BEING A ZERO: MENTAL ILLNESS AND HIV

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DISCLOSURES

- Warren Y.K. Ng, MD
  Zero Disclosures
DISCLOSURE OF UNLABELED USE

- This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. The planners of this activity do not recommend the use of any agent outside of the labeled indications.
- The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of the planners. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.
- In this activity the faculty do discuss the use of investigational antiretroviral agents and treatment regimens that are not approved by treatment guidelines.

SESSION OBJECTIVES

- Recognize the changing Mental Health challenges facing HIV-infected patients.
- Review the impact of depression on HIV/AIDS
- Review the diagnostic and screening tools for primary care and psychiatric issues
- Review strategies for treating depression, PTSD and dual diagnosed patients.
People with severe mental illnesses have a shortened life span, 15-25 years less than the general population.

Depression is associated with increased mortality among people who are medically ill.

A change in mental status, even in a person with well-established mental illness, should always prompt consideration of a medical problem.

Behavior that is disruptive in health care settings such as dual diagnosis and “drug seeking behaviors”

Non-adherence to HIV care and treatment.

Complex psychosocial needs, poor outcomes and poor quality of life despite adherence to HIV care and treatment.
Different presentations of psychiatric illnesses among HIV+ People

- Unipolar depression
- Anxiety disorders
- Alcohol/Substance use disorders
- Psychotic illnesses and bipolar disorder
- Stress disorders, including PTSD
- Somatic problems: insomnia, pain, fatigue, sexual dysfunction, body habitus changes
- Neuropsychiatric disorders due to opportunistic diseases, medication side effects, HIV itself (HIV-related neurocognitive disorders)

Reference documents at www.psych.org/aids and www.hivguidelines.org

MENTAL ILLNESSES MOST STRONGLY ASSOCIATED WITH POORER HIV/AIDS OUTCOMES IN PUBLISHED STUDIES

- Depression is associated with
  - Increased morbidity and mortality in its own right (HIV+ women with chronic depression twice as likely to die)
  - Failure to initiate antiretroviral treatment (ART)
  - Failure to adhere to ART once initiated
  - Slower virologic suppression
  - Increased sexual risk behavior

- Hazardous alcohol/substance use is associated with
  - Failure to initiate ART treatment
  - Failure to adhere to ART once initiated
  - Faster virologic failure
  - Increased sexual risk behavior
  - Increased mortality

Reference documents at www.psych.org/aids and www.hivguidelines.org
Depression and HIV

DEPRESSION IS A COMMON MEDICAL CO-MORBIDITIES OF HIV INFECTION

- Depression is present in about 30%-50% of HIV+ people in HIV care and treatment settings.

- Depression rates vary by study design (e.g. population, severity threshold, measurement tools, etc); they range from 0%-80%.

Sherr et al., Psychology, Health and Medicine, 2011 and other references
SEVERE DEPRESSION IS BEST CONCEPTUALIZED AS A MEDICAL CO-MORBIDITY OF HIV INFECTION

Major depression is as much a physical illness as it is a mental illness.

**AFFECTIVE**
- Depressed mood
- Loss of interest
- Guilt, worthlessness
- Hopelessness
- Suicidal ideation

**SOMATIC**
- Appetite/Weight loss
- Sleep disturbance
- Agitation/retardation
- Fatigue
- Loss of concentration

Evidence is emerging for a bidirectional relationship between depression and inflammation.

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**Depression Negatively Impacts the Immune System**

- Depression is associated with slower viral suppression on antiretroviral treatment (ART).

- Chronic depression is associated with increased morbidity and mortality (the likelihood of mortality doubles).

- This increase in morbidity and mortality was found prior to the availability of ART, so the effect is not simply explained by non-adherence to ART.

- We do not have studies that directly examine whether treating depression among people with HIV infection would improve lifespan (although emerging evidence shows lifespan improvement for cardiac disease).
Depression and HIV-related Mortality

HERS cohort: 765 HIV+ women at 4 sites in U.S. followed for up to 7 years

- Mortality predictors: chronic depression, CD4 count, antiretroviral treatment 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

Results repeated in other U.S. studies

Ickovics et al., JAMA, 2001 Cook et al., Am J Public Health, 2004

Depression and Mortality

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

- 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, 2007)

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

If the score is 3 or more, major depression is likely; consider further screening with the PHQ9.

