Addressing Depression in People with HIV

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October 18, 2022

Disclosure

Funding for this presentation was made possible by U1OHA29291 from the Health Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. *Any trade/brand names for products mentioned during this presentation are for training and identification purposes only.*

Objectives for Participants

- 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.

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 heath 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 Is One of the Most Frequent 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%.
- In the U.S., depressive disorders have high rates of comorbidity with other psychiatric illnesses, such alcohol/substance use disorders, anxiety disorders and PTSD

Cournos, McKinnon, Wainberg, in Comprehensive Textbook of AIDS Psychiatry: A Paradigm for Integrated Care, 2017

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 and Disability, Morbidity and Mortality

- The World Health Organization (WHO) classifies major depression as more disabling than almost all other medical illnesses and similar to having quadriplegia.

- (WHO ranks back pain is the #1 cause of disability.)

- Major depression is associated with increased morbidity and mortality from common comorbid medical conditions, suicide, and accidental deaths.

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 (does not meet full criteria for bipolar 1 or 2)

Depressive Disorders Are Associated with Numerous Negative HIV Outcomes

- Depression in people with HIV is associated with:
  - Increased morbidity and mortality
  - Problems with adherence along the HIV care continuum
  - Increased HIV risk behavior
  - Poorer quality of life

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 is emerging for 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.

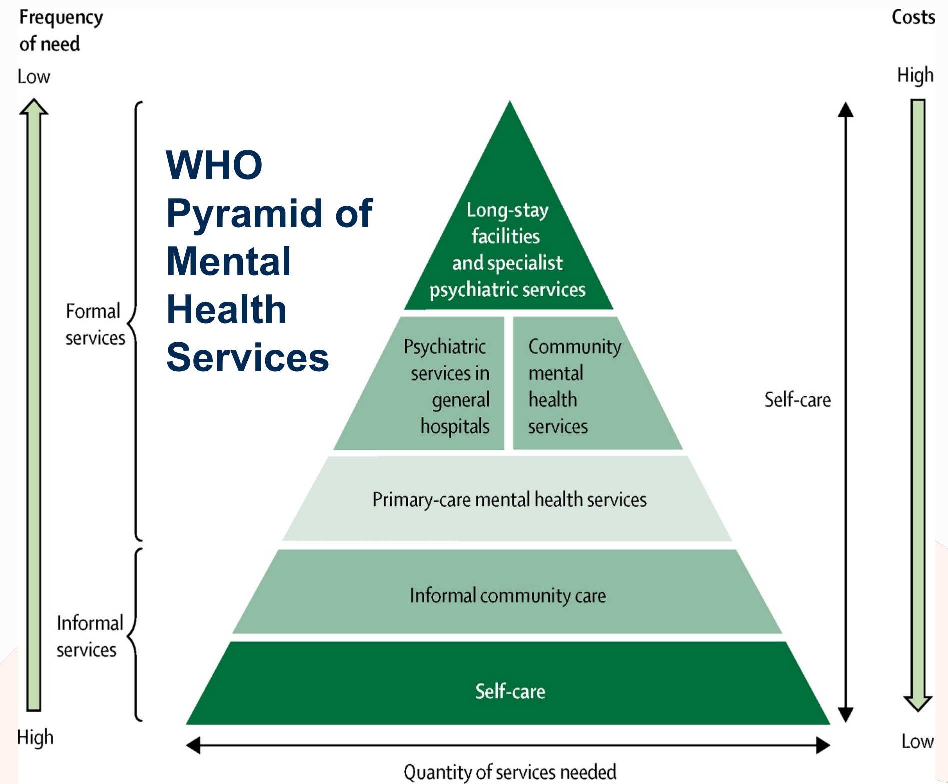
Meets recognized diagnostic criteria (ICD, DSM).

Calls for evidenced informed mental health interventions such as medication and psychotherapy.

