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Patient–Clinician Relationships and Treatment System Effects on HIV Medication Adherence

Karen S. Ingersoll^{1,2,3} and Carolyn J. Heckman¹

¹Department of Psychiatry, Virginia Commonwealth University, Richmond, Virginia

²Department of Internal Medicine, Virginia Commonwealth University, Richmond, Virginia

Abstract

The study objectives were to determine the impact of the patient–clinician relationship on patient adherence to HIV medication, to identify which aspects of the patient–clinician relationship and the treatment system influenced adherence, and to determine which of these variables remained important when the impact of mental distress and substance abuse were considered. The design was a cross-sectional study using a sample of 120 HIV+ clinic patients. The *Primary Care Assessment Survey* (PCAS) assessed the clinician–patient relationship and the treatment system. The Composite International Diagnostic Inventory—Short Form (*CIDI-SF*) screened for mental disorders, and the *Brief Substance Abuse History Form* measured recent and remote substance use. Patient adherence was assessed using five markers including 3 interview-elicited self-reports, 1 medical chart review, and 1 summary score. Logistic regression analyses identified independent predictors of each adherence behavior. PCAS scores contributed to all five models, and their effects persisted when mental distress and substance abuse were considered. Adherence behaviors are explained by a variety of factors and should be assessed using multiple methods. Further study to illuminate the mechanisms of action of the clinician–patient relationship on adherence to HIV medication is warranted.

Keywords

HIV medication adherence; patient–clinician relationship; PCAS

INTRODUCTION

The Patient–Clinician Relationship Influences General Treatment Adherence

The relationship between patient and clinician is one source of the healing that can occur in chronic illness (Simpson *et al.*, 1979, 1991). Quality patient–clinician relationships are associated with greater adherence in chronically ill patient groups (DiMatteo, 1994; Kaplan *et al.*, 1989; Sanson-Fisher *et al.*, 1989) and better clinical outcomes (Stewart, 1995). Good patient–clinician relationships are central to primary care (Institute of Medicine, 1994; Simpson *et al.*, 1991). Research on the Primary Care Assessment Scale (PCAS) in a large sample ($n = 7204$ patients) indicated that physician knowledge of the patient and patient trust in the physician were associated with adherence to physician advice regarding substance use, safe sex, diet, stress-management. These two relationship variables accounted for 14% of the variance in medical adherence (Safran *et al.*, 1998).

There is emerging evidence that the clinician–patient relationship may also be associated with patient adherence to HIV medication. Martini *et al.* (2002) found that patient satisfaction with the clinician–patient relationship was related to adherence (number of medication errors in 2 months) in outpatients with HIV in an Italian multicenter study. In a correlational study of 707 outpatients, Bakken *et al.* (2000) found that patients who were more engaged with their providers evidenced better adherence to medications and appointments and better immune health than their less-engaged peers. These results suggest that patient–clinician relationships may be related to adherence and clinical outcome of HIV treatment.

Importance of High Medication Adherence in HIV

In HIV treatment, high medication adherence is associated with slower progression to AIDS and lower mortality (Bangsberg *et al.*, 2001; DeOlalla *et al.*, 2001; Hogg *et al.*, 2002). Adherence of at least 80% with potent combinations, and possibly 90–95%, is required to avoid drug-resistant HIV and viral rebound (Flandre *et al.*, 2002; Paterson *et al.*, 2000). Unfortunately, adherence to HIV medications is uniquely challenging. Rabkin and Chesney (1999) asserted that “combination therapy for HIV illness is perhaps the most rigorous, demanding, and unforgiving of any outpatient oral treatment ever introduced” (p. 61). Therefore, it is not surprising that adherence below optimal levels is common. Catz *et al.* (2000) found that a third of HIV/AIDS patients had missed doses in the past 5 days, while 18% persistently missed doses every week over the past 12 weeks. Flandre *et al.* (2002) found that nonadherence ranged from 13 to 40% over 3 months. Ingersoll (2004) found that 28% of clinic patients reported taking fewer than 95% of protease inhibitor doses in the past week, 33% were noncompliant by medical records notations, 36% reported they did not always take medication as directed, and 44% reported they had run out of their HIV medication. Liu *et al.* (2001) also found that nonadherence rates varied by type of adherence behavior. Their estimates of nonadherence for pill count were 6–24%, for electronically monitored pill caps (MEMS) were 28–41%, and for a composite score was 24%. Paterson *et al.* (2000) reported a MEMS nonadherence rate of 25.3%. Knobel *et al.* (2002) reported nonadherence of 32.3–36.6% in a Spanish study. Spire *et al.* (2002) reported nonadherence of 26.7% in a French cohort of 445 patients. Taken together, these recent, well-designed studies suggest that nonadherence to HIV medication varies by type of adherence behavior and ranges between 6 and 44%; the majority of estimates fall between 24 and 36%.

