In the 1980s, a common reaction of both care providers and people with HIV was that depression was only to be expected among HIV-positive people. The thinking was, “Who wouldn't be depressed?” But, while rates of depression among HIV-positive people are higher than those of the general population, research has shown that they are not consistently high in absolute terms. Rather, the majority of HIV-positive people appear to be psychologically resilient most of the time.

When depression appears, however, it can be dangerous. Depression is associated with isolation, the absence of pleasure, and unemployment, even for people who are medically stable and have a strong work history. Perhaps most seriously for people with HIV, depression is correlated with the failure to maintain proper diet, to exercise, and to adhere to medications. This article reviews the types of depression, their manifestation in people with HIV, and their treatment.

Diagnosing Depression

The term “depression” has multiple meanings and approximations. In the United States, nine criteria, in various combinations, are used to define major depressive disorder and minor depression. The symptoms must be present most of the day, nearly every day for at least two weeks. The symptoms are: 1) depressed mood; 2) markedly diminished pleasure in almost all activities; 3) significant unintentional weight loss or gain, or decrease or increase in appetite; 4) insomnia or hypersomnia; 5) moving much more slowly, or being unusually fidgety or restless; 6) fatigue, low energy; 7) feelings of worthlessness or excessive guilt; 8) diminished ability to think or concentrate, or indecisiveness; 9) recurrent thoughts that one would be better off dead, or suicidal ideation.

Major depressive disorder is diagnosed when a person experiences at least five of these symptoms—always including the first or the second or both. Minor depression is diagnosed if three or four symptoms, again always including at least one of the first two, occur together for at least a two-week period. Dysthymia, a third disorder, is diagnosed when a person feels depressed and has symptoms including low self-esteem and hopelessness for more days than not in the prior two years—without a period of well-being lasting at least two months.

It is important to note that some people do not use the word “depressed” to describe their feelings: they say they feel sad or blue, or that there is joy or pleasure in their lives. It is the meaning of their words and its relationship to the diagnostic symptoms, not the label they use, that counts.

Diagnosing depressive symptoms can be complicated by medical illnesses and medications. Several somatic symptoms of depression—fatigue, poor appetite, weight loss, or insomnia—are also symptoms of HIV disease or concurrent illnesses such as hepatitis C, or are side effects of HIV-related medications. However, mood-related symptoms, such as persistent sadness or loss of interest, and cognitive symptoms, such as trouble concentrating or inappropriate guilt, are not usually caused by these physical influences. As a result, clinicians familiar with depressive disorders, HIV, and HIV medication side effects can diagnose depression even in people with advanced HIV.

Bipolar disorder, also known as “manic depressive disorder,” includes episodes of both depression and mania and is rare (rates in the general population are about 1 percent). Rates among people with HIV are no higher and a personal or family history of bipolar disorder is no more common among people with HIV than in the general population. HIV infection of the brain has been reported to cause new-onset mania late in the course of HIV disease progression, although such cases
The clinical syndrome of depression is both more significant to HIV care and prevention than ever before and less common among people with HIV than many of us might think. As Judith Rabkin points out in this issue of FOCUS, despite the fact that feeling depressed from time to time seems to be a predictable and understandable response to living with HIV, most people with HIV are psychologically resilient and only a relative few go on to develop clinical depression. In fact, people with HIV are no more likely to be depressed than other people from their particular subpopulation.

Yet, clinical depression among people with HIV can have devastating effects when it occurs, perhaps even more so today than 20 years ago. Today, depression may not only undermine quality of life, it may be a factor in threatening life itself. For example, several studies have demonstrated a connection between depression and problems with HIV medication adherence. In fact, many studies have implicated depression as undermining health-seeking behavior, and better identification and treatment of depression could both improve overall health and lower health care costs.

There is also more and more evidence of an association between depressive symptoms and HIV-related risk behavior. Recent research has clarified this relationship in more detail, identifying a range of cofactors that connect depressive symptoms to risk.

In this issue of FOCUS, Thomas Coates hones in on gay men, a group that has elevated rates not only of HIV, but also of depression, substance use, and childhood sexual abuse. Coates discusses how these factors combine to increase risk and the key role of depression in mediating these other factors.

