Adherence to Antiretroviral Therapy: Appropriate Use of Self-Reporting in Clinical Practice

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Purpose: This study investigated the factors that may affect adherence to antiretroviral therapy in people with HIV infection and compared the use of three self-report tools to determine client adherence. **Method:** A descriptive, cross-sectional study of 260 HIV-infected clients attending nine HIV outpatient centers in England was conducted using researcher-administered instruments. Self-reports of adherence were assessed using the Morisky Medication Adherence Scale (MMAS), Reported Adherence to Medication Scale (RAM), and the Patient Adjustment to Medication Scale (PAM). **Results:** Univariate analysis of clients' self-reports indicated a number of associations with adherence. Significant associations with less adherent behavior identified by two or more self-report tools were the reported use of recreational drugs, $p = .001$; living alone, $p = .041$; feeling depressed, $p = .02$; being influenced by the media, $p = .037$; and lack of a close confidant, $p = .037$. Greater adherence was associated with clients reporting a positive mental attitude to HIV infection, $p = .038$. Principal component analysis (PCA) of each self-report tool identified two well-recognized constructs: intentional nonadherence and nonintentional nonadherence. In addition, a third construct of following instructions was identified from PAM, a scale developed by the authors. Subsequent regression analysis failed to confirm the associations with adherence suggested by the univariate analysis. **Conclusion:** This study suggests that the design and use of self-report tools to identify client's adherence to complex antiretroviral regimens may need to measure individual constructs of adherence to accurately assess adherence behavior. **Key words:** *adherence, antiretroviral therapies, self-reports*

The success of combination antiretroviral therapy (ART) has rapidly changed the primary treatment options for people with HIV infection. Effective long-term suppression of viral replication significantly prolongs disease-free survival in most HIV-infected persons and reduces opportunities for the development of drug-resistant viral variants.[1,2] Clinician and client optimism surrounding the efficacy of such regimens in reducing inpatient admissions, opportunistic infections, and mortality have been tempered by the emerging reality of sustaining a life-long commitment to near total adherence to potent, toxic, and complex regimens of ART.[3] The unforgiving and inflexible nature of regimens suggests that minimal levels of nonadherence may be associated with the emergence of drug-resistant viral variants, increases in viral load, and treatment failure.[4] In addition, cross-resistance to other antiretroviral medications within the same class further reduces treatment options.[5] The implications for the client are a reduction in treatment options, treatment failure, worsening clinical outcomes, and most significantly a reduction in quality of life.[6]

The degree to which people are able to adhere to therapy is a crucial factor in the clinical management of clients. The prediction of adherence in a range of client groups has been the focus of much research during the past 30 years.[7–9] The purpose of this research has been to identify specific nonad-

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herence traits in client populations so that interventions might be targeted to increase medication adherence. However, adherence has proved difficult to measure with accuracy.[10,11] Methods used to determine client adherence include: client self-reports, physician estimates, the count of medications through prescription refills, or the use of sophisticated electronic monitoring devices that track the date and time that medication containers are opened.[12] Each of these approaches are problematic as they depend upon the candor and memory of the client, the accuracy of the physician's judgment, or the assumption that if a medication is missing from a container it has been taken by the client. Biological assays to determine serum or urinary levels may be used with some drugs,[13] but, in general, ART medications have half-lives that preclude the use of these methods in day-to-day clinical management. Although self-reports have methodological difficulties, they have been frequently used in ART adherence studies, particularly within clinical trials.[14,15] Review of the literature suggests that people are more accurate in reporting nonadherence and there is a greater likelihood that they will adhere to treatment regimens if they are asked simple questions about recent behavior.[16–18] The potential simplicity of self-reports makes it an attractive option for clinicians to use in everyday clinical practice. However, valid and reliable self-report tools that provide useful information about medication-taking behavior and assist in clinical management, as opposed to tools used in clinical trials, are in the early stages of development. This article examines the associations between demographic and personal characteristics, clinical characteristics, engagement with health care providers, and quality of life factors with adherence to ART. In addition, it describes the use of principal component analysis (PCA) to compare two validated self-report tools with the self-report adherence scale (Patient Adjustment to Medication) developed by us, and it reports on inconsistencies in self-report tools that may have an impact on their use in research and clinical practice.

