

DEPRESSION AND MANIA IN PATIENTS WITH HIV/AIDS

I. DEPRESSION

Clinical depression is the most commonly observed mental health disorder among HIV-infected patients, affecting up to 22% of patients.^{1,2} The prevalence may be even greater among substance users. Depressive symptoms have been associated with risk behavior, non-adherence to medications, and shortened survival.³⁻⁶ Although sadness and grief are normal responses to many of the consequences of HIV infection, clinical depression is not. Failure to recognize depression may endanger both the patient and others in the community. Patients with depression are at higher risk for comorbid psychiatric, alcohol, and substance use-related disorders, particularly alcohol, cannabis, and cocaine use.

A. Screening for Depression

RECOMMENDATION:

Clinicians should screen for depression as part of the annual mental health assessment and whenever symptoms suggest its presence (see [Appendix I: Mental Health Screening Tools](#) for screening tool options).

Simple screening techniques tested in a general primary care setting have been shown to be effective in detecting unrecognized depression.⁷⁻⁹ Use of the following two-question screen has been shown to be effective^{8,9}:

1. *During the past month, have you often been bothered by feeling down, depressed, or hopeless?*
2. *During the past month have you often been bothered by little interest or pleasure in doing things?*

If a patient answers “Yes” to either of these questions, further evaluation is indicated (see [Appendix I: Mental Health Screening Tools](#)).

Other questions to screen for symptoms may include:

- *When people are ill and feeling depressed, they often want to just “get it all over with.” Have you felt that way? Have you thought about killing yourself?*
- *Do you blame yourself for things you have no control over?*
- *I notice that you’ve lost/gained weight. Are you feeling more/less hungry, eating more/less than usual?*
- *Are you having trouble concentrating? Are you able to follow the plot of a TV show or a book? Is it harder than usual to make decisions?*
- *You look a little jumpy/slow; are you feeling more restless/moving more slowly than usual? Has anyone else noticed this?*
- *Are you fighting with your spouse or family?*
- *Are you having trouble enjoying sex?*

Many clinicians are reluctant to ask direct questions about psychiatric symptoms because they are afraid of insulting a patient; however, in actual clinical practice, patients are rarely offended by this line of questioning. Patients with symptoms are often quite relieved that someone has asked about their suffering. To introduce the subject, clinicians might say, *I'm concerned about your emotional well-being as well as your physical health, and I'd like to ask you a few questions.*

Although many of the somatic symptoms of depression may be attributed to HIV infection, opportunistic or other infections, or side effects of medications, the primary care clinician should recognize that the following symptoms can be caused by depression:

- Depressed mood
- Loss of interest or pleasure
- Feelings of guilt
- Suicidal thoughts
- Sleep disturbance
- Appetite/weight changes
- Attention/concentration problems
- Energy level changes/fatigue
- Psychomotor disturbance

Many HIV-infected patients may not recognize or report symptoms. They may present instead with behavioral changes that may indicate the presence of an underlying depressive disorder. Clinicians should recognize the following behavioral changes as possible indications of an underlying depressive disorder:

- A change in treatment adherence
- An inability to make life choices, including those related to medical care and adjustment to HIV disease
- A preoccupation with a particular problem, usually one that presents as minor
- A change in functioning, including an inability to perform activities of daily living, a return to substance use, or a self-imposed isolation
- Unexplained medical complaints, particularly pain or fatigue
- Interpersonal problems
- Presenting with difficult behaviors in the medical setting

In cases where patients are reluctant or unable to recognize their problem as depression, it is the responsibility of the primary care clinician to make the diagnosis and reflect it back to the patient.

HIV-infected patients do not become depressed simply because their disease progresses¹⁰; however, it is particularly important to screen for depression during the crisis points noted in Table 1. Medically ill patients may experience normal sadness, grief, and discouragement or demoralization. However, the presence of hopelessness, anhedonia (the absence of pleasure from usually pleasurable activities), ruminative guilt, and suicidal ideation may indicate accompanying clinical depression requiring psychiatric intervention.