Fortunately, for many people diagnosed with clinical depression today, there are more options for successful treatment than ever. Unfortunately, as Rabkin states, there are barriers to treatment ranging from the fatalism and inertia that can accompany depression to a health care insurance system that penalizes mental health care in more ways than I can list here.

When Tipper Gore was poised to become First Lady, it seemed that society was poised to accept—not merely tolerate—mental health care as a full partner with medical care. No one has replaced Ms. Gore as a spokesperson for this cause, and tax and health care “reform” have only worsened the mental health care financing situation. Rabkin suggests some creative approaches to navigating these barriers. But it is clear that those of us who care about mental health and psychological well-being must speak out strongly to ensure a system that prioritizes both quality and quantity of life.

References

Prevalence of Depression in People with HIV

Studies of depression and its relationship to HIV are compromised to some extent by inconsistency of methods as well as the challenges of diagnosis mentioned above. The result is that rates of depression vary enormously among these studies.

Different studies use different measures to identify depression, and different time frames (past month, past year, lifetime). They may also include additional diagnostic categories, for example, adjustment disorder with depressed mood, a diagnostic category not usually included in U.S. studies. The more reliable and valid the measure, the longer it takes to administer. The result is that large population studies almost always use abbreviated diagnostic screens that do not include detailed follow-up queries or probes to clarify answers. These tools generate less precise estimates of depression, even though their samples are larger and therefore more statistically accurate.

The “gold standard” structured clinician-administered interviews, such as the Structured Clinical Interview for DSM-IV (SCID), that generate clinical diagnoses inquire in detail about the presence and duration of diagnostic criteria and do include follow-up probes for clarification. Self-report scales are intended to assess only symptoms and severity of distress not to generate a diagnosis. Several popular self-report scales are intentionally broad in order to pick up all possible “cases,” and are meant to be followed by more detailed assessments of those who show up as “cases.” When used alone for diagnostic purposes, a common practice, these scales tend to overestimate depression prevalence.

Three major studies have used standard clinician-administered psychiatric assessments to estimate prevalence of depression in the U.S. population. While their findings were not consistent, one review of their results applied a revised system of estimation based on the clinical significance of reported symptoms to estimate prevalence.

These revised prevalence estimates indicate that the one-year prevalence rate of major
Fears of significant adverse interactions between HIV drugs and standard antidepressants are unfounded.

Depression in the total American population is about 4.5 percent.1 Studies of people with HIV have found widely varying depression prevalence rates, ranging from 4 percent to 22 percent in men and 2 percent to 18 percent or higher in women. Within this range, studies using self-rating scales reported higher rates than studies using structured diagnostic interviews.

None of 10 studies of HIV-positive participants—using rigorous diagnostic methods and including HIV-negative participants from the same communities—found a significant difference in rates of depression by HIV status. However, when the studies were combined, rates of major depression (but not the milder, more chronic dysthymia) turned out to be significantly higher in the HIV-positive participants.2 Cumulatively, 9.4 percent of HIV-positive people met criteria for current (past month) major depression, compared to 5.2 percent of HIV-negative people. In contrast, using only a diagnostic screening tool, a study of more than 2,500 HIV-positive participants—with no HIV-negative comparison group—found that 36 percent “screened positive for major depression.” In other studies, high rates of major depression have been reported for rural Black women and for both HIV-positive and HIV-negative inner-city injection drug users.

It seems likely that among HIV-positive people, a milder, persistent depression or generalized distress is considerably more common than major depression. Whether this is attributable to HIV status is unclear, since the majority of HIV-positive subjects in depression treatment studies report their first period of depression occurred years before testing HIV-positive, often during adolescence, in the context of “coming out” for gay men or of heavy drug use or domestic conflict for heterosexual men and women. After controlling for other factors such as substance use disorders, there are no systematic differences in rates of depressive disorders by ethnicity or race. As is true in the general population, women with HIV generally have higher rates of depressive symptoms and disorders than men with HIV.

Predisposing factors for depression in the general population as well as among HIV-positive people include: a prior history of depression; lifetime alcohol and substance use disorders; and loss of social support with the consequent lack of confidants. Independent of HIV status, gay men and injection drug users have elevated rates of lifetime depression.3,4 The available evidence, while inconsistent and limited, does not routinely show increasing rates of depression with advancing HIV illness, especially when studies measure progression using immunologic or virologic markers. In general, people who report many medical symptoms and behavioral limitations associated with illness are more likely to report depressive symptoms, although it is possible that this result appears because being depressed causes a heightened awareness or magnification of these physical symptoms.