Patient Predictors of Nonadherence in HIV

Demographic variables such as education level, gender, and ethnicity are unrelated to adherence in most studies (Catz *et al.*, 2000; Ingersoll, 2004; Paterson *et al.*, 2000; Singh *et al.*, 1996; Wutoh *et al.*, 2001). Factors that are associated with nonadherence include depression, severity of side effects, poor treatment adherence self-efficacy, minimal social support (Catz *et al.*, 2000; Spire *et al.*, 2002), and anxiety (Ingersoll, 2004). Active alcohol or substance use is sometimes associated with poor adherence. Cook and colleagues found that problem drinkers were significantly more likely to report missing doses of antiretroviral medications or to take them off schedule, and to attribute missed doses to forgetting, running out of medication, or consuming alcohol or drugs (Cook *et al.*, 2001). Ever using heroin quadrupled the odds of ever running out of medication among clinic patients, while recent use of crack cocaine tripled the odds of notations of noncompliance in medical records and sextupled the odds of taking fewer than 95% of protease inhibitor medications in the past week (Ingersoll, 2004). In two prospective studies, patients whose alcohol or drug use increased showed reductions in adherence (Lucas *et al.*, 2002; Spire *et al.*, 2002) and those ceasing substance use demonstrated improvements in adherence (Lucas *et al.*, 2002). However, a few studies have not found substance abuse to be associated with adherence (Catz *et al.*, 2000; Paterson *et al.*, 2000; Singh *et al.*, 1996).

No published studies have examined the impact of the clinician–patient relationship and treatment system on medication adherence in HIV+ individuals using a well-validated measure of the relationship and multiple markers of adherence. The objectives of this study were to determine whether the clinician–patient relationship and aspects of the treatment system partially explained patient adherence to HIV medication, and to identify specific aspects of the clinician–patient relationship that influenced adherence. A secondary purpose was to examine whether clinician–patient relationship variables maintained their independent predictive power when mental distress and substance abuse were considered.

METHODS

Participants

A volunteer sample of 120 patients attending an urban university hospital infectious diseases clinic during an 18-month period participated in the study. Eligibility criteria included able to give informed consent, no obvious cognitive impairment, adult, HIV+, and prescribed combination antiretroviral therapy.

Measures

Demographics—Participants provided demographic information about themselves on a self-report form developed for this study. Items included standard and HIV-specific demographic questions. Questions addressed employment and insurance status, housing status, partner status, method of transmission of HIV, history of selected transmission risk behaviors, and sexual orientation (see Table I).

Patient–Clinician Relationship—The patient’s perception of the patient–clinician relationship and treatment system was assessed using the *Primary Care Assessment Survey* (PCAS, Safran *et al.*, 1998). The PCAS is a 51-item self-report measure of primary care as defined by the Institute of Medicine Committee on the Future of Primary Care (IOM, 1994). The PCAS consists of seven constructs measured through eleven scales: accessibility (organizational, financial), continuity (longitudinal, visit-based), comprehensiveness (knowledge of patient, preventive counseling), integration of care, clinical interaction (clinician–patient communication, thoroughness of physical examinations), interpersonal treatment, and trust (Safran *et al.*, 1998). Responses to the PCAS items are summed to yield raw scores that are then converted to *T* scores, with higher scores indicating higher levels of patient-perceived quality in that care dimension. Internal consistency reliability was found to range from 0.81 to 0.95 in a sample of over 6300 employees enrolled in 12 health plans in Massachusetts (Safran *et al.*, 1998). Validity evidence includes an association between patient satisfaction and adherence to physician advice (Safran *et al.*, 1996) as well as good convergent and discriminant validities. In addition, the instrument was found to perform consistently across a number of diverse patient groups (Safran *et al.*, 1998). The doctor–patient relationship, and the use of the PCAS in particular, has recently been recommended as an important direction to improve understanding of adherence in chronic illness because many studies have focused only on patient factors (Goldstein, 2002). Patients rate their primary clinician on items such as “caring and concern for you,” “your doctor’s knowledge of your entire medical history,” and the “attention your doctor gives to what you have to say.” In this study, participants were instructed to answer the questions in regards to their primary HIV care provider. The preventive counseling scale was not used because the patients had already contracted HIV. PCAS psychometric data based on HIV+ samples have not been published, so these results provide unique information in that regard.

HIV Treatment Regimen—Participants completed a 30-min, interviewer-guided self-report questionnaire, the *Medication Adherence Form*, that elicited their current and past medication

regimens using a series of branching questions and visual aids such as colored cards depicting photographs of HIV medications with their generic and trade names to enhance memory. This form was developed for this study based on a number of other questionnaires including the *Adherence to Therapy Interview* (The Measurement Group, 1997) and included content-specific questions pertaining to HIV medications that had newly become available in 1999 and 2000. The interview covered protease-inhibitor regimens and PI-sparing combination regimens, experience with side effects, opportunistic infection prophylaxis, attitudes about medication, barriers to treatment, and adherence behaviors. The interviewer asked whether a participant was now taking each medication, the current dose, dosing schedule, dosing requirements, and side effects related to that medication. Participants reported their reasons for not taking medication. Summary statements were made by the interviewer at several checkpoints to determine completeness of the reported regimen. Following these summary statements, participants were reminded of the number of protease inhibitor pills their regimen required, then were asked to recall how many pills of each medication they missed during the past week. From these answers, the proportion of PI medications missed and taken was calculated.

