Mental Health and Adherence Issues in the Management of HIV

R. Scott Adams, RN, MSN, PMHNP
Associate in Psychiatry
Vanderbilt University School of Medicine
Vanderbilt Comprehensive Care Clinic

William Osler, 20th century physician:

- "It is more important to know what sort of person has a disease than to know what sort of disease a person has."

Objectives:

- Discuss the importance of adherence in the management of HIV
- Identify mental health issues as risk factors for non-adherence
- Identify psychiatric epidemiology in those living with HIV/AIDS

Compliance or Adherence?

- Compliance: Patient behavior coinciding with physician advice
- Adherence: Patient behavior coinciding with an agreed upon therapeutic regimen

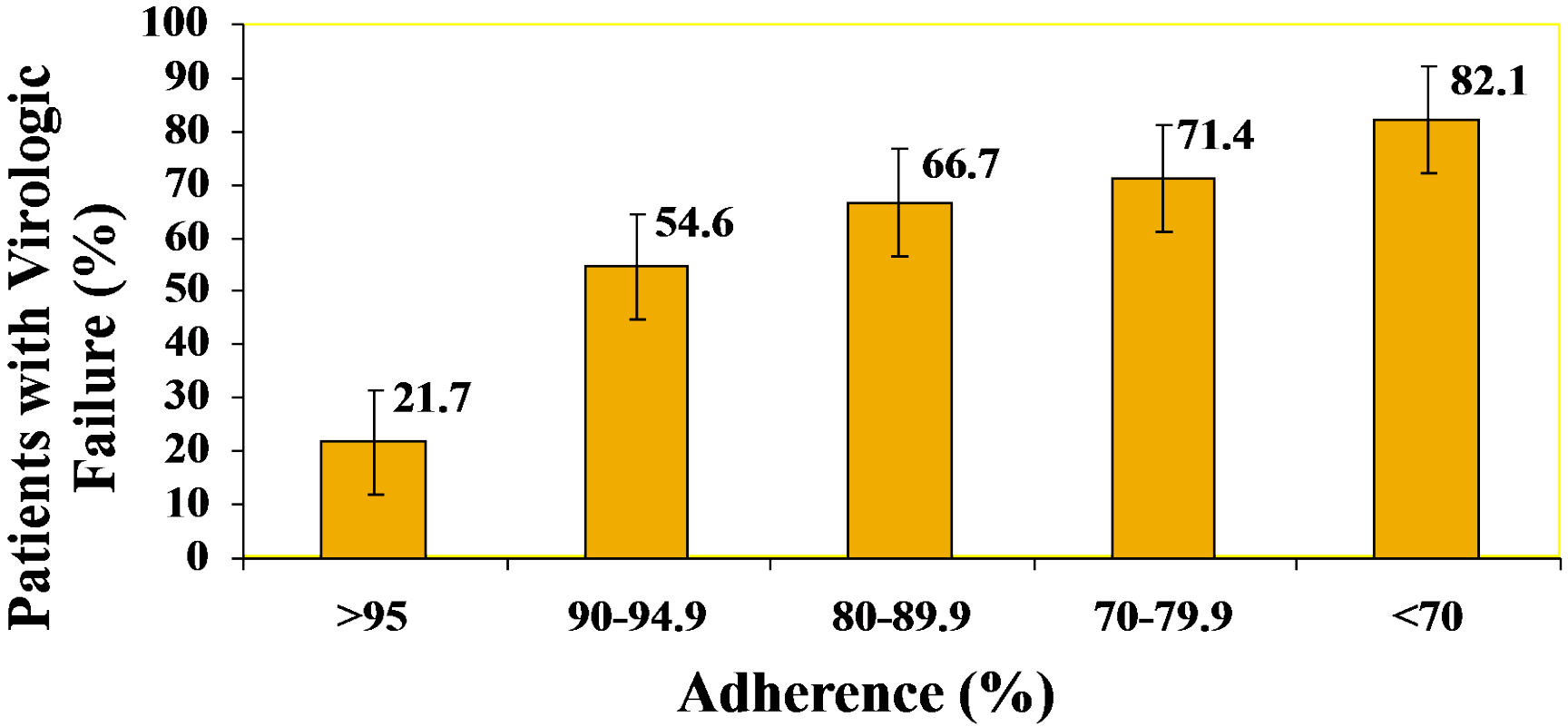
"Adherence and successful HIV management", Duke School of Medicine, 2000, pp 2

Adherence is intimately linked to treatment outcomes:

- Viral Loads
- CD4 Cell Counts
- Mortality
- A strong linear relationship was found between adherence and plasma HIV RNA levels, regardless of the method of measuring adherence.
- In a cross-sectional analysis of 34 indigent patients with a median of 12 months of PI therapy, 10% decrease in adherence was associated with a doubling of HIV RNA level.

