

Adherence to HIV Therapy: Building a Bridge to Success

Report from a Workshop Sponsored by:

**DHHS Health Resources and Services
Administration (HRSA)**

and

The Forum for Collaborative HIV Research

in collaboration with

NIH Office of AIDS Research

**November 15 – 16, 1999
Washington, DC**

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The Forum for Collaborative HIV Research, a project of the Center for Health Services Research and Policy at the George Washington University School of Public Health and Health Services, was founded in 1997. The goal of the Forum is to facilitate discussion regarding emerging issues in HIV clinical research and the transfer of research results into care. The Forum is a coalition of government agencies, clinical researchers, health care providers, pharmaceutical companies, and patient advocates. The Forum brings these constituencies together to identify gaps and impediments in the understanding of the medical management of HIV disease and develops recommendations to fill those gaps. June Bray is the Forum's Deputy Director. David Barr is the Executive Director.

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***ADHERENCE TO HIV THERAPY—
BUILDING A BRIDGE TO SUCCESS***

**November 15–16, 1999
Washington, DC**

Introduction and Welcome

Goals and Background of the Workshop

Joseph F. O’Neill, MD, MPH – Health Resources and Services Administration (HRSA)

David Barr, JD – Forum for Collaborative HIV Research

Judith D. Auerbach, Ph.D – NIH Office of AIDS Research

In November 1997, the Forum for Collaborative HIV Research, the National Minority AIDS Council, and the NIH Office of AIDS Research sponsored a conference on research into adherence to HIV therapy. The conference brought together approximately 500 experts from government, academia, health care provision, and social service agencies, who are engaged in research on adherence issues, providing primary care, or are running educational and support programs with patients. The goal of that conference was to examine existing literature on adherence to medical treatment and to develop a research agenda to better understand the issues of adherence to HIV anti-retroviral therapy.

At that time, highly active anti-retroviral therapy (HAART) for HIV was relatively new. While adherence to treatment was presumed to be an important factor in the success of these new and promising therapies, little was known about adherence and HIV treatment. The 1997 conference examined literature in adherence research in other disease areas, and identified issues in HIV care into which adherence research should be conducted¹. We examined both the biomedical and behavioral aspects of three central questions:

- What are the factors that effect a patient’s ability to adhere to therapy?
- What interventions can assist a patient’s efforts to adhere to therapy?
- How can adherence to therapy be measured?

Several things have happened since that conference. First, it is clear that HAART can have a dramatic effect on HIV disease morbidity and mortality. Since the introduction of HAART, deaths from AIDS have dropped 44% in the United States. Rates of new AIDS cases show a similarly substantial decline. However, we also now know that HAART will not eradicate HIV. Patients must stay on complex treatment regimens for life. Good treatment compliance is difficult under any circumstance, and with HAART the complexity of the regimens and the unforgiving nature of HIV replication pose particularly difficult challenges for patients.

¹ The report from that conference can be found at the Forum’s website at: www.gwumc.edu/chpr and then click on HIV Research.

The success of HAART is challenged by an HIV epidemic in the U.S. that is expanding to a population of patients who are more vulnerable, hard-to-reach and often have multiple crises in their lives. For most, HIV is now a disease of poverty. Today, people infected with HIV are 60% African-American or Latino; and of these, 70% of HIV-positive women are current and former drug users. This population is less likely to be on therapy or to have access to it. They see their physicians less often and are less likely to see a physician who is experienced in providing HIV care. An infrastructure to provide social services, medical care, housing, child care, mental health and substance abuse services, and education is essential if the promise of HAART is to be fully realized.

Two years since the conference on HIV treatment adherence research, it is also clear that without strict adherence to HIV therapy, HAART can not provide long-term suppression of HIV replication. Without adequate suppression, HIV is able to develop resistant mutations rendering HAART less or ineffective. Because of the complexity and duration of HAART regimens, adherence has emerged as a primary concern in quality and successful care. Therefore, it is important health care providers, social service providers, and patients have a good understanding of the need for and difficulties of adherence to treatment as they decide to start treatment and in order to be able to maintain good treatment adherence over the years.

To address these concerns, on November 15 – 16, 1999, the HRSA and the Forum for Collaborative HIV Research, in collaboration with the NIH Office of AIDS Research, held a workshop to see what has been learned since the 1997 conference. The workshop's primary focus was the examination of intervention efforts to educate health care providers and patients about HIV treatment adherence and to provide support to patients in their efforts to adhere to their HAART regimens. Workshop participants included academic researchers, government representatives, primary care providers, social service providers, pharmaceutical industry representatives, educators, and people with HIV and their advocates.

While two years is not enough time to develop, implement and evaluate research protocols that could determine which intervention approaches might best meet patient needs, much progress has been made to address these questions. In the last 2 years, the National Institutes of Health has funded 26 grants for research projects on adherence. HRSA has funded 12 programs to provide adherence support to underserved and vulnerable populations. Most of the HRSA-sponsored programs were represented at the 1999 workshop and many of those programs are described in this report.

For HRSA, the issue of adherence to HIV therapy is one that requires the expertise, collaboration, and coordination of services within primary care and social service settings, and ancillary treatment and support services. As HRSA performs a primary function in the provision and funding of these services, creating opportunities like this workshop to bring together the expertise, exchange information, and identify models for broader programs implementation is an important and valuable opportunity to address the challenge of treatment adherence and help to realize the promise of HAART therapy.

WHY IS ADHERENCE TO HIV THERAPY IMPORTANT?

Defining HAART Success and Failure: How Adherent Do You Have to Be?

Gerald Friedland, MD – Yale University School of Medicine

Dr. Friedland began his presentation with an overview of the goals of HAART. The biological goals include: (a) suppression of HIV replication to a level sufficient to prevent the development of drug resistant mutations and forestall the progression of HIV disease, and (b) the reconstitution of the immune system. Clinical goals are increased survival, reduced morbidity, and a better quality of life. The public health goal is to eliminate HIV transmission.

Several studies now show that patients who are able to suppress HIV replication below the level of detection of currently used assays (fewer than 20 to 50 copies/mL), have a substantially greater chance to achieve long-term viral suppression on HAART. It is also clear that even in successfully suppressed patients, HIV replication will rapidly rebound if HAART is discontinued. It is also necessary to obtain consistent and adequate drug levels in order to prevent the development of drug-resistant mutations. Therefore, to prevent progression of HIV disease, HAART must be taken regularly and continuously throughout a patient's lifetime.

The precise impact of various levels of non-adherence on antiretroviral therapy outcome has not been fully measured. While good adherence is a critical for success of HAART, a number of variables may modify the amount of adherence needed to achieve a such success. Dr. Friedland categorized and listed several factors that might modify the relationship of adherence and therapeutic outcome. These include specific features of the patient, his or her disease status, the infecting virus and, most importantly, the antiretroviral regimen. The patient's previous experience with antiretroviral agents may influence the amount of adherence needed. Antiretrovirals are usually of greatest potency in those individuals who have not received them previously. Similarly, the more advanced the state of disease, the more potent the required regimen and the more vulnerable the regimen's success may be to lapses in adherence. Close to seroconversion, with more limited viral species and resistance mutations and a more intact immune system, antiretrovirals may be more tolerant of incomplete adherence than late in HIV disease when the immune system is unable to control viral replication and multiple resistant species have emerged. Features of the predominant viral species, such as degree of resistance and fitness, may effect required levels of adherence, when stage of disease is constant. Finally, characteristics of the regimen may impact the needed levels of adherence. For example, potency and pharmacologic features such as absorption, metabolism and drug interactions may differ among regimens and, at a given level of adherence, result in differing therapeutic outcome. Emerging preliminary data from recent studies demonstrate that higher than anticipated levels of adherence are required in HIV therapeutics.

Measurement of adherence is still not precise and contributes to the difficulty of precisely relating levels of adherence to therapeutic outcome. In clinical care, adherence is usually measured by clinician's guess. This has been shown to be highly inaccurate and usually an overestimate. Other methods all have limitations including, pill counts, self-reporting, MEMS caps, pharmacy records, and metabolic drug levels. In recent studies with HIV therapies, MEMS cap measurements tend to show lower rates of adherence than self report, however, well collected self report data clearly correlates well virologic changes

and is more practical in most settings. Regardless of measurement technique several fundamental questions include:

- What is the most appropriate time elapsed for adherence measurement? - 1, 3, 7 days or a global percentage?
- Should all or individual drugs be measured?
- Should the units of measure be the percentage of doses missed, days missed, or intervals missed?

