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**HIV and Mental Illness:  
Which Came First?**

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Dr. Cournos has no conflicts of interest.



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## Learning Objectives

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- 1. Differentiate between patients who become HIV infected as a result of mental illness versus those who develop mental illness secondary to their HIV diagnosis.
- 2. Identify the major mental health diagnoses seen among patients infected with HIV.

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## Psychiatric Disorders Often Precede HIV Infection

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## Global HIV Epidemics: WHO Definitions

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- **Concentrated epidemics**
  - HIV prevalence consistently >5% in at least one defined sub-population and <1% in pregnant women
- **Generalized epidemics**
  - HIV prevalence consistently > 1% among pregnant women

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## Concentrated Epidemics

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- **Subpopulations involved**
  - Injection drug users (IDU)
  - Men who have sex with men (MSM)
  - Sex workers (SW)
  - Partners of the above three groups

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## Psychiatric Diagnoses among Injection Drug Users

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- 87-100% of opioid users meet lifetime criteria for a current and/or lifetime diagnosis of substance abuse or dependence. Many have multiple such diagnoses.
- Between 50-80% of opioid users meet criteria for at least one non-substance use psychiatric disorder, most commonly antisocial personality and mood disorders.
- Distinguishing psychiatric disorders that are manifestations of drug use/withdrawal from independent psychiatric disorders is challenging.

## Substance Use Disorders Among Opioid Users

- Brooner: 716 opioid abusers in methadone Rx in Baltimore
- Lifetime rates of drug dependence were:
  - Opioids: 100%
  - Cocaine: 65%
  - Cannabis: 51%
  - Alcohol: 50%
  - Sedatives: 45%
  - Stimulants: 19%
  - Hallucinogens: 18%

Brooner et al. Arch. Gen. Psych. 1997

## Psychiatric Diagnoses Among Men Who Have Sex With Men

Most studies of MSM show higher rates of the following disorders when compared to their heterosexual counterparts:

- Depression
- Anxiety disorders
- Alcohol and other substance disorders
- Suicide risk/attempts

## Psychiatric Disorders Among Sex Workers

- Sex-workers have elevated rates of physical and sexual traumas both during childhood and in the context of sex-workers. Physical and sexual traumas are risk factors for mental disorders.
- Elevated rates of psychiatric disorders among sex-workers include:
  - Substance abuse and dependence
  - Suicide risk/attempts
  - PTSD and other anxiety disorders
  - Mood disorders

## Overlap among Vulnerable Populations Example: Substance Use and Prostitution

- Burnett, et al studied 1,606 women and 3001 men entering substance use treatment across the U.S.
- Rates of self reported prostitution were:
  - Past year: 41% of women and 11% of men
  - Lifetime: 51% of women and 19% of men
- In both men and women, prostitution was associated with higher levels of mental health symptoms, injection drug use, and HIV infection

Burnett et al, Arch. Gen. Psych. 2008

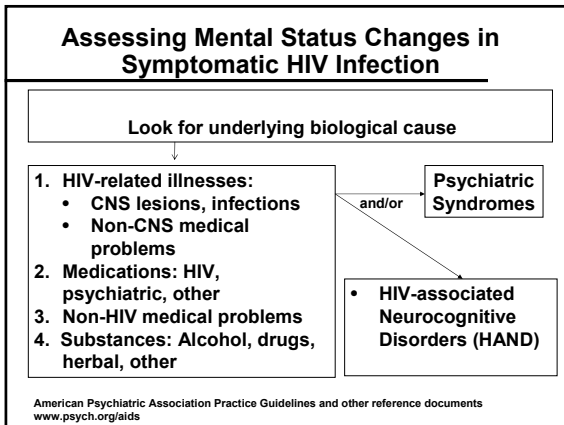
## HIV Among People with Severe Mental Illness: Summary of U.S. Studies

