians and non-neurologists.[117] The modified test eliminates the evaluation of antisaccadic eye movements, an examination deemed difficult for non-neurologists.

#### International HIV Dementia Scale (IHDS)

In 2005, the <u>International HIV Dementia Scale (IHDS)</u> was developed by Sacktor and colleagues and adopted for use in global settings to address culturally specific elements of the original HIV Dementia Scale and trouble administering the anti-saccadic errors test.[118,119] The IHDS test has three tasks that evaluate motor speed, psychomotor speed, and memory recall: timed finger tapping, timed alternating hand sequence test, and 4-item recall at 2 minutes.[119] The maximum score is 12 points.[119] Patients with a score of 10 or lower should undergo further evaluation for possible dementia.[119] A meta-analysis showed this test performed well when screening for dementia but had low accuracy for milder HAND conditions.[116]



#### **European AIDS Clinical Society (EACS) Cognitive Screen**

The European AIDS Clinical Society recommends initial screening for cognitive impairment using 3 questions related to memory loss, reasoning, and attention. The questions are graded as *never*, *hardly ever*, or *yes*, definitely; an answer of *yes*, *definitely* on at least one question is considered to be an abnormal screen.[4]



#### **Integrating Mental Health Screening into HIV Care**

#### **Integrating Screening into Primary Care**

Models for integrating the evaluation and management of mental health conditions into the primary care setting have focused primarily on depressive disorders; key elements of this integrative approach are highlighted in the recent United States Preventive Services Task Force (USPSTF) recommendation that endorses routine screening for depression in the general adult population, including pregnant and postpartum women.[120] The USPSTF statement indicates that implementation of the screening recommendation is best realized through a collaborative model of multidisciplinary, team-based care developed by the Community Preventive Services Task Force. This model uses case managers to connect primary care providers, patients, and mental health providers with stated goals of increasing screening and evidence-based treatment as well as improving clinical and community support for patient engagement in self-management. In this model, providers are responsible for screening patients, initiating treatment, and ensuring proper referral, while the case managers provide patient education, tracking, and management of the treatment plan.

#### **Integrating Mental Health Screening in HIV Care Settings**

#### **Depression Treatment Cascade**

Given the high prevalence of mental health conditions, particularly depression, among persons with HIV, collaborative care models that allow for mental health treatment within the HIV medical home are paramount.[121] A depression treatment cascade, mirroring the well-known HIV treatment cascade, has been published, and it highlights the attrition along the continuum from depression diagnosis to effective treatment; according to this cascade, 18% of individuals with HIV and depression are receiving any treatment for depression, 7% are receiving adequate treatment, and only 5% are in remission (Figure 10).[121] There is also interplay between the two cascades since depression is recognized to decrease engagement in HIV care and adherence to antiretroviral medication.[121]

#### **Collaborative Care Models**

Despite the recognized mental health treatment gap, there are limited data related to evidence-based strategies that can be integrated into HIV primary care. Some proposed solutions include co-located services and the use of embedded mental health providers. Just as the initiation of HIV care is more likely when diagnosis occurs at a site that offers co-located medical care, mental health treatment is also more likely when it is co-located within the familiar setting of a patient's medical home.[122,123] Collaborative care models to link antiretroviral and antidepressant management have also been tested in clinical trials. One such collaborative model, termed measurement-based care, has reported improvement in depression among participants. Measurement-based care is a decision support model for integrating antidepressant management into routine HIV care, in which depression case managers use metrics to give HIV primary care clinicians antidepressant treatment recommendations.[121,124]

#### **Limits of Collaborative Care Models**

It is important to note that collaborative care models in primary care are targeted for people who have mild to moderate mental health conditions and may not be able to provide the full range of services needed by people with HIV who have serious mental health conditions, such as bipolar disorder, schizophrenia, and other psychotic conditions.

#### **Summary Points**

- Among adults in the United States, the prevalence of depression, anxiety, and PTSD is significantly higher among adults with HIV than in adults without HIV.
- There is an increased risk for HIV acquisition and HIV transmission associated with certain mental health conditions, and mental health conditions have been associated with decreased utilization of antiretroviral therapy and predict worse HIV disease outcomes.
- Practical screening tools for use in the primary care setting should be brief, easily scored, free, evidence-based, and accessible to a range of providers without requiring specific training.
- Screening tools for some of the most common mental health diagnoses encountered in primary care include 2-Item PRIME-MD, PHQ2, and PHQ-9 (depression); GAD-7 (generalized anxiety disorder) PHQ-PD (panic disorder); and PC-PTSD-5 (post-traumatic stress disorder). A positive result on any screening test requires confirmation with a formal diagnostic interview.
- HAND likely affects 50% of persons living with HIV, with older age representing the greatest risk factor. Additional risk factors for HAND include low nadir CD4 count, previous central nervous system injury, detectable plasma HIV RNA levels, and comorbidities such as hypertension, insulin resistance, viral hepatitis, depression, and substance use disorder.
- HAND is subdivided into three categories based on the severity of disease: (1) asymptomatic neurocognitive impairment, (2) mild neurocognitive disorder, and (3) HIV-associated dementia.
- Screening tools for neurocognitive disorders include, among others, the MMSE, Mini-Cog, GPCOG, MIS, MOCA, European AIDS Clinical Society Cognitive Screen, HIV Dementia Scale, and International HIV Dementia Scale.
- Neurocognitive disorders screening tools work best when screening for HIV-associated dementia and they do not reliably detect milder forms of HIV-associated neurocognitive disorders.
- Co-located services, the use of embedded mental health providers, collaborative care, and decision support tools may all help to integrate mental health care into HIV primary care and improve the HIV treatment cascade.
- Meeting the needs of people with both HIV and the most serious mental health conditions, such as bipolar disorder and schizophrenia, are not well addressed in the common models proposed for integrating primary and HIV care along with care for people with mild to moderate mental health conditions. There are also no simple and reliable clinical tools for screening for psychosis. Thus, these individuals remain a challenging population to manage in the HIV clinical care setting.

#### **Citations**

- 1. Orlando M, Burnam MA, Beckman R, et al. Re-estimating the prevalence of psychiatric disorders in a nationally representative sample of persons receiving care for HIV: results from the HIV Cost and Services Utilization Study. Int J Methods Psychiatr Res. 2002;11:75-82.

  [PubMed Abstract] -
- Bing EG, Burnam MA, Longshore D, et al. Psychiatric disorders and drug use among human immunodeficiency virus-infected adults in the United States. Arch Gen Psychiatry. 2001;58:721-8.
   [PubMed Abstract] -
- 3. Carvalhal A, Baril JG, Crouzat F, et al. Recognizing cognitive and psychiatric changes in the post-highly active antiretroviral therapy era. Can J Infect Dis Med Microbiol. 2012;23:209-15.

