

Patient- and provider-reported adherence: toward a clinically useful approach to measuring antiretroviral adherence

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Abstract

We seek to develop a clinically useful measure of antiretroviral medication adherence. Because there is no gold standard for adherence, we will assess the clinical validity of patient- and provider-reported adherence by the strength of their expected associations with current viral load, depressive symptoms, alcohol and illicit drug use, and homelessness. The Veterans Aging Cohort 3 Site Study (VACS 3) is a multisite study of 881 patients at Cleveland, Houston, and Manhattan Veterans Affairs health care systems. Data was collected on adherence using patient report and provider assessment; depressive symptoms using the Center for Epidemiological Studies Depression (CESD) and provider assessment; alcohol use using the Alcohol Use Disorders Identification Test (AUDIT) and provider assessment; and homelessness using patient report only. Viral load was collected from electronic laboratory data. Although agreement between providers and patients about the patient's adherence was not better than chance (61%; weighted kappa = .07), both patient and provider-reported adherence were related to viral load ($P < .001$), current alcohol use ($P < .01$), current drug use ($P < .01$), and depressive symptoms ($P < .001$). Patient-reported adherence was also associated with homelessness ($P < .05$). In multivariate regression models, provider assessment of adherence demonstrated independent associations with viral load ($P < .001$), current alcohol use ($P < .001$), current drug use ($P < .001$), and depressive symptoms ($P < .001$) after adjustment for the patient's report of adherence (also significantly associated). The consistent and largely independent association between patient and provider reported adherence and a range of variables previously shown to be associated with adherence suggests that patient- and provider-reported adherence independently measure actual adherence. Future work will explore how patient- and provider-reported adherence might best be combined, and whether the measure may be further enhanced with pharmacy refill data. © 2001 Elsevier Science Inc. All rights reserved.

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1. Introduction

Adherence to antiretroviral therapy is thought to be of utmost importance in preventing the progression of HIV disease [1,2]. If we are to improve adherence, we must first be able to recognize those who are failing to adhere. However, there is no gold standard measure of adherence, and existing measures have strengths and weaknesses [3–13]. Pill counts err when patients dump pills prior to the visit [14,15]. Drug levels reflect a short period, and patients may improve their adherence shortly before giving a sample; they are also expensive [5,16]. The electronic monitoring system is cur-

rently considered to be “state of the art” in assessing adherence [17], but indication of opening does not prove that the drug was taken. Further, patients often remove extra pills at the time of opening, choosing to carry the pills in other containers [18]. Also, electronic monitoring systems are impractical for large-scale research and routine clinical monitoring [8,19].

Self-administered patient questionnaires have been developed and initially validated for measuring adherence in HIV [7,13] and other chronic diseases [6], and are probably the most clinically practicable. However, these surveys require further refinement before they will be clinically useful. Specifically, patient report of adherence has been shown to be correlated with pill counts, electronic monitoring systems, and drug levels [7], but appears to be optimis-

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tic [19]. Patients may report perfect adherence when they are, in fact, not adhering perfectly. Thus, we posit that a patient report of adherence is less accurate than a patient report of nonadherence. A patient report of perfect or good adherence may require further verification from the provider's assessment.

Further, many self-reported measures of adherence remain clinically cumbersome because they require a listing of all antiretroviral medications taken [20]. The patient is then asked to respond to a question or series of questions concerning *each* medication [11,12]. As suggested by Haubrich [7], we posited that patient-reported adherence might be substantially simplified without loss of information by asking a few general questions concerning the patient's adherence to their entire antiretroviral regimen—rather than asking these questions separately for each of a list of antiretroviral medications.

Finally, we have made the following clinical observation. When a provider reports that the patient is taking the medication, the provider is often wrong. However, when a provider reports that a patient is *not* taking their medication, they are usually right. Thus, we posited that provider assessment concerning antiretroviral *nonadherence* may demonstrate important associations with known correlates of adherence. Further, we suspected that provider assessment of nonadherence might add independent insight to patient report of nonadherence.

Therefore, we asked whether patient self-administered surveys and provider-independent assessment concerning general antiretroviral *nonadherence* provide clinically meaningful measures, and whether these two sources offer complimentary information.