METHOD

Study Design and Recruitment

A cross-sectional study was conducted in a sample of 260 HIV-infected men and women attending nine hospital HIV outpatient clinics in England from October 1997 to April 1998. Local research ethical approval was sought and was granted at each center. Respondents were recruited to the study if they were 18 years old or older, had a Karnofsky performance score[19] of >50, were currently being supported by a health care provider, were able to speak and understand English, and were able to give informed consent. To promote candor, researchers who were not involved in the care of the clients conducted the interviews. A member of the research team approached clients during routine clinic visits and provided verbal and written information to explain the study. Those willing to participate gave written consent; reasons for nonparticipation were recorded. All the information divulged during the interview was confidential.

Data Collection Instruments

A researcher-administered questionnaire was developed and was piloted prior to the commencement of the study. It provided demographic data and elicited responses to variables previously associated with nonadherence to medication in people with HIV infection or other chronic diseases and included medication factors, clinical characteristics of HIV disease, health status, psychological state, mental attitudes to medication and disease, and social support.[20–26]

Medication Factors

Descriptive data related to the medications prescribed, medication burden, timing and frequency of medications, information needs and resources, perceived effects of medication, and client involvement in making choices were collected using items devised by the research team.

Adherence Scales

Adherence to prescribed medication was measured using three self-report instruments: the Morisky Medication Adherence Scale (MMAS),[27] the Reported Adherence to Medication Scale (RAM),[28] and the newly developed Patient Adjustment to Medication (PAM) scale.[29,30]

MMAS (a four-item scale) measured both intentional and nonintentional nonadherence based on

forgetting, carelessness, stopping medication when feeling better, or stopping medication when feeling worse. The scale is scored 1 point for each "no" response with a possible total score ranging from 0 (*nonadherent*) to 4 (*adherent*).

RAM (also four items) measured levels of agreement with "sometimes forgetting to take, or sometimes altering the dose of medication" and the perceived frequency of forgetting and altering medication dose. These items are rated on a 5-point scale, with the total score ranging from 4 (*very adherent*) to 20 (*nonadherent*).

PAM, a new scale that we developed, measured reported adherence to instruction.[29,30] In reviewing the literature surrounding adherence, it became apparent that adherence was a multifaceted phenomena and that clients were nonadherent in a variety of ways, as opposed to simply omitting their medication. Several studies[21–23] suggested that clients made adjustments to the instructions they had been given about taking the medication, and this seemed to be relevant to the complex regimens people with HIV infection were being asked to follow. The items developed for PAM focused on eliciting how closely clients were able to follow health care providers' instructions concerning the dose, timing, and frequency of their medications. It consists of three items that are scored on a 4-point scale, with a total score ranging from 3 (*always follows instructions*; adherent) to 12 (*never follows instructions*; nonadherent). In addition, PAM collected qualitative data concerning the reasons and methods of adjusting medication.

Key Clinical Characteristics

We collected data on the date of HIV infection and AIDS diagnosis, viral load measures, CD4 counts, hospital admissions in the past 12 months, and co-morbidities.

Engagement with Health Care Provider

The relationship between the client and health care provider was measured using the Engagement with Health Care Providers questionnaire.[31] This 13-item instrument asked respondents to indicate the degree to which statements about their interactions with their key health care provider were true based on a 4-point scale, where 1 = *always true* and 4 = *never true*. Another five-item scale addressed how closely respondents were able to follow the advice and instructions given by the health care provider.

Other scales were used to collect data concerning current health status (SF 36),[32] self-reported symptoms,[33] symptoms of depression (CES-D),[34] beliefs about ART,[35] attitudes to HIV diagnosis,[36] and social support (Close Persons Questionnaire).[37]

Data Handling and Analysis

An Epi Info (version 6) data entry program was created for each section of the questionnaire; data was entered, was converted to SPSS save files using DBMS/COPY (version 5.0),[38] and was finally merged into a single database. Data analysis was completed using SPSS (version 9.0).[39]

Data analysis was carried out in two phases. In the first phase, descriptive statistics were calculated for each element of the questionnaire. The internal reliability for each of the adherence scales was calculated using Cronbach's alpha.[40] This measure ranges from 0 (*no internal reliability*) to 1 (*perfect internal reliability*). Demographic and clinical factors were related to the adherence tools using Spearman correlation coefficients.