  [PubMed Abstract] -
- European AIDS Clinical Society. Guidelines. Version 8.0. October, 2015.
   [EACS] -
- 5. Neigh GN, Rhodes ST, Valdez A, Jovanovic T. PTSD co-morbid with HIV: Separate but equal, or two parts of a whole? Neurobiol Dis. 2016;92:116-23.

  [PubMed Abstract] -
- Mudra Rakshasa-Loots A, Bakewell N, Sharp DJ, et al. Biomarkers of central and peripheral inflammation mediate the association between HIV and depressive symptoms. Transl Psychiatry. 2023;13:190.
   [PubMed Abstract] -
- Mudra Rakshasa-Loots A, Whalley HC, Vera JH, Cox SR. Neuroinflammation in HIV-associated depression: evidence and future perspectives. Mol Psychiatry. 2022;27:3619-32.
   [PubMed Abstract] -
- Centers for Disease Control and Prevention. Behavioral and Clinical Characteristics of Persons with Diagnosed HIV Infection—Medical Monitoring Project, United States, 2021 Cycle (June 2021-May 2022). HIV Surveillance Special Report 32. Published August 2023.
   [CDC] -
- Machtinger EL, Wilson TC, Haberer JE, Weiss DS. Psychological trauma and PTSD in HIV-positive women: a meta-analysis. AIDS Behav. 2012;16:2091-100.
   [PubMed Abstract] -
- 10. Hughes E, Bassi S, Gilbody S, Bland M, Martin F. Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness: a systematic review and meta-analysis. Lancet Psychiatry. 2016;3:40-8.

- 11. Wright N, Akhtar A, Tosh GE, Clifton AV. HIV prevention advice for people with serious mental illness. Cochrane Database Syst Rev. 2014;12:CD009639.

  [PubMed Abstract] -
- Falck RS, Wang J, Carlson RG, Siegal HA. Factors influencing condom use among heterosexual users of injection drugs and crack cocaine. Sex Transm Dis. 1997;24:204-10.
   [PubMed Abstract] -

13. Meade CS, Graff FS, Griffin ML, Weiss RD. HIV risk behavior among patients with co-occurring bipolar and substance use disorders: associations with mania and drug abuse. Drug Alcohol Depend. 2008:92:296-300.

- 14. Rosenberg SD, Goodman LA, Osher FC, et al. Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness. Am J Public Health. 2001;91:31-7.

  [PubMed Abstract] -
- Meade CS, Sikkema KJ. HIV risk behavior among adults with severe mental illness: a systematic review. Clin Psychol Rev. 2005;25:433-57.
   [PubMed Abstract] -
- 16. Cournos F, Empfield M, Horwath E, et al. HIV seroprevalence among patients admitted to two psychiatric hospitals. Am J Psychiatry. 1991;148:1225-30.

  [PubMed Abstract] -
- 17. Cournos F, Horwath E, Guido JR, McKinnon K, Hopkins N. HIV-1 infection at two public psychiatric hospitals in New York City. AIDS Care. 1994;6:443-52.

  [PubMed Abstract] -
- 18. Blank MB, Himelhoch SS, Balaji AB, et al. A multisite study of the prevalence of HIV with rapid testing in mental health settings. Am J Public Health. 2014;104:2377-84.

  [PubMed Abstract] -
- 19. Beyer JL, Taylor L, Gersing KR, Krishnan KR. Prevalence of HIV infection in a general psychiatric outpatient population. Psychosomatics. 2007;48:31-7. [PubMed Abstract] -
- 20. Buckingham E, Schrage E, Cournos F. Why the Treatment of Mental Disorders Is an Important Component of HIV Prevention among People Who Inject Drugs. Adv Prev Med. 2013;2013:690386. [PubMed Abstract] -
- 21. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011;365:493-505.

  [PubMed Abstract] -
- 22. Willie TC, Overstreet NM, Sullivan TP, Sikkema KJ, Hansen NB. Barriers to HIV Medication Adherence: Examining Distinct Anxiety and Depression Symptoms among Women Living with HIV Who Experienced Childhood Sexual Abuse. Behav Med. 2016;42:120-7.

  [PubMed Abstract] -
- 23. Gonzalez JS, Batchelder AW, Psaros C, Safren SA. Depression and HIV/AIDS treatment nonadherence: a review and meta-analysis. J Acquir Immune Defic Syndr. 2011;58:181-7.

  [PubMed Abstract] -
- 24. Mitzel LD, Vanable PA, Brown JL, Bostwick RA, Sweeney SM, Carey MP. Depressive Symptoms Mediate the Effect of HIV-Related Stigmatization on Medication Adherence Among HIV-Infected Men Who Have Sex with Men. AIDS Behav. 2015;19:1454-9.

  [PubMed Abstract] -
- 25. Meade CS, Bevilacqua LA, Key MD. Bipolar disorder is associated with HIV transmission risk behavior among patients in treatment for HIV. AIDS Behav. 2012;16:2267-71.

  [PubMed Abstract] -

- 26. O'Cleirigh C, Newcomb ME, Mayer KH, Skeer M, Traeger L, Safren SA. Moderate levels of depression predict sexual transmission risk in HIV-infected MSM: a longitudinal analysis of data from six sites involved in a "prevention for positives" study. AIDS Behav. 2013;17:1764-9.

  [PubMed Abstract] -
- 27. Moore DJ, Posada C, Parikh M, et al. HIV-infected individuals with co-occurring bipolar disorder evidence poor antiretroviral and psychiatric medication adherence. AIDS Behav. 2012;16:2257-66. [PubMed Abstract] -
- 28. Walkup J, Blank MB, Gonzalez JS, et al. The impact of mental health and substance abuse factors on HIV prevention and treatment. J Acquir Immune Defic Syndr. 2008;47 Suppl 1:S15-9. [PubMed Abstract] -
- 29. Sikkema KJ, Watt MH, Drabkin AS, Meade CS, Hansen NB, Pence BW. Mental health treatment to reduce HIV transmission risk behavior: a positive prevention model. AIDS Behav. 2010;14:252-62. [PubMed Abstract] -
- 30. Grossman CI, Gordon CM. Mental health considerations in secondary HIV prevention. AIDS Behav. 2010;14:263-71. [PubMed Abstract] -
- 31. Treisman G, Angelino A. Interrelation between psychiatric disorders and the prevention and treatment of HIV infection. Clin Infect Dis. 2007;45 Suppl 4:S313-7.

  [PubMed Abstract] -
- 32. Badiee J, Riggs PK, Rooney AS, et al. Approaches to identifying appropriate medication adherence assessments for HIV infected individuals with comorbid bipolar disorder. AIDS Patient Care STDS. 2012;26:388-94.