There is no direct relationship between depression and cognitive impairment. Mild cognitive problems are not uncommon among HIV-positive people, although they may not interfere with routine activities of daily living. What the two conditions may have in common is apathy: a lack of motivation and interest that is expressed emotionally as indifference and behaviorally as inaction and the tendency not to initiate a new activity unless externally prompted.

In summary, rates of depressive disorders among HIV-positive people may or may not be elevated compared to HIV-negative people from the same community, but they are clearly greater than rates for the general population. Depressive symptoms are common, and self-rating scales that include somatic symptoms such as fatigue and insomnia may show misleadingly high rates. Predictors and correlates of depression include a prior history of depression before HIV illness onset, concurrent drug use including stimulants such as cocaine and methamphetamine, and HIV-related physical limitations such as those associated with fatigue.

Treatment Options and Outcomes

The treatment of major depressive disorder is one of psychiatry’s success stories. Since 1990, researchers have published a series of studies showing that standard antidepressants have the same robust rate of success in HIV-positive patients as in any other group for patients who take their medication regularly and for sufficient time (at least eight weeks).5 Furthermore, fears that there would be clinically significant adverse drug interactions between standard antidepressants and HIV medications have turned out to be unfounded, and antidepressants have been shown to have no negative effects on measures of immune function.6 Less conventional pharmacologic treatments for depressed mood along with medications for related problems such as fatigue, wasting, or loss of libido have also shown

*It should be noted, however, that some recreational drugs such as Ecstasy and alternative treatments such as St. Johns Wort have significant interactions with protease inhibitors. The interaction affects the blood levels of both drugs, which are dangerous in combination and, according to case reports, can be fatal.
considerable effectiveness treating depression in people with HIV. These include testosterone injections (for men), dehydroepiandrosterone (DHEA) for men and women with mild but persistent depression, and stimulants including dextroamphetamine, methylphenidate and, recently, modafinil to treat clinically significant fatigue that interferes with daily activities. Researchers have conducted few studies of stimulants as antidepressant treatment, and further research is needed to assess possible interactions between such drugs and HIV antiviral medications; the modest available evidence, however, did not find negative interactions.6

There have been relatively few studies of psychosocial treatments for depressive symptoms and disorders among people with HIV. While counseling, support groups, and bereavement groups are often available in medical centers or HIV community-based organizations, and may be extremely helpful and useful for generalized distress, professional treatment is usually necessary for those with significant depression. The research literature has shown that brief, focused psychotherapies—cognitive behavioral therapy and interpersonal therapy—are effective for treating medically healthy depressed outpatients, but there have been few studies of these approaches for HIV-positive clients. One study did find that interpersonal therapy with or without concurrent antidepressant medication was superior to “supportive” psychotherapy.7 Experts in these structured treatments, however, may be hard to find, unfamiliar with HIV, and may not accept Medicaid reimbursement.

Barriers to Treatment

There are considerable barriers to treatments for depression in the context of HIV. People who are depressed are often demoralized, pessimistic, hopeless, all of which can undermine motivation to seek treatment. Although HIV primary care providers often ask about mood and quality of life during an individual’s initial visit—and some clinics include a psychiatric evaluation in all intake procedures—doctors often do not take the time to cover the issues on a regular basis.

Once depression is identified, getting effective treatment may be problematic. People who have Medicaid or AIDS Drug Assistance Program (ADAP) coverage generally have no problem getting psychiatric referrals, since they are usually seen in hospital-based clinics. People with private insurance, however, often have considerably greater difficulty getting referred to HIV-knowledgable mental health professionals who accept their insurance. When the alternative is no treatment at all, primary care providers should consider treating depression directly, referring to psychiatrists only those patients who express suicidal ideation, who do not respond to standard doses of antidepressants, or who have concurrent psychiatric conditions that also require pharmacologic management.

