

Impact of Psychiatric Conditions on Health-Related Quality of Life in Persons With HIV Infection

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Objective: Little is known about the impact of comorbid psychiatric symptoms in persons with HIV. This study estimates the burden on health-related quality of life associated with comorbid psychiatric conditions in a nationally representative sample of persons with HIV.

Method: The authors conducted a multistage sampling of urban and rural areas to produce a national probability sample of persons with HIV receiving medical care in the contiguous United States (N=2,864). Subjects were screened for psychiatric conditions with the short form of the Composite International Diagnostic Interview. Heavy drinking was assessed on the basis of quantity and frequency of drinking. Health-related quality of life was rated with a 28-item instrument adapted from similar measures used in the Medical Outcomes Study.

Results: HIV subjects with a probable mood disorder diagnosis had significantly lower scores on health-related quality of life measures than did those without such symptoms. Diminished health-related quality of life was not associated with heavy drinking, and in drug users it was accounted for by presence of a comorbid mood disorder. **Conclusions:** Optimization of health-related quality of life is particularly important now that HIV is a chronic disease with the prospect of long-term survival. Comorbid psychiatric conditions may serve as markers for impaired functioning and well-being in persons with HIV. Inclusion of sufficient numbers of appropriately trained mental health professionals to identify and treat such conditions may reduce unnecessary utilization of other health services and improve health-related quality of life in persons with HIV infection.

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With improved treatments and longer survival times for persons with HIV infection, the maintenance and improvement of their functioning and well-being (collectively referred to as “health-related quality of life”) have become major goals of treatment. We know

from studies of patient and general populations that mood disorders, particularly depression, have a substantial negative impact on a person’s health-related quality of life. In fact, for most domains of functioning and well-being, depression is more debilitating than most medical conditions (1–3). Anxiety disorders, particularly panic disorder, have also been shown to have a negative impact on social, role, and mental functioning and well-being (4, 5). Very little is known about the impact of other psychiatric conditions, such as alcohol abuse and substance dependence. However, studies have shown that persons in treatment for alcohol dependence and abuse report a much poorer health-related quality of life than subjects from the general population (6). Also, among HIV-infected individuals with a history of injected drug use, those with more severe drug problems report a poorer health-related quality of life (7). When these conditions occur in combination with HIV infection, the overall burden may be particularly great.

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Comorbid psychiatric illnesses, which are associated with diminished health-related quality of life (1, 2, 4) are more common in persons with HIV (8, 9) than in the general population (10). For example, the prevalence of depression in HIV-infected clinic populations has been estimated to range from 22%–32% (9, 11), while recent data from a nationally representative sample of HIV-infected persons receiving care show depression rates of 38% (unpublished 1999 study of E. Bing et al.). These rates are two to three times higher than those seen in general community populations (10). Other comorbid psychiatric illnesses (e.g., generalized anxiety disorder and panic disorder) and substance abuse are also relatively common in persons with HIV (unpublished 1999 study of E. Bing et al.) and result in greater utilization of general medical and mental health services (12). Yet, these conditions, particularly the affective and anxiety disorders, are treatable with psychotherapy and psychopharmacology (3, 13–16). To the extent that these conditions are associated with diminished health-related quality of life independently of the effect of HIV infection itself, their presence can serve as markers for diminished health-related quality of life, regardless of cause, and treatment for these conditions can be encouraged.

A great deal about the impact of HIV has been learned from previous observational studies of adults with HIV infection (17–19), including the considerable decrements in health-related quality of life associated with the progression of HIV itself (20, 21). Yet, little is known about the impact that comorbid psychiatric symptoms have on health-related quality of life in persons with HIV. We could find only one relevant study that assessed the impact of axis I psychiatric disorders on functioning and well-being independently of HIV disease (22). The presence of any axis I disorder was associated with substantial decrements in the health-related quality of life dimensions of mental health, social functioning, and general health perceptions but not of physical health, role functioning, or pain. That study, however, was limited to a small convenience sample (N=95).

