

Barriers to Antiretroviral Adherence among HIV-Infected Adults

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ABSTRACT

Success of highly active antiretroviral therapies (HAART) relies on HIV-infected patients being able to adhere to complicated treatment regimens for extremely long periods of time. Four focus groups with patients taking antiretrovirals ($N = 39$) were conducted to: (1) determine what strategies facilitate successful adherence; (2) determine what barriers prevent adherence; and (3) investigate the health-care provider and patient relationship and how it may impact adherence. Quantitative and qualitative information was gathered. Participants were prescribed an average of 15 pills per day ($M = 14.7$, $SD = 6.3$, range 4 to 36). Findings from the quantitative data revealed that the three strategies used most often to aid adherence were: carrying special containers for medication; having a health-care provider explain or clarify medication requirements; and carrying food and water for adherence to special instructions. The most difficult barriers for patients were sleeping through dose time, problems in following special instructions, and changes in daily routines. From the qualitative data, four main categories of barriers and aids to adherence emerged: patient characteristics, the health-care provider-patient relationship, the health-care system, and issues related to the medication regimen. Barriers related to the health care provider-patient relationship included patient satisfaction with their provider, as well as quality of communication with the provider. In addition, health-care system barriers caused difficulty in maintaining adherence. Implications for patient as well as provider interventions are discussed.

HIGHLY ACTIVE ANTIRETROVIRAL THERAPIES (HAART) have proven to be effective agents resulting in inhibition of viral replication and reduction of viral load to a point where viral particles are undetectable in the blood for many HIV-infected patients. However, success of these medications relies on patients being able to adhere to complicated treatment regimens for extremely long periods of

time. Interruptions in medication adherence permit the virus to resume its typical rapid replication—as many as 10^{10} viral particles produced per day.^{1,2} This allows the generation of resistant mutant strains that are no longer responsive to available antiretroviral drugs, which in turn poses a public health danger.³

Adherence is defined as the extent to which a patient's health-related behaviors correspond

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with medical advice. Currently, treatment guidelines state that the therapeutic regimen for acute HIV infection should include a combination of two nucleoside reverse transcriptase inhibitors and one potent protease inhibitor (Panel on Clinical Practices for Treatment of HIV Infection). Frequent dosing, with up to as many or more than 20 pills per day, is required to maintain suppression of viral replication and prevent resistance.⁴ In addition, some of these medications require following special instructions (e.g., fasting; taking the dose with a high-fat meal); and adverse side effects are common. Rates of nonadherence to antiretroviral therapy among HIV-positive adults have ranged from 37 to 70%.⁵⁻⁷ For example, studying zidovudine alone, zidovudine plus didanosine, and didanosine alone, 63% of patients were found to be compliant—with compliance defined as taking 80% or more of prescribed medication.⁷

Although researchers are currently working to find ways to simplify medication dosages, such as developing drugs with fewer side effects, combining two drugs in a single capsule, developing longer lasting drugs, or developing drugs with no adverse interactions with food or other drugs, it is clear that HIV-infected patients will continue to be faced with a significant medication adherence challenge. Studies have not yet identified estimates of the number of doses missed before resistance develops, but the following indicate the potential magnitude of the problem: there is an association between an increase in viral load and notes in individual medical records suggesting nonadherence; there is a direct relationship between the risk of developing a detectable viral load and delays in refilling prescriptions; and an increase in viral load has been reported for patients who missed three days of therapy.⁸ Due to the rapid development of resistance when doses are missed, HIV+ patients need to strive for “perfect,” or 100% compliance.

There appear to be several factors that affect adherence. One set of variables has to do with the treatment regimen itself. The more complex the regimen, the less likely a patient is to follow it, regardless of age and educational level.⁹ A linear decrease in adherence with increasing number of doses per day has been found across

medications and diseases.¹⁰⁻¹² A second set of variables has to do with the factors related to the illness for which the treatment is prescribed. Typically, noncompliance has higher associations with long-term prescriptions than with shorter term prescriptions.¹³ Nonadherence among patients also appears to be more prevalent when an illness is chronic and the treatments are largely prophylactic.^{14,15} A third set of variables have to do with patient characteristics. For example, depressed patients have been found to have poorer adherence than nondepressed patients^{7,16,17} (D.A.M., unpublished data, 1999). Finally, variables related to the health provider and patient relationships may affect compliance.¹⁷ When patients feel they are engaged in a participatory relationship with the health-care provider, adherence is improved.^{18,19}

In the current study, a series of four focus groups was conducted among HIV-infected patients who were currently on a HAART regimen. There were three aims of conducting the focus groups: (1) determine what strategies facilitate successful adherence; (2) determine what barriers prevent adherence; and (3) investigate the health-care provider and patient relationship and how it may impact adherence. Successful strategies and barriers were assessed through completion of a checklist survey as well as through open discussion; thus, quantitative and qualitative information was gathered during the focus groups.

