Adherence to HIV Therapy

A sample slide program

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[New Title slide for revised and annotated version of slide program: Adherence to HIV therapy]

[On this annotated version, I have made notes indicating which original slide the information on the new slide was derived from, so it will be possible to go back to the references. For example, this slide title is new, so it is #1 here, but only in the revised version.]

Improving Adherence in HIV Therapy

- How do we **Assess** it?
- Can we **Predict** it?
- How to **Maintain** it long-term?

[Original slide #1]

In some chronic illness conditions, adherence problems are immediately signaled with life-threatening complications. Finding problems with adherence and determining methods of enhancing adherence for patients is crucial. (Andrejak, et al, p. 185)

Although equally critical in HIV therapy, the devastating consequences of non-adherence may not be recognized for many weeks or months. By the time patients realize the implications of not following HAART* as prescribed, they will have already developed resistance to the therapy and compromised their long-term survival.

By the time clinical indications of adherence problems are obvious, it is usually too late to effectively manage the problem. Effective HIV therapy requires assessment of potential problems before they occur. We need to understand and use the predictors recognized as affecting adherence in HIV management, adapted to our individual patients, if we hope to maintain effective care over the long-term.

* (HAART is the commonly used acronym for highly active antiretroviral therapy. As all current regimens of HIV therapy are combinations of drugs, some writers are returning to the former acronym, ART. The reference papers here use HAART, so I have kept the slides consistent with that practice.)

Results of Successful HIV Therapy

- **Viral suppression**
- **Reduced resistance**
- **Increased CD4+T**
- **Enhanced long-term survival**

[Original slide #2]

We have yet to identify clear standards for measuring adherence, but we know perfect or good-enough adherence is associated with increased levels of suppression of virus and reduced rates of resistance to medications.

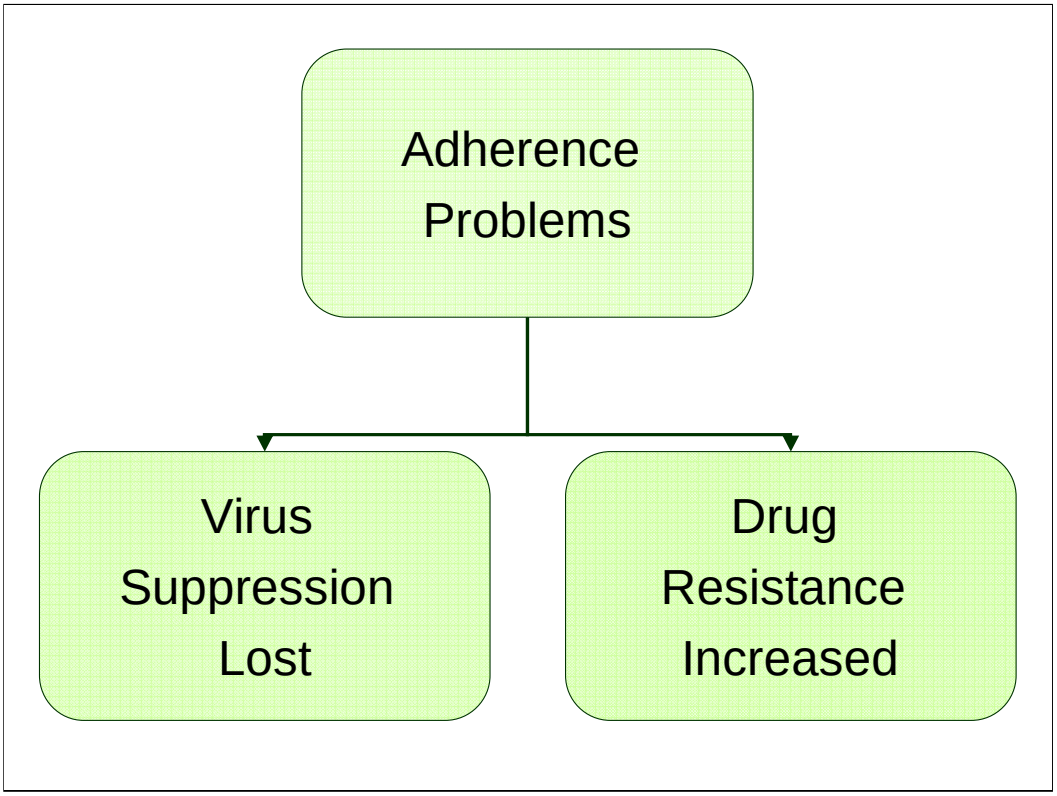
Although there is not clear consensus of what level to use as a marker of treatment success, CD4+T cell counts improve as a result of perfect adherence to HAART.

