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# A Cross-Lagged Model of Psychiatric Problems and Health-Related Quality of Life Among a National Sample of HIV-Positive Adults

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**Objectives:** To investigate the temporal association between symptoms of psychiatric disorder and physical aspects of health-related quality of life (HRQOL) in a sample of HIV-positive adults.

**Methods:** Sample included 2431 participants at baseline and the first follow-up (FU1; approximately 8 months later). Measures included 4 components of HRQOL (general health, lack of pain, physical functioning, and role functioning), and psychiatric symptoms of depressive and anxiety disorders. Covariates included demographics, and clinical and substance use-related measures. A series of regression equations was estimated to construct the cross-lagged path model. Results depicted the relationships among the 4 HRQOL components and 2 types of psychiatric symptoms over time. This model included stability effects for each measure and cross-lagged effects from both the psychiatric measures at baseline to each of the HRQOL components at FU1 and from each of the 4 HRQOL components at baseline to the psychiatric measures at FU1.

**Results:** After controlling for stability effects and covariates, symptoms of depressive disorder at FU1 were significantly predicted by baseline general health and physical functioning, whereas symptoms of anxiety disorder at FU1 were significantly predicted by baseline general health and lack of pain. Anxiety symptoms at baseline did not significantly predict FU1 HRQOL, but baseline depressive symptoms were significant predictors of general health and lack of pain at FU1.

**Conclusion:** Responses from a sample of HIV-positive adults at 2 time points approximately 8 months apart provide evidence for a

reciprocal relationship between symptoms of psychiatric disorder and physical aspects of HRQOL.

**Key Words:** HIV, psychiatric problems, health-related quality of life, cross-lagged

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A significant reduction in mortality among individuals with human immunodeficiency virus (HIV) has resulted from earlier detection of the virus and improvements in antiretroviral therapies.<sup>1</sup> However, patients living with HIV still report lower health-related quality of life (HRQOL) and higher rates of psychiatric problems compared with the general population.<sup>2,3</sup> In light of the longer survival time for HIV-infected patients, optimizing their quality of life and minimizing their risk for psychiatric problems have become important goals in their medical care. Gaining a clearer understanding of how the functioning, well-being, and mental health of HIV-infected patients affect one another, both adversely and favorably, is an integral step in achieving these goals.

Although psychiatric problems and HRQOL are positively associated, a conceptual distinction can be made between them in terms of both specificity and severity. HRQOL is a fairly general term that refers to the entire range of individual functioning, as well as perceptions of one's own physical, mental, and social well-being. The mental health component of HRQOL is equally broad in that it is designed to cover the range of general mental distress. In contrast, psychiatric problems, assessed through patients' reported experience of clusters of mental health symptoms, are more specific to diagnostic mental health functioning, and their presence may imply a need for targeted treatment.

The presence of psychiatric problems has been associated with poorer functioning and well-being in several studies. Depressed individuals have worse physical, social, and role functioning; worse perceived current health; and greater bodily pain than nondepressed individuals. In fact, the poor

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functioning uniquely associated with depressive symptoms has been found to be comparable with or worse than that uniquely associated with chronic medical illnesses.<sup>4–6</sup> Individuals with panic disorder also tend to show decrements in HRQOL compared with those with other major chronic medical conditions.<sup>7</sup> However, there is some evidence that the lower HRQOL among individuals with anxiety disorders primarily occurs in the domains of emotional well-being and functioning, rather than physical functioning and perceived current health.<sup>7,8</sup> In general, depressive and anxiety disorders account for significantly more of the variance than medical disorders in the role functioning, social functioning, and general health aspects of quality of life.<sup>9</sup>