Emerging preliminary data from recent studies demonstrate that higher than anticipated levels of adherence are required in HIV therapeutics. Paterson et al, demonstrated that very high levels of adherence are necessary to achieve desired therapeutic effect, using MEMS caps in a population of 84 experienced patients at two HIV clinics. In this study, to achieve suppression of virus below 400 copies at 3 months in greater than 80% of patients, >95% adherence was necessary. A linear relationship between levels of adherence and viral load suppression was observed. A recently published report from 5 HIV clinics studied self-reported adherence among 173 antiretroviral experienced patients. Adherence to therapy during the previous four weeks at months two and six of the study was evaluated. At six months, none of the patients with adherence levels of less than 80 % were non detectable, 17% were non-detectable with 80-95% adherence levels, 41% with levels of 95-99% and 47 % of those who were 100% adherent were non-detectable (p=0.06). Viral load measures and CD4 cell counts were significantly correlated with adherence. Among those who were <80% adherent, at six months, there was a rise in viral load of .2 log and fall in CD4 count of 18 cells. In contrast, among those who were 100% adherent, viral load fell 1.1 logs and CD4 cell count rose 72 cells.

% adherence	% non-detectable viral load
>95	81
90 – 95	64
80 – 90	50
70 – 80	25
<70	6

Striking anecdotal examples of the effect of lapses in adherence, exist as well. In patients carefully followed by MEMS caps, even short drug holidays resulted in rapid rise in viral titer, which ultimately was associated with the disappearance of predominantly wild type virus and the appearance of resistant mutant virus. The fragility of current regimen potency is illustrated in clinical trials of induction/maintenance regimens. In these studies, reducing the intensity and potency of regimens after achieving non-detectable viral load measures has resulted in rapid viral rebound in a substantial proportion of patients, providing additional, indirect support for the need for perfect or near-perfect adherence to maintain regimen potency.

Who Is on HIV Antiretroviral Therapy?

Julia Hidalgo, Sc.D. – Center for Health Services Research and Policy at the George Washington University School of Public Health and Health Services

Dr. Hidalgo provided background information about the demographics of people with HIV in the U.S., including where they live, information about their age, race, gender, and education levels. She discussed where people with HIV receive their health care, at what point in the course of HIV disease they come into care, and the quality of the care received.

At first the treatment population was composed largely of older white gay men who sought timely treatment. They were generally more educated, had higher incomes, had commercial insurance, and tended not to come from the South. After about 2 years of treatment, patients progress to HAART.

Now the epidemic is changing and concerns focus on:

- access to care
- source of primary care
- continuity of services
- continuity of health care coverage
- mental illness, substance abuse, or other co-morbidity
- incarceration
- personal, economic, and legal crises
- family and social support system
- infected family members

Systemic barriers to adherence services include:

- The HIV care system across the country is fragmented. About 40% of clinics offer on-site mental health care and two-thirds offer substance abuse treatment; on-site child care is rare. Even these clinical and support services are poorly integrated and coordinated.
- For both clinic and support services, capacity is inadequate to meet the demand.
- Support service providers are inadequately trained regarding HAART and adherence strategies.
- Formal adherence programs are limited in number and scope.
- Programs are often not culturally and linguistically competent.
- Insurance coverage varies and tends to be inconsistent.
- Treatment for substance abuse and mental health is inadequately funded.

The rise of managed care and other federal and state health care financing policies present particular barriers, including:

- HIV treatment has not been integrated into the services offered.
- HIV care providers do not generally participate in managed care.
- Some existing service strategies are deleterious to adherence, e.g. the failure of mental health services to be integrated or coordinated with primary care services.
- There is strict application of disability criteria for SSI and SSDI benefits.
- Welfare and Medicaid reform has led to loss of coverage.

How can the HIV/AIDS care system support adherence? First, adherence services must be defined - a funding agency cannot support something if they do not know what it is. In defining the services, we should:

- Integrate adherence into HIV services.
- Identify structural barriers.
- Expand programs.
- Among traditional and well-organized specialist and primary care providers, expand the multidisciplinary team approaches (e.g., CBOs, MCOs, care managers, schools, jails) to the patient, family, and informal support systems.
- Involve the whole team from the beginning.
- Expand case conferencing.
- Do not create a proliferation of small under-funded adherence programs.

Adherence services cannot be added to existing services without adding money. As for payment for providers of adherence services, the Care Act is important, but resource decisions are often made at the local level. Adherence services must be clearly articulated, measurable, and cost effective. In underwriting these services there is a clear role for sustained outside grant-giving and for industry.

FACTORS THAT AFFECT ADHERENCE:
WHAT HAVE WE LEARNED SINCE NOVEMBER 1997?

Simplification of Therapy: Fewer Pills, Fewer Doses per Day
Renslow Sherer, MD – The CORE Center, Cook County Hospital

One of the major challenges to good adherence to HAART has been the complexity of the regimens. Many drugs need to be taken three times a day (TID), and the pill burden can be overwhelming, i.e. 15-20 pills daily. Some drugs should be taken with food, some without food, and still others with high fat meals. Simplification of treatment regimens to the greatest extent possible is essential if adherence efforts are to be successful. Fortunately, in the past three years, the convenience and tolerability of regimens have improved. There are now several available twice a day (BID) regimens, and several drugs are now being tested for once-daily dosing (QD). In addition, the pill burden can now be as low as a few pills twice daily.

Table I below shows the recent alterations in dosing of common antiretroviral therapies. For a complete description of the goals of HIV therapy, recommendations for initial and subsequent antiretroviral therapies, alternate dosing strategies, common toxicities, drug interactions, and strategies and references for adherence, the reader is referred to the HHS/KFF Guidelines for the Treatment of HIV Infection in Adults and Adolescents of February, 2000 at www.hivatis.org.

Table I: Altered Dosing of Antiretroviral Agents, 2000

<u>Class</u>	<u>Agent</u>	<u>Initially recommended dose (mg)</u>	<u>Amended dose (mg)</u>
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<u>NRTIS</u>	ddl	200 BID		400 QAM
	AZT	200 TID		300 BID
	3TC	150 BID		300 QD
	Combivir	AZT+3TC BID		-----
	ABC	300 BID		-----
<u>NNRTIs</u>	NVP	200 BID		400 QD
	EFV	600 QD	QHS	-----
<u>PIs</u>	NFV	750 TID		1,250 BID
	RTV*	600 BID*	400 RTV +	400 SQV BID
	SQV-SGC*	1,200 TID*		1,600 mg BID
	AMP	1,200 BID		-----

Thus rational sequencing of HAART regimens in the year 2000 implies that the initial and subsequent regimens best fit the patient with regard to potency, food restrictions, lifestyle, drug interactions, dosing schedule, and number of doses per day. The clinician should determine what matters most to the patient—e.g., the simplest possible regimen, fewest possible side effects, or avoidance of certain side effects—while ensuring optimal potency and durability of antiviral effect. When the first regimen has been selected, the clinician should anticipate and prepare the patient for the side effects likely with that specific regimen. Nausea, vomiting, headache, and fatigue are the most common side effects that cause patients to miss a dose.

In the past three years, new and unexpected toxicities have been associated with antiretroviral agents. A syndrome of fat redistribution, hyperlipidemia, and glucose intolerance has been observed and termed “lipodystrophy (LD)”. LD may affect half or more of patients on HAART with protease inhibitors, though severe manifestations are less common, i.e. 15-30%. 5-15% of patients on NRTIs alone may have the syndrome, and it has also rarely been described on patients with HIV who have never been treated. It appears less common among patients on the NNRTI class of drugs. For this reason, and for reasons of simplicity and tolerability of the regimens, an increase in the use of so-called “protease-sparing” regimens has occurred in the past year. Several clinical trials are now testing the relative merits of regimens with protease inhibitors compared to regimens with three NRTI agents or with two NRTIs and an NNRTI, i.e. protease-sparing regimens.

For patients who have this toxicity on a protease-containing regimen in the setting of optimal virologic control, switching to a simpler regimen appears to result in continuous maximal viral suppression in the majority of patients. In addition, the simpler regimens are associated with modest improvements in adherence and quality of life.

Table II notes the updated goals of therapy for 2000. Note that the major tenets of maximal durable viral suppression remain the highest priority; it should be remembered that these goals led to the dramatic reductions in HIV mortality and morbidity in 1996-1999. At the same time, it is known that immune reconstitution with sustained rises in CD4+ T

lymphocyte counts is also associated with improved HIV outcomes, even in the presence of low level viremia of 50 – 5,000 copies/ml.

In addition, for durable virologic control and immunologic restoration to occur, additional therapeutic goals have been recognized to be essential. In addition to optimal adherence, as described in this monograph, preservation of future treatment options is an important goal of therapy. Because treatment failure rates of 30-50% or more in numerous trials and cohort studies, planning for second and third line therapy with high probabilities of success is essential. Preserving future options increases the chances of success with these regimens. There is growing evidence that genotypic and phenotypic resistance testing can improve the likelihood of success with second line agents; thus an additional goal of therapy is the use of agents to which a patient's virus is susceptible.

Table II: Update Goals of Therapy, 2000

Clinical

Reduction of mortality and morbidity

Improved quality of life

Virologic

Maximal durable suppression of viral replication

Immunologic

Immune reconstitution

Therapeutic

Rational sequencing of HAART regimens

- Preservation of future treatment options
- Optimal adherence: simplification of Rx, reduction of side effects
- Use of *optimal* and *proven* effective doses of drugs
- Selection of drugs to which a pt's virus is likely to be susceptible
- Avoidance of drugs to which a pt's virus is likely to be resistant

Finally, a note of caution for clinicians and persons living with HIV alike regarding alternative dosing strategies is warranted. Some efforts to reduce pill burden and frequency have been unsuccessful. It is important to be conservative about the use of alternate dosing strategies until there is sufficient pharmacological and clinical evidence supporting the safety and efficacy of their use.