Bangsberg, et.al., JAIDS, 2000; 14: 357-66

A prospective observational study of 81 patients showed ART adherence was significantly associated with successful virologic suppression and immune reconstitution:



Paterson, et.al., Ann.Intern.Med., 2000; 133: 21-30

Adherence and ΔCD4

A prospective, observational study found:

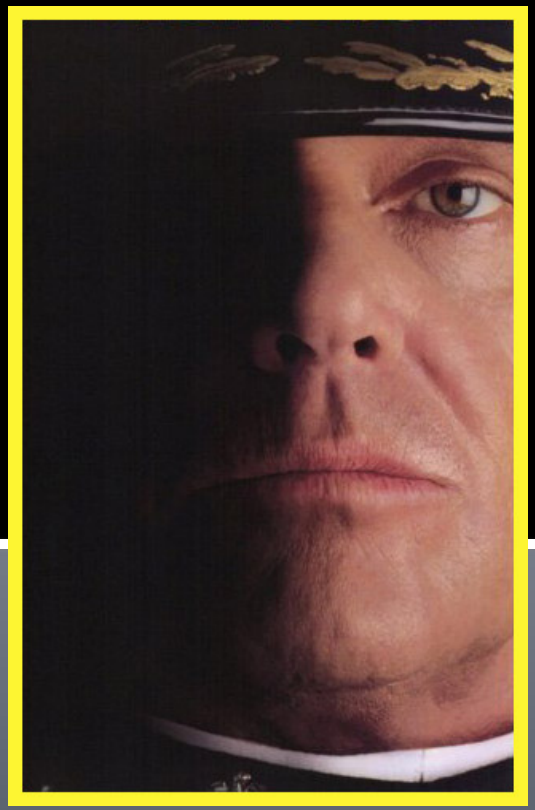
- <90% adherence = mean decrease in CD4 cell count of 5/μL
- ≥90% adherence = mean increase in CD4 cell count of 78/μL

Adherence and Mortality

A prospective, observational study of 950 HIV+ patients found:

- For every 10% drop in adherence, there was an associated 16% increase in mortality

YOU CAN'T HANDLE THE TRUTH!



How Are Patients Doing?

"Optimal Adherence" is defined as: 95% of ART doses are taken as directed.

Authors (ref.)	*n*	% Patients with adherence rates <90%	Method of Assessment
Gordillo, et.al.	366	42	pill count, patient self-report
Wenger, et.al.	1910	43	patient self-report
Eldred, et.al.	244	57	pharmacy records, patient self-report
Bangsberg, et.al.	34	62	pill count

A Patient's Perspective of Adherence

Away from home	57
Busy with other things	53
Had a change in daily routine	51
Fell asleep/slept through dose	40
Problems taking medications at specific times	40
Felt ill or sick	28
Wanted to avoid side effects	24
Felt depressed/overwhelmed	18
Had too many pills to take	14
Didn't want others to notice me taking meds	14
Felt drug was toxic/harmful	12

Adapted from Chesney, et.al., AACTG, AIDS Care, 2000; 12:255-66

Are there Predictors of Non-Adherence?

- Race
- Sex
- Educational Background
- Employment
- Income

Risk Factors for Non-Adherence

- Social Supports:
  -Unstable contact with family
  -No significant other
  -Abusive relationship
  -No close friends
- Inadequate Housing:
  -Homelessness
  -Transient status

Friedland, et.al., AIDS, 1999;13:S61-72

Kalichman, et.al., J.Gen.Intern.Med., 1999; 14:267-73

Risk Factors for Non-Adherence

Psychiatric Disorders: Depression/Affective Disorders

- Patterson, et.al.: of 99 patients studied, lower psychiatric morbidity significantly associated with ≥95% adherence.
- Chesney, et.al.: 24% of patients cited feeling depressed or overwhelmed as reason for not taking medication. Non-adherent patients reported higher mean levels of perceived stress than did adherent patients.

Risk Factors for Non-Adherence

Substance Abuse: Past or Present?