Because there is no gold standard for measuring adherence, we define a clinically meaningful measure as the measure that demonstrates a stronger and more consistent association with factors previously shown to be associated with nonadherence (Table 1). Specifically, we expect associations between nonadherence and a wide range of variables including higher viral load [21], active alcohol or drug use [22–24], depressive symptoms [3,25–28], and homelessness [24,27].

Of note, each of these variables is far from a “surrogate marker” for adherence. Although viral load is the most commonly used variable to assess measures of adherence [3], vi-

ral load is also strongly affected by antiretroviral drug resistance [29], bioavailability [30], and acute infection [30–33]. Further, viral load may be particularly limited as a method of evaluating the provider's assessment of adherence. Provider assessment may be largely determined by viral load: the patient knows whether they are taking a medication, no matter how good or bad their viral load count; the provider does not. Thus, it is also important to demonstrate strong independent associations with other variables known to be associated with adherence of which providers may be substantially less aware. If provider assessment of adherence demonstrates an expected association with these variables, we might conclude that, despite being unaware of the “causal” condition (i.e., active alcohol, drug use, or depression), the provider is aware of the result (nonadherence). This article will consider only the construct validity of patient- and provider-reported nonadherence. Future analyses will address responsiveness and predictive validity.

2. Methods

2.1. Design

VACS 3 is an observational study utilizing patient and provider surveys and electronic medical data at three Veterans Affairs Medical Center Infectious Disease Clinics. Details concerning the design of VACS 3 can be found elsewhere in this supplement [34]. The sources of cross-sectional data for this study include self-administered patient and provider surveys and computerized medical data collection including full laboratory data from each of the sites.

Patients were presented with three Likert-scale questions regarding adherence prior to the patient's first visit (Table 2) and one yes/no item asking about doses missed last weekend. After the visit, providers were independently asked to assess the patient's adherence with a Likert-scale question parallel to one of the patient's questions (Table 2) [4,35]. Patient and provider adherence questions were originally developed by Drs. Margaret Chesney and Jeannette Ickovics for the Outcomes Committee of the Adult AIDS Clinical Trials group [20].

Data regarding HIV-1 viral load were obtained from the Decentralized Hospital Computer Program (DHCP) database maintained by the Veterans Affairs. We asked both the

Table 1
Clinical variables expected to be associated with a good measure of adherence

| Variable | Expected association | Justification |
|-------------------------|---|--|
| Viral load | Better adherence should be associated with lower viral load | All else equal, poorer adherence leads to higher viral loads [21]. |
| Undetectable viral load | Better adherence should be associated with greater proportions of undetectable viral load | (see above) |
| Active substance abuse | Poorer adherence should be associated with active alcohol abuse and illicit drug use. | This has been shown in HIV and in other chronic diseases [22,23]. |
| Sadness/depression | Poorer adherence should be associated with greater degrees of sadness/depression | This has been shown in HIV [3,23–27] and in other chronic diseases |

Table 2
Likert scale questions measuring adherence

| Abbreviated phrasing | Patient questions | Provider question | Likert choices |
|----------------------|--|--|--|
| Days missed all | During the past 4 days, on how many days have you missed taking all of your doses? | | 0 days, 1 day, 2 days, 3 days, or 4 days |
| On schedule | How closely did you follow your specific schedule over the last four days? | | never, some of the time, about half the time, most of the time, all of the time. |
| Doses missed | When was the last time you missed any of your HIV medicines? | When was the last time this patient missed any of his/her HIV medications? | within the past week, 1–2 weeks, 2–4 weeks, 1–3 months, >3 months, never missed |

For all questions responses were grouped into three categories for analyses: “perfect adherence,” corresponding to a response suggesting that the patient never fails to take their medication; “intermediate adherence,” corresponding to a response that fell below perfect but above the poorest category of adherence; and “universally poor” adherence, corresponding to the worst possible response.

patient and provider about alcohol use. We also asked the patient to complete the Alcohol Use Disorders Identification Test or AUDIT [36,37]. The AUDIT is a 10-item questionnaire designed by the World Health Organization to identify drinkers “at risk” for harmful or hazardous effects on their life. A cutoff score of ≥ 8 out of 40 points for the AUDIT has been previously established to have both a sensitivity and specificity of 96% in detecting “at-risk alcohol use” [37].