- Rates of HIV Infection (3%-23%) > general population
- ↑ Rates of unsafe sexual behavior
- ↑ Rates of co-morbid alcohol/drug use
- Intermittent IDU:
  - 1%-8% recent
  - 4%-26% lifetime
- HIV Infection Rates by Type of Drug Use
  - Injected drugs 33.8%
  - Non-Injected drugs 15.4%
  - Alcohol only 10.9%

## Mental Health Problems Follow HIV Infection

### Neuropsychiatric Problems Associated with HIV/AIDS





### RAND HCSUS Study: 2,864 HIV-positive Medical Patients

<b>Any Psychiatric Disorder:</b>	<b>48%</b>
▪ Major depression	36%
▪ Dysthymia	27%
▪ Generalized anxiety disorder	16%
▪ Panic attack	11%
▪ Drug dependence	13%
▪ Problematic alcohol use	19%

Bing et al Arch. Gen. Psych. 2001

\*Later studies showed elevated rates of PTSD

### RAND HCSUS Study: 1,489 HIV-positive Medical Patients

- 27% took psychotropic medication:
  - 21% antidepressants
  - 17% anxiolytics
  - 5% antipsychotics
  - 3% psychostimulants
- About half of patients with depressive disorders did not receive antidepressants—African-Americans were overrepresented.
- Psychiatric disorders are therefore common and undertreated.

## Depression is the Most Common Psychiatric Disorder for which HIV+ Patients Seek Treatment

### Diagnosis of Depression in HIV: Affective vs. Somatic Symptoms

AFFECTIVE	SOMATIC
▪ Depressed mood	▪ Appetite/Weight loss
▪ Loss of interest	▪ Sleep disturbance
▪ Guilt, worthlessness	▪ Agitation/retardation
▪ Hopelessness	▪ Fatigue
▪ Suicidal ideation	▪ Loss of concentration

### Screening for Depression: PRIME-MD PHQ2

Over the last two weeks how often have you been bothered by any of the following problems:

- Little interest or pleasure in doing things.
  - 0=Not at all
  - 1=Several days
  - 2=More than half the days
  - 3=Nearly every day
- Feeling down, depressed or hopeless
  - 0=Not at all
  - 1=Several days
  - 2=More than half the days
  - 3=Nearly every day

The higher the score the more likely patient has depressive disorder.  
Kroenke et al, Med Care, 2003

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## Depression and its Association with Morbidity and Mortality

## Depression and Mortality

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HERS cohort (Ickovics et al JAMA 2001): 765 HIV+ women at 4 sites followed for up to 7 years

- Mortality predictors: chronic depression, CD4 count, HAART duration, age
- After adjusting for all other variables, women with chronic depressive symptoms were twice as likely to die as women with limited or no depressive symptoms

## Depression and Mortality

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WIHS cohort: 2,059 HIV + women

- Replicated HERS results: Chronic depressive symptoms associated with AIDS mortality (N = 1,761; Cook, 2004)
- Depression + illicit drug use, or recent drug use alone, associated with decreased HAART utilization (N = 1,710; Cook, 2007)

## The Effect of Depression Treatment on HIV Medical Outcomes

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- Use of antidepressants + MH therapy, or MH therapy alone, associated with increased HAART utilization (N = 1,371; Cook, 2006)
- Depression significantly worsens HAART adherence and HIV viral control. Compliant SSRI use is associated with improved HIV adherence and laboratory parameters (CD4 cell count and viral load). (Horberg, 2008)

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## What are the Causes and Approaches to Anxiety Among HIV+ People?



