OBJECTIVE: A pilot project was designed to utilize the knowledge and skills of pharmacists and social workers/mental health professionals to facilitate readiness and informed decision making to optimize antiretroviral therapy adherence for HIV-positive patients considering or beginning drug therapy.

SETTING: Group Health Cooperative in collaboration with Kaiser Permanente Northwest, both group-model health maintenance organizations (HMOs) in the Pacific Northwest.

DESIGN: The Anti-Retroviral Medication Adherence Program (ARMAP) Team at each site consisted of one pharmacist and one social worker or mental health therapist. Together, the team provided education and psychosocial support to patients contemplating, initiating, or reinitiating antiretrovirals. The focus was on increasing patient knowledge, identifying and addressing adherence barriers, and helping patients cope with lifestyle changes associated with integrating antiretroviral medications into their lives. Specific self-management adherence behaviors and therapy goals were designed individually.

MAIN OUTCOME MEASURES: Adherence as measured by refill data and patient satisfaction. Laboratory values for HIV-RNA viral load and CD4+ cell count, self-reported adherence, health status, and provider satisfaction were secondary measures.

RESULTS: Pharmacy refill data and adherence questionnaires showed three-month adherence rates of 83% and 91%, respectively. All patient respondents indicated overall satisfaction with ARMAP. Ninety-two percent reported increased understanding of antiretroviral medications. Ninety-two percent of providers were satisfied with ARMAP.

CONCLUSION: Adherence to antiretrovirals was high for ARMAP participants. Patients and providers were satisfied with ARMAP and were able to better understand readiness to initiate therapy.

KEYWORDS: HIV, antiretrovirals, adherence, patient satisfaction, multidisciplinary team

S uboptimal medication adherence is one of the most difficult and complex problems that health care providers and patients face. Nonadherence has been described for almost every situation that requires medication therapy.5,6 The National Pharmaceutical Council’s Task Force for Compliance estimated the economic impact of nonadherence in 1993 alone to be $100 billion dollars in health care and productivity costs.4

Many studies have attempted to identify predictors of nonadherence, particularly patient personality traits and sociodemographic factors.5,6 This would allow health care providers to target adherence-enhancement tools and programs to at-risk patient populations. More recently, nonadherence has been identified as a problem that spans the population and is difficult to predict, indicating that individualized treatment plans taking patients’ preferences, goals, concerns, and circumstances into account may be a more effective approach to improving adherence.7

Although personality traits and sociodemographic characteristics may not help clinicians predict adherence, characteristics of the medication regimen, the extent of patient involvement in treatment decisions, and the patient’s perception of support from the health care team have been consistently associated with adherence and should be considered when creating patient care plans.8,9 Adherence to care plans and medications also has been found to increase as patients gain knowledge.10

Treatment regimens for human immunodeficiency virus (HIV) are complex, usually involving at least three drugs and up to 25 pills daily. Many of the medications must be taken specifically with food or in a fasting state, and at prescribed intervals. Side effects are common, and patients will likely take antiretrovirals for life, factors that have been linked to nonadherence.11

Overcoming medication-adherence barriers is particularly critical in HIV treatment. Sporadic use of protease inhibitors has been associated with the emergence of drug-resistant strains of HIV.14,15 This has significant personal and public health implications. Resistance to one drug may lead to cross-resistance to other drugs in the same class, limiting future treatment options. Multidrug-resistant strains also may be transmissible.16

Some practitioners withhold triple-drug therapy in cases in which nonadherence is predicted.17 Critics of this approach say that it unfairly penalizes patients based on race, mental health status, or substance-abuse history, characteristics that are often

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ACKNOWLEDGMENT: We wish to acknowledge the contribution of our Adherence Team members Stuart O’Brochta, R.Ph., John McManus, M.A., Midge Levy, M.S.W., A.C.S.W., Jeri Thonstad, R.Ph., Phyllis Heims, M.S.W., and Dean Clay, Ph.D., without whom our successful adherence intervention would not have been possible. We also wish to express our gratitude to Ted Eytan, M.D., M.P.H., for his thoughtful input and to Heather Houston and Liz Follmer for superb project management.

