Depression as a Medical Co-morbidity of HIV Infection

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Based on a review of studies prevalence rates for depression range from 12% to 71%.

Studies use different measurement tools and cut-off points.

In the largest study of 1113 people, the rate of depression was 42% (using the HSCL-25) for symptoms compatible with major depression.

Depression is often comorbid with other psychiatric disorders including alcohol and substance use as well as the neuropsychiatric complications of HIV.

Sherr, et. al., Psychology Health & Medicine, 2011
Common Depressive Disorders

- **Major Depression**—the most common form of severe depression; may have psychotic features
- **Dysthymia**—symptoms are milder than major depression but often still debilitating; by definition symptoms have persisted for more than two years
- **Bipolar depression**—part of the cycling mood disorder known as bipolar disorder or manic-depressive disease
- The primary focus of this talk is major depression.
“We got out of my friend’s car and walked for almost 15 minutes, and then I couldn’t go any farther. I lay down fully dressed in nice clothes, in the mud. ‘Please let me stay here,’ I said, and I didn’t care about standing up ever again.”

The New Yorker, 1/12/98
Rates of severe depression are higher among medically ill people than among physically healthy people.

The presence of severe depression is associated with increased morbidity and mortality among medically ill people.
## Diagnosis of Major Depression: Affective vs. Somatic Symptoms

<table>
<thead>
<tr>
<th>AFFECTIVE</th>
<th>SOMATIC</th>
</tr>
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<tbody>
<tr>
<td>Depressed mood</td>
<td>Appetite/Weight loss</td>
</tr>
<tr>
<td>Loss of interest</td>
<td>Sleep disturbance</td>
</tr>
<tr>
<td>Guilt, worthlessness</td>
<td>Agitation/retardation</td>
</tr>
<tr>
<td>Hopelessness</td>
<td>Fatigue</td>
</tr>
<tr>
<td>Suicidal ideation</td>
<td>Loss of concentration</td>
</tr>
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</table>
Why Can’t Psychiatrists (or Others Mental Health Practitioners) Just Take Care of Depression?

- There aren’t enough of them—even if psychiatrists did nothing else, depression is too common to be treated just by them.

- Most patients don’t want to see them—it’s less stigmatizing to get treatment from someone in medical practice.
Screening for and Treating Uncomplicated Depression is Relatively Straightforward

- There are simple, valid, reliable screening tools
- Rule out bipolar disorder which requires different medication strategies than depression.
- Newer antidepressants are easier to use; many are generic so costs have gone down.
- Psychiatrists and other MHPs could concentrate on depressed patients who are bipolar, suicidal, psychotic, refractory, or have significant comorbidities.
PHQ-2 and PHQ-9 Screening Tools for Depression

- Readily available online at no charge
- Already translated into multiple languages (but not necessarily validated)
- Well studied in general medical populations
- Easy to administer or self administer
- Can be used to screen and/or make a diagnosis
- Can be used to follow patient’s progress
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, move to the PHQ9.
Diagnostic Instrument for Depression: PHQ9 – Items Rated from 0-3

- Little interest or pleasure in doing things
- Feeling down, depressed, or hopeless
- Trouble falling or staying asleep, or sleeping too much
- Feeling tired or having little energy
- Poor appetite or overeating
- Feeling bad about yourself — or that you are a failure or have let yourself or your family down
- Trouble concentrating on things, such as reading the newspaper or watching television
- 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
- Thoughts that you would be better off dead or of hurting yourself in some way
Treating Severe Depression as a Medical Co-morbidity of HIV

There is an increased understanding that severe depression is associated with increased morbidity and mortality from HIV infection, and might best be conceptualized as a medical co-morbidity of HIV infection.
Numerous studies across many countries demonstrate the association of depression with increased morbidity and mortality among people with HIV infection.

Contributing factors include the association of depression with

- Failure to access HIV care and treatment
- Failure to adhere to antiretroviral medication once it has been started
- Possible direct effects of depression on the immune system
Depression and HIV-related Morbidity/Mortality

HERS cohort: 765 HIV+ women at 4 sites in U.S. 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.

Ickovics et al., JAMA, 2001
Depression and HIV-related Morbidity/Mortality

WIHS cohort: 2,059 HIV + women in U.S.

