Antiretroviral Adherence and Use of Alternative Therapies Among Older HIV-infected Adults

Anthony K. Wutoh, PhD, RPh, Carolyn M. Brown, PhD, RPh, E. Kuor Kumoji, MSN, MPH, DrPH Cand, Monika Shah Daftary, PharmD, Tselaine Jones, PharmD, Narifa Alie Barnes, PharmD, and Nadina J. Powell, PharmD

Washington, D. C., Austin, Texas, and Baltimore, Maryland

Objective: To investigate adherence to antiretroviral therapy and use of alternative therapies among older human immunodeficiency virus (HIV)-infected adults, and to assess relationships between antiretroviral adherence and clinical outcomes.

Methods: One hundred older HIV-infected patients, aged 50 and over, treated at two large HIV clinics in Washington, DC, were enrolled. A cross-sectional methodology used structured interviews to investigate antiretroviral regimens, use of alternative therapies, and demographics. Medical records provided viral load and CD4 count within 3 months of interview.

Results: The mean self-reported adherence was 94%, and 55 patients reported 100% adherence to antiretroviral therapy. Correlation analysis showed a significant negative correlation between adherence and viral load ($r = -312$, $p = 0.005$). There was no significant difference in adherence based on race, gender, mode of transmission, or education. Twenty-one patients (21%) reported the use of an alternative therapy, with several patients using multiple alternative therapies. There was no significant difference in adherence score ($p = 0.514$) or viral load ($p = 0.860$) based upon use of alternative therapies.

Conclusions: Older HIV-infected study patients reported high levels of adherence to antiretroviral regimens, and adherence was highly correlated with HIV viral load. Use of alternative therapies did not significantly impact adherence to antiretroviral agents or viral load. High adherence among this older population may be related to older patients' familiarity with medication usage, their increasing awareness of HIV as a disease that requires optimal adherence, and educational efforts promoted by the two clinics in which they are clients. (*J Natl Med Assoc*. 2001;93:243-250.)

Advances in the treatment of human immunodeficiency virus (HIV), including earlier detection, prophylactic regimens for opportunistic infections, and antiretroviral therapies have resulted in prolonged survival among HIV-infected patients.[1,2] These factors, in addition to an increase in the incidence of HIV among older patients, have led to a growing percentage of the overall AIDS caseload that is over 50 years of age.[3] In fact, Ory and col-

leagues[4] report that the percentage of older AIDS patients in the United States is approaching 15% of the overall AIDS caseload. Several studies have also reported an increasing incidence in the use of alternative therapies among HIV patients. It has been reported in previous investigations that as many as 80% of HIV-infected patients and 100% of persons with AIDS use some form of alternative therapy to treat their medical conditions.[5-9] For example, Johnston and colleagues[9] found, among an inner city, mostly Hispanic and African American sample of HIV-infected patients, that 80% regularly used alternative therapies, including herbs, acupuncture, and traditional healers. In another study, Brauchi et al.[11] reported that more than 80% of 129 persons with AIDS used at least one form of alternative therapy from a spectrum of more than 60 different treatments. To a lesser degree, Greenblatt and colleagues found[6] among 197 AIDS patients that 29% used some form of unorthodox treatment along with their prescribed medications. Similarly, Anderson and colleagues[7] reported that 40% (70 out of 184) of HIV-infected patients in their study used some form of alternative therapy, even while enrolled in clinical trials.

One study reports pharmacists' estimates that 25.9% of patients, including those who are HIV-infected and who use alternative therapies, are generally not compliant with their prescribed medication regimens.[15] Further, among users of alternative therapies, 36.6% skipped chronic medication refills, 34.4% periodically substituted alternative therapies for prescribed medication, and 21.7% permanently replaced prescribed medication with alternative therapies. In one study involving a sample of HIV-infected outpatients in France, Malafronte et al.[17] found that use of unconventional therapy was associated with poor adherence.