- Active substance abuse (alcohol, cocaine, and opiates) associated with poorer adherence rates
- Past drug use does not seem to reduce likelihood of adherence.

Montessori, et.al., 7th CROI, 2000

Stone, et.al., 12th World AIDS Conf., 1998

Arnsten, et.al., 7th CROI, 2000

Malcolm, et.al., J.Gen.Intern.Med., 2000; 15:165

Risk Factors for Non-Adherence

Patient's Belief System:

- Higher rates of adherence in patients who believe that ART is effective and that non-adherence will lead to viral resistance.

Wenger, et.al., 6th CROI, 1999

Risk Factors for Non-Adherence

Complex Regimens:

- A meta-analysis of 23 published trials by Bartlett, et.al. involving 3257 patients on a triple-drug regimen showed a higher pill-burden was associated with a lower antiretroviral response.
- In a study involving 244 patients, those on BID regimens reported greater adherence than those on TID or more frequent dosing.

Bartlett, et.al., AIDS, 2001; 15:1369-77

Eldred, et.al., JAIDS, 1998; 18:117-25

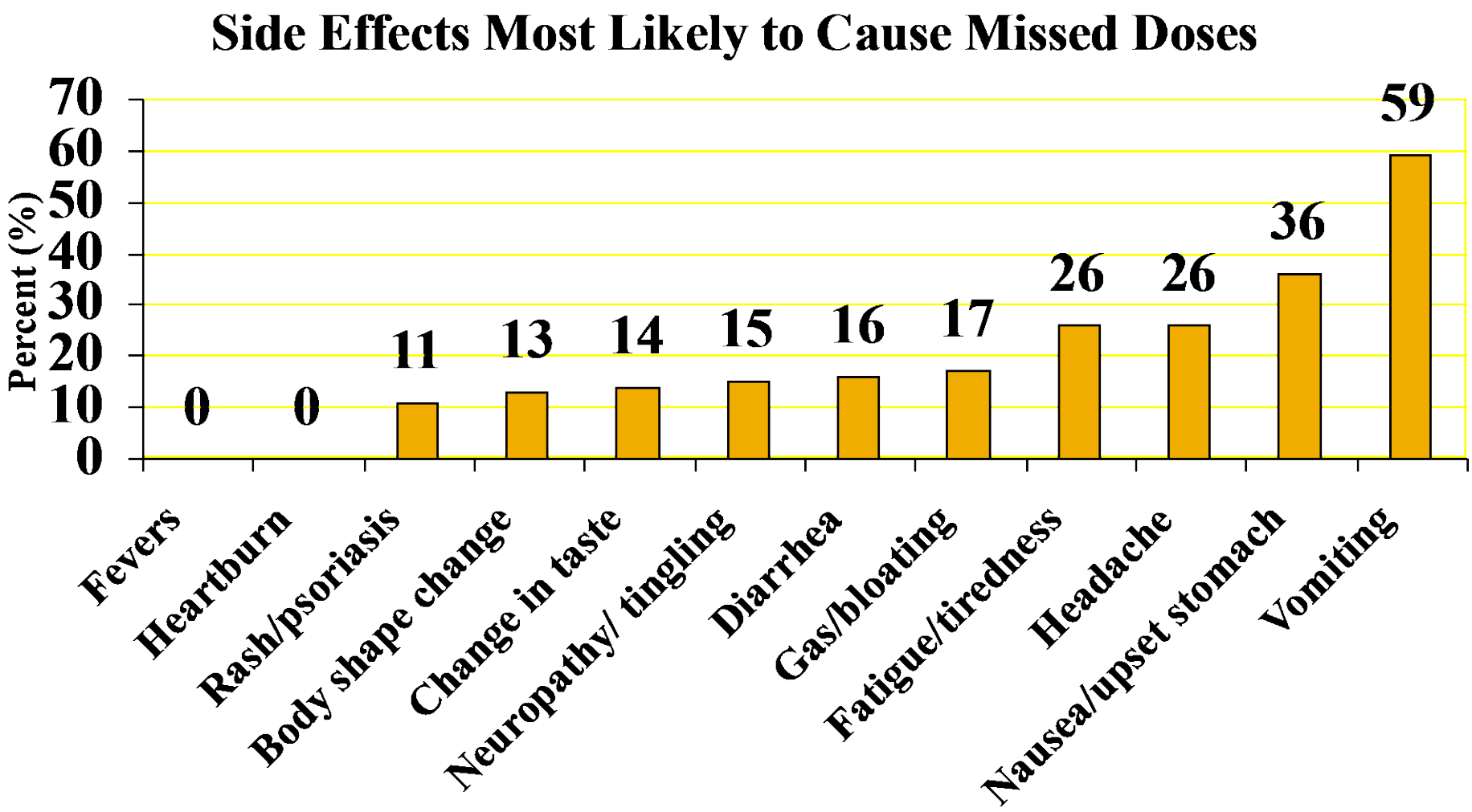
Which ART Regimen Factors Impact Adherence?