TABLE 1
CRISIS POINTS FOR HIV-INFECTED PERSONS

- Learning of HIV-positive status
- Disclosure of HIV status to family and friends
- Introduction of medication
- Occurrence of any physical illness
- Recognition of new symptoms/progression of disease (e.g., major decrease in CD4 cells, increase in viral load)
- Necessity of hospitalization (particularly the first hospitalization)
- Death of a significant other
- Diagnosis of AIDS
- A return to a higher level of functioning (e.g., re-entry into job market/school, giving up entitlements)
- Major life changes (e.g., childbirth, pregnancy, loss of job, end of relationship, relocation)
- Necessity of making end-of-life and permanency planning decisions

Data are from Duffy V. The 14 crisis points of AIDS. *AIDS Patient Care STDs* 1994;8:28-32.

B. Diagnosis

RECOMMENDATION:

Clinicians should use the diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) to diagnose depression (see Table 2).

TABLE 2
DIAGNOSTIC CRITERIA FOR MAJOR DEPRESSIVE EPISODE

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

Note: Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). Note: In children and adolescents, this can be irritable mood.
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others).
3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. Note: In children, consider failure to make expected weight gains.
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms do not meet criteria for a mixed episode.

C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

E. The symptoms are not better accounted for by bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

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In addition to major depression, there are other kinds of depression, such as minor depression and dysthymia, which share symptoms with major depression (see Table 2) but differ in duration and severity. The clinician should refer to the DSM-IV for more information on these subtypes of depression.

The following psychiatric disorders, which require a different treatment approach, may present with symptoms of depression and should be excluded as possible causes:

- Bipolar disorder
- Post-traumatic stress disorder
- HIV-associated dementia
- Alcohol and substance use

The following HIV-related medical conditions and medications may also present with symptoms of depression and should be excluded as possible causes, particularly in patients with advanced HIV disease:

- Endocrinologic abnormalities, such as hypogonadism and hypothyroidism
- Medications, such as efavirenz, interferon, corticosteroids
- B₁₂ deficiency
- Opportunistic and other infections, such as syphilis
- HIV-associated dementia

C. Depression and Co-Existing Medical Conditions

RECOMMENDATION:

The primary care clinician should work closely with a psychiatrist throughout the course of treatment if depressive symptoms are associated with medication, and the benefit of continuing the medication outweighs the risk. In these situations, antidepressant therapy should be considered.

Key Point:

Patients co-infected with HCV, patients receiving treatment with interferon, and patients with disfiguring side effects of antiretroviral therapy (ART), particularly body fat changes, are more prone to develop depressive symptoms.

1. Depression in Patients with HIV/Hepatitis C Co-Infection

RECOMMENDATIONS:

Clinicians who prescribe interferon-alfa should screen patients for depression at least every 4 weeks while they are receiving treatment.¹¹

Clinicians who prescribe interferon-alfa should consult with a psychiatrist when treating patients with a history of psychiatric disorders, including depression and substance use.

The prevalence of psychiatric disorders, depression in particular, is increased in patients infected with hepatitis C virus (HCV). It is estimated that 30% of HIV-infected patients nationally and 40% in New York State are co-infected with HCV (these findings are to be expected, given that HIV and HCV share risk factors for modes of transmission). Studies have reported depression in as many as 24% of untreated HCV-infected patients, the majority of whom required antidepressant medication. This significant association underscores the importance of screening for depression. It is also clinically significant that HCV commonly presents with symptoms of fatigue and malaise. These symptoms may mimic depression and complicate diagnosis.

Currently, the standard treatment of chronic HCV infection is the combination of ribavirin and interferon-alfa. Numerous studies have documented the association between interferon-alfa and depression, with an estimated incidence between 20% and 40%. Emergence of mood-related symptoms appears to be dose-dependent. The side effects include fatigue, hypersomnia, irritability, emotional lability, social withdrawal, and impaired concentration. When side effects are intolerable, clinicians should reduce the dose, discontinue therapy, or treat the side effect(s). Most depression emerges by 8 weeks of treatment.

Key Point:

There is a growing amount of evidence that a history of psychiatric disorders, such as depression, does not necessarily increase the risk of developing depression while receiving interferon.

At present, there are insufficient data to determine the risk factors for developing depression while receiving interferon. A history of psychiatric disorders, such as depression, should not be regarded as a contraindication to therapy. If the psychiatric problem is in remission and there is sufficient interdisciplinary support, patients with a history of depression may safely complete a course of treatment. Given the complexity of this situation, treatment of these individuals should be undertaken in consultation with a psychiatrist. There are insufficient data to recommend pre-treating depression in patients receiving interferon.

