Brian W. Pence, PhD
Pointers on depression care in people with HIV: an “opportunity for movement”

Articles by Mark Mascolini

High depression rates with HIV — and its scathing clinical impact

Depression risk factors with HIV — plus screening and diagnosis keys

When and how to treat depression — and how to make it easier
Research Initiative / Treatment Action!

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Abstract: Prevalence of major depressive disorder runs 2 to 3 times higher in people with HIV infection than in the general population. Yet depression often goes undiagnosed or untreated in HIV populations. One analysis calculated that fewer than half of depression cases get recognized clinically in people with HIV, only 18% get treated, only 7% get treated adequately, and only 5% achieve remission through treatment. Depressive symptoms may affect two thirds of people with newly diagnosed HIV infection. Research in US and Swiss cohorts links depression to greater HIV mortality and all-cause mortality. Diverse studies document the baneful impact of depression on antiretroviral adherence and, at least partly in consequence, on CD4-cell and virologic response to antiretroviral therapy. Treating depression with selective serotonin reuptake inhibitors (SSRIs) ameliorates the impact of depression on these outcomes.

More than 1 in 3 people infected with HIV in the United States has major depressive disorder, according to analysis of a national probability sample of people in care. But almost half of the 488 people with major depressive disorder determined by the Composite International Diagnostic Interview, 45%, did not have a depression diagnosis in their medical record. An 8-site US study of 803 HIV-positive people with mental health and substance abuse disorders found that only 59% received any mental health treatment in the past 3 months. And among 551 people diagnosed with mood disorders, only 40% took an antidepressant. In a Veterans Administration analysis of 434 HIV-positive and 298 HIV-negative veterans with test-determined depression, only 38% of the HIV group and 34% of the HIV-negative group took a selective serotonin reuptake inhibitor (SSRI). Fewer than half in each group got an SSRI or mental health counseling.

HIV depression experts at Duke University and other centers recently underlined three troubling facts about depression care in HIV populations:

- Although highly prevalent in people with HIV, depression remains widely unrecognized.
- When recognized clinically, depression often goes untreated.
- When treated, the therapeutic strategy typically does not follow best-practices guidelines.

Duke’s Brian Pence and depression collaborators collected and parsed data from the cited studies and others to describe a depression treatment cascade for people with HIV. The end of the cascade looks more like a trickle. They calculated that of all cases of major depressive disorder in 1 year, only 45% are recognized clinically, only 40% of those recognized get treated, only 40% of those treated are treated adequately, and 70% of those treated adequately achieve remission. To state these estimates another way, only 18% of HIV-positive people
with major depressive disorder get treated, only 7% receive adequate treatment, and only 5% emerge from their depression (Figure 1). That means 82% of HIV-positive people with depression receive no treatment, 93% do not get adequate treatment, and 95% do not attain remission.

How can healthcare professionals coax more flow through this ever-narrowing HIV depression care cascade? Pence and colleagues propose working collaboratively on multiple cascade steps, for example, “combining routine depression screening with collaborative care models that give HIV providers decision support in prescribing and adjusting antidepressants within the HIV 'medical home.’” (See page 34 for three models of such support.) This issue of RITA! aims to abet this process by helping clinicians understand (1) depression prevalence and clinical impact in people with HIV, (2) risk factors and keys to screening for and diagnosing depression, and (3) effective treatment.

**Figure 1.** According to a recent estimate of the major depressive disorder care cascade in people with HIV infection, fewer than half of cases get recognized clinically, only 18% get treated, only 7% get treated adequately, and only 5% achieve remission through treatment.4

**Depression rate 2 to 3 times higher with HIV**

Major depressive disorder affects 17% of US adults in their lifetime, according to the 2001-2003 National Comorbidity Survey of 9282 people.5 Depression prevalence in people with HIV may stand 2 or 3 times higher, depending on the population studied and how depression is determined.

A 2001 comparison of a nationally representative sample of 2864 HIV-positive US adults and 22,181 people in the National Household Survey on Drug Abuse charted nearly a 5 times higher prevalence of major depression in the HIV group (36.0% versus 7.6%).4 In other HIV populations, prevalence of major depressive disorder or moderate to major depression has ranged from 26% among 212 people in Denmark,7 to 28% among 4422 people in the Swiss HIV Cohort Study,4 to 38% among 210 people in California.8 Depressive symptoms affected 15.7% of 2863 HIV-positive people in Western Europe.
and Canada and 48.8% of 690 people in Italy. Among 180 people with newly diagnosed HIV infection in Houston, 67% had depressive symptoms.

Centers for Disease Control and Prevention (CDC) researchers used the simple 8-item Patient Health Questionnaire to identify current major depression in a nationally representative sample of 4168 people in care for HIV infection in 2009. They compared that prevalence with the rate in 267,584 people in the Behavioral Risk Factors Surveillance System. Current major depression affected 12% of adults with HIV, a prevalence 3.1-fold higher than current major depression in the general population. That prevalence ratio changed little in analyses controlled for age, race/ethnicity, or education. Controlling for both female gender and lower annual household income cut the prevalence ratio to 1.5 (95% confidence interval [CI] 1.4 to 1.7).

A 2001 meta-analysis of 10 studies comparing prevalence of major depressive disorder in 2596 HIV-positive or negative men who have sex with men (MSM) calculated an aggregated prevalence of 9.4% in men with HIV versus 5.2% in men without HIV. Those rates translated into a doubled chance of major depressive disorder in MSM with HIV (odds ratio [OR] 1.99, 95% CI 1.32 to 3.00). None of the individual studies—reported from 1988 through 1998 in the United States, Canada, Australia, and Japan—found higher odds of major depressive disorder in men with HIV, probably because none of the studies had enough participants to yield the needed statistical power to show a doubled chance of depression.
Fewer studies address depression incidence in people with HIV. Among 4422 people without a history of psychiatric disorders or depression in the Swiss HIV Cohort Study, depression developed at a rate of 3.9 cases per 100 person-years. 8 A comparison of 297 HIV-positive men and 90 HIV-negative men in the HIV Neurobehavioral Research Center at the University of California, San Diego focused on men who did not have major depression, anxiety, or substance dependence when starting 2 years of follow-up. 15 Men with symptomatic HIV disease proved significantly more likely to have a major depressive episode during those 2 years than asymptomatic HIV-positive men or HIV-negative men (about 40% versus 20%).

Research also shows that high proportions of people with HIV ponder suicide and sometimes attempt it. A review of studies published from 1995 through 2015 figured that 13.6% to 31% of HIV-positive people think about suicide and 3.9% to 32.7% try it. 16 Analysis of 1560 HIV-positive people in the US CHARTER cohort determined that 26% thought about suicide and 13% tried it. 17

Impact from quality of life to end of life

Depression wields a sledgehammer impact on the clinical course of people with HIV infection. Dozens of studies confirm links between depression and dangerous risk behavior, poor HIV control, comorbidities including cardiovascular disease, and—at the end of this train-wreck scenario—death. Glenn Treisman, a depression expert at Johns Hopkins University, lists 10 life-changing, or life-ending, consequences of depression in people with HIV. 18

- Impaired quality of life
- Decreased cognition
- Increased risk behaviors
- Unemployment
- More frequent medical visits
- Longer hospital stays
- Higher treatment costs
- Decreased antiretroviral adherence
- Suicidality
- Decreased survival

Five studies link depression to higher mortality in people with HIV. 8,19-22 Three of these five studies took place in the United States early in the combination antiretroviral era, 19-21 when regimens were less effective and many people shunned antiretroviral therapy (ART) at higher CD4 counts for fear of toxicity. And these older studies 19-21 had HIV-related death, not all-cause mortality, as an endpoint. But the most recent studies, in Switzerland 8 and the United States, 22 ran up to the most recent antiretroviral era (from 2004 to 2014) and focused on all-cause mortality.

Compared with HIV-positive women without depressive symptoms, those with chronic symptoms had a doubled risk of HIV-related death (adjusted relative risk [aRR] 2.0, 95% CI 1.0 to 3.8) in a US analysis controlled for clinical and other risk factors. 19 This analysis focused on 765 women seen from 1993 through 2000 in the prospective 4-city US HIV Epidemiologic Research Study (HERS) cohort. The HERS team also linked chronic depressive symptoms to greater drops in CD4 count. Only 38% of these women had taken ART for at least 1 year.
Prospective analysis of 1716 HIV-positive women in the US Women’s Interagency HIV Study (WIHS) in the same era (1994-2001) found that women with chronic depressive symptoms had a 70% higher risk of AIDS death than women with limited or no depressive symptoms (aRR 1.7, 95% CI 1.1 to 2.7). Half of these women had taken ART for 1 year or more. Using mental health services halved the risk of AIDS mortality in these women (aRR 0.5, 95% CI 0.3 to 0.7).

Depressive symptoms boosted the risk of AIDS death by half (adjusted hazard ratio [aHR] 1.49, 95% CI 1.00 to 2.21, \( P = 0.05 \)) in a prospective study of 338 men and 152 women, two thirds of them nonwhite, seen in five Southeastern US states in the early 2000s. There was no association between depressive symptoms and all-cause mortality. Four in 5 people were taking ART when follow-up began.