This article uses data from a nationally representative probability sample of people receiving care for HIV in the United States to examine the degree to which probable psychiatric conditions are associated with decrements in health-related quality of life in persons with HIV infection. These analyses build on our other work that has documented the morbidity of the disease at different HIV stages and shows the diminished health-related quality of life of persons with HIV compared to that of the general population and of persons with selected other chronic conditions (unpublished 1999 study of R.D. Hays et al.). In this study, we provide information on the impact that three comorbid psychiatric conditions (mood disorders, substance use, and heavy drinking) have on health-related quality of life in persons with HIV infection.

METHOD

Study Design and Sample

Data are taken from the HIV Cost and Services Utilization Study, a nationally representative probability sample of HIV-infected adults who made at least one visit (other than an emergency department visit) to a nonmilitary, nonprison medical provider in the contiguous United States during the period from Jan. 5 to Feb. 29, 1996. Full details of the design are available elsewhere (23).

Multi-stage sampling was used to select patients for enrollment. In the first stage, we randomly selected 28 metropolitan and 24 rural areas in the United States that in total contained nearly 70% of all U.S. cases of AIDS. In the second stage, we randomly selected 1) providers who had been identified by local physicians or public health officials as being known to care for patients with HIV infection and 2) providers who had confirmed in a screening survey that they cared for patients with HIV. Each provider had a probability of selection proportional to the estimated number of patients with HIV he or she was treating. For the first provider category, 100% (N=58) of those from urban areas and 79% (N=22 of 28) of those from rural areas agreed to participate in the study. For the second provider category, 70% (N=61 of 87) of those from urban areas and 83% (N=19 of 23) of those from rural areas agreed to participate.

In the final stage, patients were anonymously and randomly selected from lists of eligible patients seen by the participating providers to maintain a uniform overall probability of selection within subgroups defined by gender and health maintenance organization membership. We approached subjects for interviews only after their providers obtained their permission. Written informed consent was obtained from all subjects after the study had been explained. The RAND institutional review board and, if available, a local board reviewed all forms and materials. Of the 4,042 eligible persons sampled, we conducted a long-form computer-assisted personal interview with 71% (N=2,864).

Measures

Psychiatric conditions. During the baseline interview, all subjects were screened for “any probable mood disorder” (e.g., major depression, dysthymia, generalized anxiety disorder, or panic disorder) using the short form of the World Health Organization’s Composite International Diagnostic Interview (24). The short form was developed to provide brief and accurate diagnosis-specific information and identify persons at high risk for psychiatric disorders. Kessler et al. (24), who used the full Composite International Diagnostic Interview (25) as the standard, found the short form to have moderate to high sensitivity (0.67–0.99) and specificity (0.94–1.00). Concordance between the short form and the full interview for specific disorders was lower in our sample (unpublished 1999 study of M. Orlando et al.). The sensitivity and specificity for the “any mood disorder” category used in this study were 0.80 and 0.76, respectively. Given the high false positive rate of mood disorders, we refer to patients as having “probable” rather than “definite” diagnoses of mood disorder.

The screening instrument for drug use was also based on the short form of the Composite International Diagnostic Interview with minor modifications. Probable drug dependence was defined if any of eight classifications of drugs (sedatives, amphetamines, analgesics, marijuana, cocaine, inhalants, hallucinogens, heroin) had been used in the past year, and if the subject reported using more than intended or having emotional or psychiatric problems from using in the past year. Among those persons who used drugs but were not drug dependent, use was further specified as being either “marijuana only” or “other drug use.” Heavy alcohol use was defined as someone who drank at least half of the days during the 4 weeks before the interview and had three or more drinks on those days.

Health-related quality of life. The instrument used to measure health-related quality of life consisted of 28 items that assessed how well the subjects functioned in physical, mental, and social domains of life (26). The items were based on a broad array of measures developed for the Medical Outcomes Study (27). Eight dimensions of health are measured: physical functioning (nine items), role func-

TABLE 1. Demographic and Clinical Characteristics of 2,864 Subjects Interviewed for the HIV Cost and Services Utilization Study^a

Characteristic	%
Age (years)	
18–29	13
30–34	21
35–39	24
40–44	19
45–49	12
≥50	11
Gender	
Male	77
Female	23
Race/ethnicity	
White	49
African American	33
Hispanic	15
Other	3
Education	
<8 years	6
Some high school	19
High school diploma	27
Some college	47
Marital status	
Married	2
Separated	6
Divorced/widowed	22
Never married	69
Household income	
\$0	4
\$1–5,000	15
\$5,001–10,000	26
\$10,001–17,000	15
\$17,001–25,000	11
\$25,001–40,000	12
\$40,001–55,000	6
≥\$55,001	11
Work	
Full- or part-time	37
Unemployed	7
Disabled	47
Not working	8
Insurance, last 6 months	
No insurance	18
Medicaid	30
Medicare	19
Private insurance	33
Clinical stage	
Asymptomatic	10
Symptomatic	52
AIDS	38