Replicated HERS results: Chronic depressive symptoms associated with AIDS mortality
(N = 1,761)

Cook et al., Am J Public Health, 2004
Depression and HIV-related Morbidity/Mortality

- 996 HIV+ pregnant women in Tanzania followed for 6-8 years without HAART (vitamin supplementation study, 1995 – 2003)
- WHO clinical stage I (82%) and stage II (17%)
- 31% died during follow-up
- Depression associated with
  - A 60% increase risk of progressing to clinical stage III/IV disease
  - A greater than two-fold increased risk of death

Antelman et al., JAIDS, 2007
Associations Between Psychiatric/Substance Use Disorders and HAART

- 198 HIV+ HAART-naive patients in U.S.
- Probable depression associated with slower rate of virilologic suppression
- Probable alcohol and drug abuse/dependence associated with faster virilologic failure

Pence et al., JAIDS, 2007
Associations Between Depression Treatment and HAART Use and Outcomes

- Use of antidepressants + MH therapy, or MH therapy alone, associated with increased HAART utilization (N = 1,371)

- Compliant SSRI use associated with improved HIV adherence and laboratory parameters (CD4 cell count and viral load)

Cook et al., AIDS Care, 2006
Horberg et al., JAIDS, 2008
Associations Between Depression Treatment and HAART Use and Outcomes

- Community-based prospective cohort study
- 158 HIV+ homeless/marginally housed people followed every 3 months between 2002-2007
- Antidepressant treatment associated with
  - 4 times the likelihood of accepting HAART
  - 2 times the likelihood of achieving viral suppression

Tsai et al. Arch Gen Psych, 2010
# Associations Between Treatment for Mental Disorders and HAART Use and Outcomes


<table>
<thead>
<tr>
<th># Visits</th>
<th>Adjusted Odds Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.0</td>
<td>Referent</td>
</tr>
<tr>
<td>1</td>
<td>1.36</td>
<td>0.0013</td>
</tr>
<tr>
<td>2-5</td>
<td>0.93</td>
<td>0.43</td>
</tr>
<tr>
<td>6-11</td>
<td>0.78</td>
<td>0.052</td>
</tr>
<tr>
<td>≥ 12</td>
<td>0.60</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Himelhoch, AIDS, 2009
Interventions for HIV+ People with Depression: A Review of Studies

- 83 interventions with a placebo/control group
- Mostly in U.S., mostly conducted with gay men
- Reduce depression +/- other endpoints
- Varying measures of depression
- Diverse strategies
- Often small sample sizes

Sherr, et. al., Psychology Health & Medicine, 2011
Interventions for HIV+ People with Depression: A Review of Studies

Psychological Interventions

- Usually effective for depression, especially those that incorporate a cognitive behavioral (CB) component

- Cognitive behavioral stress management (CBSM) is particularly effective

Sherr, et. al., Psychology Health & Medicine, 2011
Interventions for HIV+ People with Depression: A Review of Studies

Pharmacological Interventions

- Antidepressants are generally effective

- Correcting testosterone deficiency with replacement hormone treatment has been shown to improve mood

Sherr, et. al., Psychology Health & Medicine, 2011
Interventions for HIV+ People with Depression: A Review of Studies

Other Interventions

- Treatments that combine psychological and pharmacologic treatment appear to be the most effective.

- Treatments that appear to be ineffective include non-specific coping interventions and herbal/vitamin supplements.

Sherr, et. al., Psychology Health & Medicine, 2011
Interventions for HIV+ People with Depression

- Many brief evidence-based psychotherapies have been manualized.
- Manualized interventions may be targeted to individuals or groups.
- Manualized interventions can be taught to providers with limited mental health background.
Antiretrovirals and Psychotropics: General Points

- Psychotropic medications maintain efficacy in the HIV+ population.
- Overlapping metabolic pathways in cytochrome P-450 system (3A4 and 2D6) → drug interactions (often theoretical).
- May facilitate or inhibit one another’s metabolism. Websites, online resources are available for information.
- Overlapping toxicities, especially liver toxicity among patients co-infected with hepatitis viruses.
- But most psychotropics can be used safely if start low, go slow.

American Psychiatric Association Practice Guidelines and other reference documents www.psych.org/aids
Somatic Treatments for Depression

- Caution with use of antidepressants among adolescents and young adults under 24-y.o.: warning about increased suicide risk
- SSRIs (easiest to use in primary care)
- SNRIs
- Tricyclics
- Other antidepressants
- Atypical antipsychotics/mood stabilizers for bipolar depression
- Brain stimulation treatments (includes ECT but many new approaches are being studied)
- Light therapy for seasonal depression
- Avoid St. John’s Wort—lowers antiretrovirals

American Psychiatric Association Practice Guidelines and other reference documents www.psych.org/aids
Antidepressant Studies in HIV: Another Summary

- > 1000 patients treated in clinical trials
- Antidepressants 50-90% effective and superior to placebo
- Placebo response rates as high as 48%
- Average # concurrent HIV medications = 4
- Women and IDUs underrepresented
- Depression diagnoses and outcome criteria vary
- HIV illness stage varies
- Duration varies (4 weeks-1 year)
- High attrition rates (19-55%)
## Reported Neuropsychiatric Adverse Effects of Medications Commonly Used in HIV Infection

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