

I. INTRODUCTION

Many HIV-infected people experience somatic symptoms, including insomnia, pain, fatigue, poor appetite, weight changes, and sexual dysfunction. Although somatic symptoms are rarely life threatening, they occur frequently, are often overlooked, are difficult to treat, and adversely affect quality of life. Somatic symptoms are not diagnostic of any particular disorders. Instead, they are commonly multifactorial and often coexist with medical and/or psychiatric conditions.

This chapter addresses the presentation, effects, and management of somatic symptoms from a mental health perspective that includes discussion of medical causes. The importance of assessing patients for medical causes of somatic symptoms cannot be overstated, particularly when multiple symptoms present concomitantly. Any of the symptoms could be an indication of a medical condition, mental health disorder, or both. For example, symptoms such as abdominal pain, fatigue, and weight loss require careful assessment. Untreated or undertreated mental health disorders can worsen patients' somatic symptoms and result in substantial emotional suffering, possibly leading to serious morbidity, even suicide.

Comprehensive medical diagnostic and treatment considerations for HIV-infected adults are available in the [Clinical Guidelines for the Treatment of HIV-Infected Adults](#).

II. SCREENING FOR SOMATIC SYMPTOMS

RECOMMENDATION:

Clinicians should assess for new somatic symptoms at each visit with direct questions that elicit accurate responses from patients.

Routine screening for somatic symptoms is essential because some patients may not consider their symptoms important until significant morbidity has resulted. In addition, the multifactorial nature of somatic symptoms may prevent patients from precisely articulating their symptoms. Clinicians should assess for new somatic symptoms at each visit with direct questions that elicit accurate responses from patients.

The questions listed below are included in the Patient Health Questionnaire 15-Item Somatic Symptom Severity Scale (PHQ-15) and detail symptoms that account for 90% of somatic symptoms encountered in the primary care setting.¹

During the past 4 weeks, how much have you been bothered by any of the following problems?

1. Stomach pain
2. Back pain
3. Pain in your arms, legs, or joints (knees, hips, etc.)
4. Menstrual cramps or other problems with your periods [Women only]
5. Headaches
6. Chest pain
7. Dizziness
8. Fainting spells
9. Feeling your heart pound or race
10. Shortness of breath
11. Pain or problems during sexual intercourse
12. Constipation, loose bowels, or diarrhea
13. Nausea, gas, or indigestion
14. Feeling tired or having low energy
15. Trouble sleeping

These questions are scored as 0 (“not bothered”), 1 (“bothered a little”), and 2 (“bothered a lot”) to help clinicians determine both the number of symptoms a patient may be experiencing and the severity of the symptoms. Total PHQ-15 scores of 5, 10, and 15 represent cutoff values for low, medium, and high somatic symptom severity, respectively.

III. ASSESSMENT, DIAGNOSIS, AND MANAGEMENT

RECOMMENDATIONS:

Clinicians should:

- **Assess for common medical and mental health disorders associated with somatic symptoms when patients present with somatic complaints** (see Table 1)
- **Review and update medication lists to identify possible drug-drug interactions or side effects that may be responsible for somatic symptoms**

Clinicians should treat both the underlying cause of the somatic symptoms and the symptoms themselves.

Clinicians should refer patients to a psychiatrist or clinical psychologist when:

- **The cause of the somatic complaints cannot be fully explained by comprehensive diagnostic tests**
- **There is significant mental distress in response to the symptoms, regardless of whether an underlying cause has been identified**

Once the presence of somatic symptoms has been established, the cause of the symptoms should be determined (see Table 1). Baseline and annual physical examination and mental health and substance use screening can ensure that possible underlying etiologies are identified and that patients receive timely treatment for any comorbid disorders.