The potential detrimental effect of mental health symptoms on HRQOL is particularly important to consider in the case of HIV-infected individuals, given the relatively high rates of psychiatric problems that have been found in this population. For example, data from the HIV Cost and Services Utilization Study (HCSUS; the same database used in this paper) indicated that the prevalence of probable psychiatric disorder (assessed after antiretroviral combination therapies became widely available) was 19% for depression, 13% for panic disorder, 4% for dysthymia, and 3% for generalized anxiety disorder.<sup>3</sup> With the exception of generalized anxiety disorder, these rates are substantially higher than the prevalence of psychiatric disorders found in the National Comorbidity Survey of the general US population.<sup>10</sup> However, few studies have investigated whether comorbid psychiatric problems are associated with poorer HRQOL in persons with HIV. Holmes et al<sup>11</sup> found that having an axis I psychiatric disorder was associated with lower HRQOL, notably poorer mental health and worse health perceptions, in a convenience sample of 95 HIV-positive men. Associations were not found with physical functioning, role functioning, or pain. Findings from HCSUS significantly extended this research by investigating whether having a probable depressive disorder based on the Composite International Diagnostic Interview–Short Form (CIDI-SF)<sup>12</sup> was associated with poorer HRQOL in a larger, more representative sample of HIV-positive adults. The CIDI-SF is a screener for disorder-specific psychiatric symptoms, and endorsement of symptoms on the screener are used to determine probable diagnosis. Results indicated that patients with a probable depressive disorder had significantly worse physical and role functioning, more pain, and poorer general health than patients without a probable disorder.<sup>13</sup>

A limitation of existing research is that it has mostly been cross-sectional. As a result, there is limited empiric evidence suggesting that psychiatric problems are causally related to HRQOL, both in the general population and among HIV-positive adults specifically. Even less work has addressed whether this association is unidirectional or reciprocal. Several prospective studies of patients with HIV have indicated that increases in depressive symptomatology over

time are associated with increases in physical symptomatology.<sup>14–16</sup> However, it is also possible that lower levels of physical functioning and well-being among persons with HIV contribute to the onset or escalation of depression, anxiety, and other psychiatric problems, as has been found with other physical conditions.<sup>17–19</sup>

The current study significantly extends our previous cross-sectional research on the relationship between psychiatric problems and HRQOL<sup>13</sup> by examining the nature of their temporal association over an 8-month period in a nationally representative probability sample of HIV-positive patients receiving care in the contiguous United States. Path modeling was used to conduct cross-lagged panel analyses assessing associations between symptoms of both depressive and anxiety disorders, and 4 physical components of HRQOL assessed in the HCSUS: general health, lack of pain, physical functioning, and role functioning. We limited our analyses to these 4 components because we were most interested in the association between psychiatric problems and physical aspects of HRQOL, rather than those with an emotional component (ie, emotional well-being, social functioning, and energy) that would be expected to overlap conceptually with psychiatric problems. To strengthen the conclusions that we can draw regarding the contribution of psychiatric symptoms to changes in functioning and well-being, we controlled for the patients' disease state in that the progression of HIV/AIDS itself is associated with significant decrements in HRQOL.<sup>20–23</sup> We also took into account patients' engagement in drug use and heavy alcohol use, given the frequent co-occurrence of substance use and mental health problems,<sup>24</sup> as well as its association with HRQOL.<sup>13</sup> We expected to find substantial stability effects for psychiatric problems and HRQOL over the 8-month follow-up period. In addition, in light of what is currently known, we expected to find evidence for either unidirectional or reciprocal causal links between depressive and anxiety disorder symptoms and each of the 4 physical components of HRQOL over time.

## METHOD

### Study Design

We analyzed data from the HCSUS. This probability sample of 2864 HIV-infected adults represents all 231,400 such patients in care in the contiguous United States in early 1996.<sup>25</sup> Using 3 stages of sampling, we selected 28 metropolitan statistical areas and 24 clusters of rural counties,<sup>26</sup> followed by 58 urban and 28 rural HIV providers from selected areas, and finally selected subjects from deidentified lists of patients who visited participating providers during the population definition period. Full details of the design are available elsewhere.<sup>27,28</sup>

## Participants and Interviews

The reference population was those at least 18 years old with known HIV infection who made at least 1 patient care visit between January 5 and February 29, 1996, at a site other than military, prison, or emergency medical departments. The RAND institutional review board and, when available, a local board reviewed and approved all forms, materials, and procedures. This study uses data from the first 2 interviews conducted January 1996 to March 1997 (baseline,  $n = 2864$ ) and January 1997 to July 1997 (first follow-up [FU1],  $n = 2466$ ). Of the 398 participants who were interviewed only at baseline, 40% ( $n = 160$ ) dropped out due to mortality. Our analyses are based on 2431 individuals who participated in both interviews and had complete information for all study measures.