METHOD

Participants

Focus group participants were recruited from an HIV clinic and through an advertisement in an AIDS publication. Inclusion criteria were that patients be at least 18 years of age, have an HIV diagnosis, and be currently prescribed HAART. Of 54 individuals invited to participate in the project, 45 were scheduled for a group, with 9 refusing participation because they did not have time. Six participants did not show up at their scheduled group, resulting in a final sample size of 39. No identifying information was collected from participants during

the groups and only first names were used in the discussion.

Participants ranged in age from 33 to 54 years ($M = 40.9$, $SD = 5.5$); 69% were male. Racial/ethnic composition of participants was as follows: 44% African-American, 39% White, 6% other or mixed race, and 6% Latino. In terms of education level, 16% of the participants had a graduate college degree; 24% an undergraduate college degree; 32% some college; 19% had completed high school or a GED; and 8% had less than a high school education. Median monthly income was in the range of \$500–1000 (see Table 1). Length of time receiving some type of antiretroviral therapy ranged from 2 months to almost 12 years ($M = 4.3$, $SD = 3.3$). (One participant reported having participated in one of the earliest clinical trials).

Procedures

Interested participants were scheduled for an enrollment interview during which the study was further explained and the informed con-

sent process was conducted. When a sufficient number of participants were identified, a focus group was scheduled; a total of four focus groups were conducted. Participants received \$30 for participation, and refreshments at the group meeting. All focus groups were audio-taped and then transcribed. Two group facilitators led each group (a male and a female), and followed a structured script.

Assessment

Adherence assessment. Participants were first asked to complete a form in which they listed their antiretroviral medication regimen, and were then asked to rate how difficult they found the instructions for taking their medications (5-point scale from 1 = not difficult at all to 5 = impossible). They were then asked to rate how closely they followed their specific medication schedule over the past 7 days (5-point rating from 1 = not at all to 5 = all of the time). Finally, to determine what participants perceive to be sufficient adherence in terms of the schedule of their regimen they were asked to describe how closely they had to follow their prescription to consider that they were successfully adherent (e.g., within 1 hour of when you are supposed to take them, within 2 hours, etc.).

Strategies and barriers to adherence checklists. Two survey checklists of strategies and barriers to adherence were completed. Successful strategies for adherence were rated on a 4-point scale of frequency used and barriers were rated as to how often they were experienced (1 = not at all to 4 = very often). The strategies checklist was developed by modifying a previous strategies coping scale (D.A.M., unpublished data, 1999) and making each item specific to medication adherence, and the barriers checklist was adapted from the AIDS Clinical Trials Group (ACTG) Adherence Baseline Questionnaire.²⁰

Open-ended discussions. Two principal topic areas were addressed in the open-ended discussions: (1) personal experiences of participants in trying to adhere successfully to their antiretroviral medication regimes, including both successful strategies they had used and

TABLE 1. FOCUS GROUP DEMOGRAPHICS (N = 39)

	%
Gender	
Male (27)	69
Female (12)	31
Hispanic	
Yes	24
No	76
Race	
Asian/Pacific Islander	3
Black/African-American	44
Latino/Latina	6
Native American/Alaskan Native	3
White	39
Other or mixed race	6
Education level completed	
8th grade	5
11th grade	3
12th grade	14
Some college	32
College degree (undergraduate)	24
College degree (graduate)	16
GED	5
Monthly income	
\$0–500	24
\$500–1000	49
\$1000–2000	14
\$2000–3000	8
>\$3000	5

barriers to adherence that they had encountered; and (2) the nature of participant's interactions with their health-care providers relative to the initiation of their antiretroviral therapy, their ability to discuss problems with that therapy with their provider, and the accuracy with which they reported their adherence to that provider. The discussion of interactions with health-care providers was structured around the following questions: (1) How did participants prefer to make their health-care decisions? Did they prefer to take an active role in decision-making or prefer having medical professionals make their decisions for them? (2) Did participants' health-care provider involve them in the decision about their current therapy? (3) Were the risks and benefits of antiretroviral therapy explained to participants during the decision-making process? (4) How do participants discuss their therapy with their providers now, including problems with side effects or with special instructions for medications? and (5) Have participants ever misled their health-care provider about their adherence to the medications prescribed for them?