It has also become increasingly clear that the effectiveness of antiretroviral therapy is highly dependent upon treatment adherence.[18-20] One study suggests that adherence to antiretroviral therapy must exceed 95% to be effective.[21] However, adherence to antiretroviral therapy has been widely varied in various studies, and has often been reported far below the 95% level.[22-24] Although various methods, including pill counts, Medication Event Management System (MEMS) caps (Aprex, Union City, CA), review of prescription records, physician report, and directly observed therapy (DOT) have been utilized to assess adherence, the most fre-

quently employed method remains patient self-report.[25-28] Another recent study has compared patients' self-report to pill count and MEMS caps and noted significant differences in adherence based upon method utilized.[29] Self-report in this study typically overestimated actual patient adherence. However, due to various factors including cost and time constraints, self-report is the method most utilized by researchers, although it is more useful when validated by clinical measure.[30]

Few studies have been conducted to examine the treatment patterns of older HIV-infected adults in terms of antiretroviral adherence and use of alternative therapies. Moreover, few studies have been conducted to assess associations between treatment behaviors and clinical outcomes among this population of patients. The goal of this study was to investigate adherence to prescribed antiretroviral agents and the use of alternative therapies among a group of older HIV-infected adults and to assess relationships between antiretroviral adherence and clinical outcomes.

MATERIALS AND METHODS

A total of 100 older HIV-infected patients, age 50 and over, who were being treated at two large HIV clinics in Washington, DC, and who agreed to participate, were included in this study. A cross-sectional methodology was employed in which patients participated in structured interviews and were queried regarding antiretroviral medication regimens, use of alternative therapies, and demographic characteristics. Patients were interviewed between April 1999 and March 2000. Reviews of patients' medical records were utilized to collect clinical status data, including the most recent viral load and CD4 count prior to interview, but within 3 months of interview date. Patients' self-report of antiretroviral medication regimen was also validated from data in the medical record. Viral load at one of the clinics was measured using a test with a lower measurable viral load limit of 400 copies/mL (Roche Molecular Systems (RMS) Amplicor[tm] HIV-1 Monitor, Hoffman-La Roche, Ltd., Basel, Switzerland). Patients at the other clinic were assessed using a test with a lower measurable limit of 50 copies/mL (Roche Diagnostics Amplicor[tm] HIV-1 Monitor Ultrasensitive Method, Hoffman-La Roche, Ltd., Basel, Switzerland). During statistical analysis, 400 copies/mL was the value used to denote unmeasurable viral

load. Each participant was offered a financial incentive of $25 in exchange for their voluntary participation. Each participant also completed an informed consent form approved by the Howard University Institutional Review Board (IRB) and each clinic. These patients participated in a 30-min structured interview designed to address the objectives of this study.

The structured patient interview, conducted by trained study investigators, covered risk behaviors for transmitting HIV, adherence to antiretroviral medications, use of alternative therapies, and demographic characteristics. All interviews were held at the clinics in private, quiet patient rooms during weekday mornings and afternoons.

Adherence to antiretroviral medications was defined as the percentage of prescribed antiretroviral doses reportedly taken during the 7 days prior to the interview. This method assures greater patient recall of recent medication behavior.[31] Adherence scores were calculated as $(100 \{A/7(B \times C)\})$, where A = reported number of pills (capsules, tablets, or packets) taken in the past 7 days, B = number of doses prescribed per day, C = number of pills per dose.[31] Doses were defined as the total number of capsules of each specified medication taken in the previous 7 days. Participants identified each of the medications taken by name or by pictured chart. Patient self-report of antiretroviral regimen was verified through review of medical records. An adherence score was calculated for each individual medication and a mean cumulative adherence score across all antiretroviral medications taken was then calculated. Seven patients taking antiretroviral medications did not have recorded viral loads within the previous 3 months.

Alternative therapies were described as any treatment other than prescribed antiretroviral medications used by the patient to treat or ameliorate their HIV condition. Examples provided to patients included herbal therapies, acupuncture, high-dose vitamins, spiritual healing, and other treatments described in previous literature.[11]

Ethnicity was assessed by patients' self-report, and categorized as black, non-Hispanic white, Hispanic, Asian/Pacific Islander, Native American, Alaskan Native, or other. Income was assessed by patient self-report in $10,000 incremental categories from less than $10,000 to greater than $50,000. Educational achievement was assessed by self-report and categorized as less than high school, high school

graduate, some college, college graduate, or graduate/professional school.

Descriptive statistics including means and standard deviations were obtained. In addition, Spearman's correlation analysis was performed to determine associations between nonparametric study variables. Group comparisons were conducted using either the Student's t-test for continuous data or chi-square analysis was used for analysis of noncontinuous data.