According to Jordan, et.al. in a survey of 550 HIV+ patients, responses in order of importance were:

1) Total pills per day
2) Dietary restrictions
3) Dosing frequency
4) Pill size and drug combinations

Which ART Regimen Factors Impact Adherence?

Side Effects



Characteristics which Differentiate Excellent from Sub-Optimal Adherers

•Believe that 90-100% adherence is necessary to benefit from medication	•Believe that taking 33-75% of their medication is enough for viral suppression
•Be motivated by desire to stay physically healthy for their own sakes	•Be motivated by a desire to stay alive to care for others or to avoid suffering
•Have a great degree of respect and trust for their PCPs	•Be suspicious of their PCP's intentions and motivations
•Be open about their HIV status with friends and family and receive strong social support	•Be secretive about their HIV status and lack social support
•Take their medication even when drinking or using substances	•Identify obtaining a substance of use as a first priority and refrain from taking HAART when using substances
•Take steps to monitor emotions on an ongoing basis (including taking antidepressants and receiving counseling)	•Be depressed and report feeling hopeless and out of control

Adherence Now, Cedars-Sinai M.C., 2001; pp 11

Methods for Measuring Adherence

Method	Advantages	Disadvantages
Directly Observed Therapy	•Only method associated with 100% adherence •Serves as effective monitor as well as intervention promoting adherence	•Labor intensive •Impractical with certain antiretroviral agents
Patient Self-Reporting	•Convenient and relatively inexpensive •Certain methods (e.g. diaries) can help promote adherence	•Less accurate than more objective measures
MEMS Caps	•Relatively accurate, objective measure •Continuous measure of adherence •Ability to calculate variety of adherence measures •Serves as an effective monitor as well as an intervention promoting adherence	•Expensive •Not readily available in clinical practice •Caps do not fit all medication bottles •Presumptive measure of adherence

Methods for Measuring Adherence

Methods	Advantages	Disadvantages
Prescription Refill Monitoring	•Relatively accurate, objective measure •When combined with telephone prompts, also serves as an intervention promoting adherence	•Presumptive measure of adherence
Viral Load Assay	•Objective measure, complementary to patient self-reports	•Not a primary measure of adherence
Plasma Drug Testing	•Objective measure	•Not a continuous measure of adherence •Pharmacokinetic profile of drug needs to be understood

Adherence and Successful HIV Management, Duke School of Medicine, 2000; pp 11

Strategies for Enhancing Optimal Adherence

- The patient-provider relationship is critical; establish mutual trust and respect
- Patient's readiness: Assess for true readiness to begin therapy
- Stages of patient's attitude:

Adherence and Successful HIV Management, Duke School of Medicine, 2000; pp 17

Stage	Patient behavior and perceptions	Patient signs	Appropriate physician intervention
Precontemplation	•Not ready to begin therapy in next 6 months •Ambivalent about why therapy is necessary •Possible denial about disease and its severity	•"I don't have any symptoms" •"I've heard that the therapy is worse than the disease"	•Empathic understanding •Provide general HIV disease/medication educational information
Contemplation	•Considering change in the next 6 months •On the verge of accepting HIV status •Seeking relevant information and help from others	•"I would like to really do something positive to control my disease"	•Continue empathic understanding •Enlist support of family •Continue to provide educational information

Stage	Patient behavior and perceptions	Patient signs	Appropriate physician intervention
Preparation	•Ready to make change in the next 30 days	•"I want to begin a medication regimen"	•Question patient about any obstacles to adherence •Provide tools for a "dry run" with candies •Follow-up in 2 weeks or earlier
Action	•Successfully engaged in dry run •Agrees to accept certain interventions (e.g. follow-up phone calls)	•"I feel confident that I will use my medications every day just as you prescribed"	•Have a patient sign a therapeutic contract •Suggest certain interventions (e.g. pill box, timers) •Notify patient about follow up phone-calls
Maintenance	•Patient has maintained adherent behavior for the past 6 months	•"I've been using my HIV pills every day for the past 6 months"	•Provide feedback on viral load/CD4 counts •Ask if patient would like to continue with certain interventions