Finally, while depression is common among people who use substances, its management is complicated and understudied. It is also difficult to diagnose depression when a person regularly uses drugs that reliably cause mood crashes, for example, methamphetamine. It is generally recommended that substance abuse treatment accompany depression treatment, but some patients are not seeking sobriety. To further complicate diagnosis and treatment, substance abuse is often associated with additional psychiatric disorders such as anxiety disorders and personality disorders.

Conclusion

Depression is a disorder, not a normal part of life with HIV, and it responds well to appropriate treatment. Providers need to take the time to properly screen for, monitor, and treat depression or refer people with HIV for appropriate care.

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Depression, Gay Men, and HIV Acquisition

Thomas Coates, PhD

Recent research has continued to define the relationship between depression, depressive symptoms, and the behaviors most likely to lead to HIV transmission. In particular, studies suggest a complex interplay among a variety of factors that interact with depression and the conditions that increase risk or undermine risk reduction. This article looks at the manifestation of depression in men who have sex with men and the ways in which other conditions common within this population combine with depression to increase HIV-related risk.

A recently published, national, multicenter study of an HIV prevention counseling intervention found that men who have sex with men in the intensive counseling group were 18 percent less likely to contract HIV than their counterparts who received only semi-annual voluntary HIV antibody counseling and testing. The study also found that the counseling intervention was successful in improving safer sex self-efficacy, the perception of affirmative social norms about safer sex, and communication skills about sex. That is the good news.

The bad news is that the intervention did not reduce alcohol and drug use, and depressive symptoms. Further, over the course of the study's three-and-a-half-year follow-up substance use, enjoyment of unsafe sex, and depressive symptoms each independently predicted whether or not participants would acquire HIV. While substance use and enjoyment of unsafe sex seem to have a logical link to risk-related sexual behavior and HIV acquisition, the relationship of depressive symptoms to HIV transmission is less clear. Why would depressive symptoms, which often decreases libido and whose treatment may decrease libido, increase a person's chances of getting HIV?

Depression among Gay Men

Another large study of psychological distress and depression was notable for sophisticated recruitment strategies that enabled researchers to obtain a random sample of gay men in four cities: Los Angeles, San Francisco, Chicago, and New York. The study found that 17.2 percent of participants were depressed, a significantly higher rate than the 3 percent to 8 percent depression rates observed in the general, U.S. male population.

The study identified four predictors of depression: being single; not identifying as “gay,” “queer,” or “homosexual”; experiencing multiple episodes of anti-gay violence in the previous five years; and very high levels of community alienation. Depression was also associated with histories of attempted suicide, a history of childhood sexual abuse, and recent sexual dysfunction.

These findings are important. They suggest that the ongoing stresses of being gay, experiencing harassment and anti-gay violence, childhood sexual abuse, and other factors lead a higher proportion of gay men to experience depressive symptoms as adults than their heterosexual peers. If depression is linked to HIV acquisition, these findings also contribute to the explanation of why gay men continue to contract HIV despite years of HIV prevention efforts.

Ron Stall, the lead researcher on the four-city study now at the Centers for Disease Control and Prevention, used the same sample to examine what he termed a “syndemic,” highly related sets of health problems experienced by a single population, in this case urban gay men. The study sought to explore further the three key relation-

References


ships between substance use and HIV, depression and HIV, and violence and HIV.

Stall suggests that the “additive interplay” of these health problems magnifies the vulnerability of gay men to serious health conditions like HIV disease. He and his colleagues found first that depressive symptoms were associated with more polydrug use, more childhood sexual abuse, and more partner violence. Further, the researchers found that someone with depressive symptoms, polydrug use, and childhood sexual abuse was at higher risk than someone with only depressive symptoms and polydrug use, and those people were at higher risk than someone with depressive symptoms alone. All of these health problems—depression, polydrug use, childhood sexual abuse, and partner violence—was related both to a greater likelihood of having high-risk sexual behavior and of having HIV.

Depression and HIV Infection

Rates of depression are nearly two times higher among people with HIV than among similar people who do not have HIV. While the majority of HIV-positive individuals are resilient and do not suffer from depression, HIV infection is a risk factor for depressive disorders. It is important to note, however, that depressive symptoms among people with HIV may be caused by physiological factors, for example, fatigue related to HIV disease may be caused by physiological factors, for example, fatigue related to disease progression or other symptoms related to HIV antiviral treatment.