RESULTS

A total of 100 older HIV-infected patients were recruited to participate in this cross-sectional study from two metropolitan Washington, DC HIV clinics. The demographic characteristics of the sample are listed in Table 1. The majority of study participants were black (75%) and male (78%). Most had a high school education or better (74%). The mean age of participants was 54.5 years, and they had been diagnosed with HIV for an average of 7.2 years.

Sexual activity was the most common route of HIV transmission, with male-to-male transmission reported by 35% of the study group, and heterosexual transmission reported by 21%. Intravenous transmission of HIV was reported by 24% of the study group. The mean number of antiretroviral medications taken by the participants during the study period was 2.8. The majority of patients were on multiple drug combinations, including 55% who were receiving protease inhibitors as part of their combination therapy (Table 2). There was also a significant correlation between the number of antiretroviral medications taken and increased adherence ($r = 0.223$, $p = 0.041$). It must be noted that 13 patients reported no use of antiretroviral medications in the previous week. Two of those patients had been hospitalized in the previous week and so were unable to take their antiretroviral medications that week, although they still considered themselves current antiretroviral users.

In terms of clinical measures, the mean CD4 count, within 3 months of interview, was 432.0 cells/ mm^3 (median = 386.5 cells/mm^3) (Table 3). The mean viral load was 52,557.7 copies/mL (HIV RNA), but the median value was 1061.0 copies/mL. Respondents reported very high levels of adherence to antiretroviral therapy. Of the 87 patients who were taking antiretroviral medications, only 14 participants reported adherence rates less than 90%.

25

Table 1. Demographic Characteristics (n = 100)

	Frequency	Percent	Mean ± SD
Gender			
Male	78	78%	
Female	22	22%	
Race			
Black (non-Hispanic)	75	75%	
White (non-Hispanic)	20	20%	
Hispanic	3	3%	
Native American/Alaska Native	2	2%	
Education			
Less than high school graduate/degree	26	26%	
High school graduate/degree	27	27%	
Some college	19	19%	
College graduate/degree	14	14%	
Graduate/professional school graduate/degree	14	14%	
Marital Status			
Unmarried	44	44%	
Married or intimate relationship	24	24%	
Divorced/separated	22	22%	
Widowed	10	10%	
Annual Income			
Less than $10,000	53	53%	
$10,000–$19,000	19	19%	
$20,000–$29,000	9	9%	
$30,000–$39,000	3	3%	
$40,000–$49,000	3	3%	
Greater than $50,000	4	4%	
Don't know	1	1%	
No answer	8	8%	
Mode of Transmission			
Male-to-male (homosexual)	35	35%	
Intravenous drug use	24	24%	
Heterosexual (sex with HIV-infected person)	21	21%	
Transfusion	4	4%	
Unknown/don't know	14	14%	
Other	2	2%	
Age (in years)			54.5 ± 5.1
Number of years since diagnosis of HIV			7.2 ± 5.2
Number of antiretroviral medications			2.8 ± 0.9
Number of non-HIV medications			1.6 ± 1.8

The mean self-reported adherence was 94.4% (median = 100%).

Twenty-one patients (21%) reported the use of some form of alternative therapy to treat or ameliorate their HIV infection, with several patients using multiple forms of alternative therapies. The most frequently mentioned treatments included high-dose megavitamins (n = 8), garlic products (n = 5), spiritual healing (n = 4), herbal teas (n = 4), and use of various other herbal products including cha-

Table 2. Antiretroviral Therapy at Study Entry

Classification of therapy	n = 100
No antiretroviral therapy	13 (13.0%)
Monotherapy (PI)*	1 (1.0%)
Multidrug antiretroviral therapy	86 (86.0%)
Includes protease inhibitors	55
No protease inhibitors	31

*PI = Protease inhibitor.