For recommendations regarding the medical management of HIV/HCV co-infected patients, refer to the Adults guidelines [Hepatitis C](#).

2. Depression in Patients Experiencing Body Fat Changes

RECOMMENDATION:

Clinicians should assess mood at every visit in patients who develop changes in body fat.

Change in body fat is a common side effect of ART. It has generally been associated with long-term protease inhibitor (PI) therapy; however, this association is an active area of research. The symptoms include central obesity, peripheral fat depletion, and metabolic disturbances. In qualitative studies, body fat changes have been associated with bodily discomfort, decreased self-esteem, interpersonal difficulties, social withdrawal, demoralization, depression, and high-risk sexual behaviors. Body fat changes have also been associated with a higher incidence of high-risk sexual behavior, regardless of the patient's knowledge of viral load.¹²

Key Point:

Patients report that clinicians minimize the importance of body fat changes.

Clinicians should assess the mood of patients who experience body fat changes at every visit and should ask in a sensitive manner about its emotional impact on their lives. Facial wasting may be particularly difficult for patients who are concerned that their appearance may reveal that they are infected with HIV. These patients may become extremely distressed if they believe that other people are able to discern their serostatus.

For recommendations regarding the medical management of body fat changes in HIV infection, refer to the Adults guidelines [Long-Term Complications of Antiretroviral Therapy](#).

D. Management of HIV-Infected Patients With Depression

RECOMMENDATION:

Clinicians should implement interventions, such as medications or psychotherapy, for patients with moderate to severe depression or mild depression that does not resolve in 2 to 4 weeks.

Depression varies in severity from mild to severe. Its course may range from one acute episode that resolves with treatment to a chronic relapsing disorder whose treatment is only partially effective. Mild depression may resolve within 2 to 4 weeks with support and education alone. For some patients, medication alone may be sufficient to ease their depression; for others, the combination of medication and psychotherapy will provide a more effective and perhaps faster response.

1. Referral

RECOMMENDATION:

Patients at high risk for suicide or other violent behavior should be referred for immediate psychiatric intervention (see [Suicidality and Violence in Patients With HIV/AIDS](#)).

Indications for referral to a psychiatrist include:

- Depression associated with dementia, psychotic symptoms, manic symptoms
- No response to trials of two different antidepressants
- Worsening of symptoms despite appropriate medication
- Requiring higher-than-usual doses of medication to control symptoms
- Patient inability to tolerate side effects or clinician concern about side effects
- Depressive symptoms presenting in a patient with a history of bipolar disorder

2. Antidepressant Medications

RECOMMENDATION:

Clinicians should individualize therapy, considering drug-drug interactions with HIV-related medications, presence of comorbid psychiatric disorder(s), presenting symptoms, and side effect profile.

Because of potential side effects and drug-drug interactions, clinicians should become familiar with the safety profiles and interactions of antidepressants and HIV-related medications (see [Appendix II: Interactions Between HIV-Related Medications And Psychotropic Medications](#)). When an antidepressant is indicated, the choice can be guided by patient history, family history, target symptoms, and the side effects and safety profiles of the medications. For example, if a patient has responded to a specific medication in the past, he/she probably will again. If a patient has a relative who responded well to a specific medication, the patient may do the same. Drug characteristics and side effects may also guide medication choice. For example, a patient whose main complaint is insomnia may benefit from antidepressants with more sedative effects.

Key Point:

As in other vulnerable populations, the concept “start low, go slow” remains the cornerstone of psychiatric medication prescribing for HIV-infected patients.

Table 3 lists commonly used antidepressants. Selective serotonin reuptake inhibitors (SSRIs) have become the first-line treatment for depression. If SSRIs are not used, the novel antidepressants are a good second choice in many cases; however, for some patients, tricyclic antidepressants (TCAs) may be preferable. Clinicians should consult with a psychiatrist when making this decision. Dosing information, side effect profile, and drug-drug interactions can be found in [Appendix II: Interactions Between HIV-Related Medications And Psychotropic Medications](#).

