

Suggested Replication Training: **Health Promotion and Adherence for Clinicians**

Table of Contents

Introduction	page 2
Session 1: Icebreaker (5 minutes) Activity: Defining Adherence	page 5
Session 2: A Broad Perspective on Adherence: Part 1 (10 minutes) Presentation: Why Do We Need to Focus on Adherence for Substance Users?	page 7
Session 3: The Politics of Adherence (15 minutes) Activity: Agree or Disagree?	page 15
Session 4: A Broad Perspective on Adherence: Part 2 (10 minutes) Activity: Factors Affecting Adherence	page 17
Session 5: Medical Issues Specific to HIV-Infected Substance Users (40 minutes) Presentation: Medical Issues	page 21
Session 6: Talking With Patients About HIV and Substance Use? (15 minutes) Presentation: Improving Provider-Patient Communication	page 34
Session 7: Managing HIV in the Context of Substance Use (20-60 minutes) Activity: Case Study Exercise	page 38
Session 8: Conclusion (5 minutes) Activity: Take-Home Points	page 53
References	page 54

Introduction

Background and Purpose

The purpose of this module is to provide participants with strategies and tools to promote the health of HIV-infected substance users. Specifically, this module focuses on the importance of adherence and emphasizes the need to consider adherence within the broader context of overall health promotion for this population.

Providing HIV medical care to persons with past or present substance use presents special challenges. First, drug and alcohol use complicate the planning and delivery of care. Providers must be aware of biological issues, including interactions between HIV medications and recreational drugs, as well as changes that prolonged drug or alcohol use can have on the absorption and effectiveness of medications. In addition, HIV-infected substance users often have co-morbid conditions, such as hepatitis C infection, which may complicate the management of HIV disease and create competing healthcare priorities. Providers must also be knowledgeable about the social context of different kinds of substance use. Social factors may affect the ways that people become engaged in medical care, their retention in care, and their adherence to treatment.

The second major challenge to providing HIV medical care to this population is that providers may have preconceptions about drug and alcohol use. Like everyone else, providers are exposed to and influenced by the many media portrayals of people who use alcohol or drugs. Almost all of these images are negative; even the relatively few sympathetic or compassionate portrayals rarely show substance users as whole, complex human beings. Stereotypes and myths about substance use and substance users can limit a provider's capacity to support adherence and provide optimal care.

As trainers, we have the responsibility to help the people we train acknowledge and analyze their preconceptions, and then consciously put them aside. We – and the people we train – need to recognize that these negative images may make substance users feel powerless to adopt changes that will promote their health. Consequently, we also need to help HIV-infected substance users recognize that they have the capacity to protect and improve their health. We can raise their awareness of the behavioral and environmental resources that promote health. We can also work with them to develop dynamic strategies for HIV adherence that fit into the context of their lives.

A third, and perhaps even larger challenge, is to distinguish the true biological and social challenges from the harmful stereotypes of substance use and substance users. In this module, we deal with both the truths and the myths that affect the quality of care that substance users receive and their ability to adhere to HIV treatment. However, it is important to recognize that learning the distinctions between these truths and myths is a difficult, ongoing process – certainly not something that can be fully sorted out and mastered in the short time allotted for this training. What we can accomplish is to help participants understand that HIV-infected substance users do not fit any stereotype. We can encourage participants to explore the adherence challenges substance users face and to consider the vast range of adherence interventions that may promote their health.

Resource Materials

Slides:

A PowerPoint presentation for this adherence module is included in the curriculum. This presentation should be run concurrently with the module. To help participants follow the presentation, we have listed the specific slides that correspond to each session in the module.

Suggested Reading List:

A reading list has also been prepared for participants. A full citation provided in the “References” section at the end of the module, includes the items listed below.

- *Addressing the challenges of adherence. Navigating emerging challenges in long-term HIV therapy*
- *Factors affecting adherence to antiretroviral therapy*
- *The challenge of adherence*
- *Adherence: Keeping up with your meds*
- *Building a cooperative doctor/patient relationship*
- *Medical progress: Medical care for injection-drug users with HIV infection*

Handouts:

1. Alphabetical lists of HIV medications (Page 6)
2. *Adherence Now* packets (See Page 13*)
3. Reprint: *Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents* (See Page 16*)
4. Worksheet for participant notes (Page 19)
5. Interactions between Antiretroviral Medications and Methadone (Page 30)
6. Interactions between Antiretroviral Medications and Recreational Drugs (Page 31)
7. Commonly Abused Substances and Possible Interactions with HIV drugs (Page 32*)
8. Pre-Appointment Questionnaire from *Adherence Now* (Page 36)
9. Case presentation summaries (Pages 42-46)

**The facilitator needs to acquire these resources in advance of the training.*

Other Materials Needed:

- Self-stick notes
- Flipcharts
- LCD projector
- Screen
- Colored Markers
- Tape

Objectives

By the end of this module, participants will be able to:

- Define adherence broadly and understand its significance
- Recognize that substance users may experience different medical complications of HIV infection than those experienced by other risk groups
- Assess persons' readiness for starting and maintaining antiretroviral therapy
- Identify effective techniques and useful resources for supporting adherence
- Develop approaches for tailoring health promotion interventions to the specific needs of substance-using patients

Key Facts

- Health promotion is more than just adherence to medications.
- A broad view of adherence actively engages patients in health care and treatment and provides them with more opportunities for success.
- In order to be effective, providers need to recognize their biases and judgments about adherence issues—especially for substance users.
- Substance users are not a homogeneous population—each individual has unique needs and challenges to overcome.
- With the proper support services and primary care, substance users can achieve equal levels of success as non-substance users.

Session 1: Introductions and Icebreaker

Activity: Defining Adherence

Purpose: To introduce training participants to each other and the instructor, to gain an initial “read” on the participants, and to start the interactive process.

Time: 10 minutes

Materials

- Handout 1, “Alphabetical Lists of Antiretroviral Drugs Used in HIV Treatment”

Instructor Notes

1. Once the participants have arrived, take three minutes to introduce yourself, talk briefly about the presentation style, remind people to approach the day with an open mind, encourage interaction, and add any personal touch that you feel is appropriate. If you wish, you may also talk briefly about the terminology you will use throughout the presentation. For example, the use of the words “patient” versus “client,” “ART” (antiretroviral therapy) versus “HAART” (highly active antiretroviral therapy), and “substance user” versus “substance abuser” or “addict.”
2. Ask the participants to introduce themselves by name, agency, and job.
3. Use a brief ice-breaker of your choosing to get an initial “read” on the participants and begin the interactive process. Here is one suggestion:
 - Ask each of the participants to give a one-sentence description of what they believe adherence to be, as part of their introduction.
4. Distribute Handout 1, “Alphabetical Lists of Antiretroviral Drugs Used in HIV Treatment” and note that it will be useful throughout the training as an easy reference on the many different antiretroviral drugs that are now used.

Handout 1: Alphabetical Lists of Antiretroviral Drugs Used in HIV Treatment

The following table was developed to reduce confusion concerning the different names of drugs used for HIV treatment. It is derived from the publication “Antiviral Drug Names” (Fact Sheet 401) from the New Mexico AIDS InfoNet.

Protease Inhibitors

- Agenerase (Amprenavir)
- Crixivan (Indinavir)
- Fortovase (Saquinavir)
- Invirase (Saquinavir)
- Kaletra (Lopinavir/ritonavir)
- Lexiva (Fosamprenavir)
- Norvir (Ritonavir)
- Reyataz (Atazanavir)
- Viracept (Nelfinavir)

Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs or “non-nukes”)

- Rescriptor (Delvirdine)
- Sustiva (Efavirenz)
- Viramune (Nevirapine)

Nucleoside Reverse Transcriptase Inhibitors (NRTIs or “nukes”)

- Combivir (Lamivudine/3TC + zidovudine/AZT)
- Emtriva (Emtricitabine)
- Epivir (Lamivudine/3TC)
- Hivid (Zalcitabine)
- Retrovir (Zidovudine/AZT)
- Trizivir (Abacavir + lamivudine/3TC + zidovudine/AZT)
- Videx (Didanosine/DDI)
- Viread (Tenofovir)
- Zerit (Stavudine/D4T)
- Ziagen (Abacavir)

Fusion Inhibitor

Fuzeon (Enfuvirtide/T-20)

Note that lopinavir is actually only available in combination with a small dose of ritonavir and sold under the trade name Kaletra.

Session 2: A Broad Perspective on Adherence: Part 1

Purpose

- To illustrate that adherence is *not only* about taking one's medications; in some cases, a patient is not ready to be on a regimen but can still be "adherent" to medical treatment in many other ways
- To show that non-adherence to medications is pervasive in both substance-using and non-substance-using populations
- To introduce the wide variety of psychosocial factors that impact adherence
- To show how thinking about adherence broadly gives a patient more opportunity for success
- To establish the need to improve adherence, in the broad sense, for HIV-infected substance users
- To illustrate why adherence to antiretroviral medications is so important if an individual is ready to take them

Materials

- Flipchart, colored markers, and tape
- Handout 2, "'Adherence Now' Teaching Cards" (from "Adherence Now" packet)
- Slide 2, "Expanded Definition of Adherence"
- Slide 3, "Why Adopt a Broad View of Adherence?"
- Slide 4, "What is Health Promotion?"
- Slide 5, "Adherence Support = Health Promotion"
- Slide 6, "Why Focus on HIV Adherence in Substance Users?"
- Slide 7, "Why Is Adherence to Antiretroviral Medications So Important?"
- Slide 8, "Problems With Poor Adherence"
- Slide 9, "Goals of Medical Adherence"
- Slide 10, "Medication Adherence Is Not Easy!"
- Slide 11, "How Much Adherence Is Enough?"
- Slide 12, "Treatment Failure"
- Slide 13, "What Do We Know About HIV Drug Resistance?"
- Slide 14, "Relationship Between Level of Adherence and Risk of Resistance"

Time: 10 minutes

Instructor Notes

1. Slide 2 is a sample of an expanded definition of adherence. Use Slide 3 to summarize the importance of adopting a broad view of adherence. Slide 4 provides examples of a broad perspective of adherence. You may want to ask participants if they can offer other examples.

Expanded Definition of Adherence

Any action that improves, supports, or promotes the health of a person living with HIV with respect to HIV treatment and care, including physical, mental, and psychosocial well-being.

Slide 2

Why Adopt a Broad View of Adherence?

A broad view of adherence:

- recognizes that adherence is not only about taking one's medications
- actively engages patients in health care and treatment
- values the health impacts of "non-medical" interventions, including controlled drug use, stable housing, social supports, harm reduction, and good nutrition
- improves patients' self-efficacy
- provides more opportunities for success

Slide 3

What Is Health Promotion?