The biggest assessment of depression and mortality used all-cause mortality as the endpoint and ran from January 2010 through July 2013 in the Swiss HIV Cohort Study (SHCS). This analysis of 4422 SHCS members without initial depression involved 3294 men (74%), 1934 MSM (44%), 1128 women (26%), and 432 injection drug users (10%). The researchers identified depression through diagnosis by a psychiatrist (63%) or an SHCS infectious diseases specialist. HIV care is free and accessible to all in Switzerland.

During follow-up 193 people died, mostly from non-AIDS deaths (59%), AIDS deaths (11%), or suicide (9%). Overall mortality measured 0.96 per 100 person-years, and mortality proved more than one third higher in people with than without depression (1.17 versus 0.86 per 100 person-years, \( P = 0.033 \)). Eliminating drug injectors from the analysis rendered this difference nonsignificant. The researchers did not perform an adjusted analysis.

Defining depression as a Patient Health Questionnaire-9 (PHQ-9) score at or above 10, the investigators determined that 1246 people (31%) had depression in their first year of CNICS enrollment. At the end of follow-up, 121 people (3%) had died of any cause. A Cox proportional hazards model adjusted for adherence, CD4 count, HIV suppression, and other variables determined that people with depression had almost a two thirds higher risk of death (adjusted hazard ratio 1.64, 95% CI 1.06 to 2.53).

The Swiss and US studies offer strong contemporary evidence that depression shortens survival, and the intuitive strength of that conclusion speaks for itself. As the CDC observes, depression has strong associations with undeniable correlates of mortality such as smoking, drinking, and a sedentary lifestyle.

**Depression, heart failure, and the HIV care cascade**

It’s easy to add other factors that correlate with both depression and mortality, like injecting drugs, abusing other substances, and multiple comorbidities. A recent US general-population trial randomized 20 primary care practices to evidence-based depression care or usual care. During 2 years of follow-up involving 1204 older...
primary care patients, those in usual-care practices with
the highest comorbidity and depression levels had a
tripled risk of death compared with depressed patients
who had minimal comorbidities (HR 3.02, 95% CI 1.32
to 8.72). In contrast, patients in depression-care practices
with the highest levels of comorbidity and depression
did not run a higher death risk than depressed patients
with minimal comorbidity. The bottom line is that
active depression management contributes to prolonged
survival in older people with a list of comorbid diseases—
like a growing proportion of people with HIV infection.

One US study tied major depressive disorder to heart
failure in people with HIV. This Veterans Aging Cohort
Study (VACS) involved 26,908 veterans with HIV and
54,519 without HIV. After 5.8 years of follow-up, HIV-
positive vets with major depressive disorder had a two
thirds higher risk of heart failure than HIV-negative vets
without depression (aHR 1.68, 95% CI 1.45 to 1.95).
A separate fully adjusted analysis limited to veterans
with HIV determined that major depressive disorder
independently boosted heart failure risk (aHR 1.29, 95%
CI 1.11 to 1.51). Among veterans with major depressive
disorder, those taking antidepressants when follow-up
began had a 24% lower risk of heart failure (aHR 0.76,
95% CI 0.58 to 0.99).

And for people with HIV, comorbidities represent
only one set of hurdles to healthy longevity. To control
HIV and comorbidities, they have to get into care, stay
in care, start and adhere to antiretroviral therapy, gain
CD4 cells, and make their viral load undetectable.
Research from the past decade offers evidence that
depression can narrow passage through each of these
gateways in the HIV care continuum—starting
with linkage to care and retention in care, and
proceeding through antiretroviral adherence, CD4 gains,
and viral control.

Retrospective analysis of 3359 HIV patients in the
Kaiser Permanente healthcare system addressed the
last three intertwined outcomes in people starting their
first antiretroviral regimen from January 2000 through
December 2003. This 8-state analysis included 1961
people (58%) starting ART without depression and
1398 (42%) starting ART with depression. Among
people diagnosed with depression, only 508 (36%) got a
prescription for a selective serotonin reuptake inhibitor
(SSRI) antidepressant. Most study participants, 83%,
were men, and median age stood at 40 when follow-
up began. The Kaiser team calculated adherence by
pharmacy refills.
An analysis adjusted for age, gender, antiretroviral regimen, and temporal trend determined that people with depression but not taking an SSRI had about a 20% lower chance of at least 90% antiretroviral adherence than the control group of people starting ART without depression (adjusted odds ratio [aOR] 0.81, 95% CI 0.70 to 0.98, \( P = 0.03 \)) (Figure 2). But antiretroviral adherence did not differ significantly between the control group and people with depression taking an SSRI.

In an analysis adjusting for the same variables plus baseline CD4 count, odds of reaching a viral load below 500 copies/mL 12 months after starting ART proved 23% lower in people with depression and not taking an SSRI than in the control group of HIV-positive people without depression (aOR 0.77, 95% CI 0.62 to 0.95, \( P = 0.02 \)). Chances of viral control in 12 months did not differ significantly between SSRI takers with depression and people with depression taking an SSRI.
and the control group. Twelve-month CD4 responses were similar in people with and without depression. But among people with depression, those with better than 80% SSRI adherence had significantly greater 12-month CD4 gains than people not taking an SSRI (+19 versus -19 cells/mm$^3$, $P = 0.01$).

CDC analysis of a nationally representative sample also linked depression to lower chances of reaching an undetectable viral load.$^{35}$ Among 18,095 HIV-positive people in the Medical Monitoring Project in 2009-2012, 25% had a depression diagnosis, 91% took antiretroviral therapy, and 69% had a viral load below 200 copies/mL on all measures in the past 12 months. An analysis adjusted for antiretroviral adherence and race determined that a depression diagnosis independently conferred a 7% lower chance of attaining sustained viral suppression (adjusted prevalence ratio 0.93, 95% CI 0.91 to 0.96).

**The worse the depression, the worse the adherence**

The link between depression and poor antiretroviral adherence appears to grow stronger as depression deepens. That conclusion emerged from a cross-sectional study of 624 HIV-positive adults at the Washington University HIV Clinic in 2009.$^{33}$ Participants completed the Patient Health Questionnaire-9 (PHQ-9), which focuses on nine diagnostic criteria for DSM-IV depressive disorders, and researchers used responses to rate patients as having no depression, minimal depression, mild depression, moderate depression, moderately severe depression, or severe depression.

Ninety-six people (15%) had symptoms of major depressive disorder. Statistical analysis adjusted for age, race, tobacco use, and treatment with a protease inhibitor versus a nonnucleoside determined that more severe depression predicted a greater chance of worse than 95% antiretroviral adherence. For example, probability of poor adherence lay around 20% or lower in people with minimal or mild depression, above 20% in those with moderate or moderately severe depression, and as high as 40% in people with severe depression ($P < 0.05$).

If depression fosters poor adherence, one might assume treating depression improves adherence. Meta-analysis of 29 studies involving 12,243 people with HIV confirms that assumption.$^{27}$ Overall odds of antiretroviral adherence proved 83% greater in people treated for depression (standardized odds ratio 1.83, 95% CI 1.27 to 2.55). In contrast, people not treated for depression ran a 35% higher risk of nonadherence (standardized relative risk 1.35, 95% CI 1.13 to 1.60). Compared with people not treated for depression, treated people had a doubled chance of improvement in depressive symptoms (standardized odds ratio 2.07, 95% CI 1.38 to 3.30). Adherence definitions varied from study to study.

In a review of major depression and other psychiatric disorders, Andrew Angelino and Glenn Treisman from Johns Hopkins call these conditions “a vector for infection with HIV and a barrier to its successful treatment.”$^{36}$ Evidence like that reviewed in this article led them “to conclude that treatment of these disorders greatly improves patient adherence and outcomes of HIV infection.”

continued...


33. Taniguchi T, Shacham E, Onen NF, Grubb JR, Overton ET. Depression severity is associated with increased risk behaviors and decreased CD4 cell counts. *AIDS Care*. 2014;26:1004-1012.


Pointers on depression care in people with HIV: an “opportunity for movement”

An interview with Brian W. Pence, PhD

Dr. Pence has become a leading researcher on mental health and behavioral issues in people with HIV infection. His recent work includes the randomized SLAM DUNC trial assessing the impact of measurement-based antidepressant therapy and a study of psychiatric comorbidity and consequences in HIV-positive people with depression. With Kathryn Whetten, Dr. Pence coauthored the second edition of You’re the First One I’ve Told: The Faces of HIV in the Deep South (Rutgers University Press, 2013), integrating qualitative findings from the first edition with quantitative findings on more than 600 HIV-positive people in the US Coping With HIV/AIDS in the Southeast (CHASE) longitudinal cohort. He holds an MPH in epidemiology from Columbia University and a PhD in epidemiology from the University of North Carolina-Chapel Hill.

Keys to screening for and diagnosing depression

Mascolini: Should clinicians screen everyone with HIV for depression?

Pence: I think they should. We have good data that depression is prevalent in the HIV population—up to 30% of patients in care may have a depression diagnosis. It is often chronic but can also arise as a result of new circumstances. The US Preventive Services Task Force recommends routine depression screening for patients in primary care, and those recommendations have continued to expand to other populations, including geriatric populations and women during the perinatal period. Given the prevalence of depression in people with HIV infection and the negative clinical consequences observed with depression, it’s a high-priority condition to identify and treat.

