Published in final edited form as:

AIDS Behav. 2011 February ; 15(2): 376–388. doi:10.1007/s10461-010-9836-3.

Challenges in Addressing Depression in HIV Research: Assessment, Cultural Context, and Methods

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Abstract

Depression is one of the most common co-morbidities of HIV infection. It negatively impacts self-care, quality of life, and biomedical outcomes among people living with HIV (PLWH) and may interfere with their ability to benefit from health promotion interventions. State-of-the-science research among PLWH, therefore, must address depression. To guide researchers, we describe the main diagnostic, screening, and symptom-rating measures of depression, offering suggestions for selecting the most appropriate instrument. We also address cultural considerations in the assessment of depression among PLWH, emphasizing the need to consider measurement equivalence and offering strategies for developing measures that are valid cross-culturally. Finally, acknowledging the high prevalence of depression among PLWH, we provide guidance to researchers on incorporating depression into the theoretical framework of their studies and employing procedures that account for participants with depression.

Keywords

HIV/AIDS; Depression; Research Methods; Measurement

Depression is one of the most common co-morbidities of HIV infection, with prevalence estimates of major depressive disorder among persons living with HIV (PLWH) ranging from 20% to as high as 37%.^(1, 2) This is a three-fold greater prevalence of major depression in the general population.⁽³⁾

Why is depression so prevalent among PLWH? HIV is a chronic and life-threatening illness and, like other such illnesses, can be stressful to manage. Its life-threatening nature may instigate fears of impending mortality. Moreover, the medical sequelae of HIV infection, its associated opportunistic infections, and side effects of antiretroviral treatment can mimic symptoms of depression (i.e., fatigue, concentration problems, somatic symptoms, decreased appetite/weight loss). From a cognitive-behavioral perspective,⁽⁴⁾ these physical symptoms can be part of a cycle of continued depression. Specifically, individuals can develop negative cognitions about side effects (e.g., “They remind me of my illness”) that maintain depression, potentially increasing the likelihood of behavioral symptoms of depression such as avoidance or reduced engagement in other activities.

Furthermore, the underlying biological process of HIV may contribute to risk for depression and depressive symptomatology in several ways. Viral illnesses like HIV can cause cytokine-induced sickness behavior,⁽⁵⁾ which has a similar symptom pattern to depression (e.g., depressed mood, lethargy, social isolation, anorexia, altered sleep patterns, decreased “grooming”). Interleukin 1, which activates immune response, appears to have an important role in these physiological and behavioral sequelae associated with “sickness behavior”.^(5, 6) Markers of immune activation such as elevated neopterin levels have been shown to predict depressive symptoms in HIV patients.⁽⁷⁾ Moreover, depressed HIV patients show higher rates of tryptophan degradation.⁽⁷⁾ As tryptophan is a precursor to serotonin, its depletion by an activated immune system impacts the synthesis of serotonin (a key neurotransmitter implicated in depression).

Other factors that might account for the high level of depression among PLWH are related to risk factors for HIV. Specifically, PLWH disproportionately come from marginalized groups in the U.S., including the economically disadvantaged, ethnic and sexual minorities, and those with a history of substance use, sex work, and trauma.⁽⁸⁾ Individuals in these at-risk groups are often subject to discrimination and stressors that can contribute to poor mental health outcomes, even before acquiring an HIV diagnosis.⁽⁹⁾ Because HIV is associated with these marginalized statuses, the disease itself has become highly stigmatized – leading to problems such as nondisclosure of one’s HIV status⁽¹⁰⁾ and social isolation –further increasing the risk of depression.⁽¹¹⁾

Depression rates do not appear to decline with age in HIV populations as they do in the general population.⁽¹²⁾ This is important because as many as one quarter of all U.S. HIV-positive adults are now 50 years or older.⁽¹³⁾ As people live longer due to medical advances, depression in a gradually aging HIV cohort will remain an issue that needs to be addressed clinically and accounted for in HIV research.