- Taking all antiretrovirals, on time exactly as prescribed
- Taking meds to prevent opportunistic infections
- Primary and Preventive Care (PAPS)
- Keeping regular medical appointments
- Eating a nutritious diet
- Exercising regularly
- Participating in a drug treatment program
- Controlling drug use or sobriety
- Practicing safer sex and drug injection
- Taking a multivitamin
- Stopping smoking
- Connecting with a support network

Slide 4

2. Present slides 5 and 6. Emphasize that substance users are often discriminated against and have:
 - Less access to care
 - Less access to ART
 - Slower decline in morbidity and mortality

Part of the reason for substance users' reduced access and poorer response to care is that providers lack training to care for this special population and may have negative attitudes toward substance users.

Adherence Support = Health Promotion

“..helping a patient who uses drugs adhere to a complex medical regimen can support an upward spiral of self-esteem and the adoption of healthier practices.”

Eldin, 2001

Slide 5

Why Focus on HIV Adherence in Substance Users?

- There is systemic discrimination against substance users
 - Less access to care
 - Less access to ART
 - Slower decline in morbidity and mortality
- Providers often lack training in the care of substance users and may have negative attitudes towards them

Slide 6

3. Tell the participants that, with proper support, substance users can achieve better outcomes.

Why Is Adherence to Antiretroviral Medications So Important?

- Medications cannot work if they aren't taken
- Successful HIV treatment requires consistent and long-term therapy

Slide 7

Problems With Poor Adherence

- Sub-therapeutic levels of medications
- Less viral suppression
- More drug resistance, which limits future treatment options
- Higher morbidity and mortality

Slide 8

Goals of Medical Adherence

- Maximally suppress viral load
- ↓ drug resistance
- ↑ length of regimen effectiveness
- All of the above leading to ...
 - ↓ HIV disease progression
 - ↑ survival

Slide 9

4. Emphasize that adherence is not an easy task and that the high adherence standard of 95%—that has been established by research—is extremely difficult for most people to achieve. If this adherence goal is not presented to HIV-infected patients in a sensitive way, then it may set them up for failure. It is also important to note that, even when people achieve 95% adherence, they can still experience treatment failure (Slides 10 and 11). It is important to educate patients on the importance of adherence, but also make it known to them that treatment failure is not patient failure (Slide 12). In addition, patients need to know that many supports are available to help them meet the challenge of adherence. We will talk about supports shortly.

Medication Adherence Is Not Easy!

- Rate of nonadherence to ART is generally 50% to 70%
- Substance users' adherence rates are lower (inconsistent data)
- Even >95% adherence is associated with treatment failure almost 20% of time

Golin, 2002; Samet, 1992; Broers, 1994; Gordillo, 1999; Arnsten, 2002; Chesney, 2000

Slide 10

How Much Adherence Is Enough? (After 3 Months)

<u>% of doses taken correctly</u>	<u>% with viral suppression</u>
>95%	81%
90% - 95%	64%
80% - 90%	50%
70% - 80%	25%
<70%	6%

Chesney, 2000

Slide 11

Treatment Failure

- Defined as
 - increased viral load
 - decreased CD4+ T cell count
 - progression of HIV disease
- Treatment failure is *not* patient failure—it can even happen if a patient is adherent.
- Assess why failure occurred and move on. Don't dwell on the failure; instead set up a new plan to address the underlying reasons.

Slide 12

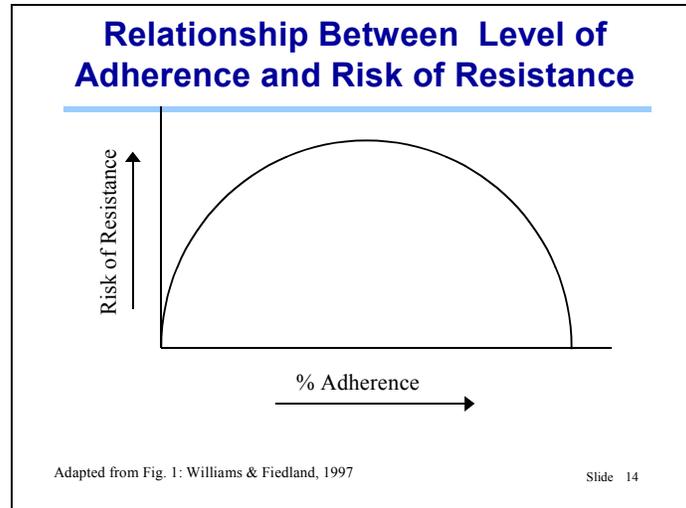
5. Remind participants about antiretroviral drug resistance, transmission of resistant strains of HIV, and the relationship between adherence and drug resistance (Slides 13 to 14). Note that one of the main arguments that is made against prescribing ART to drug users is that they won't adhere and that, as a result, their HIV infection will become resistant to HIV meds. This in turn would lead to the transmission of drug-resistant HIV to others. Be sure to cover the following points:
- If a person is completely nonadherent (takes none of his or her medications), the chances of drug resistance are extremely low, because the virus is not exposed to any antiretroviral drug to become resistant to.
 - Conversely, if person's adherence is very high (takes close to 100% of his or her medications correctly), then the risk of drug resistance is quite low. This is because an effective regimen should suppress viral replication to such an extent that very few viruses are produced.
 - The greatest risk for drug resistance occurs when a person takes his or her HIV medications intermittently. Taking medications intermittently gives the virus the perfect opportunity to develop resistance, because it has an opportunity to multiply in the presence of medications.
 - To summarize, if there is no medication in the body, there is nothing for the virus to work with to become resistant. Conversely, if there is a consistently high level of medication around, the virus has little opportunity to grow and change. Use Slide 14 to illustrate these points graphically. The take-home message is that, if people start using recreational drugs again or feel for any reason that they cannot stick with their regimen, they should stop all their medications at once and not "wean" themselves off.

What Do We Know About HIV Drug Resistance?

- An estimated 78% of people on HIV treatment experience have resistance to at least one antiretroviral agent.
- An estimated 50% of all people living with HIV (irrespective of current treatment status) have evidence of resistance to at least one agent.

Richman, 41st ICAAC, 2001

Slide 13



6. Distribute Teaching Cards from the Adherence Now packet. These laminated cards can help you illustrate the benefits of adherence to your patients. The front of each card contains a graphic image demonstrating the benefits of adherence, while the back of the card contains bullet points that a provider can emphasize. Additional copies of the “Adherence Now” materials can be obtained at no cost from:

World Health CME	Tel: (800) 433-4584, ext. 1776
41 Madison Ave	E-mail: erivera@whcom.com
New York, NY 10010-2202	

7. Finally, remind participants that it is crucial to remember the broader perspective on adherence when thinking about adherence to antiretroviral medications. Each element of a patient’s treatment plan will have a direct impact on his or her ability to adhere to the medications. Taking HIV medications is only part of the patient’s overall well-being. *It is rarely, if ever, an emergency to start antiretroviral therapy.* In fact, it may be more harmful than helpful to prescribe antiretroviral medications if a person is not ready to take them.

Session 3: The Politics of Adherence

Activity: Agree or Disagree?

Purpose: To raise some controversial issues and allow participants to express their opinions about these issues

Time: 15 minutes

Materials

- Colored markers, newsprint paper, and tape
- Slide 15, “Politics of Adherence”
- Slide 16, “Agree or Disagree?”
- Slide 17, “Abstinence and Antiretroviral Therapy”

Instructor Notes

1. In preparation for the session, make three signs that say “Agree,” “Disagree,” and “Both Agree and Disagree.” Post these signs in three different parts of the room.
2. Introduce the activity. Acknowledge that some of the issues related to adherence and substance use will be controversial and that this exercise gives participants a forum to discuss their opinions. You may use Slide 16 to summarize the main points.

Politics of Adherence

- What are your opinions about this controversial adherence issue?
- Decide whether you
 - Agree
 - Disagree
 - Both agree and disagree
- Let us know what you think!



Slide 15

3. Tell participants that you are going to put up a series of statements. When they read each statement, they should move to the part of the room that matches their opinion about that statement – agree, disagree, or both agree and disagree. Once participants have moved to

their respective positions, facilitate a discussion by asking the people in each position to explain some of the reasons for their stance. Let participants know that the position they pick does not have to be permanent; that is, they can later change their minds and switch to another position.

4. Slide 16 gets at the issue of priorities in substance use treatment settings. Should HIV issues be paramount in early recovery, or should there be a narrow focus on concerns directly related to substance use? Use Slide 17 to help facilitate your discussion.

Agree or Disagree?

“An individual should be drug free for *one month* before they can start antiretroviral therapy.”

“An individual should be drug free for *three months* before they can start antiretroviral therapy.”

“An individual should be drug free for *six months* before they can start antiretroviral therapy.”

Slide 16

Abstinence and Antiretroviral Therapy

- There is no right answer.
- Studies have shown active drug use is associated with less adherence.
- What is the influence of drug of choice, housing, support network, and so forth?
- The decision to start ART depends on the person's specific circumstances.
- Providers and patients should make informed decisions about ART.

Golin, 2002; Stone, 2001

Slide 17

Session 4: A Broad Perspective on Adherence: Part 2

Activity: Factors Affecting Adherence

Purpose: To emphasize that *it is rarely, if ever, an emergency to start ART*; that one must consider patients' specific needs when evaluating their readiness to start treatment; and to help participants identify what factors may facilitate or hinder a patient's adherence

Time: 10 minutes

Materials

- Handout 3, Table 6 from *Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents*
- Handout 4, "Worksheet for Participant Notes"
- Large copy of Handout 4, written on newsprint
- Self-stick notes (3-5 sheets per participant)
- Slide 18, "HIV Treatment Guidelines"
- Slide 19, "Adherence Issues to Consider for Substance Users"
- Slide 20, "Medication Adherence and Drug of Choice"

Instructor Notes

1. Pass out Handout 3, Table 6 from *Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents*. Obtain the most recent version of the guidelines from http://www.aidsinfo.nih.gov/guidelines/default_db2.asp?id=50 before the training.
2. Show Slide 18 and note where the most recent treatment guidelines can be obtained.

HIV Treatment Guidelines

The best time to start therapy in individuals with a CD4 count ≥ 200 and no symptoms is unknown. Below are general guidelines:

Symptomatic (AIDS)	Treat
No symptoms, CD4<200	Treat
No symptoms, 200<CD4 \leq 350	Offer treatment, but controversial
No symptoms, CD4>350, VL>55,000	Some recommend treating, others recommend waiting
No symptoms, CD4>350, VL<55,000	Wait and continued monitoring of CD4 counts

The most recent treatment guidelines can be found at: CDC, MMWR 2002
http://www.aidsinfo.nih.gov/guidelines/default_db2.asp?id=50

Slide 18

3. Ask participants to write down 3-5 potential adherence barriers to or facilitators of adherence. Then post on these comments on the appropriate area of the large newsprint copy of the Handout 4 worksheet. Note those challenges that are client-focused, regimen-focused, and clinical care/provider focused.
4. Remind participants that medication is not the only important part of a patient's treatment plan, and that initiation of anti-retroviral therapy is rarely, if ever, an emergency.
5. Also, emphasize that factors that influence adherence vary from person to person (Slide 19). One important factor that influences adherence is the drug or drugs of choice. Slide 20 shows some of the ways in which the drug of choice may affect adherence. In this discussion, you may refer to a study (Arnsten, 2002) in which active cocaine use was associated with a 41% decline in median adherence and was a strong predictor of failure to maintain viral suppression. In this study, active heroin users also had lower adherence than nonusers, but the difference was not statistically significant.