Key Point:

Identification of a medical disorder does not exclude the existence of a mental health or substance use disorder. Poor physical health is frequently accompanied by a mental health disorder, particularly depression.²

The distinction between a medical disorder and a mental health disorder is not always clear. For example, depression accompanies a variety of medical disorders and is independently associated with physiological changes in the body. Back pain, headache, abdominal pain, weight loss, and fatigue can all be somatic manifestations of depression. Shortness of breath, palpitations, abdominal pain, and dizziness can be manifestations of anxiety. Schizophrenia, bipolar mania, and other psychiatric disorders can all present with somatic symptoms.

Patients with mental health disorders may also present with somatic *delusions*. A somatic delusion is a false fixed belief of suffering from a disease that does not exist. For example, the depressed patient may say, *My body is rotting inside*. Somatic symptoms and somatic delusions, in the context of severe mental health disorders, can lead to self-destructive behaviors, including intentional or unintentional self-harm or suicide. Early identification and appropriate referral and treatment can be lifesaving in these cases.

For a comprehensive discussion regarding suicide assessment and treatment, refer to [Suicidality and Violence in Patients With HIV/AIDS](#). Information regarding depression and mania can be found in [Depression and Mania in Patients With HIV/AIDS](#).

Assignment of symptoms to malingering or somatoform disorders, such as hypochondriasis, requires a careful initial assessment for other causes. When malingering or a somatoform disorder is suspected, consultation with a psychiatrist may be necessary for confirmation.

TABLE 1
ASSESSMENT FOR DISORDERS ASSOCIATED WITH SOMATIC SYMPTOMS

Medical Assessment	
Physical examination	<ul style="list-style-type: none"> • Refer to Primary Care Approach to the HIV-Infected Patient: Table 2. HIV-Related Physical Examination
Laboratory assessment	
Immunologic and virologic assessment	<ul style="list-style-type: none"> • CD4 count • Viral load • Significant decline in immune function and high levels of viremia are often associated with somatic complaints
Hematologic assessment	<ul style="list-style-type: none"> • Neutropenia and anemia can be detected by complete blood count with a differential
Metabolic assessment	<ul style="list-style-type: none"> • Muscle enzyme elevations • Abnormal hormonal levels (especially testosterone levels) • Electrolyte imbalances • Liver enzyme elevations • Thyroid dysfunction • Vitamin deficiencies, including B₁₂ and folate
Syphilis screening	<ul style="list-style-type: none"> • Syphilis screening can help identify acute versus latent infection • Acute syphilitic meningitis, as well as neurosyphilis, may result in physical or mental (or both) symptoms
Mental Health and Substance Use Assessment	
Mental health assessment	<ul style="list-style-type: none"> • Assess for the following: <ul style="list-style-type: none"> ○ Cognitive impairment ○ Depression ○ Anxiety ○ Sleep habits ○ Appetite ○ Post-traumatic stress disorder ○ Psychosocial status ○ Suicidal/violent ideation ○ Past psychiatric history, including diagnoses, hospitalizations, and psychotropic medications
Substance use assessment	<ul style="list-style-type: none"> • Types of drugs; past and current use <ul style="list-style-type: none"> ○ Street drugs—Marijuana, cocaine, heroin, methamphetamine, MDMA/ecstasy ○ Illicit use of prescription drugs ○ Alcohol ○ Tobacco ○ Frequency of use and usual route of administration • Risk behaviors—Drug/needle sharing, exchanging sex for drugs, sexual risk-taking while under the influence of drugs or alcohol • Toxicology screening (with the patient’s consent) may detect acute intoxication, addiction, or withdrawal

The management of somatic symptoms in combination with existing chronic illnesses, drug side effects and interactions, and the psychological and emotional state of the patient is a clinical challenge. When physical health disorders are accompanied by mental health disorders, it is important to treat both simultaneously. Knowledge about potential drug-drug interactions, dosing, and side effects is essential. Psychiatric medications and psychotherapy may be required in addition to medical treatment.

Refer to [*Interactions Between HIV-Related Medications And Psychotropic Medications: Indications And Contraindications.*](#)

IV. INSOMNIA

A. Assessment and Diagnosis

RECOMMENDATIONS:

Clinicians should ask patients at routine monitoring visits about quality of sleep and difficulty initiating or maintaining sleep.