Analysis

Simple descriptive statistics were used to assess data from the adherence assessment and the strategies and barriers survey questionnaire. For the qualitative information, a content analysis was performed on interview data. A line-by-line review of the transcripts was performed and first-level codes (descriptors of important components of the interviews) were noted; all coded segments were entered into Ethnograph, a software program for computer-based text search and retrieval. Data corresponding to each of the first-level codes were printed and reviewed, and subcodes were established to divide the first-level codes into smaller categories. The results correspond to the emergent categories, and all quotations are drawn directly from the groups.

RESULTS

Adherence assessment

Descriptive summaries of the data were chosen over comparative statistics (e.g., testing

percentage or mean differences) because of the heterogeneity of the groups (see Table 1). Overall, participants took about 15 pills each day ($M = 14.7$; $SD = 6.3$), with a range of 4 to 36 pills each day. Regarding antiretroviral medication use, the most frequent medications used by participants were D4T (56%), 3TC (49%), Nelfinavir (33%), and Ritonavir (33%). A wide variety of combination therapies were prescribed; the most common was the three-drug combination of Nelfinavir, DDI, D4T ($n = 4$), followed by the combination of D4T, 3TC, Nel-

TABLE 2. DRUG COMBINATIONS REPORTED BY FOCUS GROUP PARTICIPANTS

Participant ID	Medications taken
1	Ritonavir, D4T, Saquinavir, 3TC
2	D4T, 3TC, Nelfinavir
3	Nelfinavir, D4T, 3TC
4	Nelfinavir, D4T, 3TC
5	3TC, D4T
6	DDI, Nelfinavir, 3TC
7	Ritonavir, 3TC, AZT
8	Combivir
9	Fortovase, Combivir
10	Nelfinavir, 3TC, D4T
11	Nelfinavir, DDI, D4T
12	Combivir, Fortovase, Ritonavir, Nevirapine
13	Nelfinavir, Combivir, Saquinavir, Nevirapine, DDI
14	Hydroxuria, D4T, 3TC
15	D4T, 3TC, Indinavir
16	D4T, Ritonavir
17	D4T, Nevirapine, Abacavir, Preveon, Sustiva
18	Indinavir, D4T, DDI
19	AZT, Indinavir
20	Nelfinavir, DDI, Combivir
21	Nevirapine, Ritonavir, Fortovase
22	3TC, Ritonavir, Myambutol, Nevirapine, Neurontin
23	Ritonavir, Saquinavir, 3TC, D4T
24	Saquinavir, Combivir
25	3TC, D4T, Nelfinavir, DDI
26	3TC, D4T, Ritonavir
27	Ritonavir, Saquinavir
28	Indinavir, Ritonavir, D4T, Sustiva
29	D4T, 3TC, Saquinavir, Ritonavir
30	Sustiva, Nelfinavir, DDI, D4T, Indinavir
31	AZT, 3TC, Ritonavir, Fortovase
32	Ritonavir, Fortovase, DDI, D4T
33	3TC, D4T, Indinavir
34	Nelfinavir
35	Saquinavir, 3TC, AZT
36	Nelfinavir, DDI, D4T, Nevirapine
37	Fortovase, Combivir, Nelfinavir
38	Indinavir, Nevirapine, AZT, DDI
39	Rescriptor, 3TC, D4T, Indinavir

finavir ($n = 4$), and Ritonavir, D4T, Saquinavir ($n = 4$). Table 2 shows the full compliment of drug combinations reported by focus group participants.