**Adherence Issues to Consider
for Substance Users**

- Relationship to the medical sector
 - Access to care
 - Access to ART
 - Discrimination
- Drug interactions
- Side effects and Pain
- Drug of choice variations
- Scheduling doses

Slide 19

Medication Adherence and Drug of Choice

- Heroin
 - Use may be more regimented
 - Users may have an easier time with adherence
- Cocaine/Crack
 - Use may be more sporadic
 - Intense mood swings may interfere with adherence
- Methamphetamine
 - Unclear, but use may be more sporadic and interfere with adherence
- Alcohol
 - May have most negative impact on adherence due to blackouts and memory loss

Slide 20

Areas of Challenge Worksheet

	Client Focused	Regimen Focused	Clinical Care/Provider Focused
Issues			
Interventions			

Session 5: Medical Issues Specific to HIV-Infected Substance Users

Presentation: Medical Issues

Purpose: To learn about medical complications that may be relevant when treating HIV-infected substance users

Time: 40 minutes

Materials

- Handout 5, “Interactions Between HIV-Related Medications and Methadone”
- Handout 6, “Interactions Between Antiretroviral Medications and Recreational Drugs”
- Handout 7, “Commonly Abused Substances and Possible Interactions With HIV Drugs”
- Slide 21, “Medical Issues Related to HIV and Substance Use”
- Slide 22, “Drug Interactions: What Do We Know?”
- Slide 23, “How Do Drug Interactions Affect Medication Adherence?”
- Slide 24, “Methadone Interactions With PIs”
- Slide 25, “Methadone Interactions With NNRTIs”
- Slide 26, “Methadone Interactions With NRTIs”
- Slide 27, “Buprenorphine Interactions with ART”
- Slide 28, “Recreational Drug Interactions With ART”
- Slide 29, “Illicit Drug Interactions with ART”
- Slide 30, “Talking About Recreational Drug Interactions”
- Slide 31, “Hepatitis C (HCV) Infection”
- Slide 32, “HCV and HIV”
- Slide 33, “HCV Treatment Issues”
- Slide 34, “HCV Treatment Issues (continued)”
- Slide 35, “Tuberculosis (TB)”
- Slide 36, “TB and HIV”
- Slide 37, “TB and HIV Drug Interactions”
- Slide 38, “HIV and Mental Illness”
- Slide 39, “Priorities and Motivations”

Instructor Notes

1. Introduce the topic by noting that HIV-infected substance users may experience medical complications that are specific to their substance use. As we have already seen, there are many factors to consider when assessing a patient’s readiness for antiretroviral therapy. Substance use does not necessarily preclude a patient from receiving – or adhering to –

antiretroviral therapy, especially if he or she has formed a good relationship with a provider and is prepared to take on the challenge.

2. Recognize that competing health priorities can complicate both access to ART and adherence if people are feeling ill or if they have other health conditions that may urgently require treatment. A few examples of such conditions are presented below:
 - Hepatitis C (HCV) coinfection is common among HIV-infected injection drug users. In this population, HIV infection has been linked to more aggressive progression of HCV disease (Lauer, 2001; Soto, 1997; Bruno, 2002; Landau, 2001; Nasti, 2001).
 - Mental illness may also create significant adherence barriers if a person's mental health status interferes with memory or motivation. For example, depression, which is the most common mental illness among substance users, may affect both memory and motivation (Stone, 2001; Sherer, 1998; Elliot, 1997).
3. Present the material in Slides 21 to 37, and refer participants to Handouts 5 to 7 as good sources of additional information.

**Medical Issues Related to
HIV and Substance Use**

- Drug interactions
- Hepatitis C
- Tuberculosis (TB)
- Mental Illness
- Complex relationship with medical providers

Slide 21

4. In general, research has shown that active substance users are less adherent than former users or nonusers. Consequently, it may be prudent to defer ART until a person's substance use and psychosocial climate have stabilized. However, this does not mean that a person must stop using before starting ART. If a person is using and wishes to begin ART, then stabilizing the environment can be helpful in promoting adherence. Each person's situation should be assessed individually. Flexibility is essential when tailoring a treatment plan to meet the needs of an active substance user.
5. Introduce the discussion of drug interactions, referring to the relevant information in Handouts 5 through 7 and Slides 22 through 30. It is important to note that there are many drugs that have not yet been studied and also that many of the studies have been conducted are on a small number of patients making it hard to generalize from them.
 - Explain how drug interactions may affect adherence, and talk about the basic science behind the interactions. Focus on a few common interactions, and then refer participants to their handouts for more information.

- Note that the coadministration of methadone with protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs) often leads to significantly decreased methadone levels.
- Also note that the coadministration of methadone with nucleoside reverse transcriptase inhibitors (NRTIs) generally does not affect methadone levels, although the effects of some NRTIs have not yet been determined. Methadone may also effect the levels of some NRTI, but in clinical practice the only change in dosing that may be required is with didanosine. (If participants ask about the increased clearance of methadone for abacavir, let them know that in clinical practice it is still generally not necessary to change methadone dose).

Drug Interactions: What Do We Know?

- Most drug interactions occur in the liver
- Most drug interactions are due to the following factors:

Speeding up metabolism of drug ↓ Drugs cycle out of the body more quickly	Slowing down metabolism of drug ↓ Drug levels build up in the blood
---	---

Slide 22

How Do Drug Interactions Affect Medication Adherence?

- Concerns about methadone levels may lead to less adherence
- If medications levels are too low, the effect may be the same as nonadherence
- If patients are not disclosing drug use to their providers, it can be harder to determine why treatments are failing in an otherwise adherent client

Slide 23

Methadone Interactions with PIs

Protease Inhibitor	Effect on Methadone
Indinavir	No change
Ritonavir	↓37%
Nelfinavir	↓ level
Amprenavir	↓ 13-35%
Fosamprenavir	↓ level
Lopinavir/ritonavir	↓28-53%
Saquinavir	↓ 0-40%
Atazanavir	No data

Beauverie, Gourevitch, Antoniou, Clarke 2002, Bart, Shelton, Stevens, McCance-Katz 2003, Gerber, DHHS
Slide 24

Methadone Interactions With NNRTIs

NNRTI	Effect on Methadone
Nevirapine	↓ by 46%
Efavirenz	↓ by 48-52%
Delavirdine	No data (expect ↑ or no change)

Altice, 1999; Staszewski, 1998; Gourevitch, 2000; Antoniou, 2002; Clarke, 2001

Slide 25

Methadone Interactions With NRTIs

NRTI	Effect on NRTI
Zidovudine	↑ 40%
Stavudine	↓ 18-27%
Didanosine	↓ 41-60% *
Abacavir	↓
Tenofovir	No data
Lamivudine	No change
Zalcitabine	No data
Emtricitabine	No data

Rainey, Gourevitch, Antoniou, McCance-Katz, 1998, Bart, Rainey 2000 & 2002, DHHS

Slide 26

Buprenorphine Interactions with ART

- NRTIs
 - No change in AZT
- NNRTIs
 - Likely ↓ buprenorphine levels
- PIs
 - ↑ Buprenorphine with ritonavir > indinavir > saquinavir
- Fusion inhibitor
 - No data

McCance-Katz 2001, Iribarne, Sullivan

Slide 27

Recreational Drug Interactions With ART

- Interactions are complex, inconsistent, and difficult to predict.
- Interactions may be affected by drug purity, mode of ingestion, and baseline liver and kidney function.
- Interactions with HIV meds may be extremely dangerous or even fatal.
- “Take heed, club lovers - there’s no map for these trips.” (Horn, 1998)

Slide 28

Illicit Drug Interactions With ART

Drug	Effect
Amphetamines	may ↑ level 2-3 fold with ritonavir
Methamphetamine	↑ HIV replication, fatal OD with ritonavir/saquinavir
Cocaine	↑ HIV replication, ↓ immune system function
Ecstasy (MDMA)	Over dose or death with ritonavir
GHB (liquid X)	↑ levels with ritonavir or saquinavir
Heroin	levels may ↓ or ↑ with ritonavir

Antoniou, Henry, Harrington, Roth, Bagastra, Peterson 1991 & 1992, Ellis, Gavrilin, Urbina, Hales
Slide 29

6. We know very little about the interactions between HIV medications and recreational drugs. However, most of the interactions that have been reported involve ritonavir.

7. The most important point to emphasize about drug interactions is that little is known. One of the reasons is that it is very difficult to do controlled clinical trials with recreational drugs, so we can only make educated guesses based on limited research, medical records, and anecdotal reports. Note that some of the drug interaction information is conflicting. Fortunately, the data are better for legal substances, such as methadone and alcohol. The take-home message is that drug interaction information is not always clear. In addition, the interactions may vary, based on such factors as the person's metabolism, the mode of injection, and the purity of the drug.

Talking About Recreational Drug Interactions

- There is no way to identify “safe drugs” with HIV medications.
- Relapse is not necessarily a reason to stop ART.
- Start “slow and low” on drugs of choice while taking ART.
- Share information and resources, but stress that our knowledge of drug interactions is an *inexact* science.

Slide 30

8. Introduce the topic of co-morbidities, referring to the information in Slides 31 through 38. Explain how co-morbidities, such as Tuberculosis (TB) and Hepatitis C, are fairly common among substance users and should be considered in their treatment plans. **Note to Instructor: Discussion of TB is optional depending on location of training**
9. Here are some other points to raise:
- HCV infection is very common among drug users – much more common than HIV infection.
 - Note some of the challenges of current treatment for HCV. For example, some HCV medications are administered through injection, which may be problematic for some substance users. In addition, HCV treatment has a low to moderate success rate, and the side effects are very difficult to tolerate.

HCV Infection

Epidemiology

- 5 times more widespread than HIV
- Leading cause of liver disease in the U.S.
- Up to 88% of HIV-infected IDUs are coinfecting with HCV

Lauer, NEJM 2001

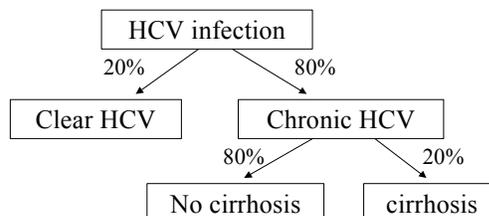
Slide 31

HCV and HIV

- HIV's effect on HCV
 - Accelerates hepatitis C disease
 - Leads to cirrhosis more quickly
 - No difference in response to HCV treatment
- HCV's effect on HIV
 - Conflicting data about HIV disease progression
 - Liver disease may complicate ART

Slide 32

HCV Treatment Issues



Lauer, NEJM 2001

Slide 33

HCV Treatment Issues (continued)

- Peginterferon injections weekly for 6 to 12 months
- Cure rate approximately 56% overall
- Severe side effects—Flu-like symptoms, depression, irritability, emotional lability, severe anemia
- Up to 1/3 of patients stop treatment due to intolerance

Fried, 2002

Slide 34

Explain how the comorbidity of Tuberculosis (TB) is fairly common among substance users and should be considered in their treatment plans

- TB's epidemiology, interaction of TB and HIV, and TB's effect on HIV drugs
- Note that the TB drug rifampin has such significant drug interactions with PIs and NNRTIs that it is contraindicated for nearly all of these antiretroviral agents. Rifampin also dramatically reduces methadone levels. Rifabutin is the preferred choice in the treatment of TB, because it has fewer drug interactions with PIs and NNRTIs and causes no change in methadone levels.