The second phase of analysis involved PCA of the three tools to identify possible multidimensional components for inclusion in a self-report instrument for measuring adherence. The factor structure of the adherence scale items was investigated. All questionnaire items that made up the MMAS, RAM, and PAM were entered into a PCA.[40] The adequacy of the data for this statistical model was tested using Bartlett's test of spherically and the Kaiser-Meyer-Olkin[40] measure of sampling adequacy. The resulting factor structure was rotated obliquely, which allowed the resulting factors to be correlated.

Scale scores for each factor were computed by rescaling all items loading on a factor to a range of 0–1 to give variables equal weighting and multiplying by 100 to give scores ranging from 0–100. Higher scores represented greater adherence. The goal of the PCA was to identify the underlying constructs making up the self-report measures and to determine the best performing items for future use. Cronbach's alpha[40] was used to determine the internal reliability of each scale. The analysis is fully described in the Results section.

RESULTS

Response Rate

Researchers approached 369 clients attending outpatient appointments. Of these, 260 agreed to participate in the study and met the entry criteria. This gave an overall response rate of 70% (range, 57%–82%). There were no significant differences between responders and nonresponders in terms of age and sex, although black women were less likely to agree to participate. Reasons given for nonparticipation included lack of time (n = 11), the length of the interview (n = 4), concerns regarding confidentiality (n = 7), failure to keep appointments or return completed questionnaires (n = 16), and difficulties with language and literacy (n = 4). Analysis demonstrated no significant differences between demographic or clinical characteristics of clients at each center, and data were therefore pooled for further analysis. Key demographic and clinical features of the study population are summarized in Table 1.

Demographic and Personal Characteristics

The mean age (±*SD*) of respondents was 39.9 years (± 9.9 years), with 57% of respondents (147) being under the age of 40. Almost half of the respondents (48%; 125) lived alone, 31% (81) owned their own home, and 30% (77) lived with a partner. Respondents were predominantly male (87%; 225) and white (85%; 222); 11% were black, (5 black Caribbean, 22 black African, 1 black other), <1% (2) were Asian, and 3% (8) were from other ethnic groups. A total of 13% (34) of the respondents were born outside the United Kingdom.

Living alone was associated with less adherent medication behavior for all three adherence scales (Table 2). Greater adherence to medication was associated with having a nonprofessional person identified as a caregiver (MMAS, p = .021). Age, social class, ethnicity, and level of education were not significantly associated with adherence for any of the measures.

Lifestyle Factors

In terms of risk factors, 74% (193) of participants described themselves as homosexual. Six percent (6%; 15) had a history of injecting drug use and 34% (88) used recreational drugs regularly or occasionally. Seventeen percent (17%; 44) smoked more than 20 cigarettes per day and 17% (44) drank more than 16 units of alcohol per week.

The use of recreational drugs was associated with nonadherence to medication regimens (MMAS, p = .001; RAM, p = .001) (Table 2). Current or previous use of intravenous drugs, current smoking, or alcohol consumption were not significantly associated with nonadherence.

Table 1. Demographic, personal, and clinical characteristics of study population (N = 260)

Characteristics	Percent	Number
Demographic features		
Age distribution		
18–19	<1	1
20–29	13	34
30–39	43	112
40–49	29	75
50–59	9	24
60–60+	5	14
Male	87	225
Caucasian	85	222
Social class 1 or 2	46	102
Employed	29	74
Student	10	27
Home owners	31	81
Living alone	48	125
Car available	62	162
Registered disabled	60	157
Left school at age 16 or >16	40	103
No educational qualifications	13	34
Personal features		
Homosexual	74	193
Current smoker	47	122
Current drinker	80	207
History of injecting drug use	6	15
Clinical features		
Diagnosed HIV pre-1990	37	95
Diagnosis of AIDS	39	100
CD4 currently rising	40	104
CD4 below 200	38	94
Viral load rising	17	45
Viral load less than 400	34	72
Hospital in past year HIV related	35	90
Opportunistic infections in past year	52	134

Table 2. Associations with adherence behavior as identified by MMAS, RAM, and PAM (N = 222)