Further, as noted above, certain experiences in childhood and adolescence predispose people to adult depression. The need to treat depression leads people to use various substances—some by prescription and some off the street—to make themselves feel better. Depression makes it difficult to form friendships and intimate relationships, which buffer people from many life difficulties; the lack of these connections makes people feel more depressed. In response, depression may lead some people to use sexual encounters to make themselves feel better. The combination of substance use and high-risk sexual behavior may result in unsafe sexual encounters and a greater chance of catching or transmitting HIV.

These phenomena are not limited to gay men. Other researchers have found similar evidence among adolescents and among patients at sexually transmitted disease clinics. Further, a meta-analytic review of many individual studies found that such findings hold across sexual orientation groups.

Conclusion

Why does libido, which usually decreases with depression, paradoxically seem to increase in depressed gay men? There are several possible explanations that need to be further researched. One possibility is that these men seek out sexual partners to alleviate depression. Another is that depression decreases self-esteem, leading these men to engage in sexual behavior that they might otherwise not find acceptable. Rather than driving away a potential sexual partner by trying to negotiate sexual behavior, these individuals may be willing to accept whatever sexual activities the partner wants as a way of achieving relief from depression and isolation.

A third possibility is that people who are depressed self-medicate with alcohol or stimulants such as methamphetamine in order to overcome depression. They may also use Viagra or other drugs in order to compensate for loss of libido due to depression, alcohol use, or drug use. Research is beginning to uncover a powerful relationship between the combination of Viagra and methamphetamine and both increased HIV-related risk and increased seroconversion rates.

Clearly, we need treatment models that can help people respond to depression, to the childhood and adolescent antecedents of this depression, and to the adult consequences of depression. We need to examine the efficacy of antidepressants in helping people not only to overcome depression, but also to curb drug use. We might also need to examine the efficacy of various drugs other than antidepressants in assisting with drug use or misuse. Finally, community mental health treatment and prevention models that acknowledge the extent of depression in the community and also provide psychotherapy and other supportive experiences are essential in helping people to deal with past difficulties, current depression, and the health consequences that result.

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Comments and Submissions

We invite readers to send letters responding to articles published in FOCUS or dealing with current AIDS research and counseling issues. We also encourage readers to submit article proposals. Send correspondence to rmarks@itsa.ucsf.edu or to Editor, FOCUS, UCSF AIDS Health Project, Box 0884, San Francisco, CA 94143-0884.
Depression and HIV Risk Behaviors

Depression among sexually transmitted disease clinic patients was associated with a range of HIV-related risk behavior including trading sex and having sex while "high," according to a large Baltimore study. However, depression was not associated with unprotected sexual intercourse, multiple sex partners, anal sex, or STD diagnosis among this primarily African American, heterosexual sample.

Researchers recruited 320 male and 351 female patients at the Baltimore City Health Department STD clinic between July 2000 to August 2001. Participants answered questions about sex and drug use behaviors, symptoms of depression, and overall health status using an audio, computer-assisted self-interview. Of the 671 participants, 96 percent were African American, 74 percent were single or not married, and 83 percent were heterosexual. According to the Beck Depression Inventory, 14 percent of female subjects and 23 percent of male subjects were depressed.

In the preceding 30 days, depressed women were significantly more likely than nondepressed women to have traded sex for drugs or money and to have had sex while “high” on alcohol, cocaine, or heroin. Depressed women were also significantly more likely to report a history of trading sex for drugs or money. In the preceding 30 days, depressed men were significantly more likely than nondepressed men to have had sex while high on cocaine or heroin and to have abused alcohol or drugs. Depressed men were also significantly more likely than nondepressed men to report a greater number of lifetime sex partners, a past sex partner who used injection drugs, and a history of trading sex for drugs or money.

AIDS-related death was more common among HIV-positive women with chronic depressive symptoms than HIV-positive women without these symptoms.

Psychosocial Factors of Treatment Adherence

A small Miami study found that HIV medication adherence was positively associated with social support and “positive states of mind” and negatively associated with depressive symptoms.