(Frank, p. S10, citing Paterson, et al, 2000)

(GUARVA)

Perfect or good-enough adherence is required to ensure long-term survival. Patients need to be educated to understand what clinicians have learned: the best therapy is the first HAART regimen, if it can be effectively maintained.

(GUARVA, p. 20)



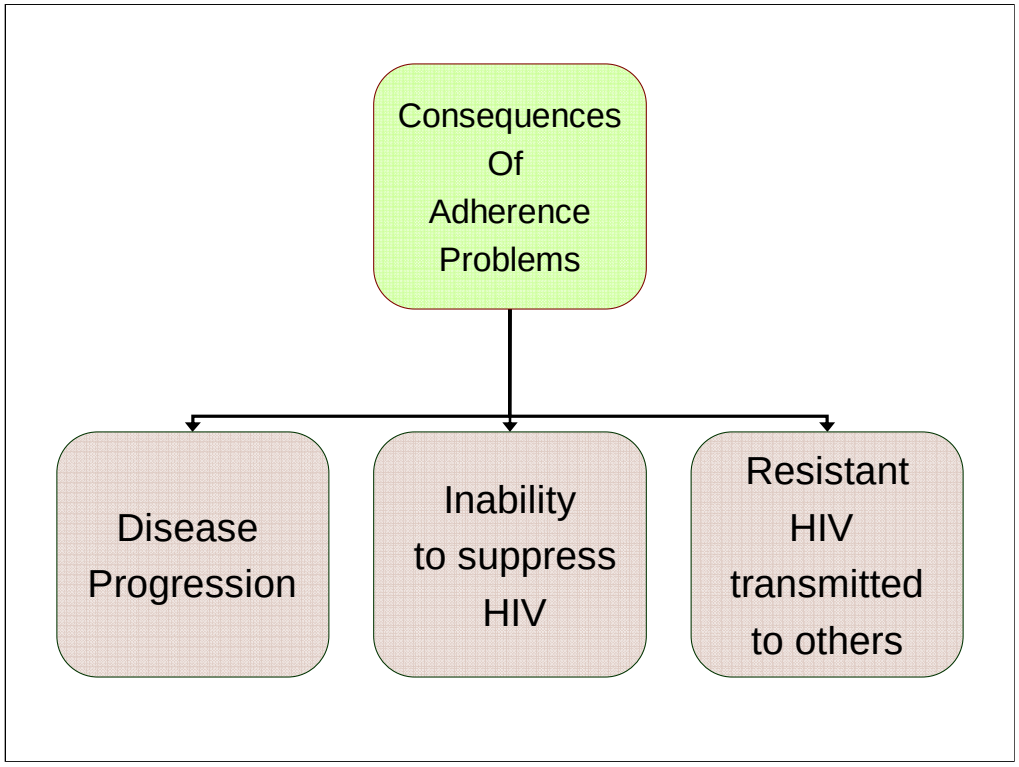
[I've divided the original slide #3 into two new slides (revised slides #4 and #5). This reduces information overload, and allows the speaker to concentrate on each level of problems that occurs.]