In terms of dosage adherence over the past week, only 33% of the participants said they had been fully adherent; 40% said they had adhered most of the time; 19% said they adhered about half of the time; and 8% said they had adhered only a little or not at all. In terms of their prescribed schedule, patients varied widely in terms of what they considered "successful adherence." 10% of the patients defined it as taking medication at the exact time prescribed; 8% within one-half hour; 30% within an hour; 11% within 1 to 2 hours; 8% within 2 to 5 hours; and 22% sometime within the day. Ten percent of the patients varied the time of their adherence schedule, but took their medications either with their main meals (breakfast, lunch, and dinner) starting whenever they had breakfast, or spaced throughout the day (morning, noon, and night) from whenever their day began.

Strategies and barriers to adherence checklists

For adherence strategies, Table 3 contains the percent of participants using each adherence strategy. Adherence strategies may be considered any behavioral action or use of a physical object to help participants remember to take their medication. The three most frequently

noted adherence strategies included carrying special carriers/containers for medication storage and transport (58%), asking a doctor or nurse to help explain/clarify medication dosage (42%), and carrying food and water for dosage (37%). The least reported strategies used were agreements with family/friends to remind the person to take their medication (8%), using diaries/schedules of dosages (5%), and wrist alarms/reminders of dosage time (3%). It should be noted that the percentages reported for these adherence strategies are indicative of the strategies used most or least frequently, and thus are not necessarily indicative of success rate of a particular strategy.

Table 4 contains the percentage of participants listing each of the barriers surveyed. An adherence barrier was considered to be any issue that prevented participants from taking their medications as prescribed. These included issues related to: (1) the participants' health status (e.g., participants felt too sick to take their medication, or felt healthy and decided they did not need to take their medication); (2) the physical nature of the regimen (e.g., participants had to take too many pills, or their medication needed refrigeration); (3) the participants' emotions (e.g., depression, confusion); (4) participant avoidance (e.g., participants did not take their medication because they wanted to avoid side effects or they wanted to be able to drink alcohol later); and (5) the participants' schedule (e.g., the medication regimen did not

TABLE 3. PERCENTAGE OF PARTICIPANTS WHO FOUND THE FOLLOWING STRATEGIES HELPFUL IN TAKING THEIR MEDICATIONS

<i>Strategy category</i>	<i>Frequency</i>	<i>%</i>
Assistance device strategies		
Using special carriers/containers	22	58
Carrying food and water for dosage	14	37
Diaries/schedules of dosage, carry and record dose	2	5
Wrist alarms/reminders of dosage time	1	3
Social support strategies		
Asking doctor/nurse to explain/clarify dosage	16	42
Having health-care provider ask if you are taking medications as prescribed	14	37
Join support group to share problems/concerns	11	29
Disclosing HIV status to family/friends/co-workers—no need for privacy	6	16
Agreements with family/friends to remind you to take medications	3	8
Medication management strategies		
Changing medications to get easier dosage schedule	12	32
Changing medications for fewer side effects	7	18
Changing daily routine including breaks for medications	7	18

TABLE 4. PERCENTAGE OF PARTICIPANTS IDENTIFYING THE FOLLOWING BARRIERS TO ADHERENCE

<i>Barrier</i>	<i>Frequency</i>	<i>%</i>
Slept through dose time	20	53
Had problems taking pills with special instructions	19	50
Had change in daily routine	18	47
Did not have medications with you	16	42
Busy and did not want to stop to take medications	16	42
Simply forgot	15	40
Felt depressed or overwhelmed	14	37
Felt angry, depressed, or hopeless that you have to deal with this	13	34
Wanted to forget the whole thing	12	32
Wanted to avoid side effects	10	26
Had too many pills to take	8	21
Felt like drug was toxic or harmful	8	21
Felt sick or ill	8	21
Confused about what you were supposed to do (No. of pills, when)	8	21
Forgot how many pills you already took	8	21
Did not want others to notice you taking medications	6	16
Already missed medications on a day, so you missed more for the day	6	16
Felt healthy and did not think you needed to take medications	5	13
Doubled up on a dose because you missed a dose	4	11
Were confused about the dose	3	8
Had difficulty keeping medications refrigerated during the day	2	5
Had questions and had trouble getting a hold of a doctor/nurse	2	5
Had not refilled the prescription	2	5

fit well into their daily routine). The barrier reported most frequently by participants was falling asleep or sleeping through a dose (53%), which suggests a strong accidental component in missing doses. The second most reported barrier was problems following special instructions (50%), followed third by changes in daily routine (47%). The least problematic barriers included not refilling the prescription, trouble getting a hold of a doctor/nurse, or medicine refrigeration issues (5%), confusion about a dose (8%), and feeling healthy so no need to take medication (13%).