We asked both the patient and provider about illicit drug use. We asked the patient to complete questions that were written to parallel those in the alcohol-based AUDIT, but the references were changed to ask about illicit drugs. We called this score the AUDIT-D. The complete patient survey may be found in the appendix to the paper by Smola *et al.* also found in this supplement [28].

We asked both the patient and provider about depression. We used the self-administered 10-Item Center for Epidemiological Studies Depression (CESD)[38] to assess depressive symptoms. The CESD is a 10-item short-form self-completed survey to identify patients at high risk of clinical depression. A score of 10 or higher is thought to be associated with depression.

We asked the following two questions of the patient only: *In the past 4 weeks, have you ever been without a permanent address that you call home?* And *Have you ever been without a permanent address that you call home?* In both cases, the options were yes or no.

2.2. Statistical analysis

All data was analyzed using STATA version 6.

Based on the distribution of responses we developed a three-level score for each Likert-scale question in which the score was 2 if the report was of poor adherence (see Table 1), 0 if the report was for perfect adherence, and 1 for all others. These scores and the strength of expected associations are reported. We did not analyze the yes/no item concerning weekend nonadherence for this report because it was formatted differently. Of the 881 patients who completed the survey, 793 responded that they take medication to treat their HIV infection. Viral loads were avail-

able on all 793 patients. We used this group for our analyses. Of these, 83% had viral loads within 90 days prior to baseline.

Prior to regression analyses, HIV-1 RNA viral load values (copies/mL) were \log_{10} transformed to improve the fit to a normal distribution. HIV-1 RNA viral load was also dichotomized by a cut point of above/below 400 copies. CESD-10 scores were analyzed as a continuous variable and as a dichotomous variable representing a cut point of 10 or above for depressions.

We calculated percent agreement and weighted kappa scores [39] for patient and provider report of adherence and of current alcohol use, current illicit drug use, and current depressive symptoms. Agreement and kappa scores were not sensitive to the method of weighting, so we used the numeric values previously assigned. We report bivariate and multivariate analyses of the patient and provider survey questions related to adherence and the strength of their association with variables previously demonstrated to be related to adherence. We generated medians and simple proportions as appropriate to describe the data. We used nonparametric tests of trend across ordered groups (an extension of the Wilcoxon rank-sum test and is a useful adjunct to the Kruskal-Wallis test) to compare antiretroviral adherence levels by viral load, alcohol use, illicit drug use, depression, and homelessness variables. Details of how each of these expected associates were measured are included in the presentations of the tables.

For continuous conditions (log 10 viral load), linear regression was used. For dichotomous conditions (undetectable viral load, current alcohol use, current drug use, depression, and homelessness), logistic regression was used. We report the coefficients (linear regression) or odds ratios (logistic regression) for each of the three patient and the one provider items addressing adherence. Because we expect covariance among questions concerning adherence completed by the patient and between the patient and the provider report, we consider any question that demonstrates an independent contribution at the level of $P = .1$ significant. To explore the degree to which patient and provider report of adherence offered independent association with viral load, we used logistic regression. For each model, viral load (above/below 400 copies) was regressed on the patient ad-

herence questions, the provider adherence question, and on both. ROC curves of each were plotted, and the area under the curve was calculated.

Multivariate regression analyses were also employed to determine whether provider reported adherence demonstrated independent relationships with the expected associated variables before and after adjustment for viral load and the providers awareness of the condition (active alcohol use, drug use, and depressive symptoms).

3. Results

Patient and provider report of adherence did not agree. Patient and provider report of adherence demonstrated poor agreement and poor agreement beyond chance (agreement: 61%; kappa $-.03$; CI: $-.09, .03$). Patient and provider report of current alcohol use (agreement: 63%; kappa $.13$; CI: $.08, .19$), current drug use (agreement: 85%; $.28$ kappa; CI: $.19, .38$), and current depressive symptoms (agreement: 60%; kappa $.22$; CI: $.19, .33$) also demonstrated poor agreement beyond chance.