What Do We Know about Adherence Levels in Different Populations?

Laura Cheever, MD – HRSA

Dr. Cheever discussed recent data on how various demographic variables affect adherence to HIV treatment. She cautioned that much of this data is preliminary and in abstract form. Much of the data has only been subjected to a univariate analysis, which does not account for confounding variables, of which there could be many. Further, the sample sizes of the studies are often too small to detect differences that could exist.

In the literature on adherence to treatment of chronic diseases, demographic variables generally do not predict adherence. However, the AIDS epidemic has a unique demographic profile. Also, the legacy of Tuskegee may have an impact on the attitudes of African-Americans towards the acceptance and use of HIV anti-retroviral therapy. This remains to be studied.

Citing several studies², age, race, stage of disease, and sex were shown to be inconsistent adherence predictors. Depression, literacy levels, active drug and alcohol abuse predict poorer adherence. In one study, women were more likely to be less adherent than men. Insurance status, education and income levels, a physician's experience with HIV, and attitudes regarding the efficacy of medication were not predictors of adherence. Health beliefs and attitudes which correlated with better adherence included:

- Medications will often fit into daily routine;
- Poor adherence leads to drug resistance;
- Taking all doses is important;
- Feeling comfortable taking medications in front of people.

In conclusion, Dr. Cheever stated that the data provides epidemiologic predictors. The data does not provide any information about particular patients. Each patient needs to be assessed and treated individually. The data may be important, however, in exploring barriers in different populations and in designing adherence interventions in different populations.

HIV Treatment and the Rest of Our Lives: How Does It Affect Adherence?
Margaret Chesney, Ph.D. – UCSF Prevention Sciences Group

Dr. Chesney, a leader in the field of HIV treatment adherence research, spent much of her time talking about the dangers of over-emphasis on poor adherence as a cause of treatment failure. She stressed the need for physicians to be better informed about the appropriate use of anti-viral therapy. Stressing adherence to a sub-optimal regimen is harmful and, unfortunately, not uncommon. She cited an analysis of ACTG studies where 25% of patients did not understand the instructions regarding when to take which medicines. Non-adherence can undermine clinical trials and treatment. Conversely, adherence is necessary, but not sufficient, for successful treatment.

Dr. Chesney discussed a recent study in San Francisco, which screened people who had experienced symptoms of HIV infection (fever, sore throat, night sweats, diarrhea within 3 weeks of exposure). Of 390 persons screened for primary HIV infection (the first 12 months), 137 were found to be infected. The average patient was a 34-year-old white man, college-educated, whose annual income was about \$30,000. Adherence in this population (determined by self-reporting) declined with time.

People with symptoms adhere better, whereas drug toxicity and concomitant side effects become more important later in treatment. The UCSF Prevention Sciences Group found

² HCSUS Survey. Wegner, 6th CROI, Chicago 1999, Abs. 98; Cheever, 39th ICAAC 1999, Abs. 591; Patterson, 6th CROI 1999, Abs. 92; Kaplan, 6th CROI 1999, Abs. 96

that during 1 to 12 weeks of treatment, adherence was at 80%; by 24 to 48 weeks of treatment, adherence had declined to 61%. Reasons for missing a dose early in treatment were forgetting, sleeping, being away, changing routine, being too busy, feeling sick, being depressed. In the UCSF group, the number of pills per day did not predict adherence.

Urban poor women are already stigmatized. They often have psychiatric disorders, such as post-traumatic stress disorder (many live in virtual combat zones). Substance abuse, demoralization, and parenting demands beyond their competence are also characteristic. How do they prioritize adherence to treatment in the context of these other, often more critical, crises?

Providers tend to focus on how much adherence is enough, and the relation between disease state and viral load. Often they fail to see the challenge of adherence in the broader context of people's lives. While it is true that non-adherence is linked to increases in viral load, it is not always true. For some people, as adherence decreases, viral load increases, but for others, as adherence decreases, viral load remains unchanged. Therefore, assumptions based on stable viral loads can be deceptive. Conversely, there are many reasons for treatment failure other than poor adherence. Assumptions that patients are non-adherent because of increases in viral load may also be wrong.

Providers may inadvertently enforce skipped doses (e.g., "Just keep doing whatever you're doing"). They must stress the importance of sustaining adherence and to do this we need to teach self-management skills.

We need to know more about the impact of side effects and co-morbidities on adherence efforts. Some side effects and symptoms—such as fat redistribution, lipid changes—have serious consequences. But, in clinical trials, side effects are reported only if the patient complains and patients are encouraged not to complain; therefore side effects are underreported.

Dynamics of Patient Adherence

-Predicting an Individual's Ability to Adhere to Treatment;

-Provider Attitudes toward Patients and Their Adherence Abilities

Ruth Finkelstein, ScD – New York Academy of Medicine

Predicting the ability of a patient to adhere to treatment can be an important component to determine whether or not that person should start antiretroviral therapy. Dr. Finkelstein discussed the difficulties that physicians face in trying to predict adherence, the assumptions that are often made about how adherence can be predicted, and the implications such assumptions can have on patient's lives and public health policy.

The ability of physicians to accurately report on the treatment adherence of their patients is limited and often inaccurate. Dr. Finkelstein cited three studies. In the Miller study, of

patients identified by their physician as adherent, 30% were taking <80% of their medication, while 22% of so-called non-adherent patients were taking >80% of medication. Patterson, et al, found that 1/3 fewer patients identified by physicians as >80% were so. Of patients identified by physicians as <80% adherent, 1/5 were actually 95% adherent and 1/3 were 80 – 90% adherent.

Multiple studies indicate variations in how treatment gets prescribed. The HCSUS study showed yearly increases in prescribing HAART for all patients from 1996 – 1998. But, despite lessening differences between sub-populations, in 1998, patients who were Black, Latino, women, uninsured, or Medicaid-insured were less likely to be on HAART. Also, differential decline in AIDS-related mortality by race, gender and transmission indicate that not all groups are being provided access to HAART, even when they are receiving medical care. Much of this difference is due to provider assumptions about the ability of different groups to adhere to therapy.

Several factors have been identified as affecting adherence, including:

- complexity of the treatment regimen, including number of pills/drugs, frequency, duration of therapy;
- patient's knowledge and beliefs about disease and medicine;
- access to social support;
- co-morbidities, esp. substance abuse and depression;
- stigma associated with illness;
- coping style;
- missed clinic appointments;
- meaningful life
- feeling comfortable with and trusting the physician;
- level of medication supervision;
- side effects management.

Dr. Finkelstein cited three major factors that effect treatment decision-making. First is the belief system of the physician. If the physician believes the best antiretroviral approach is to “hit hard, hit early”, then she is more likely to be aggressive in prescribing therapy. If she believes that crack addicts cannot adhere to treatment, she is less likely prescribe therapy to patients she perceives to be crack addicts. The second factor is an individualized assessment of adherence risk/readiness. The third factor is an assessment using evidence about adherence.

Evidence can be assessed taking multiple factors into account. These include:

- Environmental factors: What is the patient's living situation? Does he have a telephone, a refrigerator, adequate water supply? Who does the patient live with and can they provide support?
- Mental/emotional health: Is the patient depressed? Are they undergoing treatment for depression or other problems?

- Substance use: Is the patient addicted to drugs or alcohol? What is the severity of the addiction? Does the patient use drugs/alcohol recreationally? If so, how often and how does this use affect his daily schedule? Is substance abuse treatment available?
- Knowledge about HIV and HIV treatment: Does the patient understand the need for good adherence? Does he understand the consequences of poor adherence? Does he know which pills to take, how many to take, how often and when to take them? Does he understand about any dietary restrictions? Does he understand about possible side effects? Can the patient read/understand basic health words and concepts?
- Attitudes and beliefs: Does the patient believe that she has the ability to follow through on the treatment decision? Does she believe in the efficacy of HIV medication? Is she open about her HIV status? Is she scared of people seeing her medication? What are her goals and expectations for treatment?
- Social support: Is the patient isolated? Who can assist the patient in taking medication regularly? What other responsibilities does the patient have which may affect the ability to adhere to HIV medication?
- Past experiences: What is the patient's previous history adhering to medication? Does the patient miss appointments, fill prescriptions, etc.?

Health care providers should also take the patient's payor source and the stability of that source into account. Finally, the provider should then engage the patient in a decision-making process where the advantages and disadvantages of starting therapy are weighed.

How Do We Define "Effective" Adherence Interventions?

