

# Addressing Depression in People with HIV

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## Learning Objectives

- Learn approaches to distinguishing between distress, major depression, and bipolar depression.
- Understand which treatments for depression can be most realistically implemented in HIV/primary care.
- Be able to cite some of the common psychiatric conditions that are comorbid with depression and how they can affect treatment.

# Disclosures

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## Globally, Depression Is Referred to As a “Common Mental Disorder”

- Depressive disorders and anxiety disorders are called “common mental disorders” because they are frequently seen in the general population.
- These disorders appear to be more common in the general U.S. population than in many other countries.
- Common mental disorders affect not only patients, but also their health care workers.
- Although the stigma of depression has lessened, it remains a major barrier to diagnosing and treating depressive disorders among patients and providers.

## Depression During the COVID-19 Pandemic

- Rates of depression increased during the COVID-19 pandemic, and health care workers were among the most severely impacted groups.
- The COVID-19 pandemic further exposed the social determinants of health and mental health in the U.S., including racial discrimination and income inequality.
- Discussion continues about our “mental health crisis”.
- While this talk is focused on people living with HIV, COVID-19 has taught us that we’re all in this together, patients and health care workers alike.

## Depression and Disability, Morbidity and Mortality

- Globally, mental illnesses account for 23% of years of life lived with disability (YLD) (Vos, et.al., Lancet, 2012)
  
- Of the 20 most common causes of years lived with disability, mental illnesses account for seven of them; depression ranks highest
  - Major depression (#2)
  - Anxiety disorders (#7)
  - Drug use disorders (#12)
  - Alcohol use disorders (#15)
  - Schizophrenia (#16)
  - Bipolar disorder (#18)
  - Dysthymia (#19)

## Depression As an Illness Is Found in Two Types of Psychiatric Disorders

- Depressive disorders, which include:
  - Major depression
  - Persistent depressive disorder (includes what was previously called dysthymia)
  
- Bipolar disorders (depressive phase), which include:
  - Bipolar 1 (mania is/has been present)
  - Bipolar 2 (hypomania is/has been present)
  - Cyclothymia (cycling moods that don't meet full criteria for bipolar 1 or 2)

# Major 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 suggests a bidirectional relationship between depression and inflammation  
*Khandaker, et. Al., Psychol Med, 2017.*



## Mental Illnesses Are also Physical Illnesses Because the Brain and the Body are One

- The brain controls life's essential involuntary bodily functions, such as breathing and heart rate.
- The brain tells the body what voluntary physical actions it must take to survive, such as eating or running away.
- The body provides continuous feedback to the brain, such as my stomach is full, or my muscles are tired.
- Strong emotions are expressions of the brain and body acting in unison, e.g., “a knot in my stomach”, “a lump in my throat”, “chills ran down my spine”, etc.

# Distinguish Between Mental Distress And Mental Disorders

## ■ Mental Distress

- Can occur in response to any adversity.
- Often does not meet criteria for a psychiatric diagnosis or require specialized mental health interventions.
- Often responds well to supportive strategies.