Factors	MMAS	RAM	PAM
Demographic			
Female	r = -.078 (p = .25)	r = -.017 (p = .806)	r = .041 (p = .544)
Lifestyle			
Recreational drug use	r = -.223 (p = .001)	r = .225 (p = .001)	r = .074 (p = .284)
Current/previous IV drug use	r = -.098 (p = .145)	r = .06 (p = .380)	r = .098 (p = .149)
Clinical			
CD4 count	r = .043 (p = .534)	r = -.091 (p = .194)	r = .015 (p = .831)
HIV RNA viral load	r = -.088 (p = .211)	r = .026 (p = .714)	r = -.146 (p = .038)
Depression	r = -.158 (p = .02)	r = .256 (p = .001)	r = .120 (p = .077)
Medication			
Total no. of medications taken/day	r = .043 (p = .555)	r = .045 (p = .51)	r = -.210 (p = .003)
Total no. of dose events per day	r = .0 (p = .997)	r = .025 (p = .714)	r = -.172 (p = .012)
Medication information and instructions			
Not recognizing the importance of following instructions	r = .243 (p < .001)	r = -.337 (p < .001)	r = -.208 (p = .002)
HCP provides with information	r = -.151 (p = .026)	r = .158 (p = .021)	r = .048 (p = .487)
Influenced by general media	r = -.141 (p = .037)	r = .138 (p = .043)	r = .083 (p = .222)
Influence by HIV media	r = -.097 (p = .152)	r = .147 (p = .03)	r = .189 (p = .005)
Social Support			
Living alone	r = -.137 (p = .041)	r = .197 (p = .003)	r = .148 (p = .028)
Nonprofessional carer	r = .155 (p = .021)	r = -.055 (p = .423)	r = -.063 (p = .351)
Could rely on close confident	r = .139 (p = .045)	r = -.140 (p = .045)	r = -.214 (p = .002)
Access to practical help	r = .125 (p = .07)	r = -.059 (p = .397)	r = -.161 (p = .02)
Being comforted in someone's arms	r = -.143 (p = .037)	r = .150 (p = .03)	r = .018 (p = .798)
Perceived relationship with HCP			
Involves patient as a partner in care	r = .097 (p = .151)	r = -.071 (p = .298)	r = .143 (p = .036)
Helps patient to understand their care	r = -.078 (p = .251)	r = -.029 (p = .671)	r = .134 (p = .049)
Supports decisions	r = -.091 (p = .192)	r = .137 (p = .05)	r = -.015 (p = .832)
Accessible	r = -.137 (p = .045)	r = .127 (p = .064)	r = .057 (p = .403)
Mental attitude			
Plans for future	r = -.204 (p = .003)	r = .162 (p = .019)	r = .064 (p = .355)
Hopeful about future	r = -.164 (p = .016)	r = .172 (p = .012)	r = .068 (p = .321)
Active coping	r = -.212 (p = .002)	r = .152 (p = .028)	r = .059 (p = .392)
Positive evaluation	r = -.144 (p = .038)	r = .178 (p = .01)	r = .10 (p = .152)

Note: In this analysis, a high Morisky Medication Adherence Scale (MMAS) indicated good adherence and a high Reported Adherence to Medication Scale (RAM) and Patient Adjustment to Medication Scale (PAM) indicated poor adherence, therefore, any correlations reflect this difference. HCP = health care provider.

Key Clinical Characteristics

Key clinical characteristics are shown in Table 1. Of those interviewed, 37% (95) of participants had been diagnosed with HIV infection before 1990 and 39% (100) had an AIDS diagnosis. Respondents were asked to describe their current CD4 levels as rising, stable, or falling: 45% (117) reported rising CD4 levels, 38% (99) reported stable CD4 levels, and 17% (44) reported falling CD4 levels. Actual CD4 counts were recorded for the last two available measures; the time lapse between measures ranged from 1–3 months. The median CD4 for the most current and previous measures was 230 cells/mm^3 and 213 cells/mm^3, respectively. Similarly, viral load was described as rising by 24% (62) of the respondents, stable by 35% (91) of the respondents, and falling by 41% (107) of the respondents. Actual viral load was recorded for the last two available measures, with the time lapse between measures ranging from 1–3 months. The median plasma viral load was 1,400 HIV RNA copies/mL and 3,500 HIV

RNA copies/mL, respectively, for the most current and previous measures. Of the sample, 57% (149) participants reported HIV as their only health problem, and 35% (91) had been admitted to hospital in the past 12 months with an HIV-related illness. One or more opportunistic infections had been experienced by 52% (134) of respondents in the past 12 months, and 5% (14) had a diagnosis of tuberculosis. Sixty-four percent (64%; 140) of respondents had a CES-D score of 16 or above.[34] The mean CES-D score for the sample population was 19.8 ± 7.8 ($\alpha = 0.77$).