When the inhibitory concentration (IC) of one or more drugs drops, the consequences of adherence problems follow.

Patients develop drug-resistant strains of HIV.

Changing therapy, even to very intensive regimens, cannot suppress viral replication.

*(Note – None of the studies included in the research gave times to development of resistance. This is important and should be added.)



[Second slide revised from original slide #3.]

The further compromise of the immune system results in serious and often *fast* *development of additional disease states

that cannot be controlled, despite the addition of multiple agents, which further overload the patient's immune system.

The uncontrolled, drug-resistant virus is also passed onto partners, reducing their chances for successful therapy.

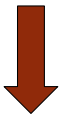
(Gifford, et al, p. 387,

citing, Havlir, et al, 1998; Pialoux, et al, 1998; Reijers, et al, 1998; Montaner, et al, 1998; Hecht, et al, 1998; Shafer, et al, 1998)

(Howard et al, p. 2176, citing Wainberg and Friedland, 1998)

*(Note – None of the studies included in the research gave times to development of resistance. This is important and should be added.)

When Adherence Is Good



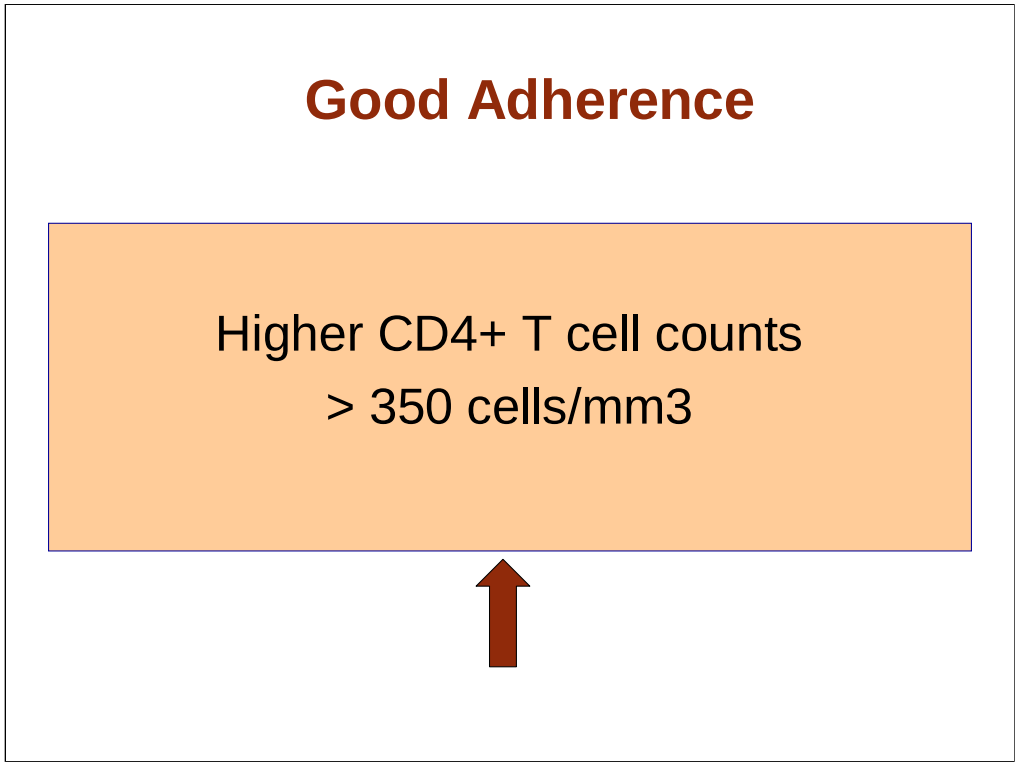
Decreased HIV concentration
in plasma
< 400 OR < 50 copies/mL

[Again, to allow the speaker to emphasize the subject, I've divided the original slide #4 into two new slides with the same information (revised slides # 6 and #7).]