Not only is depression a distressing and impairing condition, but it also negatively affects a variety of self-care behaviors needed for optimal management of HIV disease.⁽¹⁴⁾ For example, patients with depression have been found to initiate ART at lower CD4+ cell counts and higher HIV-1 RNA levels compared to patients without depressive disorders,⁽¹⁵⁾ and depressive symptoms have been related to poor adherence to ART once initiated.⁽¹⁶⁾

Individuals with depressive symptoms and non-adherence according to pharmacy refills were at almost a 6-fold greater risk for mortality.(17) Additionally, depression and substance abuse are co-morbid,(18, 19) with as many as one-third of depressed patients having co-occurring substance use disorders.(20) Among PLWH in particular, depression has been associated with substance use,(21, 22) leading to poorer health-related quality of life and antiretroviral non-adherence.(23) Finally, suicidality is an important symptom of depression that must be routinely assessed. Although suicide rates have decreased among PLWH with the introduction of ART, they remain higher than in the general population and are associated with older age, male gender, injection drug use, and advanced clinical stage.(24, 25)

Evidence from a number of treatment trials suggests that depression in patients with HIV can be effectively treated.(26, 27) Although psychopharmacologic treatment can be complicated by side effects and drug interactions, trials clearly show that serotonin reuptake inhibitors, newer agents such as nefazadone and venlafaxine, and older agents such as tricyclics are all useful for the treatment of depression in persons with HIV.(28) Additionally, psychotherapeutic treatments of depression, particularly cognitive-behavioral approaches, appear to be effective for individuals with HIV. (29–32)

More work is necessary in order to get timely and appropriate treatment to those in need and to understand the impact of depression among those affected by HIV. However, a number of methodological issues have slowed research in this area, including the multiplicity of instruments, the challenges of cultural context, and the impact of co-morbid depression on clinical trials for individuals living with or at risk for HIV.

In the current paper, we aim to stimulate further research on depression and HIV by (1) describing the main assessment measures of depression and offering suggestions for selecting the most appropriate; (2) considering how cultural issues can impact the assessment of depression and the optimal choice of an instrument; and (3) highlighting methodological challenges that arise in HIV research because of the involvement of individuals living with and at risk for depression.

Diagnostic, Screening, and Symptom-Rating Measures of Depression

Depression as a clinical and categorical diagnosis requires specific criteria: persistent depressed mood or anhedonia (i.e., loss of interest or pleasure), along with at least four additional symptoms including sleep problems, excessive feelings of guilt or worthlessness, loss of energy, concentration problems, appetite or weight changes, psychomotor retardation or agitation, and suicidality.(33) The diagnosis of depression is generally (and optimally) made after a face-to-face clinical interview by a trained mental health professional based on either ICD or DSM criteria. In the field, detection and diagnosis of depression often comprises two stages: screening and then referral for diagnosis by clinical assessment. Note, however, that symptoms of depression that do not meet diagnostic criteria also can be distressing and can affect health behaviors. Accordingly, depression can be examined continuously (i.e., in terms of symptom severity) as well as categorically (i.e., in terms of the presence or absence of a clinically significant diagnosis). Researchers should keep in mind that screening, diagnosing, and quantifying the symptoms of depression are somewhat different tasks, and that instrument choice should be driven by several considerations, including the population of interest, study hypotheses, and comparisons that the investigators might want to draw with other studies and populations.

In research settings, *standardized diagnostic interviews* are commonly used as the “gold standard” to assess the categorical diagnosis of depression based on DSM or ICD criteria. However, they are lengthy and usually require a clinician or an interviewer with extensive

training to administer reliably. In international settings, the requirement of highly trained interviewers is particularly burdensome. Numerous depression *screening instruments* have been developed that do not require much time or a clinician to administer. They provide empirically based cut-offs useful as the basis for referrals to more comprehensive evaluations or to estimate the prevalence of possible depression. *Symptom-rating scales* offer a continuous measure of the extent of depressive severity. They usually do not require a clinician to administer; in fact, they are typically brief and easy to self-administer. They may or may not include a recommended cutoff for screening purposes. Symptom rating scales can be useful for monitoring change in depression symptoms over time.