  [PubMed Abstract] -
- 33. Vranceanu AM, Safren SA, Lu M, et al. The relationship of post-traumatic stress disorder and depression to antiretroviral medication adherence in persons with HIV. AIDS Patient Care STDS. 2008;22:313-21.

  [PubMed Abstract] -
- 34. Brownley JR, Fallot RD, Wolfson Berley R, Himelhoch SS. Trauma history in African-American women living with HIV: effects on psychiatric symptom severity and religious coping. AIDS Care. 2015;27:964-71.

[PubMed Abstract] -

35. Yiaslas TA, Kamen C, Arteaga A, et al. The relationship between sexual trauma, peritraumatic dissociation, posttraumatic stress disorder, and HIV-related health in HIV-positive men. J Trauma Dissociation. 2014;15:420-35.

- 36. Antelman G, Kaaya S, Wei R, et al. Depressive symptoms increase risk of HIV disease progression and mortality among women in Tanzania. J Acquir Immune Defic Syndr. 2007;44:470-7. [PubMed Abstract] -
- 37. Charlson FJ, Baxter AJ, Dua T, Degenhardt L, Whiteford HA, Vos T. Excess mortality from mental, neurological and substance use disorders in the Global Burden of Disease Study 2010. Epidemiol Psychiatr Sci. 2015;24:121-40.

  [PubMed Abstract] -

- 38. Sundermann EE, Tang B, Kim M, Paolillo EW, Heaton RK, Moore RC. Neuropsychiatric predictors of cognitive functioning over a one-year follow-up period in HIV. J Affect Disord. 2023;336:92-6. [PubMed Abstract] -
- 39. Goodkin K, Evering TH, Anderson AM, et al. The comorbidity of depression and neurocognitive disorder in persons with HIV infection: call for investigation and treatment. Front Cell Neurosci. 2023;17:1130938.

- 40. Cruess DG, Kalichman SC, Amaral C, Swetzes C, Cherry C, Kalichman MO. Benefits of adherence to psychotropic medications on depressive symptoms and antiretroviral medication adherence among men and women living with HIV/AIDS. Ann Behav Med. 2012;43:189-97.
  [PubMed Abstract] -
- 41. Cook JA, Cohen MH, Burke J, et al. Effects of depressive symptoms and mental health quality of life on use of highly active antiretroviral therapy among HIV-seropositive women. J Acquir Immune Defic Syndr. 2002;30:401-9.

  [PubMed Abstract] -
- 42. Horberg MA, Silverberg MJ, Hurley LB, et al. Effects of depression and selective serotonin reuptake inhibitor use on adherence to highly active antiretroviral therapy and on clinical outcomes in HIVinfected patients. J Acquir Immune Defic Syndr. 2008;47:384-90.
  [PubMed Abstract] -
- 43. Himelhoch S, Brown CH, Walkup J, et al. HIV patients with psychiatric disorders are less likely to discontinue HAART. AIDS. 2009;23:1735-42.

  [PubMed Abstract] -
- 44. Saag LA, Tamhane AR, Batey DS, Mugavero MJ, Eaton EF. Mental health service utilization is associated with retention in care among persons living with HIV at a university-affiliated HIV clinic. AIDS Res Ther. 2018;15:1.

  [PubMed Abstract] -
- 45. Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: a systematic review and metaanalysis. Alzheimers Dement. 2013;9:63-75.e2. [PubMed Abstract] -
- 46. Heaton RK, Clifford DB, Franklin DR Jr, et al. HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy: CHARTER Study. Neurology. 2010;75:2087-96. [PubMed Abstract] -
- 47. Vance DE, Wadley VG, Crowe MG, Raper JL, Ball KK. Cognitive and Everyday Functioning in Older and Younger Adults with and without HIV. Clin Gerontol. 2011;34:413-426.

  [PubMed Abstract] -
- 48. Sacktor N, Skolasky RL, Seaberg E, et al. Prevalence of HIV-associated neurocognitive disorders in the Multicenter AIDS Cohort Study. Neurology. 2016;86:334-40.

  [PubMed Abstract] -
- 49. Eggers C, Arendt G, Hahn K, et al. HIV-1-associated neurocognitive disorder: epidemiology, pathogenesis, diagnosis, and treatment. J Neurol. 2017;264:1715-27.

  [PubMed Abstract] -

- 50. The HIV and Aging Consensus Project: Recommended Treatment Strategies for Clinicians Managing Older Patients with HIV. American Academy of HIV Medicine. Last Updated May 2017
  [AAHIVM] -
- 51. Ahern E, Semkovska M. Cognitive functioning in the first-episode of major depressive disorder: A systematic review and meta-analysis. Neuropsychology. 2017;31:52-72.

  [PubMed Abstract] -
- 52. Roca M, Vives M, López-Navarro E, García-Campayo J, Gili M. Cognitive impairments and depression: a critical review. Actas Esp Psiquiatr. 2015;43:187-93.

  [PubMed Abstract] -
- 53. Letendre SL, Chen H, McKhann A, et al. Antiretroviral Therapy Intensification for Neurocognitive Impairment in HIV. Clin Infect Dis. 2023 May 15. [Online ahead of print] [PubMed Abstract] -
- 54. Saylor D, Dickens AM, Sacktor N, et al. HIV-associated neurocognitive disorder pathogenesis and prospects for treatment. Nat Rev Neurol. 2016;12:309.

  [PubMed Abstract] -
- 55. Antinori A, Arendt G, Becker JT, et al. Updated research nosology for HIV-associated neurocognitive disorders. Neurology. 2007;69:1789-99.

  [PubMed Abstract] -
- 56. Gutiérrez F, Navarro A, Padilla S, et al. Prediction of neuropsychiatric adverse events associated with long-term efavirenz therapy, using plasma drug level monitoring. Clin Infect Dis. 2005;41:1648-53. [PubMed Abstract] -
- 57. Foster R, Taylor C, Everall IP. More on abacavir-induced neuropsychiatric reactions. AIDS. 2004;18:2449.

  [PubMed Abstract] -
- 58. Foster R, Olajide D, Everall IP. Antiretroviral therapy-induced psychosis: case report and brief review of the literature. HIV Med. 2003;4:139-44.

  [PubMed Abstract] -
- 59. Boly L, Cafaro V, Dyner T. Depressive symptoms predict increased incidence of neuropsychiatric side effects in patients treated with efavirenz. J Acquir Immune Defic Syndr. 2006;42:514-5. [PubMed Abstract] -
- 60. Nightingale S, Ances B, Cinque P, et al. Cognitive impairment in people living with HIV: consensus recommendations for a new approach. Nat Rev Neurol. 2023 Jun 13. [online ahead of print] [PubMed Abstract] -
- 61. Spitzer RL, Williams JB, Kroenke K, et al. Utility of a new procedure for diagnosing mental disorders in primary care. The PRIME-MD 1000 study. JAMA. 1994;272:1749-56.