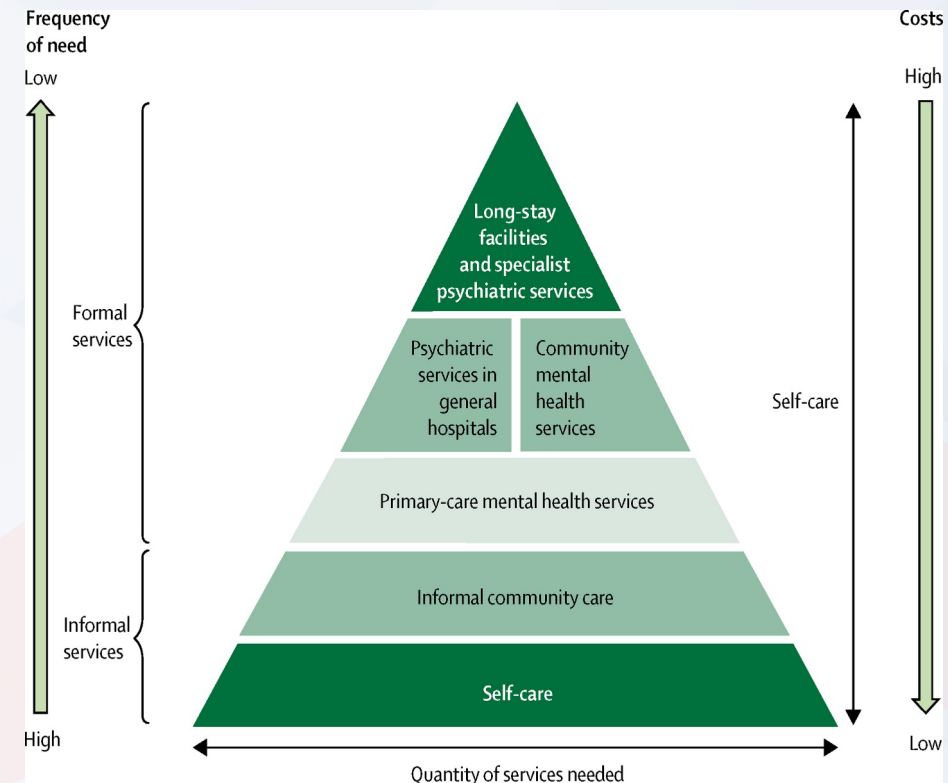
## ■ Mental Disorders

- Usually cause either persistent severe subjective distress and/or functional impairment.
- Meets recognized diagnostic criteria (ICD, DSM).
- Calls for evidenced informed mental health interventions such as medication and psychotherapy.

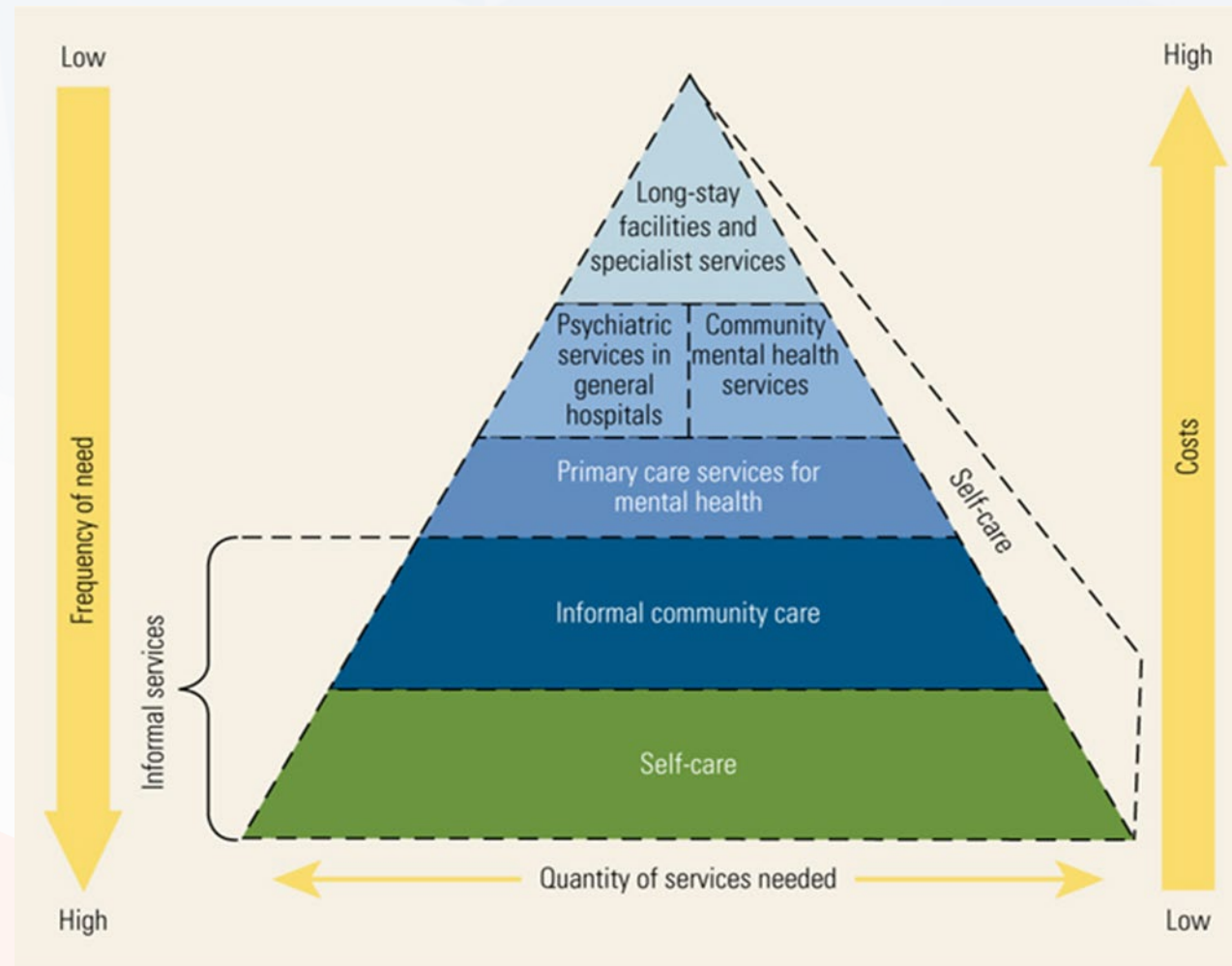
# Conceptualizing Depression Care with The WHO Pyramid of Mental Health Services