TABLE 3 COMMONLY USED ANTIDEPRESSANT MEDICATIONS	
Drug Class	Generic Name (Brand name)
SSRIs—First-line medications for depression	<ul style="list-style-type: none"> • Citalopram (Celexa) • Sertraline (Zoloft) • Fluoxetine (Prozac Sarafem) • Paroxetine (Paxil) • Escitalopram (Lexapro)
Novel antidepressants	<ul style="list-style-type: none"> • Bupropion (Wellbutrin) • Venlafaxine (Effexor) • Mirtazapine (Remeron)
Tricyclic antidepressants	<ul style="list-style-type: none"> • Nortriptyline (Aventyl, Pamelor) • Desipramine (Norpramin, Pertofrane) • Doxepin (Adapin, Sinequan) • Imipramine (Tofranil)
Psychostimulants	<ul style="list-style-type: none"> • Methylphenidate (Concerta, Metadate, Methylin, Ritalin) • Dextroamphetamine (Adderall)

Selective Serotonin Reuptake Inhibitors and Novel Antidepressant Medications

RECOMMENDATIONS:

Clinicians should ask patients who are receiving SSRIs about sexual side effects.

Clinicians should monitor patients for suicidal ideation during the initiation phase of SSRI treatment. Clinicians should consider discontinuing medication in patients whose depression is persistently worse or whose emergent suicidality is severe, abrupt in onset, or was not part of the presenting symptoms.

SSRIs are relatively safe and are usually well tolerated by patients. Although not necessarily more effective than the older TCAs, SSRIs have become the first-line treatment for depression because they are associated with fewer drug interactions and a more benign side effect profile than TCAs.

For many people, the most troubling side effect of SSRIs is sexual dysfunction (e.g., anorgasmia, decreased libido, or erectile and ejaculatory dysfunction). Dose reductions, drug holidays, or switching to another drug in the same class may ease these effects and, therefore, improve adherence. Other patients will require the use of another class of drug.

Most drug-drug interactions involving cytochrome P450 isoenzymes are theoretical, and most SSRIs can be used safely with HIV medications. However, drug interactions between drugs with serotonergic activity may result in serotonin syndrome, a potentially dangerous reaction characterized by autonomic instability, neuromotor hyperactivity, and mental status changes. Consult [Appendix II: Interactions Between HIV-Related Medications And Psychotropic Medications](#) for details of interactions with NNRTIs and PIs.

Currently there is debate about whether antidepressants play a role in worsening depression and causing the emergence of suicidality in certain patients. It is particularly important to monitor patients for suicidal ideation during the initiation phase of treatment. Clinicians should consider discontinuing medication in patients whose depression is persistently worse or whose emergent suicidality is severe, abrupt in onset, or was not part of the presenting symptoms. All psychotropic medications should be stopped slowly.

Other agents such as bupropion, mirtazapine, and venlafaxine are also relatively safe and well tolerated. As with SSRIs, clinicians should be aware of drug interactions involving cytochrome P450 isoenzymes that may alter medication serum levels (see [Appendix II: Interactions Between HIV-Related Medications And Psychotropic Medications](#)). These agents and SSRIs may require a trial of up to 6 to 8 weeks at maximal doses to achieve the expected benefit.

Tricyclic Antidepressants

RECOMMENDATION:

Clinicians should monitor serum drug levels to ensure appropriate dosing of tricyclic antidepressants when there are concerns about adherence, absorption, or drug interactions.

If patients cannot tolerate SSRIs or any of the newer antidepressant medications, TCAs may be equally effective. TCAs have anticholinergic side effects, such as sedation and constipation, which may be useful to patients suffering from insomnia and chronic diarrhea, respectively. TCAs also cause weight gain and may be useful in treating neuropathic pain. However, HIV-infected patients, particularly those with more advanced disease, are more sensitive to and less able to tolerate anticholinergic side effects of TCAs. Anticholinergic effects include dry mouth, blurred vision, cognitive impairment, or orthostasis and may lead to non-adherence or treatment failure.

Treatment failure is primarily caused by underdosing or inadequate length of treatment. Monitoring serum levels and ensuring a full 6-week trial at appropriate dosing is necessary to achieve the best effect and may be particularly important when there are concerns about adherence, absorption, or drug interactions. Because TCAs can be lethal in overdose, an SSRI may be a safer choice for patients at risk for suicide.

Increased levels of TCAs may result when concomitantly used with PIs or NNRTIs (see [Appendix II: Interactions Between HIV-Related Medications And Psychotropic Medications](#)).