^a Study sample represents 231,400 adults with known HIV infection who were receiving medical care at eligible sites during the first 2 months of 1996.

tioning (two items), pain (two items), general health perceptions (three items), emotional well-being (seven items), social functioning (two items), energy (two items), and disability days (one item). The items within each dimension had a high degree of internal consistency (Cronbach's $\alpha=0.74$ – 0.91). The subdimensions were scored by using simple summated scale methods. Scores were linearly transformed into T scores with a mean of 50 and standard deviation of 10. Higher scores indicate better health-related quality of life. Disability days ranged from 0–28 days in the past 4 weeks.

Physical and mental health composite scores were derived from all subdimensions by means of factor scoring coefficients derived from a two-factor oblique model with a moderate ($r=0.70$) correlation among factors. Final scores for the composites were also transformed linearly into T scores, with estimated reliabilities (28) of 0.96 and 0.94, respectively. The composites provide a global sense for

whether comorbid conditions are associated with physical and mental health, whereas the subdimensions provide detailed information about how the conditions affect the specific profile of health-related quality of life. Emotional-well being was not studied separately because of its high ($r=0.98$) correlation with the mental health composite score.

Other covariates. A variety of demographic and clinical data, obtained as part of the interview, were included as controls in multivariate models. Demographic variables included age, gender, race, education, annual income, and occupational status. Clinical data included self-reported immune function (lowest CD4 cell count), HIV disease stage, and 13 HIV-related clinical symptoms experienced in the previous 6 months (new or persistent headaches; fevers, sweats, or chills; pain in the mouth, lips, or gums; white patches in the mouth; painful rashes or sores on the skin; nausea or loss of appetite; trouble with the eyes; a sinus infection, pain, or discharge; numbness or tingling in the hands or feet; Kaposi's sarcoma lesions; persistent cough or difficulty breathing; diarrhea or watery stools; and weight loss). Recent findings suggest that self-report CD4 data provide good estimates of true CD4 counts (29).

We imputed missing values for covariates and health-related quality of life measures by using a standard hot-deck strategy (30). We imputed 4.9% of the CD4 cell count values, less than 4% of the income values, less than 3% of the values for health-related quality of life measures, and less than 0.5% of the missing values for other variables.

Analysis

Multiple linear regression analyses were conducted to examine both the total and unique relationship of psychiatric conditions to health-related quality of life, controlling for demographic and clinical characteristics. The disability days measure was the only dependent variable with a skewed distribution. Because analyses using log of disability days found similar results, for simplicity, we report analyses from the nontransformed analysis. Models were estimated with each psychiatric condition entered singly (total relationship) and again with all entered simultaneously (unique relationship). Interactions between different psychiatric conditions were examined to see if the burden associated with these comorbid psychiatric conditions was greater with multiple conditions. All models included controls for the aforementioned covariates. We adjusted for multiple comparisons by using the method developed by Hochberg (31).

Data from each respondent were weighted to assure valid inference to the reference population by using an analytic weight (which can be interpreted as the number of persons represented by that respondent). This weight is constructed from the product of the "sampling weight" (which adjusts for differential sampling probabilities), a "multiplicity weight" (which adjusts for patients who could have entered the sample through their visits to multiple providers), and a "nonresponse" weight (which adjusts for differences in rates of cooperation). To compensate for the complex multistage sampling design and differential weighting, we adjusted all standard errors and statistical tests by means of linearization methods (32).

RESULTS

The sample of 2,864 patients with full interview data from the HIV Cost and Services Utilization Study represents 231,400 adults with known HIV infection receiving medical care at eligible sites during the first 2 months of 1996. Table 1 shows demographic and clinical characteristics of this population.