Clinical characteristics such as date of diagnosis, having an AIDS diagnosis, and CD4 counts were not significantly associated with adherence in this sample. However, higher viral loads were associated with greater adherence (PAM, $p = .038$) (Table 2). Depression, as measured by CES-D,[34] was significantly associated with nonadherence (MMAS, $p = .02$; RAM, $p = .001$).

Self-Reported Adherence to Medication

Medication burden and adherence data are reported on 222 of the 260 respondents who were taking ART at the time of interview; the following results relate to this group.

Medication Factors

No respondents were taking monotherapy, 27% (60) were taking two-drug combinations, 59% (130) were taking triple-drug combinations, 12% (26) were taking four-drug combinations, and 2% were taking five or more drugs in combination. The length of time respondents had been on ART therapy ranged from 3 months to 3 years: 69% (153) had been taking therapy for less than 1 year, 12% had been taking therapy for 1–2 years, and 19% (42) had been on therapy for 2–3 years. Over half of the respondents (63%; 139) were prescribed one or more protease inhibitors. Clients on therapy for more than a year were more likely to have taken other ART combinations. In addition, 74% (164) of those interviewed took prescribed medications other than ART therapy. Respondents also reported the number of tablets/capsules/elixir taken and the number of dose events in a 24-hour period. The proportion of respondents taking 1–9 tablets/capsules/elixir was 38% (84), 37% (82) reported taking 10–14, 15% (32) reported taking 15–19, and 10% (22) respondents reported taking in excess of 20 in a 24-hour period. When combined with other prescribed medications, 72% (160) were taking 10 or more tablets/capsules/elixir per day. The number of dose events in a 24-hour period ranged from twice (39%; 87), three times (32%; 71), four times (14%; 31), five times (8%; 18), and six or more times (7%; 15). Eighty percent (80%; 172) of respondents stated that they always or sometimes experienced side effects, and 15% (34) of respondents said that this impacted on their decision to take prescribed therapy. The most frequently reported side effects included nausea, vomiting, and gastric upset, loose stools and diarrhea, skin rash and irritation, numbness and tingling, and lethargy and tiredness.

The total number of medications being taken (PAM, $p = .003$) and the number of dose events in 24 hours (PAM, $p = .012$) were significantly associated with poorer adherence (Table 2). The type of medications, pill burdens, side effects, or restrictions on lifestyle were not significantly associated with nonadherence.

MMAS

Nearly half the respondents (45%; 99) reported that they forgot to take their medication, 10% (21) reported being careless about taking their medication, 8% (18) reported that they stopped taking their medication when they felt better, and 9% (22) reported that they stopped taking their medication when they felt worse. The mean MMAS nonadherence score in this sample was 3.3 ± 0.77 ($\alpha = 0.31$).

RAM

On the RAM scale, 38% (82) respondents strongly agreed or agreed that they sometimes forgot to take their medication and 14% (31) strongly agreed or agreed that they sometimes altered their medication to suit their own needs. However, when they were asked how often they forgot to take medications, only 4% (9) reported forgetting often or very often, 16% (35) reported sometimes forgetting, and 16% (36) reported rarely forgetting to take their medication. Reporting on how often doses were missed or adjusted to suit their own needs, 3% reported that they did this often or very often, 9% (20) reported that they did this some-

times, and 29% (49) reported that they rarely missed or adjusted doses. The mean RAM score for the study sample was 7.3 ± 3.07 (α = 0.66).

PAM

On the PAM scale, 30% (67) of respondents rarely or never followed the instructions they were given about the dose of their medications, 30% (67) rarely or never followed instructions regarding the frequency with which they took their medications, and 50% (111) altered the time that they took their medications. In addition, 41% (60) never discussed the changes they made to their regimen with their physician. The mean score for PAM was 5.4 ± 2.86 (α = 0.84).