Table 3. Study Variables (n = 100)

	Mean ± SD	Median
Clinical status		
CD4 Count (cells/mm³) (within 3 months of study interview)	432.0 ± 283.3	386.5
Viral Load (copies/mL HIV RNA) (within 3 months of study interview)	52,555.7 ± 159,606.0	1061.0
Health behaviors		
Compliance/adherence to antiretroviral therapy (percentage)	94.4 ± 13.8	100

momile tea, echinacea, and ginseng (see Table 4). Of the 21 patients reporting use of alternative therapies, 16 used alternative therapies in conjunction with prescribed antiretroviral medications (76.2%), whereas the other 5 patients (23.8%) used alternative therapies in lieu of prescribed antiretroviral medications. However, there was no significant difference in the usage of alternative therapies whether or not patients used prescribed antiretroviral medications (p = 0.097). There was also no significant difference in the use of alternative therapies by gender (p = 0.553), mode of transmission (p = 0.573), income level (p = 0.450), insurance coverage (p = 0.111), or educational achievement (p = 0.274). However, in terms of race, black patients were significantly less likely than nonblack patients to report use of alternative therapies (p = 0.007).

Fifty-five patients reported 100% antiretroviral adherence, whereas 25 patients reported less than 100% adherence. Seven other patients taking antiretroviral medications did not have recorded viral loads within the previous 3 months. Further, patients who did not report any anitretroviral usage (n = 13) were also excluded from the correlation analysis assessing adherence and viral load. Spearman's correlation analysis showed a significant negative correlation between adherence and viral load (r = –312, p = 0.005). Patients who reported 100% adherence (n = 55) had significantly lower viral loads compared with patients who reported less than 100% adherence (n = 25; p = 0.016). There was no significant difference in adherence based on race, gender, mode of transmission, or education. Also, there was no significant difference in adherence score (p = 0.514) or viral load (p = 0.860) based upon use of alternative therapies.

DISCUSSION

The demographic characteristics of the study population were representative of the demograph-

ics of AIDS cases in Washington, DC, because more than three quarters of the study participants were male, and three out of four were black. According to the latest available data (June 1998) from Washington, DC, 78% of living AIDS cases were among males, and 79% were black patients.[32] (AIDS case data are reported because HIV is not a reportable disease in Washington, DC). In the nation's capitol, the percentage of newly reported AIDS cases in patients over 50 years of age was 12.8% in 1997. Further, the high rate of transmission due to sexual contact (56%) is the same as the rate of transmission due to sexual contact among younger living AIDS cases in Washington, DC.[32] This may reflect the frequency of unprotected sexual intercourse among older Americans.[33] In comparing this data with national statistics, only 47% of newly diagnosed AIDS cases, throughout the United States in 1999, were among black, non-Hispanic patients.[34] In ad-

Table 4. Alternative Therapies Used by Study Patients

Alternative therapy	Number of patients reporting use*
High-dose megavitamins	8
Garlic products	5
Spiritual healing	4
Herbal teas	4
Noni Juice®	3
Ginseng	2
Chinese herbs	2
CoEnzyme Q	2
Evening primrose	2
Golden Seal	1
Fish oil	1
Kelp	1
Wheat grass	1
Interferon	1
Acupuncture	1

*Total exceeds 21 as several patients used multiple therapies.

dition, 77% of these newly diagnosed AIDS cases throughout the United States were among male patients, and 52% were related to sexual contact (44% male to male, 8% heterosexual).

The mean age of study participants was 54.5 years old (SD ± 5.1 years). Of the 100 study patients, there was documentation of the age at initial HIV diagnosis for 88 patients. Of those 88 patients, the average time since initial HIV diagnosis was 7.2 years (SD ± 5.2 years). This may suggest that many of these patients may have been infected prior to reaching age 50. However, 30 patients were infected at or above age 50. In fact, the oldest age at diagnosis was 73 years of age. This highlights the potential for infection with HIV at any age.

Twenty-one patients reported use of some form of alternative therapy. The most frequently mentioned treatments among this population, including high-dose megavitamins, garlic products, spiritual healing, and other herbal therapies, are consistent with other studies investigating the use of alternative therapies among other populations of HIV-infected patients.[11] The use of certain alternative therapies among these patients may be of particular concern, especially since other studies have noted clinicians' lack of awareness of alternative therapy usage among their patients.[35,36] This concern is heightened with increasing reports of drug interactions between antiretroviral medications and certain herbal products.[37] Further, there is research evidence to suggest that many patients may use alternative therapies as a substitute for prescription pharmaceuticals.[15] Although there was no significant difference in the use of prescribed antiretroviral medications among alternative therapy users in this study ($p = 0.097$), the small number of patients who solely treated themselves with alternative therapies ($n = 5$) limits the conclusions that can be made regarding this issue. Although patients were not specifically queried regarding their use of non-HIV prescription medication, there may also be concern regarding the use of alternative therapies with other prescription medications. Although herbal therapies and other alternative therapies are often viewed as innocuous, there remains the potential for drug interactions with medications including warfarin, benzodiazepines, and cardiac glycosides.[38–40]