## ■ Main Points

- The number of available behavioral health (BH) care providers is always limited.
- For minimal/mild depressive symptoms that do not cross the threshold into disorders, we need to rely primarily on self care, community care and primary care



# The WHO Pyramid of Mental Health Services



*Patel V, et. al., Mental, Neurological and Substance Use Disorders, World Bank, 2015".*

# The National HIV Curriculum Has Tools to Screen for Depression and other Psychiatric Illnesses



The screenshot shows the homepage of the National HIV Curriculum website. At the top, there is a navigation bar with icons and labels for: Antiretroviral Medications, Course Modules, Question Bank, Clinical Challenges, Tools & Calculators, Clinical Consultation, and HIV Resources. Below the navigation bar, the main heading reads "National HIV Curriculum" with the URL "www.hiv.uw.edu". A sub-heading states "FREE CME, MOC, CNE, Pharmacology CE, and CE" and a descriptive sentence: "Free, up-to-date website for novice to expert clinicians to learn about HIV diagnosis, treatment, and prevention". The main content area features a dark blue background with a microscopic image of a cell. Text on the page includes: "The National HIV Curriculum is an AIDS Education and Training Center Program and led by the University of Washington." and "Funded by Health Resources and Services Administration (HRSA)".

**National HIV Curriculum**  
www.hiv.uw.edu

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**National HIV Curriculum**

The National HIV Curriculum is an AIDS Education and Training Center Program and led by the University of Washington.

[Contributors](#) [Site Overview](#)

Funded by Health Resources and Services Administration (HRSA)

Recertified for CE in fall 2020, six modules with 37 lessons and corresponding question bank topics address:

- Screening and Diagnosis
- Basic HIV Primary Care
- Antiretroviral Therapy
- Co-Occurring Conditions
- Prevention of HIV
- Key Populations

The National HIV Curriculum is an AIDS Education and Training Center (AETC) Program supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services as part of an award totaling \$1,000,000 with 0% financed with non-governmental sources.

# Some Tools in the National HIV Curriculum Are Linked to Automatic Calculators

Screening Calculators & Tools: The HIV National Curriculum: [www.aidetc.org/nhc](http://www.aidetc.org/nhc)

## ■ Mental Disorders Screening

- Anxiety: GAD-2
- Anxiety: GAD-7
- Dementia: IHDS
- Depression: PHQ-2
- Depression: PHQ-9
- PTSD: PC-PTSD-5

## ■ Substance Use Screening

- Alcohol: AUDIT-C
- Alcohol: CAGE
- CAGE-AID
- Drug Abuse: TICS
- Opioid: Risk Tool

## 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 probable diagnosis
- Can be used to follow patients' progress

## Screening for Depression: PHQ-2

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. This screener can also be used as a yes/no questionnaire; if yes to either question, screen with the PHQ9.**

*Kroenke, et. al. Medical Care 2003*



## PHQ-9 for Depression: 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\*

[\*Asking about suicide is safe and does not encourage suicidal behavior]

*Spitzer et., al., JAMA, 1999*

## The Differential Diagnosis of Depressive Symptoms

- Evaluate for and address underlying medical disorders and contributing biological factors, for example hypothyroidism, hypogonadism, prescribed medications, alcohol and other substances, etc.
- Remember that depression is often associated with significant cognitive impairment.
- Try to rule out bipolar disorder.