Adherence—Because adherence can best be understood as a set of related behaviors, and due to the lack of a single “gold-standard” for adherence measurement, multiple markers of adherence should be used to fully characterize the behaviors (Dunbar-Jacob, 2002). Empirical data also support the predictive validity of composite adherence measures for subsequent viral load (Liu *et al.*, 2001). The first marker was proportion of PI medications taken during the past week. Proportions of 95% or greater were categorized as High, with 94% and below as Low, based on Paterson *et al.*’s (2000) finding that those with at least 95% adherence showed significantly greater virological response than others. The second marker was the self-report, yes/no response to the question “Have you ever run out of your HIV medications?” The third marker was the self-report, yes/no response to the question “Do you always take all of your medications as directed?” These questions were embedded in different sections of the *Medication Adherence Form*. The last marker was a collateral report of adherence derived from the electronic medical record. Researchers queried the electronic medical record to identify any provider notations of noncompliance in the medical chart; if notations such as “noncompliant,” “having trouble taking medications,” “possible noncompliance,” or “long history of poor adherence” were present, the participant was categorized as non-adherent by the medical record. Lastly, it was of interest to determine the extent of overlap of the four indicators of adherence and to develop a summary marker of adherence, as recommended by Liu *et al.* (2001). Therefore, an adherence score was devised that gave a point for each of the measures on which the person was categorized as adherent. Because a minority of participants were taking PI regimens and therefore were not queried on proportion of PI doses taken in the past week, their scores on the summary measure could range from 0 to 3, with 0 meaning they were adherent on none of the measures and 3 indicating perfectly adherent by all of the measures. For those taking PI regimens, scores could range from 0 to 4, with 4 indicating adherence on all four measures.

Health Status—The participant’s health status, including CDC classification that indicated HIV or AIDS, history of opportunistic infections, currently prescribed regimen, three most recent CD4 and three most recent viral load counts, diagnostic codes, and staff comments regarding adherence were derived by querying the participant’s electronic medical record.

Substance Abuse—The *Brief Substance Abuse History*, a structured, interviewer-administered form, was adapted from the *Drug History form* (NIDA, 1993) and queried whether the participant had ever used a list of commonly abused substances including nicotine, alcohol, amphetamines, cocaine, heroin/opioids, hallucinogens, marijuana, drug combinations,

and other drugs. In each case when the participant had ever used/tried a substance, a series of branching questions was used to determine the extent of use, recency of use, and number of days used in the past 30. Additionally, participants answered whether they considered themselves to have a “primary drug” or a “drug of choice” and whether any drug was causing problems for them or had in the past. Participants also indicated whether they had undergone various types of drug abuse treatment.

Mental Disorders—A range of DSM-IV Axis I acute mental disorders was screened for using a brief, interviewer-administered questionnaire, the Composite International Diagnostic Interview—Short Form (CIDI-SF; WHO, 1998). The CIDI-SF takes 7 min to administer and is convergent with the full-length CIDI (Kessler *et al.*, 1998). The short form also has good sensitivity, specificity, and predictive validity (Kessler *et al.*, 1998). For this study, CIDI-SF modules were used to assess symptoms of Major Depression, Anxiety Disorders (Panic Attacks, Agoraphobia, Generalized Anxiety Disorder, Social Phobia, and Obsessive-Compulsive Disorder), and Drug and Alcohol Dependence in the past 12 months.

Procedures

The study utilized procedures that protected vulnerable human subjects and that were approved by the Institutional Review Board. Patients attending the infectious diseases clinic were approached in the waiting room by a research assistant and asked to participate in the study. Patients were also invited to participate via hospital flyers and personal recruitment by clinic staff. Patients were provided with information about the study and were scheduled to meet with a research assistant at their convenience, typically around their other scheduled hospital appointments. The assessment required between 2 and 3 hr. Participants were offered frequent breaks and snacks in addition to transportation vouchers and compensation. Although the procedures were rather long, participants did not seem bothered by the inconvenience, and some referred others for screening. Research assistants helped patients read and understand the survey items if necessary. Interviewers were trained to develop a good rapport with the participant, ask all questions neutrally and nonjudgmentally, and correct inconsistencies that arose over the course of the interview before proceeding. These procedures were developed to reduce potential response bias in which participants would be tempted to “please” the interviewer by overreporting adherence. Participants received \$30 merchandise gift cards from a major discount department store as compensation for their participation.