The project was supported by grant #101-9063 from the Garfield Memorial Fund.

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viewed as predictive of nonadherence, despite the lack of consistent evidence in the literature. Preliminary evidence exists that effective therapy is being withheld from certain populations.

Readiness to change health behaviors has been described in the literature and has been used to predict treatment success. The asymptomatic HIV-positive population contemplating the lifestyle changes necessary to initiate antiretroviral therapy has not been well studied. The nonurgent nature of initiating drug therapy in these patients has been described, allowing patient readiness to become a crucial component of the decision to start antiretroviral drug therapy. A major limitation of early aggressive HIV treatment without regard to readiness to adhere is that poor adherence leads to treatment failure. In a study of the link between protease-inhibitor adherence and treatment success, researchers found that while 95% adherence correlated to an 80% success rate (defined as an undetectable plasma HIV RNA level), 80% adherence was associated with a 50% success rate.

Once an individual’s state of readiness to begin antiretroviral therapy is understood, regimen-specific barriers to adherence may be addressed. Programs that demonstrate success by enhancing adherence are complex, making it difficult to justify offering only one adherence-enhancement tool to patients and to determine the merits of an individual tool. Essential HIV-specific elements of a treatment plan have been proposed. These include the use of jellybean trials, viral load and T-cell counts, and medication diaries as patient-feedback tools. Other tools that have been used to support adherence include having patients associate pill taking with other activities, reminder timing devices, social supports, and drug-information hotlines.

**Program Description**

This report describes the Anti-Retroviral Medication Adherence Program (ARMAP) pilot project implemented at Group Health Cooperative (GHC) and Kaiser Permanente Northwest (KPNW). The program’s patient and provider acceptability and its association with adherence and disease regression are reported. The program was initiated in order to use the combined knowledge and skills of pharmacists and social workers/mental health professionals to facilitate informed decision making, help patients set realistic goals for adherence through better understanding of personal barriers, and optimize antiretroviral therapy adherence by providing regular follow-up for drug management.

The program was developed in response to issues raised in a consumer focus group on HIV care. A general lack of awareness of the importance of adherence and lack of knowledge about available adherence tools were identified in the focus group.

In preparation for ARMAP, the adherence team members were trained in interview and motivation techniques. A thorough review of adherence issues and current HIV treatment recommendations was provided.

The pilot program was launched in October 1998, and enrollment occurred through February 1999. The ARMAP team at each site consisted of one clinical pharmacist and one social worker (at GHC) or mental health therapist (at KPNW). At GHC, primary care providers located throughout the service region manage HIV-positive patients, while at KPNW HIV-positive patients are treated at a centrally located Immune Deficiency Clinic. Adult patients were eligible for inclusion if they were candidates for antiretroviral therapy and had not been on antiretrovirals in the previous three months.

The ARMAP teams were established to address the educational needs of the providers and patients in order to optimize adherence potential prior to the initiation of therapy. Troubleshooting once therapy has been initiated is the more common approach described in the literature but is less ideal because of the substantial evidence that frequent missed doses, drug holidays, and discontinuation of antiretroviral therapy contribute to drug resistance and more rapid disease progression.

The initial patient consultations were scheduled for 90 minutes. Patients completed personal general information sheets, informed consent forms, and MOS-HIV status questionnaires, and provided baseline adherence data using a questionnaire developed by Chesney et al. at the University of California, San Francisco. In the initial consultations, patients’ perceptions of their illness and therapy were elicited and clarified through discussion that acknowledged patients’ feelings in a nonjudgmental manner. Adherence barriers and social supports were identified through direct or open-ended assessment questions about daily routine, employment, use of alcohol or drugs, emotional stability, relationships, living situation, and past experiences with medications. Patients were encouraged to build their social support system, in some cases necessitating discussion of issues of HIV-status disclosure and privacy. Patient education was provided on HIV disease, available medications, side effects, combination therapy, drug resistance, and common adherence problems and strategies. Patients were encouraged to ask questions and express concerns, and an effort was made to respond fully to each of them.