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Mascolini: Should a clinician screen an HIV patient at the first evaluation? And how regularly should screening be repeated as care continues?

Pence: Clinical practices will differ. To identify depression in our SLAM DUNC trial, we worked with our partnering clinics to start with one-time screening of all patients. Then we rescreened patients every 6 months at their regular clinical appointments. Certainly we know that a new HIV diagnosis and entry into care are very vulnerable periods for patients and a real opportunity to link patients into additional service and try to set them up for success in the long term. So early screening makes a lot of sense. Updated semiannual or annual screening in my opinion is quite important to try to catch new-onset depression and to try to link patients into services that can help them. [The European AIDS Clinical Society also recommends initial screening of all HIV patients and regular rescreening thereafter. See page 27.]

Mascolini: How should clinicians screen for depression and then go on to establish that someone with depressive symptoms has major depressive disorder?

Pence: There are a number of good, low-burden, self-report screening tools out there. In our studies we used the Patient Health Questionnaire-9 (PHQ-9), which is a 9-item patient self-report that has been widely used and validated (http://patient.info/doctor/patient-health-questionnaire-phq-9). It’s an easy thing to integrate into standard intake paperwork when patients register. Some clinics already have PDAs [personal digital assistants] that allow patients to enter certain information on intake. So there’s a pretty low-burden way to screen.

Of course the screens aren’t diagnostic, but they’re a good first cut at picking up the patients who need to be assessed further. In our studies we trained social workers, nurses, and other personnel in the clinic to confirm that diagnosis. Clinicians can also confirm the diagnosis themselves, relying on a standardized assessment (Table 1) as well as on clinical judgment.

### Table 1. DSM-IV Diagnostic Criteria for Depression

For major depressive disorders, at least five of the following symptoms must be present most of the day, nearly every day, for at least 2 weeks. At least one of the first two bolded symptoms must be present.

1. **Depressed mood**
2. **Markedly diminished interest in usual activities**
3. Significant increase/loss in appetite/weight
4. Insomnia/hypersomnia
5. Psychomotor agitation/retardation
6. Fatigue or loss of energy
7. Feelings of worthlessness or guilt
8. Difficulty with thinking, concentrating, or making decisions
9. Recurrent thoughts of death or suicide
**Deciding how to start therapy**

**Mascolini:** When a patient needs treatment for depression, how should the clinician decide whether to recommend psychotherapy or antidepressant therapy or both?

**Pence:** It’s really a personal decision between the provider and the patient. The evidence base is that psychotherapy and antidepressant treatment are comparably effective, but they don’t always work for the same people. Some patients respond really well to antidepressants and some don’t; some respond really well to psychotherapy and some don’t.

Partly it’s a matter of patient preference for medication versus therapy. At the same time, providers and patients have to weigh the pros and cons of each. Antidepressants have a faster onset of action than psychotherapy, but after a few months they have about the same efficacy. For treatment-resistant depression or chronic depression, a combination of antidepressant medication plus psychotherapy may be the most helpful for patients.

**Mascolini:** Is a selective serotonin reuptake inhibitor (SSRI) always the first choice for antidepressant therapy?

**Pence:** SSRIs have been the workhorse for quite a while, and a lot of them are generic now, which is a big plus. Also, SSRIs have a pretty low side-effect burden and tend not to interact with antiretrovirals. Those are all good things.

For all of these medications, there are tradeoffs. If a patient really does not want sexual side effects, then an SSRI may not be the first choice. If a patient is really concerned about sleep or weight gain, that might drive a particular choice. SSRIs have been the first choice for a long time and for good reason. But some newer agents work better for some patients and may provide a preferable side-effect profile.

**Mascolini:** What are those other agents?

**Pence:** Bupropion is one, mirtazapine is another. Also venlafaxine, desvenlafaxine, and duloxetine. The last three are SNRIs—serotonin and norepinephrine reuptake inhibitors. Those are five agents that provide alternatives to the SSRI class. [See pages 33-37 of reference 5.]

**Mascolini:** How do standard therapies for depression compare in efficacy in people with versus without HIV?

**Pence:** They work just fine in people with HIV. Several meta-analyses that specifically address that question demonstrate that standard interpersonal counseling—psychotherapy—is effective, with effect sizes comparable to what you see in general primary care. Similarly, meta-analyses of antidepressant trials show effect sizes comparable to what you would expect to see in general clinical care. And there have been several trials of collaborative care models for depression integrated into routine HIV care that have shown positive impacts on depression.

We have to remember, though, that HIV patients may present not only with depression, but also with co-occurring posttraumatic stress disorder, panic disorder, substance abuse, or alcohol dependence. In those individuals antidepressant therapy or psychotherapy may be helpful but may not be enough to address those other comorbidities. To me that’s the main difference between HIV patients with depression and a typical primary care patient population: People with HIV
often have additional psychiatric diagnoses that can complicate the response to treatment.

**Advice on referrals and management algorithms**

**Mascolini:** When is referral to a specialist appropriate for depression diagnosis or treatment?

**Pence:** There's been a big push in medical training toward training nonpsychiatrists to manage antidepressant treatment in nonpsychiatric care settings. We know that primary care doctors can do a great job prescribing and managing first- or second-line antidepressants, and HIV providers can do that as well. We demonstrated that in our trial, and other trials have relied on the HIV provider as that first prescriber. There are good tools providers can use [see references 5 and 9].

But there are situations when more specialized treatment is helpful. As I said, patients with co-occurring psychiatric conditions have a more complicated picture and can be harder to treat. If posttraumatic stress disorder or substance abuse is part of the picture, for example, more specialized resources may be helpful. Clinics usually have protocols in place if there are acute safety or suicidality concerns, and such concerns can certainly be one indication for referral. If the depressive illness is really bipolar disorder or a psychotic illness with depressive features, those can be more complicated conditions and may be out of the comfort zone of many HIV providers.

**Mascolini:** SLAM DUNC and other trials in HIV populations used response-driven algorithms interpreted by nonphysicians to guide depression management. [See pages 34-40.] Can these algorithms be adapted to clinical practice?

**Pence:** The algorithm we used in SLAM DUNC was heavily based on what was used in the original STAR*D depression trial in primary care 10 years ago. It's an adaptation of a standard chronic disease management approach to managing depression, and that algorithm was designed for use in primary care. The Depression Management Tool Kit, a great resource from the MacArthur Foundation, details the same approach using the PHQ-9 [see page 20 of reference 5] and offers primary care clinicians other practical guides to depression screening, diagnosis, and treatment. The University of Washington also has a toolkit for collaborative care for depression that presents many of these same elements. We have also published our adaptation of the approach for HIV care so others can use it.

In SLAM DUNC we specifically looked carefully at interactions between antiretrovirals and antidepressants, but there really weren't many interactions to be very concerned about. So the principles present in the toolkits available are just as applicable to HIV clinical care.
The really key aspect of these algorithms is the emphasis on measuring depressive symptom severity regularly—in particular about 4 weeks after any new prescription or dose adjustment—to see if the treatment is working. If the patient is still depressed, the treatment plan probably needs to be adjusted. One of the big gaps in primary care and other nonpsychiatric management of depression is that an antidepressant may be started, but it may be many months before there’s any sort of assessment of whether it’s helping. Several scales, like the PHQ-9 for example, are well validated as tools that can measure depressive severity and guide treatment adjustment decisions.

**Mascolini:** What other issues should HIV clinicians be aware of in caring for people with depression?

**Pence:** I think there are great lessons to be learned from the experience of primary care over the last 10 to 15 years in expanding depression identification and treatment. That primary care model could be very helpful in structuring depression management in the HIV clinic.

We know depression is highly prevalent in people with HIV infection; we know that it can be identified reliably; and we know that much of it can be managed well in the HIV clinical home with the algorithms we discussed. At the same time we know that many HIV-positive patients don’t have access to good mental health care elsewhere. Even though we really wish they could all be treated by a psychiatrist or a specialty mental health clinic, that’s simply not the reality for many of these patients.

There’s a real opportunity within HIV clinical care to greatly improve quality of life for a substantial proportion of patients and at the same time try to head off some of the disengagement from care, poor adherence, disease progression, and poor clinical outcomes—all consequences that have been linked to depression. I think there’s opportunity for movement in improving primary HIV care of depression.

“*One of the big gaps in primary care and other nonpsychiatric management of depression is that an antidepressant may be started, but it may be many months before there’s any sort of assessment of whether it’s helping.*”

— Brian Pence (see page 15)
References

Abstract: Independent risk factors for depression in people with HIV infection can be grouped into sociodemographic variables (including female gender, unemployment, and financial difficulties), behavioral factors (including injection drug use and other substance use and abuse), clinical factors (including less antiretroviral experience, poor antiretroviral adherence, and a detectable viral load), and psychological factors (including a family or personal history of depression and low self-efficacy). Research throughout the Western world shows that depression often goes undiagnosed and untreated in HIV-positive people. HIV health experts in the United States and Europe recommend screening everyone with HIV for depression. European AIDS Clinical Society (EACS) guidelines offer straightforward advice on screening for and diagnosing depression in people with HIV.