Clinician Contributing Factors in Adherence

- Consistent provider
- Satisfaction with relationship
- Knowledge of clinical regimen
- Treatment expertise
- Time for client teaching

Frank, Miramontes, 1997

Clinician Contributing Factors in Adherence

- Style matched to client
- Belief in client
- Belief in treatment
- Knowledge of adherence
- Enthusiasm
- Cultural competence

Frank, Miramontes, 1997

Question Patient about any Issues which Could be a Barrier to Adherence

- Insurance issues
- Transportation
- Housing/Food
- Job situation
- Cultural issues

Assess for Affective Disorders and/or Substance Abuse

- Referral to psychiatry clinician for evaluation/treatment of affective disorder
- Referral for therapy services
- Referral for case management (mental health)
- Referral to A&D rehabilitation program
- Referral to AA/NA or other support groups

Identify Psychosocial Support Network

- Family members
- Partner or spouse
- Friends or neighbors
- Religious or spiritual support
- Community network (e.g., Nashville Cares)

Educate and Motivate

- Provider: thorough discussion of advantages/benefits of treatment, and physiology involved
- Adherence Counselor: one-on-one counseling sessions

Simplify Regimen

- Lower pill burden
- Frequency of dosing
- Tailor regimen to patient’ s lifestyle

Anticipate and Manage Side-Effects

- Nausea/Vomiting - phenergan
- Diarrhea - lomotil
- Etc.

Educational Techniques

- Tailor to individual educational/literacy level
- Handouts which include pictures
- Individual educational sessions