Tuberculosis (TB)

Epidemiology

- TB is common in IDUs before HIV.
- Up to 23% of IDUs have TB exposure (PPD+).
- TB and HIV coinfection is concentrated among IDUs and minorities.
- HIV infection is the strongest risk factor for the progression of TB exposure to active disease.

CDC, 2002; Selwyn, 1989

Slide 35

TB and HIV

- TB's effect on HIV
 - ↑ HIV replication
 - accelerate the progression of HIV disease
 - ↑ risk for opportunistic infections and death
- HIV's effect on TB
 - Clinical presentation of TB may be different
 - Early response to TB therapy is no different
 - Unknown relapse rates of TB

Slide 36

CDC, 2002; Whalen, 1995

TB and HIV Drug Interactions

Numerous complex drug interactions between ART and TB medications

- Rifampin
 - *Cannot use* in most patients on NNRTIs and PIs
 - ↓ NNRTI and PI levels, making them ineffective
 - ↓ methadone levels
- Rifabutin
 - More favorable for use with HIV medications
 - Still needs dose modification with many NNRTIs and PIs
 - No effect on methadone levels

Slide 37

10. Note the prevalence of mental illness, and briefly discuss the implications this has for treatment. Although this module does not consider this topic in detail, it is essential to mention the importance of screening for mental illness and providing the necessary referrals and treatment (Slide 38).

HIV and Mental Illness

- Up to 50% to 80% of HIV-infected persons are affected by mental illness.
- Triple diagnosis of HIV, substance use, and mental illness is common.
 - Up to 80% of HIV-infected patients in methadone maintenance require psychiatric consultation for mental illness.
- Untreated depression can compromise medication adherence and make HIV infection more disabling.

Sherer, 1998; Elliot, 1997; Ferrando, 2001

Slide 38

11. The most important implication of the medical issues raised in this session may be summed up as follows: *Providers need to pay special attention to tailoring medication and treatment regimens to each patient's specific situation and needs.*

12. A patient's readiness to start, continue, or resume ART should be considered in light of their other personal and health priorities. For example, a patient who considers securing housing, resolving an acute illness, and reconnecting with his or her hepatitis C doctor as his or her top three priorities may not yet be ready to start ART. After some of these "front-burner" concerns are addressed, that patient might feel more ready to consider ART. Similarly, education and support can often help patients who are not yet considering ART – to move to the next level of readiness. The Stages of Change model provides a template for talking with patients about their degree of readiness and the steps they might take to prepare for treatment, even if they are not ready to start ART now. In this respect, each step towards readiness is viewed as a healthy behavior change. Patients are not set up for "failures" if they are not yet ready or able to adhere to therapy. On the contrary, they are given more opportunities for "success" in their health-promotion efforts (Slide 39).

Priorities and Motivations

Adherence goals cannot be considered outside the spectrum of psychosocial and medical service needs.

- Service planning, short- and long-term goals, patient needs, and resources
- Spectrum of health promotion opportunities
- Stages of Change application

Slide 39

Handout 5: Interactions Between HIV-Related Medications and Methadone

HIV Medication	Effect on Methadone	Effect on HIV Medication	Clinical Effect
Pis			
Indinavir Ritonavir	Unchanged ↓ levels by 37%		Monitor and titrate methadone dose, if needed; might require increase in methadone dose
Saquinavir [§] Nelfinavir	- ↓ levels		Has minimal effect on maintenance dose; monitor and titrate dose, if needed; might require increased methadone dose
Amprenavir	↓ by 35%		Monitor and titrate dose, if needed; might require increase in methadone dose
Lopinavir	↓ AUC by 36%, level by 53%		Monitor and titrate dose if needed; might require increased methadone dose
NNRTIs			
Nevirapine	↓ by 46%	Unchanged	Withdrawal symptoms may occur if dosage is not adjusted; titrate methadone dose to effect; might require increased methadone dose
Efavirenz	↓ by 48-52%		Titrate methadone dose to effect; might require increased methadone dose
Delavirdine	Not studied		
NRTIs			
Zidovudine	Unchanged	↑ AUC by 40%	Unclear; methadone may increase zidovudine-related toxicities
Stavudine	Unchanged	↓ AUC by 18%, level by 27%	No dose adjustment
Didanosine	Unchanged	↓ AUC by 41%, level by 60%	Consider increasing dose of didanosine
Tenofovir	Not studied		
Lamivudine	Unchanged		
Abacavir	↑ clearance	↓ peak concentration	
Zalcitabine	Not studied		
Other Medications Sometimes Used by HIV-Infected Persons			
Rifampin	↓ levels sharply		Titrate methadone dose to effect; might require increased methadone dose
Rifabutin	Unchanged		Unknown clinical significance
Fluconazole	↑ level by 30%		Titrate methadone dose to effect; might require increased methadone dose
Phenytoin	↓ levels sharply		Titrate methadone dose to effect; might require increased methadone dose
Phenobarbital	↓ levels sharply		Titrate methadone dose to effect; might require increased methadone dose
Carbamazepine	↓ levels		Titrate methadone dose to effect; might require increased methadone dose

[§]Drug interaction studies were conducted with the Invirase formulation of saquinavir; therefore, the observations and recommendations might not apply to the Fortovase formulation of saquinavir.

AUC = Area under the curve

Adapted from the following sources:

Centers for Disease Control and Prevention, 2002

Gourevitch, M.N., Friedland, G.H., 2000

Handout 6: Interactions Between Antiretroviral Medications and Recreational Drugs

Drug	Effect	Comment
Alcohol	↑ abacavir level	Unknown significance
Amphetamines	Ritonavir may ↑ amphetamine level two- to three-fold	Avoid combining with ritonavir; alternatively, use one-quarter to one-half the amount of amphetamine
Methamphetamine	↑ HIV replication, overdose with ritonavir/saquinavir ¹²³⁴	Avoid combining with ritonavir
Cocaine	Possibly ↑ HIV replication and ↓ immune system ⁵⁶⁷⁸	Studies conducted only in test tubes and mice
Ecstasy (MDMA)	Overdose and death with ritonavir ⁹¹⁰ Possibly ↑ levels with other PIs and NNRTIs	Avoid combining with ritonavir; alternatively, use one-quarter to one-half the amount of MDMA and watch for signs of toxicity
GHB (liquid X)	↑ levels and toxicity with ritonavir/saquinavir ⁵ , possibly ↑ with delavirdine	Use cautiously with PIs, as well as delavirdine and efavirenz
Heroin	Ritonavir may ↓ levels by 50%; Ritonavir and other PIs may also ↑ levels	
Ketamine	Possibly ↑ levels with ritonavir, delavirdine, and efavirenz	Use cautiously with ritonavir, nelfinavir, and efavirenz
LSD	Unknown	Use cautiously with PIs, delavirdine, and efavirenz
Marijuana	PIs may ↑ levels	Efavirenz may cause false-positive screening test for marijuana
PCP	Possibly ↑ levels with antiretrovirals	Use cautiously with PIs, delavirdine, and efavirenz

Adapted from: Antoniou, T., Tseng, A.L., 2002

¹ Ellis RJ, Childers ME, Cherner M, et al. Increased human immunodeficiency virus loads in active methamphetamine users are explained by reduced effectiveness of antiretroviral therapy. *J Infect Dis.* 2003 Dec 15;188(12):1820-6.

² Gavrilin MA, Mathes LE, Podell M. Methamphetamine enhances cell-associated feline immunodeficiency virus replication in astrocytes. *J Neurovirol.* 2002 Jun;8(3):240-9.

³ Hales G, Roth N, Smith D. Possible fatal interaction between protease inhibitors and methamphetamine. *Antivir Ther.* 2000 Mar;5(1):19.

⁴ Urbina A, Jones K. Crystal methamphetamine, its analogues, and HIV infection: medical and psychiatric aspects of a new epidemic. *Clin Infect Dis.* 2004 Mar 15;38(6):890-4.

⁵ Roth, M.D., Tashkin, D.P., Choi, R., et al., 2002

⁶ Bagasra, O., Pomerantz, R.J., 1993

⁷ Peterson, P.K., Gekker, G., Chao, C.C., et al, 1991

⁸ Peterson, P.K., Gekker, G., Chun, C.C., et al., 1992

⁹ Harrington, R.D., Woodward, J.A., Hooton, T.M., et al., 1999

¹⁰ Henry, J.A., Hill, I.R., 1998

**Handout 7: Commonly Abused Substances and Possible Interactions With HIV drugs
(From STATSCRIPT Pharmacy – The Boston Living Center Medication Adherence
Program and the Treatment Information Clinic, September, 2000)**

(The instructor will hand this out.)

Session 6: Talking with Patients About HIV and Substance Use

Presentation: Improving Provider-Patient Communication

Purpose: To improve provider-patient communication in general, as well as in the specific areas of substance use and adherence to medications

Time: 10 minutes

Materials

- Handout 8, “Pre-appointment Questionnaire From ‘Adherence Now’ Materials”
- Slide 40, “Talking About Adherence”
- Slide 41, “Talking About Adherence (continued)”
- Slide 42, “Talking About Substance Use”
- Slide 43, “Talking About Substance Use (continued)”
- Slide 44, “Provider-Patient Relationship (continued)”

Instructor Notes

1. Introduce why it is important for providers to talk with their patients about adherence. Focus on how assessing adherence is an important way for providers to tailor interventions to their patients’ needs (Slides 40 and 41).

Talking About Adherence

Ask specific questions

- How many pills did you take yesterday?
 - What are the names? What do they look like? (show pictures of meds if they have problems recalling)
- What time did you take them?
- Do you link your medications to any activity?
- How many times did you miss medication doses in the last three days? In the last week?

Slide 40

Talking About Adherence (continued)

Probe about missed doses

- Why do you think you missed doses?
- Are you using again?
- How much are you using?
- Do you bring your meds with you when you leave home?
- Can you link your meds to activities you do regularly in your life?

Slide 41

2. Next, focus on talking about substance use and finding out more about the patient's patterns of use (Slides 42-43).

Talking About Substance Use

- Nonjudgmental attitude is crucial!
- Some questions to ask
 - When is the last time you used?
(*Not* "Are you using drugs?"--different mindsets)
 - What is the pattern of your use?
 - Why do you think you use?
 - How are you using--injecting, snorting, inhaling, eating, or drinking?
 - Are you sharing needles or "works"?
 - How do you get the money to use?