Patients who decided to proceed with antiretroviral therapy initiation were offered a one- to two-week placebo (jellybean) trial that simulated the burden of their potential drug regimens. Other adherence tools were utilized depending on the needs of the individual patient. Motivational counseling was used in some cases, emphasizing the fact that taking antiretrovirals is a way to maintain health rather than to treat illness. Medications were dispensed as one-month supplies to allow for closer monitoring and were cycled together to avoid multiple trips to the pharmacy within the month. Other available tools were HIV calendar medication boxes, pagers, and alarm watches.

Shared decision making was employed to arrive at clinically appropriate, individualized treatment plans for patients who chose to initiate therapy. This process involved the providers, the ARMAP teams, and the patients.

Following initiation of drug therapy, the pharmacist made a
phone call to the patient after three to four days to address problems, concerns, or specific drug side effects. At two to three weeks, the social worker called to provide additional support. A 30-minute visit or phone consultation was scheduled at one and three months to address further concerns and elements of therapy effectiveness. Additional visits were arranged as needed.

To assess the impact of the ARMAP program, the Chesney et al. adherence questionnaire was administered at the one- and three-month visits and the MOS-HIV questionnaire was administered at the three-month visit. Patient and provider satisfaction questionnaires were administered at the end of the study period. Adherence to antiretroviral medication was the primary outcome of interest. Pharmacy refill data and self-reported adherence were used as primary adherence measures. Laboratory values for HIV viral load and CD4+ cell counts were collected as additional adherence indicators.

Multiple measures of adherence were collected to obtain a more complete picture than could be derived from a single measure. Pharmacy dispensing records do not capture the timing of doses or actual taking of medication; patient reports are subject to inaccuracy because of patients’ inability to remember or unwillingness to report failed drug dosing; HIV viral load and CD4 count are influenced by many factors (e.g., drug absorption, resistance of HIV strain) in addition to adherence.

#### Practice Innovation

The two characteristics that made this program unique are its focus on determining patients’ readiness to integrate antiretroviral therapy into their daily lives and the coupling of pharmacists and social workers/mental health professionals as adjunct health care teams offering educational and psychosocial support to patients contemplating, beginning, or restarting complex drug regimens.

The ARMAP program was rooted in the belief that waiting to treat is preferable to poor adherence to treatment, and that patients, if provided with adequate information and clarification of the issues associated with antiretroviral therapy, are best able to identify their readiness to start medication. Although the patient was encouraged to determine his or her readiness, dialogue with the ARMAP team was an integral part of this determination. Having a pharmacist and a social worker or mental health professional help the patient with this decision removed the pressure to treat the disease from the prescriber. Although delaying antiretroviral therapy has not been shown to be detrimental to future treatment success, the high visibility of the disease and the political volatility surrounding it contribute to an environment in which physicians may not feel comfortable waiting to treat an identified case of HIV.

Traditionally, social workers and pharmacists have not been paired in the provision of health care, yet they have complementary skills and knowledge to contribute to adherence enhancement. Patients with HIV face unique challenges that pharmacists and mental health professionals are able to address. Among these challenges are quickly changing knowledge about disease pathology and treatment options; the large amount of conflicting information available through the media and other sources; social stigma; the psychological burden of having a chronic and, most likely, terminal disease; the high cost of treatment; and the complexity of the currently preferred treatment regimens.

#### Results

Thirty-two participants (18 at KPNW and 14 at GHC) were enrolled in the program’s pilot phase. The average age of program participants was 39 years, and the majority (31/32, 97%) was male. Five (16%) were nonwhite. Thirty-eight percent of study participants were classified as having acquired immunodeficiency syndrome (AIDS), using the Centers for Disease Control and Prevention classification. While 32 participants entered the study, 26 patients (81%) were eligible for analysis at the one-month follow-up and 23 (72%) went on to complete the entire three-month pilot program, including all questionnaires and medication refills.