## PHQ-9 Scores

- 1-4: Minimal depression
- 5-9: Mild depression
- 10-14: Moderate depression
- 15-19: Moderately severe depression
- 20-27: Severe depression

## Responding to Minimal/Mild Symptoms of Depression (while addressing modifiable medical conditions)

- There aren't enough behavioral health providers to refer all people with minimal/mild depressive symptoms to specialized care.
- Self-care and informal supports at lower levels of care on the WHO pyramid can improve symptoms and play a role in preventing the onset of more severe symptoms.
- Informal care can address the social determinants of health (food, shelter, income support, etc.).

# Self Care for Minimal/Mild Depressive Symptoms

- All health care providers can review advice and/or employ behavioral change strategies with their patients focused on wellness and self care:
  - Identifying and utilizing pre-existing coping strategies
  - Reaching out to social supports
  - Physical activity, exercise
  - Eating and sleeping well
  - Mindfulness and meditation
  - Listening to music
  - Productive and pleasurable activities
  - Reducing negative stimuli, such as interpersonal conflict and excessive exposure to distressing news
  - Caution using alcohol and other substances for coping

## Evidence-based Psychotherapies for Depression

- Best studied psychotherapies for depression
  - Cognitive behavioral psychotherapies
  - Interpersonal psychotherapy
  
- How psychotherapies are used to treat depression
  - By themselves for mild to moderate depression
  - In combination with antidepressant treatment

## Antidepressant Treatment for Depression

- There's no “penicillin” for depression.
- There are no clinically relevant biological tests that predict therapeutic responses to different antidepressants. There are some tests to assess drug metabolism, but they don't directly predict medication efficacy.
- We largely treat patients by trial and error, monitoring tolerability to side effects and degree of improvement.
- Response (>50% reduction of symptoms) is a much less desirable outcome than remission (few or no symptoms).

## Treatment of Unipolar Major Depression in the STAR\*D Study: Overview

- There were two endpoints: response (>50% reduction of symptoms) and remission (few or no symptoms). Step one was treatment with citalopram.
- If citalopram treatment was not successful, step two contained seven options for either augmentation (with another medication or 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.

*Rush et. al., Am J Psychiatry, 2006*



## 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 in the STAR\*D Study: Implications

- It is valuable for prescribers in primary/HIV care to know how to use several antidepressants and be willing to switch patients from one to another depending on patient outcomes (symptom improvement and tolerance of side effects).
- If the patient does not improve sufficiently after both trials, refer to mental health specialty care if available. Refractory depression causes severe suffering and disability.
- Other reasons to refer to specialty care, if available, include bipolar depression, psychotic depression, risk for suicide and/or violence, and diagnostic uncertainty.

## Classes of Antidepressants

- SSRIs
- SNRIs
- Bupropion
- Tricyclics
- MAO inhibitors
- Zuranolone—just approved as a short-term treatment for post-partum depression (corrects hormonal imbalance)
- Adjunctive treatment with mood stabilizers and other medications

## There are Treatments For Depressive Disorders that Are Refractory to Usual Psychotropic Medications

- Brain stimulation treatments: Electroconvulsive therapy (ECT) was the first such treatment, but now there are two other FDA approved treatments, vagus nerve stimulation (VNS) and repetitive transcranial magnetic stimulation (rTMS).
- Ketamine, a veterinary anesthetic, (also known as a drug of abuse and a psychedelic), has been approved by the FDA for refractory depression; must be used with specific safeguards.
- Other psychedelic drugs (e.g psilocybin, MDMA, LSD) combined with guidance/therapy are under study for refractory depression, but clinical trials can be difficult to access.

# Bipolar Depression

- Bipolar disorder is marked by extreme changes in mood (highs and lows), thought, energy and behavior. Changes in mood are intense and can last for hours, days, weeks or months.
- People with this disorder typically seek help when they are in the depressive phase and are often initially diagnosed with unipolar depression. The average length of time to correct diagnosis and treatment is 10 years.