Kroenke, et al. Medical Care 2003
Diagnostic Instrument for Depression: PHQ9 – Items Rated from 0-3

- 1. Little interest or pleasure in doing things
- 2. Feeling down, depressed, or hopeless
- 3. Trouble falling or staying asleep, or sleeping too much
- 4. Feeling tired or having little energy
- 5. Poor appetite or overeating
- 6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down
- 7. Trouble concentrating on things, such as reading the newspaper or watching television
- 8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual
- 9. Thoughts that you would be better off dead or of hurting yourself in some way

Spitzer et al. JAMA, 1999

ASSESSING MENTAL STATUS CHANGES

Look for underlying causes (or more than 1)

1. Medications: HIV, psychiatric
2. Substances: Alcohol, drugs
3. Non-HIV medical problems
4. HIV-related illnesses:
   - CNS lesions, infections
   - Non-CNS medical problems

Psychiatric Syndromes
- Personality Disorder

HIV-neuropsychiatric manifestations:
- Minor Cogn Motor Disorder
- HIV Assoc Dementia
## ENDOCRINOLOGICAL ISSUES

### Hypogonadism
- **Testosterone- patch/gel ("Low T")**
  - helpful in alleviating depressive symptoms with hypogonadism (especially fatigue, anorexia, and diminished libido).
  - Improvement in energy, mood, libido

### Hypothyroidism
- **Thyroid replacement**
- **Test: TSH, T3, T4, Free T**
- **Synthroid/Thyroxine**
  - Mimics symptoms of depression with fatigue, lethargy, weight gain, poor concentration, depressed mood

### Major Depressive episode 5+ symptoms 2 weeks

**DSM V**

- Depressed mood
- Loss of pleasure
- Weight change (5%)
- Insomnia/ hypersonnia
- Psychomotor agitation/retardation
- Fatigue
- Worthlessness/guilt
- Diminished ability thinking/ concentration
- Recurrent thoughts of death/ suicide
- Significant impairment
- Rule out other causes
PERSISTENT DEPRESSIVE DISORDER
(DYSTHYMIA)

- Depressed mood for most of the day for more days than not for 2 years
- While depressed 2+
  - Poor appetite/overeating
  - Insomnia/hypersomnia
  - Low energy/fatigue
  - Low self esteem
  - Poor concentration
  - Hopelessness
- Never without symptoms for 2 months
- Criteria for MDD may be present 2 years
- Never manic/hypomanic
- r/o Schizophrenia/etc
- Not substances/medical
- Impairment/distress

ANTIDEPRESSANTS: LIMITED STUDIES IN HIV TREATMENT; SSRIS ARE THE MOST STUDIED

- In general, SSRIs are well tolerated, safe, and have lower rates of drug discontinuation in studies with HIV-infected patients – all have equal efficacy.
- SSRIs have proven efficacy in clinical trials with HIV+ depressed patients.
- Avoid paroxetine in pregnancy (category D).
BIPOLAR MOOD DISORDERS
DSM V
OFTEN DEPRESSIVE EPISODES PRECEDE MANIA

- Bipolar Disorder
  - Type 1 mania (MDD plus mania)

  Manic episode 1 week, 3 or more: 4 if irritable

  1. Inflated self-esteem or grandiosity
  2. Decreased need for sleep (rested after 3 hours)
  3. More talkative than usual or pressure to keep talking
  4. Flight of ideas or subjective experience that thoughts are racing
  5. Distractibility
  6. Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
  7. Excessive involvement in activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

PSYCHOTHERAPY FOR DEPRESSION

- Effective psychotherapies (e.g. CBT, IPT) are available as the sole treatment for mild-moderate depression and/or to augment antidepressant medication in moderate-severe depression.

- These therapies are often not available in settings where HIV care takes place; problems include cost of training providers, poor reimbursement for therapy, poor dissemination of research-based approaches, lack of priority.
STAR*D is the largest and most inclusive clinical trial ever conducted on the treatment of non-psychotic unipolar major depression.

This multisite, multistep, prospective, randomized, federally funded clinical trial enrolled about 4000 patients, many with medical and psychiatric co-morbidities.

There were four sequenced treatment steps in the algorithm. The first step for everyone was treatment with the SSRI antidepressant citalopram.

There were two endpoints: response (>50% reduction of symptoms) and remission (few or no symptoms).

If citalopram treatment was not successful, step two contained seven options for either augmentation (including with cognitive behavioral therapy) or switching to another antidepressant.

If step two failed there were further options in steps three and four.