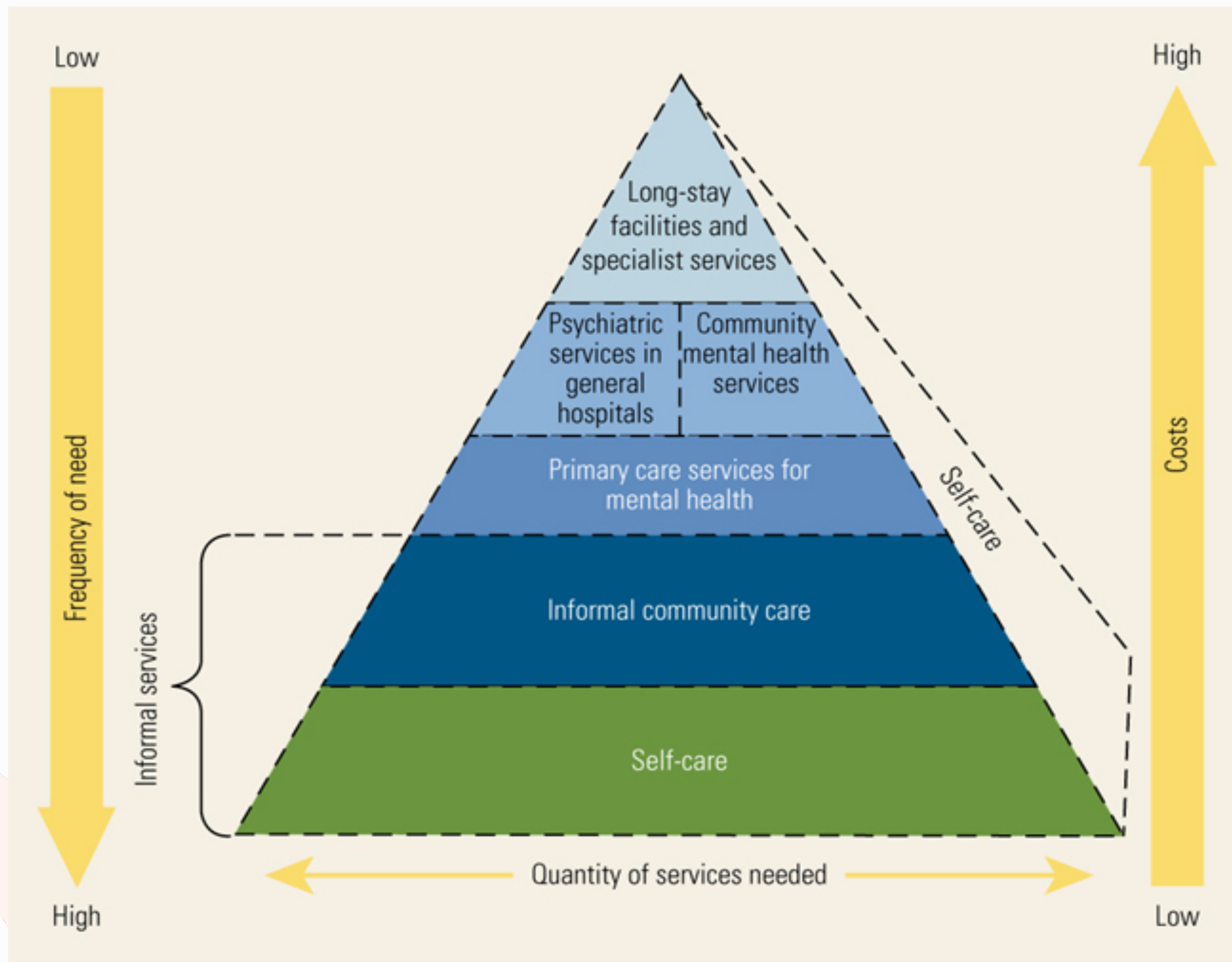
Conceptualizing Depression Care with The WHO Pyramid of Mental Health Services

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

www.hiv.uw.edu

FREE CME, MOC, CNE, Pharmacology CE, and CE

Free, up-to-date website for novice to expert clinicians to learn about HIV diagnosis, treatment, and prevention

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.aidsetc.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

- 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's no equivalent of testing patients for sensitivity to different antidepressants, and there are very limited biological tests that are relevant to clinical practice.
- 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 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.
- The 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, 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
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.
- Other reasons to refer to specialty care, if available, include bipolar depression, psychotic depression, risk for suicide and/or violence, and diagnostic uncertainty.