Psychostimulants

Psychostimulants may be used when depressive symptoms include psychomotor slowing and fatigue in patients with more advanced immunosuppression and/or CNS involvement with HIV. Advantages include more rapid onset of action and fewer drug-drug interactions with ART.

3. Psychotherapy

RECOMMENDATION:

Clinicians should refer patients for psychotherapy in the following situations:

- **When basic supportive psychoeducational interventions are deemed ineffective in alleviating mood symptoms**
- **When patients with depressive symptoms refuse (or prefer not to take) recommended psychotropic medication**
- **When situational events precipitate mild to moderate depressive symptoms**
- **When patients appear to have difficulty accepting the diagnosis of a mood disorder (especially when this appears to cause high-risk behavior or non-adherence to medication)**
- **When patients request a referral**

Key Point:

Combining psychotherapy with antidepressant and mood-stabilizing medications is the most effective treatment option for many patients. If treatment with medications is not possible (e.g., some patients in recovery are opposed to taking psychotropic medications), psychotherapy alone may be as effective as medication in cases of mild to moderate depression.

There are several different types of individual and group psychotherapies that may be useful for treatment of depression. Interpersonal therapy and cognitive-behavioral therapy are time-limited, focused treatments for depression. In controlled clinical trials, both therapies were effective in reducing depressive symptoms in HIV-infected individuals.

4. Alternative Therapies for Depression

RECOMMENDATIONS:

Clinicians should inform patients who decide to use alternative treatments of the following:

- **Drug interactions and toxicities may occur**
- **These treatments may take longer to be effective**
- **These medications are not well studied**

Clinicians should inform patients that concomitant use of St. John's Wort with PIs or NNRTIs is contraindicated because it may lead to subtherapeutic ART drug concentrations.

In addition to body therapies and acupuncture, herbal supplements such as St. John's Wort (SJW) are commonly used alternative therapies for depression. To make an informed choice, patients should be aware of current knowledge about SJW. SJW induces the cytochrome P450 metabolic pathway. Consequently, it has numerous drug interactions, including the potential to lead to subtherapeutic concentrations of ART drugs. In addition, well-designed clinical trials of SJW have failed to demonstrate efficacy.

S-Adenosylmethionine (SAM-e) is another compound used for depression. To date, there are no documented serious drug interactions. Further study is needed to determine its efficacy for depression.

5. Treatment Follow-Up

RECOMMENDATIONS:

After initiating treatment, clinicians should schedule a brief visit or phone conversation every 1 to 2 weeks to support adherence, assess response and side effects, and remind the patient that it may take 3 weeks or longer for mood to improve. After 3 to 4 weeks, the clinician should perform an in-person assessment of symptom improvement.

During the maintenance phase of treatment with anti-depressant medication, clinicians should schedule a brief visit every 4 to 12 weeks to assess adherence, sustained therapeutic response, and side effects.

After referring patients to another provider for medication or psychotherapy, primary care clinicians should schedule a brief visit or phone conversation within 1 to 4 weeks after the referral to ensure that the patient followed through.¹³

Clinicians should encourage patients who experience recurrent depression to remain on medication indefinitely.

Primary care clinicians should maintain ongoing coordination of care with the patient's mental health care provider.

Sleep, energy level, and the ability to meet obligations tend to improve before mood. A brief visit or phone conversation every 1 or 2 weeks is advisable at the beginning of treatment. After 3 to 4 weeks, improvement in a patient's symptoms should be assessed in person. Little or no improvement suggests the need to change treatment. If side effects are tolerable, the first option is generally to increase the dose. If a trial for several weeks at the maximum dose is not effective, options include changing the medication, augmenting it with another agent, or referral.

Depression is usually a chronic condition characterized by intermittent relapses. After the first episode of depression resolves, treatment should be continued for 6 months to 1 year. Repeated episodes of depression suggest the need for lifelong treatment with medications, preferably in combination with psychosocial treatment (e.g., monthly individual psychotherapy sessions).

E. Treatment of Depression in Pregnant Women

RECOMMENDATIONS:

Clinicians should screen all HIV-infected pregnant women for depression at least once each trimester, including the first prenatal visit, and should educate patients about the risks of perinatal depression.