Why is depression so prevalent in people with HIV infection? One inescapable reason is that depression ranks high among risk factors for HIV infection, so depression often precedes HIV infection and the two coexist after seroconversion. Depression goes hand-in-hand with behaviors that boost HIV risk, such as injecting drugs, abusing alcohol and other substances, and frequent sex without condoms. The link between depression and HIV risk also holds true in people without a substance abuse history. One study from the first decade of the US HIV epidemic charted a 7-fold higher rate of lifetime mood disorders in nonabusers seeking HIV testing than in the general population.

Thus any survey of depression risk in people with HIV must be read with the understanding that relevant research rarely establishes causality. But a grasp of which variables hold the strongest associations with depression in HIV populations can be a crucial step toward heightened awareness of depression in people with HIV—and toward possible diagnosis and treatment.

Depression risk factors fit in four bins

European AIDS Clinical Society (EACS) guideline writers believe depression poses such a threat to people with HIV that everyone infected should be screened for depression immediately after HIV diagnosis and every 1 to 2 years thereafter (see “Screening and diagnosis simplified” on page 26). These guidelines offer a

continued...
7-point framework as a starting point for identifying HIV-positive people at high risk for depression:

- Family history of depression
- Personal history of depressive episode
- Older age
- Adolescence
- History of drug addiction or psychiatric, neurologic, or severe somatic comorbidity
- Efavirenz use
- Use of neurotropic or recreational drugs

Specific depressive symptoms in men may include feeling stressed or burned out, venting feelings in angry outbursts, and coping through overwork and heavy drinking. But this list is hardly immutable. For example, some HIV research shows a diminishing risk of depression with age, and research does not consistently confirm a link between efavirenz and depression.

Analysis of 11 studies from the combination antiretroviral era (Table 1) suggests several other variables independently associated with depression that fit into four broad bins: (1) sociodemographic, (2) behavioral, (3) clinical, and (4) psychological (Table 2). The research explored includes three prospective and eight cross-sectional studies involving 15,480 people with HIV infection. Six studies came from the United States (n = 4766), two from Denmark (n = 417), and one each from Switzerland (n = 4422), Spain (n = 5185), and Italy (n = 690) (Table 1). Participants in most of these 11 studies averaged about 40 years in age except for one study of people 50 or older and one study of US youth. About half of participants in the study of US youngsters were female, while women made up one quarter to one third of the other study groups.

Among sociodemographic factors, certain variables consistently predict depression from study to study: female gender, homosexual orientation, living alone, and unemployment or low income (Table 2). Three studies found a consistent association between female gender and higher depression risk, though some experts question the strength of this link on the grounds that men are less likely than women to admit depressive symptoms on testing. Living without a spouse or partner boosted depression risk in the Swiss HIV Cohort Study and made suicidal ideation more likely in a 4-city US study. Unemployment or limited ability to work got tied to depression in the United States, Italy, and Switzerland. A single-center study in St. Louis, Missouri found that having one or more minor dependents (versus none) made depression more likely. Financial straits or low access to medical care contributed to depression in Houston and Denmark. Homosexual versus heterosexual orientation made depression or suicidal ideation more likely in Denmark or 4 US cities. In a study of 186 HIV-positive youngsters at five US sites, those behaviorally infected rather than perinatally infected ran a higher risk of depression.

Analysis of these studies yields no tidy take-home on how age affects depression risk. The study of HIV-positive US youth found depression more likely in older youngsters, while a study of US HIV patients 50 or older found depression more likely in younger cohort members. A 4422-person Swiss HIV Cohort Study analysis found incident depression more frequent in people under 45 (versus over 55), while cumulative prevalent depression proved more frequent in people over 45 (versus under 45). Studies of middle-aged adults in St. Louis and Denmark found
Table 1. Eleven US/European studies assessing depression risk factors with HIV

<table>
<thead>
<tr>
<th>First author</th>
<th>Year(s)</th>
<th>n</th>
<th>Location</th>
<th>Type of study, age</th>
<th>How depression was determined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anagnostopoulos</td>
<td>2010-2013</td>
<td>4422</td>
<td>Switzerland (SHCS)</td>
<td>Prospective</td>
<td>Psychiatrist or physician report</td>
</tr>
<tr>
<td>Bhatia</td>
<td>2006-2007</td>
<td>200, 32% F</td>
<td>Houston</td>
<td>Prospective, mean age 38 (range 18-70)</td>
<td>CES-D-20</td>
</tr>
<tr>
<td>Carrico</td>
<td>2000-2002</td>
<td>2902, 24% F</td>
<td>4 US cities</td>
<td>Cross-sectional, mean age 41</td>
<td>Suicidal ideation by BDI</td>
</tr>
<tr>
<td>Grov</td>
<td>2005</td>
<td>914 &gt;50 years old, 29% F</td>
<td>New York City</td>
<td>Cross-sectional, median age 54 (range 50-78)</td>
<td>CES-D &gt;23</td>
</tr>
<tr>
<td>Gutierrez</td>
<td>2004-2010</td>
<td>5185, 26% F</td>
<td>Spain, CoRIS cohort</td>
<td>Prospective, median age 41</td>
<td>&quot;Clinically significant depression;&quot; unclear how determined</td>
</tr>
<tr>
<td>Justice</td>
<td>2001-2002</td>
<td>50</td>
<td>VACS 5 sites</td>
<td>Cross-sectional</td>
<td>PHQ-9</td>
</tr>
<tr>
<td>Marando</td>
<td>Current ART era</td>
<td>690, 27% F</td>
<td>Italy</td>
<td>Cross-sectional, median age 45</td>
<td>CES-D-20</td>
</tr>
<tr>
<td>Rodkjaer</td>
<td>2005</td>
<td>205, 24% F</td>
<td>Denmark</td>
<td>Cross-sectional, 83% 30 to 59 years old</td>
<td>BDI-II</td>
</tr>
<tr>
<td>Shacham</td>
<td>2007</td>
<td>514, 32% F</td>
<td>St. Louis</td>
<td>Cross-sectional, mean age 42</td>
<td>PHQ-9</td>
</tr>
<tr>
<td>Slot</td>
<td>2013</td>
<td>212</td>
<td>HIV clinic in Denmark</td>
<td>Cross-sectional</td>
<td>BDI-II</td>
</tr>
<tr>
<td>Tanney</td>
<td>2000s</td>
<td>186 youth, ~50% F</td>
<td>5 US sites</td>
<td>Cross-sectional</td>
<td>BSI</td>
</tr>
</tbody>
</table>

ART, antiretroviral therapy; BDI, Beck Depression Inventory; BSI, Brief Symptom Inventory; CES-D, Center for Epidemiologic Studies Depression; F, female; PHQ-9, Patient Health Questionnaire; SHCS, Swiss HIV Cohort Study; VACS, Veterans Aging Cohort Study.

depression more likely in younger study participants. A comparison of HIV-positive and negative US veterans at five sites determined that depressive symptom frequency dropped with age in HIV-negative vets but not HIV-positive vets. Depression prevalence rose with age in veterans with HIV compared with HIV-negative veterans. The message from this drove of data may be to consider age a less reliable depression predictor than other factors.

Among behavioral factors tied to depression, injection drug use looms large. In the Swiss HIV Cohort Study, men who inject drugs ran a higher risk of incident

continued...
depression and cumulative prevalent depression than white men who have sex with men (MSM), while women who inject drugs had a higher risk of cumulative prevalent depression. Research elsewhere in Europe and the United States also confirms illicit drug use, recent substance abuse, regular marijuana use, previous alcohol abuse, and smoking as depression risk factors. In the Swiss study, lack of physical activity boosted chances of incident or prevalent depression, and sexually active people ran higher risks of both incident and prevalent depression. The study of US youth found an unsurprising link between more behavioral problems and depression.

These 11 US and European studies turned up several links between antiretroviral therapy, its benefits, and depression. In a 5185-person Spanish cohort, both starting ART and longer ART exposure (including longer efavirenz use) lowered the risk of clinically significant depression. Lower nadir CD4 count heightened risk of incident depression in Switzerland, while a pre-ART CD4 count below 200 cells/mm³ raised depression risk in a US study. Having a detectable viral load made depression more likely in Switzerland and the United States. Two studies in Denmark linked poor antiretroviral adherence to depression. Other clinical variables tied to depression or suicidal ideation include worse HIV symptom severity, decreased cognitive function, cirrhosis, self-reported poor health, and reduced energy.

A previous depression diagnosis raised odds of a new episode almost 10-fold in the Italian cohort. Related variables that made depression more likely include previously seeking help for psychological problems; guilt, shame, stigma, or leading a double life with HIV; low self-efficacy (belief in one's ability to accomplish things); increased loneliness; dissatisfaction with one's current life; self-reported stress; constant thoughts about HIV; and the perception that HIV affects all aspects of life.

Table 2 outlines the risk factors summarized in the preceding paragraphs, creating a checklist clinicians can use when evaluating a patient for depression.