Sheryl Catz, Ph.D. – Medical College of Wisconsin

Measuring adherence to treatment is one important aspect of measuring treatment effectiveness. In measuring adherence, it is important to examine the role of the patient, the health care provider, and the system through which health care is provided. No one form of measurement is complete or adequate. The ideal evaluation standard—unobtrusive, objective, practical—is lacking; therefore we must use a multi-method approach.

Methods for Measuring Adherence Outcomes:

Direct Measures

- directly observed therapy – is accurate, but may not be practical when pills must be take several times a day for long periods of time;
- biomedical assay of blood and urine analysis – are objective and do not rely on patient reports, but are not always an accurate method due to pharmacokinetic factors, difficulties with timing tests with ingestion times, and susceptibility to “white coat effects.” They are also expensive and not always available;

Indirect Measures

- pill counts – are inexpensive and relatively easy to do, but do not provide information about whether the pills are actually taken and if taken according to schedule. Pill “dumping” can occur, and assessments can be impractical if the assessment period

does not coincide with prescription refills or if there are too many pills to fit into containers;

- pharmacy refill records – are unobtrusive and do not rely on patient report, but have limitations similar to pill counts;
- service utilization records – can be used to calculate the percentage of appointments kept (a direct measure of appointment adherence and an indirect measure of medication adherence), but are only as accurate as the record-keeping system and the record review can be time-consuming and expensive;
- MEMS caps - these devices electronically record when a pill bottle is opened. Benefits of electronic monitoring include objectivity, the identification of specific patterns of medication-taking over time, higher rates of missed doses detected as compared to other measures, they are not easily tampered with; and graphs of MEMS data can provide behavioral feedback useful for motivating patients. However, the system is expensive and cumbersome when multiple medications are used. Accuracy is compromised by how often the patient opens the bottle and removes a pill (or not) but does not take the medication. We need MEMS technology in dosette boxes and technology that can accommodate liquids.
- patient reporting - self-reporting in the form of diaries, questionnaires, or interviews are an inexpensive and necessary component of adherence assessment. But, reports of poor adherence tend to be more accurate than reports of good adherence and there are problems with recall and comprehension. Reporting may be more accurate if you “give the patient permission” to admit skipping a dose, use the patient’s language, and provide recall cues over a brief time period.
- provider reporting - provider ratings tend to overestimate good adherence, but can be useful supplements to other adherence measures;
- collateral reports – can be most useful with children’s caretakers;
- clinical outcomes – should not be conceptualized as a measure of adherence. Viral load is not perfectly correlated with adherence. Some people with excellent adherence don’t achieve reduced viral load; some with reduced viral load are not consistently adherent. However, the idea of validating adherence measures against clinical outcomes makes sense given the end goal of taking medications consistently is to achieve medical benefit from them.

Process Evaluation of Adherence Interventions

To examine how different kinds of adherence interventions work or don’t work we need to evaluate interventions which target changes at the level of the individual, provider, and system. Several process evaluation questions can be asked, including:

Individual level: Does the intervention effectively -

- Identify adherence barriers;
- Build problem-solving skills;
- Increase integration into daily life;
- Increase adherence self-efficacy;
- Increase knowledge;
- Increase motivation;

Provider Level: Does the intervention effectively –

- Increase provider communication skills;
- Build trust and rapport;
- Increase provider assessment skills;
- Match medical management to changing needs;
- Meet “best practice” goals ;
- Provide tailored feedback and educational materials;

System Level: Does the intervention effectively –

- Increase access to care;
- Provide continuous access to medications;
- Meet appropriate service utilization guidelines;
- Provide consistent environmental supports;
- Protect confidentiality

To define an effective intervention we need to address three issues. How much will adherence increase? What kind of adherence is being measured? Which components of individual, provider, and systemic interventions are the “active ingredients” necessary to increase adherence over time?

INTERVENTIONS TO ASSIST ADHERENCE

The majority of time at the workshop was devoted to presentations of various interventions to assist adherence efforts. These efforts included ways to educate providers and patients about the need for good adherence and the proper use of treatment regimens, as well as provide support and assistance for patients on therapy. The presentations were meant to provide representations of the types of programs being implemented. Many of them are still in fairly early stages of development. There are several other programs in operation. Time prevented us from providing a more comprehensive review of adherence intervention programs.

ARMAP: Antiretroviral Medication Adherence Projects

Diana Antoniskis, MD – Kaiser Permanente

Kaiser Permanente, a managed care organization with a large HIV-infected patient population, and Group Health Cooperative, a primary-care based organization, collaborated in an effort to maximize the cost-effectiveness of ART. Their premise is that the adherence team should provide intensive educational and psychosocial evaluation before initiating antiretroviral therapy and that the team should include a pharmacist and a social worker.

The pre-therapy visit is the most important aspect of their program; it lasts 1-1/2 to 2 hours. The pharmacist reviews medications. The social worker reviews the patient’s routine, perceptions, previous therapeutic experience, access to therapy, treatment for substance abuse, mental health issues, and self-advocacy, and offers a placebo (jellybean)

regimen and support group. To aid adherence, team members use phone calls, follow-up visits (at 1 and 3 months), and a monthly support group.

The average clients were 38-year-old white men. During treatment, their quality of life improved, especially in mental health and overall health. Controls receive treatment but not the social interventions of the program. The program was well-received by both patients and providers. A continuation study with longer follow-up (9 months) is being planned.

TREAT — a Clinical Management Tool with Adolescents
Audrey Rogers, PhD – NICHHD

TREAT is an adherence intervention that focuses primarily on assessing patient's readiness to participate in treatment. The program relies on Prochaska's Trans-Theoretical Model of Change (TMC), which consists of the following four stages (relapse is a reversion to a previous stage):

1. Pre-contemplation—no intention of changing behavior
2. Contemplation—aware of the problem, but not committed to action
3. Preparation—intend to take action within 30 days
4. Action and maintenance—committed to change; has devised strategies to prevent relapse

TREAT is one arm of a program that includes REACH (observational) and ACCESS (social marketing). TREAT is offered in 15 cities to REACH subjects in whom HAART is indicated. Each is referred to a social worker to overcome barriers to treatment.

Clients are mostly minority girls, a third of whom are high school dropouts, and a fourth of whom have no health care coverage. Most were infected through sex. Few exhibited AIDS-defining conditions. For this group, disclosure is critically important; it is the first step out of denial.

The TREAT program is stage specific; at each stage, each client is given the following:

1. a binder with a videotape, an audiotape, and an illustrated booklet
2. counseling and an audiotape
3. counseling, an audiotape, a choice of drug regimen, a surrogate pill trial
4. audiotape

At relapse, each is given an audiotape.

The program has been in the field only a couple of months and implementation is not complete. The goal of 15 cities is an organizational problem, and the program hasn't been implemented as planned. A considerable proportion of the patients are in the pre-contemplation or contemplation stages of whom 57% are receiving no treatment. Evaluation is nested case-control. Acceptability ranges are good—more than 75% have accepted the program.

Harlem Adherence to Treatment Study (HATS)
Sharon Manheimer, MD – Harlem Hospital Center

The Harlem Hospital Infectious Disease Clinic, a primary care clinic, undertook HATS, a randomized clinical trial, in an attempt to change peer-centered social support intervention for promotion of adherence to ART. The study's three components are: peer support, concrete services, and education.

- Peer support comes from trained HIV-infected peers who are successfully taking HAART. These peers address mistrust of the system and lack of support. They show the client how to navigate the system and communicate with providers, serve as role models and educators, and give feedback.
- Concrete services include HIV primary care, nutrition, and gynecological and psychological services.
- Education is directed to clients as well as clinical and non-clinical staff members and peers.

For this study, data were collected through detailed interviews. The client population was half men; average age 44 years; 75% African American, 20% Latino; 58% heterosexual; 78% unemployed; 75% on Medicaid; 20% in unstable housing; 60% didn't discuss their condition with friends, 35% felt ashamed, 30% would stop taking ART if they were using street drugs. Self-reported adherence was 64%; provider-reported adherence was 69%. The most common reason for non-adherence (50%) was forgetting.

Barriers to adherence were:

- low confidence in taking HIV medications alone and no one to help
- depression
- active substance abuse

Health Care Provider Adherence Training Curriculum (HCPATC)

Linda Frank, PhD – University of Pittsburgh

AETCs train clinicians (including dentists), and offer clinical consultation and technical assistance to build clinic capacity. HCPATC is a national AETC.

The training is targeted for low-, medium-, and high-volume providers. For low-volume providers (fewer than 10 cases a year), the question is when to refer. For medium-volume providers (fewer than 50 cases a year), the focus is on co-management. High-volume providers (more than 50 cases a year) are AETC faculty members and serve as experts.

Adherence must be addressed at every level. Strategies are intertwined with case conservation, mini-residencies, and on-site and distance consultation. The curriculum was devised to circulate guidelines, both of which must be continually updated. The curriculum refers the reader to the Web site.