When treatment is indicated, clinicians and HIV-infected pregnant women should discuss the risks and benefits of antidepressant therapy. The discussion should include the following:

- **Patient's history of depression**
- **Patient's past response to medication**
- **Increased risk for postpartum depression**
- **Risks of prenatal exposure to psychotropic medication versus the benefit of stabilizing the patient's depressive symptoms**
- **Possible drug-drug interactions between antidepressants and ART medications**

Clinicians should evaluate pregnant patients for the use of antidepressant medication, alone or in combination with nonpharmacologic treatment, when patients present with moderate to severe depression, a history of postpartum depression, or recurrent major depression.

Primary care clinicians should refer HIV-infected pregnant women with depression to a psychiatrist when treatment considerations are complicated by:

- **The presence of a co-occurring mental health disorder or when the patient's depression is a feature of an underlying mental health disorder**
- **Previous non-response to antidepressive therapy**
- **Possible drug-drug interactions with other medications**
- **Allergic reactions to antidepressant medications**

Routine screening for prenatal depression among HIV-infected pregnant women can prevent significant complications, including:

- Relapse of a major depressive disorder during pregnancy if treatment is interrupted¹⁴
- Poor adherence to ART, which can increase the risk of mother-to-child transmission of HIV¹⁵
- Impaired neurobehavioral function, including lower cognition and language development, in the child^{15,16}
- Postpartum depression¹⁵

A validated screening tool for depression should be used at least once each trimester, including the first prenatal visit. Perinatal depression screening tools include the Edinburgh Postnatal Depression Scale¹⁷ and the Postpartum Depression Screening Scale¹⁸ (also see [Appendix I: Mental Health Screening Tools](#) and the [Mental Health Quick Reference Card](#)).

Pharmacologic treatment may be indicated when an HIV-infected pregnant patient presents with depressive symptoms, particularly when nonpharmacologic treatment does not stabilize the symptoms.

Pharmacologic treatment of moderate to severe depression, including major depressive disorder, is prudent in HIV-infected pregnant women because of the significant morbidity that can result if these conditions are not treated effectively. The SSRI fluoxetine and tricyclic antidepressants do not appear to adversely affect neurobehavioral function in preschool and early-school children.^{16,19} However, an increased risk for preterm birth has been noted with all antidepressants, and possible drug-drug interactions between antidepressants and HIV medications require consideration (see [Appendix II: Interactions Between HIV-Related Medications and Psychotropic Medications](#)). Although the health risks associated with these psychotropic medications are considered low, other adverse effects during pregnancy are listed in Table 4. Additional studies are required to definitively weigh the risks of pharmacologic treatment versus the risks of foregoing such treatment.

TABLE 4 CONSIDERATIONS FOR PSYCHOTROPIC MEDICATIONS DURING PREGNANCY	
Tricyclic antidepressants	<ul style="list-style-type: none"> • Small association with cardiovascular defects with the use of clomipramine²⁰
SSRI antidepressants	<ul style="list-style-type: none"> • Risk of persistent pulmonary hypertension in the newborn²¹ • Transient neonatal abstinence symptoms may be present after use in late pregnancy²²: agitation, irritability, feeding and sleep disturbances, or respiratory distress • <i>Paroxetine is not recommended by the FDA for use during pregnancy (class D)</i> <ul style="list-style-type: none"> ○ <i>May confer an increased risk of cardiovascular defects resulting from exposure during the first trimester</i>²³
Atypical antidepressants	<ul style="list-style-type: none"> • Few data are available for the use of atypical antidepressants, including: <ul style="list-style-type: none"> ○ Venlafaxine ○ Duloxetine ○ Bupropion ○ Mirtazapine ○ Reboxetine
Monoamine oxidase inhibitors	<ul style="list-style-type: none"> • <i>Not generally prescribed during pregnancy</i> <ul style="list-style-type: none"> ○ <i>May cause sudden and severe maternal hypertension (e.g., hypertensive crisis)</i>

Screening and Treatment of Postpartum Depression

RECOMMENDATIONS:

Primary care clinicians or obstetrical care providers should screen for postpartum depression in HIV-infected women at the routine 4- to 6-week postpartum obstetrical visit; a depression screen should also be performed at 2 to 3 weeks postpartum in women with a current or previous diagnosis of depression.