Slide 42

Talking About Substance Use (continued)

Working with substance use

- Is your use causing any problems?
- Do you want to address these problems?
- How do you think you can address these problems?
- Use motivational interviewing techniques
- Give options
 - Interdisciplinary approach
 - Drug treatment programs
 - Support from social network
 - Support from provider

Slide 43

3. End the presentation with some general points on establishing a good provider-patient relationship (Slide 44). Keep in mind that some substance users have an extraordinarily difficult time with communicating with their providers as a result of past negative experiences with the medical system. Providers can help their patients by reviewing treatment options, and encouraging patients to discuss their questions and concerns.

Provider-Patient Relationship

Goals of “medical” care

- Patient-centered
- Reasonable and acceptable goals
- Small steps over time
- Put it all on the table (no hidden agenda)
- Redefine “success”

The above approach leads to less provider and patient frustration.

Slide 44

Handout 8: Preappointment Questionnaire From “Adherence Now” Materials
 (This handout is included in the “Adherence Now” materials that were passed out earlier.)



ADHERENCE NOW
 PREAPPOINTMENT QUESTIONNAIRE

*Please complete this questionnaire prior to seeing your provider,
 to address important issues about your care that have come up since your last visit.*

SECTION ONE

Are you currently taking HIV medications? (please circle) Yes No

If no, why not? _____

If you are not taking medications, please proceed to Section Two.

Do you find your HIV drugs easy to take? (please circle) Yes No

If no, why not? _____

Please list your HIV medications below:

Trade name	Generic name	Number of pills per dose	Number of doses per day	What times do you take your doses? (ie. 12 AM / 12 PM)	Special instructions (eg. with/without food)

Please estimate the number of doses

you have missed (if any): Today _____ Yesterday _____ Last week _____ Last month _____

Why did you miss the dose? Forgot _____ Sleeping _____ Side effects/felt sick _____ Other _____

How much of your HIV medications do you estimate that you take? (circle one)

None (0%)	Some (10%-30%)	Less than half (30%-50%)	About half (50%)	More than half (60%-75%)	Most (80%-85%)	Almost all (90%-95%)	All (100%)
--------------	-------------------	-----------------------------	---------------------	-----------------------------	-------------------	-------------------------	---------------

Some people forget to take their pills on the weekends. Did you forget a dose last weekend? Yes No

Do you have family or friends who remind you to take your HIV medications? Yes No

Do you have transportation or any means of getting to the pharmacy to fill a prescription? Yes No

Would you like an alarm or reminder device to help you to remember to take your medications? Yes No

Would you be interested in receiving a pillbox with dividers for each dose and day to help you to remember to take your medications? Yes No

Would you be interested in learning about ways to take your medications better? Yes No

SECTION TWO OPTIONAL QUESTIONS

Have you had unprotected sex since your last visit? Yes No

How many alcoholic drinks (can of beer, glass of wine, mixed drink) have you had in the past week?

Have you used any drugs to get high since your last visit? Yes No

Do you think you might be depressed? Yes No Maybe

Comments: _____

Provider name: _____ Provider signature: _____

Patient name: _____ Date: _____

MASTER COPY FOR DUPLICATION PURPOSES

Session 7: Managing HIV in the Context of Drug Use

Activity: Case Study Exercise

Purpose:

- To synthesize what participants have learned in this module
- To illustrate that adherence is a multidimensional challenge for all parties involved and requires an interdisciplinary approach

Time: 20-60 minutes

Materials

- Handout 9, “Case Studies for Small Group Exercise”
- Slide 45, “Some Strategies for Improving Health and Adherence”
- Slide 46, “Managing HIV and Substance Use: Case Studies”
- Slide 47, “Case Study 1: Melissa”
- Slide 48, “Case Study 2: Raymond”
- Slide 49, “Case Study 3: Krista”
- Slide 50, “Case Study 4: Marlon”
- Slide 51, “Case Study 5: Rosanna”

Instructor Notes

1. For this exercise, allow 20 minutes to conduct one case study, and 10-15 minutes for each additional case study.
2. Introduce the exercise (Slide 44-46) by telling participants that they will be working with a case study as a way to help synthesize the knowledge and skills they have gained through this module and apply them to hypothetical patient situations. Ask participants to consider how they can best develop a plan to promote the patient’s health. Remind participants to consider lifestyle, substance use, and medical information in determining an appropriate response plan for each case.

Some Strategies for Improving Health & Adherence

- Clarify the regimen
- Identify the patient's motivation
- Make medications part of daily routine
- Manage side effects
- Address alcohol and drug use
- Build good provider-patient communication
- Identify social supports

Slide 45

Managing HIV and Substance Use: Case Studies



- Identify key adherence issues
- Consider adherence barriers and supports
- Set realistic goals
- Highlight HIV health concerns
- Develop a tailored HIV health and adherence plan

Slide 46

3. Divide the participants into groups of five to seven people. In forming the groups, try to ensure that each group includes people representing a range of disciplines, such as physicians, nurses, substance abuse treatment providers, case managers, and so forth. This approach will give participants the opportunity to practice working as part of an interdisciplinary team.
4. Depending on time examine 1-3 case studies. Give the participants 12 minutes to work on their cases, and allow five minutes each for the small groups to present their cases to the entire group. To save time, use Slides 47 through 51 to provide brief synopses of the cases and ask participants to focus mainly on the information and issues contained in the slides.

Case Study 1: Melissa

- 25 years old
- Commercial sex worker
- Injects heroin 3-4 times/day
- Intermittently incarcerated
- Recent 15 pound weight loss
- History of STDs and respiratory infections.
- Smoker - 1 pack/day
- CD4 count = 480/mm³
- Viral load = 45,000 copies/mL

Slide 47

Case Study 2: Raymond

- 50 years old
- Corporate manager
- Married with teenage children
- Alcoholic and occasionally uses cocaine
- HCV co-infected
- Drug and alcohol free for 6 months
- CD4 count = 350/mm³
- Viral load = 85,000 copies/mL

Slide 48

Case Study 3: Krista

- 35 years old
- Homeless
- Smokes crack daily
- Alcoholic
- Connected with shelter/meal program
- Earlier connection with Department of Mental Health
- CD4 count = 50/mm³
- Viral load = 380,000 copies/mL

Slide 49

Case Study 4: Marlon

- 21 years old
- MSM with HIV-infected partner
- Attends circuit parties and has anonymous sex
- Diagnosed at age 17 years
- Recent genotype test indicates resistance
- Feels like a “failure”
- CD4 count = 300/mm³
- Viral load = 90,000 copies/mL

Slide 50

Case Study 5: Rosanna

- 60 years old
- Living with AIDS and HCV
- Recovery from heroin for 8 years
- Currently on MMTP (120 mg)
- Raising grandchildren who are not aware of her health status
- Involved with church
- Attending college classes to obtain degree
- Viral load = undetectable on treatment
- Interested in HCV therapy

Slide 51

5. In each of the five cases, participants should try to identify the following types of issues:
 - *Lifestyle and psychosocial issues* that present barriers or supports to medication adherence and HIV health.
 - *Medical issues* that may affect the person’s access to health care, his or her baseline health status, or the appropriateness of treatment recommendations or present therapy in his or her particular situation.
 - *Specific issues related to substance use*, including the drug of choice, drug interactions, timing of drug use, and stage of recovery.

Following each case, a list of suggested questions and planted issues are given to help facilitate discussion.

6. Note that the case studies do not give information on the race and ethnicity of the persons discussed. This was done intentionally to allow instructors to adjust the scenarios in ways that address the circumstances of different population groups. However, the case studies do include information about each person’s age, gender, sexuality, incarceration history, housing

status, and drug of choice. Participants should be encouraged to consider the extent to which social and cultural issues are relevant to HIV adherence and health promotion.

7. Keep in mind that these cases do not necessarily reflect the standard of care for prescribing HIV medications, including the timing of therapy and the specific medications selected by the health care provider in each scenario. Part of the challenge of this exercise is to determine what role the social service provider has in responding to medical information.
8. Also, note that each case also has specific instructor's notes that the participants should not receive.

Handout 9: Case Studies for Small Group Exercise

Case Study 1: Melissa

Melissa is a 25-year-old woman living with HIV. She is a heroin user, has never been in a methadone maintenance program, has been incarcerated intermittently, and smokes about a pack of cigarettes each day. She works in the commercial sex industry and lives with roommates in a small apartment. Only one of her roommates is aware of her HIV status. She uses heroin three to four times a day. Melissa receives her HIV care from a local community health center, and goes to the doctor at least every few months when she's not in jail. Most of her visits to the doctor are prompted by symptoms consistent with either sexually transmitted diseases (STDs) or upper respiratory infections. Melissa has health insurance coverage through the state's Medicaid program.

Melissa's most recent CD4 count was 480/mm³ and her viral load was 45,000 copies/mL. Her current health problems include genital herpes and an upper respiratory infections. Melissa has been on and off antibiotics for the past year during episodes of pneumonia, and she takes acyclovir to manage the herpes infection. Melissa went to see her doctor last week because she was concerned about a weight loss of 15 pounds during the past month. At that appointment, her doctor suggested that she "just start eating more and try to stay out of jail." The doctor also recommended that she begin antiviral therapy "right away" and gave her a prescription for efavirenz and Combivir (lamivudine plus zidovudine). Melissa thinks her doctor may be angry with her because she recently started using heroin again. Melissa also isn't sure whether she should trust her doctor's advice. Melissa comes to meet with you and asks what you think about her situation.

Discuss the Following Questions

- Is it appropriate for the provider to prescribe ART now?
- What factors would make you *not* want Melissa to begin HIV medications?
- What factors would make you want her to start medications?
- What are some ways in which you could help Melissa adhere to treatment (in the broadest sense of the word)?

Planted Issues

- Safer sex with a sex worker's "clients"
- Confidentiality and Melissa's nondisclosure of her status at home
- Symptom-driven contact with medical sector
- Doctor-patient communication issues, including trust and access to care
- Health care plan during incarceration
- Connection to methadone maintenance program

Case Study 2: Raymond

Raymond is a 50-year-old man living with HIV and Hepatitis C (HCV). He works full time as a corporate manager and is married with two teenage children. His family is aware of his HIV status. He is an alcoholic and occasionally uses cocaine. He was first diagnosed with HCV in 1990, when it was still referred to as non-A, non-B hepatitis. He first tested positive for HIV during a stay in drug treatment in 1995.

Raymond has excellent health insurance through his employer, but no one at work is aware of either his HIV or HCV status. He is prone to relapse, especially during periods of stress at home or work, and often drops out of contact for days at a time. He's been sober from alcohol and cocaine for six months. At his last appointment, Raymond's doctor suggested he begin antiviral therapy because his numbers were "taking a turn for the worse." His most recent CD4 count was 350/mm³, and his viral load was 85,000 copies/mL. Raymond's liver function tests remain within a normal range. Raymond wants to start therapy and is anxious to stay healthy for his wife and kids, but he is concerned that he won't be able to stick with a regimen. His doctor has prescribed indinavir, ritonavir, lamivudine, and stavudine. Raymond comes to meet with you and asks whether you think he can handle the suggested ART regimen. He confides that he's been feeling "very vulnerable lately" and that he "really wants to drink."