Adherence is placed in the context of the client-provider relationship and the individual client. The curriculum, implemented by all 14 AETCs, is driven by the premise that the patient is the decision-maker. New modules will be developed to address changing trends in the epidemic. Current components of instruction are:

- introduction

- pathogenesis and viral dynamics
- principles of HAART
- adherence principles and strategies
- psychosocial issues of adherence
- cultural issues of adherence
- slide set
- experiential exercises
- process evaluation and outcome evaluation

For researchers a fundamental question is how to get information from a study into the field. The answer is to work with the AETC.

Action Point—San Francisco

Josh Bomberger, MD – San Francisco Department of Health

Action Point is a store-front clinic, which is street-based and geographically appropriate. The program stores and dispenses medications for 100 to 150 homeless people and offers whatever other services they need to succeed with an individual adherence plan. The patient decides how much medicine to take away.

The clinic offers monetary incentives and needle exchange three days a week. Adherence must be integrated into the patient's drug life. Such a clinic must offer flexible hours (6 days/week, 12:00 to 6:00 pm), adequate staff support (including a nurse, a case manager, a pharmacist, an acupuncturist), and supervision by flexible and imaginative people. Action Point offers love, respect, and social support. The clinic forms a sense of community. It is a link to primary health care, and drug and mental health treatment. Referrals come from providers, self, friends, CBO staff, and jail.

Their goals are:

- reduce harm
- reduce viral load
- increase immune response
- refer clients to drug and mental health treatment
- improve stability of housing and access to food
- reduce multi-drug resistance
- reduce drug use and dependency
- raise the standard of care among the HIV-infected urban poor
- reduce costs of health care to the public sector
- improve clients' self-esteem

To be enrolled, clients must be documented HIV positive with a CD4 of less than 500 or a viral load greater than 10,000, and TB negative. Within six weeks of enrollment, they must have established a relationship with a primary care provider.

Clients tend to be over 40 years of age; 29% are white, 25% African American, 13% Latino; 98% use illicit drugs; some are women and transsexuals; 60% started HAART

within a month. Most come in once a week. The most common regimen is D4T, 3TC, NLF.

Action Point offers its clients:

- individual adherence plans with frequent reassessment (which is time-consuming and intense)
- medication storage and dispensing
- medi-set filling and management
- case management, including finding housing, food, mental health care, etc
- a pager reminder system
- referrals for drug and mental health treatment
- \$10 weekly incentive pay
- acupuncture
- treatment advocacy
- referral to primary care
- “hang out” space

The program costs about \$4200 per year per active clients. Sustainability of staff may become a problem—it’s staff-draining work.

Structured Training and Monetary Reinforcement

Marc Rosen, MD – VA Connecticut Healthcare System

Contingency management in the VA Connecticut Healthcare System involves paying the patient to take medication at the right time. Intervention involves detailed review and discussion. Patient and provider meet once a week for counseling for 4 weeks; then again at week 8 and week 12. All patients get MEMS caps, but counseling is given only for the drug of poorest compliance. Review of MEMS-generated printouts gives the patient feedback. In addition to MEMS feedback, patients are paid \$2 to \$10.

The average age of clients was 48 years; 93% were male; 75% African American; many use illicit drugs.

Contingency management produced a significant effect. Adherence began at 95 to 100%. This level decreased but still remained higher than in the control group. The same interventions in a non-VA population showed that contingency management with MEMS caps still gave better results than the control.

However, the study is limited by its small size and cannot be generalized as done because clinics will not pay patients \$10/day indefinitely. Nevertheless, some findings are generally useful. MEMS compliance reports are helpful for patients and providers. Self-reports differ from MEMS-generated reports, probably because patients want to please providers. Although it is hard to estimate the percentage of compliance, details of the MEMS reports reveal patterns, which can then be addressed, e.g., are doses missed on weekends, mornings, or afternoons? Cost—\$80 per cap—is a drawback to MEMS.

***ADHERE—Adherence to Drugs for HIV,
an Experimental Randomized Enhancement***
Jeffrey Samet, MD – Boston University Medical Center

ADHERE is a 24-month prospective study of 240 HIV-infected people with different levels of problems with alcohol use. The study focuses on the relationship between alcohol use and outcomes of HIV infection with regard to testing an intervention to enhance adherence to ART.

Program components are:

- brief clinical intervention for the alcohol problem
- medication timer
- counseling on efficacy of ART and the importance of adherence
- nurse's home visit to tailor an individual approach of adherence assessment
- self-reporting for each ART medication
- MEMS caps

Intervention adds nurse's visits to the baseline of a visit and a home visit at 1 month and 3 months.

Of 106 subjects enrolled so far: 19% are women; 40% are African American, 23% Latino, 31% white; 22% are homeless; and 59% are injected-drug users.

Challenges are:

- adherence measures—MEMS or self-report
- recruitment
- follow-up—at 6 months, 71 of 81 were captured
- selection of outcome variables

The Role of Social Service Providers in HIV Treatment Education
Carlos Arboleda – Gay Mens' Health Crisis

Social service providers have important opportunities to provide treatment education and support to their clients. Clients are often more comfortable talking with case managers than with physicians and are usually given more time to do so. In order for social service providers to provide treatment information, adherence support, and advocate for better care for their clients, they need education and training on HIV treatment issues.

To meet this need, Gay Mens' Health Crisis, a large social service provider and educator in New York City, offers a workshop entitled "The Role of Treatment Education in Client Services." Workshop participants solve problems in scenarios based on fact. The problem-solving scenarios provide participants with background information about HIV disease and treatment, along with opportunities for them to understand how HIV treatment issues impact their work in social services. All participants are given background materials on treatment issues, including clinical practice guidelines, fact sheets, and GMHC's treatment newsletter. The participants are then placed on a mailing list and are sent regular information about treatment forums. GMHC also runs a treatment library that

provides providers and people with HIV comprehensive treatment and medical information.

The most important aspect of the workshop is its attempt to help social service providers understand how treatment issues directly impact their work, even though they do not provide medical care. The scenarios are designed to show how a knowledge of HIV pathogenesis, disease manifestations, and treatment impact primary prevention programs, case management, housing services, nutrition services, drug treatment services, etc.

More than 400 people have completed the workshop. Participants come from social service organizations throughout the New York metropolitan area including drug treatment centers, housing services, child services, HIV primary prevention programs, and case management services. GMHC staff are often asked to bring the workshop to a particular agency and the workshop has been performed in all boroughs since its inception. The majority of participants are people of color. Evaluation of the workshop includes a survey asking participants what they thought of the event, what they learned, what aspects of the workshop were most useful. Responses are very positive. Most important, participants frequently refer their co-workers to the workshop.

Directly Observed Therapy (DOT)

Tim Flanigan, MD – Brown University

Dr. Flanigan described a program of directly observed therapy (DOT), where workers watch patients take medication on a regular basis. At Miriam Hospital, 80% of the HIV-infected are poor and on Medicare. They tend to be co-impacted by substance abuse including alcohol, depression, and violence, and have spent time in jail. There is also an ongoing epidemic of TB, but TB is curable with daily or twice-per-week medication. Adherence to HAART competes with the client's other priorities and crises.

Directly observed therapy is a time-consuming way to encourage adherence, but it does not have to be continued forever. In some circumstances, such as incarceration, DOT works well, but is difficult to sustain after release. At Miriam Hospital, a pilot program of modified DOT, using community health education workers, enrolled the hardest to reach patients. DOT is best done by people from the community. This program employs near-peers. They are high school graduates who get salary plus fringe benefits totaling about \$20,000/year. The goal is to teach patients strict and sustained adherence and then to gradually move them off the program. Each patient is met by a near-peer outreach worker every weekday morning in a location selected by the patient. At each visit the worker delivers the day's prepackaged doses of medications chosen by the primary care physician. The morning dose is observed; the others are self-administered and self-recorded.

Clients enrolled in this study were: an average age of 38 years; 65% are women; 68% have been in jail; 84% are HAART-experienced; 46% are substance abusers. Of the 37 patients enrolled, 24 have completed 6 months on the program and 2 have completed 12 months on the program and now take medications entirely on their own. All believe the outreach worker helps, and 87% feel they are better able to take their medications.

Adherence Support for HAART: A Multi-Site Evaluation
Mark Waters, RN, MPH – New York State AIDS Institute

The New York State AIDS Institute, in conjunction with the New York Academy of Medicine, is conducting a multi-site evaluation of adherence support programs in New York State. The project goals are to increase adherence, empower clients to make informed treatment decisions, and to identify effective adherence interventions. The project objectives are to provide consumers with access to adherence services, integrate adherence services into the continuum of HIV care, and develop a collaborative infrastructure across provider organizations.

The project involves 10 organizations that provide both clinical and non-clinical support for persons at greatest risk for non-adherence. The New York Academy of Medicine is conducting the program evaluations to assess the effectiveness of the interventions. Adherence is measured using self-reports, MEMS caps, pill counts, viral load, clinic attendance, prescription refills, patient diaries, and CD4 cell counts. The multi-site evaluation collects data on program characteristics, client characteristics, intermediate outcomes, adherence rates, and health outcomes.