As seen in table 2, the screening instrument detected a probable diagnosis of any mood disorder during the previous 12 months in nearly half the sample (specific probable diagnoses within this group included depression [36%], dysthymia [26%], generalized anxiety disorder [16%], and panic disorder [11%]). Screening for

TABLE 2. Health-Related Quality of Life Scores of HIV-Infected Subjects With and Without Probable Psychiatric Conditions^a

Health-Related Quality of Life Measure	Any Mood Disorder				Heavy Drinking				Drug Use							
	Yes (N=1,423)		No (N=1,441)		Yes (N=176)		No (N=2,683)		Marijuana Only (N=341)		Other Drugs, No Dependence (N=744)		Dependence (N=368)		No Drugs (N=1,407)	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Physical composite	48.1 ^b	0.3	51.7	0.2	50.6	0.4	50.0	0.2	50.4	0.3	50.3	0.3	48.5	0.6	50.1	0.3
Mental composite	45.6 ^b	0.3	54.1	0.2	49.4	1.0	50.1	0.2	51.0 ^c	0.5	49.4 ^{b,d}	0.4	46.7 ^b	0.6	50.9	0.3
Physical functioning	49.6 ^b	0.3	51.4	0.3	51.5	0.4	50.5	0.2	51.1	0.4	50.9	0.3	49.8	0.7	50.4	0.3
Role functioning	49.4 ^b	0.3	51.4	0.3	51.1	0.4	50.4	0.3	50.4	0.4	51.2	0.3	50.1	0.6	50.2	0.3
Pain	49.0 ^b	0.2	51.5	0.2	50.1	0.6	50.3	0.2	50.4	0.4	50.5	0.4	48.4 ^e	0.7	50.6	0.3
General health	48.7 ^b	0.3	52.4	0.2	50.6	0.5	50.6	0.2	50.8	0.4	50.7	0.3	49.9	0.5	50.7	0.2
Social functioning	47.3 ^b	0.4	53.4	0.3	51.4	0.7	50.4	0.2	51.1 ^f	0.5	50.2 ^{d,g}	0.3	48.2 ^b	0.6	51.1	0.3
Energy	48.2 ^b	0.3	52.4	0.2	51.0	0.6	50.3	0.2	51.3 ^f	0.4	50.4 ^d	0.3	48.3 ^h	0.7	50.6	0.2
Disability days	4.2 ^b	0.2	3.0	0.2	3.9	0.3	3.6	0.1	3.3	0.2	3.5	0.2	4.6	0.6	3.4	0.1

^a Health-related quality of life measures except for disability days (which range from 0 to 28 days in the past month) were linearly transformed to T scores with a mean of 50 and standard deviation of 10. Two tailed t tests were used to compare groups (df range=2820–2827 owing to missing data).

^b Significantly different from the group without the condition ($p<0.0001$).

^c Significantly different from subjects reporting other drug use ($p=0.02$) and drug dependence ($p<0.001$).

^d Significantly different from subjects with drug dependence ($p=0.01$).

^e Significantly different from the group without the condition ($p=0.006$).

^f Significantly different from subjects with drug dependence ($p<0.001$).

^g Significantly different from the group without the condition ($p=0.005$).

^h Significantly different from the group without the condition ($p=0.002$).

drug abuse resulted in 12% being classified as dependent on drugs, 12% as marijuana users only, and 26% as users of other drugs. Six percent of the sample were classified as being heavy drinkers.

Table 2 also presents the health-related quality of life composite scores for subjects with and without probable psychiatric conditions, controlling for demographics and other covariates. These results are from models with each psychiatric condition entered separately and thus represent the total relationship between each probable condition and health-related quality of life. Subjects with a probable diagnosis of any mood disorder had significantly worse functioning and well-being than those without a mood disorder diagnosis on all health-related quality of life measures, including the physical and mental health composites (all t values >4.43 , $df=2827$, all p values <0.0001 using a two-tailed test). The magnitude of differences in health-related quality of life scores between subjects with and without probable mood disorders were smaller for the physical health subscales and composite (effect sizes ranged from 0.2 SD to 0.4 SD) than for the mental health subscales and composite (effect sizes ranged from 0.4 SD for energy, 0.6 SD for social functioning, and 0.8 SD for the mental health composite).