Thirteen patients reported no use of antiretroviral medications in the previous week. Among patients using antiretroviral therapies, the mean number of medications taken was 2.8. Interestingly, an increase in the number of antiretroviral medications taken was associated with increased adherence. This result is consistent with similar findings reported by other researchers.[41]

Patients reported a high level of adherence to antiretroviral therapy (mean adherence reported was 94.4%), whereas only 14 patients reported adherence below 90%. Although this value initially appeared high, there was a significant negative correlation between self-reported adherence and viral load ($r = -0.312$, $p \leq 0.005$) providing some validation of the self-reported measure. Fifty-five patients (69%) reported 100% antiretroviral adherence, whereas 25 patients (31%) reported less than 100% adherence. This result is similar to those stated by Kleeburger and colleagues,[42] who found that 77.7% of their study participants reported 100% antiretroviral adherence. Further, they also reported significant associations between higher self-reported treatment adherence and decreased viral load ($p = 0.015$).

Several other recent studies also report similarly high mean adherence levels by self-report, although none of the populations were among older HIV-infected patients.[43,44] Waters and colleagues[43] report that 61% of their patient population reported 100% adherence. Further, Jones and colleagues[44] note that 74% of patients in their study reported 100% antiretroviral adherence, although neither study correlated medication adherence with clinical outcomes. The high self-reported adherence among this older population, as validated by lower viral loads, may be related to several factors including: older patients' familiarity with medication usage for chronic diseases, increasing awareness of HIV as a disease that requires high medication adherence, and patient educational efforts promoted by the two clinics. However, the possibility of exaggerated self-reported compliance estimates can not be dismissed, as reported in previous studies.[24,29] Further, the lack of adherence by a number of study patients, as evidenced by higher viral loads, is of concern due to the potential for development of resistant strains of HIV, more rapid disease progression, and the possibility of adherence failure with other clinical protocols.[18–21] Additionally, recent studies have shown that patients with high viral loads are far more likely to transmit HIV to an uninfected partner than patients with lower viral loads, further

highlighting the importance of adherence to antiretroviral regimens.[45]

STUDY LIMITATIONS

The conclusions from this study are limited by the sample size ($n = 100$). Further, the self-reported method of assessing adherence may limit the validity of this measure, although the high correlation of adherence and viral load provides some measure of validity. Moreover, the fact that viral loads were not necessarily taken at the same time as adherence self-reports may impact the validity of those values as well. However, there was no more than 3 months separating the date of the most recent viral load and the date of the adherence measure. Another potential limitation may be the generalizability of the study results. The demographic characteristics of the study population may not be consistent with other groups of older HIV-infected adults. A final limitation involves the cross-sectional nature of the study. It represents one point in time and does not reflect changes in behavior or regimens over time. Despite these potential limitations, the results of this study provide important insight regarding the treatment behaviors of older HIV-infected adults. Future research considerations will include evaluations of methods to improve antiretroviral adherence among older HIV-infected adults, assessment of the various types of alternative therapies used among older patients, the development of specific prevention strategies, and assessment of specific treatment regimens that will improve antiretroviral adherence.

ACKNOWLEDGMENTS

REFERENCES

1. Palella FJ, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. *N Engl J Med.* 1998;338:853–860.

2. Hammer SM, Squires KE, Hughes MD, et al. A controlled trial of two nucleoside analogues plus indinavir in persons with human immunodeficiency virus infection and CD4 cell counts of 200 per cubic millimeter or less. *N Engl J Med.* 1997: 337:725–733.

3. Centers for Disease Control and Prevention. AIDS among persons aged greater than or equal to 50 years—United States, 1991–1996. *MMWR Morb Mortal Wkly Rep.* 1998;47:21–27.

4. Ory MG, Mack K. Middle-aged and older people with AIDS: trends in national surveillance rates, transmission routes, and risk factors. *Res Aging.* 1998;20(6):653–664.

5. Kassler WJ, Blanc P, Greenblatt RM. The use of herbs by human immunodeficiency virus-infected patients. *Arch Intern Med.* 1991;151:2281–2288.