## Study Variables

### Health-Related Quality of Life

Four components of HRQOL were assessed at both interviews. All questions were framed to reflect respondents' impressions during the past 4 weeks. General health was measured as the average of responses to participants' ratings of their health (1 = excellent to 5 = poor), and 2 items reflecting participants' extent of agreement with the statements "I seem to get sick a little easier than other people" and "I have been feeling bad lately" (1 = definitely true to 5 = definitely false). Cronbach  $\alpha$  for this 3-item scale was 0.80. Respondents' lack of pain score was based on responses to 2 items ( $\alpha = 0.84$ ) indicating the extent to which pain interfered with work (1 = not at all to 5 = extremely) and severity of bodily pain (1 = none to 6 = very severe). Physical functioning was measured with 9 items ( $\alpha = 0.91$ ) indicating respondents' limitations in performing activities such as climbing a flight of stairs, shopping, walking 1 block, and preparing meals or doing laundry (1 = yes, limited a lot to 3 = no, not limited at all). The role functioning score was based on responses to 2 items ( $\alpha = 0.85$ ) reflecting whether health has prevented respondents' ability to (1) work at a job, do work around the house, or go to school; and (2) do certain kinds or amounts of work, housework, or schoolwork (1 = yes, for all of the time to 3 = none of the time; Hays et al, unpublished).<sup>2</sup> For the analyses reported here, all component scores were rescaled to range from 0 to 10 points, with higher scores reflecting better HRQOL.

### Psychiatric Symptoms

Continuous symptom scores ranging from 0 to 4 points were derived for major depression, dysthymia, general anxiety disorder (GAD), and panic disorders based on responses to the CIDI-SF,<sup>12</sup> administered as part of the baseline and FU1 surveys. The original CIDI-SF scoring corresponded to the number of symptoms endorsed for each disorder, and yielded scores from 0 to 7 points for depression, 0 to 4 points

for dysthymia, 0 to 7 points for GAD, and 0 to 6 points for panic. We obtained comparable score ranges across disorders by collapsing the symptom scores and recoding the depression, GAD, and panic scales to range from 0 to 4 points.<sup>3</sup> From these 4 scales, we derived 2 psychiatric symptom scores, each ranging from 0 to 8 points, for both the baseline and FU1 samples. The first reflected symptoms of a depressive disorder and was calculated as the sum of the derived depression and dysthymia scales; the second, reflecting symptoms of an anxiety disorder, was calculated as the sum of the derived GAD and panic disorder scales.

### Covariates

All covariates were measured at the baseline assessment and included demographic information regarding participants' gender, ethnicity, age, and education level, as well as 4 measures reflecting respondents' HIV clinical status and 2 substance use measures. Participants were classified into one of 3 HIV disease stages (asymptomatic, symptomatic, and AIDS) and were also asked to report their most recent CD4<sup>+</sup> count (less than 50, between 50 and 200, between 200 and 500, and greater than 500). Participants also identified whether they experienced any of 13 HIV-related physical symptoms in the previous 6 months.<sup>29</sup> Due to potential overlap between HIV physical symptoms and mental health-related symptoms,<sup>30</sup> responses to the 5 questions (fevers, chills, or sweats; pain in the mouth, lips, or gums; white patches in the mouth; painful rashes or sores on the skin; a sinus infection) with the least likelihood of overlap were summed to create a 0- to 5-point count of HIV-related physical symptoms. Finally, participants indicated whether they had received antiretroviral drugs during the 6 months prior to baseline. A dichotomous summary measure of any illicit drug use in the past 30 days was derived based on participants' indicated use of each of 8 classes of drugs (heroin, cocaine, amphetamines, marijuana, inhalants, sedatives, analgesics, and hallucinogens) in the past 30 days "without a doctor's prescription, in larger amounts than prescribed, or for longer periods than prescribed." Participants' description of the quantity and frequency of their alcohol consumption during the past 4 weeks was used to create a dichotomous summary measure of engagement in any heavy drinking (defined as 5 or more drinks on 1 occasion). The time between baseline and FU1 interviews was used to control for variation in interview gaps.