Open-ended discussions

From the content analysis of the focus group interview data, four main categories of barriers to adherence and of aids to adherence with antiretroviral medications emerged. These categories were: patient characteristics, the health-care provider-patient relationship, the health-care system, and issues related to the medication regimen.

Patient characteristics: adherence barriers and successful strategies. Some of the focus group

participants had beliefs regarding adherence that led them to nonadhere. For example, one participant believed that it was all right for HIV-positive patients to miss antiretroviral doses as long as they felt healthy and got good results on laboratory tests: "I think a lot of this probably has to do with how good a person feels. If a person feels like they're healthy and they [miss], they're like, 'Well, if I missed my dose, that's okay, as long as I feel good or as long as I get a good report on my health.'"

Other participants had conflicting information regarding what they should be doing that led to adherence problems. Illustrative of this problem, one person explained, "I think the hardest thing about . . . sticking with [medication adherence] is the eating problem. . . . It's like you're wasting, so you got to eat to keep up your strength. But then you can't eat because you got to take the pills."

Next, those who had erratic daily schedules, who traveled, or left their homes during the day without their pills found it difficult to adhere. One participant disclosed: "My schedule isn't as regimented. Every day is totally different. I'm a night owl and some days I sleep to 11:00 and some days I'm up at 6:00 a.m. And

with such an unorganized schedule, it's pretty difficult for me to, every eight hours, take the medication."

The final patient-related barrier was an unwillingness to take doses in public places, including when they were at work, or with certain friends or family members. One individual stated: "During May and June and July, I may go home to Memphis and stay anywhere from two to four months. So, the biggest problem I was having there was ducking and dodging my nieces and nephews and sister-in-law, in taking my medication."

Those participants who believed that adhering to their antiretroviral regimens would allow them to live longer and healthier lives found this to be an aid to adherence. One person said, "I find it very easy because what motivates me to take it is that I want to live. And that alone helps me to remember to take my medication."

Participants who had predictable daily schedules often had an easier time adhering. A common strategy was tying their medication doses to routine daily events: "When I get up in the morning, I'll eat breakfast, take my meds. . . . And when I come in for dinner at night, I take my second regimen, and before I go to bed, I have a liquid that I take at bedtime."

Some respondents found particularly creative ways to tie doses to their daily schedules, such as taking a dose whenever they fed their pet.

Another strategy was carrying medications when leaving home during the day. A respondent maintained: "When I go visiting my friend . . . I make sure that I always carry a bottle of liquid and just pills . . . I might not bring clothes . . . but I've got that medication." Similarly, because many of the medications must be taken with food or a lot of water, another strategy was to carry food and water: "Usually what I do is I'll pack a little snack with me. Sometimes carrots, sometimes a little box of raisins."

Finally, interactions with other people sometimes aided patients' adherence. Some respondents had friends or family members who were vigilant about reminding them to take their doses. One person said: "My wife keeps me on schedule. Yeah, she does. 'Time to get your pills.' Regardless of what I'm doing, if I'm

asleep, if I'm awake, if I'm sick over the toilet or something like that [laughs], she gives them to me."

Another respondent developed a buddy system for pill reminders with a friend also on an antiretroviral regimen: "We call each other . . . 'Take the pills and have you taken yours?' If you have somebody who's on the same schedule as you, it's easier because then you can . . . keep up with each other. It helps."

Health-care professional-patient relationship: adherence barriers and successful strategies. Barriers related to the health-care provider-patient relationship included patient satisfaction with their provider, as well as quality of communication with the provider. One respondent disclosed: "The first time that I started playing with antiretrovirals and protease inhibitors, it was a mess. It just didn't happen. I wasn't into it and I stopped doing it . . . mostly because of the hatred I developed for my health-care provider. [The provider was] so completely indifferent and basically threw things up and said, 'Do this,' and . . . scheduled . . . appointments for like 10 minutes apart from each other."

Respondents also experienced adherence problems when they received confusing instructions from their providers about how to take their pills. For example, one person stated that his provider gave him instructions for taking his pills that were different than the instructions that were printed on his pill bottles. This resulted in him having an incomplete understanding of the best way to take the medicine.