The health-related quality of life of subjects who reported heavy drinking did not differ from those who did not drink heavily. The health-related quality of life of subjects who reported marijuana use only did not differ from subjects who reported no drug use. Subjects who reported other drug use but not dependence had significantly lower mental health ($t=4.16$, $df=2820$, $p<0.0001$) and social functioning ($t=2.92$, $df=2820$, $p=0.005$) scores than did subjects who reported no drug use. Probable drug dependence was negatively related to the mental composite scores ($t=5.67$, $df=$

2820, $p<0.0001$) and the subdimensions of freedom from pain ($t=2.87$, $df=2820$, $p=0.006$), social functioning ($t=3.99$, $df=2820$, $p<0.0001$), and energy ($t=3.20$, $df=2820$, $p=0.002$).

There were health-related quality of life differences among subjects reporting different types of drug use. Subjects who reported using marijuana only or who reported other drug use (but not dependence) had significantly better levels of mental health (composites), social functioning, and more energy than did subjects with substance dependence ($t=2.60$ – 6.42 , $df=2821$, $p=0.02$ to <0.0001).

Models were also estimated with each psychiatric condition entered simultaneously to test the unique relationship of each condition with health-related quality of life. Results for any mood disorder and heavy drinking were similar to those reported for the total relationship models. In all cases, the health-related quality of life burden was most severe in subjects with a probable mood disorder diagnosis. The relationship between health-related quality of life and drug use became weaker. After controlling for presence of any mood disorder and heavy drinking, subjects with probable drug dependence only differed in their mental health composite score ($t=3.54$, $df=2814$, $p=0.001$) from persons without any psychiatric condition. Differences among categories of drug use were also less pronounced after controlling for other psychiatric conditions.

Only three of 64 tests of interactions among psychiatric conditions were significant (presumably due to chance), which suggests that the burden on health-related quality of life related to comorbid psychiatric conditions was not greater than the additive effect for subjects with combinations of mood disorders, substance dependence, and alcohol use.

DISCUSSION

This study is the first to show in a nationally representative sample of persons with HIV infection the detrimental burden on health-related quality of life associated with comorbid psychiatric conditions. HIV subjects with a probable diagnosis of any mood disorder had poorer physical and mental health and well-being than did those without such symptoms. While the relationship of mood disorders to mental functioning is to be expected, since one is defined substantially by the other, the additional burden in all subdomains including physical health, role functioning, pain, general health perceptions, and disability days is noteworthy. The effect sizes are not large for the physical health measures. However, the difference of 0.3 SD for the physical health composite is equal to the difference between working and being unemployed in the whole sample (unpublished 1999 study of R.D. Hays et al.). These results do not reflect differences in HIV disease stage, which was controlled for in the analyses. These results are in contrast to those reported before on a convenience sample of persons with HIV (22) but substantiate the considerable additional illness burden associated with mood/anxiety disorders in persons experiencing other physical illnesses (1–3).

Heavy drinking was not associated with diminished health-related quality of life. Our measure of heavy drinking may not have segregated those at the most severe end of the drinking continuum from those whose drinking was moderate but not necessarily morbid. However, other analyses (data not shown) with an alternate measure that focused on moderate and binge drinkers (low binge: drank in past month and had five or more drinks on 1–4 days; high binge: five or more drinks on more than 4 days) found similar nonsignificant results. Other studies that have found diminished health-related quality of life in persons being treated for alcohol abuse and dependence may have been capturing a more severely ill population (15).

Probable drug dependence was associated with poorer health-related quality of life, although most of this impairment disappeared after controlling for presence of a probable mood disorder. Users of drugs other than marijuana but who were not dependent did have lower mental health and social functioning—but not physical health—scores than did nonusers. However, these differences also became nonsignificant after controlling for presence of a probable mood disorder. These results are in contrast with the severe social and role functioning disabilities that typify people seen in treatment for drug dependence (16). It may be that depression and anxiety are so intrinsic to the problems of drug dependence that there is little relationship between dependence and health-related quality of life after adjusting for mood disorders. This may be supported by the fact that in our sample, 76% of subjects with drug dependence also had a mood disorder. Alternately, it may be that the people usually seen in treatment for drug dependence have more severe limita-

tions than the present sample because they are in treatment for chronic problems (e.g., poor employment history). These chronic problems that define a treatment sample may not be captured by our drug use measures, which ask about drug use in the past 12 months regardless of whether the respondent was currently or ever in treatment. There is some evidence in the literature that substance abusers who do seek care are different than those who do not and tend to be more dysfunctional (33).