### Analyses

To examine the causal relationship between the 4 physical components of HRQOL and the 2 psychiatric symptom measures, we estimated a series of multivariate regression models to obtain the components of the complete cross-lagged path analytic model using Stata version 6 statistical software.<sup>31</sup> A total of 6 models were estimated. The set of

independent variables for each model was identical. Models differed only with respect to the dependent variables, which included 1 of each of the FU1 measures of general health, lack of pain, physical functioning, role functioning, depressive disorder symptoms, and anxiety disorder symptoms. Independent variables in each of the 6 models included baseline demographic, clinical, and substance use covariates; and baseline measures of general health, lack of pain, physical functioning, role functioning, depressive disorder symptoms, and anxiety disorder symptoms. All models adjusted standard errors for the complex survey design using Stata's linearization methods, and incorporated analytic weights, which allow extrapolation of the results to the represented target population.<sup>27</sup>

## RESULTS

### Sample Description

The 2431 respondents in this study were an average age of  $38.81 \pm 8.71$  years (standard deviation), with 23% female, 50% white, 32% black, 15% Hispanic, and 3% of some other ethnicity. Twenty-four percent of the sample had less than a high school education, 28% had a high school diploma, 28% had some college education, and 20% had earned a bachelor's degree or higher. At baseline, most of the sample was in the symptomatic stage (53%), with 11% asymptomatic and 36% classified as having AIDS. Only 10% of the sample had CD4 counts at or above 500 at baseline; 39% were between 200 and 500, 30% were between 50 and 200, and 21% had CD4 counts less than 50. Participants reported an average of 1.58 HIV-related symptoms at baseline, and 24% had been exposed to antiretroviral drugs 6 months prior to the baseline survey. With respect to the substance use variables, 6% of the baseline sample was classified as heavy drinkers and 11% were classified as drug users.

Table 1 lists the means and standard errors for the baseline and FU1 measures of HRQOL and psychiatric symptoms used in the path model. All 4 components of HRQOL improved slightly from baseline to FU1, and both types of

psychiatric symptoms declined during this period. This general positive trend in outcomes has been acknowledged in other studies of these data and has been linked to the fact that the time period between study measurements coincided with the dissemination of HAART.<sup>29,32</sup>

### Cross-lagged Model Results

Our series of equations tested the cross-lagged associations from baseline to FU1 among general health, lack of pain, physical and role functioning, and symptoms of depressive and anxiety disorders controlling for relevant participant characteristics. Table 2 lists the path coefficients of interest (ie, those involving the HRQOL and psychiatric measures) from this model along with their standard errors. All 6 stability effects were strong and significant. The cross-lagged results between the 4 HRQOL components and 2 psychiatric symptom measures revealed a largely reciprocal relationship: More positive values of general health at baseline were predictive of fewer depressive and anxiety symptoms at FU1, higher baseline physical functioning was associated with fewer depressive symptoms at FU1, and greater lack of pain was predictive of fewer anxiety symptoms at FU1. Conversely, although anxiety symptoms at baseline were not associated with FU1 measures of HRQOL, higher depressive disorder symptom counts were associated with poorer values of general health and greater pain at FU1.

Although not of main interest in this study, we note several predictive associations among the 4 HRQOL components from baseline to FU1. General health at baseline was positively associated with lack of pain and physical and role functioning at FU1; lack of pain at baseline was predictive of general health and physical functioning; physical functioning at baseline showed positive relationships with general health, lack of pain, and role functioning at FU1; and role functioning at baseline was predictive of physical functioning at FU1. Finally, symptoms of depressive and anxiety disorder were positively associated with each other over time.