Correlation assessment studies of adherence show relationships between
better adherence and decreases in HIV concentration in plasma.
(Gifford, et al, p. 389)

Studies of electronic monitoring of adherence showed significant correlations
between:
1)Higher adherence rates and "virologic success"
(We assume this means reduced rates of virus and reduced rates of developing drug-resistant viral strains.)
(Frank, p. S10, citing Paterson, et al, 2000)

2) Higher adherence rates and higher CD4+ T cell counts
(Frank, p. S10, citing Paterson, et al, 2000)
(Howard, et al, p. 2180)



[Second slide revised from original #4.]

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(Gifford, et al, p. 389)

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   (We assume this means reduced rates of virus and reduced rates of developing drug-resistant viral strains.)

   (Frank, p. S10, citing Paterson, et al, 2000)

2) Higher adherence rates and higher CD4+ T cell counts

   (Frank, p. S10, citing Paterson, et al, 2000)

   (Howard, et al, p. 2180)

What Predicts Adherence?

- **Older age**
- **Being employed**
- **Having a college degree**
- **Longer duration of therapy**
- **Feeling therapy regimen "fits"**

[Original slide #5; minor editing, see title.]

In study of women with HIV, older age of women and employment of women both correlated with better adherence.

Also, women who had been in therapy longer had better adherence with therapy.
(Howard, et al, p. 2179)

In study of people with Type 2 diabetes, older patients had better adherence profiles.
(Dezii, et al, p. 70)

Having a college degree correlated with better adherence.
(Gifford, et al, p. 388)

Feeling the regimen "fits" with daily activities is associated with better adherence,
(Gifford, et al, p. 389)

and also with lower plasma concentrations of HIV.
(Gifford, et al, p. 390)

Psychosocial Components

- **Social support**
- **Healthy diet**
- **Medicare**
- **Access to meds**

[The original slide (# 6) has too much information. The revised slides (#9 & 10) demonstrate a better way to divide the material into subject areas, which aids the presentation by giving more organization and focus.]

We know several ways that emotional factors affect adherence.

One of the most crucial is having in place some type of social support.

(Gifford, et al, p. 387, citing Morse, et al, 1991; Samet, et al, 1992; Muma, et al, 1995; Singh, et al, 1999; Kalichman, et al, 1999)
(Frank, p. S11)

Having Medicare, and having better perceived access to medications, and better social support for using medications
are correlated with better adherence...

(Gifford, et al, p. 389) ...as is the ability to keep clinic appointments.
(Frank, p. S11)

Eating healthier food and having a higher sense of self-efficacy about using medications
also correlate with better adherence in both previous and current studies.

(Gifford, et al, p. 389)
(Frank, p. S11, citing Paterson, et al, 2000;
Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents [GUARVA 2002]; Gebo, Keruly, Moore, 2001)

Patient Value System

Keeps appointments

Believes medication helps

Understands adherence

[Second slide revised from original slide #6.]

A patient's attitudes about particular medications may affect adherence.
Having positive beliefs and knowledge about medications,
specifically about how antiretroviral medication works,
and belief in the efficacy of the prescribed medications are all correlated with better adherence.

(Gifford, et al, p. 387, citing Morse, et al, 1991; Samet, et al, 1992; Muma, et al, 1995; Singh, et al, 1999; Kalichman, et al, 1999)
(Frank, p. S11)

In addition to having access to medications and medical care,
patients who are able to keep appointments have better adherence.
(Gifford, et al, p. 389)
(Frank, p. S11)

Understanding that non-adherence leads to HIV resistance,
also correlates with better adherence in both previous and current studies.
(Gifford, et al, p. 389)
(Frank, p. S11, citing Paterson, et al, 2000; Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents [GUARVA 2002]; Gebo, Keruly, Moore, 2001)

What Predicts Non-adherence?

Stress or depression

Current use of drugs or alcohol

Change in daily schedule

[Original slide #7 revised into two slides (#11 & 12).]