**Frequent depression underdiagnosis and undertreatment**

Research in the United States and Western Europe shows that clinicians routinely fail to diagnose or treat HIV patients who meet standard criteria for depression. The largest US study addressing this issue focused on a national probability sample of HIV-positive adults in the HIV Cost and Services Utilization Study (HCSUS) who completed the Composite International Diagnostic Interview (CIDI) in the first years of the combination antiretroviral era. Of the 1140 study participants, 76% were men, 59% white, 22% black, and 14% Hispanic. Two thirds were between 26 and 40 years old and 5% were younger.

Among 448 people (39% of 1140) with CIDI-defined depression, only 203 (45%) had a depression diagnosis on their chart. Compared with people who had a college education, those who did not complete high school had 2.5 times higher odds of a missed depression diagnosis. Older patients—those with Medicare—had a two thirds lower chance of a missed diagnosis than privately insured
Table 2. Independent predictors of depression in 11 cohort studies

<table>
<thead>
<tr>
<th>Check for yes</th>
<th>Variable</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sociodemographic</strong></td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td>(^{4,8,12})</td>
</tr>
<tr>
<td>Homosexual vs heterosexual orientation</td>
<td>(^{5,9})</td>
</tr>
<tr>
<td>Behavioral vs perinatal HIV acquisition in youth</td>
<td>(^{14})</td>
</tr>
<tr>
<td>Single (living alone, (^{4}) not in primary relationship)</td>
<td>(^{9})</td>
</tr>
<tr>
<td>One or more minor dependents (vs none)</td>
<td>(^{6})</td>
</tr>
<tr>
<td>Not working (unemployed/occasionally employed, (^{6,12}) decreased ability to work)</td>
<td>(^{9})</td>
</tr>
<tr>
<td>Financial difficulty (low income, (^{4}) finances &quot;hopeless,&quot; (^{5}) low access to care)</td>
<td>(^{9})</td>
</tr>
<tr>
<td><strong>Behavioral</strong></td>
<td></td>
</tr>
<tr>
<td>Injection drug use</td>
<td>(^{4})</td>
</tr>
<tr>
<td>Other substance use or abuse (illicit drug use, (^{12}) recent substance abuse, (^{8}) regular marijuana, (^{9}) previous alcohol abuse, (^{13}) smoking)</td>
<td>(^{12})</td>
</tr>
<tr>
<td>No physical activity</td>
<td>(^{4})</td>
</tr>
<tr>
<td>Sexual activity</td>
<td>(^{4})</td>
</tr>
<tr>
<td>More behavioral problems (in youth)</td>
<td>(^{14})</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
</tr>
<tr>
<td>Less ART experience (not starting ART, (^{7}) less ART exposure)</td>
<td>(^{7})</td>
</tr>
<tr>
<td>Detectable viral load</td>
<td>(^{4,6})</td>
</tr>
<tr>
<td>Lower CD4 nadir, (^{4}) baseline CD4 count below 200</td>
<td>(^{4})</td>
</tr>
<tr>
<td>Poor antiretroviral adherence</td>
<td>(^{5,13})</td>
</tr>
<tr>
<td>More severe HIV symptoms</td>
<td>(^{9})</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>(^{12})</td>
</tr>
<tr>
<td>Decreased cognitive function</td>
<td>(^{10})</td>
</tr>
<tr>
<td>Self-reported poor health</td>
<td>(^{13})</td>
</tr>
<tr>
<td>Reduced energy</td>
<td>(^{10})</td>
</tr>
<tr>
<td><strong>Psychological</strong></td>
<td></td>
</tr>
<tr>
<td>Depression history (previous diagnosis, (^{12}) previously sought psychological help)</td>
<td>(^{12})</td>
</tr>
<tr>
<td>Stigma, (^{10,14}) shame, guilt, double life with HIV</td>
<td>(^{5})</td>
</tr>
<tr>
<td>Other psychological problems (loneliness, (^{10}) dissatisfaction with current life, (^{13}) self-reported stress)</td>
<td>(^{10})</td>
</tr>
<tr>
<td>Low self-efficacy (belief in one's ability to accomplish things)</td>
<td>(^{8,9})</td>
</tr>
<tr>
<td>Constant thoughts about HIV, (^{7}) perception that HIV affects all aspects of life</td>
<td>(^{13})</td>
</tr>
</tbody>
</table>

Independent associations reported in 11 studies, 3 prospective, 8 cross-sectional; 6 USA (n = 4766), 2 Denmark (n = 417), 1 Switzerland (n = 4422), 1 Spain (n = 5185), 1 Italy (n = 690) (total n = 15,480). See Table 1 for more details.

continued...
people. People with more clinic visits during the study period also had lower odds of a missed diagnosis.

A more recent US analysis looked at 803 HIV-positive adults with a baseline visit in 2000-2002 in the HIV/AIDS Treatment Adherence, Health Outcomes, and Cost Study.16 One third of participants were women and two thirds black. According to the Structured Clinical Interview for DSM IV Axis I Disorders (SCID), 69% of participants had a mood disorder, 57% a personality disorder, and 27% anxiety disorder. The SF-36 mental health composite score lay in the lowest (worst) quartile in 194 people (24%). Among people with both mental illness and substance use, only 59% received any mental health care in the past 3 months; among those with a mood disorder, only 40% were taking a psychotropic drug.

Analyzing these data15,16 and other findings, Duke University depression expert Brian Pence and colleagues estimate that only 45% of major depressive disorders in people with HIV get recognized clinically, only 40% of those recognized get treated, and only 40% of those treated get treated adequately.17

A single-center Danish study used the Beck Depression Inventory II (BDI-II) to determine how many HIV patients had symptoms of depression (BDI-II >14) or major depression (BDI-II >20).5 The 2005 study involved 205 people with HIV who reflected the general HIV population in Denmark (76% male, 83% 30 to 59 years old, 80% white). Seventy-seven people (38%) had symptoms of depression and 53 (26%) had major depression. Of these 53 people, 36 agreed to see a psychiatrist, and 18 of those 36 had untreated depression. Among the 17 people who declined a visit to a psychiatrist, 12 had not seen a mental health specialist before. Thus 30 of 53 people with major depression (57%) received no care for their illness.

A cross-sectional survey reported in 2015 involved HIV-positive adults seen at one of 24 centers across Italy.15 Of these 690 people, 155 (22%) had severe depression, defined as a Center for Epidemiologic Studies Depression (CES-D) score of 26 to 60. In contrast, physicians identified severe depression in only 6 patients (4%). Physician evaluations rated 135 of 155 severely depressed people (87%) as having no, mild, or moderate depression.

Screening and diagnosis simplified

Guidelines for primary care of people with HIV from the US HIV Medicine Association and the Infectious Diseases Society of America18 echo European guidelines3 in recommending depression screening for everyone with HIV. “All patients should be evaluated for depression and substance abuse, and if present, a management plan that addresses these problems should be developed and implemented in collaboration with appropriate providers,” the US guidelines state. European AIDS Clinical Society (EACS) Guidelines call for a depression questionnaire at HIV diagnosis, before starting antiretroviral therapy, then “as indicated” for “at-risk persons.”3

What depression screening options do HIV clinicians have? A multicenter study of 190 HIV-positive people in Ontario rated three short screening instruments—
and two of three ultrashort forms—highly reliable in
detecting depression identified by the Mini International
Neuropsychiatric Interview.\textsuperscript{19} The six screening
tools were the Center for Epidemiologic Depression
Scale (CES-D-20), the Kessler Psychological Distress
Scale (K-10), and the Patient Health Questionnaire
depression scale (PHQ-9) and their ultrashort forms
(CES-D-10, K-6, and PHQ-2). The three primary
screening instruments had excellent accuracy and
validity (defined at area under the curve >0.9) and good
reliability (Kappa statistic 0.71 to 0.79 and Cronbach's
alpha 0.87 to 0.93). Except for PHQ-2, all tools had good
to excellent sensitivity (0.86 to 1.0) and specificity (0.81
to 0.87), excellent negative predictive value (>0.90), and
moderate positive predictive value (0.49 to 0.58).

EACS guideline writers suggest two questions that can
help clinicians identify depressed HIV patients:\textsuperscript{3}
1. Have you often felt depressed, sad, or without
hope in the last few months?
2. Have you lost interest in activities that you
usually enjoy?

These guidelines then advise clinicians to rule out
organic causes, which may include hypothyroidism,
hypogonadism, Addison's disease, non-HIV drugs, and
vitamin B12 deficiency.\textsuperscript{3}

The MacArthur Foundation's Depression Management
Tool Kit also suggests a simple two-question screen:\textsuperscript{20}

During the past month, have you been bothered by:
1. Little interest or pleasure in doing things?
2. Feeling down, depressed, or hopeless?

A positive response to either question calls for further
evaluation, perhaps with the PHQ-9 (see page 17 of
reference 20).

The EACS also offers a straightforward scheme to
diagnose depression and advises clinicians to evaluate
symptoms regularly (\textbf{Figure 1}).\textsuperscript{3} (For a similar
approach, see DSV-IV criteria for diagnosing depression
on page 14 of reference 20.)