## Distinguish Between Major Depression and Bipolar Depression

- Bipolar depression accounts for most of time that people with bipolar disorder spend unwell.
- This may help explain why, in primary care, over 3 in 20 patients diagnosed with a depressive disorder have unrecognized bipolar disorder.
- First line pharmacologic treatment of bipolar depression is mood stabilizers (lithium, anticonvulsants, atypical antipsychotics), whereas for major depression it's antidepressants.
- Giving antidepressants alone, especially to people with bipolar 1 depression, may precipitate mania.

*McIntyre, et al, Curr Med Res Opin, 2019; Devaney, et al, Gen Hosp Psych, 2019*

# Diagnosing Bipolar Disorder

- There are no brief screens for bipolar disorder. The Mood Disorders Questionnaire (MDQ) is available but has 13 items.
- Ask if the patient or a close relative has ever been told s/he has manic-depressive illness or bipolar disorder?”
- Consider a few questions from the MDQ (based in the DSM-5):
  - Has there ever been a period of time when you were not your usual self, and you had much more energy than usual?”
  - Has there ever been a period of time when you got much less sleep than usual and found you didn’t really miss it?
- If you get yes answers to any of the above questions, you might consider completing the MDQ ([www.aidsetc.org/nhc](http://www.aidsetc.org/nhc)) and/or referring the patient for a diagnostic evaluation.

# Managing Bipolar Disorder

- On average, bipolar disorders are more severe illnesses than depressive disorders. The DSM-5 has now created two separate categories for these conditions instead of lumping them together.
- Most people with bipolar disorder need lifetime ongoing management for this condition to maximize social/occupational functioning and well being.
- At the same time, there's a long list of famous artists, fiction writers, inventors, politicians etc. with bipolar disorder.
- People with bipolar disorder are most amenable to treatment during the depressive phase of the illness. Those who feel euphoric and energized during (hypo)mania often reject care while in that state.



## Bipolar Disorder is Associated with Creativity

- Alvin Ailey was an American modern dancer who had bipolar disorder, alcohol and drug use, and HIV infection. He died of AIDS in 1989, but his work lives on through the Alvin Ailey American Dance Theater.



## Alcohol/Substance Use Co-morbidity

- Psychiatric disorders, including depressive disorders, carry a high degree of comorbidity with one another:
  - Our diagnoses are descriptive.
  - We have yet to understand the underlying biology that may tie our diagnoses together as different manifestations of the same vulnerability.
  - Siloed services for mental illness and substance use disorders are a major barrier to good care.
  - Most people with alcohol/substance use disorders receive no treatment for these conditions.

## Alcohol/Substance Use Co-morbidity

- A review of studies among people with bipolar disorders shows a 42% prevalence of alcohol use disorders, a 20% prevalence of cannabis use disorders and a 17% prevalence of other illicit drug use disorders.
- In general, outcomes tend to be significantly worse among patients diagnosed as having both major depressive disorder and an alcohol/substance use disorder, compared with patients who have only one of these diagnoses.

*Hunt, et al, J Affect Disord, 2016; Iqbal et al, Focus (Am Psychiatr Publ). Spring 2019*

## Alcohol/Substance Use Co-morbidity

- Alcohol and substance use disorders tend to be one of the most problematic of psychiatric comorbidities among persons with depressive disorders and HIV because of their added negative impact on morbidity, mortality, and outcomes along the HIV care continuum.
- **In this case, two disorders = two treatments**
- Depressive disorders and alcohol/substance use disorders each require their own treatment because treating only one condition doesn't usually result in sufficient improvement of the other condition.

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## Outcomes of Depression Treatment in People with HIV

- People with HIV often achieve comparable outcomes with depression treatment as the general population (relevant antidepressant research is very limited).
- General outcomes include:
  - Relief of suffering and improved quality of life
  - Reduced disability and cognitive dysfunction
  - Increased ability to function
  - Reduced mortality due to suicide and, in some studies, medical illness.

## Conclusions

- Depressive disorders are common among people with HIV, and they are highly treatable if providers persevere.
- Rule out medical causes of depression among people with HIV.
- Distinguish between depressive symptoms and depressive disorders. Symptom severity helps determine treatment.
- Consider whether depression is part of a bipolar disorder.
- Psychotherapies and medications are effective treatments. Self care is always essential. Addressing social determinants helps.
- The treatment chosen will depend on patient preference and the treatment capacities of a specific (HIV) care setting.