Since 2003, hundreds of papers have been published about the STAR*D results.
Rates of acute remission (few or no symptoms):
- Step 1: 37%
- Step 2: 31%
- Step 3: 14%
- Step 4: 13%

Rates of response (>50% reduction of symptoms):
- Step 1: 49%
- Step 2: 29%
- Step 3: 17%
- Step 4: 16%

Rates of medication intolerance, relapse and dropout are not shown in this slide.

Rush et al., Am J Psychiatry, 2006

It is valuable for prescribers in primary/HIV care to know how to use two antidepressants and be willing to switch patients from one to the other depending on patient response (symptom improvement and tolerance of side effects).

If the patient does not improve sufficiently after both trials, refer to mental health specialty care.

Other reasons to refer to specialty care include bipolar depression, psychotic depression, risk for suicide and/or violence, and diagnostic uncertainty.
HEPATITIS C CO-INFECTION

- It is estimated that 30% of HIV-infected patients nationally and 40% in New York State are co-infected with HCV
- 24% of untreated HCV-infected patients
- HCV treatment: Sofosbuvir (Sovaldi)
- Ribavirin and interferon-alfa
  - Estimated incidence between 20% and 40%
  - Emergence of mood-related symptoms appears to be dose-dependent.
  - The side effects include fatigue, hypersomnia, irritability, emotional lability, social withdrawal, and impaired concentration.

HIV-Associated Neurocognitive Disorders (HAND)
FREQUENCY OF HIV-ASSOCIATED NEUROCOGNITIVE DISORDERS: CHARTER STUDY

N= 1555 community dwelling HIV+ participants in the U.S. without confounding factors

- HIV-associated dementia: 2%
- HIV-associated mild neurocognitive disorder: 12%
- Asymptomatic neurocognitive impairment: 33%

Heaton, et. al. Neurology 2010

CHALLENGES TO SCREENING FOR AND TREATING HIV-RELATED NEUROCOGNITIVE DISORDERS

- There are no simple screening tools to diagnose asymptomatic impairment or mild neurocognitive disorder. Simple tools (such as the MMSE) pick up advanced cortical deficits.

- Neuropsychological testing takes 1-4 hours

- Multiple co-morbidities and aging complicate the differential dx

- There are no clear treatments beyond achieving undetectable viral load (degree of ARV CNS penetration remains of uncertain benefit).

Valcour, et. al. CID, 2011
5-10 MINUTE SCREENS FOR SEVERE NEUROCOGNITIVE IMPAIRMENT

- HIV Dementia Scales: original (includes saccadic eye movements), modified (removes eye movements), and international versions—validated in HIV
  - WWW.HIVGUIDELINES.ORG

- Montreal Cognitive Assessment (MoCA)—free, on-line, translated into multiple languages; not yet validated in HIV; may also pick up milder impairment
  - WWW.MOCATEST.ORG

OTHER STRATEGIES TO MEET THE CHALLENGE OF NEUROCOGNITIVE DISORDERS

- The brain is protected by beginning ART before the CD4 count is less than 200.

- Treat contributing co-morbid medical problems—numerous disorders and substance use contribute to cognitive impairment.

- Assess for and treat depression, which is commonly accompanied by cognitive impairment (there is a bi-directional relationship).

- Changing antiretroviral treatment may help in individual cases.

Reference documents at www.psych.org/aids and www.hivguidelines.org
Alcohol/Substance Use and HIV

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 ≥ 2 may be suggestive of a problem

References and more tools: www.hivguidelines.org

Screening for Substance Use: Cage-AID (CAGE Adapted to Include Drugs)
HARM REDUCTION: CREATING STABLE CHANGE
TRANSTHEORETICAL MODEL*

- Precontemplation
- Contemplation
- Preparation
- Action
- Maintenance
- Relapse & Recycle

* Prochaska & DiClemente

**MOTIVATIONAL INTERVIEWING**

- Clinician helps patient identify conflicts between patient’s current behaviors and patient’s goals/values
- Clinician reflects on discordance
- Patient realizes change is necessary and develops own solutions

Chanut et al., Can J Psych, 2005
SUMMARY

- Psychiatric disorders are common with Individuals living with HIV/AIDS
  - 50% Mood and Anxiety disorder
  - 25% current Substance abuse or dependence
  - 26% Personality Disorder
- Psychiatric dx are linked to slower rates of virologic suppression and treatment (Pence et al 2007)
- Treatment of Psychiatric disorders is associated
  - Slower disease progression and mortality (Belanoff 2005)
  - Improved treatment adherence (Wyatt 2004)
  - Decrease in HIV transmission risk behavior (Sikkema 2008, Wyatt 2004)
  - Improved quality of life (Sikkema 2005)

THANK YOU