Behavioral Techniques

- Positive reinforcement
- Wellness contracts
- Behavioral cues

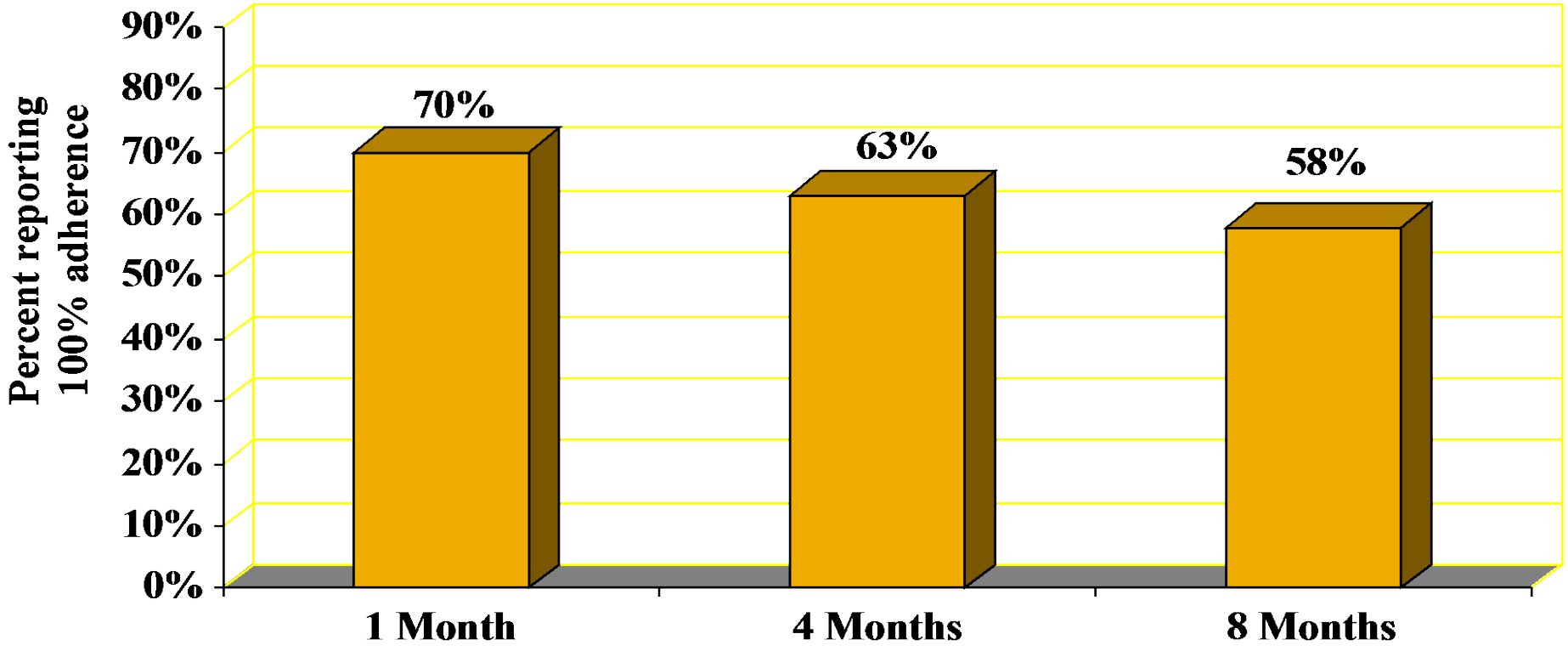
Provide Adherence-Promoting Devices

- Pill boxes
- Diaries
- Alarms
- Bubble packs

Frequent Follow-up and Support are Key!

How Long Should the Focus on Adherence Last?

- Adherence declines over time, (P<0.01)



Mannerheimer, et.al., 13th Int'l.AIDS.Conf., 2000

- Adherence counseling is in everyone’s job description
- Each patient encounter is an opportunity to assess adherence
- Identify and solve problems, and reinforce the importance of adherence

Major Depressive Disorder DSM-5 Criteria: (5 or more)

- Depressed Mood
- Marked diminished interest or pleasure
- Greater than 5% weight loss or decrease/ increase in appetite
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feelings of worthlessness or excessive guilt
- Diminished ability to think or concentrate
- Recurrent thoughts of death

Psychiatric Epidemiology

- Depression
  - > 2 fold increase in HIV seropositive individuals (Ciesla & Roberts 2001)
  - Risk factor for HIV infection (Regier 1990)
  - 2.5 fold increase when CD4 cell <200 cells/mm^3 (Lyketsos 1996)

Psychiatric Epidemiology

- Depression has been linked to lower ART adherence rates (Dimatteo 2000)
- Depression is associated with increased mortality and disease progression (Ickovics 2001)

Psychiatric Epidemiology

- In a meta-analysis across 29 studies of 12,243 persons living with HIV/AIDS found that the treatment of depression and psychological distress improved adherence to antiretroviral regimen.
- The odds of adherence were 83% better in individuals treated for depression. (Sin & DiMatteo 2013)

Bipolar I Disorder
DSM-5 Criteria: Manic

- Distinct period of abnormally and persisted elevated, expansive or irritable mood, or increased activity/energy lasting at least one week
- 3 or more of the following:
  - Inflated self-esteem or grandiosity
  - Decreased need for sleep
  - More talkative or pressure to keep talking
  - Flight of ideas/ racing thoughts
  - Distractibility
  - Increased in goal-directed activity/ psychomotor agitation
  - Excessive involvement in activities with a high potential for painful consequence

Bipolar I Disorder
DSM-5 Criteria: Manic

- Mood disturbance causes marked impairment in social or occupational functioning
- Episode not attributable to the physiological effects of a substance or to another medical condition

Bipolar I Disorder
DSM-5 Criteria: Hypomanic

- Distinct period of abnormally and persisted elevated, expansive or irritable mood, or increased activity/energy lasting at least four days
- 3 or more of the following:
  - Inflated self-esteem or grandiosity
  - Decreased need for sleep
  - More talkative or pressure to keep talking
  - Flight of ideas/ racing thoughts
  - Distractibility
  - Increased in goal-directed activity/ psychomotor agitation
  - Excessive involvement in activities with a high potential for painful consequence

Bipolar I Disorder
DSM-5 Criteria: Hypomanic

- The episode is associated with unequivocal change in functioning
- Disturbance of mood and functioning are observable by others
- Episode is not severe enough to cause marked impairment in social or occupational functioning
- Episode not attributable to the physiological effects of a substance or to another medical condition

Bipolar II Disorder
DSM-5 Criteria:

- Criteria is met for hypomanic episode
- Criteria is met for a major depressive episode

Psychiatric Epidemiology

- Bipolar Disorder
  - Prevalence rate 10 times higher in HIV seropositive individuals (Lyketsos 1993)

Posttraumatic Stress Disorder DSM-5 Criteria

- Exposure to actual threatened death, serious injury, or sexual violence:
  - Directly experiencing a traumatic event
  - Witnessing in person a traumatic event
  - Learning traumatic event occurred to a close family member or friend
  - Experiencing repeated or extreme exposure to aversive details to a traumatic event