## Anxiety and Milestones of HIV Disease / Progression

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- Anxiety may be related to milestones:
  - HIV testing
  - News of HIV positive status
  - Appearance of first illness symptoms
  - Changes in CD4 count & viral load
  - Onset of AIDS-defining illness

## Anxiety May be Caused by Substance Use / Withdrawal

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### **USE:**

- Amphetamines
- Ecstasy
- Caffeine
- Cocaine
- Nicotine

### **WITHDRAWAL:**

- Alcohol
- Benzodiazepines
- Opiates

## Questions to Identify Anxiety

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- Do you often worry or feel nervous?
- Are you often fearful of interacting with other people?
- Do you ever feel jittery, short of breath, or like your heart is racing?
- Do you ever feel as if you might lose control or fear that you may be “losing it”?

References and more tools: [www.hivguidelines.org](http://www.hivguidelines.org)

## Questions to Identify PTSD

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In your life, have you ever had any experience that was so upsetting, frightening, or horrible that you:

- Have nightmares about it or think about it when you do not want to?
- Try hard not to think about it or go out of your way to avoid situations that remind you of it?
- Are constantly on guard, watchful, or easily startled?
- Feel numb or detached from others, activities, or your surroundings?

References and more tools: [www.hivguidelines.org](http://www.hivguidelines.org)

## Screening for Substance Use: Cage-AID (CAGE Adapted to Include Drugs)

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Target Population: Adults and Adolescents > 16

- Have you ever felt the need to *Cut* down on your use of alcohol or drugs?
- Has anyone *Annoyed* you by criticizing your use of alcohol or drugs?
- Have you ever felt *Guilty* because of something you've done while drinking or using drugs?
- Have you ever taken a drink or used drugs to steady your nerves or get over a hangover (*Eye-opener*)?

A total of  $\geq 2$  may be suggestive of a problem.

References and more tools: [www.hivguidelines.org](http://www.hivguidelines.org)

## Management of Anxiety

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- Try non-pharmacological strategies first—stress reduction techniques, psychosocial support, etc.
- Reduce / discontinue anxiety-provoking substances
- Consider CBT, IPT and other EBT interventions if available

## Using Psychotropic Medication with HIV+ People: Brief Summary

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Medically asymptomatic and not on antiretroviral treatment

- Most psychotropics can be used as usual
- Monitor use of typical antipsychotics for increased incidence of extrapyramidal side effects
- Evaluate for testosterone deficiency if depressed or fatigued

## Using Psychotropic Medication with HIV+ People: Brief Summary

### Medically Ill and/or on antiretroviral treatment

- For most psychotropics, start with low doses and increase slowly
- Check for interactions and overlapping toxicities between psychotropics and antiretrovirals
- Protease inhibitors are especially potent inhibitors of cytochrome P450 enzymes—use caution

## Medications for Depression/Anxiety

### ▪ Pharmacology of Depression

- Caution in adolescents and young adults under 24 y.o.
- SSRIs – most studied in HIV
- SNRIs
- TCAs
- Other antidepressants
- Atypical antipsychotics/mood stabilizers for bipolar depression

### ▪ Pharmacology of Anxiety

- Decrease caffeine, nicotine and stimulant use
- Antidepressants, especially SSRIs
- Buspirone
- Benzodiazepines – fewest drug interactions with lorazepam, oxazepam and temazepam

[www.psych.org/aids](http://www.psych.org/aids)

## Pharmacotherapy of Psychosis

- Older neuroleptics – high rates of extrapyramidal side effects
- Newer “atypical” antipsychotics – easier to use, but have metabolic complications

American Psychiatric Association Practice Guidelines and other reference documents [www.psych.org/aids](http://www.psych.org/aids)

## Treatment of Mania

### ▪ Psychopharmacology

- Antipsychotics for acute management
- Mood stabilizers ± antipsychotics for long-term management:
  - Lithium – do not use if HIV nephropathy
  - Anticonvulsants, however,
    - Carbamazepine: potent CYP3A4 enzyme inducer, may decrease levels of PIs and NNRTIs - AVOID
    - Valproic acid: inhibitor of glucuronidation; increases zidovudine, but dosage adjustment not recommended
    - Consider side effects & toxicities; labs
  - Benzodiazepines as adjunct
- Electroconvulsive therapy (ECT)