In Table 1, we provide information on 23 instruments assessing depression, a sampling of the most commonly used and the potentially most useful. For each, we indicate whether they can be used for diagnostic, screening, or symptom rating purposes; who can administer them; whether they have a specific cut-off for screening; whether they directly assess suicidality; and examples of studies among HIV-positive populations in which they have been used.

There are a variety of instruments that have been shown to be valid in primary care settings, although relatively few of these instruments have been evaluated specifically in PLWH. Williams and colleagues (2002) reviewed the literature from 1970 to 2000 seeking instruments tested in general primary care settings against a standard interview such as the Structured Clinical Interview (SCID) to make a criterion-based diagnosis of depression.(34) They found 28 studies using 11 different instruments, all of which performed acceptably. Of the measures, the BDI and the CES-D have perhaps the longest history of use in behavioral studies of HIV.(8) The BDI and PHQ are considered sensitive to clinically relevant change and are often used to measure outcomes in depression intervention research. Note there are several versions of the BDI. The original version was published in 1961 and revised in 1978 (BDI-1A). The current version, the BDI-II, was published in 1996 in response to the publication of the DSM-IV, which changed the criteria for the diagnosis of depression. The BDI-II can be separated into 2 subscales, an affective component and a somatic component. The BDI was developed to assess depression severity, not as a diagnostic instrument, but a 7-item version called the BDI-PC (PC for Primary Care) was introduced in 1997 that was intended for use in screening.

A number of studies have examined the diagnostic performance of depression screening instruments in PLWH,(35–40) four of which used diagnostic interviews as the basis for making a criterion diagnosis.(35–37, 39) One reason to specifically examine the diagnostic performance of a diagnostic instrument in an HIV-specific group is that the somatic symptoms of depression can be difficult to disentangle from the disease-associated symptoms of HIV (e.g., fatigue, weight loss, poor concentration). For example, Voss and colleagues studied the relation between symptoms of depression and of fatigue in PLWH and found correlations of >0.60 .(41) Kalichman et al. tried to separate somatic symptoms of HIV from depression symptoms using both the BDI and the CES-D, concluding that the clinical utility of both instruments was improved when these HIV-related somatic symptoms were removed.(40) Cockram and colleagues conducted a small pilot study among hospitalized HIV patients referred for depression ($N = 34$), comparing two self-administered symptom rating scales (BDI and CES-D) and two clinician-administered scales (HAMD and MADRS); they used a standard clinical interview to diagnose major depression by DSM-III-R criteria. In contrast to earlier reports in non-HIV populations,(42) investigators found all four scales performed equally well, despite the inclusion of somatic/vegetative symptoms in two of the scales.(39) This problem is in no way unique to HIV. Others have used a variety of methods to distinguish disease-related and depression-related somatic symptoms in the

elderly and in cancer patients and have concluded that there is little advantage to attempting to do so.(43–46)

We would encourage investigators to continue to examine this question in their studies of PLWH. The size of this potential effect will likely be related to HIV stage and the presence of co-morbid conditions such as hepatitis C and complications of HIV disease such as opportunistic infections. Note the impact of somatic symptoms may differ depending on whether one is assessing overall levels of depression versus examining whether the symptom level of depression is associated with health behaviors or health outcomes. In testing a depression treatment, for example, one may not expect to see changes in the somatic items if they are related directly to HIV disease. However, if the depression treatment affects the cognitive/affective items on a scale, this would still be apparent in an overall change score. When the research focuses on the association between depression and other health behaviors or outcomes, it may be more important to isolate the cognitive/affective items, which may be uniquely related to the health outcomes of interest.