Project services include:

- individualized treatment plans
- HIV treatment education
- Treatment readiness
- Medication reminders
- Medication delivery
- Modified DOT
- Adherence monitoring
- Home visits
- Skills-building
- Counseling
- Phone support
- Peer support
- Case management

Of the 406 clients included in the evaluation, 58% are male, 37% are Latino, 36.7% are African American, 27.5% have a history of mental illness, and 83% have a history of drug or alcohol use. 50.2% report having previous adherence difficulties. 18.7% are new to HAART. Self-reported adherence rates from 213 clients show that 59.1% missed a dose in the last two weeks, and 36.4% missed a dose in the last three days. The mean adherence rate in the last three days was 81%. Most common reasons for missing doses were:

- simply forgot
- slept through dose
- didn't fit daily routine
- too hard
- depressed/overwhelmed

Bienestar

Rafael Landa – Los Angeles, California

Bienestar, a nonprofit founded in 1989, serves about 1500 clients at six locations in Los Angeles. It has filled a linguistic and cultural gap by serving the Latino community (97% of their patients). HIV infection has increased among minorities, women, and children. 87% of Bienestar's clients are between the ages of 20 and 37.

Complicating treatment of HIV and other infections among immigrants is distrust of authority engendered by the political chaos that often characterizes undeveloped countries. Bienestar has had to break down fear and guilt among those HIV-positive immigrants arriving from Central and South America, where they are regarded as sexual criminals. (Such attitudes are addressed with mental health interventions.)

Bienestar began connecting with other agencies and health care providers to increase the patients' network of services. A combination of all services, including education and social service, is required to attain adherence. They support a peer program in which the client is connected to another person, which encourages communication. The patient can choose services from the whole HIV program. Health care providers are bilingual foreign doctors who are waiting to qualify for US medical license.

Services include:

- education services
- pre- and post-HIV test counseling
- counseling and services for patients and their loved ones
- social services
- medication seminars and workshops
- exercise
- meditation
- peers who visit the client once or twice a week to follow up

Peer Education and Adherence to HIV Therapy in Children

John Farley, MD – University of Maryland–Baltimore (UMB)

This program will enroll 160 HIV-infected children. Most of the mothers discovered their HIV-positive diagnosis when they were pregnant. This program provides support and guidance in child development and parenting, disclosure, and coping. Adherence in the pediatric population is challenged by the dual illness of parent and child. There is often active illicit drug use within the family structure. Disclosure of HIV status and secrecy is an important issue, with the child often not knowing that either he or the parent have HIV. Secrecy about one's HIV status also makes obtaining social support difficult, if not impossible. Other significant problems include unstable living conditions, the need to plan for multigenerational care, and low literacy. Treatment is long-term, many patients have no symptoms, and palatability problems are significant. The situation is further complicated in adolescence by developmental issues.

The UMB Compliance Critical Path involves:

- psychological assessment
- caregiver/family assessment
- determine whether backup exists
- determine need for case management
- environmental assessment (home, school)
- medications-specific issues (dosage form)
- family education and training
- tools and reminders
- child/caregiver reinforcement (token economy, e.g., McDonalds coupons)

A study to measure adherence levels is underway using MEMS caps. The study focuses on caregivers of HIV-positive children who were younger than 13 at enrollment and who are taking three or more antivirals. It excluded people who don't use pill boxes or do not set out pills in advance (which implies secrecy) or who use liquids. The remainder were given MEMS caps for one of their medications. Pharmacy re-fill information is collected for all medications.

To this was added a peer-educator and home visits for the test group. The peer-educator's visits changed from weekly to monthly, and they encouraged visits with a child psychologist.

Family support was determined by adding to the survey the question: "How many in your network know you have HIV?" To address the distrust issue, African-American psychologists embedded true-or-false questions including:

- "HIV medications work better for white people."
- "HIV was devised to infect minority groups."
- "Doctors give patients medications without telling them."

To date 40 subjects aged 2 to 11 have been enrolled. Most don't know their diagnosis. Most are African American. The caregivers include biological mother, biological father, biological grandmother, aunt, adopted parent, or foster parent.

Preliminary results revealed very high parenting stress scores, but neither health beliefs, nor distrust are major issues. The peer educator's home visitor was popular, however there's a significant disconnect in social support; that is, firm support networks exist, but few people in those networks know the patient is HIV-positive.

About 20% of the client's using HAART were in pre-contemplation and contemplation stages of Prochaska's model. A unique problem to the pediatric population is that children must be taught how to swallow pills.

As determined by MEMS and self-reporting, about 75% had missed at least one pill in the last 2 weeks. Overall adherence 3 months after intervention was 75% (before the intervention, it was 58%). A related issue is that non-administration of medication becomes Child Protective Services issue under the law.

AIDS Action Committee

Michael Immel – Boston, Massachusetts

This adherence program establishes different levels of education and support for clients with varying needs and understanding about their treatment. The program is one of 12 funded by the Department of Public Health in Massachusetts.

Acceptance and understanding of the issue within the social service agency is a challenge. Adherence must be incorporated into a broad range of issues; it's too narrow a specialty to be independent from related programs. And it must be integrated among staff and every aspect of their daily routine.

Counseling or social support was added to the existing treatment educational program. The social support is a buddy system—one volunteer per client. Buddies telephone their assigned client regularly. Forgetting (the convenience factor) was the primary reason for missed doses.

Readiness measures and techniques are extremely important to avoid the “intuition trap.” Another component is social services education regarding financial, legal, and housing issues; care providers must be taught to listen for indicators of problems in these areas. In addition, social marketing on a broader scale is needed. The public and the community needs to know and acknowledge that adherence goes on.

Among the education tools they produce are bilingual brochures written to be readable for various literacy levels. More detailed packet are given to more literate clients. Social services providers are given a poster intended for office use to stimulate discussion.

AIDS Project Los Angeles (APLA)

Nancy Wongvipat, M.P.H. & Janelle L'Heureux, M.S., R.D.

APLA, founded in 1983, serves about 8000 clients and is one of the largest AIDS social service organization in the United States with a staff of 170. Their services include mental health, nutrition, education, a dental clinic, food, housing, transportation, benefits management, legal services, a women's program, and a health education and advocacy program. Their clients' demographics--10% women, 90% men; 40% Caucasian, 22% African American, 32% Latino/a, 2% Asian Pacific Islander, 1% Native American, 3% other/unknown--represent the epidemic of Los Angeles County.

APLA has a Health Education and Advocacy (HEA) department comprised of five treatment advocates (TAs), two nutrition advocates (R.D.'s), an HIV resource center assistant, program manager, and a health education specialist (M.P.H.). APLA's Treatment and Nutrition Advocacy components are unique in its adherence support in that support is provided in a community-based setting, consultations are not time-limited, and is provided within a one-stop shop setting, with the exception of primary medical care provisions. Treatment education consists of one-on-one consultation, community education forums (e.g. Treatment 101, on dealing with medication side effects), educational materials (e.g. fact sheets, newsletter with a monthly “Adherence Matters” column providing practical

adherence tips) and intensive Treatment Advocacy Trainings. The Treatment Advocacy Training provides a comprehensive overview of adherence and practical case study exercises.

To better understand the adherence needs of our client, a survey was conducted in 1997, which resulted in 1322 responses. Results of the survey found the following: About 60% reported good adherence; 43% reported side effects from medication; 30% had problems with the number of pills; 27% forgot to take medication; 25% were unable to eat at the necessary times; 21% had difficulty taking pills as prescribed; and 11% had difficulty or were unable to take their medications at work.

To support adherence efforts, APLA employed a staff person devoted to the issue. A standardized assessment tool was developed and used by TAs to assess demographic and medical information, reasons for intake, and adherence concerns. The adherence section served three purposes: as an assessment instrument, an educational and skills intervention, and a follow-up evaluation tool. Adherence tools, including an illustrated medication schedule with pill stickers, daily routine and activities reminders, and food facts and suggestions, and pill boxes were provided to clients. Practical tips and support from TAs that were reported to be helpful with clients' adherence included identifying regular activities to serve as cues to taking doses, creating a personalized meal/medication schedule, utilizing pillboxes, and providing strategies to deal with side effects. Since TAs are not time-limited in their consultations with clients and given clients' comfort levels in a community-based peer setting, clients open up and disclose to TAs more so than they would to their clinicians. This openness and flexibility of the interaction help TAs find clues to assessing whether the client truly has an adherence concern and allow TAs to become more specific in their adherence assessment. Adherence data collected from the intake forms showed a 16% increase in overall reported adherence.

APLA has a centralized case management database, which aids in follow-ups and process monitoring, and in working with other staff and departments to achieve a more integrated adherence effort. They would like to see more reinforcement of adherence and integration of adherence support such as through case management and mental health staff, which is the direction they are heading in their adherence efforts.