Data Analyses

Means, standard deviations, and frequencies were used to describe continuous and discrete demographic, mental disorder, substance use, and adherence characteristics of the sample. The relationship between adherence score and recent CD4 (above or below 200) and viral load (detectable vs. undetectable) were examined using *t* tests. Internal consistency reliability (Cronbach’s coefficient alpha) was calculated on the score items of the *Medication Adherence Form* and the *PCAS*. Stepwise multivariate logistic regression was used to develop explanatory models of all five types of adherence behavior including running out of medication, not taking medication as directed, low proportion of protease inhibitor pills taken, noncompliance noted by a clinician in the medical chart, and overall adherence score. All PCAS scales were entered into these initial models. After significant models and significant PCAS explanatory variables were identified, mental distress and substance abuse variables previously identified as significantly related to the four adherence behaviors (Ingersoll, 2004) were added to the PCAS models.

RESULTS

Thirty-eight percent of the sample was female, slightly more women than among the clinic population in general. The mean educational level of the sample was 10th grade, with years of formal education completed ranging from 0 to 18. The mean age was 40.4 years. Participants' average viral load was 77,493 copies (SD 188,416), while their average CD4 (t cell) count was 378.3 (SD 313.8). Participants averaged 3.2 (SD 1.6) medications for HIV and 6.2 (SD 3.6) medications total. The typical participant was an African American heterosexual single man who was disabled and diagnosed with AIDS (rather than asymptomatic HIV disease) for 4 years, had a detectable viral load and CD4 count above 200, and was on a triple combination protease inhibitor-sparing medication regimen, often due to failing previous regimens. Demographic characteristics are provided in Table I.

A large proportion of the sample reported psychiatric and substance use problems within the previous 12 months (Table II). Over 50% of the participants reported a major depression, almost 45% reported an anxiety disorder, and 26% reported problems with alcohol or drug dependence. In addition to substance dependence criteria, over half of the sample reported having a "primary drug," with most of these being illicit, and 40% of participants admitted to illicit substance use within the past 6 months.

Rates of nonadherence in the current sample were high, ranging from 30 to 44%, depending on the criterion employed (See Table II). The strictest measure of adherence was the composite score. Composite adherence rates (scoring as fully adherent by always taking medication as prescribed, never running out of medication, and not having noncompliance noted in the medical records) were very low; only 29% scored 3 out of 3.

Adherence was related to immune health in this sample. Those with detectable viral loads ($n = 67$) had lower mean adherence scores (1.69, SD 0.91) than those with undetectable viral loads ($n = 48$), whose mean adherence score was 2.19 (SD 0.68); this difference was significant ($t = 3.04$, $p = .003$). Among those with CD4 counts below 200, the mean adherence score was 1.64 (SD 0.86), while among those with CD4 counts above 200, the mean adherence score was 2.06 (SD 0.90), and this difference was also significant; $t = 2.45$, $p = .02$.

Internal Consistency of the MAF and PCAS

The *Medication Adherence Form* (MAF) is an interview process that yields primarily discrete variables. The four behavioral measures of adherence, and the two composite scores, were converted from categorical yes/no to numeric variables to permit assessment of the item-scale correlations. Therefore, scores of 1 or 0 were assigned to each of the items: always takes medication as directed, notations of non-compliance in the chart, proportion of protease inhibitors taken is 95% or greater, and has ever run out of medication. The composite scores ranged from 0 to 3 for those not taking protease inhibitors and 0 to 4 for those taking PIs as previously described. The internal consistency of these six score items of the MAF was very good, with a standardized Cronbach's coefficient alpha of .81.

The internal consistency of the PCAS scale for this sample of HIV+ patients was excellent, with a standardized Cronbach's coefficient alpha of .88 for the total scale. Scale coefficient alphas ranged from a low of .24 for the Trust scale to a high of .95 for integration of care (see Table III). Two scales (Trust and Organizational Access) failed to achieve an alpha of .70 and therefore have inadequate internal consistency to yield reliable measurement of their purported constructs in this sample. This may be due to the limited range of responses to these scales, with almost all participants rating both the provider and clinic very highly on these scales. However, we retained all scales for predictive analyses to allow comparison with previous research.

Patients with HIV-generated PCAS scale scores that were consistent with those reported for patients in primary care in terms of financial and organizational accessibility, visit continuity, integration of specialty care, quality of physician exam, interpersonal treatment, and communication. In contrast, the mean longitudinal continuity score in this sample was 13 points lower than the norm group mean and 12 points lower than the 50th percentile of the normative group. In two areas, this sample of patients scored higher than the normative sample. In contextual knowledge of the patient, this sample's mean of 74.16 was 20 points higher than the mean and 6 points higher than the 75th percentile of the normative sample. In trust, this sample's mean of 92.60 was 17 points higher than the mean of the normative group and 5 points higher than the 75th percentile of the normative group. In other words, while patients reported being seen in the clinic or by their provider for a relatively short period of time, they reported very good relationships with their providers. PCAS Scale scores are provided in Table III.