Researchers reviewed baseline interviews from a subsample of 90 women of any sexual orientation and men who have sex with men who had participated in a larger longitudinal psychosocial intervention study. Participants ranged in age from 18 to 65 years and were currently prescribed a regimen of HIV antiviral combination treatment. Subjects with cognitive impairment, psychosis, or alcohol or drug dependence within the past three months were excluded. Participants filled out questionnaires to measure depressive symptom severity (Beck Depression Inventory) and completed interviews to assess medication adherence over the course of four days.

Among all potential demographic and health-related control variables, only age and alcohol consumption were significantly related to medication adherence. Adherent patients were older and reported less alcohol consumption in the prior week than non-adherent patients. Researchers therefore controlled for these two factors when performing analyses.

Perceived quality of social support was significantly associated with medication adherence, fewer depressive symptoms, and higher levels of positive states of mind. Depression and positive states of mind were each independently related to medication adherence. Depression was negatively associated with adherence, while positive states of mind were positively associated with adherence. The relationship between positive states of mind and medication adherence was independent of depression levels, suggesting that a positive state of mind represents a mindset beyond the mere absence of depression.

Depression and Immunity in Women

A small multisite study of 103 women with HIV found associations between depression and measures of HIV disease
progression, including higher HIV viral loads, higher CD8 cell counts, and lower natural killer cell levels.

Forty-nine women from Pennsylvania—35 HIV-positive and 14 HIV-negative—and 44 women from Florida—28 HIV-positive and 16 HIV-negative—participated in the study. Demographic and behavioral characteristics were similar between the two sites. The racial composition at the sites was predominantly African American: 73 percent in Pennsylvania and 75 percent in Florida. Participants ranged in age from 18 to 69 years old. Researchers excluded women who were pregnant, who had a significant chronic, systemic illness, a significant neurological disorder, or a history of schizophrenia or severe psychotic disorder, or who met the criteria for current substance or alcohol abuse or dependence.

Rates of current major depression did not differ significantly between HIV-positive women (16 percent) and HIV-negative women (10 percent), although HIV-positive women did experience higher levels of depressive symptoms compared to HIV-negative women. Both groups had similar levels of anxiety symptoms.

Depressive symptoms and anxiety symptoms were each significantly associated with higher activated CD8 cell counts and higher viral load levels. CD8 cells may have damaging effects on the immune system in HIV-infected individuals with progressive disease. Further, major depression, depressive symptoms, and anxiety symptoms were each associated with significantly lower natural killer cell activity. Natural killer cells have the capacity to destroy HIV-infected cells and may play a role in the host defense against viral infection.

There was no relationship between major depression, depressive symptoms, or anxiety symptoms and CD4+ cell count, or CD56+ cell count. Because CD4+ cells are affected early and profoundly by HIV infection, this cell population may be more sensitive or reliable measure for demonstrating over time the relationship between depression and HIV.

Depression and Mortality among Women
Cook JA, Grey D, Burke J, et al. Depressive symptoms and AIDS-related mortality among a multisite cohort of HIV-positive women. American Journal of Public Health. 2004; 94(7): 1133–1140. (University of Illinois, Chicago; Mount Sinai Medical Center, New York; Georgetown University Medical Center; and University of California, San Francisco.)

AIDS-related death was more common among HIV-positive women with chronic depressive symptoms than women without depression, according to a large multi-site study on depression.

Researchers recruited 2,059 HIV-positive women from Brooklyn, the Bronx, Chicago, Los Angeles, San Francisco, and Washington, D.C. between October 1994 and November 1995. Using the Center for Epidemiologic Studies Depression Scale (CES-D), they measured depressive symptoms at each six-month visit over the course of 7.5 years. They also collected health-related information and data on AIDS-related deaths.

In order to assess depression longitudinally, researchers excluded women with less than three study visits. Of the remaining 1,716 women, 17 percent died over the course of the study: 9 percent from AIDS-related causes and 9 percent from other causes. Of those who died from AIDS-related causes, 66 percent reported depressive symptoms at their final study visit.

Only 6 percent of the women with few or no depressive symptoms and only 7 percent of the women who experienced intermittent symptoms died from AIDS-related causes. Thirteen percent of the women who experienced chronic depressive symptoms, however, died from AIDS-related causes, and this represented a statistically significant difference. Further, among women with CD4+ cell counts higher than 200 at baseline, those who had chronic depressive symptoms were 2.3 times more likely to die than those who had limited or no depressive symptoms.
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