  [PubMed Abstract] -
- 62. Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. JAMA. 1999;282:1737-44.

  [PubMed Abstract] -
- 63. Fuchs CH, Haradhvala N, Hubley S, et al. Physician actions following a positive PHQ-2: implications for

the implementation of depression screening in family medicine practice. Fam Syst Health. 2015;33:18-27.

[PubMed Abstract] -

- 64. Yonkers KA, Smith MV, Lin H, Howell HB, Shao L, Rosenheck RA. Depression screening of perinatal women: an evaluation of the healthy start depression initiative. Psychiatr Serv. 2009;60:322-8. [PubMed Abstract] -
- 65. Katon WJ, Lin EH, Von Korff M, et al. Collaborative care for patients with depression and chronic illnesses. N Engl J Med. 2010;363:2611-20.

  [PubMed Abstract] -
- 66. Croft P, Altman DG, Deeks JJ, et al. The science of clinical practice: disease diagnosis or patient prognosis? Evidence about "what is likely to happen" should shape clinical practice. BMC Med. 2015;13:20.

[PubMed Abstract] -

67. US Preventive Services Task Force, Barry MJ, Nicholson WK, et al. Screening for Depression and Suicide Risk in Adults: US Preventive Services Task Force Recommendation Statement. JAMA. 2023;329:2057-67.

[PubMed Abstract] -

- 68. Thompson MA, Horberg MA, Agwu AL, et al. Primary Care Guidance for Persons With Human Immunodeficiency Virus: 2020 Update by the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis. 2021;73:e3572-e3605
  [HIVMA] -
- 69. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16:606-13.

[PubMed Abstract] -

70. Huang FY, Chung H, Kroenke K, Delucchi KL, Spitzer RL. Using the Patient Health Questionnaire-9 to measure depression among racially and ethnically diverse primary care patients. J Gen Intern Med. 2006;21:547-52.

[PubMed Abstract] -

71. Moriarty AS, Gilbody S, McMillan D, Manea L. Screening and case finding for major depressive disorder using the Patient Health Questionnaire (PHQ-9): a meta-analysis. Gen Hosp Psychiatry. 2015;37:567-76.

[PubMed Abstract] -

72. Levis B, Benedetti A, Ioannidis JPA, et al. Patient Health Questionnaire-9 scores do not accurately estimate depression prevalence: individual participant data meta-analysis. J Clin Epidemiol. 2020;122:115-128.e1.

- 73. Maurer DM. Screening for depression. Am Fam Physician. 2012;85:139-44. [PubMed Abstract] -
- 74. Chang BP, Tan TM. Suicide screening tools and their association with near-term adverse events in the ED. Am J Emerg Med. 2015;33:1680-3. [PubMed Abstract] -
- 75. Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item

National HIV Curriculum

depression screener. Med Care. 2003;41:1284-92. [PubMed Abstract] -

76. Levis B, Sun Y, He C, et al. Accuracy of the PHQ-2 Alone and in Combination With the PHQ-9 for Screening to Detect Major Depression: Systematic Review and Meta-analysis. JAMA. 2020;323:2290-2300. [PubMed Abstract] -

77. Tamburrino MB, Lynch DJ, Nagel RW, Smith MK. Primary care evaluation of mental disorders (PRIME-MD) screening for minor depressive disorder in primary care. Prim Care Companion J Clin Psychiatry. 2009;11:339-43.

[PubMed Abstract] -

- 78. Whooley MA, Avins AL, Miranda J, Browner WS. Case-finding instruments for depression. Two questions are as good as many. J Gen Intern Med. 1997;12:439-45.

  [PubMed Abstract] -
- 79. Preljevic VT, Østhus TB, Sandvik L, et al. Screening for anxiety and depression in dialysis patients: comparison of the Hospital Anxiety and Depression Scale and the Beck Depression Inventory. J Psychosom Res. 2012;73:139-44.

  [PubMed Abstract] -
- 80. Whelan-Goodinson R, Ponsford J, Schönberger M. Validity of the Hospital Anxiety and Depression Scale to assess depression and anxiety following traumatic brain injury as compared with the Structured Clinical Interview for DSM-IV. J Affect Disord. 2009;114:94-102.

  [PubMed Abstract] -
- 81. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res. 2002;52:69-77. [PubMed Abstract] -
- 82. Herr NR, Williams JW Jr, Benjamin S, McDuffie J. Does this patient have generalized anxiety or panic disorder?: The Rational Clinical Examination systematic review. JAMA. 2014;312:78-84. [PubMed Abstract] -
- 83. US Preventive Services Task Force, Barry MJ, Nicholson WK, et al. Screening for Anxiety Disorders in Adults: US Preventive Services Task Force Recommendation Statement. JAMA. 2023 Jun 20. Online ahead of print.

- 84. Kroenke K, Spitzer RL, Williams JB, Monahan PO, Löwe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. Ann Intern Med. 2007;146:317-25. [PubMed Abstract] -
- 85. Löwe B, Decker O, Müller S, et al. Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. Med Care. 2008;46:266-74.

  [PubMed Abstract] -
- 86. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006;166:1092-7.

  [PubMed Abstract] -
- 87. Plummer F, Manea L, Trepel D, McMillan D. Screening for anxiety disorders with the GAD-7 and GAD-2: a systematic review and diagnostic metaanalysis. Gen Hosp Psychiatry. 2016;39:24-31.

#### [PubMed Abstract] -

88. Wittkampf KA, Baas KD, van Weert HC, Lucassen P, Schene AH. The psychometric properties of the panic disorder module of the Patient Health Questionnaire (PHQ-PD) in high-risk groups in primary care. J Affect Disord. 2011;130:260-7.

[PubMed Abstract] -

89. Spoont MR, Williams JW Jr, Kehle-Forbes S, Nieuwsma JA, Mann-Wrobel MC, Gross R. Does This Patient Have Posttraumatic Stress Disorder?: Rational Clinical Examination Systematic Review. JAMA. 2015;314:501-10.

[PubMed Abstract] -

90. Freedy JR, Steenkamp MM, Magruder KM, et al. Post-traumatic stress disorder screening test performance in civilian primary care. Fam Pract. 2010;27:615-24.

[PubMed Abstract] -

91. Prins A, Bovin MJ, Smolenski DJ, et al. The Primary Care PTSD Screen for DSM-5 (PC-PTSD-5): Development and Evaluation Within a Veteran Primary Care Sample. J Gen Intern Med. 2016;31:1206-11.