Explanation of Adherence

Explanation of Adherence Using Patient–Clinician Variables Only—According to the logistic regression (see Table IV), PCAS scores did not predict running out of medication and the model was not significant ($LR\chi^2_{(2df)}=4.07, p < .09$). In contrast, the model of not taking medication as directed was significant, explaining 10% of the variance ($LR\chi^2_{(4df)}=12.53, p < .02$). The PCAS interpersonal treatment variable increased the risk of nonadherence, whereas organizational access predicted better adherence. In addition, PCAS continuity of care was retained in the model but was not an independent predictor. The model of low proportion of protease inhibitor pills taken was also significant, with five PCAS variables explaining a moderate amount of the variance, 29% ($LR\chi^2_{(5df)}=15.56, p < 0.01$). Two variables contributed independently to low proportion of pills taken, financial accessibility, which was a protective factor, and continuity of care, which was a risk factor. Other variables in the model included comprehensive knowledge of the patient, communication skills, and physical exam (see Table IV).

The model of chart noncompliance was not significant, with PCAS variables explaining only 3% of the variance ($LR\chi^2_{(2df)}=3.28$). In contrast, the predictive model of poor adherence score was significant, and PCAS variables explained 9% of the variance ($LR\chi^2_{(4df)}=11.39$). It had two independent predictors, PCAS interpersonal treatment, a risk factor, and organizational access, a protective factor. PCAS scales that had no relationship to adherence as measured by any of the four behavioral or the composite indicators included visit-based continuity, integration of care, quality of physical exam, and trust.

Explaining Adherence With Both Patient–Clinician and Patient Mental Distress and Substance Use—The final models that include both PCAS and patient variables (mental distress and substance use) are presented in Table IV. Some PCAS variables remained in these models as independent predictors. The model of running out of medication was significant and included three variables that accounted for 13% of the variance ($LR\chi^2_{(2df)}=13.81, p < .01$). Variables that contributed independently to this model were contextual knowledge of the patient, which was slightly protective, and depression, which nearly tripled the risk of running out of medication.

The model of not taking medication as directed was also significant, explaining 16% of the variance ($LR\chi^2_{(6df)}=17.35, p < .01$). Variables that contributed independently to not taking medication as directed were one risk factor, PCAS interpersonal treatment, and two protective factors, PCAS contextual knowledge of the patient, and any CIDI-SF anxiety disorder. Anxiety disorder decreased the risk of not taking medication as directed more than fourfold.

The model of low proportion of protease inhibitor pills taken was significant, with its eight variables explaining a large amount of the variance, 45% ($\text{LR}\Pi^2_{(8\text{df})}=25.04, p < .01$). However, only one variable contributed independently to low proportion of pills taken, PCAS financial accessibility, which was a protective factor.

The model of chart noncompliance was still insignificant, explaining only 6% of the variance ($\text{LR}\Pi^2_{(3\text{df})}=5.80$), and had no independent predictors. Similarly, the overall predictive model of poor adherence score remained insignificant, explaining only 8% of the variance ($\text{LR}\Pi^2_{(5\text{df})}=8.65$). It had one independent risk factor, PCAS communication.

DISCUSSION

Medication regimens for HIV/AIDS are complex and demanding, and these results confirm that many individuals prescribed antiretroviral medication are not adequately adherent. Rates of nonadherence were high, ranging from 30 to 44% depending on the measure. Using the composite measure of adherence, or consistently scoring as adherent across three behaviors, the rate of consistent adherence across behaviors was very low, 29%. These figures indicate that patients are willing to self-report various nonadherent behaviors.

These data demonstrate that the patient–clinician relationship and treatment system influence medication adherence in HIV, even when patient factors such as substance abuse and mental health variables are considered. Scales from the PCAS were important in all five models predicting different aspects of adherence. PCAS scales better explained adherence behavior than past year depression, substance use, or anxiety. In addition, some clinician–patient relationship factors served as protective, and some served as risk factors for adherence to HIV medication. Of special interest are the counterintuitive findings that some of the “positive” relationship variables conferred risk to adherence, while recent anxiety symptoms provided protection.

Contextual knowledge of the patient as a person includes perceptions that the clinician knows one’s history, understands one’s responsibilities at work, home, or school, and understands one’s core values and beliefs. Patients who perceived their clinicians to know them well were less likely to report they had run out of medication or to report they did not always take it as directed. It is notable that the study sample’s mean on this scale was much higher than the normative group’s mean; this likely indicates that the HIV care providers of this sample of patients are perceived to understand their patients’ life situations in much greater depth than other primary care providers.

Financial accessibility, or the fairness/value of the cost of care, was an independent and protective predictor of the proportion of PI medication taken. Financial considerations may play a more important role in adherence to the most costly regimens, although many participants in this study were likely eligible for treatment at no or low cost either through the charity care of the institution or the state’s AIDS Drug Assistance Program.

