IMPACT OF MENTAL HEALTH DISORDERS ON HIV ILLNESS

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HIV in 2014

- ART (potent antiretroviral treatments)
- Emerging treatments
- Resistance testing
- Living longer
- Improved quality of life
- Chronic disease model
- Treatment as Prevention
The Use of Antiretrovirals for Primary Prevention
# RCT Evidence for Preventing Sexual HIV Transmission

Recent advances: 6/2010 to 7/2011

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect size (CI)</th>
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<tbody>
<tr>
<td><strong>Treatment for prevention</strong></td>
<td></td>
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<tr>
<td><em>(HPTN 052)</em></td>
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<tr>
<td>PrEP for discordant couples*</td>
<td>96% (73; 99)</td>
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<tr>
<td><em>(Partners PrEP with FTC/TDF)</em></td>
<td>73% (49; 85)</td>
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<tr>
<td>PrEP for heterosexuals</td>
<td>63% (21; 48)</td>
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<td><em>(Botswana TDF2 with FTC/TDF)</em></td>
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<tr>
<td>Medical male circumcision</td>
<td>54% (38; 66)</td>
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<td><em>(Orange Farm, Rakai, Kisumu)</em></td>
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<tr>
<td>PrEP for MSMs</td>
<td>44% (15; 63)</td>
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<tr>
<td><em>(iPrEX with FTC/TDF)</em></td>
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<td>STD treatment</td>
<td>42% (21; 58)</td>
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<td><em>(Mwanza)</em></td>
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<tr>
<td>Microbicide (topical PrEP)</td>
<td>39% (6; 60)</td>
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<tr>
<td><em>(CAPRISA 004 tenofovir gel)</em></td>
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</table>
Prevention of HIV-1 Infection with Early Antiretroviral Therapy

HIV Suppression Stops Transmission

96%

HPTN 052: If an HIV-infected person adheres to ART, the risk of transmitting the virus is reduced by 96%

“HPTN 052 is a game changer”

Michel Sidibe, UNAIDS
"We've reached a point where the goal of an AIDS-free world – once a far-off dream – is now within sight."

Kathleen Sebelius, Secretary of Health and Human Services
“Now we know beyond a doubt: If we take a comprehensive view of our approach to the pandemic, treatment doesn’t take away from prevention. It adds to it.

So let’s end the old debate over treatment versus prevention and embrace treatment as prevention.”

Secretary of State Hillary Rodham Clinton
Washington, D.C., November 7, 2011
Seek, Test, Link, Treat, Adhere, Retain: The Implementation Cascade
Gaps in the Implementation Cascade

72% of HIV+ Americans (850,000!) lack viral control!
In the Life of People Living with HIV and AIDS (PLWHA)

There are multiple, and at times, competing needs and challenges across several domains:

- Accessing and maintaining healthcare (adherence)
- Obtaining social support (dealing with stigma, disclosure, etc.)
- Seeking & maintaining employment and housing, etc.
- Reducing sexual and other transmission risk behaviors (dating, disclosure, family planning, etc.) … while
- Coping with the stigma associated with their sexuality and for some, the desire to have children
- Assessing and addressing mental health problems

Remien RH & Mellins CA. Long-term psychosocial challenges for people living with HIV: Let's not forget the individual in our global response to the pandemic. AIDS 2007; 21 Suppl 5:S55-63
Prevalence of Depression and Other Mental Health Disorders
Neuropsychiatric Problems Are Common among HIV+ People

- Mood disorders
- Anxiety disorders
- Alcohol/Substance use disorders
- Psychotic illnesses
- Somatic problems: insomnia, pain, fatigue, sexual dysfunction, body habitus changes
- Neuropsychiatric disorders due to opportunistic diseases, medication side effects, HIV itself (neurocognitive disorders)

Reference documents at www.psych.org/aids and www.hivguidelines.org
In the U.S., HIV, Substance Use, and Mental Illness Travel Together

Among the HIV infected in care, psychiatric disorders are common, under-diagnosed and under-treated:

- Alcohol and other drugs (AOD) ~ 40-75%
- Depression ~50-60%
- Anxiety almost as prevalent & commonly associated with depression
- Neurocognitive disorders are common in spite of ART and are hard to assess

Psychiatric patients have higher rates of HIV infection than the general population.