Feeling stressed, overwhelmed, or depressed are all factors associated with reduced rates of adherence and also with increased levels of HIV plasma concentrations.

(Gifford, et al, p. 388, 389-390); (Frank, p. S11)

Current, but not past, use of alcohol and illegal drugs are negative predictors,

associated with reduced levels of adherence.

(Frank, p. S11); (Howard, et al, p. 2179);

(Gifford, et al, p. 387, citing Haubrich, et al, 1999; Chesney, et al, 2000; Roca, Gomez, Amedo, 1999; Gordilla, et al, 1999)

Disruptions in daily schedule that interfere with adherence include: being too busy, forgetting,

being away from home, having a break in routine, taking a “drug holiday,” or running out of medications.

(Gifford, et al, p. 388)

Medical Non-adherence

Using Medicaid

Current illness

Adverse effects of meds

Complicated dosage regimen

[Second slide revised from original slide #7.]

Having to rely on Medicaid for treatment may be stressful, and it independently correlates with decreased adherence.

(Gifford, et al, p. 388)

Experiencing symptoms of disease, related to HIV or not, and experiencing adverse effects of medication are both associated with negative adherence behaviors.

(Gifford, et al, p. 388); (Frank, p. S11)

Perhaps the area that has received the greatest amount of analysis is treatment regimens.

How many pills, and how many times daily, and with what precision must patients take the pills for the rest of their lives?

Inconvenient treatment regimens and high pill counts have both been correlated with poor adherence and negative response to treatment.

(Frank, p. S11, citing, Bartlett, et al, 2001; Cahn, 2000)

Adherence **Red Flags**

- Adverse events from medication
- 4-drug regimens
- Taking too many pills daily
- More than once-daily dosing

[Original slide #8; minor changes, see title]

Class of antiretroviral shows a correlation with adherence. Protease inhibitors, for example, are associated with negative adherence behavior. Future studies may clarify relationships between difficult adverse event profiles and negative adherence.
(Howard, et al, p. 2179)

Four-drug regimens also correlate with negative adherence. In a study of self-administered therapy and directly observed therapy, taking four drugs was still associated with reduced adherence.
(Frank, p. S10)

Reducing the number of pills (pill count) and reducing one component of the treatment regimen from twice-daily to once-daily has positive correlations with improved adherence. Immunologic responses also improved.
(Cardiello, et al, p. 464, 469); (Frank, p. S11, citing, Bartlett, et al, 2001; Cahn, 2000)

Researchers analyzed the relationships between once-daily, twice-daily, and thrice-daily dosages. They found a strong negative correlation between taking pills three times a day and adherence.
(Howard, et al, p. 2179)

Once-daily dosing was associated with better adherence. (Frank, p. S13)

In studies with medication for other diseases, researchers found reducing the number of daily doses from two to one correlated with improved adherence, even when the total number of pills daily was not reduced.
(Dezii, et al, p. 68, Type 2 Diabetes)
(Andrejak, et al, p. 190, Hypertension)

Education Improves Adherence:

- **HIV and CD4+ T counts**
- **Role of resistance**
- **Myths and misconceptions**

[Original slide #9 revised into slides (# 14 & 15).]

Patients need to understand how their specific medication affects viral load, what drug resistance means and how it will affect them, and how these critical aspects of care are affected by adherence to the regimen.

(Frank, p. S11)

Patients – but also physicians and nurses – have misconceptions about many aspects of HIV treatment and adherence.

Get the latest facts from research updates, because these expectations can affect outcome.

(Frank, p. S11, citing Paterson, et al, 2000)

Medication Education

- **Benefits of therapy**
- **Once-daily or twice-daily**
- **Adverse effects**

[Second slide revised from original #9.]

If patients are prescribed a once-daily regimen, they need to understand that it works as well or better than a twice-daily regimen, if they can make sure they take all the medications every day as prescribed.