Nevertheless, both patient- and provider-reported measures of adherence were strongly associated with viral load (Table 3) ($P < .001$). In multivariate analyses, provider- and patient-reported adherence were each independently associated with viral load (Table 4).

The association between patient and provider reports of adherence and alcohol consumption was also strong (Table 5). Current alcohol consumption as reported by the patient was strongly related to provider reported poorer adherence ($P < .001$). Provider reported current alcohol use was also strongly related to patient-reported poorer adherence for all of the patient adherence questions ($P < .05$). In multivariate analyses, provider- and patient-reported adherence responses were independently associated with current alcohol consumption (Table 6).

Table 3
Bivariate association of adherence measures of viral load (HIV-1 RNA)

| | Level of adherence | n | Median viral load | Viral load <400 copies/mL |
|---------------------------|--------------------|-----|-------------------|---------------------------|
| (Patient) days missed all | Perfect | 532 | 176 | 55.4% |
| | Intermediate | 188 | 2147 | 35.6% |
| | Poor | 63 | 25266 | 22.2% |
| | P | | <.001 | <.001 |
| (Patient) on schedule | Perfect | 400 | 222.5 | 53.8% |
| | Intermediate | 337 | 900 | 43.2% |
| | Poor | 42 | 17267.5 | 31.0% |
| | P | | <.001 | <.001 |
| (Patient) doses missed | Perfect | 217 | 141 | 56.7% |
| | Intermediate | 368 | 393.5 | 50.0% |
| | Poor | 199 | 1679 | 32.5% |
| | P | | <0.001 | <0.001 |
| (Provider) doses missed | Perfect | 208 | 76.5 | 67.1% |
| | Intermediate | 338 | 554.5 | 47.2% |
| | Poor | 134 | 10938.5 | 25.9% |
| | P | | <.001 | <.001 |

Of note, the overall AUDIT score of 8 or above, the usual threshold for identifying “at risk” drinking was associated with adherence questions for both the patient and their provider ($P < .05$, data not otherwise shown). Binge drinking (six or more drinks at a time), was associated with two of the adherence questions ($P < .05$). The trend for the proportions is very similar to that for the AUDIT (data not otherwise shown). Because these associations were no stronger than those for the question of current alcohol use, and more patients reported current alcohol use than reported “at-risk” drinking, we used this item for the outcome of the regression analysis (Table 6).

Drug use reported by both the provider and the patient was also strongly associated with reported adherence (Tables 7 and 8) ($P < .01$). The patient report of doses missed demonstrated a relationship with illicit drug use, specifically for the modified AUDIT questions including presently using drugs, regular drug use, inability to stop using drugs, failed to do what was normally expected of them, and guilt over drug use ($P < 0.02$, data not otherwise shown). The relationship with adherence was strongest for the question reporting current illicit drug use so this was the question employed in the multivariate analyses (Table 8). Patient and provider report each offered independent associations with nonadherence in multivariate analyses of current drug use (Table 8).

Patient-reported depression based upon the 10-item CESD, demonstrated strong relationships with both provider and patient reports of adherence (Tables 9 and 10, $P < .001$). In multivariate analyses both provider and patient report of adherence was strongly associated with a CESD score of 10 or greater (the usual cutoff for depression) (Table 10).

Only the patient report of adherence was associated with homelessness (Tables 11 and 12). In multivariate analyses, provider reported nonadherence failed to demonstrate an association with homelessness.