[PubMed Abstract] -

92. Ouimette P, Wade M, Prins A, Schohn M. Identifying PTSD in primary care: comparison of the Primary Care-PTSD screen (PC-PTSD) and the General Health Questionnaire-12 (GHQ). J Anxiety Disord. 2008;22:337-43.

[PubMed Abstract] -

93. Das AK, Olfson M, Gameroff MJ, et al. Screening for bipolar disorder in a primary care practice. JAMA. 2005;293:956-63.

[PubMed Abstract] -

- 94. Merikangas KR, Akiskal HS, Angst J, et al. Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. Arch Gen Psychiatry. 2007;64:543-52. [PubMed Abstract] -
- 95. Carvalho AF, Takwoingi Y, Sales PM, et al. Screening for bipolar spectrum disorders: A comprehensive meta-analysis of accuracy studies. J Affect Disord. 2015;172:337-46.

  [PubMed Abstract] -
- 96. Hirschfeld RM, Williams JB, Spitzer RL, et al. Development and validation of a screening instrument for bipolar spectrum disorder: the Mood Disorder Questionnaire. Am J Psychiatry. 2000;157:1873-5. [PubMed Abstract] -
- 97. Price AL, Marzani-Nissen GR. Bipolar disorders: a review. Am Fam Physician. 2012;85:483-93. [PubMed Abstract] -
- 98. Zimmerman M, Galione JN. Screening for bipolar disorder with the Mood Disorders Questionnaire: a review. Harv Rev Psychiatry. 2011;19:219-28.

  [PubMed Abstract] -
- 99. Lin JS, O'Connor E, Rossom RC, Perdue LA, Eckstrom E. Screening for cognitive impairment in older adults: A systematic review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013;159:601-12.

100. Mind Exchange Working Group. Assessment, diagnosis, and treatment of HIV-associated neurocognitive disorder: a consensus report of the mind exchange program. Clin Infect Dis. 2013:56:1004-17.

[PubMed Abstract] -

101. Ebell MH. Brief screening instruments for dementia in primary care. Am Fam Physician. 2009;79:497-8, 500.

[PubMed Abstract] -

102. Michels TC, Tiu AY, Graver CJ. Neuropsychological evaluation in primary care. Am Fam Physician. 2010;82:495-502.

[PubMed Abstract] -

103. Petersen RC, Stevens JC, Ganguli M, Tangalos EG, Cummings JL, DeKosky ST. Practice parameter: early detection of dementia: mild cognitive impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2001;56:1133-42.

[PubMed Abstract] -

- 104. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12:189-98.

  [PubMed Abstract] -
- 105. Tombaugh TN, McIntyre NJ. The mini-mental state examination: a comprehensive review. J Am Geriatr Soc. 1992;40:922-35.

  [PubMed Abstract] -
- 106. Nakazato A, Tominaga D, Tasato D, et al. Are MMSE and HDS-R neuropsychological tests adequate for screening HIV-associated neurocognitive disorders? J Infect Chemother. 2014;20:217-9. [PubMed Abstract] -
- 107. Skinner S, Adewale AJ, DeBlock L, Gill MJ, Power C. Neurocognitive screening tools in HIV/AIDS: comparative performance among patients exposed to antiretroviral therapy. HIV Med. 2009;10:246-52.

[PubMed Abstract] -

- 108. Borson S, Scanlan J, Brush M, Vitaliano P, Dokmak A. The mini-cog: a cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. Int J Geriatr Psychiatry. 2000;15:1021-7.

  [PubMed Abstract] -
- 109. Holsinger T, Plassman BL, Stechuchak KM, Burke JR, Coffman CJ, Williams JW Jr. Screening for cognitive impairment: comparing the performance of four instruments in primary care. J Am Geriatr Soc. 2012;60:1027-36.

- 110. Brodaty H, Pond D, Kemp NM, et al. The GPCOG: a new screening test for dementia designed for general practice. J Am Geriatr Soc. 2002;50:530-4.

  [PubMed Abstract] -
- 111. Buschke H, Kuslansky G, Katz M, et al. Screening for dementia with the memory impairment screen.

  Neurology. 1999;52:231-8.

  [PubMed Abstract] -
- 112. Janssen MA, Bosch M, Koopmans PP, Kessels RP. Validity of the Montreal Cognitive Assessment and

the HIV Dementia Scale in the assessment of cognitive impairment in HIV-1 infected patients. J Neurovirol. 2015;21:383-90. [PubMed Abstract] -

- 113. Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005;53:695-9.

  [PubMed Abstract] -
- 114. Power C, Selnes OA, Grim JA, McArthur JC. HIV Dementia Scale: a rapid screening test. J Acquir Immune Defic Syndr Hum Retrovirol. 1995;8:273-8.

  [PubMed Abstract] -
- 115. Valcour V, Paul R, Chiao S, Wendelken LA, Miller B. Screening for cognitive impairment in human immunodeficiency virus. Clin Infect Dis. 2011;53:836-42.

  [PubMed Abstract] -
- 116. Zipursky AR, Gogolishvili D, Rueda S, et al. Evaluation of brief screening tools for neurocognitive impairment in HIV/AIDS: a systematic review of the literature. AIDS. 2013;27:2385-401. [PubMed Abstract] -
- 117. Davis HF, Skolasky RL Jr, Selnes OA, Burgess DM, McArthur JC. Assessing HIV-associated dementia: modified HIV dementia scale versus the Grooved Pegboard. AIDS Read. 2002;12:29-31, 38. [PubMed Abstract] -
- 118. Haddow LJ, Floyd S, Copas A, Gilson RJ. A systematic review of the screening accuracy of the HIV Dementia Scale and International HIV Dementia Scale. PLoS One. 2013;8:e61826.

  [PubMed Abstract] -
- 119. Sacktor NC, Wong M, Nakasujja N, et al. The International HIV Dementia Scale: a new rapid screening test for HIV dementia. AIDS. 2005;19:1367-74.

  [PubMed Abstract] -
- 120. Siu AL. Behavioral and Pharmacotherapy Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Women: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2015;163:622-34.

  [PubMed Abstract] -
- 121. Pence BW, O'Donnell JK, Gaynes BN. Falling through the cracks: the gaps between depression prevalence, diagnosis, treatment, and response in HIV care. AIDS. 2012;26:656-8. [PubMed Abstract] -
- 122. Torian LV, Wiewel EW, Liu KL, Sackoff JE, Frieden TR. Risk factors for delayed initiation of medical care after diagnosis of human immunodeficiency virus. Arch Intern Med. 2008;168:1181-7.