Pharmacy refill data and self-administered questionnaires were used as measures of adherence for patients who initiated therapy. Seventy-eight percent of participants were “very” or “extremely” sure that they would be able to take all or most of the study medication when asked at baseline. At one month, 26 patients had initiated therapy and completed follow-up questionnaires. Among the six not eligible for analysis at one month, three GHC and one KPNW participant chose not to start antiretroviral therapy. Reasons patients decided not to start included substance abuse, better understanding of disease status and therapy consequences, denial of disease status, and fear of disease disclosure. Two patients dropped out of the study before completing the one-month questionnaire. Seventy-three percent of patients reported taking all their medications in the previous four days. Pharmacy refill data indicated that 88% had filled their prescriptions and had medication available on those four days.

At three months, 23 participants were available for analysis; two were lost to follow-up and one did not complete the self-assessment questionnaire. Ninety-one percent reported taking all of their medications in the previous four days; pharmacy refill data indicated that 83% had medication available.

Almost all study subjects reported that they were able to adhere to their dosing schedules all or most of the time (96% at one month, 95% at three months). A significant proportion (100% at one month, 94% at three months) reported that they were able to follow special instructions, such as “take with food” or “take on an empty stomach.” When asked if they missed any medications the previous weekend, 85% at one month and 90% at three months responded no. The most commonly cited reasons for missing doses were “had a change in my daily routine” and “busy with other things.”
HIV-related lab values were used as additional measures of adherence as well as an adherence encouragement tool. The average baseline CD4+ count for ARMAP participants was 313 cells/mm³. Twenty-three of 24 (96%) participants who began therapy and had a repeat CD4+ count at three months showed an improvement over baseline. The average three-month CD4+ count was 436 cells/mm³. The baseline viral load for ARMAP participants ranged from 967–500,000 copies per milliliter (ml) (median 42,595 copies/ml). All patients initiating therapy experienced a drop in viral load. At one month, three patients achieved undetectable levels of the HIV virus (<50 copies/ml). Eight additional patients reached undetectable levels of virus at three months. The percentage decrease in viral load at three months among patients who started antiretroviral medication ranged from 67% to over 99%, with the majority of patients experiencing a drop of at least 95% from baseline.

Patients participating in ARMAP were satisfied with the program. Table 1, right, shows the distribution of responses to two participant-satisfaction-survey questions. Five-point Likert scales were used to assess both ARMAP's perceived helpfulness and participants' overall satisfaction with the program, with 1 corresponding to “very unsatisfied” or “very unhelpful” and 5 corresponding to “very satisfied” or “very helpful.” Although 23 patients completed all questionnaires, 78% of those initially enrolled completed the satisfaction questionnaire. Eighty percent of participants responding to the satisfaction survey reported that the program was “helpful” or “very helpful” for taking their medications. All respondents indicated overall satisfaction with ARMAP. The most widely reported benefit of ARMAP was an increased understanding of antiretroviral medications (92%). Over 75% of respondents also believed that ARMAP benefited them by helping them to understand their readiness to begin taking medications, teaching them to identify challenges to taking medications, and improving their ability to succeed with medication taking (see Table 2, right).

Providers who had referred patients to the team also indicated overall satisfaction with ARMAP. Five-point Likert scales were used to assess its perceived usefulness or helpfulness, with 1 being “not useful/helpful at all,” 3 being “neutral,” and 5 being “very useful/helpful.” The mean provider rating of the program’s overall usefulness was 4.42, with 92% (11/12) of providers indicating that ARMAP was “useful” or “very useful” to them. The program was most helpful, according to the mean response, with supporting patients on retroviral therapy (mean=4.64). The program was also deemed helpful by providers in reducing the time they spent discussing medications and providing patient education (4.33 and 4.17, respectively). The adherence team’s assessment of readiness to begin therapy and patient follow-up after starting therapy were identified as useful by most providers (mean response=4.42 and 4.58, respectively).