Researchers should remember that the screening and symptom-rating instruments that we note here (and that are described in more detail in the reviews cited(34, 47)) are not themselves diagnostic instruments. If the goal of the research study is to identify individuals with a clinical diagnosis of major depressive disorder, investigators should consider following up individuals who screen positive with a full diagnostic interview such as the SCID or Composite International Diagnostic Interview (CIDI), which has been validated with PLWH in both developed and developing countries.(48)

Given that the diagnostic performance of commonly used instruments is similar, more practical considerations should guide decisions of which instrument to use. These include the length of the instrument; whether it measures only depression or other mental health concepts (e.g., anxiety, substance use) that might be relevant to a particular study; if it assesses specific aspects of depression, such as suicidality or somatic symptoms separately; how user friendly the instrument is in terms of reading level, response formats, need for training to administer; and whether it can be used to assess depression severity and treatment response in addition to providing a diagnosis of depression. For example, the HAM-D and the BDI both emphasize somatic symptoms of depression (e.g., fatigue) more than some other instruments. Depending on the clinical population, the outcomes of interest, and the comparisons of interest, such a somatic emphasis could be either a positive or a negative factor in an investigator's instrument choice. Researchers also might want to consider how often the instrument has been used in the area of HIV, which could bolster the acceptability of the approach and facilitate comparison of results.

Several other practical and conceptual factors may influence instrument selection. For example, the BDI uses different response options for each item, which increases the time of administration, makes it difficult for individuals with impaired cognitive or attentional abilities, and complicates telephone administration. The CES-D, which was designed for telephone administration, has 20 items with the same response format, but not all versions are DSM-IV compatible (i.e., early versions do not include items that map directly onto DSM symptoms). In contrast, the depression scale of the PRIME-MD PHQ (i.e., PHQ-9) has only 9 items (one for each of the nine DSM-IV depression symptoms) and is therefore relatively simple to administer. It also has undergone preliminary performance testing in PLWH (38, 49) and its psychometric properties among HIV-infected persons have recently been assessed.(50) While the PHQ-9 had high reliability and validity, suggesting it is appropriate for use with individual HIV-positive patients, differences in the interpretation of questions across subgroups of the population (e.g., differing by race, gender, age), indicate it may not be ideal for longitudinal studies across group.(50)

One consideration worthy of mention with respect to depression assessment and its relation to health behaviors has to do with a potential for a curvilinear association. For example, some health behaviors such as adherence likely have a linear relation with depression: the more severe the depression, the greater the impact on the behavior. With other behaviors, such as sexual risk-taking, the relation with depression may be curvilinear.(51) In this respect, individuals with increasing depression may be proportionately more risky, except during severe depression, during which individuals may experience a loss of interest in sex and, hence, be essentially abstinent. In selecting the most appropriate depression instrument, researchers should, therefore, consider the potential pattern of association between depression and the health behavior of interest. If a curvilinear relation is possible, a continuous measure of depression is required.

Cultural Context in the Assessment of Depression

HIV has impacted a vastly diverse population of individuals across the globe, and assessing depression among them must take into account their important cultural differences. Unfortunately, researchers from developed countries have largely operated from a universalist or “etic” assumption that individuals are very similar and cultural differences are minimal; this Eurocentrist approach assumes psychological disorders, symptomatology, and measures apply cross-culturally.(52)

Significant disagreement stems from the “emic” perspective that sound research must attend to cultural differences. According to the emic view, which we support, culture plays a central role in shaping emotional experience and provides the language people use to describe their experience.(53) Consequently, terms for emotional states often do not match precisely across languages or cultures; indeed, English language words such as “depression” and “anxiety” are difficult to translate into non-Western languages.(54) Furthermore, terms for depressive symptoms and questionnaire items often lack cultural equivalence (e.g., “I feel downhearted and blue”(55)). Many instruments developed to assess depression in people from Western countries emphasize cognitive and affective symptoms of depression over somatic aspects of depression.(56) These can be problematic because World Health Organization (WHO) studies have shown that patients from non-Western countries tend to report more somatic than psychological symptoms of depression.(57, 58)