(Cardiello, et al, p.465, 468-469)

(Frank, p. S12-S14)

Patients need to know potential adverse events before therapy begins.

The medical team must explain management strategies before problems arise.

(Frank, p. S12-S14)

Caring Partnership

- **Develop trust and insight**
- **Assess readiness for therapy**

[Original slide # 10 revised into two slides (#16 & 17).]

Education about adherence requires more than giving patients information.

True collaboration means patients become active participants in their own care.

A therapeutic collaboration is based on trust.

Patients have to be completely honest about the details of their lives with all members of the health care team.

It is not the physician's job to insist the patient start therapy, but to assess if the patient is ready to make that commitment.

Assessment forms and questionnaires can start the process...

(Gifford, et al, p. 387-388, 392, 393-394)

(Frank, p. S11)

...as can helping the patient make a self-assessment.

Therapeutic Collaboration

- **Convenient regimen**
- **Lowest dosage possible**
- **Support adherence**

[Second slide revised from original slide #10.]

A convenient regimen needs to “fit” the patient’s lifestyle and should be as simple as possible.

This requires insight into the patient’s life and careful monitoring of HIV plasma concentrations and CD4+ T cell counts.

(Cardiello, et al, p. 469)

Patients need to know what they can do to enhance adherence.

The medical team needs to assure they are available for support when needed.

Address Emotional Issues

Accept lifelong therapy

Create self-efficacy

Provide drug and alcohol treatment

[Original slide # 11 revised into two slides (# 18 & 19).]

The management team must include resources for emotional support.

Emotional issues are part of care; they are best addressed before they interfere with treatment.

It is necessary to help patients feel effective in managing their own care.

No treatment plan can be successful without an involved patient who wants to do well.
(Frank, p. S11)
(Gifford, et al, p. 392)

Drug and alcohol treatment programs are an expected part of any management strategy, and will contribute to the patient's sense of self-management.
(Howard, et al, p. 2181)

Medication Support

Assess ability to follow regimen

Involve patients in monitoring

[Second slide revised from original #11.]

Because the patient's ability to follow the complicated, life-long regimen of HAART is essential for effective treatment, plan to address all issues that can make adherence to the regimen difficult.

(Gifford, et al, p. 392)

(Frank, p. S11)

Be sure patients understand the results of viral monitoring and CD4+ T cell counts.

Knowing the meaning of clinical indicators can bolster the patient's sense of self-efficacy and their efforts to adhere to the regimen.

(Frank, p. S12-S13)

Work on Adherence

Before therapy begins

For the duration of care

[Original slide # 12 revised into two slides (# 20 & 21).]

There is no advantage, but there are serious disadvantages to beginning HAART unprepared.

Therapy for HIV management requires structured communication before treatment begins and throughout the duration.

Lifelong care means making a commitment to support the patient, including during difficult times and life changes.

The health care team must continue to educate, collaborate, and support the patient for the duration of care, hopefully growing old along with their patients.

(Howard, et al, p. 2180)

Critical Times

When changing regimens

During an illness

When hospitalized

[Second slide revised from original #12.]

All patients will need special support during the times when adherence to HAART is strained to impossible: when the patient is ill, or hospitalized, and when it is time to change to a different HAART regimen.

There is no one approach; every patient will require individual attention.

(Howard, et al, p. 2180)

The medical team will need to assure patients that even in difficult times,it is important to monitor viral suppression and immune markers.

Need to Learn About

- **Past IV use on viral load**
- **Effect of race/demographics**
- **Attitudes/beliefs about health**
- **Approach to care system**

[Original slide #13 revised into two slides (#22 & 23).]

Although certain characteristics appear in most studies of adherence to HAART, the exact roles of these factors are not clear.

We need further study to understand the relationship, if any, they may have on treatment outcome and on the patient's ability to adhere to a specific regimen.
(Gifford, et al, p. 393)

For example, the characteristic of race, particularly being African-American,
has been analyzed as an independent factor and also as part of a broad study of socioeconomic factors and education level.