  [PubMed Abstract] -
- 123. Willenbring ML. Integrating care for patients with infectious, psychiatric, and substance use disorders: concepts and approaches. AIDS. 2005;19 Suppl 3:S227-37.

  [PubMed Abstract] -
- 124. Pence BW, Gaynes BN, Adams JL, et al. The effect of antidepressant treatment on HIV and depression outcomes: results from a randomized trial. AIDS. 2015;29:1975-86.

  [PubMed Abstract] -

#### References

- Aberg JA, Gallant JE, Ghanem KG, Emmanuel P, Zingman BS, Horberg MA. Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV medicine association of the Infectious Diseases Society of America. Clin Infect Dis. 2014;58:e1-34.
   [HIVMA] -
- Archer J, Bower P, Gilbody S, et al. Collaborative care for depression and anxiety problems. Cochrane Database Syst Rev. 2012;10:CD006525.
   [PubMed Abstract] -
- Beer L, Tie Y, Padilla M, Shouse RL. Generalized anxiety disorder symptoms among persons with diagnosed HIV in the United States. AIDS. 2019 Sep 1;33:1781-87.
   [PubMed Abstract] -
- Blair JM, Fagan JL, Frazier EL, et al. Behavioral and clinical characteristics of persons receiving medical care for HIV infection - Medical Monitoring Project, United States, 2009. MMWR Surveill Summ. 2014;63 Suppl 5:1-22.
   [PubMed Abstract] -
- Crepaz N, Marks G. Are negative affective states associated with HIV sexual risk behaviors? A metaanalytic review. Health Psychol. 2001;20:291-9.
   [PubMed Abstract] -
- Do AN, Rosenberg ES, Sullivan PS, et al. Excess burden of depression among HIV-infected persons receiving medical care in the united states: data from the medical monitoring project and the behavioral risk factor surveillance system. PLoS One. 2014;9:e92842.
   [PubMed Abstract] -
- Eisinger RW, Dieffenbach CW, Fauci AS. HIV Viral Load and Transmissibility of HIV Infection: Undetectable Equals Untransmittable. JAMA. 2019;321:451-2. [PubMed Abstract] -
- Golden J, Conroy RM, O'Dwyer AM. Reliability and validity of the Hospital Anxiety and Depression Scale and the Beck Depression Inventory (Full and FastScreen scales) in detecting depression in persons with hepatitis C. J Affect Disord. 2007;100:265-9.
   [PubMed Abstract] -
- Golin CE, Haley DF, Wang J, et al. Post-traumatic Stress Disorder Symptoms and Mental Health over Time among Low-Income Women at Increased Risk of HIV in the U.S. J Health Care Poor Underserved. 2016;27:891-910.
   [PubMed Abstract] -
- Heslin M, Jewell A, Croxford S, et al. Prevalence of HIV in mental health service users: a retrospective cohort study. BMJ Open. 2023;13:e067337.
   [PubMed Abstract] -
- Honarmand K, Feinstein A. Validation of the Hospital Anxiety and Depression Scale for use with multiple sclerosis patients. Mult Scler. 2009;15:1518-24.
   [PubMed Abstract] -
- Kroenke K, Wu J, Yu Z, et al. Patient Health Questionnaire Anxiety and Depression Scale: Initial Validation in Three Clinical Trials. Psychosom Med. 2016;78:716-27.



#### [PubMed Abstract] -

- Lu H, Surkan PJ, Irwin MR, et al. Inflammation and Risk of Depression in HIV: Prospective Findings From the Multicenter AIDS Cohort Study. Am J Epidemiol. 2019;188:1994-2003.

  [PubMed Abstract] -
- Mimiaga MJ, Reisner SL, Grasso C, et al. Substance use among HIV-infected patients engaged in primary care in the United States: findings from the Centers for AIDS Research Network of Integrated Clinical Systems cohort. Am J Public Health. 2013;103:1457-67.
   [PubMed Abstract] -
- Mitchell AJ, Yadegarfar M, Gill J, Stubbs B. Case finding and screening clinical utility of the Patient Health Questionnaire (PHQ-9 and PHQ-2) for depression in primary care: a diagnostic meta-analysis of 40 studies. BJPsych Open. 2016;2:127-138.
   [PubMed Abstract] -
- Moore CL, Grulich AE, Prestage G, et al. Hospitalization for Anxiety and Mood Disorders in HIV-Infected and -Uninfected Gay and Bisexual Men. J Acquir Immune Defic Syndr. 2016;73:589-597.
   [PubMed Abstract] -
- Mustanski BS, Newcomb ME, Du Bois SN, Garcia SC, Grov C. HIV in young men who have sex with men: a review of epidemiology, risk and protective factors, and interventions. J Sex Res. 2011;48:218-53.
   [PubMed Abstract] -
- Nel A, Kagee A. Common mental health problems and antiretroviral therapy adherence. AIDS Care. 2011;23:1360-5.

- Siu AL, Bibbins-Domingo K, Grossman DC, et al. Screening for Depression in Adults: US Preventive Services Task Force Recommendation Statement. JAMA. 2016;315:380-7.
   [PubMed Abstract] -
- Springer SA, Dushaj A, Azar MM. The impact of DSM-IV mental disorders on adherence to combination antiretroviral therapy among adult persons living with HIV/AIDS: a systematic review. AIDS Behav. 2012;16:2119-43.
   [PubMed Abstract] -
- Underwood J, Winston A. Guidelines for Evaluation and Management of Cognitive Disorders in HIV-Positive Individuals. Curr HIV/AIDS Rep. 2016;13:235-40.
   [PubMed Abstract] -
- van der Zwaan GL, van Dijk SE, Adriaanse MC, et al. Diagnostic accuracy of the Patient Health
  Questionnaire-9 for assessment of depression in type II diabetes mellitus and/or coronary heart
  disease in primary care. J Affect Disord. 2016;190:68-74.
   [PubMed Abstract] -
- Vodermaier A, Millman RD. Accuracy of the Hospital Anxiety and Depression Scale as a screening tool in cancer patients: a systematic review and meta-analysis. Support Care Cancer. 2011;19:1899-908.
   [PubMed Abstract] -
- Wei SC, Messina L, Hood J, et al. Methods to include persons living with HIV not receiving HIV care in the Medical Monitoring Project. PLoS One. 2019;14:e0219996.
   [PubMed Abstract] -

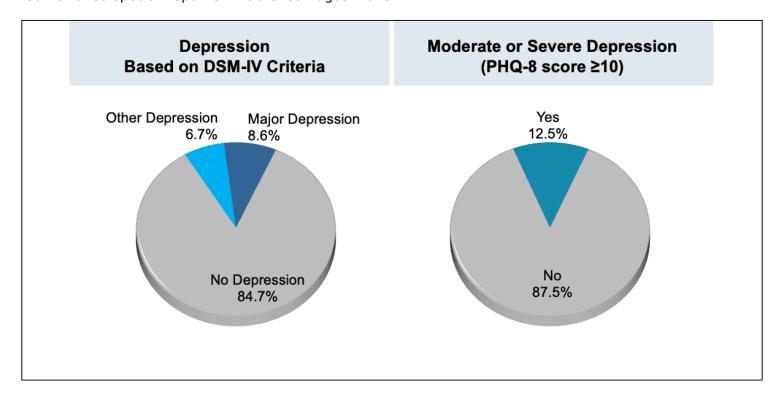


#### **Figures**

# Figure 1 Depression in Persons with HIV During the 2 Weeks Before Interview—Medical Monitoring Project, United States, 2020 Cycle

Using the DSM-IV criteria, major depression was defined as having at least 5 symptoms of depression and other depression defined as having 2–4 symptoms of depression.