Among those triply diagnosed (HIV, substance use and mental illness), HIV rates are higher than those for people with substance use disorders alone.
Psychopathology and Risk Behaviors (transmission risk and adherence to care)

- There is an association:
  - People with mental illness have higher rates of unsafe sexual behavior and are thus vulnerable to becoming infected with HIV/STDs
  - Among people living with HIV, co-morbidity (substance use and other mental disorders) increases the risk of ongoing HIV transmission and contributes to poor treatment adherence, thus complicating clinical course and outcomes

Mental Health Diagnoses

- Major Depression
- Other Depression
- Panic Disorder
- Generalized Anxiety Disorder
- Psychosis
- Alcohol Abuse
- Drug Abuse
- Post Traumatic Stress Disorder
RAND HCSUS Study:  
2,864 HIV-positive Medical Patients

Any Psychiatric Disorder: 48%

- Major depression 36%
- Dysthymia 27%
- Generalized anxiety disorder 16%
- Panic attack 11%
- Drug dependence 13%
- Problematic alcohol use 19%


- Later studies showed elevated rates of PTSD.
Prevalence of Depression Among PLWHA

- Current Disorder
  - Major Depression: 29 – 36%

- Lifetime Disorder
  - Major Depression: 36 - 60%
  - Depression can be the silent killer
    - HIV treatment failure
    - suicide risk
**Prevalence of PTSD**

- HIV Cost Services Utilization Study HCSUS
  - PTSD (10.4%) (Vitiello, 2003)
- HIV+ Women
  - PTSD (35-38%) (HCSUS, Mellins, 2001)
Abuse/sexual assault

- 230 HIV-positive women in New York City, 50% experienced abuse in childhood, 68% as adults, and 7% reported physical assault or rape in the previous 90 days. (Simoni, 2000)

- Among 357 men and women living with HIV/AIDS, 68% of women (and 35% of men) reported a history of sexual assault since age 15 (Kalichman, 2002)
Neurocognitive Sequelae

- HIV has affinity for the central nervous system
  - Crosses blood brain barrier
  - “Inflammatory cascade”
  - Direct neurotoxic effect
  - Inflammatory proteins may lead to oxidative stress and neuronal injury or apoptosis

Nath (2002)
Steiner, Haughey, Li, Venkatesan, Anderson, Reid, et al. (2006)
HIV-Associated Dementia

- Prevalence pre-HAART:
  - 17% - 25%

- Prevalence post-HAART:
  - 1% - 10%

- While incidence and prevalence have dropped since HAART, prevalence now on the rise as patients live longer

Dore et al. (2003)
McArthur et al. (1994)
Grant et al. (1999)
Sacktor et al. (2001)
Neurocognitive Impairment

- Attention/Concentration
- Memory/Learning
- Language
- Visuospatial Ability
- Executive Functioning
- Speed of Information Processing
- Motor Functioning
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)
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
Neurocognitive Function in HIV

- Combination antiretroviral treatment (ART) reduces the incidence of HIV dementia, whereas overall prevalence of neurocognitive deficits remains high and comparable to pre-ART levels.

- Symptoms have changed with ART-- more memory and executive dysfunction problems.

- The best prevention of neurocognitive deficits appears to be earlier treatment of HIV that prevents low CD4 cell counts (< 200).

Neurocognitive Function in HIV

• The importance of the penetration of antiretrovirals into the CNS remains undecided.

• Nonetheless, it is worth trying a regimen with greater CNS penetration when providing clinical care to a well-controlled HIV+ patient with cognitive impairment.
# CNS Penetration of ARVs

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<th></th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
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<td>Zidovudine</td>
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<td>Emtricitabine</td>
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<td>Nevirapine</td>
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<td>PIs</td>
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<td>Lopinavir-r</td>
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<td>Darunavir-r</td>
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<tr>
<td>Tipranavir-r</td>
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<tr>
<td>Fusion Inhibitors</td>
<td></td>
<td></td>
<td>Enfuvirtide</td>
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<tr>
<td>Entry Inhibitor</td>
<td>Maraviroc</td>
<td></td>
<td>Letendre et al. (2008)</td>
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Impact
Impact of Mental Health Problems for PLWHA

- Mental health problems affect interpersonal relationships
- Mental health and physical health are often inseparable
- HIV/AIDS-associated social, psychological and neurological conditions have serious consequences for mental health of PLWHA
Impact of Mental Health Problems (cont.)

