
Major Depression: A Medical Comorbidity of HIV Infection

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Disclosures

Francine Cournos has nothing to disclose

Learning Objectives

1. To identify signs and symptoms, screening tools, and treatments for depression.
2. To improve knowledge and skills in the treatment of depression at the individual practitioner and systems levels.

Depression Among HIV+ People

- Based on a review of studies, prevalence rates for depression range from 12% to 71%.
- Studies use different measurement tools and cut-off points. They most often focus on small convenience samples rather than large representative populations.
- In one of the larger studies of 1113 people, the rate of depression was 42% (using the HSCL-25) for symptoms compatible with major depression.

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 may or may not be as severe as major depression and 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.

Depression Is Strongly Associated with Poorer HIV/AIDS Outcomes in Published Studies

- **Depression is associated with:**
 - Failure to initiate antiretroviral treatment (ART)
 - Failure to adhere to ART once initiated
 - Slower virologic suppression
 - Increased morbidity and mortality
 - Increased HIV-related risk behavior

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

Major Depression Is As Much a Physical Disorder As It Is a Mental Disorder

Anatomy of Melancholy by Andrew Solomon

“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

Severe Depression is Best Conceptualized as a Medical Co-morbidity of HIV Infection

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.

Depression May Negatively Impact the Immune System

- The increase in morbidity and mortality among people with HIV who also have chronic depression 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; however, emerging studies show that treating depression in people with cardiovascular disease (CVD) eliminates the increased mortality seen in depressed vs. non-depressed patients with CVD.

Reference for CVD citation: Gallo, et al, BMJ, 2013

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 HIV-related Mortality

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

Antelman et al., JAIDS, 2007

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, major depression is likely; consider further screening with the PHQ9. Can also be used as a yes/no questionnaire; if yes to either question, screen 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

Assessment for Depression

- Evaluate for contributing biological factors, for example prescribed medications, alcohol and other substances, hypothyroidism, hypogonadism, etc.
- Try to rule out bipolar disorder
 - Ask: Past or family history of mania?
 - Ask: In the past year, while not high or intoxicated, did you ever feel extremely energetic or irritable and more talkative than usual?

Case: A 26 year old woman you evaluate tests positive for HIV infection with a CD4 cell count of 234 and a viral load of 32,000. After conducting resistance testing, you explain the importance of beginning ARV treatment. The patient stares at you blankly but nods in agreement that she's ready to start medication. You give her a prescription for a single pill regimen but she doesn't come back for her first follow-up visit. You regret that you didn't:

- Spend more time explaining the importance of starting treatment right away.
- Screen her for depression.
- Refer her to the on-site social worker since her blank stare made you feel concerned that something was wrong.

Case: A 26 year old woman with HIV infection who stared at you blankly but agreed to start ARV medication. She hasn't returned for the first follow up appointment and you regret you didn't do more.

- **The problem with explaining more about the importance of ARVs is that a patient with a blank stare is probably not absorbing what you're saying. It turned out that the patient was severely depressed.**
- **Depression is a medical co-morbidity of HIV infection and practitioners should be able to screen for its presence without referring to other providers.**
- **Screening for depression will become the first mental health indicator of quality care under the ACA. But screening only works if it's coupled with treatment.**

There Are Many Somatic Treatments for Depression

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

American Psychiatric Association Practice Guidelines and other reference documents
www.psych.org/aids

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

Antidepressants: Limited Studies in HIV Treatment; SSRIs Are the Most Studied

- In general, SSRIs were well tolerated, safe, and had lower rates of drug discontinuation in studies with HIV-infected patients – all had equal efficacy.
- Drug interactions need to be considered with fluoxetine and paroxetine.
- Avoid paroxetine in pregnancy (category D).
- Assess for testosterone deficiency, which may contribute to depressive symptoms; treat if present.

www.psych.org/aids

Associations Between Depression Treatment and ART Use

- Use of antidepressants + MH therapy, or MH therapy alone, was associated with increased ART utilization (Cook, N = 1,371).
- Compliant SSRI use was associated with improved HIV adherence and laboratory parameters (CD4 count and viral load).
- However, two small randomized controlled clinical trials of depression treatment (antidepressants* and cognitive behavioral therapy**) showed engagement in care only improved when an adherence component was also included.