Characteristics of the Health Care Provider

In 93% (206) of responses, the key health care provider was identified as the physician. Where respondents identified a second key health care provider, 33% (61) stated that it was a nurse. The interpersonal, supporting, and empowering skills of the key health care provider were perceived positively by respondents as shown in Table 2, with 66% (170) being very satisfied with the care provided by their health care provider. The mean satisfaction score for the sample population was 16.7 ± 5.1 (α = 0.92).

Respondents who perceived that their health care provider provided them with information (MMAS, p = .026; RAM, p = .021); supported his/her decisions (RAM, p = .049); were accessible (MMAS, p = .045); helped them understand things about their care (PAM, p = .49); and involved them as a partner in their care (PAM, p = .036) were more likely to be adherent to therapy (Table 2).

Information and Control Factors

When asked to give an opinion on a range of information and control of medication variables, 14% (31) of participants did not feel sufficiently informed to make decisions about their medications. Thirty-one percent (31%; 69) felt that they had been given little choice in the medications they had been prescribed, and 22% (48) had not been involved in decisions about changes in medication regimens. In addition, 12% (27) of respondents did not consider that it was important for them to be in control of their medication, and 39% (87) were not worried about the possibility of developing viral resistance.

Factors significantly associated with nonadherence were not recognizing the importance of following instructions (MMAS and RAM, p = .001; PAM, p = .002), being influenced by information presented in the general media (MMAS, p = .037; RAM, p = .043), and being influenced by the information in the HIV-specific media (RAM, p = .03; PAM, p = .005) (Table 2).

Locus of Control

Respondents who reported having plans for the future (MMAS, p = .003; RAM, p = .019) and being hopeful about the future (MMAS, p = .016; RAM, p = .012) were more likely to be adherent than those who were not. Similarly, those who perceived that they coped actively with their HIV (MMAS, p = .002; RAM, p = .028) and who evaluated themselves positively (MMAS, p = .038; RAM, p = .01) were more likely to adhere to their medication regimens (Table 2).

Social Support

Half of the respondents lived alone, but 78% reported that they had a nonprofessional available to help them with their care. For 30% of respondents, this person was their partner. Only 5 respondents reported that they had no close confidants, and 30 respondents reported having one or two people in whom they could confide. Forty-three percent (43%) of the respondents never saw any relatives, and 26% reported seeing friends less than once a month.

Those people who reported relying a great deal on their close confidant were more likely to be adherent (MMAS, p = .045; RAM, p = .045; PAM, p = .002). In addition, those who reported that this person gave a great deal of practical help were more likely to be adherent (PAM, p = .02). Respondents who reported that they had been comforted in someone's arms every day were more likely to be adherent (MMAS, p = .037; RAM, p = .03) (Table 2).

Principal Component Analysis (PCA)

The range of factors associated with adherence behavior and their significance varied between the

three adherence tools used in this study. PCA indicated that the relationships between the questionnaire items from MMAS, RAM, and PAM might usefully be represented by four underlying constructs: forgetting to take medication, not following instructions, altering/missing doses, and difficulties with regimen. These four factors accounted for 61% of the variance in 14 questionnaire items and 63% of the variance in 12 questionnaire items, with two poorly performing items excluded. Table 3 shows the resulting factor structure and the four coherent groupings referred to previously.

The first and third factors to emerge from the analysis combined items from MMAS and RAM scales and can be seen to represent unintentional (forgetting) and intentional (altering dose) nonadherence. However, the second factor (not following instructions) was derived solely from PAM, the novel items devised by the researchers, and suggests that following instructions represents a distinct area of nonadherence not measured by MMAS or RAM.

The internal reliability for each of the scales was forgetting to take medication ($\alpha = 0.7$), not following instructions ($\alpha = 0.9$), altering/missing doses ($\alpha = 0.5$), and difficulty with regimen ($\alpha = 0.3$). Because the internal reliability of the last scale, difficulties with regimen, was unacceptably low, this scale was dropped from further analysis. The internal reliability for the scale "altering/missing doses" was borderline at best, but because it represented the only explicit measure of intentional nonadherence it was included in further analyses. These discrete facets of adherence were entered into a regression analysis. None of the associations previously attributed by MMAS, RAM, or PAM reached significance (Table 4).