6. Greenblatt RM, Hollander H, McMaster JR, et al. Polypharmacy among patients attending an AIDS clinic: utilization of prescribed, unorthodox, and investigational treatments. *J Acquired Immune Defic Syndromes.* 1991;4:136–143.

7. Anderson W, O'Connor BB, MacGregor RR, et al. Patient use and assessment of conventional and alternative therapies for HIV infection and AIDS. *AIDS.* 1993;7:561–566.

8. Connett S, ed. More clinicians supporting alternative therapies. *AIDS Alert (American Health Consultants) Newsletter.* 1996; 11:121–32.

9. Digman DJ. Contemporary issues in HIV/AIDS. *AIDS Wkly Plus.* 22 July 1996:2–15.

10. Johnston BE, Ahmad K, Smith C, et al. Alternative therapy use among HIV-infected patients of the inner city [Abstract 42391]. Presented at the XII International AIDS Conference in Geneva, Switzerland, July, 1998.

11. Brauchi P, Reuteler I, Burki B. Use of complementary therapies for HIV/AIDS in Switzerland. *Schweiz Med Wochenschr.* 1996;126:1297–1305.

12. Standish LJ, Calabrese C, Reeves C, et al. A scientific plan for the evaluation of alternative medicine in the treatment of HIV/AIDS. *Altern Ther Health Med.* 1997;3:58–67.

13. Vogl D, Smith M, Rapkin BD, et al. Use and cost of alternative therapies in an HIV-infected Medicaid population [Abstract no. 42387]. Presented at the XII International AIDS Conference in Geneva, Switzerland, July, 1998.

14. Heurtin-Roberts S, Reisin E. Health beliefs and compliance with prescribed medication for hypertension among black women—New Orleans, 1985–1986. *MMWR Morb Mortal Wkly Rep.* 1990;39:701–704.

15. Brown CM. Experiences of community pharmacists with the use of alternative therapies among patients and its impact on compliance with medication regimens. *J Am Pharm Assoc.* 1998; 38:603–608.

16. Druss BG, Rosenheck RA. Association between use of unconventional therapies and conventional medical services. *JAMA.* 1999;282:651–656.

17. Malafronte B, Perbost I, Dunais B, et al. Unconventional medicine and AIDS: Trends in behaviour among patients receiving protease inhibitors [Abstract no.14119]. Presented at the XII International AIDS Conference in Geneva, Switzerland, July, 1998.

18. D'Arminio Monforte A, Testa L, Adorni F, et al. Clinical outcome and predictive factors of failure of highly active antiretroviral therapy in antiretroviral-experienced patients in advanced stages of HIV-1 infection. *AIDS.* 1998;12:1631–1637.

19. Hott R, Yip B, Chan K, et al. Non-adherence to triple combination therapy is predictive of AIDS progression an death in HIV-positive men and women (TuOrB419). Presented at the

XIII International AIDS Conference in Durban, South Africa, July 9–14, 2000.

20. Carmona A, Knobel H, Guelar A, et al. Factors influencing survival in HIV infected patients treated with HAART (TuOrB417). Presented at the XIII International AIDS Conference in Durban, South Africa, July 9–14, 2000.

21. Paterson D, Swindells S, Mohr J, et al. How much adherence is enough? A prospective study of adherence to protease inhibitor using MEMSCaps. Presented at the 6th Conference on Retroviruses and Opportunistic Infections in Chicago, IL, February 1999.

22. Muma RD, Ross, MW, Parcel GS, Pollard RB. Zidovudine adherence among individuals with HIV infection. *AIDS Care.* 1995;7:439–447.

23. Jung R, Etzel JV, Brocavich JM. Evaluation of drug usage and compliance in patients infected with the human immunodeficiency virus. *American Society of Health System Pharmacy Midyear Clinical Meeting.* 1995;30:P-469(R).

24. Samet JH, Libman H, Steger KA. Compliance with zidovudine therapy in patients infected with human immunodeficiency virus, type 1: a cross-sectional study in a municipal hospital clinic. *Am J Med.* 1992;92:495–502.

25. Mannerheimer S, Friedland G, Matts J, et al. Self-reported antiretroviral adherence correlates with HIV viral load and declines over time (TuORB421). Presented at the XIII International AIDS Conference in Durban, South Africa, July 9–14, 2000.