Cook et al., *AIDS Care*, 2006 Horberg et al., *JAIDS*, 2008

*Tsai et al, N=158; **Saffren et al, N=89

Treatment of Unipolar Major Depression

The STAR*D Study: Overview

- 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.

Treatment of Unipolar Major Depression

The STAR*D Study: Overview

- There were two endpoints: response (>50% reduction of symptoms) and remission (few or no symptoms).
- If citalopram treatment was not successful in step one, 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.

Treatment of Unipolar Major Depression

The STAR*D Study: 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

Treatment of Unipolar Major Depression

The STAR*D Study: Implications

- 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.

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.**

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

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

Models for Treating Depression in Primary/HIV Care: Why Can't Specialists Do It Alone?

- There aren't enough of them — even if psychiatrists and other mental health specialists did nothing else, depression is too common to be treated just by them.
- Most patients don't want to see specialists — it's less stigmatizing to get treatment from their current medical practitioners.

What's the Evidence for Integrating Mental Health Care into HIV Care?

- The care of people with HIV infection has offered some wonderful clinical models for providing integrated care to complex patients.
- Special HIV funding streams such as Ryan White have contributed to the ability of HIV clinical programs to integrate mental health/substance use treatment into HIV care, and there are published program descriptions of doing so.
- However, there is very limited research on the outcomes of incorporating mental health/substance use treatment into HIV care. The few studies that have been conducted have small sample sizes.

What's the Evidence for Integrating Mental Health Care into Medical Care?

- There have been a substantial number of studies focused on integrating mental health care into medical care.
- Most of these studies examine integrating depression treatment into primary care.
- Improved mental health and physical health outcomes have been demonstrated.

What Does It Take to Get Good Outcomes?

- **Teamwork.** Integration of mental health into primary care does not work well if HIV/primary care clinicians are left to do it on their own without support and consultation.
- **Targeted and monitored outcomes for both medical and psychiatric outcomes.** Objectively set the desired endpoints (including depression symptom score).
- **A comprehensive (but not necessarily expensive) set of program elements that includes screening, patient support, and input from mental health specialists.**
- **Training to build the capabilities of team members.**

Common Psychiatric Comorbidities of Major Depression Among People with HIV Infection