Previous research has shown that mood disorders, especially depression, have a strong impact on a person's daily functioning (10, 34, 35), yet they often go undetected and untreated in general practice (36). In addition, limitations in functioning and well-being in persons with symptoms that do not reach the threshold for disorder often persist over time (2), possibly due to untreated or partially treated depression. HIV itself is associated with diminished health-related quality of life, especially during the later stages of the disease (20). This study found additional burden on health-related quality of life associated with comorbid mood disorders after controlling for HIV symptoms, CD4 count, and stage of disease. To provide a sense of the magnitude of burden, previous analyses showed that while the average score on physical and mental health aggregates in the sample was 50 (SD=10), those scores for patients with the lowest CD4 levels were 49.58 and 48.80, respectively, compared to 50.91 and 51.14 for those with the highest CD4 levels (unpublished 1999 study of R.D. Hays et al.). In comparison, physical and mental composite scores for patients with any mood disorder were 48.1 and 45.6 while those for patients with drug dependence were 48.5 and 46.7.

Our study has several limitations. First, the screening tests for anxiety and mood disorders, drug dependence, and alcohol abuse, although high in sensitivity and specificity in a general population, have lower concordance in persons with HIV (unpublished 1999 study of M. Orlando et al.). Although the short form of the Composite International Diagnostic Interview provides useful information about mental health distress in HIV-positive adults, it is less accurate for providing disorder-specific diagnoses in this population. In particular, there appears to be some confounding of HIV symptomatology and interview-defined caseness. However, while subjects identified may not have these disorders, they may, in fact, have subthreshold symptoms and be at high risk for developing the full psychiatric or drug use disorders. Given the consistently poorer health-related quality of life associated with these symptoms, it is expected that the burden would be even greater in persons with the disorders (10). Second, data are from cross-sectional analyses and do not address issues of the causal relationship between psychiatric symptoms and health-related quality of life.

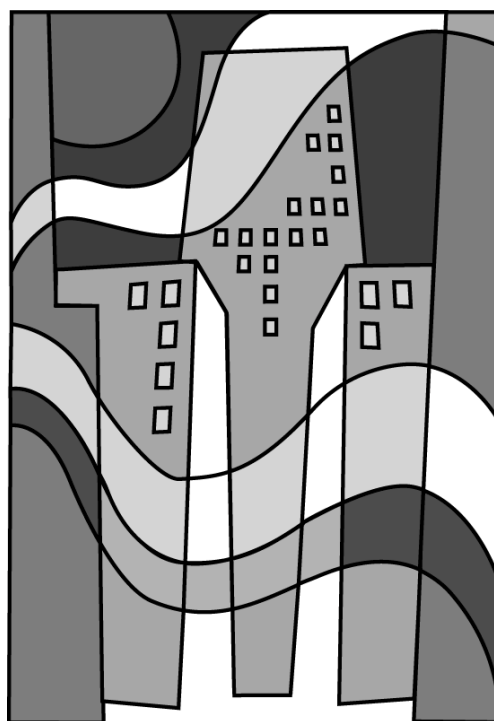
The fact that the health-related quality of life of HIV-infected persons with probable psychiatric comorbidity, as measured by these screening tests, was diminished suggests that these conditions are clinically

important and should be identified and treated early, regardless of confirmed disorder status. Such treatment may reduce total utilization of health services and improve health-related quality of life. These initial results show no additional decrement in health-related quality of life associated with heavy alcohol use or marijuana and other drug use. It will be important to confirm whether or not the lack of relationship between health-related quality of life and these conditions remains for subjects at the severe end of the use/abuse continuum and for those currently in treatment. Improvement in health-related quality of life is particularly important now that HIV is a chronic disease with the prospect of long-term survival. Comorbid mood disorders may result in poorer prognosis and response to treatment for persons with HIV, and the associated poor health-related quality of life may be one of the most important indicators of overall disease status. The high prevalence of mood disorders in persons with HIV emphasizes the need for coordinated general medical and mental health services and joint management plans for this population. Sufficient numbers of appropriately trained mental health professionals are needed at the clinical level to provide needed assessments and interventions to this at-risk population.

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