Nutrition Support

Diet is part of adherence as well as to the overall well being of persons living with HIV/AIDS, but often overlooked in primary care settings, research studies and other settings. Whether we are dealing with body's response to medication, drug regimens, whether the client is experiencing weight loss or gain, or the development of opportunistic infections, all are issues involving nutrition. Registered dietitians at APLA offer nutrition education classes and meet with clients on a 1:1 basis to build self-management skills. Classes include; basic nutrition and HIV, food & water safety, meals and medication, dealing with side effects, measuring lean body mass, managing high blood sugars/diabetes, high cholesterol and triglyceride levels and a fitness class. Nutrition must be constantly reinforced, especially with complicated medication regimens. A dietitian can assist the client in interpreting in terms of food, the food requirements of specific medications.

Recognizing that there have been early and ongoing indications that nutritional issues are closely linked to progression of disease and treatment outcomes, an expert panel is being

formed to develop national HIV nutrition guidelines. The goal of this document is to provide guidance about medical nutrition therapy as part of HIV healthcare management. The intent of these national guidelines would be to raise awareness of the important role of nutrition in HIV health care, guide physicians in their recommendations to patients, and provide guidance for patients themselves.

The project has been spearheaded by collaboration of government and non-government agencies. These are the Office of HIV/AIDS Policy at Department of Health and Human Services, the HIV/AIDS Bureau at the Health Resources and Services Administration, the Office of Special Health Issues at the Food and Drug Administration and the Nutrition & HIV Program of AIDS Project Los Angeles. It is anticipated that the document will become a companion to the US Public Health Service Treatment Guidelines, and expected to be available in approximately a year. Nutrition fact sheets for each protease inhibitor can be found on the APLA website: www.apla.org

Project TEACH (Treatment, Education, and Access, Central Harlem)

Bradley Walrond – Minority Task Force on AIDS, New York, NY

Project TEACH is a peer-based project in which each peer is responsible for a constituency and for recruitment. Peers work less than 10 hours per wk at \$10 per hour; usually the peer is HIV-positive. Once a week peers have access to insurance people, health care professionals, and pharmacists to keep abreast of trends. Peers reflect the constituency; they are true advocates for the client base.

HIV-positive people live with an illness that will probably take their life. Nevertheless, treatment should be the client's informed choice, made with consciousness and responsibility. Because the person is not adherent does not mean the person is not responsible, and providers and caregivers must respect how clients choose to live and die with their disease, and not become "pill-pushers."

HIV/AIDS is not the only chronic disease, and the HIV/AIDS community can learn from other long-term chronic diseases, such as terminal cancer.

HIV University

Rebecca Dennison – WORLD, Oakland, California

Nine years ago, when Dennison was diagnosed HIV-positive, women and non-addicts had no place to turn, so Dennison started a monthly newsletter, which is now sent to over 12,000 women. Confidentiality is a huge problem. They send the newsletter in a security envelope and they don't sell their mailing list. More than 300 women have shared their experiences in the newsletter, some anonymously, some not. They have a monthly pot-luck dinner. In 1992 they had their first women's retreat; now they offer a retreat twice a year and there's a waiting list. Most of the women are low-income and get health care at under-funded clinics.

To enable these women to understand and combat their condition, Dennison and a group of women designed and developed a curriculum for their own “university.” Courses include: anatomy and physiology, HIV and cellular infection, HIV disease, gynecology, sexually transmitted diseases, pregnancy, and perinatal transmission. Education sessions are now given in African American churches.

The support program began with volunteer AIDS activists, but now, through Ryan White Title IV funding, some of the volunteers can be paid. A new issue is arising as experienced volunteers age and die. Besides education, HIV University also offers alternative and complementary therapy (acupuncture), clinical trials, and addiction recovery and relapse prevention.

Spirituality is important. They all know there’s no cure, but they maintain hope day to day—hope that treatment will get better, hope for supportive relationships. What does it mean to take medication if you believe life and death are God’s decision? We must figure out how to treat without being arrogant and pushy. Not everyone wants treatment; not everyone wants longer life at any expense.

Many research questions remain to be addressed, and a large meeting of patients talking about their problems and solutions they need would be helpful. For instance:

- About half of the women are co-infected with hepatitis C. What will medications do to the liver?
- People are very concerned about side effects. What can be done?
- Which medications may contribute to depression?
- Are scheduled interruptions harmful; if so, how so?
- What are drug effects peculiar to women and African-Americans?
- Are people not on medication because they’re not informed and not getting good care, or because it’s an informed choice?
- What is each drug’s metabolism in pregnant women?
- What are the drug effects on the fetus and on children?
- Is a natural low viral load the same as a drug-induced low viral load?
- How do medications work with the immune system?
- What sequencing strategies should be used for people who want to have a baby one day?

Quality of life and the will to live are involved with adherence issues. Looking for assessment tools without considering the individual’s desire to live is useless.

T.H.E. Course[®]

Valerie Scott & Maddy Rice – Glaxo Wellcome

Learning to live with HIV/AIDS requires behavior change and the ability to maintain that change. Can HIV self-management skills be learned? Adherence is a by-product of improved self-management skills. T.H.E. Course[®] is (T.H.E. stands for “Tools for Health and Empowerment”) a program that teaches life skills, premised on the idea that self-

empowerment is the active participation in one's health care. It stresses that an HIV-infected person:

- needs to actively participate in their health care decisions with a trusted health care team
- understands the importance of a personal support system and learns how to put one in place
- understands the rationale for strict adherence and if he/she decides to initiate therapy, is fully committed to taking their medications as prescribed
- knows the effects and side effects of those medications

T.H.E. Course[®] provides tools for the HIV-positive person and caregivers (friends, family members, partners), tools for trainers. These tools are designed to reinforce behavior change.

T.H.E. Course[®] is delivered in an interactive, small-group setting and facilitated by a health care professional or peer educator (the “trainer”). Trainers attend a two-day Train-the-Trainer Program focused on the principles of adult learning, as well as procedures for organizing and delivering T.H.E. Course[®] curriculum. T.H.E. Course[®] uses participant-centered skills-building activities and discussions, aimed at improved HIV self-management behavior organized into 12 two-hour modules.

The modules focus on:

- patient self-empowerment and the importance of working collaboratively with one's health care team
- medication self-management planning, adherence strategies, pharmacology and nutrition
- HIV pathogenesis
- recognizing signs and symptoms of HIV specific to women
- accessing medical and emotional care and paying attention to self-needs
- parenting, pregnancy, and contraception
- prevention of transmission: sexual, household, and maternal-fetal HIV transmission
- assessing risk behaviors and harm reduction strategies for alcohol and drug use
- principles, benefits and risks of combination antiretroviral therapy
- symptom management
- preventing opportunistic infections
- employment issues
- death and dying, wills, and advance directives

Participants are awarded an Empowerment Message Button for completing each module.

A clinical trial of the education modules was conducted in 11 different treatment sites: Immediate and delayed intervention groups served as active and control populations. Only participants who completed at least 7 of a possible 11 sessions were included in the analysis. Trial participants included 69 patients—28% were women; 33% were African American, 46% white, 17% Latino; average age was 43. Results of the trial showed statistically significant improvement in adherence lasting 12 months. A trend toward reduced viral load was also seen, however there was no change in CD4 cell count.

Even though medication adherence was good prior to T.H.E. Course[®] intervention it still improved and yielded improved sustained behavior changes in knowledge and empowerment as well. Program participants would like to have had T.H.E. Course[®] earlier in their disease. Trainers saw changes in the clients, as clients took a more active role in treatment. The trainer's ability to motivate was crucial. They used incentives, maintained the materials current, and made learning fun. Participants need to be actively involved in the program and the curriculum should be flexible.

Medicaid Managed Care Contract Specifications

Jeff Levi, PhD – Center for Health Services Research and Policy (CHSRP) at the George Washington University School of Public Health and Health Services

Dr. Levi discussed the systemic approaches to the incorporation of adherence support into health care and social services. Adherence services need to be seen as an essential element of the continuum of care for people with HIV. To achieve this goal, adherence services must be part of the payment system through an expanded definition of case management and as a separately defined service. The impact will be greatest on the public sector, which pays for over half of HIV care costs.

Nearly half of HIV-positive persons receive health benefits from Medicaid, and more than half of the states (54%) use managed care for their Medicaid programs. Therefore, providers must learn to deal with managed care. State's contract with managed care organizations to provide services for their Medicaid recipients. That contract describes the services that the managed care company is expected to provide to patients. The negotiation of the contract specifications offers an important opportunity to assure that high quality care is available to patients. Furthermore, contract specifications offer an opportunity to define a broader set of services than normally provided by Medicaid. In this context, purchasers of health care services can more clearly define their expectations of contractors and can better determine appropriate reimbursement rates; providers can better understand purchaser's expectations and can better determine costs; and consumers can more clearly understand what services to expect.

CHSRP's purchasing specifications project has devised effective language to be used in such contracts. Three elements are critical:

- screening for HIV and sexually transmitted diseases
- following treatment and prevention guidelines
- ensuring access to an experienced provider

The specifications specify the need for an interrelationship between support services and primary care services and call for adequate reimbursement in a capitated setting. Adherence support services are included as an essential element of care. Specifications for

adherence services describe the services and include counseling as a necessary part of treatment to initiate and sustain the course.