26. Maggiolo F, Migliorino M, Caprioli S, et al. Once-a-day therapy for HIV infection (TuPpB1167). Presented at the XIII International AIDS Conference in Durban, South Africa, July 9–14, 2000.

27. Rawlings K, Farthing C, Brown L, et al. H.E.A.R.T. (helping to enhance adherence to antiretroviral therapy) NZT 4006 (TuPeB3223). Presented at the XIII International AIDS Conference in Durban, South Africa, July 9–14, 2000.

28. Brown CM, Wutoh AK, Jones T, et al. Health beliefs and treatment practices of older HIV-infected adults (WePeD4606). Presented at the XIII International AIDS Conference in Durban, South Africa, July 9–14, 2000.

29. Miller L. Providers estimates of adherence overestimate reports from medication as Monitoring systems (MEMS) for patients on protease inhibitors (PIs) [Abstract 97]. Presented at the 6th Conference on Retroviruses and Opportunistic Infections in Chicago, IL, February 1999.

30. Arnsten J, Demas P, Gourevitch M, et al. Adherence and viral load in HIV-infected drug users: Comparison of self-report and medication event monitors (MEMS). Presented at the 7th Conference on Retroviruses and Opportunistic Infections, Chicago, IL, February 2000.

31. Eldred LJ, Wu AW, Chaisson RE, et al. Adherence to antiretroviral and Pneumocystis prophylaxis in HIV disease. *J Acquired Immune Defic Syndromes Hum Retrovirology.* 1998;18:117–125.

32. Washington D.C. Department of Health D.C. Report on HIV/AIDS AIDS Surveillance Branch, HIV/AIDS Epidemiology Division, 2000. (http://www.washingtondc.gov/agencies/detail.asp?id=27).

33. Rose MA. HIV/AIDS knowledge, perceptions of risk, and behaviors of older adults. *Holistic Nurs Pract.* 1995;10:10–17.

34. Centers for Disease Control and Prevention. HIV/AIDS Surveillance Report 11(No. 2), 1999.

35. Drivdahl CE, Miser WF. The use of alternative health care by a family practice population. *J Am Board Fam Pract.* 1998; 11:193–199.

36. Ayuk-Egbe P, Wutoh AK, Hailemeskel B, et al. A survey of nurses' knowledge and attitudes regarding herbal therapies. *Natl Academies Pract Forum.* 2000;2:191–194.

37. Piscitelli SC, Burstein AH, Alfaro MS. Indinavir concentrations and St. John's wort. *Lancet.* 2000;355:547–548.

38. Cupp MJ. Herbal remedies: adverse effects and drug interactions. *Am Fam Physician.* 1999;59:1239–1245.

39. Miller LG. Herbal medicinals: selected clinical considerations focusing on known or potential drug-herb interactions. *Arch Intern Med.* 1998;158:2200–2211.

40. Klepser TB, Klepser ME. Unsafe and potentially safe herbal therapies. *Am J Health-System Pharmacists.* 1999;56:125–138.

41. Singh N, Squier C, Sivek C, Wagener M, Nguyen MH, Yu VL. Determinants of compliance with antiretroviral therapy in patients with human immunodeficiency virus: prospective assessment with implications for enhancing compliance. *AIDS Care.* 1996 Jun;8:261–9.

42. Kleeberger C, Jacobson LP, Strathdee S, et al. Determinants of heterogenous adherence to HIV-antiretroviral therapies (ART) in the multicenter AIDS cohort study (MACS) (ThPeB4984). Presented at the XIII International AIDS Conference in Durban, South Africa, July 9–14, 2000.

43. Waters M, Finkelstein R, French T, et al. Characteristics of a cohort of patients enrolled in treatment adherence demonstration projects (ThPeB4982). Presented at the XIII International AIDS Conference in Durban, South Africa, July 9–14, 2000.

44. Jones T, Pillay D, Sabin C, et al. Assessing the role of treatment adherence in a clinical setting (ThPeB4986). Presented at the XIII International AIDS Conference in Durban, South Africa, July 9–14, 2000.

45. Quinn TC, Wawer MJ, Sewankambo N,. et al, for the Rakai Project Study Group. Viral load and heterosexual transmission of human immunodeficiency virus type 1. *N Engl J Med.* 2000;342:921–929.