As well as attending to linguistic and cultural (or content) equivalence, researchers who use measures cross-culturally must pay special attention to construct equivalence (e.g., Does the construct of “depression” exist and is it operationalized similarly in both contexts?); normative equivalence (Are appropriate norms and cut-offs available?); technical equivalence (Does the method of assessment, such as pencil-and-paper or computer-assisted self-interviewing, yield comparable data?); and scale equivalence (e.g., Does differential familiarity with multiple-choice and true-false formats lead to invalidity).(52) Studies of depression and somatization in non-Western countries often have used interview styles of questioning as opposed to self-report measures, particularly in countries where literacy rates are low. In the WHO studies mentioned earlier, the researchers examined those patients who met criteria for major depression using symptom-directed interview questions, which typically inquire about specific symptoms in a closed-ended yes/no manner (e.g., “Have you been depressed or down in the past month?”). This type of questioning reflects what Kleinman termed a category fallacy, a situation that imposes Western constructs onto non-Western cultures.(59) However, Simon and colleagues found that patients tended not to present psychological symptoms unless specifically asked, and thus argue that without symptom-directed questioning, psychological symptoms are apt to go unrecognized.(58)

Despite the limitations of using Western-based instruments, many studies of depression among people with HIV conducted in non-Western countries have used instruments developed in the West and pointed to noteworthy findings about the existence of depression among PLWH. For example, Jin et al., using the Chinese CIDI and the BDI, found high rates of major depression and suicidal thoughts among people with HIV in Beijing and Anhui province in China.(60)

Before using Western instruments and diagnostic categories, researchers would benefit from conducting prior investigation into the applicability of these instruments and categories across cultures. This type of prior investigation will help to identify instruments used within the country of interest as well as identify local norms and values around the stigma and non-disclosure of depression. For example, stigma around depression within specific cultural contexts may make it difficult for participants who already face the stigma of HIV to disclose their depressive symptoms to researchers. Prior investigation into communication patterns within the culture may help a researcher find guidelines, or ways of inquiring about depression, that are sensitive and appropriate. One approach is to couple a Western-based instrument with an instrument that was validated in a non-Western country. For example, a researcher might wish to use the BDI(61) for a study of depression among PLWH in India and couple it with the Explanatory Model Interview Catalogue (EMIC), an instrument that was developed and has been used extensively in India.(62) The EMIC uses open-ended questions to capture culturally specific as well as universal symptoms of depression from participant report. Several studies have used the Kannada language version of the EMIC, coupled with the HAM-D, to assess depressive symptoms with people in Bangalore, South India.(63, 64) Similarly, many instruments, such as the CIDI,(57) have been used with success across cultures and thus may have cultural relevance in the countries where they have been used. Information on the psychometric properties of depression measures as used across cultures is limited, but Table 1 notes several international studies on HIV that used the specific depression measures described, which can provide some information on the measures' psychometric properties in different countries.

In those instances when depression measures have not yet been used in a particular cultural context, a researcher may wish to adapt an existing measure or build a more culturally relevant one. In adapting a questionnaire, researchers should know their profession's standards for adapting instruments cross-culturally, paying particular attention to issues around translation and the multiple types of equivalence. Adapting a questionnaire to a particular culture will require more effort than simply translating the wording of the questionnaire. A researcher can better achieve semantic equivalence and ensure that the wording of questions conveys the original meaning through a process of forward translation, expert panel review, back translation, and discrepancy resolution.(65) In addition, a researcher can conduct cognitive interviews with a small sample of participants in the target group, asking them specifically about the meaning of each item after translation.(66)

In the development of a new measure to assess depression in PLWH from a particular culture, a best practice approach would be ethnographically informed and involve qualitative inquiry (e.g., interviews in the participants' own language) aimed at understanding depression within the local context. From this work, the researcher can identify prominent themes and develop a conceptual model of depression among PLWH. Survey items can be created based on the themes from this qualitative work and items from existing measures of depression, thereby incorporating culturally specific issues into the resulting questionnaire. (67) Once the items are developed and used within the population of interest, gathering information on the psychometric properties of the instrument will yield helpful information on the instruments' reliability and validity as used within this context. Finally, if a researcher wishes to use an instrument in two distinct cultures, in order to ensure item

equivalence for cross-cultural comparability of the survey, a best practice approach would be to use item-response theory techniques to investigate differential item functioning across responses of the two groups.(68) Generally, these methods require that the researcher make use of both qualitative and quantitative methodological approaches.