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, an agent used primarily by veterinarians for anesthesia (and also known as a drug of abuse), was recently approved by the FDA for refractory depression; must be used with specific safeguards.
- Patients with refractory depression should be referred to the next level of care whenever possible because depression causes severe suffering and disability.

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 to people with bipolar depression may precipitate mania.

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

Diagnosing Bipolar Disorder

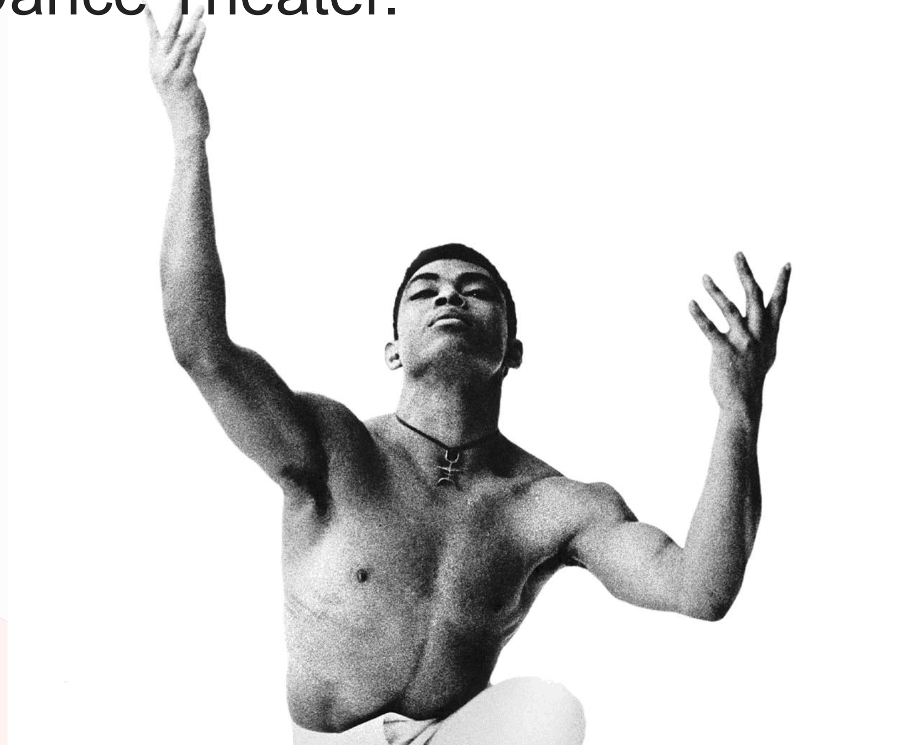
- There are no brief screens for bipolar disorder. The Mood Disorders Questionnaire (MDQ) is available but has 13 items.
- Ask if the patient or a close relative has ever been told s/he has manic-depressive illness or bipolar disorder?"
- Consider a few questions from the MDQ (based in the DSM-5):
  - 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) 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.

Outcomes of Depression Treatment in People with HIV

- People with HIV likely 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

Outcomes of Depression Treatment in People with HIV

- Evidence is mixed regarding whether successful treatment of depressive illness by itself is associated with improved rates of viral suppression; the addition of a specific adherence intervention is advised.
- Evidence is not available regarding whether the successful treatment of depressive illness reverses the shortened life span of people with both chronic depression and HIV

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 both effective treatments. Self care is always essential. Other support helps.
- The treatment chosen will depend on patient preference and the treatment capacities of a specific (HIV) care setting.