Other respondents had not communicated enough with their health-care providers and left the providers' offices without a clear understanding of how to take their pills. For instance, one participant said: "When I'd get that queasy feeling or I'd get a real bad dose of diarrhea, automatically I would stop, not knowing or understanding that maybe I have to feel bad or stay on the pot for 2 weeks until it got into my system and I got used to it, and then all these things would stop. So, my body became resistant to a lotta the medicine." Had this individual communicated thoroughly with his provider about the potential side effects he could expect, how long such problems typically

lasted, and what to do if these effects were experienced, he may not have stopped taking the medication.

Changing a medication regimen that was too complicated was a common occurrence among this sample. Many of the participants reported they had communicated with their health-care professionals about their adherence problems and were subsequently able to switch to more manageable regimens. After switching to a regimen better suited to their lifestyles, their adherence improved. One person reported: "I told them I'm just not taking it the way I should . . . so then they gave it to me in a liquid form which is a lot easier to take, and I've been sticking to that."

Being involved in initial decision-making about their regimen also appeared to improve adherence. Those who were actively involved were able to help select a regimen that best fit their lifestyle: "I was given choices of what I thought would work best for me, pill-wise, and number, and of course, the schedule of my eating. And I chose the schedule that I'm on right now. I chose it myself." Being actively involved in other aspects of health care, such as gathering information regarding their disease, also improved adherence for some participants: "I started getting more medical information and more information period about the pills. . . . I also found out . . . that it's very important to take 'em as recommended. It was no play thing. So, I started taking it very seriously . . . and I've been taking 'em faithfully ever since."

Health-care system: adherence barriers and successful strategies. Numerous participants reported that they occasionally had difficulty obtaining refills of their antiretroviral medicines, at times due to their health-care plan policies. One participant discussed this sort of difficulty: "I'm on that ADAP program . . . and if you lose some of them [antiretroviral pills] or misplace them, and then you go back and try to get new medications, they will fight you because they don't want to give them to you until the 30 days are up."

If participants ran out of medicine when they were away from home, it was particularly problematic to get their prescriptions refilled.

One person stated: "I've been on the road and the medicine got too low. I had somebody here go to the clinic for me and get my medicine. It was a bunch of phone calls, they had to mail it to me, and it was panic, you know."

Refills also proved to be problematic if pharmacies happened to be short of the medicine that respondents required. One individual said: "The only time I get into a panic is when I can't get my medication, which is almost all the time. . . . I was getting it through Rite Aid and called in the prescription and they told me they didn't have it, and I had just like a day and I didn't have a lotta time to get it and I had to be at work, etc., etc. And then they called all around, nobody had it . . . I was in a panic."

This example highlights contextual factors that may impinge on patient adherence. Someone may have every intention of adhering to their regimen, but if they are unable to obtain their medications due to bureaucratic complexities, nonadherence will be the result.

Adherence improved when patients were able to arrange for routine home delivery of their prescription refills. Such delivery was helpful because it eliminated the need for patients to remember to call in or bring in a refill order, as well as actually travel to the pharmacy to pick up the order. One participant said: "I finally worked it out with my nurse practitioner so now it's being mailed to me. . . . So now it works out smooth."

One respondent's adherence also was improved when his health-care clinic supplied him with a beeper to remind him to take his antiretroviral doses. He explained, "One of the tools that I received . . . is this beeper deal from my doctor. . . . They issue beepers out and it's set and everything to the time when you take your medications . . . and it goes off when you're supposed to. . . . Very cool."

Finally, one participant appreciated the fact that the health-care clinic he frequented allowed him enough time with his health-care provider to ask all the questions that he had about his medication regimen. He stated: "They give me basically all the time I need. I mean, they'll sit there with me for 45 minutes to an hour if I want to just sit and talk. . . . They work with me. . . . They're incredible, I think."

This is a good example of the links between health-care clinic policies (i.e., scheduling of appointments), provider-patient communication regarding adherence issues, and patients' actual adherence patterns. If patients do not have enough time with their health care professional, they are unlikely to disclose any adherence problems, and their adherence may subsequently suffer.