All clinicians involved in the care of the mother and newborn (e.g., the obstetrician, the HIV primary care clinician, the pediatrician) should be vigilant for signs and symptoms of postpartum depression. If the mother is identified as having postpartum depression, the identifying clinician should inform all other providers of the mother’s depression after obtaining her consent.

Many women develop subclinical depression (e.g., “baby blues”) 3 to 4 days postpartum that remits within 2 weeks after onset.²⁴ Patients who experience depressive symptoms after delivery that do not remit within 2 weeks are at high risk for postpartum major depression, a condition that, if left untreated, can have severe consequences for both the mother and the long-term development and behavior of the child. The *DSM IV-TR* defines postpartum major depression as a major episode of depression that occurs within the first 4 weeks after delivery. Screening with a validated screening tool, such as the Edinburgh Postnatal Depression Scale¹⁷ or the Postpartum Depression Screening Scale,¹⁸ should be performed at the routine 4- to 6-week postpartum obstetrical visit; a depression screen should also be performed at 2 to 3 weeks postpartum in

women with a current or previous diagnosis of depression. Depression screening can also take place during a routine well-child visit.²⁴ Pharmacologic treatment of postpartum depression follows the same guidelines as those for pharmacologic treatment of depressive disorders in nonpregnant adults.

Key Point:

Because pediatricians see the mother and infant more often in the first few weeks postpartum, they are in a unique position to detect depressive symptoms in mothers, including difficulty forming a maternal bond with the infant.

II. MANIA

RECOMMENDATION:

Clinicians should immediately refer patients experiencing mania for psychiatric evaluation and care.

In addition to mania seen in patients with bipolar disorders that predate their HIV infection, HIV-infected patients may develop mania that is thought to be secondary to HIV CNS involvement. The rate of secondary mania, or “AIDS mania,” may be as high as 4% in a clinic population.^{25,26} This form of mania tends to occur in patients with more advanced immunosuppression and to be associated with HIV-related cognitive impairments. It may also have a more chronic course. Mania may be a risk factor for HIV transmission because manic patients may experience symptoms of impulsivity, disinhibition, and hypersexuality, which may impede their use of safer-sex practices (see *Determination of Decisional Capacity in HIV-Infected Patients With Mental Health Disorders* chapter for a discussion on involuntary confinement in these situations). In addition, patients with bipolar disorder are at greater risk for having comorbid alcohol or other substance use disorders, which also magnify impediments to safer-sex behavior.

A. Clinical Presentation

In its full-blown form, mania is a period of abnormally elevated or irritable mood and is easy to identify. Mania may or may not be accompanied by psychotic symptoms. The same symptoms that define mania and hypomania (same symptoms as mania but less severe) in bipolar disorder are also present in AIDS mania. However, AIDS mania is much more likely to be accompanied by cognitive deficits that are usually present at the time of initial presentation but, in some cases, may not be evident until later in the course of illness.

B. Diagnosis

RECOMMENDATIONS:

Clinicians should consult with or refer patients to a psychiatrist when there is doubt concerning the diagnosis.

Clinicians should consult with or refer patients to a psychiatrist when it is not clear whether patients are hypomanic or depressed.

Clinicians should use the *DSM-IV* diagnostic criteria for mania (see Table 5).

If the patient's mood is expansive, at least three symptoms should be present in order to make the diagnosis. If the mood is irritable, four symptoms should be present (see Table 5). For the clinician to make a diagnosis of mania, the patient's symptoms should impair usual functioning and persist for at least 1 week.

TABLE 5
DIAGNOSTIC CRITERIA FOR MANIC EPISODE

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 week (or any duration if hospitalization is necessary).

B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:

1. Inflated self-esteem or grandiosity
2. Decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
3. More talkative than usual or pressure to keep talking
4. Insomnia or hypersomnia nearly every day
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
6. Flight of ideas or subjective experience that thoughts are racing
7. Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)
8. Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
9. Excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

C. The symptoms do not meet criteria for a Mixed Episode.

D. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

E. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).