Source: Centers for Disease Control and Prevention. Behavioral and Clinical Characteristics of Persons with Diagnosed HIV Infection—Medical Monitoring Project, United States, 2021 Cycle (June 2021-May 2022). HIV Surveillance Special Report 32. Published August 2023.

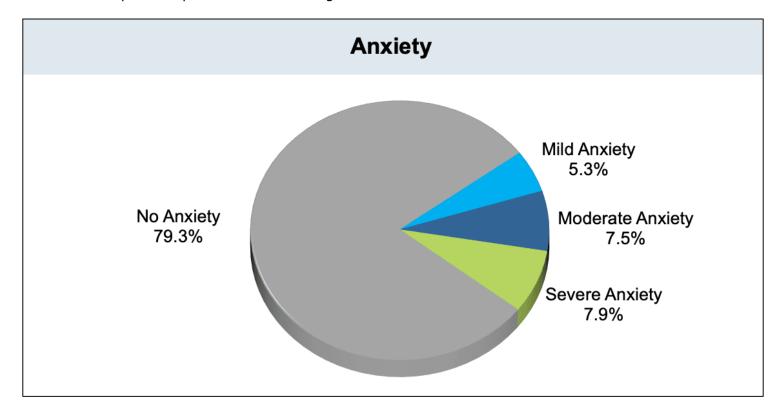




# Figure 2 Anxiety in Persons with HIV During the 2 Weeks Before Interview—Medical Monitoring Project, United States, 2020 Cycle

Anxiety definitions were according to criteria from the DSM-IV and based on GAD-7 scores. Severe anxiety was defined as having a score of  $\geq 15$ , moderate anxiety as having a score of 10-14, and mild anxiety as having a score of 5-9.

Source: Centers for Disease Control and Prevention. Behavioral and Clinical Characteristics of Persons with Diagnosed HIV Infection—Medical Monitoring Project, United States, 2021 Cycle (June 2021-May 2022). HIV Surveillance Special Report 32. Published August 2023.

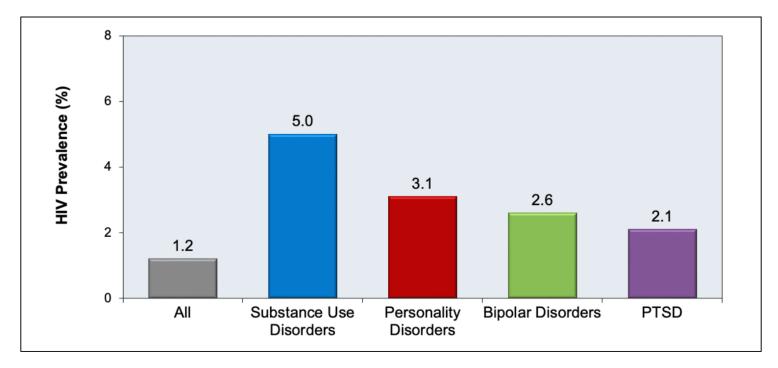




#### Figure 3 HIV Prevalence in General Outpatient Psychiatric Population

These data were obtained through general outpatient psychiatric clinics at Duke University Medical Center during 2001-2004.

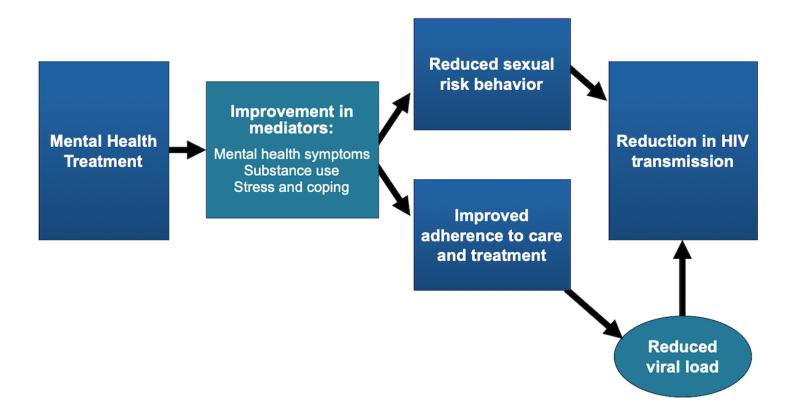
Source: Beyer JL, Taylor L, Gersing KR, Krishnan KR. Prevalence of HIV infection in a general psychiatric outpatient population. Psychosomatics. 2007;48:31-7.





## Figure 4 Positive Prevention Model Showing Hypothesized Effects of Mental Health Treatment on HIV Transmission Risk Behavior

Source: Sikkema KJ, Watt MH, Drabkin AS, Meade CS, Hansen NB, Pence BW. Mental health treatment to reduce HIV transmission risk behavior: a positive prevention model. AIDS Behav. 2010;14:252-62.

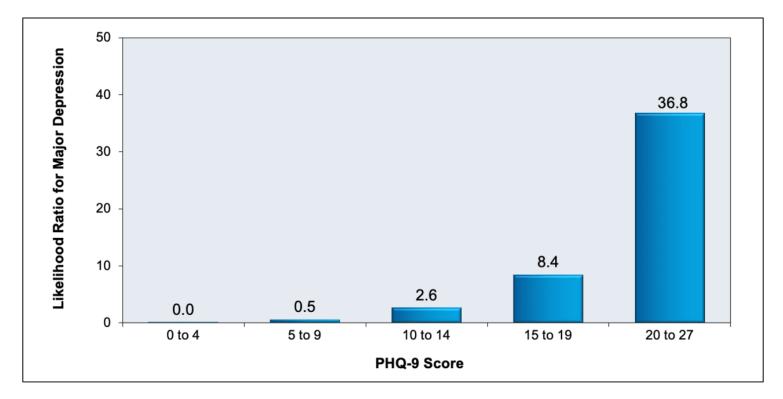




#### Figure 5 PHQ-9 Scores and Likelihood Ratio for Major Depression

These data are based on surveys from 580 patients who completed the PHQ-9 and had a structured interview by a mental health professional to determine the presence or absence of major depression.