Preliminary analysis of health status via the HIV-MOS instrument at baseline and 12 weeks showed no significant change in health status after initiation of antiretroviral therapy, even after adjusting for adherence. These findings will be reported separately.

Discussion

<table>
<thead>
<tr>
<th>Reported Benefit</th>
<th>Yes N (%)</th>
<th>No N (%)</th>
<th>Not Applicable N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shared and compared experiences with others with similar problems</td>
<td>10 (40)</td>
<td>5 (20)</td>
<td>10 (40)</td>
</tr>
<tr>
<td>Increased my understanding of how to take antiretroviral medications</td>
<td>23 (92)</td>
<td>1 (4)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Helped me understand whether I was ready to start taking medications</td>
<td>20 (80)</td>
<td>3 (12)</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Made specific changes to better manage my medications</td>
<td>16 (64)</td>
<td>6 (24)</td>
<td>3 (12)</td>
</tr>
<tr>
<td>Learned to identify challenges to taking my medications</td>
<td>21 (84)</td>
<td>3 (12)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Learned to avoid situations that interfere with taking my medications</td>
<td>17 (68)</td>
<td>4 (16)</td>
<td>4 (16)</td>
</tr>
<tr>
<td>Improved my ability to be successful with medication taking</td>
<td>22 (88)</td>
<td>2 (8)</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>

Note: N=25.

Table 1.

<table>
<thead>
<tr>
<th>Response</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Helpfulness of ARMAP in Medication Taking (mean=4.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5: Very helpful</td>
<td>15</td>
<td>60%</td>
</tr>
<tr>
<td>4: Somewhat helpful</td>
<td>5</td>
<td>20%</td>
</tr>
<tr>
<td>3: Neutral</td>
<td>3</td>
<td>12%</td>
</tr>
<tr>
<td>2: Not at all helpful</td>
<td>1</td>
<td>4%</td>
</tr>
<tr>
<td>1: Very dissatisfied</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Overall Satisfaction with ARMAP (mean=4.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5: Very satisfied</td>
<td>22</td>
<td>88%</td>
</tr>
<tr>
<td>4: Somewhat satisfied</td>
<td>3</td>
<td>12%</td>
</tr>
<tr>
<td>3: Neutral</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>2: Not at all satisfied</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>1: Very dissatisfied</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

Note: N=25.

*One KPNW survey respondent did not answer this question.
The major limitation of this pilot study was that no control group was included, which makes us unable to attribute the high adherence rates solely to the team's interventions. The high adherence rates may also be attributable to patient knowledge of adherence monitoring or to the fact that participants were a self-selected group that may have been more likely to adhere and be receptive to the team's interventions than the general HIV-positive population would be. Adherence rates to most medications also have been shown to decrease with duration of therapy, so the adherence rates in this three-month pilot cannot be extrapolated.

The reasons for the shift from higher patient-reported rates of nonadherence compared to pharmacy refill data at one month to lower rates of patient-reported nonadherence at three months are unclear. Patients' clearer understanding of the survey instrument or less attention to missed doses over time may have played a role.

The project's initial success has led to its extension in both organizations, and six- and nine-month data will soon be available, allowing us to examine potential concurrent control groups.

Conclusions

The ARMAP pilot was well received by both patients and providers and has proven successful in supporting adherence, contributing to an improved state of readiness to start medications and positive clinical outcomes. Patient readiness to start antiretroviral medication was more clearly understood by patients, physicians, and the ARMAP team as a result of the closer collaboration. High adherence rates to newly initiated antiretrovirals were documented, and no decline in health status was noted in these patients.

The successful collaboration between allied health professionals and prescribers in this program may serve as a prototype for future collaborations intended to improve clinical outcomes in ambulatory populations. As more time demands are placed on prescribers and conflicting health and drug information is made available to the public, allied health professionals are in a good position to support prescribers by helping patients with chronic diseases to understand how medications and behaviors may affect their health.

References