Regimen: adherence barriers and successful strategies. Given the arduous nature of the antiretroviral medication regimens, it is not surprising that participants encountered various barriers to adherence related to the regimens themselves. First, the difficulty of complying with the special instructions of the antiretroviral medications was discussed in the group. Such instructions relate to the timing of doses (e.g., take every 8 hours), food requirements (e.g., take on an empty stomach), water requirements (e.g., take with a lot of water), and refrigeration requirements (e.g., keep cold). One respondent explained the difficulties she had with these types of special instructions: "It's so crazy with the food . . . I had gone for like six months just really taking them pretty erratic . . . because it was two hours before, or an hour before, or on an empty stomach. I just . . . felt it wasn't worth bothering so much for it."

Next, participants complained about the taste, smell, size, and shape of the assorted antiretroviral medicines. For example, one person stated, "Ritonavir—yeah, that liquid is nasty . . . I haven't been doing very good takin' [it] twice a day." Some respondents even disclosed that they had stopped taking their antiretroviral medications due to these issues; one participant stated: "I stopped taking [my medicine]. I can't stand the taste of it."

Side effects constituted yet another regimen-related barrier to adherence for respondents. One respondent explained: "[I] have a lot of problems with medications. The side effects . . . because I'm a very active person, so it slows me down a great deal. . . . It's very difficult. I don't like the sickness that I have."

Finally, the sheer magnitude of the antiretroviral regimens, in terms of the total num-

ber of pills per day, was an adherence barrier. The magnitude of patients' daily pill-taking regimens was even greater for those individuals who also had to take medications for other conditions, such as diabetes or heart problems. For example, a respondent said, "I am a diabetic. . . . I take . . . insulin and I'm also hypertensive, I take medication for that. There's a lot of medications that I have to juggle every day. . . . Sometimes it's just very hard to adhere."

Respondents noted that the easier an antiretroviral regimen was, the easier it was to adhere to. Hence, the initial choice of which antiretroviral regimen to take was integrally related to patient adherence patterns. As one person noted, "You pick the one that's easiest, rather than the ones that you can't eat at this period of time, or you have to take more pills."

To cope with some of the unpleasant aspects of taking the antiretroviral medications, such as their bitter taste or unsavory smell, respondents developed a number of strategies that helped them to adhere to their regimens. A couple respondents, for example, discussed using a syringe to "shoot" the medicine down their throats, thereby bypassing the tongue all together. Another person discussed experimenting with the placement of the pill on the tongue: "It kind of also depends on where you put it on the tongue. . . . The different taste buds . . . taste different things in different places. . . . It's one place I figured out that . . . it doesn't leave a nasty taste in your mouth."

Another respondent stated: "I found that the chocolate Ensure, if you line the mouth with it, must a spoon, just to line the mouth, and drink the Norvir down, and then take another spoon and line . . . the mouth again . . . get all your pills down with Ensure . . . you'll do all right." Other participants found that drinking lemonade, chocolate milk, or eating sour candy was helpful in coping with the unpleasant taste of the medicines.

Finally, participant used alarm clocks, beepers, pill-boxes (containers that contain a day's, week's, or month's worth of medication), or written reminder schedules to remind themselves to take their antiretroviral doses at the correct time each day. One person reported: "I

have one of those plastic boxes with the days of the week . . . so I can separate all my pills because I take so many and I don't want to forget them."

DISCUSSION

A number of patient characteristics emerged as factors related to the level of successful adherence that patients can achieve that have implications for intervention and for providers. First, participants who reported a belief that taking their medication as prescribed was important to maintenance of their health reported high levels of treatment adherence, whereas participants who reported the belief that taking medication is important only when one feels sick were less likely to take their medication as prescribed. A belief that taking one's antiretroviral medication as prescribed will help to maintain health may form the foundation on which other adherence efforts are based. That is, communication with patients should emphasize the importance of *preventing* illness through continuous efforts at taking the medication as prescribed, with education materials that assist in patients understanding that HIV remains active during periods of apparent wellness.

Scheduling also emerged as an important patient factor: participants who could tie taking their medications with regular daily activities reported that such strategies were helpful, whereas those without regular daily schedules appeared unable to make such connections. Among this population, it is possible that adherence should be viewed as more than a problem of taking medication—that it may entail certain lifestyle changes to accommodate the treatment regimen. This observation is consistent with prior research on health behaviors such as smoking cessation, in which changing environmental factors can assist in breaking maladaptive behavior chains, and has been shown to be an important factor in achieving the desired behavioral goals.