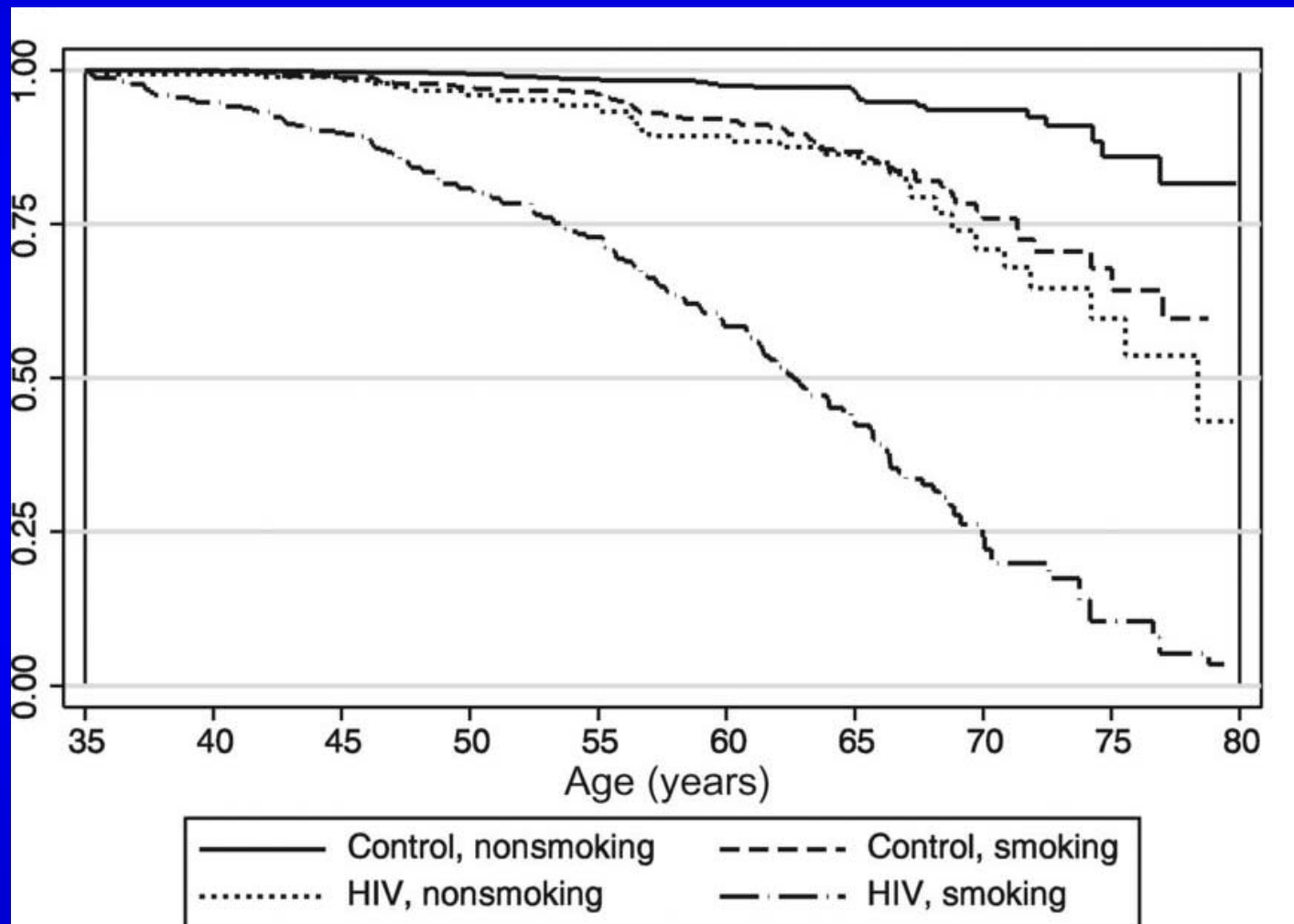
- Alcohol use disorders
- Other substance use disorders
- Posttraumatic stress disorder

In Discussions of Substance Use Problems, Tobacco is Now Receiving More Attention

- A study of tobacco smoking was conducted from 1995-2010 in Denmark where HIV care and treatment is free.
- 2,921 HIV positive patients age 35 or over were followed for 14,281 person years and compared to controls.
- The number of life-years lost in association with HIV was 5.1
- The number of life-years lost in association with HIV and smoking combined was 12.3

Helleberg M et al. Clin Infect Dis. 2013;56:727-734

Kaplan-Meier curve showing survival by age, stratified by human immunodeficiency virus and smoking status for all study subjects



Helleberg M et al. Clin Infect Dis. 2013;56:727-734

Smoking and Mental Illness: US National Comorbidity Survey-Replication 2001-2003

Rates of smoking by type of mental disorder:

- No mental disorder: 21 %
- Any anxiety disorder: 38 %
- Any mood disorder: 45 %
- Any substance use disorder: 64 %

Lawrence D et. al., BMC Public Health, 2009

Other Facts about Smoking and Mental Illness from the Peer-Reviewed Literature

- **Almost half of all cigarettes in the U.S. are consumed by people with a mental disorder.**
- **Bupropion and varenicline increase smoking abstinence rates in smokers with mental illness and studies suggest they are safe to use in this population.**

Major Depression and HIV: Summary

- Major depression is a common medical comorbidity of HIV infection.
- Untreated major depression interferes with HIV care and treatment, shortens life span and increases suffering and functional impairment.
- Screening for depression is straightforward.
- Effective psychotherapies and medications are available. At present, finding an effective medication involves some trial and error.
- Alcohol and other substance use disorders, including tobacco smoking, are common comorbidities and require their own treatment.