Practice Guideline for the Treatment of Patients with Bipolar Disorder, 2<sup>nd</sup> Ed. Available online at <http://www.psychiatryonline.com/pracGuide/pracGuideHome.aspx>

## Use of Psychotropic Medications: Other Key Points

- Protease inhibitors increase the levels of many psychotropic medications including:
  - Newer sleep medications, including zolpidem/Ambien, zaleplon/Sonata, eszopiclone/Lunesta
  - Antianxiety agents, including most benzodiazepines and bupropion
  - Antidepressants, including most SSRIs, tricyclics, and trazadone
  - Stimulants
  - Antipsychotics
  - Lamotrigine
- Do not use benzodiazepines to treat delirium in medically ill HIV+ patients.

## Interactions Between Antiretrovirals and Alternative / Recreational Drugs

- Interactions can occur -- much is unknown
- Concerns about the interaction between ritonavir and ecstasy
- Methadone dose may need to increase (or, less often, decrease) depending on the antiretroviral regimen
- St. John's Wort may lower levels of NNRTIs and protease inhibitors

### Reported Neuropsychiatric Adverse Effects of Medications Commonly Used in HIV Infection

Medication	Neuropsychiatric Adverse Effect(s)
Zidovudine (AZT)	Insomnia, agitation, mania, depression
Didanosine (ddl)	Insomnia, agitation, mania, depression
Abacavir	Fatigue, depression, suicidal ideation, headache, psychosis
Nevirapine	Vivid dreams/nightmares, depression
Efavirenz	Depression, suicidal ideation, insomnia, vivid dreams/nightmares, anxiety, psychosis, cognitive dysfunction and antisocial behavior
Interferon alpha 2a and ribavirin	Depression, suicidal ideation, anxiety, sleep disturbance, fatigue, mania, psychosis, delirium, cognitive dysfunction

### HIV Associated Neurocognitive Disorders

*NIMH working group, Neurology 2007*

- Asymptomatic neurocognitive impairment (ANI),
- HIV-associated mild neurocognitive disorder (MND)
- HIV-associated dementia (HAD)
- Milder impairment is under-diagnosed and may be present even when patients are otherwise well controlled (e.g., stable ARV regimen, undetectable viral load): To date, no consistent diagnostics or therapeutics are available for this problem.

### Hepatitis C:

### Another Comorbidity of HIV, Mental Illness and Substance Use

### Hepatitis C (HCV) Infection

- HCV is over-represented among people with HIV/mental illness/substance use
- In the U.S., HCV infection is a leading cause of death among HIV-infected people
- HCV is neurotropic and replicates in the CNS
- HCV is associated with cognitive impairment even in the absence of liver failure
- HCV treatment (peginterferon + ribavirin) is associated with psychiatric morbidity

### Treating the Whole Person Involves the Integration of Care for Multiple Diagnoses

#### The Multiply Diagnosed Patient:

- HIV infection
- Substance use
- Other mental disorders
- Common non-HIV medical comorbidities, e.g., hepatitis C

### Educational Resources on HIV and Mental Health

- Local and national AETCs
- NYS AIDS Institute:  
[www.hivguidelines.org](http://www.hivguidelines.org)
- American Psychiatric Association Office of HIV Psychiatry:  
[www.psych.org/AIDS](http://www.psych.org/AIDS)
- HIV InSite  
<http://hivinsite.ucsf.edu>

## **AETC National Programs**

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- **National Resource Center (FXB/UMDNJ)**
  - Provides virtual library of online training resources for adaptation to meet local training needs
  - [www.aidsetc.org](http://www.aidsetc.org)
- **Warmline/PEpline (UCSF)**
  - Telephone consultation for HIV clinical management and post-exposure prophylaxis management
  - Warmline: 800-933-3413
  - PEpline: 888-448-4911