## DISCUSSION

This study is the first to demonstrate reciprocal cross-lagged associations between psychiatric symptoms and physical components of HRQOL among HIV-positive adults. Patients who initially had a greater number of symptoms of depressive disorder showed increased pain and declines in general health perceptions over an 8-month follow-up, and patients who initially had higher perceptions of general health, lack of pain, and physical functioning exhibited significant decreases in the number of symptoms of either depressive or anxiety disorders or both. Considering the psychiatric symptom variables together, the association between these symptoms and the general health and lack of pain components of HRQOL was largely reciprocal. However, we did not find the expected reciprocal associations of either type

**TABLE 1.** Descriptive Statistics for HRQOL and Psychiatric Symptom Measures

Study Variable	Baseline, Mean (SE)	First Follow-Up, Mean (SE)
General health	5.53 (0.13)	5.86 (0.12)
Lack of pain	6.97 (0.10)	7.32 (0.09)
Physical functioning	8.05 (0.11)	8.14 (0.11)
Role functioning	6.84 (0.13)	7.12 (0.15)
Depressive disorder symptoms	1.79 (0.08)	1.39 (0.08)
Anxiety disorder symptoms	0.72 (0.05)	0.52 (0.04)

**TABLE 2.** Cross-Lagged Path Coefficients for 4 HRQOL Components and 2 Measures of Psychiatric Symptoms at First Follow-Up

Baseline	General Health	Lack of Pain	Physical Functioning	Role Functioning	Depressive Symptoms	Anxiety Symptoms
General health	0.39 (0.03) <sup>†</sup>	0.07 (0.02) <sup>†</sup>	0.06 (0.02) <sup>†</sup>	0.14 (0.04) <sup>†</sup>	-0.10 (0.02) <sup>†</sup>	-0.03 (0.01)*
Lack of pain	0.07 (0.02) <sup>†</sup>	0.32 (0.03) <sup>†</sup>	0.06 (0.02)*	0.04 (0.03)	-0.04 (0.02)	-0.04 (0.01) <sup>†</sup>
Physical functioning	0.06 (0.03)*	0.12 (0.03) <sup>†</sup>	0.37 (0.03) <sup>†</sup>	0.23 (0.04) <sup>†</sup>	-0.06 (0.02)*	-0.03 (0.02)
Role functioning	0.04 (0.02)*	0.00 (0.02)	0.08 (0.02) <sup>†</sup>	0.28 (0.03) <sup>†</sup>	0.01 (0.03)	0.02 (0.01)
Depressive symptoms	-0.11 (0.03) <sup>†</sup>	-0.09 (0.02) <sup>†</sup>	-0.02 (0.02)	-0.04 (0.03)	0.30 (0.03) <sup>†</sup>	0.09 (0.02) <sup>†</sup>
Anxiety symptoms	-0.03 (0.03)	-0.03 (0.04)	-0.01 (0.04)	0.02 (0.05)	0.16 (0.03) <sup>†</sup>	0.20 (0.04) <sup>†</sup>

\* $P < 0.05$ . <sup>†</sup> $P < 0.01$ .

Path coefficients are from multivariate regression models that also included baseline measures of gender, ethnicity, age, education level, HIV stage, most recent CD4<sup>+</sup> count, experience of 5 HIV-related symptoms, receipt of ARVs, illicit drug use, and heavy alcohol use.

of psychiatric symptoms with the physical or role functioning components of HRQOL. In the case of physical functioning, the temporal association was unidirectional, with initially poorer physical functioning associated with increases in the number of depressive symptoms over time. The lack of temporal association from psychiatric symptoms to declines in physical functioning may have been due to the relatively short follow-up period in this study. There is some evidence for delayed adverse health effects due to psychiatric morbidity.<sup>6,33</sup> Thus, we may have found the expected reciprocal effects if examined over a longer period of time. It is also possible that physical functioning was not predicted by depressive or anxiety symptoms because it is a relatively more objective measure than perceptions of general health or lack of pain.

Role functioning was not temporally related to either type of mental health symptom in our analyses. This was somewhat surprising in light of our previous cross-sectional analyses demonstrating that patients with a probable depressive disorder reported poorer role functioning than other patients.<sup>13</sup> This lack of temporal association may imply that there is no time lag between psychiatric symptoms and role functioning. That is, perhaps poorer role functioning (eg, unable to do household chores) is an expression of depression or other psychiatric symptoms that is evident immediately, and recovery from psychiatric symptoms is coincident with increased role functioning.