Interpersonal treatment was an independent risk factor for not taking medication as directed and contributed to the prediction of noncompliance notations in the chart. A related area, communication skill, was an independent risk factor for a poor adherence score, again conferring only a slight increase in the risk. These results initially seem counterintuitive. Why might communication and interpersonal skill be detrimental to medication adherence in HIV patients? Providers who discuss adherence issues but are not confrontational may be perceived as more interpersonally skilled. Patients may misconstrue these providers’ empathy for permission to be less adherent. Alternatively, providers who are good communicators and have

higher levels of interpersonal interest may discuss a broad range of issues with their patients, rather than focusing only on adherence. Patients may then fail to grasp the critical nature of adherence because it did not stand out enough from other topics of discussion. It is also important to recognize that interpersonal treatment was rated by patients, whereas professionals might rate “skill” level differently. Patients might rate interpersonal treatment based on kindness alone, as opposed to a balance of appropriate challenge and support that might better foster adherent behaviors.

Continuity of care, or the length of the patient’s relationship with the clinician, contributed to three models but was not an independent predictor. This scale mean was lower in this sample than in the normative group, and the lower mean may indicate that patients completing the original PCAS experienced longer relationships with their PCPs than HIV+ patients had with their HIV care providers. This makes sense given that in this adult sample, HIV had not been a lifelong illness, and this result may reflect the shorter duration of their HIV care. Longer continuous care could be related to nonadherence as it conveys a longer duration of living with HIV. Maintaining excellent adherence over longer periods may be particularly challenging and remains an area in need of further study.

Trust has previously been identified as an important predictor of patient outcome and adherence (Safran *et al.*, 1998). Carr (2001) conducted qualitative interviews with 14 HIV+ patients to explore trust. Several patients explicitly identified trust as an important relationship factor that provided curative benefits. Trust appeared to be based on a variety of factors such as the length of the relationship, a general feeling of comfort on the part of the patient, and several provider variables such as their apparent clinical skills and knowledge, willingness to impart information, apparent enthusiasm, nonjudgmental attitude, understanding of the patient’s personal situation, reassuring behaviors, and general willingness to collaborate in care. The absence of trust as a predictor in this study is most likely due to its unusually low reliability in this sample due to a restriction of range in the responses to this scale. The participants uniformly rated their trust in their clinician as extremely high. Thus, trust did not vary by level of adherence in this sample. This finding should not be misconstrued as meaning that trust is unimportant to HIV treatment adherence. In fact, we did find that some of the elements of trust suggested by patients (longitudinal continuity, comprehensive knowledge of patient) were, in fact, predictive of adherence in this study. In the setting of more variation in trust and a more reliable measure of trust, the role of trust in facilitating adherence in HIV might emerge more clearly.

Although mental disorders (Major Depression and Anxiety) and substance use contributed to the prediction of adherence, substance use was not an independent predictor in any model. Depression has been identified in numerous other studies as an important predictor of adherence (e.g., Catz *et al.*, 2000; Spire *et al.*, 2002), and although it contributed to predicting running out of medication, it did not predict other types of nonadherent behavior. A patient with active major depression may experience lethargy and demoralization that result in failing to obtain a prescription refill on time, leading to running out of medication. Moreover, he/she may be passively suicidal and therefore, not take medications for this reason. Anxiety was a significant protective factor in not taking medication as directed, but was not independent in any other model. A patient with an anxiety disorder may be vigilant about his or her health, and this anxiety helps him/her to adhere closely to taking medication as directed. Substance disorders did not independently explain any aspect of adherence measured in this study. While previous studies have demonstrated such effects (Cook *et al.*, 2001; Lucas *et al.*, 2002; Spire *et al.*, 2002) as might be expected given the cognitive, emotional, and social impairments caused by substance problems, the current study did not obtain such results. It may be that such discrepancies with existing literature are related to measurement timeframe. This study screened for disorders during the past year, but perhaps recent psychiatric and substance

problems (e.g., past 30 days) would be more related to adherence. Alternatively, it is possible that patient–clinician relationship factors and a range of psychiatric disorders are more strongly related to adherence than is substance use. In summary, aspects of the doctor–patient relationship were important across the broad behaviors that comprise adherence, while patient mental health factors contributed only to specific types of nonadherent behavior in this sample.

Clinical Recommendations

These findings should encourage clinicians caring for people with HIV to enhance their relationships with patients to improve adherence. Results suggest that this enhancement might include both support and challenge, as some of the results are counterintuitive with regard to the clinician–patient relationship. Relationship building can be challenging, as HIV/AIDS can raise issues for clinicians that may impact their relationship with patients negatively due to its severity and prognosis, contagion issues, homophobia, substance abuse, as well as isolation and stigmatization (Battegay *et al.*, 1991). Developing a deeper knowledge of the patient in context may be an important bridge to improved adherence. Clinicians should also examine their method of discussing adherence. Physicians providing HIV care vary widely as to the timing, content, and extensiveness of their communication about adherence (Roberts and Volberding, 1999). Those clinicians with smoother interpersonal skills, who enjoy open communication, may cover a range of issues; therefore, their patients may not perceive the critical nature of adherence.