Purchasing specifications and other information are posted on the Web site (www.gwu.edu/~chsrp).

Correctional Institutions

Ellen Rappaport, MPH – Correctional Medical Services for Massachusetts Department of Correction

Of the 11,000 inmates in the Massachusetts state correctional system, 4% are HIV-positive. Our HIV Case Management program was developed to clinically manage HIV+ inmates and is very comprehensive. The program was implemented based on recommendations from a local AIDS Task Force. This task force was made up of Department of Public Health officials, community resources, prison advocates, Department of Correction, contracted medical providers, and the local public health hospital. The program includes Nurse Case Managers (the mainstay of the program), on-site Infectious Disease specialists (physicians that have been “leant” by our public health hospital who provide care behind the prison walls), dietitians, HIV test counselors, and a discharge planner for inmates being released from custody.

Of the HIV patients, 77% of the population are taking some type of HIV medication. 84% of the patients on medications are taking triple therapy (usually includes a protease inhibitor). Most inmates participate in the Keep-on-Person (KOP) medication program. The program gives the inmate responsibility to self medicate and more control for their own health. Medication is packaged in “blister cards”. When there are peculiarities with various medications, e.g. need for ritonavir in the refrigerator or dry storage of Crixivan in original container, custody staff is educated about storing medication in containers other than the blister packs. The KOP program resorts to Directly Observed Therapy (DOT) if the patient is in segregation, and unable to participate in the KOP program or if the patient is not adherent with his/her medication.

A large amount of the Nurse Case managers’ time is spent on educating the inmates about when and how to take their medication. Case managers provide a very supportive environment and for the most part, the inmates are highly educated about HIV disease and HIV medication. There is close monitoring on how adherent the inmate is. In prison the way to monitor adherence may be different than is usually seen. Some ways we monitor adherence is to see if the inmate comes to pick up their medication on time or if they re-order their medication on time.

Medical providers in the prison setting have a unique opportunity to provide health care. For some, prison is the first place many inmates are introduced to health care. In a structured environment the inmates do well. The struggle for us as care givers, as well as, for some inmates, is when they transition into the community. Inmates must get help applying for benefits and services while they are still inside the prison. They are currently unable to apply for public benefits (e.g. Medicaid) while they are incarcerated. This makes it difficult in ensuring continuity of care for the inmate. Many of our inmates have other chronic diseases and on medications for those diseases. We discharge inmates

who's HIV medications are paid for through AIDS Drug Assistance Program (ADAP) but the non-HIV medications are not covered.

The incarcerated patient population is getting sicker; currently 57% of our HIV+ patients are co-infected with hepatitis C; and they are aging. The case management model, as an intervention, is effective in the correctional setting. The challenge before us as a society is to provide the incarcerated patients the tools to acquire a sense of self worth, the capacity to be a self advocate and ultimately feel empowered.

WORK GROUPS

After hearing the presentations on background information and the various types of interventions in development around the country, participants were assigned to one of four work groups: Hospital-based Clinics, Community-based Organizations (Free-standing Clinics), Social Service Agencies, Behavioral Health Service Agencies. The function of the groups was to identify the kinds of services needed within each of these settings to provide adherence support and education to/with people with HIV. Each group was to consider the same six questions for 2 hours and report the results of their discussion to the group. Below is a summary of those workgroup discussions. These summaries can be useful in planning broader implementation of adherence support services.

Questions posed to Work Groups

1. What are the components necessary to develop comprehensive adherence interventions within your respective setting?
2. Identify opportunities during the provision of care where adherence support/education could be provided.
3. Which adherence interventions seem most appropriate and promising for this care setting?
4. What are the opportunities for and potential risks and benefits of directly-observed therapy (DOT) within the care setting?
5. How do adherence support programs coordinate efforts and strategies and exchange information?
6. What are appropriate and feasible methods to evaluate the effectiveness of the interventions?

Summary of Work Group Discussions

- Need for a Team Approach: Underlying any components must be agency commitment. There should be vertical as well as horizontal “buy-in.” Consensus favors a team approach, albeit expertise-focused, which takes more time, money, and resources. Ideally the team should be composed of a primary care physician, a research director, a pharmacist, nurses, social workers, case managers, peer educators, and someone who is responsible for coordination and communication. All team members should be “on the same page”; that is, they should share the principles, values, mission, and philosophy of the program, and should use the core protocol and receive the same training.
- Coordination of services: Services must be integrated and linked with other services. Collaboration among and within agencies with providers and with clients would include referrals for mental health, substance use, and social services (often episodic over time); and sharing client information, but information sharing is risky—clients must consent, informed consent forms must be released, and the information must be protected.
- Adherence support requires looking at a patient’s life, not just their HIV treatment. Issues such as child care, housing, mental health, pregnancy, drug use, access to social support, disclosure of HIV-status, and economic security must be addressed as they will drastically effect a patient’s ability to adhere to therapy.

- Treatment should be client-centered with individualized care plans that address the client's concerns, in her or his chosen order. Time should be allowed to develop and address issues of adherence and to reinforce desired behavior over time. Adherence should be kept on the agenda, and the program's success and progress reevaluated from time to time. Input from clients should be sought. Care provision should be seen as ongoing process, not a series of individual encounters. If better adherence depends, in part, in the development of a trusting doctor-patient relationship, then consistent interaction between those parties is essential.
- To enable access to services, clinics should focus on a specific population in a geographically limited area. Hours of operation should be flexible and should accommodate the clients' schedules.
- Coordination of care and services is an important and efficient means of providing adherence services. Assuming appropriate training is available, any service where an client interacts with a professional or peer is an opportunity to provide adherence support. Programs such as home health visits, meal delivery, adult day care, drug treatment, transportation, support groups, and peer-based education can incorporate adherence support services. Conduct case conferences with primary care provider, case manager, and other service providers to strengthen coordination and eliminate duplicative services.
- Making a detailed assessment with the client before starting therapy is perhaps the most important opportunity to intervene and ensure better adherence. Clients should be assessed to determine their readiness to accept a complicated and demanding treatment regimen. To encourage personal responsibility, the choice to accept treatment must be the client's. Continued follow-up and re-assessment is also necessary, as adherence and the relationship to treatment will change over time.
- Community organizing, community awareness, and client advocacy are important parts of the social program. The communities affected by HIV need to understand the difficulties people with HIV trying to adhere to these treatment regimens. In this way, the community can offer support, and not stigmatize people if and when adherence difficulties arise.
- Life transitions are particularly stressful times and need close attention to ensure that adherence to medication is maintained. These include release from prison, changing residency and/or jobs, having children, etc. The crises that these transitions can create are both emotional and logistical. Ensuring continuity of care is an essential component of transition management.
- Training and education should be available for staff members, people with HIV, social workers, volunteers, peers, and providers. Training is important in areas such as needs assessment, readiness evaluation, collaboration with other agencies, patient education, and leadership development. Social service providers need training into the pathogenesis of HIV, its disease manifestations, and therapeutic regimens. Cross-training would be useful for staff members of medical and behavioral health agencies in HIV/AIDS, mental health, and substance use.
- Treatment information is an important component of adherence services. Patients need to understand why they are being given these drugs, why adherence is essential, have information about side effects, understand the various components of their treatment regimens and that they have choices to make. Treatment information should be culturally appropriate, easy to read, and accessible.

- Adherence services require space, staffing, and materials.
- Funding for adherence services should be incorporated in care plans and health delivery specifications.
- Assist clients in setting up a support system by identifying who they trust and depend on for care and support. Provide those persons with information about drug regimens and the need for adherence to therapy.
- Bring pharmacists into the team; they can alert the team regarding prescription re-fills. Work with pharmacies to ensure delivery of medications. Increase pharmacy services—longer hours and perhaps follow-up.
- DOT is an option for some people if it is included in a larger picture. It can provide positive reinforcement if an appropriate provider is available once a day to observe. It is helpful if DOT can be done on-site—perhaps a hospital-based clinic—which offers a chance for daily check-in and regular contact. The contact that comes with DOT allows providers to deal with issues of diversity, culture, and language and possible complications.
- DOT can work for diseases like TB, which require finite treatment for cure. However, with a chronic illness like HIV, the effectiveness and practicality of DOT is unclear. DOT is labor intensive and expensive. If resources to provide treatment are limited, then the use of DOT can lessen the availability of treatment. How long should DOT last? Can/should it be provided for a patient indefinitely? Will DOT be effective in helping patients with treatment adherence after DOT stops? Does DOT teach patients skills for adherence? Geographic limitations can make DOT untenable in many areas, particularly rural ones. The use of monetary and other incentives may be effective in getting people to take their drugs, but is it coercive? Do monetary incentive impact of patients' decisions to start therapy?
- There is no gold standard for evaluation of adherence intervention. But, evaluation is essential. Evaluations should utilize both as to process and outcome measures, including biologic outcomes, clinical outcomes, virologic effects, and adherence measures.
- Partnerships between CBOs and the research community are an important and underutilized avenue for program evaluation.