Discuss the Following Questions

- Is it appropriate for the provider to prescribe ART now?
- What factors would make you *not* want Raymond to begin HIV medications?
- What factors would make you want him to start medications?
- How should you talk with Raymond about his concerns about being able to "handle" an HIV regimen?
- What are some ways you could help Raymond adhere to treatment?

Planted Issues

- HCV coinfection
- Alcohol use and adherence
- Cocaine use and adherence
- Relapse planning
- Sobriety and decision-making about ART
- Doctor's selection of a regimen containing indinavir and ritonavir; concerns about fluid requirements for indinavir and storage of ritonavir in a refrigerator

Unstable lifestyle and adherence

Case Study 3: Krista

Krista is a 35-year old woman living with HIV. She is currently homeless, and typically stays on the street, in crack houses, or in “wet” shelters. Krista sometimes stays at her mother’s home, but she can only go there when she is sober. Krista uses crack cocaine and is an alcoholic. She drinks whatever she can get, and she typically uses crack in the evenings when she gets bored and lonely and “hits the streets.” Krista considers herself a loner, but she has connected with a local street outreach program that provides free lunches, as well as day shelter services in the winter. At one point, Krista was also connected with the local Department of Mental Health (DMH) and was diagnosed with bipolar disorder, but she did not follow up with mental health support treatment. She is not on psychotropic medications.

Krista receives her HIV care from the public health clinic connected with a major urban medical center. She goes to the doctor often because she thinks he is very kind, she likes the medical staff, and she appreciates being able to hang out in the waiting room and watch TV. Krista’s doctor is very concerned about her plummeting CD4 count (now at 50/mm³) and her high viral load, which is 380,000 copies/mL. Last year, her doctor put her on trimethoprim/sulfamethoxazole (more commonly known by the trade name Bactrim) and now wants to add antiretrovirals. He gives her a prescription for nelfinavir and Combivir (lamivudine plus zidovudine), in addition to the antibiotic azithromycin. He also tells her to keep taking the trimethoprim/sulfamethoxazole. Krista is scared and doesn’t understand why she needs this treatment. She asks you for help.

Discuss the Following Questions

- Is it appropriate for the provider to prescribe ART now?
- What factors would make you *not* want Krista to begin HIV medications?
- What factors would make you want Krista to start medications?
- What are some ways you could help Krista adhere to treatment (in the broad sense of the word)?

Planted Issues

- Challenges of homelessness
- Mental illness and adherence
- Potential to build on the positive relationship with her doctor and other medical staff
- Urgency of prophylaxis because of low CD4 count
- Potential to incorporate street supports into adherence plan
- Fear, anxiety, and lack of understanding about treatment need to be addressed
-

Case Study 4: Marlon

Marlon is a 21-year-old man who has unprotected sex with other men who are infected with HIV. He works at a fast-food restaurant. He attends circuit parties, likes to have anonymous sex, and uses recreational drugs at parties only. He has a steady boyfriend who is also infected with HIV and taking ART. They live together in a studio apartment. Marlon was diagnosed with HIV infection when he was 17 years old. At that time, he had a CD4 count of $180/\text{mm}^3$ and a viral load of 80,000 copies/mL.

His doctor started him on therapy almost immediately with zidovudine, lamivudine, and nevirapine, as well as trimethoprim/sulfamethoxazole. Until recently, Marlon's HIV treatment was very successful. His viral load was undetectable, and his CD4 count was back up to $400/\text{mm}^3$. In fact, Marlon was doing so well that his doctor told him he could stop taking trimethoprim/sulfamethoxazole. Unfortunately, Marlon's last few blood tests have indicated that his viral load is rising. Marlon's most recent viral load was 90,000 copies/mL, and his CD4 count is down to $300/\text{mm}^3$. Marlon's doctor performs a genotype test, which shows that his HIV infection is now resistant to nevirapine and lamivudine. His doctor suggests a switch in therapy to stavudine, abacavir, ritonavir, and indinavir. Marlon is devastated and feels like a failure, especially when he compares himself with his partner, who is still doing very well on his medications. Marlon doesn't understand what he's doing wrong.

Discuss the Following Questions

- How would you approach Marlon when you discuss adherence with him?
- How would you assess his adherence?
- What specific questions would you ask him?
- What are some ways in which you could help Marlon improve his adherence to treatment?

Planted Issues

- Drug interactions between recreational drugs and ritonavir
- Feelings concerning "treatment failure"
- Individual responses to therapy
- Possibility of HIV superinfection and the importance of safer sex between HIV-infected partners.
- Significance of genotype test

Case Study 5: Rosanna

Rosanna is a 60-year-old woman living with AIDS and HCV infection. She is a heroin addict who has been in recovery for eight years. Rosanna is currently in a methadone maintenance program and is dosed every morning at 7 a.m. She had to increase her methadone dose to 120 mg last year when she started getting dope sick. Rosanna is also a grandmother and has been raising her three grandchildren on her own since her daughter died two years ago. She receives a monthly SSDI check and also has a Section 8 subsidy to help pay the rent on her spacious three-bedroom apartment.

Rosanna is very busy attending to her grandkids' school and activities, maintaining the household on her own, and volunteering at her church. She has also been taking classes at a local community college with the goal of obtaining an associate degree. Rosanna hopes to go back to work as a human service professional or a community organizer. She is very closeted about her HIV status, especially in church and around the grandchildren. However, the staff at the methadone clinic are aware of her status, and she also told some fellow classmates at school. Rosanna started taking antiretroviral drugs last year, but she has had a hard time sticking to her complex regimen of didanosine, stavudine, ritonavir, and amprenavir. Even though Rosanna's viral load is now undetectable, she would like to change to an easier HIV regimen, but she's afraid to ask her doctor about this. Rosanna also thinks that her doctor is not paying attention to her HCV. She has heard about interferon-based combination therapy for her HCV infection, but her doctor has never brought it up. She asks for your advice.

Discuss the Following Questions

- How would you approach Rosanna when you discuss adherence with her?
- How would you assess her adherence?
- What specific questions would you ask her?
- What are some of Rosanna's potential barriers to adherence? What supports for adherence does she have?
- What could you suggest to make it easier for Rosanna to adhere to her HIV medications?

Planted Issues

- Drug interactions between methadone and antiretrovirals
- HCV coinfection
- Adherence challenges and supports associated with a busy lifestyle (juggling the demands of kids, work, and household)
- Support and confidentiality in various settings – and their impact on adherence
- Doctor-patient communication about the complexity of the regimen and options for change

Instructor Notes for Melissa

The goal in this case is to facilitate a discussion about the variety of issues facing Melissa. Some of the key lifestyle and psychosocial issues include Melissa's intermittent incarceration and commercial sex work. Both of these issues may have serious health implications. Incarceration can interfere with adherence to both antiretroviral and preventative medications if medications are stopped or unavailable during periods of incarceration. Since Melissa is involved with commercial sex work, her provider should try to engage her in a discussion about prevention issues for people infected with HIV (also called "positive prevention"). The provider should also try to talk with Melissa about the specific health risks she may face as a commercial sex worker (evidenced by her recurrent STDs) as well as her options for negotiating safer sex.

It should also be noted that, according to her most recent blood work, Melissa does not meet the current guidelines for antiretroviral therapy: her CD4 count is greater than 350/mm³ and her viral load is below 55,000 copies/mL. Participants should be encouraged to discuss why Melissa's doctor might think therapy is appropriate at this time, including the possibility that Melissa's provider is not an HIV specialist and may not be familiar with current clinical recommendations.

Other medical issues that the participants should consider include the antiretroviral medications chosen for Melissa, the significance of her recent weight loss, her continued smoking, and her history of respiratory infections. Participants should also be encouraged to be critical of the provider-patient relationship in this case, since Melissa may be receiving suboptimal care. Also ask participants to identify Melissa's opportunities and barriers to accessing high-quality HIV care.

In addition, we know from her case that Melissa has taken antibiotics in the past and currently uses acyclovir for herpes. When assessing Melissa's readiness to start HIV medications, it would be worthwhile to ask about her adherence experience with antibiotics and acyclovir. It would also be useful to ask whether Melissa's ongoing substance use affects her ability to adhere to medications and access medical care. We know that Melissa uses heroin three to four times a day. The participants may note the Melissa could use her heroin use as cues for taking her HIV medications. Participants should also consider how Melissa feels about starting ART, as well as her willingness to consider drug treatment as part of her HIV health and adherence plan.

Instructor Notes for Raymond

Raymond's case is complex because of the psychosocial and medical issues he faces, including his polysubstance use (both alcohol and cocaine). As the instructor, it is important not to have the unrealistic expectation that all of Raymond's issues will be addressed in the short time available. Instead, this case should be seen as a rich opportunity to explore a wide variety of issues.

Participants should pay special attention to Raymond's work and family situation and consider the impact that his "disclosure status" concerning his HIV and HCV infection may have on his ability to adhere to medications. Participants should also consider the unique challenges related to his corporate lifestyle, the adherence barriers associated with full-time employment, and the strategies Raymond might adopt to help him adhere to ART in a workplace where he is not open about his status.

Clearly, one of the major issues facing Raymond is the nature of his substance use. Cocaine and alcohol have negative effects on adherence rates because of the way they are used (sporadically and inconsistently). In addition, heavy alcohol use can lead to memory lapse and periods of blackout. Although Raymond has been drug-free for six months, participants should still pay special attention to his risk for relapse, the importance of stress as a trigger for his drug use, and his tendency to "disappear" when he picks up. Participants should discuss strategies for determining other aspects of Raymond's "treatment readiness."

Participants should also be encouraged to consider the variety of medical issues that Raymond faces. He is coinfecting with HCV and HIV, which places him at risk for accelerated HCV disease progression. His alcohol consumption presents a major health risk. Another point to notice is the selection of ritonavir as part of his treatment regimen. Ritonavir is known to be especially hard on the liver and is probably not an ideal choice for someone with pre-existing liver disease and a history of alcohol abuse.

On the other hand, ritonavir is a powerful antiretroviral in terms of efficacy, and may be more forgiving than other protease inhibitors in terms of missed doses and the risk of viral resistance. Although some providers would elect to start ART when the CD4 count and viral load have reached the levels seen in Raymond, others would not. The most recent guidelines indicate that treatment should be offered, but controversy exists. Participants should carefully consider his provider's decision to prescribe therapy at this stage and may question whether the provider is aware of the extent of Raymond's substance use.

Instructor Notes for Krista

The challenge in this case is to identify both the barriers and – perhaps more important – the supports for HIV adherence and health promotion in Krista’s life. For example, we know that Krista has a relationship with her mother, is connected with outreach and shelter services, had a previous connection with DMH, and seems to have an open and positive relationship with her medical provider. However, both her homelessness and mental health status are important psychosocial challenges that participants need to recognize and discuss.