In a fully adjusted multivariate model of provider assessment of adherence, patient-reported current alcohol use ($P < .001$) and patient-reported symptoms of depression ($P = .08$)

Table 4
Multivariate association of adherence measures to viral load (HIV-1 RNA)

| | Log ₁₀ viral ^a | | | Viral load <400copies/mL ^b | | |
|---------------------------|--------------------------------------|--------------|-------|---------------------------------------|------------|-------|
| | OR | 95% CI | P | OR | 95% CI | P |
| (Patient) days missed all | .25 | 0.06, 0.45 | 0.01 | 0.77 | 0.54, 1.10 | 0.2 |
| (Patient) on schedule | .12 | -0.29, 0.05 | 0.16 | 1.20 | 0.89, 1.62 | .2 |
| (Patient) doses missed | .04 | -0.19, 0.11 | .6 | 0.98 | 0.75, 1.28 | .9 |
| (Provider) doses missed | .53 | -0.67, -0.39 | <.001 | 1.97 | 1.53, 2.52 | <.001 |

^aLinear regression.

^bLogistic regression.

Table 5
Bivariate association of adherence measures to alcohol consumption

| | Level of adherence | n | Patient | |
|---------------------------|--------------------|-----|-------------------------|-------------------------|
| | | | Presently drink alcohol | Presently drink alcohol |
| (Patient) days missed all | Perfect | 532 | 35.0% | 8.4% |
| | Intermediate | 185 | 50.2% | 17.0% |
| | Poor | 63 | 46.0% | 22.0% |
| | P | | .00 | .00 |
| (Patient) on schedule | Perfect | 400 | 33.8% | 9.0% |
| | Intermediate | 337 | 46.1% | 13.2% |
| | Poor | 42 | 52.4% | 23.7% |
| | P | | .00 | .01 |
| (Patient) doses missed | Perfect | 217 | 25.7% | 7.6% |
| | Intermediate | 368 | 38.5% | 10.6% |
| | Poor | 199 | 57.9% | 18.1% |
| | P | | <0.001 | <0.001 |
| (Provider) doses missed | Perfect | 208 | 34.9% | 7.5% |
| | Intermediate | 338 | 35.9% | 10.1% |
| | Poor | 134 | 54.5% | 27.1% |
| | P | | .00 | .00 |

Table 7
Bivariate association of adherence measures to illicit drug use

| | Level of adherence | n | Patient ^a | |
|---------------------------|--------------------|-----|----------------------|---------------------|
| | | | Presently use drugs | Presently use drugs |
| (Patient) days missed all | Perfect | 532 | 8.9% | 7.1% |
| | Intermediate | 188 | 18.7% | 11.7% |
| | Poor | 63 | 20.6% | 23.7% |
| | P | | <.001 | <.001 |
| (Patient) on schedule | Perfect | 400 | 8.0% | 6.5% |
| | Intermediate | 337 | 16.1% | 12.6% |
| | Poor | 42 | 21.4% | 16.2% |
| | P | | <.001 | <.001 |
| (Patient) doses missed | Perfect | 217 | 8.1% | 6.7% |
| | Intermediate | 368 | 11.0% | 10.5% |
| | Poor | 199 | 19.2% | 11.3% |
| | P | | <0.001 | 0.13 |
| (Provider) doses missed | Perfect | 208 | 7.9% | 2.5% |
| | Intermediate | 338 | 12.3% | 8.3% |
| | Poor | 134 | 19.4% | 27.1% |
| | P | | <.001 | <.001 |

^aProportion responding “Yes.”

remained associated with provider assessment after adjustment for viral load (P < .001) and for the provider’s awareness of current alcohol use (P = .2), current drug use (P < .001), and depression (P = .01). Patient-reported current drug use did not significantly influence provider assessment (P = .9).

4. Discussion

Provider- and patient-reported adherence, based on a few general questions regarding overall antiretroviral use, demonstrated strong and mutually independent associations with HIV-1 RNA viral load. Further, although provider and patient report of adherence, current alcohol use, drug use, and depressive symptoms did not agree, provider- and patient-reported adherence was strongly (and independently) associated with patient reports of alcohol use, drug use, and depressive symptoms. The strong, consistent, and often independent expected relationships between patient and provider report of adherence and viral load, active substance use, and depressive symptoms supports our hypothesis that these two sources of information on patient adherence are complimentary. These results also support prior research demonstrating an associa-

tion between adherence and alcohol use [23–25], illicit drug use [23,25], and depression and depressive symptoms [3,26–29] measured in a variety of ways.