Posttraumatic Stress Disorder DSM-5 Criteria

- Presence of one or more intrusion symptoms:
  - Recurrent involuntary and intrusive distressing memories
  - Recurrent distressing dreams of traumatic event
  - Dissociative reactions (flashbacks)
  - Intense or prolonged psychological distress at exposure to internal or external cues
  - Marked physiological reactions to internal or external cues

Posttraumatic Stress Disorder DSM-5 Criteria

- Persistent avoidance with stimuli associated with traumatic event:
  - Efforts to avoid distressing memories, thoughts, or feelings
  - Efforts to avoid external reminders (People, places, situations)

Posttraumatic Stress Disorder DSM-5 Criteria

- Negative alterations in cognitions and mood associated with traumatic event: (2 or more)
  - Inability to remember aspects of event
  - Persistent/exaggerated negative beliefs about oneself, others, or the world
  - Distorted cognitions about cause or consequences (self-blame)
  - Persistent negative emotional state
  - Marked diminished activities
  - Detachment or estrangement from others
  - Persistent inability to experience positive emotions

Posttraumatic Stress Disorder DSM-5 Criteria:

- Marked alterations and arousal associated with an event: (2 or more)
  - Irritable behavior/ angry outburst
  - Reckless/ self-destructive behavior
  - Hypervigilance
  - Exaggerated startle response
  - Problems with concentration
  - Sleep disturbance

Posttraumatic Stress Disorder DSM-5 Criteria:

- Duration > one month
- Disturbance causes clinically significant distress or impairment in functioning
- Disturbance not attributed to physiological effects of a substance or another medical condition

Psychiatric Epidemiology

- PTSD
  - 42% of HIV positive women in County Medical Clinics met the diagnostic criteria for PTSD (Cottler 2001)

Panic Disorder
DSM-5 Criteria:

- Recurrent unexpected panic attacks with 4 or more of the following:
  - Palpitations/ accelerated heart rate
  - Sweating
  - Trembling or shaking
  - Shortness of breath
  - Feeling of choking
  - Chest pain/ discomfort
  - Nausea/ abdominal distress
  - Feeling dizzy or light headed
  - Chills or heat sensation
  - Paresthesias (numbness or tingling)
  - Derealization/ depersonalization
  - Fear of losing control or "going crazy"
  - Fear of dying

Panic Disorder DSM-5 Criteria:

- Attack followed by one month or more of one or both of the following:
  - Persistent concern or worry about additional attacks
  - Significant maladaptive change in behavior

Panic Disorder
DSM-5 Criteria:

- Disturbance is not attributable to the physiological effects of a substance or another medical condition
- Disturbance is not attributable to another mental disorder

Generalized Anxiety Disorder DSM-5 Criteria:

- Excessive anxiety and worry more days than not for at least 6 months about a number of events and activities
- Individual finds it difficult to control worry
- Associated with 3 or more of the following symptoms:
  - Restlessness/ keyed up/ on edge
  - Easily fatigued
  - Difficulty concentrating/ mind going blank
  - Irritability
  - Muscle tension
  - Sleep disturbance

Generalized Anxiety Disorder DSM-5 Criteria:

- Clinically significant distress or impairment in social/ occupational or other functioning
- Disturbance not attributable to physiological effects of a substance or another medical condition
- Disturbance not attributed to another mental disorder

Psychiatric Epidemiology

- Panic Disorder and Generalized Anxiety Disorder
  - >4 times more prevalent in HIV seropositive individuals (Bing 2001)

Conclusions

- Adherence to therapy for HIV is uniquely challenging
- Adherence has been intimately linked to markers of HIV disease progression, including viral load, CD4 counts, and mortality
- Adherence rates of ≥95% are required to meet the goals of ART (i.e. viral suppression, immunologic reconstitution)
- Potential barriers to adherence are numerous and complex
- There are enhancing practices/tools which have shown efficacy and should be individualized to reduce these potential barriers
- All patients are potential defaulters in terms of adherence, however all patients are potentially excellent adherers, provided that obstacles are identified and effectively addressed

Conclusions

- Comorbid psychiatric disorders are of increased prevalence among HIV seropositive individuals and represent unique challenges
- The identification and effective management of comorbid psychiatric disorders can improve adherence, treatment outcomes, and quality of life for those living with HIV/AIDS.