Some researchers have found race to be correlated with adherence,
(Gifford, et al, p. 388-389)

while others have not (Frank, p. S11).

This is an area that needs further study.

Other factors affect patient's physiological response to medication,
and the role of psychological concepts in accessing and obtaining healthcare.

Subjective Advantages

Daily pill count

Vs.

Dosing schedules

[Second slide revised from original slide #13.]

We cannot make assumptions about therapy options.
Once-daily dosing seems like an advantage, but it may not be for all patients.

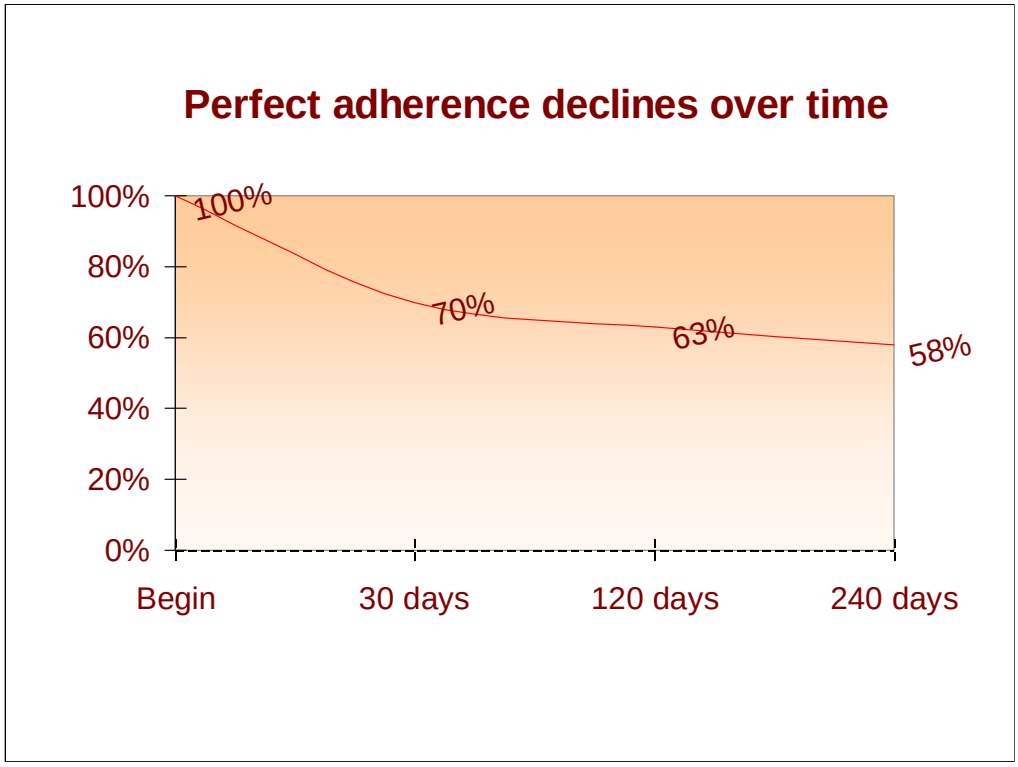
Many studies have shown better adherence with once-daily dosing, using variations of HAART to provide sufficient IC over a 24-hour period. But not all agents can be used in a once-daily regimen.
(Frank, p. S13, reviewing studies and specific drugs)

Assessing the subjective aspects of therapy is difficult.

Treatment studies use devices to measure adherence, so we cannot know for sure
if the results under these circumstances will be similar to real-life situations.

We also have to look at the outcome.

In a study of patients with hypertension, disease management did not improve
even with electronic surveillance showing better adherence to once-daily dosing.
(Andrejak, et al, p. 189)



[Original slide #14; minor changes to slide body.]