Earlier we noted the conceptual overlap between mental health components of HRQOL and psychiatric problems. An alternative analysis could have examined the cross-lagged associations between the mental and physical aspects of HRQOL rather than introducing psychiatric symptoms. Our rationale for examining psychiatric symptoms rather than the mental health components of HRQOL was that endorsement of these symptoms can be indicative of more than a general feeling of distress. Not only are the psychiatric symptom

measures disorder specific, they also reflect potentially serious mental health problems that can be alleviated with targeted treatments. To ensure that this distinction held up empirically, we ran sensitivity analyses that included the baseline measure of emotional well-being as an independent variable in the 6 regression models and found that the pattern of cross-lagged associations involving the psychiatric symptom variables remained stable with the inclusion of this variable. These results lend support to the notion that although psychiatric symptoms and emotional well-being overlap conceptually, psychiatric symptoms reflect something unique that is worthy of study.

The reciprocal nature of the association between psychiatric symptoms and certain physical components of HRQOL emphasizes the importance of addressing poor HRQOL among HIV-infected individuals, as well as detecting and treating psychiatric problems in this population. Given that improvements in HRQOL can lead to improved mental health, identifying and treating HIV-positive people experiencing high levels of pain, for example, may prevent development and escalation of mental health symptomatology. On the other hand, adequately addressing psychiatric problems in this population should result in improved functioning and well-being. Indeed, several studies have shown that antidepressant treatment of major depression<sup>34,35</sup> and dysthymia<sup>36</sup> improves HRQOL compared with placebo (for an exception, see Elliott et al<sup>37</sup>). Such improvements in HRQOL, in turn, should prevent further psychiatric morbidity. Despite effective therapies for depressive and anxiety disorders, psychiatric illness among patients often goes undetected, as noted by others.<sup>38,39</sup> Given the relatively high prevalence of psychiatric disorders among HIV-positive patients,<sup>40-43</sup> and the reciprocal associations with HRQOL demonstrated in this study, it is particularly important to increase awareness of mental health issues among health professionals working with this population, and to emphasize

the importance of identifying psychiatric symptoms and referring patients with such symptoms for treatment as appropriate.

Strengths of this study include the large nationally representative sample of HIV-positive patients and the use of cross-lagged analyses to examine reciprocal associations among psychiatric symptoms and HRQOL. Another strength of this study is that we examined these associations controlling for HIV disease stage, HIV-related symptoms, and recent drug use and heavy drinking, all of which could affect patients' reports of mental health symptoms and HRQOL. Several study limitations should also be noted. First, the sample is restricted to patients receiving HIV care; thus, findings may not be generalizable to HIV-positive patients not in care. Second, all data are based on self-report. Third, the correlational design of this study precludes us from drawing strong conclusions regarding the causal relationship between psychiatric symptoms and HRQOL, although this study provides some of the best evidence to date that a causal association exists. Fourth, the time frame between assessments was only 8 months, and results may not generalize to longer time frames. Unfortunately, available data precluded study of these relationships over a longer time period. Finally, we did not include an indicator of time since first HIV-positive notification in our analyses. Although this variable was assessed in the baseline survey, it had missing values for more than 250 respondents. Therefore, its inclusion would cause a significant loss of sample size due to listwise deletion of missing cases. We conducted sensitivity analyses that included this variable to determine whether its inclusion would alter any substantive results. We found that time since first HIV-positive notification was significantly related only to physical functioning, and its inclusion did not alter the pattern of significance of the other predictors in the models. Therefore, we elected to omit this variable in our final set of analyses.

Results from this study suggest that HIV-positive patients with psychiatric symptoms experience declines in general health and increases in pain over time (independent of their HIV disease state and symptoms), which in turn worsen their psychiatric problems. An important implication is that early identification and treatment of psychiatric problems such as depression and anxiety is likely to improve HRQOL among patients with HIV.

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