Krista also has some complex and urgent medical issues: Her CD4 count is low (50/mm³), and her viral load is high (380,000 copies/mL). Because we know that Krista’s doctor prescribed trimethoprim/sulfamethoxazole last year, we can assume that her CD4 count has been low at least since then. Encourage participants to consider why Krista’s doctor decided to prescribe ART now even though he didn’t prescribe it earlier. Also ask them to think about approaches for determining Krista’s readiness for ART. For example, how well has she been adhering to her trimethoprim/sulfamethoxazole? Guide the participants to ensure that they spend some time devising strategies to support Krista’s efforts to stay healthy and to determine whether antiretroviral therapy is right for her at this stage. Also ask participants to consider interventions that might help Krista adhere to her medications if she decides to start ART at this time. For example, they might suggest linking adherence cues with Krista’s participation in the outreach program, and helping her reconnect with DMH services, and encouraging her to try a “mock or rehearsal regimen.” By ‘rehearsing’ their regimen, people can see whether they are ready to start treatment and learn ways to improve their adherence before starting the actual drugs.

Participants might lose sight of Krista’s substance use issues when they consider everything else she is facing. Encourage participants to talk about the nature of her substance use, to discuss whether drug treatment is appropriate for her, whether she should initiate psychiatric treatment, and to consider the specific health and adherence challenges arising from Krista’s continuing alcohol and crack use. Remind them that the focus should be on adherence challenges, supports, and interventions.

Instructor Notes for Marlon

A discussion of adherence in Marlon's case can focus on his experience with taking medications during the past four years. Since Marlon was able to maintain an undetectable viral load until recently, in all likelihood he had been adherent to his medications. Participants should consider what factors may have contributed to the current failure of his treatment. The possibilities include recent nonadherence to his regimen or the development of viral resistance despite excellent adherence. It is important that participants discuss the latter possibility – that even “perfect” adherence does not lead to viral suppression 100% of the time.

Participants should be prompted, if necessary, to discuss some other important medical issues about Marlon's case. Marlon's doctor stopped his trimethoprim/sulfamethoxazole treatment when his CD4 count rose back to a safe level – typically over 300/mm³ or 400/mm³. Marlon may not understand why this medication was stopped and then later restarted when his CD4 count declined. The rapid and sudden increase in Marlon's viral load is evidence that his HIV infection has developed resistance to his current medications, which is further evidenced by the results of his genotype test. Make sure that participants understand what a genotype test is – a blood test that looks at the genetic structure of a person's virus to identify mutations that are believed to confer resistance to specific antiretroviral medications.

Marlon is also facing some psychosocial issues, including his relationship with his partner and his feelings of personal failure since his medications stopped working. There is an opportunity here for participants to identify important information to pass on to Marlon, such as how people may respond to medications differently (his experience versus his partner's experience), and how it is the medications that “fail,” not the people who take them. In addition, Marlon's disclosure about anonymous sex and recreational drug use should prompt a discussion about the possible health risks of these behaviors.

Marlon's doctor is proposing a new treatment regimen that includes ritonavir, a medication that is known to have potentially dangerous interactions with recreational drugs. Because Marlon is also engaging in unprotected sex with people whose HIV status he does not know, he risks transmitting the virus to others and potentially re-exposing himself to HIV, which can result in “superinfection” and possible accelerated HIV disease progression. Remind participants that, although there is only limited information about superinfection and interaction between ART and recreational drugs, these are important possibilities to consider.

Instructor Notes for Rosanna

There is no shortage of issues to discuss here. Don't expect that the participants will be able to address all issues in the limited time available. Participants should be guided, if necessary, to discuss some key psychosocial issues, including Rosanna's disclosure of her HIV and HCV status: She has told people at the methadone clinic and some friends at school, but not her grandchildren or members of her church. Be sure that the participants discuss how Rosanna's disclosure may affect her current and future adherence. Keep in mind that her current regimen seems to be working well (her viral load is undetectable), which indicates that she is probably adhering well but that she wants to change to something easier.

Participants may also question why Rosanna is taking such a complex regimen of HIV medications in the first place, since the case indicates that this is her first treatment combination. In addition, participants should pay special attention to the provider-patient relationship. The case indicates that Rosanna feels afraid to talk with her doctor about changing medications, and she also seems to think that her doctor may not be paying adequate attention to her HCV coinfection. Other medical issues in this case include the following: assessing the need for education about HIV and HCV coinfection, drug interactions between antiretrovirals and methadone, and strategies to talk with her medical provider about next steps. Regarding drug interactions, it is important to note that the increase in Rosanna's methadone dose may have been necessitated by drug interactions with ritonavir and amprenavir. Encourage participants to develop strategies to help Rosanna advocate for herself in the medical setting – perhaps by doing role plays with her or helping her develop a list of questions before her next appointment.

Other than Rosanna's participation in a methadone maintenance program, substance use issues are not paramount in this case. However, participants may consider ways to connect Rosanna's HIV and HCV health promotion behaviors with her successful recovery program. Participants should note that Rosanna has a lot going on in her life, including her commitments to her grandchildren, school, church, methadone maintenance, antiretroviral therapy – and now she is considering switching her HIV medications and starting interferon-based therapy for HCV. If necessary, prompt participants to consider what barriers to adherence Rosanna may face in the future, what existing supports she has, and what interventions might provide additional support for her health promotion efforts.

Session 8: Conclusion

Presentation: Take-Home Points

Purpose: To summarize the main points of this module

Time: 5 minutes

Materials: Slide 52, “Take-Home Points”

Instructor Notes

1. Briefly summarize the main themes concerning adherence in HIV-infected substance users (Slide 52). Be sure to include the following points:
 - Individualize treatment plans to each patient’s needs.
 - Recognize that there are specific challenges when working with HIV-infected substance users, but that these challenges can be overcome.
 - Consider the boundaries that non-medical providers face when they offer counseling on HIV adherence and health promotion.
 - Explore opportunities to link with providers across disciplines to strengthen adherence support for substance-using patients.
2. Take Q & A.

Take-Home Points

- Individualize treatment plans to each patient’s needs.
- Recognize the specific challenges of working with HIV infected substance users.
- Use knowledge and tools to overcome these challenges and to advocate for patients.
- Consider the boundaries for nonmedical providers offering HIV adherence and health promotion counseling.
- Explore opportunities to link with providers across disciplines to strengthen adherence support.

Slide 52

References

- Altice, F.L., Friedland, G.H., Cooney, E.L. (1999). Nevirapine induced opiate withdrawal among injection drug users with HIV infection receiving methadone. *AIDS*, 13(8), 957-962.
- Antoniou, T., Tseng, A.L. (2002). Interactions between recreational drugs and antiretroviral agents. *Annals of Pharmacotherapy*, 36(10), 1598-1613.
- Arnsten, J.H., Demas, P.A., Farzadegan, H., et al. (2001). Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: Comparison of self-report and electronic monitoring. *Clinical Infectious Diseases*, 33(8), 1417-1423.
- Arnsten, J.H., Demas, P.A., Grant, R.W., et al. (2002). Impact of active drug use on antiretroviral therapy adherence and viral suppression in HIV-infected drug users. *Journal of General Internal Medicine*, 17(5), 377-381.
- Bagasra, O., Pomerantz, R.J. (1993). Human immunodeficiency virus type 1 replication in peripheral blood mononuclear cells in the presence of cocaine. *Journal of Infectious Diseases*, 168(5), 1157-1164.
- Bamberger, J., Bangsberg, D., Chamber, D., et al. (June 2000). Adherence to HIV therapies: Critical issues. *Science to Community, Clinical #1*. University of California-San Francisco, San Francisco, California.
- Bart PA, Rizzardi PG, Gallant S, et al. Methadone blood concentrations are decreased by the administration of abacavir plus amprenavir. *Ther Drug Monit*. 2001 Oct;23(5):553-5.
- Broers, B., Morabia, A., Hirschel, B. (1994). A cohort study of drug users' compliance with zidovudine treatment. *Archives of Internal Medicine*, 154(10), 1121-1127.
- Beauverie, P., Taburet, A. M., Dessalles, M. C., et al. (1998). Therapeutic drug monitoring of methadone in HIV-infected patients receiving protease inhibitors. *AIDS*, 12(18), 2510-2511.
- Bruno, R., Sacchi, P., Puoti, M., et al. (2002). HCV chronic hepatitis in patients with HIV: Clinical management issues. *American Journal of Gastroenterology*, 97(7), 1598-1606.
- Carmona, A., Knobel, H., Guelar, A., et al. (2000). Factors influencing survival in HIV-infected patients treated with HAART [Abstract TuOrB417]. Presented at 13th International AIDS Conference, Durban, South Africa, July 9-14, 2000.
- Cedars-Sinai Medical Center. (2001). *Adherence Now: Best Practices and Practical Tools. Proceedings of a roundtable symposium in November 2001*. World Health CME, New York, New York.
- Centers for Disease Control and Prevention. (2002). Guidelines for using antiretroviral agents among HIV-infected adults and adolescents: Recommendations of the Panel on Clinical

Practices for Treatment of HIV. *MMWR*, 51(RR-7), 1-55.

(<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5107a1.htm>)

Centers for Disease Control and Prevention. (1998). Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: Principles of therapy and revised recommendations. *MMWR*, 47(RR-20), 1-58.

(<http://www.cdc.gov/mmwr/preview/mmwrhtml/00055357.htm>)

Chesney, M.A. Factors affecting adherence to antiretroviral therapy. (2000). *Clinical Infectious Diseases*, 30(Suppl 2), 171-176.

Chesney, M. (January 1999). The challenge of adherence. *Bulletin of Experimental Treatments for AIDS* 12(1), 10-13.

(<http://www.sfaf.org/treatment/beta/b39/b39adhere.html>)

Clarke S., Mulcahy F., Bergin C., et al. (2002). Absence of opioid withdrawal symptoms in patients receiving methadone and the protease inhibitor lopinavir-ritonavir. *Clinical Infectious Diseases*, 34(8), 1143-1145.

Clarke, S., Mulcahy, F., Tija, J., et al. (2001). The pharmacokinetics of methadone in HIV-positive patients receiving the non-nucleoside reverse transcriptase inhibitor efavirenz. *British Journal of Clinical Pharmacology*, 51(3), 213-217.

Department of Health and Human Services (DHHS). Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. March 23, 2004: 1-97. Accessed at http://www.aidsinfo.nih.gov/guidelines/adult/AA_032304.pdf on July 21, 2004.

Eldin, B.R., Seal, K., Lorvick, J., et al. (2001). Is it justifiable to withhold treatment for hepatitis C from illicit injection drug users? *New England Journal of Medicine*, 345(3), 211-214.

Ellis RJ, Childers ME, Cherner M, et al. Increased human immunodeficiency virus loads in active methamphetamine users are explained by reduced effectiveness of antiretroviral therapy. *J Infect Dis*. 2003 Dec 15;188(12):1820-6.

Elliot, A. Depression and HIV. (1997). Retrieved December 2002 at the Project Inform website at <http://www.projectinform.org>.

Ferrando, S.J. (2001). Substance abuse and HIV infection. *Psychiatric Annals*, 31(1), 57-62.

Fried, M.W., Shiffman, M.L., Reddy, K.R., et al. (2002). Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. *New Journal of Medicine*, 347(13), 975-982.