Methodological Challenges of Depression in Research on HIV

Given the high prevalence of depression among individuals living with or at high risk of HIV, it is likely that substantial numbers of depressed individuals participate in trials of health promotion and prevention interventions for HIV. This raises several challenges with respect to theory and methodology. To optimize both efficacy and potential effectiveness (i.e., generalizability of interventions to PLWH post-trial), researchers developing and testing interventions should make informed decisions about how to incorporate depression into their theoretical conceptualization and to assess and address depression in these studies, both in the recruitment and the intervention phases.

Most health-promotion interventions in the field of HIV are based on conceptual models of health behavior change rooted in social-cognitive theory. Generally, these health psychology models, along with their corresponding intervention strategies, do not account for the impact of clinical depression on the predictors of health behavior change. However, symptoms of clinical depression such as persistent sadness, impaired concentration, hopelessness, and suicidality may theoretically affect motivations, perceived self-efficacy, and the intentions to engage in health-promoting behaviors such as safer sexual practices and adherence. Failing to account for these mental health factors—both in the theoretical foundation of the intervention trial as well in trial procedures—may limit the impact of an intervention.(69) Addressing depression in the intervention itself, either directly or through assessment and triage for treatment, may allow for a more potent intervention, potentially reaching those in the greatest need for help. For example, one adherence intervention trial integrated cognitive behavioral therapy for adherence with cognitive behavioral therapy for depression to help PLWH with co-morbid depression.(70) Theories that incorporate depression may be better able to account for the variance in key outcomes, such as one cognitive–affective model of medication adherence that incorporated the indirect effects of negative affect.(71)

Researchers conducting HIV-related trials need to decide as well whether to screen for depression when recruiting participants and, then, whether to include those exceeding clinical cut-offs. There are advantages and disadvantages to each approach with respect to internal and external validity. Screening out potential participants with depression may increase the internal validity of a trial and may raise the likelihood of finding an effect because it produces a more homogeneous sample, and a sample unimpaired by depression may be more likely to adhere to the intervention protocol and less likely to attrite. On the other hand, including those with depression in a behavioral intervention trial allows for a test of the mediating and moderating role of depression. Additionally, such a sample will make the study's findings more generalizable to the population of PLWH, although substantial outreach and recruitment efforts may be needed because those with clinical depression may lack the initiative to join a clinical trial. Perhaps most importantly, if the prevalence of depression is as high as published estimates suggest, and depression is associated with worse health outcomes such as nonadherence and increased HIV transmission risk behavior, including those with depressive symptoms will ensure inclusion of those most in need of the intervention and those most likely to receive the intervention once it is disseminated more widely. Of course, including depressed individuals in a trial raises the ethical issue of how to refer for or treat the depression once it is discovered. Ideally, a trial should include protocols for ongoing monitoring of depression, making effective referrals, or offering treatment – either as part of the actual intervention or not.

Another area of HIV research includes trials evaluating psychopharmacological and psychotherapeutic treatments for depression among PLWH, which are often complicated by disease-specific factors as well as HIV stigma, the co-morbid conditions of substance abuse and mental illness, and complex HIV treatment regimens. These may pose unique challenges specifically to recruitment and retention in trials as well as to the generalizability of findings resulting from efficacy trials.

Determining an appropriate control group in treatment trials is increasingly challenging, as there is a growing array of effective depression treatment interventions available and it is thus difficult for researchers to argue for a control group that does not include an active state-of-the-science intervention. In some cases, there may be enough evidence to warrant a shift away from asking whether an intervention works to asking how the intervention works, under what conditions, and for whom. In addition, comparative effectiveness studies will be important in determining the relative effects of various interventions for both depression and HIV-related outcomes.