Finally, perceived support emerged as a patient factor in promoting adherence. Those participants who indicated they had friends, family, or partners who encouraged them to take

their medications reported high levels of adherence. On the other hand, reluctance to take medication publicly or when with friends or family was also reported as a barrier to adherence. Social support for taking antiretroviral medications is closely linked to awareness of family and friends of the patient's HIV disease. Because HIV remains stigmatized, issues of whom to inform of one's HIV status, and how and when to inform them may be important factors in establishing treatment adherence. Findings that certain support is viewed as positive or helpful, whereas other support is negative^{21,22} suggest that assisting patients in identification of appropriate support people may be especially important.

There were also a number of provider-patient relationship factors that emerged as being significantly influential in adherence. Participants who had open lines of communication and positive relationships with their health-care providers also said that they took their medications as prescribed, while those who characterized their communications with their providers as poor reported poor levels of medication adherence. Provider-patient communication appears to have three components as described by the participants: (1) accuracy of the information; (2) clarity of the instructions provided; and (3) the nature of the relationship. All appear necessary for the communication to be effective. Accuracy includes completeness of information, including special instructions and possible side effects (and how long they last). Providers can maximize patient level of understanding by asking the patient to recap her or his understanding of how the medication should be taken, and correcting misunderstandings that emerge. Providers can promote trust in their patient relationships by encouraging questions when patients do not understand what is being presented, by involving patients in the treatment decision-making process, and encouraging patients to contact them if unexpected side effects or other problems arise. Several participants noted that they had communicated to their providers that their regimens were too complicated, and that their providers worked with them to change to a simpler one. Such collaboration and communication in the context of treatment is crucial in

promoting treatment adherence, and could not occur outside of a trusting relationship.

Although factors such as beliefs about medication and its role in the treatment of HIV and scheduling may be targets of patient-level intervention, barriers in the health-care system can undermine the best of efforts. In this study, issues related to the health-care system emerged as factors in adherence. Although establishing policy-limiting prescriptions to a 30-day supply and maintaining limited inventory confers certain advantages such as cost containment and ensuring that medication in stock has not expired, it may have the unwanted and unintended consequence of placing barriers in the way of adherence. Under these circumstances, even the best-intended patient may be forced to forgo doses of medication. In recognition of this problem, some specialty pharmacies have begun programs that deliver medications to patients on schedule. Other mechanisms for reducing or eliminating such obstacles may exist; for example, if a patient loses or misplaces his or her medication, the pharmacist might call the provider for rapid approval of new prescription. In view of the findings that for people contemplating workforce entry or reentry one of the greatest sources of concern was whether or not they would be able to take their medications as prescribed,^{23,24} this issue is especially important.

Consistent with earlier research, simplified medication regimens emerged as a major factor in improved adherence. In recognition of this fact, pharmaceutical companies have begun marketing medications that are easier to take. Unfortunately, as patients become increasingly experienced with different antiretroviral medications (i.e., they have taken more medications in the past), their regimens typically also become more complicated, with more pills and more complicated medication schedules. A corollary of this observation is that people with histories of poor medication adherence also have more complicated regimens than those who adhere as prescribed from the beginning. In addition, adherence is typically assessed for dosage rather than for schedule; however, as can be seen in this study, patients vary widely in terms of what they consider successful adherence in terms of sched-

ule. Almost one quarter of the participants felt they were successful as long as they got all their doses in sometime within a 24-hour period. Continuous coverage of the antiretrovirals is considered important to reduce the development of resistance; therefore, adhering to schedule may be particularly important for these regimens. Therefore, assisting people with HIV to develop strategies to take their medications as prescribed, and simplifying medication regimens early in treatment may be important in setting the stage for long-term adherence. Moreover, as people with HIV live longer, additional complications such as hypertension and diabetes will emerge, not to mention complications that may result from these medications themselves, further complicating medication adherence.

A major challenge faces all of those involved in HIV care if HIV-infected patients are to be able to maintain full adherence to complicated medication regimens over extremely long periods of time, and perhaps for their entire lifetime. Patient-level intervention, provider-level intervention, and health-care system modification may all be necessary if this challenge is to be met successfully.

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