\textbf{EACS algorithm for diagnosing }
\textbf{depression in people with HIV}

\begin{itemize}
  \item \underline{Depressed mood for at least 2 weeks} OR
  \item \underline{Loss of interest} OR
  \item \underline{Diminished sense of pleasure} OR

\begin{itemize}
  \item 1. 5% weight gain in 1 month or
  persistent change in appetite
  \item 2. Insomnia or hypersomnia
  most days
  \item 3. Change in speed of thought and
  movement
  \item 4. Fatigue
  \item 5. Feelings of guilt and worthlessness
  \item 6. Diminished concentration and
decisiveness
  \item 7. Suicidal ideation or suicide attempt
\end{itemize}

\textbf{Figure 1. HIV care guidelines from the European AIDS Clinical
Society (EACS) offer a simple diagnostic algorithm for depression
in people with HIV infection.}\textsuperscript{3}
Johns Hopkins University depression expert Glenn Treisman advises clinicians to distinguish between major depressive disorder and demoralization (sadness or grief). Major depression is marked by persistent sadness and anhedonia (utter lack of pleasure). In contrast, demoralization is “a psychological reaction to life stresses” usually “related to a specific event or circumstance.” People with demoralization say they feel fairly normal when distracted from the event that caused their sadness. But when they are reminded of that event, their sadness returns. Table 3 outlines the main features distinguishing major depressive disorder from demoralization.

Table 3. Features distinguishing major depressive disorder from demoralization proposed by Glenn Treisman

<table>
<thead>
<tr>
<th>Major depressive disorder</th>
<th>Demoralization (sadness or grief)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anhedonia</td>
<td>Can be distracted from loss</td>
</tr>
<tr>
<td>(pervasive loss of rewards from activity)</td>
<td>(maintains rewards from activity)</td>
</tr>
<tr>
<td>Family history</td>
<td>No family history</td>
</tr>
<tr>
<td>History of similar episodes</td>
<td>Unique episode</td>
</tr>
<tr>
<td>Disrupted life course</td>
<td>Stable life course</td>
</tr>
<tr>
<td>Unresponsive to positive events</td>
<td>Responsive to positive events</td>
</tr>
</tbody>
</table>

From Glenn Treisman, Johns Hopkins University.

“Given the prevalence of depression in people with HIV infection and the negative clinical consequences observed with depression, it’s a high-priority condition to identify and treat.”

— Brian Pence (see page 15)


When and how to treat depression—and how to make it easier

By Mark Mascolini

Abstract: A simple symptom checklist can guide clinicians in deciding when and how to start treating depressive symptoms in people with HIV and when to refer a patient to a specialist. Among nondrug therapies, cognitive behavioral therapy has proved particularly effective in people with HIV, especially young adults. Systematic reviews establish the value of multiple antidepressant classes in people with HIV, but selective serotonin reuptake inhibitors (SSRIs) have become the mainstay of treatment. Besides relieving depression, SSRIs promote better antiretroviral adherence, better viral control, and higher CD4 counts. Three strategies tested in randomized trials show that measurement-guided care can help prescribing clinicians reach the optimal tolerable antidepressant dose with the aim of attaining remission of depressive symptoms in people with HIV. With appropriate therapy, HIV-positive people achieve remission of depression as often as or more often than people without HIV.

Analyzing recent data, Pence and coauthors estimate that only 45% of major depressive disorder cases get recognized clinically in people with HIV, only 18% receive any treatment, only 7% receive adequate treatment, and only 5% achieve remission. But systematic reviews of clinical trials show that both psychotherapy and antidepressants can be effective in treating depression in people with HIV.

A decade ago the National Comorbiditiy Study Replication (NCS-R) figured that only 64% of the general US population in care with mental health specialists received adequate depression treatment, while only 41% of those treated in general practice got adequate treatment for depression. In a US national probability sample of people with HIV, more than one third had test-determined major depressive disorder. But 45% of those with depression did not have that diagnosis listed in their medical record.

Core principles of treating depression

European AIDS Clinical Society (EACS) guidelines map out a straightforward approach to treating depression in people with HIV. The first step in planning treatment, EACS says, is determining the number of depressive symptoms a person has from a simple list of 10 (see Figure 1 on page 27 of the preceding article):

1. Depressed mood for at least 2 weeks
2. Loss of interest
3. Diminished sense of pleasure
4. 5% or greater weight gain in 1 month or persistent change in appetite
5. Insomnia or hypersomnia most days
6. Change in speed of thought and movements
7. Fatigue
8. Feelings of guilt and worthlessness
9. Diminished concentration and decisiveness
10. Suicidal ideation or suicide attempt

From that point, it’s a numbers game (Figure 1). A person with fewer than four of these 10 symptoms probably does not have depression and needs no treatment, the EACS advises. A person with four of the 10 symptoms may benefit from problem-focused consultation, physical activity, and possibly antidepressant therapy. A person with five or six symptoms should start antidepressant therapy. And a person with more than six symptoms must be referred to a specialist (Table 1).

**Table 1.** EACS advice on when to refer a depressed patient to a specialist

- If treating clinician is unfamiliar with using antidepressants
- If depression is not responding to treatment
- If patient has suicidal ideation
- If patient has more than six of 10 symptoms in list on page 27
- In complex situations including drug addiction, anxiety disorder, personality disorder, dementia, or acute severe life events

HIV depression mavens Brian Pence and Glenn Treisman stress a fundamental principle of treating people with antidepressants: “The first step in antidepressant treatment is to get the patient to consistently take the medicine,” Treisman writes, “and to use an adequate therapeutic dose.” Start with a low dose, Treisman and Pence advise, then evaluate patients regularly for response and side effects, escalating the dose slowly until a response becomes apparent. The final section of this article (see “Three tested measurement-based antidepressant strategies”) describes three models...
of treatment monitoring by a professional other than the prescribing clinician.)

EACS HIV care guidelines include an outline of doses, safety, and side effects of four selective serotonin reuptake inhibitors (SSRIs), the dual-action reuptake inhibitor venlafaxine, and the mixed-action agent mirtazapine (available online at reference 6). Finally, EACS offers a clear yet comprehensive list of interactions between major antidepressants and antiretrovirals.6

**Psychological treatment of depression in HIV populations**

One systematic review analyzed diverse psychotherapies and related interventions for depression in people with HIV,2 while two other reviews focused on group psychotherapies for HIV-positive people.8,9

The diverse psychotherapy analysis examined 90 studies (81 from North America or Western Europe) published through September 2009 that assessed an intervention and a comparison group.2 Two thirds of the studies involved men, mostly men who have sex with men. Psychological interventions—especially cognitive-behavioral stress management—proved most effective in relieving depression, with 15 of 22 strategies (68%) having a significantly greater impact than control conditions. Three of four studies combining psychological and pharmacological therapy had a significantly greater impact than control conditions. Five of nine HIV-specific therapies proved effective; these approaches included adherence support, self-care symptom management, enhanced risk prevention, and modified directly observed therapy. Studies of physical therapies (like exercise, acupuncture, and massage) yielded less clear-cut evidence of success, while psychosocial therapies (like art psychotherapy, life review, and mantra repetition) generally proved ineffective. This analysis also covered antidepressant interventions, summarized in the next section of this article.

A 2007 meta-analysis examined eight double-blind randomized controlled trials of group psychotherapy involving 665 people with HIV, including five studies of cognitive behavioral therapy, two studies of supportive therapy, and one study of coping effectiveness training.8 Supportive therapy and coping effectiveness training did not relieve depressive symptoms more than control strategies. Pooled analysis of the five group cognitive behavioral therapies found significant relief of depressive symptoms, but that impact did not reach significance in studies that excluded people with major depression. Almost all study participants were men, so these findings may not apply to women with HIV.

A 2013 analysis9 homed in on four randomized controlled trials10-13 of group cognitive behavioral therapy for HIV-positive adults—always men—with depressive symptoms. All trials were small, single-center studies, with the largest randomizing 95 people.12 One trial took place in Hong Kong10 and three in the United States. All four studies used waiting-list controls, and two also used active controls.11,12 Pooled analysis of the four trials determined that cognitive behavioral therapy reduced depressive symptoms. But an analysis limited to the two comparisons with active control arms found the impact of group therapy “less impressive.”
Together these three analyses\textsuperscript{2,8,9} single out cognitive behavioral therapy as an effective way to ease depressive symptoms in adults (at least men) with HIV infection. Cognitive behavioral therapy also proved effective in a small trial of young adults with HIV (31% of them women) detailed on page 38. Experts define cognitive behavioral therapy as short-term, goal-oriented psychotherapy “that takes a hands-on, practical approach to problem-solving” and aims "to change patterns of thinking or behavior that are behind people's difficulties, and so change the way they feel.”\textsuperscript{14}

In their HIV-depression review article, Pence and colleagues advise that psychotherapy for depression “generally requires at least eight sessions.”\textsuperscript{1} A US study of 399 adults who screened positive for depression on the 9-item Patient Health Questionnaire (PHQ-9) showed the value of each visit for psychiatric or psychological treatment.\textsuperscript{15} Most study participants (79%) were men taking antiretroviral therapy (81%); their age averaged 43.9 years, and 52% were nonwhite. Statistical analysis adjusted for demographics, antiretroviral adherence, and CD4 count calculated a 0.63 drop (improvement) in PHQ-9 with each additional depression treatment visit.