DISCUSSION

The results of this study have shown that some self-report tools may compound the facets of intentional and nonintentional adherence. Although there are a range of clinical, demographic, and health care-related variables that can be individually associated with adherence behavior, there is little consistency in these relationships between studies.[41–52] Nonadherence has been closely associated with treatment failure in ART studies.[4,5] However, other factors such as inadequate absorption, existing resistance to some elements of the prescribed regimen, or suboptimal prescribing may result in increases in plasma RNA.[46] Lifestyle factors may be important determinants of adherence behavior. Factors associated with nonadherence, such as living alone and recreational drug use, may be explained as much by the lack of daily routines and patterns of activity that would normally provide a structure for taking medications as by the presence or absence of substance use or significant others. The association between higher HIV RNA viral load and greater adherence has not been reported in other studies; in fact, most studies report adherence as being associated with low or undetectable viral load.[44,53] In our study, many of the respondents stated that bringing about a fall in their viral load was their main reason for taking ART. It is possible that clients with higher viral load may have a greater motivation to adhere to their medication regimens. Some of the apparent disparities between published research may also be due to differences in populations and approaches to measurement across studies.[46] The lack of consistent associations between MMAS, RAM, and PAM and potential determinants of adherence in this study emphasizes this point.

The use of behavioral measures of adherence such as self-reports are not considered to be as objective as the use of biological markers or to provide the detailed information that is available from electronic monitoring devices.[54–56] However, self-reporting has the potential to be the most useful measure of adherence, because only the patient is actually able to report what has been taken.[57] In addition, as a method, it has the advantage of being relatively inexpensive and quick and easy to administer. The criticism of self-report measures has so far been leveled at the ability and inclination of patients to accurately report adherence behavior. Research suggests that patients are more accurate when they are asked about missed doses than when they are asked if they have taken their medication. In addition, recall is enhanced if patients are asked about periods of time no longer than 1 month.[53]

Our analysis suggests that different tools may give different associations and that tools that combine well-described facets of adherence behavior may lead to flawed assumptions, particularly if such measures have low reliability. In this study, regression analysis after PCA failed to confirm the associations of adherence suggested by the

Table 3. Factor loadings for four-factor solution of adherence items (63% of variance explained) (*N* = 222)

Item	F1 Forget	F2 Follow instructions	F3 Alter dose	F4 Difficulties
I sometimes forget to take my medication.	**.89**	-.18	.14	-.16
Do you forget to take any of your medication?	**.86**	-.09	.24	-.17
Some people forget to take their medication. How often does this happen to you?	**.80**	-.14	.28	-.27
Do you exactly follow the instructions about the frequency of your medication?	.18	**.90**	.06	-.15
Do you exactly follow the instructions about the time of your medication?	.14	**.89**	.09	-.03
Do you exactly follow the instructions about the dose of your medication?	.07	**.86**	.07	-.14
When you feel better do you stop taking any of your medication?	.08	.00	**.75**	.07
I sometimes alter the dose of my medication.	.26	-.08	**.64**	-.16
Are you careless about taking any of your medication?	.29	-.06	**.61**	-.02
If you feel worse when you take any medications, do you stop taking them?	.07	-.10	**.60**	-.23
Some people miss doses of their medication. How often does this happen to you?	.11	-.06	.09	**-.81**
How difficult has it been to follow your health care providers advice and instructions?	-.27	.14	-.12	**.71**

Table 4. Hierarchical multiple regression predicting self-reported adherence (N = 222)

	Forget		Follows instructions		Alters dose		Difficulties with regimen		
Variable	R^2	Change in R^2	R^2	Change in R^2	R^2	Change in R^2	R^2	Change in R^2	p
Block 1: Ethnicity	0.007	0.007	0.026	0.026	0.070	0.070	0.041	0.041	NS
Block 2: Person	0.067	0.06	0.050	0.024	0.106	0.036	0.179	0.138	NS
Block 3: Clinical features	0.101	0.033	0.101	0.051	0.138	0.032	0.243	0.063	NS
Block 4: Symptoms	0.126	0.025	0.135	0.034	0.179	0.041	0.259	0.016	NS
Block 5: Functional status	0.185	0.059	0.166	0.031	0.197	0.018	0.330	0.072	NS
Block 6: Quality of life	0.202	0.016	0.208	0.042	0.216	0.019	0.341	0.010	NS
Block 7: Resources	0.207	0.005	0.227	0.020	0.306	0.090	0.371	0.030	NS
Block 8: Social support	0.224	0.017	0.283	0.055	0.373	0.067	0.385	0.015	NS

univariate analysis using individual self-report tools. The factors identified by the PCA correspond closely to the way in which adherence is commonly construed as nonintentional nonadherence or forgetting and intentional nonadherence or missing doses.[58] MMAS and RAM measure both of these concepts and give a composite score of adherence. The PAM scale measures a single construct independent of those measured by the other two scales.