Works Cited

- "Adherence and successful HIV management", Duke School of Medicine, 2000, pp 2, 11, 17
- Adherence Now, Cedars-Sinai M.C., 2001; pp 11
- Arnsten J, Demas P, Courevitch M, et.al. Adherence and ciral load in HIV-infected drug users: comparison of self-report and medication event monitors (MEMS) [abstract 69]. 7th CROI, Jan. 30-Feb. 2, 2000
- Bangsberg DR, Hecht FM, Charlebois ED, et.al. Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population. AIDS, 2000;14:357-66
- Bartlett JA, Demasi R, Quinn J, et.al., Overview of the effectiveness of triple-combination therapy in antiretroviral-naïve HIV-1-infected adults. AIDS, 2001; 15:1369-7
- Bing EG, Burnam MA, Longshore D, et al. Psychiatric disrorders and drug use among human immunodeficiency virus-infected adults in the United States. Arch Gen Psychiatry. 2001;58:721-728.
- Chesney MA, Ickovics JR, Chambers DB, et.al., Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: The AACTG adherence instruments. AIDS Care, 2000;12:255-66
- Ciesla JA, Roberts JE. Meta-analysis of the relationship between HIV infection and risk for depressive disorders. Am J Psychiatry. 2001; 158:725-730
- Cottler LB, Nishith P, Compton WM III: Gender differences in risk factors for trauma exposure and post-traumatic stress disorder among inner-city drug abusers in and out of treatment. Compr Psychiatry. 42:111-117, 2001.
- Cramer JA. Partial medication compliance: the enigma in poor medical outcomes. Am. J. Managed Care, 1995;1:45-52
- DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: Meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med.* 2000; 160(14):2101-2107.
- Eldred LJ, Wu AW, Chaisson RE, et.al. Adherence to antiretroviral and *Pneumocystis* prophylaxis in HIV Disease, JAIDS, 1998;18:117-25
- Linda Frank, Helen Miramontes, Understanding HIV Treatment For You And Your Client Training Curriculum, 1997.

Works Cited

- Friedland GH, Williams A. Attaining higher goals in HIV treatment: the central importance of adherence. AIDS, 1999;13(Supplement):S61-72
- Ickovics JR, Hamburger ME, Vlahov D, et al. Illicit drug use, depression and their association with highly active antiretroviral therapy in HIV-positive women. Drug Alcohol Depend. 2007;89:74-81.
- Kalichman SC, Ramachandran B, Catz S. Adherence to combination antiretroviral therapies in HIV patients of low health literacy. J.Gen.Intern.Med., 1999;14:267-73
- Lyketsos CG, Hoover DR, Guccione M, et al. Depressive symptoms as predictors of medical outcomes in HIV infection. Multicenter AIDS Cohort Study. JAMA. 1993;270:2563-2567.
- Lyketsos CG, Hoover DR, Guccione M, et al. Changes in depressive symptoms as AIDS develops. Am J Psychiatry. 1996; 153:1430-1437.
- Malcolm SE, Ng JJ, Rosen RK, et.al. Which patients get an "A" for adherence? [abstract 57]. J.Gen.Intern.Med., 2000;15:165
- Mannerheimer S, Friedland G, Matts J, et.al. Self-reported antiretroviral adherence correlates with HIV viral load and declines over time [abstract TuOrB421]. 13th Int' l.AIDS.Conf., Jul 9-14, 2000
- Montessori V, Heath KV, Yip B, et.al. Predictors of adherence with triple combination antiretroviral therapy [abstract 72]. 7th CROI, Jan.30-Feb.2, 2000
- Paterson DL, Swindells S, Mohr J, et.al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Ann.Intern.Med., 2000;133:21-30
- POZ. 1998;6(2).

Works Cited

- Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. Jama. 1990;264:2511-2518.
- Sin NL, DiMatteo MR. Depression Treatment Enhances Adherence to Antiretroviral Therapy: a Meta-Analysis. Ann. Behavioral Medicine. Nov. 2013.
- Stone VE, Adelson-Mitty J, Duefield CA, et.al. Adherence to protease inhibitor (PI) therapy in clinical practice: usefulness of demographics, attitudes and knowledge as predictors [abstract 32337]. 12th World AIDS Conf., Jun.28-Jul.3, 1998.
- Wenger N, Gifford A, Liu H, et.al. Patient characteristics and attitudes associated with antiretroviral (AR) adherence [abstract 98]. 6th CROI, Jan.31-Feb.4, 1999.