Diagnostic Criteria for Mixed Episode

- A. The criteria are met both for a Manic Episode and for a Major Depressive Episode (except for duration) nearly every day during at least a 1-week period.**
- B. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.**
- C. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).**

Diagnostic Criteria for Hypomanic Episode

- A. A distinct period of persistently elevated, expansive, or irritable mood, lasting throughout at least 4 days, that is clearly different from the usual nondepressed mood.**
- B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:**

1. Inflated self-esteem or grandiosity
2. Decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
3. More talkative than usual or pressure to keep talking
4. Flight of ideas or subjective experience that thoughts are racing
5. Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)
6. Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
7. Excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., the person engages in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

- C. The episode is associated with an unequivocal change in functioning that is uncharacteristic of the person when not symptomatic.**
- D. The disturbance in mood and the change in functioning are observable by others.**
- E. The episode is not severe enough to cause marked impairment in social or occupational functioning, or to necessitate hospitalization, and there are no psychotic features.**
- F. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).**

Note: Hypomanic-like episodes that are clearly caused by somatic antidepressant treatment (e.g., medication, electroconvulsive therapy, light therapy) should not count toward a diagnosis of Bipolar II Disorder.

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1. Bipolar Disorder

The first episode in bipolar disorder may be a depressive episode. Regardless of how many episodes of depression patients have, a single manic episode indicates that the diagnosis is bipolar disorder, and treatment should be prescribed accordingly. A single manic episode without a history of depression also indicates a diagnosis of bipolar disorder.

2. Hypomania

Symptoms of hypomania are similar to those of mania, but the impairment in functioning is not as extreme. Patients with symptoms of hypomania that include irritable mood may be difficult to differentiate from patients with depression. Correct diagnosis is essential because treatment of hypomania with an antidepressant medication, instead of an appropriate mood stabilizer, may provoke a full-blown episode of mania.

3. Other Causes of Mania

Manic symptoms can also be caused by HIV-related medications, alcohol, cocaine, amphetamines, and anabolic steroids. Medical illness, including some opportunistic infections, may also induce mania.

C. Management of HIV-Infected Patients With Mania

RECOMMENDATION:

Until patients with mania are stabilized, clinicians should maintain consultation with a psychiatrist or the patient should be under psychiatric care.

1. Emergency Evaluation

A patient experiencing mania requires emergency psychiatric intervention. For primary care clinicians, this means immediately referring the patient to a psychiatrist or emergency department. Patients with mania often have severely impaired judgement and are unable to listen to advice. In addition, manic patients often enjoy their symptoms, which makes them resistant to treatment. To overcome this resistance, it is often helpful to involve such patients' families and friends. If necessary, the police can transport a patient to the emergency department. In these cases, the clinician should then contact the emergency department to follow up with the disposition of the patient.

2. Medications

Treatment of both the acute and maintenance phases of mania in more immunocompetent patients usually involves use of a mood stabilizer and/or antipsychotic medication. Valproic acid, gabapentin, or other anticonvulsant medications are most often used to control symptoms.

Key Point:

Treating hypomanic patients with antidepressants may lead to a full-blown episode of mania.

The treatment of both AIDS mania and bipolar disorder in sicker patients requires even more careful attention to medication toxicity, drug interactions, and adherence. Use of a single agent, usually an antipsychotic medication, if possible, may be preferable. Serum drug level monitoring is not needed with antipsychotic medications, and they can be administered on a once-daily basis. Lithium is problematic because of risk of CNS toxicity and difficulty maintaining therapeutic serum drug levels, even when medication-taking is supervised. The “atypical” antipsychotic medications are more commonly used because of their more favorable side effect profiles and tolerability. These medications include risperidone, olanzapine, quetiapine, and aripiprazole (see Table 6). Some mood stabilizers have significant associated liver and bone marrow disorders.

ART medications also have a role in the treatment of AIDS mania. Suppression of systemic viral load may result in corresponding reduction of viral replication in the CNS. The degree of ART CNS penetration may be one factor used to guide choice of ART medication.

TABLE 6 COMMONLY USED MEDICATIONS TO TREAT MANIA
Lithium
Valproic acid (Depakene, Depakote)
Lamotrigine (Lamictal)
Gabapentin (Neurontin)
Risperidone (Risperdal)
Olanzapine (Zyprexa, Zydys)
Quetiapine (Seroquel)
Aripiprazole (Abilify)
Ziprasidone (Geodon)

3. Psychotherapy

Psychotherapy that focuses on adaptation to illness(es), identification of early symptoms to prevent recurrence of illness, and treatment adherence may be combined with medications to enhance the management of selected patients.

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