Although patient-reported adherence was associated with homelessness, provider-reported adherence was not. Without explicit interventions to support adherence among homeless patients, homelessness clearly complicates the task of adhering to antiretroviral medication [27,40]. The finding that provider assessment of adherence was not associated with homelessness deserves further evaluation.

Our study partially contradicts previous research that found clinicians managing HIV-positive patients inaccurately assess their patient’s adherence to HIV medications [7,41,42]. Of note, in one of these studies providers were not asked to assess the patients’ adherence. They were instead instructed to record the patient’s report of adherence [7,41]. The independent information offered by the physician *assessment* may actually reflect the physicians ability to “see behind” the patients overly optimistic report. Other studies have shown that providers assessment of adherence independently predict virologic response to HIV medications [43–45].

Table 6
Multivariate association of adherence measures to alcohol consumption

| | Patient | | | Provider | | |
|---------------------------|---|------------|--------|---|------------|-------|
| | Presently drink alcohol compared to not presently drinking ^a | | | Presently drink alcohol compared to not presently drinking ^a | | |
| | OR | (95% CI) | P | OR | (95% CI) | P |
| (Patient) days missed all | 0.82 | 0.58, 1.16 | 0.3 | 1.19 | 0.74, 1.91 | 0.5 |
| (Patient) on schedule | 0.75 | 0.56, 1.01 | 0.06 | 0.79 | 0.51, 1.24 | .3 |
| (Patient) doses missed | 1.88 | 1.40, 2.50 | <0.001 | 1.10 | 0.74, 1.64 | 0.6 |
| (Provider) doses missed | 0.87 | 0.68, 1.10 | 0.3 | 0.56 | 0.38, 0.82 | 0.003 |

^aLogistic regression.

Table 8
Multivariate association of adherence measures to illicit drug use

| | Patient | | | Provider | | |
|---------------------------|----------------------------------|------------|------|----------------------------------|------------|-------|
| | Presently use drugs ^a | | | Presently use drugs ^a | | |
| | OR | 95% CI | P | OR | 95% CI | P |
| (Patient) days missed all | 1.20 | 0.76, 1.94 | 0.40 | 1.13 | 0.67, 1.91 | 0.70 |
| (Patient) on schedule | 0.72 | 0.46, 1.11 | .1 | 0.71 | 0.42, 1.17 | .2 |
| (Patient) doses missed | 1.33 | 0.90, 1.98 | 0.20 | 0.75 | 0.48, 1.17 | 0.20 |
| (Provider) doses missed | 0.81 | 0.56, 1.16 | .2 | 0.30 | 0.19, 0.47 | <.001 |

^aLogistic regression

An important limitation to every study of adherence is that there is no gold standard for measuring adherence. Viral load is the most commonly used variable to assess candidate measures of adherence [3], but viral load is also affected by antiretroviral drug resistance [29], bioavailability [30], and acute infection [30–33]. Further, provider assessment of adherence may be largely determined by viral load. The patient knows whether or not they are taking the medications no matter how good or bad their viral load count, but the provider does not. Indeed, provider assessment was more closely associated with viral load than was the patient report of adherence.

Thus, it is important to also demonstrate strong associations with other variables known to be associated with adherence of which providers are less aware. Providers were clearly less aware of patient-reported current alcohol use, drug use, and depressive symptoms (as witnessed by the poor kappa scores). Nevertheless, provider assessment of *adherence* was significantly and often independently associated with patient reported current drug use, alcohol use, and depressive symp-

Table 9
Bivariate association of adherence measures and depression

| | Level of adherence | n | Patient | Provider |
|---------------------------|--------------------|-----|-------------------|------------|
| | | | CESD ^a | Depression |
| (Patient) days missed all | Perfect | 532 | 42.2% | 39.2% |
| | Intermediate | 188 | 47.0% | 38.8% |
| | Poor | 63 | 61.9% | 54.7% |
| | P | | <.001 | .11 |
| (Patient) on schedule | Perfect | 400 | 39.5% | 36.7% |
| | Intermediate | 337 | 50.5% | 44.4% |
| | Poor | 42 | 56.1% | 44.7% |
| | P | | <.001 | .05 |
| (Patient) doses missed | Perfect | 217 | 44.4% | 33.9% |
| | Intermediate | 368 | 41.2% | 41.1% |
| | Poor | 199 | 53.1% | 46.2% |
| | P | | 0.09 | 0.02 |
| (Provider) doses missed | Perfect | 208 | 37.0% | 33.7% |
| | Intermediate | 338 | 43.7% | 40.5% |
| | Poor | 134 | 59.1% | 54.0% |
| | P | | <.001 | <.001 |

^aCESD level with cutoff at 10 (proportion above 10).