Gavrilin MA, Mathes LE, Podell M. Methamphetamine enhances cell-associated feline immunodeficiency virus replication in astrocytes. *J Neurovirol*. 2002 Jun;8(3):240-9.

- Gerber JG, Rosenkranz S, Segal Y, et al. Effect of ritonavir/saquinavir on stereoselective pharmacokinetics of methadone: results of AIDS Clinical Trials Group (ACTG) 401. *J Acquir Immune Defic Syndr*. 2001 Jun 1;27(2):153-60.
- Gordillo V., del Amo, J., Soriano, V., et al. (1999). Sociodemographic and psychological variables influencing adherence to antiretroviral therapy. *AIDS*, 13(13), 1763-1769.
- Golin, C.E., Liu, H., Hays, R.D., et al. (2002). A prospective study of predictors of adherence to combination antiretroviral medication. *Journal of General Internal Medicine*, 17(11), 756-765.
- Gourevitch, M.N., Friedland, G.H. (2000). Interactions between methadone and medications used to treat HIV infection: A review. *Mount Sinai Journal of Medicine*, 67(5-6), 429-436.
- Hales G, Roth N, Smith D. Possible fatal interaction between protease inhibitors and methamphetamine. *Antivir Ther*. 2000 Mar;5(1):19.
- Henry, J.A., Hill, I.R. (1998). Fatal interaction between ritonavir and MDMA. *Lancet*, 352(9142), 1751-1752.
- Harrington, R.D., Woodward, J.A., Hooton, T.M., et al. (1999). Life-threatening interactions between HIV-1 protease inhibitors and the illicit drugs MDMA and γ -hydroxybutyrate. *Archives of Internal Medicine*, 159(18), 2221-2224.
- Horn, G. (1998). Party favors – Do yourself one: Get the dope on the protease effect. *POZ*, 36. Available on the *POZ* web site at <http://www.poz.com/archive/june1998/partner/warning.html>
- Horn, T. (2001). HIV drug resistance and drug resistance testing: Just the FAQ's. *CRIA Update*, 10(4).
- Iribarne C, Berthou F, Carlhant D, et al. Inhibition of methadone and buprenorphine N-dealkylations by three HIV-1 protease inhibitors. *Drug Metab Dispos*. 1998 Mar;26(3):257-60.
- Landau, A., Batisse, D., Piketty, C., et al. (2001). Long-term efficacy of combination therapy with interferon-alpha 2b and ribavirin for severe chronic hepatitis C in HIV-infected patients. *AIDS*, 15(16), 2149-2155.
- Lauer, G.M., Walker, B.D. (2001). Hepatitis C virus infection. *New England Journal of Medicine*, 345(1), 41-51.
- McCance-Katz, E.F., Rainey, P.M., Jatlow, P., et al. (1998). Methadone effects on zidovudine disposition (AIDS Clinical Trials Group 262). *Journal of Acquired Immune Deficiency Syndrome Human Retrovirology*, 18(5), 435-443.
- McCance-Katz EF, Rainey PM, Friedland G, Kosten TR, Jatlow P. Effect of opioid dependence pharmacotherapies on zidovudine disposition. *Am J Addict*. 2001 Fall;10(4):296-307.

McCance-Katz EF, Rainey PM, Friedland G, Jatlow P. The protease inhibitor lopinavir-ritonavir may produce opiate withdrawal in methadone-maintained patients. *Clin Infect Dis*. 2003 Aug 15;37(4):476-82. Epub 2003 Aug 01.

Murphy, E.L., Collier, A.C., Kalish, L.A., et al. (2001). Highly active antiretroviral therapy decreases mortality and morbidity in patients with advanced HIV disease. *Annals of Internal Medicine*, 135(1), 17-26.

Nasti, G., DiGennaro, G., Tavio, M., et al. (2001). Chronic hepatitis C in HIV infection: Feasibility and sustained efficacy of therapy with interferon alfa-2b and ribavirin. *AIDS*, 15(14), 1783-1787.

O'Connor, P.G., Selwyn, P.A., Schottenfeld, R.S. (1994). Medical progress: Medical care for injection-drug users with human immunodeficiency virus infection. *New England Journal of Medicine*. 331(7), 450-459.

Paterson, D.L., Swindells, S., Mohr, J., et al. (2000). Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of Internal Medicine*, 133(1), 21-30.

Peterson, P.K., Gekker, G., Chao, C.C., et al. (1991). Cocaine potentiates HIV-1 replication in human peripheral blood mononuclear cell cocultures. *Journal of Immunology*, 146(1), 81-84.

Peterson, P.K., Gekker, G., Chun, C.C., et al. (1992). Cocaine amplifies HIV-1 replication in cytomegalovirus-stimulated peripheral blood mononuclear cell cocultures. *Journal of Immunology*, 149(2), 676-680.

Project Inform. (May 1996). Building a cooperative doctor/patient relationship. Retrieved December 2002 at the Project Inform website
<http://www.projectinform.org/pdf/doctorpatient.pdf>.

Rainey, P.M., Friedland, G., McCance-Katz, E.F., et al. (2000). Interaction of methadone with didanosine and stavudine. *Journal of AIDS*, 24(3), 241-248.

Rainey PM, Friedland GH, Snidow JW, et al. The pharmacokinetics of methadone following co-administration with a lamivudine/zidovudine combination tablet in opiate-dependent subjects. *Am J Addict*. 2002 Winter;11(1):66-74.

Reiter, G.S., Stewart, K.E., Wojtusik, L., Hewitt, R., Segal-Maurer, S., Johnson, M., et al. (2000). Elements of success in HIV clinical care: Multiple interventions that promote adherence. *Topics in HIV Medicine*. 8(5), 21-30.

Richman, D. D., Bozette, S., Morton, S., Chien, S., Wrin, T., Dawson, K., Hellmann, N. "The Prevalence of Antiretroviral Drug Resistance in the U.S." (Abstract LB-17), 41st Interscience Conference on Antimicrobial Agents and Chemotherapy, 2001.

Roth, M.D., Tashkin, D.P., Choi, R., et al. (2002). Cocaine enhances human immunodeficiency virus replication in a model of severe combined immunodeficient mice implanted with human peripheral blood leukocytes. *Journal of Infectious Diseases*, 185(5), 701-705.

Samet, J.H., Libman, H., Steger, K.A., et al. (1992). Compliance with zidovudine therapy in patients infected with human immunodeficiency virus, type 1: A cross-sectional study in a municipal hospital clinic. *American Journal of Medicine*, 92(5), 495-502.

Selwyn, P.A., Hartel, D., Lewis, V.A., et al. (1989). A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. *New England Journal of Medicine*, 320(9), 545-550.

Selwyn, P.A., Feingold, A.R., Hartel, D., et al. (1988). Increased risk of bacterial pneumonia in HIV-infected intravenous drug users without AIDS. *AIDS*, 2(4), 267-272.

Shapiro, M.F., Morton, S.C., McCaffrey, D.F., et al. (1999). Variations in the care of HIV-infected adults in the United States: Results from the HIV Cost and Services Utilization Study. *JAMA*, 281(24), 2305-2315.

Shelton MJ, Cloen D, DiFrancesco R, et al. The effects of once-daily saquinavir/minidose ritonavir on the pharmacokinetics of methadone. *J Clin Pharmacol*. 2004 Mar;44(3):293-304.

Sherer, R. (1998). Adherence and antiretroviral therapy in injection drug users. *JAMA*, 280(6), 567-568.

Soto, B., Sanchez-Quijano, A., Rodrigo, L., et al. (1997). Human immunodeficiency virus infection modifies the natural history of chronic parenterally-acquired hepatitis C with an unusually rapid progression to cirrhosis. *Journal of Hepatology*, 26(1), 1-5.

Strathdee, S.A., Palepu, A., Cornelisse, P.G., et al. (1998). Barriers to use of free antiretroviral therapy in injection drug users. *JAMA*, 280(6), 547-549.

Staszewski, S., Haberl, A., Gute, P., et al. (1998). Nevirapine/didanosine/lamivudine once daily in HIV-1-infected intravenous drug users. *Antiviral Therapy*, 3(Suppl 4), 55-56.

Stein, J.A., Gelberg L. (1997). Comparability and representativeness of clinical homeless, community homeless, and domiciled clinic samples: Physical and mental health, substance use, and health services utilization. *Health Psychology*, 16(2), 155-162.

Stevens RC, Rapaport S, Maroldo-Connelly L, Patterson JB, Bertz R. (2003). Lack of methadone dose alterations or withdrawal symptoms during therapy with lopinavir/ritonavir. *J Acquir Immune Defic Syndr*. Aug 15;33(5):650-1.

Stone, V.E. (2001). Strategies for optimizing adherence to highly active antiretroviral therapy: Lessons from research and clinical practice. *Clinical Infectious Diseases*, 33(6), 865-872.

Sullivan L. Drug interaction guide: Opioids and HIV antiretroviral agents. Draft. July 22, 2004. Supported by NY/NJ AETC, HRSA.

Urbina A, Jones K. (2004). Crystal methamphetamine, its analogues, and HIV infection: medical and psychiatric aspects of a new epidemic. *Clin Infect Dis*. Mar 15;38(6):890-4.

Walsh, J.C., Hertogs, K., Gazzard, B. (2000). Viral drug resistance, adherence and pharmacokinetic indices in HIV-1 infected patients on successful and failing protease inhibitor (PI) based highly active antiretroviral therapy (HAART) [Abstract 699]. Presented at the 40th Interscience Conference of Antimicrobial Agents and Chemotherapy, Toronto, Canada, September 17-20, 2000, 294.

Whalen, C., Horsburgh, C.R., Hom, D., et al. (1995). Accelerated course of human immunodeficiency virus infection after tuberculosis. *American Journal of Respiratory Critical Care Medicine*, 151(1), 129-135.

Williams, A., Friedland, G. (1997). Adherence, compliance, and HAART. *AIDS Clinical Care*, 9(7), 51-54, 58.

Reading List

University of California San Francisco. (2002). *Addressing the challenges of adherence. Navigating emerging challenges to long-term HIV therapy*. World Health CME, New York, New York.

Chesney, M.A. Factors affecting adherence to antiretroviral therapy. (2000). *Clinical Infectious Diseases*, 30(Suppl 2), 171-176.

Chesney, M. (January 1999). The challenge of adherence. *Bulletin of Experimental Treatments for AIDS* 12(1), 10-13.

(<http://www.sfaf.org/treatment/beta/b39/b39adhere.html>)

O'Connor, P.G., Selwyn, P.A., Schottenfeld, R.S. (1994). Medical progress: Medical care for injection-drug users with human immunodeficiency virus infection. *New England Journal of Medicine*. 331(7), 450-459.

Project Inform. (October 2002). Adherence: Keeping up with your meds. Retrieved December 2002 from the Project Inform website at <http://www.projectinform.org/pdf/adherence.pdf>.

Project Inform. (May 1996). Building a cooperative doctor/patient relationship. Retrieved December 2002 from the Project Inform website at <http://www.projectinform.org/pdf/doctorpatient.pdf>