Research to improve PLWH outcomes, including depression, that is conducted at the individual-level within HIV clinics does not account for the wide variability of resources and level of provider training with regard to mental health issues across clinics. Randomization at the clinic level is one methodological approach that could be considered in this case; however, clinic-level randomized studies can be large and costly. In clinic-randomized studies, meaningful outcomes may not be conceptualized as individual-level change but, rather, could include structural changes at the clinic-level, including provider behavior, clinic policy, or practice guidelines.

Alternatively, research that does not rely on the standard randomized controlled trial (RCT) may be necessary to answer questions about the effectiveness of depression treatment among PLWH. Several alternative designs are available and some have been tested in clinical trials of depression treatment, including equipoise-stratified randomization and random encouragement designs.^(72–74) Alternative designs can include adjustments to randomization or use of observational data that allows for some degree of confidence in a signal of causal inference.⁽⁷⁵⁾ Quantitative assessment designs, for example, may be useful when treatment assignment must be determined by differential participant need, merit or risk. In the case of PLWH, the high prevalence of depression suggests the need to characterize the factors associated with HIV and depression risk which, in turn, could serve as the basis for treatment assignment. Propensity scores can be useful in the context of observational studies when preexisting or constructed groups exist and will receive different treatment conditions. This type of design would allow for understanding of the effectiveness of depression treatment for PLWH across diverse settings in which PLWH are already receiving depression treatment (e.g., primary care, HIV care, community mental health treatment). Thus, determining the most appropriate research design should begin with the research question, acknowledge treatment and contextual constraints, and take into account basic ethical principles to provide human subjects protection.

Conclusion

The prevalence of depressive symptoms among PLWH is alarming, underscoring the need for increased attention to the psychological well-being of this group to alleviate their suffering as well as to minimize the impact of depression on aspects of self-care and associated risk behaviors. Unfortunately, there is no “gold standard” for assessment of depression among PLWH. Based on the available evidence, we offer instead suggestions for best practices to researchers working in the area. The most appropriate strategy in HIV research—whether for assessing depression or designing a study—involves making an

informed choice based on the characteristics of the study population, including cultural considerations; the purpose of the research; and any restrictions based on the limitations of study, personnel, or site resources. Additional research is warranted to systematically evaluate different measures of depression among persons living with HIV, especially in international contexts. Furthermore, more research on the unique and complex interface of depression and HIV infection is needed to inform clinical interventions that may reduce risk behaviors and promote self-care, thereby improving the quality of life for PLWH as well as fostering the public's health.

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Table 1

Brief Description of Diagnostic, Screening, and Symptom-Rating Measures of Depression