Table 10
Multivariate association of adherence measures and depression

| | Patient | | | Provider | | |
|-------------------------------------|---------------------|------------|-------|----------------------------------|------------|-------|
| | CESD ^{a,b} | | | Depression symptoms ^b | | |
| | OR | 95% CI | P | OR | 95% CI | P |
| (Patient) days missed all (n = 783) | 1.11 | 0.79, 1.55 | 0.56 | 0.91 | 0.64, 1.29 | 0.60 |
| (Patient) on schedule (n = 779) | 0.75 | 0.56, 1.01 | 0.06 | 0.86 | 0.64, 1.17 | .3 |
| (Patient) doses missed (n = 778) | 0.92 | 0.71, 1.19 | 0.51 | 1.15 | 0.88, 1.51 | .3 |
| (Provider) doses missed (n = 680) | 0.70 | 0.55, 0.89 | 0.004 | 0.71 | 0.55, 0.91 | 0.008 |

^aCESD level with cutoff at 10 (proportion above 10).

^bLogistic regression.

toms. When we directly adjusted for the provider's awareness of these conditions *and* for viral load (a partial determinant of the provider's assessment) patient-reported current alcohol use and depressive symptoms remained associated with the provider's assessment. Thus, despite being unaware of the "causal" condition (i.e., alcohol, drug use, or depression), the provider was aware of the result (nonadherence). The consistent association between patient and provider reported adherence and a wide range of variables (viral load, substance use, depression, and homelessness) suggests that these questions are independently measuring adherence.

In future studies we will evaluate the additional independent information offered by the patient's report of nonadherence on the weekend and by electronic pharmacy refill data. If, as we expect, these sources also offer information, a weighting schema will be developed and validated that combines all patient and provider report items and electronic pharmacy data. We will then make use of multivariate modeling techniques to develop a clinical index of ad-

Table 11
Bivariate association of adherence measures to homelessness

| | Level of adherence | n | Patient |
|---------------------------|--------------------|-----|--|
| | | | Have you ever been without a permanent address that you could call home? |
| (Patient) days missed all | Perfect | 532 | 27.5% |
| | Intermediate | 188 | 34.6% |
| | Poor | 63 | 50.0% |
| | P | | .00 |
| (Patient) on schedule | Perfect | 400 | 27.4% |
| | Intermediate | 337 | 34.8% |
| | Poor | 42 | 39.0% |
| | P | | .02 |
| (Patient) doses missed | Perfect | 217 | 25.0% |
| | Intermediate | 368 | 31.5% |
| | Poor | 199 | 37.4% |
| | P | | 0.01 |
| (Provider) doses missed | Perfect | 208 | 28.3% |
| | Intermediate | 338 | 33.0% |
| | Poor | 134 | 33.6% |
| | P | | .26 |

Table 12
Multivariate association of adherence measures to homelessness

| | Patient | | |
|---------------------------|---------|------------|------|
| | OR | 95% CI | P |
| (Patient) days missed all | 1.57 | 1.15, 2.23 | 0.01 |
| (Patient) on schedule | 0.92 | 0.67, 1.26 | .6 |
| (Patient) doses missed | 1.07 | 0.81, 1.41 | 0.60 |
| (Provider) doses missed | 1.06 | 0.82, 1.37 | 0.70 |

^aLogistic regression

herence using these three sources of information on adherence. Such an index could be used to identify nonadherent individuals for targeted adherence interventions. It might also provide a more precise measure of clinical adherence for use in large clinical studies in which electronic monitoring systems are not a feasible alternative.

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