Multiple regression analysis is currently the statistical method that is used to analyze adherence data and should, in theory, allow us to isolate which, if any, of a set of variables are the most useful in determining a level of adherence. This is only true if the measure of adherence being used is coherent and measures a single construct. Logically, we would not expect the variables correlated with forgetting to be the same as those correlated with intentional nonadherence, but this is exactly the assumption that is made by a regression analysis using MMAS and RAM. The problem with some existing self-report tools is that they assign a single value to a case that can mean different things in different cases. For example, a respondent with a MMAS score of 1 might mean that the respondent was forgetful, whereas for another respondent the same score of 1 might mean that they intentionally altered the dose of medication. This lack of consistency may be one of the reasons for the variation in findings related to the determinants of adherence in HIV and other diseases. Our results suggest that in addition to patient honesty and recall in reporting, the measurement of individual constructs of adherence within self-reports may be important to the accurate identification of the possible determinants of adherence behavior.

A number of tools currently under development[57,59] for use within HIV clinical trials have been designed to take into account the impact that adherence may have on the scientific integrity of AIDS clinical trials. These tools tend to focus on the recollection of missed doses (intentional nonadherence) and the surrounding circumstances, including "forgetting" or nonintentional nonadherence over a period of 4–7 days prior to the appointment. As with our study, these tools use a multifactorial approach to exploring determinants of adherence; but unlike MMAS or RAM, they do not appear to compound the facets of intentional and nonintentional nonadherence. Clinical trials offer researchers the opportunity to follow populations of patients and assess adherence behavior as part of the evaluation of therapeutic outcomes. However, clinical trials are generally well resourced and patients have access to information and professional support that may be in excess of that available to nontrial patients. The personal and economic costs of treatment failure mean that the assessment of adherence in everyday clinical practice must form a central part of the clinician–patient interview.

The strength of self-reporting in the assessment of adherence may not be in its use to identify determinants of adherence in populations but in its use to build an individual profile of adherence behavior for a particular client. A consistent and reliable approach to monitoring adherence in individuals may offer clinicians a greater opportunity to tailor regimens and provide appropriate support for people facing the real problems of adhering to complex, toxic regimens that have far-reaching effects on their quality of life.

There are a number of limitations associated with our study. The range of factors being investigated in our study meant that the questionnaire contained a battery of instruments and took between 1 and 2 hours to complete; this time scale was of concern to some of the clients who were approached. The response rate may have improved if the questionnaire had been shorter. The sample consisted of patients who were attending outpatient departments (OPD), who were currently taking ART, and who were judged to be representative of the clinic population. There were slight differences in the way in which clients were recruited in each OPD, but comparative analysis of the sites demonstrated no differences between the main clinical and demographic characteristics of respondents from each clinic. When compared to national data from the Survey of Prevalent Diagnosed HIV Infections (SOPHID) for 1997,[60] our sample had a higher proportion of whites (85% of the sample vs. 61% in the SOPHID data). The reluctance of non-whites to participate in the study may have been due to language or literacy difficulties and concern about the confidentiality of information. This was particularly true of black men and women. Two percent (2%) of the study sample were between 15–18 years old compared with 4% in the SOPHID data. This was accounted for by the exclusion of 15–17 year olds within the study entry criteria. Females accounted for 13% of the sample

compared with 18% in SOPHID data. The small number of injecting drug users within the sample population was related to the fact that these clients tend to be seen in specialist clinics.

Our study suggests that existing adherence tools may be confounded by their inability to distinguish between well-recognized facets of adherence behavior and may lead to flawed assumptions about the determinants of adherence in individuals and populations. If self-reporting is to be of use in everyday clinical practice, it needs to be designed to measure single constructs of adherence, and it should be used to monitor the dynamic and multifactorial nature of adherence in individuals rather than to predict adherence in a collective population. The items developed in PAM may form one element of such a self-report tool. Further development will improve its reliability and practicability for use in clinical settings through cross-validation in other client populations.

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