Providers may be able to improve patient adherence by facilitating the treatment of depression and fostering healthy “anxiety” about the risk of not taking medications as directed. This is not to suggest that providers leave anxiety disorders untreated. Rather, they can help patients understand the potential clinical outcomes of sporadic adherence and explore their ambivalence about taking medication. In addition, while substance use may have negative consequences for patients’ lives in general, its impact on medication adherence may not be so important as previously thought, especially when other variables are taken into consideration.

Limitations of the Study

This study’s primary limitation was its convenience sampling strategy among volunteer participants who were patients of an infectious diseases clinic, which could introduce biases into the study that limit generalizability. Factors that moderate this concern include a sample that reflected the demographic characteristics of the larger clinic population and adequate variability in most predictor and outcome variables. Future research should use representative sampling strategies among patients with HIV.

A second limitation is the use of self-report screening instruments rather than structured clinical interviews to generate hits for mental health and substance abuse disorders. However, several authors (Chesney *et al.*, 2000; Duong, *et al.*, 2001) found that self-report measures, despite their risk of under-estimating nonadherence, provide satisfactory concurrent and predictive validity (e.g., predicting viral load). While the CIDI-SF has excellent psychometric properties that compare well to structured interviews, its diagnoses are not definitive. Thus, the rates of recent Major Depression, Anxiety Disorder, and Alcohol or Drug Dependence identified in this study may vary from rates ascertained using other instruments. Therefore, the relationship of these mental disorders, or a lifetime rather than recent history of symptoms, to adherence should be examined further.

A third limitation is that without a “gold standard” for adherence, it is difficult to know the true rates of adherence in the sample. Although some studies have used electronic monitoring, that approach is expensive, not feasible in most clinical settings, and presents practical concerns

about requiring patients to use individual pill bottles rather than pillboxes, that can serve as a memory aid.

Future Directions

Methodology improvements in adherence research remain a pressing need. A recent meta-analytic review of the relationship of adherence to clinical outcomes revealed that method of measuring adherence was the largest source of variance in the relationship between adherence and outcomes (DiMatteo *et al.*, 2002). We have attempted to address this need by developing separate models for each indicator of adherence. The use of multiple self-report measures, behavioral measures, pill counts, electronic monitoring, pharmacy reporting, and other technology-based reporting methods should be pursued to maximize the reliability, validity, and practicality of adherence measurement, and researchers should avoid reporting these using composites alone. Future studies that report a range of adherence behaviors will facilitate greater understanding of the facilitators and barriers of each type of adherence.

These data suggest that adding measures of the patient–clinician relationship into future adherence studies could yield improved understanding of adherence. Although this study provides some hypotheses about the nature of the relationships between adherence and patient–clinician variables, these merit further study, using both self-report and observational methods such as rating relationship processes. In addition, characterizing the nature of the patient–clinician relationship may be fruitful. There may be different patterns of adherence behaviors in relationships that are paternalistic, mentoring, collaborative, or autonomous in nature (Balint and Shelton, 1996). The goal is to specify the mechanism of action of the patient–clinician variables on subsequent adherence behaviors. To that end, prospective studies that examine the patient–clinician relationship over time, and observe changes in adherence and outcomes, are highly desirable. Finally, intervention researchers should examine the most effective ways to facilitate adherence through improving the patient–clinician relationship.

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Table I

Demographic Characteristics of the Sample

Variable	<i>n</i>	%
Sex		
Men	74	62
Women	46	38
Ethnic/racial		
African American/Black	100	83
Caucasian	18	15
Native American	2	2
Education		
Less than high school	59	49
High school or equivalence	29	24
Some college	32	27
Employment		
Disabled	57	48
Unemployed	37	31
Part time	19	16
Full time	7	6
Partner/marital status		
Single	66	56
Divorced, separated, or widowed	28	24
Living with spouse/partner	23	20
Sexual orientation		
Heterosexual	70	61
Lesbian, gay, bisexual	44	39
Insurance type		
Government	78	66
None	30	25
Private	10	8
Housing status		
Home/apartment	61	51
Another's home/apartment	39	33
None	17	14
Institutionalized	3	2

Table II

Rates of Mental Disorders, Substance Abuse Problems, Health Status, and Adherence in 120 Patients With HIV

Measure	Disorder/characteristic	N	%
CIDI-SF (past year)	Major depression	60	52.6
	Anxiety disorder	50	43.9
	Alcohol or drug dependence	30	26.3
Brief substance abuse history	Has a "primary drug"	65	55.1
	Primary drug is alcohol	21	17.5
	Primary drug is illicit	42	35.0
	Recent illicit drug use (within 6 months)	47	39.8
Medical record	Noted to be a substance abuser by provider	47	39.8
Medication adherence form	a. Does not always take medication as directed	43	36.8
	b. Has ever run out of medications	52	44.4
	c. Noted to be noncompliant in records	38	32.2
	d. Proportion of PI taken below 95% past week ^a	14	30.4
	e. Sometimes skips protease inhibitor dose ^d	26	56.5
Composite Adherence Score (To how many items is patient scored as adherent of a, b, and c, above?)	0	10	8.62
	1	29	25.0
	2	44	37.9
	3	33	28.5
Composite Protease Adherence Score (To how many items is patient scored as adherent of a, b, c, and d, above?) ^d	0	2	4.1
	1	7	14.3
	2	16	32.7
	3	10	20.4
	4	14	28.6
Disease status	AIDS	71	65
	HIV	38	35
Most recent viral load by chart	Detectable (>400)	70	59
	Undetectable	48	41
Most recent CD4 count by chart	Over 200	70	59
	Below 200	48	41
Has regular HIV care provider	Yes	112	96