**Insights on antidepressant therapy for people with HIV**

A 2005 meta-analysis of randomized controlled trials in people with HIV found that antidepressant therapy has at least a moderate impact in relieving depression, but this analysis is dated.\textsuperscript{16} The 7 trials involving 494 adults with depression appeared from 1994 through 1999 and only 1 took place in the combination antiretroviral therapy era. Two studies tested the tricyclic antidepressant imipramine, 1 tested imipramine and the SSRI paroxetine, and 4 tested the SSRI fluoxetine. Three studies documented a significant benefit with antidepressant therapy, 2 testing fluoxetine or paroxetine and 1 testing imipramine. The 7-trial pooled effect size of 0.57 (95% confidence interval [CI] 0.28 to 0.85) indicated that these antidepressants have a moderate impact in relieving depression in people with HIV. Because the trials enrolled almost no women and few minorities, the findings cannot be applied to those groups.

A 2011 systematic review of depression therapy for people with HIV included a subanalysis of trials involving 10 psychotropic medications: the SSRIs fluoxetine, fluvoxamine, paroxetine, and sertraline, the tricyclics desipramine and imipramine, the central nervous system stimulants dextroamphetamine and methylphenidate, the serotonin modulator trazodone, and the benzodiazepine clorazepate.\textsuperscript{2} Treatment proved effective in 6 of 11 placebo-controlled trials (55%). Effective antidepressants in these studies were fluoxetine, fluvoxamine, sertraline, desipramine, imipramine, dextroamphetamine, methylphenidate, and testosterone replacement (the last two of which were not effective in certain trials). In two trials (18%) antidepressant therapy had no impact, and in 3 trials (27%) the impact was unclear. Treatment also relieved depressive symptoms in 2 of 3 trials with a placebo or control group but without random allocation.

SSRIs have become the mainstay of antidepressant therapy for people with and without HIV. Four of the six antidepressants listed in EACS guidelines are SSRIs (citalopram, escitalopram, paroxetine, and sertraline).\textsuperscript{6} An open-label study of three SSRIs and three randomized trials comparing an SSRI with placebo or a tricyclic antidepressant establish the efficacy of SSRIs in men and women with HIV.\textsuperscript{17-20}
Retrospective analysis of 3359 US patients with HIV linked SSRI therapy to better antiretroviral adherence, better viral control, and higher CD4 counts. Ample research links depression to faulty antiretroviral adherence (see page 10 of this issue). This US study in 8 states and Washington, DC is the largest to explore the impact of depression and SSRI therapy on antiretroviral adherence in people starting antiretrovirals.

The study involved 1961 people never diagnosed with depression and 1398 with depression, 508 of whom (36% of 1398) took an SSRI for more than 2 months. Most study participants (83%) were men, and median age stood at 40 years when antiretroviral therapy began. Depression without SSRI therapy lowered odds of antiretroviral adherence almost 20% (adjusted odds ratio [aOR] 0.81, 95% CI 0.70 to 0.98) and sliced the odds of reaching an undetectable viral load almost 25% in the first 12 months of treatment (aOR 0.77, 95% CI 0.62 to 0.95). In the same adjusted analysis, people taking an SSRI for depression did not differ from people without depression in antiretroviral adherence and viral control. Among study participants with depression, those taking an SSRI gained significantly more CD4 cells with antiretroviral therapy (adjusted CD4 change at 12 months −19 cells/mm$^3$ without SSRI, +9 cells/mm$^3$ with SSRI, +19 cells/mm$^3$ with greater than 80% SSRI adherence, $P = 0.01$ comparing first and third groups).

Because depression remains highly prevalent in people with HIV (42% in this study group) these clinical investigators urge colleagues to screen HIV patients for depression and to offer SSRI therapy to those with depression. Although this study did not directly measure the impact of SSRIs on depressive symptoms, the HIV-related benefits linked to SSRIs suggest these antidepressants did relieve depression.


**Three tested measurement-based antidepressant strategies**

Low depression treatment rates in HIV-positive people underline a need for plans to assist clinicians in prescribing antidepressants with or without psychotherapy, tracking side effects and response, and titrating doses. Three US groups developed innovative collaborative care plans that can help primary HIV providers offer optimal antidepressant therapy to their patients (Table 2).

“SSRIs have been the first choice for a long time and for good reason. But some newer agents work better for some patients and may provide a preferable side-effect profile.”

— Brian Pence (see page 15)
Table 2. Response-driven strategies to support treatment of depression with HIV

<table>
<thead>
<tr>
<th></th>
<th><strong>SLAM DUNC</strong>&lt;sup&gt;22&lt;/sup&gt;</th>
<th><strong>HITIDES</strong>&lt;sup&gt;24&lt;/sup&gt;</th>
<th><strong>ATN plan</strong>&lt;sup&gt;25&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What is it?</strong></td>
<td>Measurement-based care with antidepressants</td>
<td>Measurement-based care with antidepressants plus phone support</td>
<td>Cognitive behavioral therapy plus measurement-based care with antidepressants</td>
</tr>
<tr>
<td><strong>What treatments are involved?</strong></td>
<td>Antidepressant therapy</td>
<td>Antidepressant therapy, phone support by nurse</td>
<td>Cognitive behavioral therapy, antidepressant therapy</td>
</tr>
<tr>
<td><strong>What staff is needed besides prescribing clinician?</strong></td>
<td>Depression case manager</td>
<td>Nurse depression care manager, clinical pharmacist, psychiatrist</td>
<td>Psychotherapist</td>
</tr>
<tr>
<td><strong>How is response monitored?</strong></td>
<td>PHQ-9</td>
<td>PHQ-9</td>
<td>QIDS-SR</td>
</tr>
<tr>
<td><strong>Plan details available?</strong></td>
<td>Strategy described in Pence;&lt;sup&gt;22&lt;/sup&gt; treatment algorithms online at Adams&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Strategy described in Pyne;&lt;sup&gt;24&lt;/sup&gt; medical management algorithm not currently online&lt;sup&gt;*&lt;/sup&gt;</td>
<td>Strategy described in Brown;&lt;sup&gt;25&lt;/sup&gt; medical management algorithm at <a href="http://links.lww.com/QAI/A732">http://links.lww.com/QAI/A732</a></td>
</tr>
<tr>
<td><strong>Test population?</strong></td>
<td>304 HIV+ US adults with depression</td>
<td>249 HIV+ US veterans with depression</td>
<td>44 HIV+ US 18- to 24-year-olds with depression</td>
</tr>
<tr>
<td><strong>Length of test?</strong></td>
<td>12 months</td>
<td>12 months</td>
<td>24 weeks plus 24 weeks follow-up</td>
</tr>
<tr>
<td><strong>How well did it work?</strong></td>
<td>Depressive severity similar with intervention and usual care at 12 months; 16% greater probability of depression remission and 29 more depression-free days in 12 months with intervention</td>
<td>Response and remission rates initially higher with intervention than usual care but not by 12 months; 19 more depression-free days through 12 months with HITIDES versus usual care</td>
<td>Significantly fewer depressive symptoms at 24 and 48 weeks with intervention than with usual care; significantly higher response rates and remission rates at 24 and 48 weeks</td>
</tr>
</tbody>
</table>

<sup>*</sup>A similar system is available at [https://aims.washington.edu/resource-library/care-management-tracking-system-cmts](https://aims.washington.edu/resource-library/care-management-tracking-system-cmts)
A 304-person 4-clinic US trial that randomized HIV-positive people to measurement-based antidepressant therapy or enhanced standard care found that the measurement-based plan significantly improved some depression outcomes through 6 and 12 months. The 2010-2014 SLAM DUNC trial enrolled adults on or about to start antiretroviral therapy with depression indicated by the Patient Health Questionnaire-9 (PHQ-9) and the Mini International Neuropsychiatric Interview.

Measurement-based care follows straightforward antidepressant algorithms interpreted by trained depression case managers and emphasizes “vigorous antidepressant dosing.” Cases managers can be medical assistants, nurses, clinical social workers, or other professionals. The algorithms, available online at reference 23, guide case managers through treatment steps at initial and follow-up visits. The case managers then relay antidepressant therapy recommendations to providers. The aim is depression remission, and decisions are driven by side effects and response on the PHQ-9 (Figure 2). The treatment plan follows six principles:

1. The goal of depression treatment is remission.
2. Assess depressive symptoms systematically.
3. Monitor side effects early and often.
4. Start with a low dose.
5. Increase the dose to remission, using the full dosing range if needed.
6. Ensure an adequate trial before switching or referring.

**Figure 2.** A measurement-based plan for antidepressant therapy relies on regular checkups by a case manager who makes recommendations to the prescribing clinician based on side effects and response to therapy gauged on Patient Health Questionnaire-9 (PHQ-9). Algorithms detailing decisions based on side effects and symptom response are online at reference 23.
Age averaged 42.8 years in the 149 people randomized to measurement-based care and 44.9 in the 155 randomized to usual care. Respective proportions of men were 75% and 64%, blacks 56% and 68%, whites 36% and 25%, and Hispanics 6% and 3%. Three quarters in both study groups were unemployed. Depression severity (by the Hamilton Depression Rating Scale) and psychiatric comorbidity prevalence were high. Participants in the measurement-based care arm averaged 8.9 contacts with case managers over 12 months.