Source: Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16:606-13.



#### Figure 6 Operating Characteristics of PHQ-2 for Major Depression

This table shows the sensitivity, specificity, positive predictive value, and likelihood ratios for the range of PHQ-2 scores in diagnosing major depressive disorder. These data are based on surveys from 580 patients who completed the PHQ-2 and had an independent mental health professional interview.

Source: Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: Validity of a Two-Item Depression Screener. Medical Care. 2003;41:1284-92.

# Operating Characteristics of PHQ-2 Screen for Major Depression PHQ-2 Score Sensitivity Specificity Positive Predictive Value Likelihood Ratio 1 97.6 59.2 15.4 0.3

#### Figure 7 Operating Characteristics of GAD-7 for Generalized Anxiety Disorder

This table shows the sensitivity, specificity, and likelihood ratios for the GAD-7 scores in the range of 8 to 15 as a diagnosis for generalized anxiety disorder. These data are based on 995 patients who completed the GAD-7 and underwent structured psychiatric interviews by a mental health professional as an evaluation for generalized anxiety disorder.

Source: Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006;166:1092-7.

Operating Characteristics of GAD-7 Screen for Generalized Anxiety Disorder				
GAD-7 Score	Sensitivity	Specificity	Likelihood Ratio	
8	92	76	3.8	
9	90	79	4.3	
10	89	82	5.1	
11	82	85	5.5	
12	73	89	6.5	
13	66	91	7.7	
14	56	92	7.2	
15	48	95	8.7	

#### Figure 8 Diagnostic Characteristics for the Primary Care PTSD Screen for DSM-5 (PC-PTSD-5)

These data are based on surveys from 399 adult Veterans seen at a primary clinic. The Primary Care PTSD Screen for DSM-5 (PC-PTSD-5) screening tool was used.

Source: Prins A, Bovin MJ, Smolenski DJ, et al. The Primary Care PTSD Screen for DSM-5 (PC-PTSD-5): Development and Evaluation Within a Veteran Primary Care Sample. J Gen Intern Med. 2016;31:1206-11.

### Diagnostic Characteristics of the PC-PTSD-5 Screen by Cut-Off Score

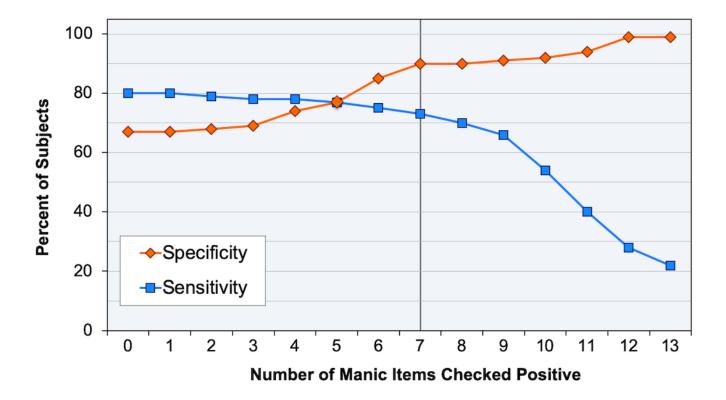
Cut-off Score	Sensitivity	Specificity	Likelihood Ratio
0	-	-	-
1	99	67	2.99
2	98	78	4.41
3	95	85	6.33
4	83	91	8.79
5	56	97	17.40



#### Figure 9 Operating Characteristics of the Mood Disorder Questionnaire

This graphic is based on data from 198 individuals seen at five outpatient clinics. A score of 7 or higher (gray vertical line) was chosen as the optimal cutoff.

Source: Hirschfeld RM, Williams JB, Spitzer RL, et al. Development and validation of a screening instrument for bipolar spectrum disorder: the Mood Disorder Questionnaire. Am J Psychiatry. 2000;157:1873-5. Reprinted with permission from the American Journal of Psychiatry, (Copyright ©2000). American Psychiatric Association. All Rights Reserved.

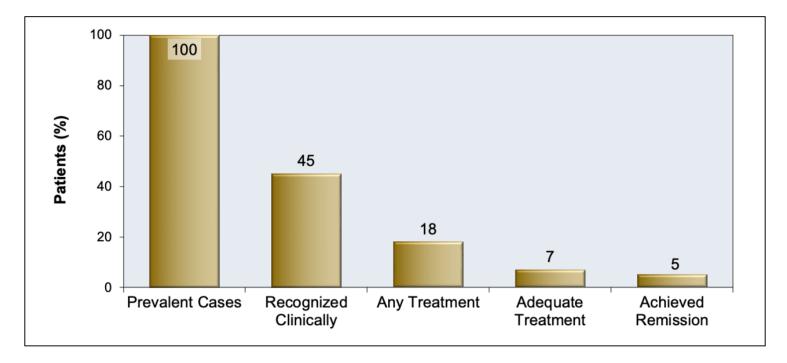




#### Figure 10 Depression Treatment Cascade for Patients with HIV

This graphic shows the estimated proportion of all HIV patients with a major depressive episode in the past year who had depression recognized clinically, received any treatment, received adequate treatment, and achieved remission.

Source: Pence BW, O'Donnell JK, Gaynes BN. Falling through the cracks: the gaps between depression prevalence, diagnosis, treatment, and response in HIV care. AIDS. 2012;26:656-8.





#### Table 1.

#### Summary of Recommendations from the International HIV-Cognition Working Group

**Recommendation 1:** HIV-associated brain injury (HABI) should be considered as one cause of cognitive impairment alongside other potential causes of brain injury occurring in people living with HIV.

**Recommendation 2:** HABI should be differentiated on the basis of HIV RNA suppression and the activity of pathology.

**Recommendation 3:** Low performance on cognitive tests should not be labelled as cognitive impairment without clinical context.

**Recommendation 4:** When interpreting cognitive data, the false-classification rate should be considered.

**Recommendation 5:** A research classification of cognitive impairment in people living with HIV should consider a combination of cognitive symptoms, low performance on cognitive testing, and abnormality on neurological investigations.

**Recommendation 6:** Cognitive symptoms should refer to any change in cognition that has been noticed by the individual or an observer, whether or not this change has an impact on daily functioning.

#### Source:

 Nightingale S, Ances B, Cinque P, et al. Cognitive impairment in people living with HIV: consensus recommendations for a new approach. Nat Rev Neurol. 2023 Jun 13. [online ahead of print] [<u>PubMed Abstract</u>]