- May impair the quality of one’s life
- May interfere with HIV treatment adherence
- May interfere with a range of self-care behaviors
- May impair ability to cope with daily events, including childcare
- May result in acting out verbally or physically
- Mental health problems may be associated with unsafe sexual and drug use behaviors
Public Health Concern: Adherence & Sexual Risk

- High levels of medication adherence is an integral factor in the success of antiretroviral therapy
  - Poor adherence can lead to the development of drug resistant virus
  - Drug resistant virus can be transmitted to uninfected partners
- There is a relationship between adherence to antiretroviral therapy and adherence to safer sex practices and both are negatively affected by mental health problems

Remien et al., *AIDS and Behavior* 2007, 11(5), 663-675
Depression and HIV-related Morbidity/Mortality

- 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
HIV Clinical Outcomes in Untreated Mental Illness

- HIV+ women with untreated chronic depressive symptoms have 50% higher mortality rates\(^1\)
  - For HIV+ women with CD4<200, RR=4.3 (CI 1.6-11.6)
- Slower rate of virologic suppression and faster rate of virologic failure in patients with untreated psychiatric disorder\(^2\)
- Lack of psychological resources associated with increased mortality in HIV+ women\(^3\)

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Depression and Mortality In HIV+ Women

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 In HIV+ Women

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)
Psychiatric Disorders, especially Depression and mild Neurocognitive disorder, are common, under-diagnosed, under-treated, and negatively impact quality of life, adherence, HIV transmission, morbidity and mortality and prevention.
Mental Illness Often Untreated

- Nearly half of all Americans who have a severe mental illness do not receive any treatment

- Especially among people living with HIV, lack of treatment associated with increased suffering, impairment, premature mortality
Screening
Some Easy to Use Screening Tools: PHQ-2, PHQ-9 and GAD-7

- Readily available online at no charge
- Already translated into multiple languages
- 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

- 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
- 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
Diagnostic Instrument for Generalized Anxiety Disorder: GAD-7 – Items Rated from 0-3

- 1. Feeling nervous, anxious or on edge
- 2. Not being able to stop or control worrying
- 3. Worrying too much about different things
- 4. Trouble relaxing
- 5. Being so restless that it is hard to sit still
- 6. Becoming easily annoyed or irritable
- 7. Feeling afraid as if something awful might happen
Questions to Identify PTSD

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
Screening for Hazardous Alcohol Use: Audit-C Questionnaire

- There are 3 questions:
  - How often do you have a drink containing alcohol?
  - How many standard drinks containing alcohol do you have on a typical day?
  - How often do you have six or more drinks on one occasion?

- Each item is rated on a five-point scale used to identify hazardous alcohol use.

- The Audit-C is easily accessed online at no charge.
Screening for Substance Use: Cage-AID (CAGE Adapted to Include Drugs)

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
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

Valcour, et. al. CID, 2011
Cognitive Impairment

- Quick assessment:
  - Signature: look for any changes including orientation
  - Write a sentence: watch execution and look for full sentence (subject, object, verb)
  - Repeat a phone number
  - Draw a square – then turn it into a cube
Referral
Depression: When to Refer for Urgent Psychiatric Evaluation

- Patient is suicidal and/or has just made a suicide attempt

- Patient has symptoms of psychosis or severe agitation

- Patient has mixed depression and mania
Referrals

■ Provide clear directions and communications

■ If possible have the name of the referral…
  ■ If known to you…better
  ■ If not…can you develop a network of referrals

■ Even better if the patient can meet the referral while with you in advance…
Treatment
Barriers to Treatment

- **Patient Level:** stigma of mental illness; desire to be strong and tough; there’s nothing wrong

- **Intervention Level:** the side effects of antidepressants manifest before the therapeutic effects

- **Provider Level:** failure to screen, detect, discuss, treat

- **System Level:** limited funding/availability of mental health services; lack of provider training
Barriers to Treatment (cont.)