Six months after randomization, the intervention arm did better in three measures of depression:

- Depressive severity significantly lower (mean difference –3.7)
- Probability of depression remission higher (relative advantage 13%)
- Suicidal ideation lower (risk difference –18%)

By month 12 differences from the usual-care arm disappeared for two of these three outcomes. But the management-based care group maintained significant advantages by two measures:

- Probability of depression remission higher (relative advantage 16%)
- Depression-free days over 12 months (29 more days)

Measurement-based care had no impact on antiretroviral adherence at 6 months by unannounced telephone pill count, possibly because participants were not selected for low adherence and baseline adherence was high in both groups. Nor did the groups differ in appointment adherence, HIV symptoms, or viral load.

The authors propose that depression treatment models like this one “efficiently leverage clinic staff time to provide antidepressant prescription decision support to HIV medical providers.” They believe the trial “demonstrates that such a real-world strategy can significantly shorten the course of depressive illness for HIV patients and reduce overall morbidity from depression.”

A randomized trial at three Veterans Affairs (VA) HIV clinics found that a collaborative team using a treatment decision system lessened symptom severity and yielded more depression-free days, though the intervention did no better than standard care in improving response rate or remission rate. The trial enrolled 249 HIV-positive veterans who screened positive for depression on the PHQ-9. Substance-dependent veterans could enroll. Researchers randomized them to standard care or to the HITIDES intervention, which relies on a three-person team—a registered nurse depression care manager, a clinical pharmacist, and a psychiatrist. This trio makes treatment suggestions to prescribing clinicians via electronic medical record progress notes. These suggestions follow a stepped-care model that heightens treatment intensity when a participant does not respond. The provider makes all treatment decisions. The depression care manager supports each patient by phone, discussing treatment barriers and resolution, depression symptom and treatment monitoring, and substance abuse monitoring. The team monitors treatment response by PHQs completed by each participant and delivered at each clinic visit.

continued...
Both treatment groups averaged 49.8 years in age, and 97% were men. Almost two thirds of participants were black, and about 90% had at least a high school education. Three quarters of both groups had major depression verified by the Mini International Neuropsychiatric Interview, and about 80% had a current antiretroviral prescription.

Six months after randomization response rates (at least a 50% drop in the 20-item Hopkins Symptom Checklist [SCL-20]) measured 33.3% in the HITIDES group and 17.5% in the standard-care group. Those results yielded more than twice higher odds of response in the HITIDES group in an analysis adjusted for relevant variables (aOR 2.60, 95% CI 1.39 to 4.86, \( P = 0.003 \)). At 6 months rates of remission (mean SCL-20 item score below 0.5) measured 22% in the intervention group and 11.9% in the standard-care group, also yielding more than twice higher odds of success in the HITIDES group (aOR 2.40, 95% CI 1.10 to 5.22, \( P = 0.03 \)). At 12 months, as in the SLAM DUNC study, these between-group differences dwindled to nonsignificance.

But veterans in the HITIDES group reported significantly fewer depression-free days through 12 months (\( \beta = 19.3 \) days, \( P < 0.001 \)), and veterans in the intervention group had significantly lower HIV symptom severity at 6 months (\( \beta = -2.6, P < 0.001 \)) and at 12 months (\( \beta = -0.82, P = 0.03 \)).

In both the SLAM DUNC and HITIDES studies, the intervention improved depression faster than usual care (through 6 months) but the usual-care arms caught up with the intervention arms in some measures of depression (through 12 months). VA researchers suggest two reasons for delayed response in the control arms that could apply to both trials: First, all participants were receiving care in the context of a clinical trial in which providers and patients accepted the need for improved depression care. Second, as the trials proceeded, clinicians in the control arm became more practiced in prescribing antidepressants and monitoring responses because of their involvement in the trials. If these speculations are true, they suggest that providers who begin paying more attention to depression care in routine practice will improve the mental health of their depressed patients.

A small randomized trial involving young adults with HIV found that 24 weeks of combined “measurement-guided psychotherapy and medication management” tailored for this age group yielded significantly higher depression remission rates at 24 and 48 weeks in the intervention group than in a standard-care contingent. More psychotherapy in the measurement-guided group probably contributed to better outcomes in this arm.

The trial recruited 18- to 24-year-olds in care at one of four US Adolescent Trials Network (ATN) sites. Participants had a diagnosis of nonpsychotic depression with significant symptoms defined as a Quick Inventory of Depressive Symptomatology-Self-Report (QIDS-SR) score of 7 or higher. Enrollees could not have psychosis, bipolar disorder, or a diagnosis of alcohol or substance dependence in the last 6 months.

Researchers randomized two ATN sites to use the combination psychotherapy and medication management (COMB) plan and two to treat patients according to standard practice. Clinicians in the COMB
arm implemented and adjusted antidepressant therapy (starting with an SSRI) according to an algorithm online at http://links.lww.com/QAI/A732). As in the SLAM DUNC trial,22 this algorithm uses depression response as the primary driver of treatment decisions. The trial offered all COMB participants cognitive behavioral therapy conducted by a site psychotherapist. Psychotherapists and prescribing clinicians in the COMB arm received 2 or 1 day of training respectively. Therapy continued for 24 weeks, and participants in both arms completed QIDS-SR at 6, 12, 24, 36, and 48 weeks.

Both study groups averaged 21.5 years in age and included similar proportions of blacks (83% overall) and Hispanics (21% overall). The intervention group had a significantly higher proportion of men than the control group (96% versus 40%, \( P < 0.001 \)). The study arms had similar QIDS-SR scores when entering the trial. After 24 weeks this measure showed significantly fewer depressive symptoms in the intervention COMB group than in controls (mean 4.3 versus 11.1, \( P < 0.001 \)) and that advantage persisted through 48 weeks (mean 4.1 versus 10.2, \( P < 0.001 \)). Response rates (at least 50% drop in QIDS-SR) proved significantly greater in the COMB group at week 24 (85% versus 20%, \( P < 0.001 \)) and week 48 (88% versus 33%, \( P < 0.001 \)) (Figure 3). Remission rates (QIDS-SR below 5) were also better with COMB than standard care at weeks 24 (65% versus 10%) and 48 (71% versus 7%).

**Figure 3.** A trial of measurement-guided psychotherapy and medication management for young adults with HIV and depression found significantly greater depression response and remission rates in the combination (COMB) intervention arm than the usual-care arm through 24 weeks of treatment and for an additional 24 weeks after the interventions ended.25

continued...
A significantly higher proportion of young adults in the COMB group received psychotherapy (95% versus 45%, $P < 0.001$) and attended more psychotherapy sessions through 24 weeks (12.6 versus 5.0, $P < 0.001$). Antidepressant use did not differ significantly between the two groups. At week 24 only 35% in the COMB arm and 45% in the usual-care arm took an antidepressant. These findings suggest that cognitive behavioral therapy explained much of the improved response in the COMB arm.

This is a small feasibility study without reported statistical power calculations. The researchers caution that results may not apply to all young people with HIV because they excluded those with substance use disorders. But the impact of the intervention proved significant and sustained. And because existing staff at study sites carried out these interventions, the authors propose that this approach “is feasible in other US medical care sites.”

These three studies in distinct HIV groups with depression22,24,25 show that response-guided treatment strategies conducted by trained professionals supporting prescribing clinicians can improve depression outcomes over the course of 12 months (Table 2). The three strategies differ in their details, but all three involve treatment response plans to guide the prescribing HIV provider.

All three trials randomized participants to the study intervention or to standard care. The study in 18- to 24-year-olds25 differed from the two studies in middle-aged people22,24 in finding significantly better response and remission rates at both 6 and 12 months, while the other studies recorded more depression-free days through 12 months with the intervention. The strategy for young adults also differed in aiming to combine cognitive behavioral therapy and antidepressant therapy, while the other two studies focused primarily on antidepressants. As detailed above, cognitive behavioral therapy appeared to explain the response advantage in the intervention arm of this trial in young adults,25 but the trial was small and results should be confirmed in bigger groups.

The larger trials in middle-aged adults with HIV and depression22,24 relied on gradual antidepressant dose escalation guided by test-measured responses and patient reports of tolerance. Both studies used algorithms to inform antidepressant adjustment recommendations, though the algorithm for the VA study24 is not currently available online.

All three response-guided strategies22,24,25 rely on regular patient monitoring, especially during the first months of a new antidepressant, to ensure reaching a dose that leads to symptom remission without causing side effects. But the strategies differ in the type and number of supporting professionals required. The SLAM DUNC approach is the simplest, requiring a quickly trained professional who may be a medical assistant, nurse, or clinical social worker.22 The strategy for young adults needs a trained psychotherapist.25 And the HITIDES approach creates a three-person team: nurse, clinical pharmacist, and psychiatrist.

Clinicians who see a need for support in offering patients response-guided depression care could profit by exploring the three approaches described here and picking one that seems to mesh best with that clinician’s practice.
References

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