With HIV therapy, perfect, or near-perfect adherence is required for a lifetime.

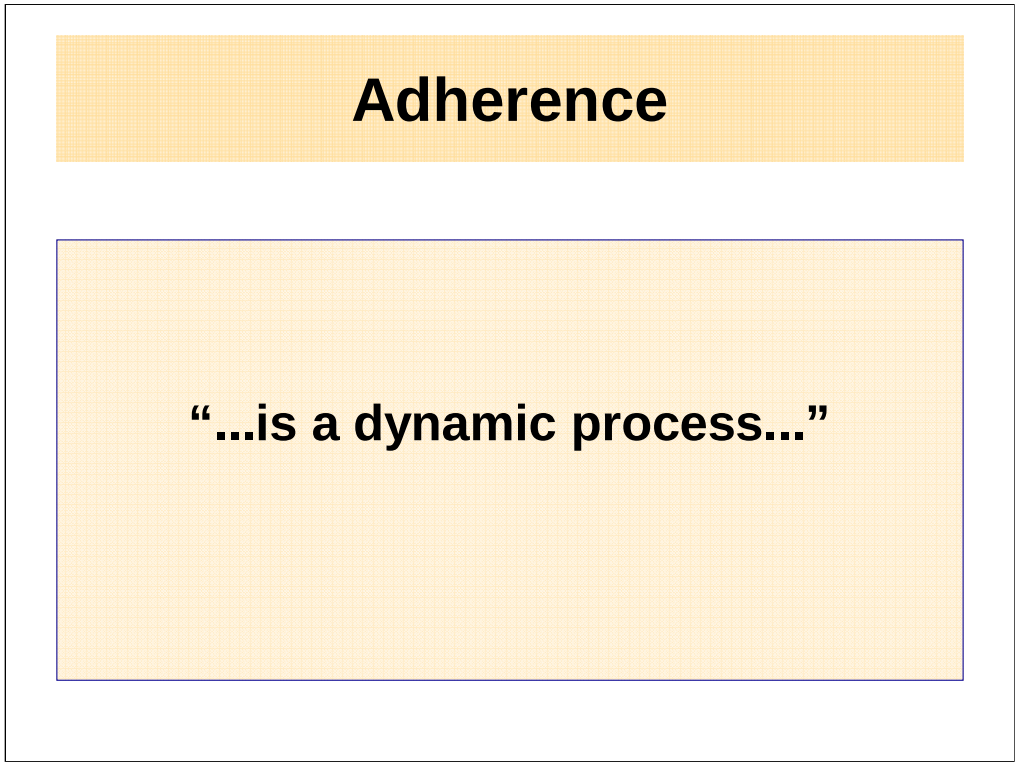
We know from studies of adherence rates, adherence declines over time.
(Dezii, et al, p. 68)

Typical real-life results are much lower than 100% adherence, and are much lower than a "good enough" level needed for therapeutic control of HIV.

For example, in a study with a theoretical 100% adherence possible,

the actual measured adherence after 1 month was 70%
(this was only 70% of patients taking 100% of medications on time).
At 4 months only 63% patient had perfect adherence;
and at 8 months, only 58%.

(Frank, p. S11, citing Mannerheimer [sic], et al, 2000)



[Original slide #15; edited slide body.]

“...adherence is a dynamic process, and its predictors vary over time.”
(Howard, et al, p. 2176, citing Liu, et al, 2001; Carrieri, et al, 2001; Mannheimer [sic], et al, 2002)

Many factors have been associated with both positive and with negative adherence behaviors, and these may be used to predict which patients will need extra levels of support.

We also need to expect these factors to be in a constant state of change, and be prepared with new levels of support.

Assessing problems with adherence requires considerable time and individual patient management.

While it is possible to look at potential predictors of adherence...
(Gifford, et al, page 392-393),
...no single or simple predictor is precise or infallible.

This means, in the end, adherence will depend on the relationship between patient and providers.