- Individual Barriers to Treatment
  - Lack of awareness/ denial of mental health needs
  - Hopelessness and embarrassment about seeking and receiving care
  - Stigma
  - Fear of hospitalization
  - Cultural beliefs
  - Negative experiences to previous treatment
Associations Between Depression Treatment and ART 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 ART 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 ART
  - 2 times the likelihood of achieving viral suppression

Tsai et al. Arch Gen Psych, 2010
Agents Used for Depression in Patients with HIV

- Antidepressants
  - SSRIs
  - SNRIs
  - TCA (tricyclic antidepressants)
  - Other antidepressants

- Psychostimulants

- Hormonal treatment—check for / treat ↓ testosterone levels in men and women
Antidepressants: SSRIs

- 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.

- Drug interactions need to be considered with fluoxetine and paroxetine.

- Side effects: nausea, jitteriness, weight loss, insomnia, sexual dysfunction.
Non-Medical Mental health treatment helps, but we don’t tend to use evidence-based psychotherapies.
Using Evidence-based Psychotherapies for Psychiatric Disorders: Brief Summary

- Many brief evidence-based psychotherapies have been studied, proved efficacious in research settings (and sometimes effective in clinical settings), and manualized.

- These manualized interventions include treatment for depression, anxiety disorders, and alcohol/substance use disorders.

- Manualized interventions may be targeted to individuals or groups.
Using Evidence-based Therapies for Psychiatric Disorders: Brief Summary

- Manualized interventions can be taught to providers with limited mental health background.

- Common techniques incorporated into manualized interventions include cognitive behavioral therapy, interpersonal therapy, exposure therapy, psychodynamic strategies, and supportive approaches.
Using Evidence-based Therapies for Psychiatric Disorders: Brief Summary

- Manualized psychotherapies can be used with or without psychotropic medications.

- Manualized interventions are rarely adopted by clinical programs. They are much more time intensive than prescribing pills, and remain a largely untapped resource for treating mental disorders.
Essential Components for Treatment

- Coordination of comprehensive care including medical care, mental health services, substance abuse services

- Easy access

- Cultural sensitivity

- Multidisciplinary team with integrated case management

- Family based interventions providing support
Summary
Mental Health Disorders are Common Among PLWHA

- Major Depression
- Other Depression
- Panic Disorder
- Generalized Anxiety Disorder
- Psychosis
- Alcohol Abuse
- Drug Abuse
- Post Traumatic Stress Disorder
Depression and HIV Progression

- Depression (and substance use disorders) are associated with non-adherence to HAART and transmission risk behaviors

- Controlling for adherence, depression remains associated with more rapid progression of HIV and increased morbidity and mortality

- The treatment of depression improves medical and behavioral outcomes

- The diagnosis and treatment of depression is an essential component of HIV care
Multiply Diagnosed Patients

- On-site integrated care models are best
- Split Care → Case management
- Split Care → Provider Communication
Resources
Psychiatric Medications and HIV Antiretroviral: A Guide to Interactions for Clinicians

- Start Low, Go slow
- Side effects
- Drug-Drug interactions
- Risk of dependence with Benzodiazepines
Online Resources

- NYS AIDS Institute:  
  www.hivguidelines.org

- American Psychiatric Association Office of HIV Psychiatry:  
  www.psych.org/AIDS

- Local and national AETCs
AETC National Programs

- National Resource Center (FXB/UMDNJ)
  - Provides virtual library of online training resources for adaptation to meet local training needs
  - 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
To schedule a Psychiatric Consultation please contact James Satriano, PhD, at

SATRIAN@PI.CPMC.COLUMBIA.EDU

OR 212/543-5591

To schedule a Training Activity, please contact Veronica Pinho at

VAP2112@COLUMBIA.EDU

OR 212/543-6028

OR visit us on the web at:
http://www.columbia.edu/cu/hivmentalhealthtraining
“…AIDS can be beaten. A plague that 30 years ago was blamed on man's iniquity has ended up showing him in a better, more inventive and generous light.”

The Economist

The end of AIDS?

How 5 million lives have been saved, and a plague could now be defeated
Thank you

Questions? Comments?