Measure	Measure Type	Admin. Type	Clinical Cut-offs	Suicidality Assessed	Use in HIV research [*]	Notes
CIDI (76)	Diagnostic	Clinician	No	Yes	HIC (35, 77) LMIC-none	Designed for cross-cultural epidemiologic studies; measures both DSM-IV and ICD-10 criteria
MINI (78)	Diagnostic	Clinician Self	No	Yes	HIC -none LMIC(36, 79, 80)	Assesses 19 disorders (MINI-Plus includes 23); designed for primary care.
SCID (81)	Diagnostic	Clinician	No	Yes	HIC (70, 82) LMIC (83, 84)	6 modules for 14 DSM-IV disorders, including major depressive, dysthymic, and bipolar
CIS-R (85)	Diagnostic	Interviewer	Yes	No	HIC-none LMIC (86)	Common in health care and epidemiologic research
PRIME-MD (87)	Diagnostic	Clinician	Yes	Yes	HIC (88) LMIC-none	Often adapted; superseded by PHQ-9
PHQ-9 (89)	Diagnostic	Self	Yes	Yes	HIC (90-92) LMIC (38)	Also measures depression severity
PHQ-2 (93)	Screening	Self	Yes	No	HIC-none LMIC (38)	Primarily used as an initial screening test
SDDS-PC (94)	Diagnostic Screening	Self Clinician	No	Yes	HIC-none LMIC-none	Developed for use in primary care settings
HADS (95)	Diagnostic	Self	Yes	No	HIC-none LMIC (96-99)	Emphasizes anhedonic symptoms
BDI (61, 100)	Diagnostic Symptom rating	Self	Yes	Yes	HIC (82, 101, 102) LMIC (103-107)	BDI-II extends timeframe for assessment to past 2-weeks from past 7 days in BDI-I
IDS (108)	Diagnostic Symptom rating	Clinician Self	No	Yes	HIC-none LMIC-none	Precursor to QIDS
QIDS (109)	Diagnostic Symptom rating	Clinician Self	No	Yes	HIC-none LMIC-none	Adapted to Interactive Voice Response system for data collection; translated into multiple languages
IDD (110)	Diagnostic Symptom rating	Self	No	Yes	HIC (111) LMIC-none	Infrequently used
MDI (112)	Diagnostic Symptom rating	Self	Yes	No	HIC-none LMIC-none	Classification of depression can vary depending on choice of scoring criteria(DSM-IV vs, ICD-9/10)
CES-D (113)	Screening Symptom rating	Self	Yes	No	HIC (114) LMIC(79, 115-123)	Numerous revisions, including 10-item (124), 9-item (125) and 8-item (126) versions, version type rarely specified
HSCL (127)	Screening Symptom rating	Self	Yes	No	HIC (128) LMIC (103, 129, 130)	Subscale for assessing anxiety
SCL-90 (131); SCL-90-R (132)	Symptom rating	Self	No	No	HIC (133) LMIC(107, 123, 134)	Evolved from Hopkins Symptom Checklist

Measure	Measure Type	Admin. Type	Clinical Cut-offs	Suicidality Assessed	Use in HIV research*	Notes
ZSDS (135)	Screening Symptom rating	Self	Yes	Yes	HIC (136) LMIC-none	Developed to measure severity among those already diagnosed
GHQ-12 (137)	Symptom rating	Self	No	No	HIC-none LMIC (138)	Composite scoring for psychiatric distress rather than a specific indication of depression
HAM-D / HDRS (139)	Symptom rating	Clinician	No	Yes	HIC-none LMIC-none	Weighted toward somatic items
K10 (140)	Symptom rating	Self	Yes	No	HIC-none LMIC (141, 142)	Used in WHO World Mental Health Surveys
K6 (140)	Symptom rating	Self	Yes	No	HIC-none LMIC-none	Subset of K10
MADRS (143)	Symptom rating	Clinician	No	Yes	HIC (39) LMIC (144, 145)	Developed to assess symptom change in drug studies; scores compared at 2 time points

Abbreviations: CIDI=Composite International Diagnostic Interview; MINI=Mini-International Neuropsychiatric Interview; SCID=Structured Clinical Interview for DSM Disorders, research version; CIS-R=Revised Clinical Interview Schedule; PRIME-MD=Primary Care Evaluation of Mental Disorders; PHQ=Patient Health Questionnaire; SDDS-PC=Symptom-Driven Diagnostic System for Primary Care; HADS=Hospital Depression and Anxiety Scale; BDI=Beck Depression Inventory; IDS=Inventory of Depressive Symptoms; QIDS=Quick Inventory of Depressive Symptoms; IDD=Inventory to Diagnose Depression; MDI=Major Depression Inventory; CES-D=Centers for Epidemiologic Studies Depression Scale; HSCL=Hopkins Symptom Checklist; ZSDS=Zung Self-Rating Depression Scale; GHQ-12=General Health Questionnaire-12; HAM-D or HDRS=Hamilton Depression Rating Scale; K10=Kessler Psychological Distress Scale; K6= Kessler Psychological Distress Scale; MADRS=Montgomery-Asberg Depression Rating Scale; SCL-90-R=Symptom Check List Revised; GDS=Geriatric Depression Scale.

* HIC denotes use in High Income Countries; LMIC denotes use in Low Middle Income Countries. References indicate selected settings in which measures have been used.