Measure	Disorder/characteristic	N	%
On OI Prophylaxis	No	5	4
	Yes	42	36
Taken and discontinued a PI	Yes	48	41
	None	62	53
Current PI	Nelfinavir	25	21
	Ritonavir	13	11
	Indinavir	7	6
	Kaletra	5	4
	Amprenavir	4	3
	Saquinavir	2	2

^aSample for these analyses consists of the 46 patients who were on a current protease inhibitor regimen from the total sample of 120, which included patients on PI-sparing regimens.

Table III
Primary Care Assessment Scale *t* Scores and Scale Reliability in 120 Patients With HIV

Scale name	<i>n</i>	Mean	<i>SD</i>	Correlation with total	Subscale coefficient alpha
Financial accessibility	106	64.70	21.53	.33	.90
Organizational accessibility	107	66.23	18.83	.74	.85
Longitudinal continuity ^a	107	63.32	32.09	.09	
Visit continuity	107	82.99	25.22	.37	.84
Comprehensive knowledge	106	74.16	19.75	.85	.66
Integration ^b	52	71.69	21.69	.85	.95
Physical exam ^a	107	81.68	20.21	.79	
Interpersonal treatment	107	81.12	18.65	.88	.94
Communication skill	107	82.17	17.36	.83	.94
Trust	107	92.60	15.90	.74	.24

^aThe Longitudinal continuity and physical exam scores are calculated based on one item each and thus interitem correlations and reliability cannot be calculated for these scales.

^bThe Integration of Care scale is only scored for those patients who indicated that their primary HIV care provider had referred them to a different specialist.

Table IV

Final Logistic Regression Models

Measure	Variable	B	SE	OR	CL	Wald χ^2
Model 1: Predicting running out of medication						
PCAS	Knowledge of patient	-0.03	.01	0.97	0.94-0.99	6.54*
PCAS	Length of continuity of care	0.01	.01	1.01	0.99-1.02	1.26
CIDI-SF	Depression	0.52	.22	2.85	1.20-6.77	5.67*
Model 2: Not taking medication as directed						
PCAS	Organizational access	-0.03	.02	0.97	0.94-1.00	3.45
	Longitudinal continuity	0.02	.01	1.02	1.00-1.03	3.60
	Interpersonal skill	0.06	.02	1.06	1.02-1.11	7.24**
	Knowledge of patient	-0.04	.02	0.94	0.90-0.98	4.16*
CIDI-SF	Any anxiety disorder	-0.60	.26	0.25	0.08-0.74	5.48*
Substances	Recent illicit drug use	0.26	.25	1.66	0.64-4.36	1.07
Model 3: Taking below 95% of protease inhibitor pills						
PCAS	Financial access	-0.09	.04	0.91	0.84-1.00	4.29*
	Scientific knowledge	-0.11	.06	0.90	0.80-1.01	3.36
	Longitudinal continuity	0.06	.03	1.07	1.00-1.14	3.51
	Communication skill	0.12	.08	1.13	0.96-1.33	2.19
	Knowledge of patient	0.08	.06	1.09	0.97-1.22	2.16
CIDI-SF	Any anxiety disorder	-0.72	.62	0.24	0.02-2.74	1.33
	Drug or alcohol dependence	1.38	.80	15.65	0.68-361.61	2.95
Substances	Recent illicit drug use	0.71	.58	4.10	0.42-40.12	1.47
Model 4: Predicting noncompliance (per chart)						
PCAS	Interpersonal skill	-0.03	.02	1.05	0.99-1.11	1.22
	Communication skill	0.05	.03	1.05	0.99-1.11	2.33
Substances	Recent illicit drug use	0.41	.23	2.27	0.93-5.53	3.27
Model 5: Predicting poor adherence score (≤ 1 of 3)						
PCAS	Organizational access	-0.03	.02	0.97	0.94-1.01	2.65
	Communication	0.04	.02	1.04	1.00-1.09	3.93*
	Knowledge of patient	-0.03	.02	0.97	0.94-1.01	2.48

Measure	Variable	B	SE	OR	CL	Wald χ^2
Substances	Recent illicit drug use	0.39	.25	2.18	0.82–5.76	2.45
	Primary drug identified	−0.36	.25	0.48	0.18–1.30	2.07

Note. The confidence limits of some significant Odds Ratios appear to contain 1.00 due to rounding.

* $p < .05$.
** $p < .01$.