Clinicians should determine whether a patient’s insomnia is acute, chronic, primary, or secondary.

Insomnia, or “problem sleeping,” is a common complaint among people with HIV. Insomnia can be multifactorial and, therefore, a complex condition to treat. Insomnia involves not only how many hours a patient sleeps at night but also how a patient feels upon waking and the patient’s perception of his/her quality of sleep. Insomnia can be acute or chronic and can be a primary or secondary condition attributable to a physiologic or mental health disorder. Patients who suffer from insomnia tend to have impaired daytime cognitive function,³ which can lead to increased absenteeism from work and other disruptions in life,⁴ including missed appointments. Other problems associated with insomnia include the following:

- Insomnia may be associated with nonadherence to ARV therapy⁵
- Physical and mental health disorders, including acute episodes of most severe mental illnesses, can cause insomnia and/or worsen preexisting primary insomnia
- Insomnia can be an early sign of relapse in patients with a history of mental health disorders⁶
- Insomnia may become even more severe in advanced HIV infection⁷
- A patient with insomnia has greater risk of a first episode of depression than a patient without insomnia⁸

Possible medical, mental health, and substance use etiologies of insomnia are listed in Table 2.

TABLE 2
DIFFERENTIAL DIAGNOSIS FOR PATIENTS WITH INSOMNIA

General Medical and HIV-Related Etiologies	
<ul style="list-style-type: none"> • Medications that may cause insomnia side effects 	<ul style="list-style-type: none"> ○ β-blockers ○ Bronchodilators ○ Calcium channel blockers ○ Corticosteroids ○ Decongestants
<ul style="list-style-type: none"> • ARV medications 	
<ul style="list-style-type: none"> – Efavirenz 	Has been associated with a variety of disturbances in sleep-wake patterns and nightmares
<ul style="list-style-type: none"> – Lamivudine 	Has been associated mood disturbances
<ul style="list-style-type: none"> • Medical conditions 	<ul style="list-style-type: none"> ○ Hyperthyroidism ○ Chronic renal failure ○ Lung disease ○ Congestive heart failure ○ Pain ○ Diarrhea ○ Incontinence ○ Fever ○ Dyspnea and sleep apnea ○ Periodic limb movements in sleep or restless limb syndrome
Mental Health Etiologies	<ul style="list-style-type: none"> ○ Side effects of psychotropic medications, including selective serotonin-reuptake inhibitors (SSRIs) ○ Severe psychiatric disorders, including mania and psychosis ○ Mood and anxiety disorders
Substance Use Etiologies	<ul style="list-style-type: none"> ○ Illicit drug use, particularly stimulant drugs ○ Alcohol and caffeine consumption ○ Nicotine

B. Management

A careful evaluation of the possible causes of insomnia should be conducted before initiating treatment. Lack of response to treatment after a reasonable period may require a mental health referral to assess for an underlying mental health disorder.

1. Nonpharmacologic Treatment

RECOMMENDATIONS:

Clinicians should use nonpharmacologic approaches for treating insomnia before prescribing medications.

Clinicians should discuss sleep hygiene with patients with insomnia (see Table 3).

Behavioral therapy may benefit some patients with insomnia. Techniques may include cognitive therapy, relaxation training, sleep restriction, and phototherapy. When possible, patients with insomnia should be evaluated at least once by a psychiatrist or clinical psychologist, who may be more likely to identify an underlying mental health disorder that warrants more aggressive monitoring and management.

Clinicians should offer practical nonpharmacologic methods of improving sleep. Table 3 lists specific strategies.

TABLE 3 STRATEGIES TO IMPROVE SLEEP
<ul style="list-style-type: none"> • Avoid napping during the day • Avoid caffeine (coffee, tea, chocolate, soda), alcohol, and nicotine before bedtime, or abstain completely • Take hot baths before bedtime • Exercise for ≥ 30 min/day most days of the week; however, avoid exercise before bedtime • Place the bedroom clock out of sight • Practice a bedtime routine, such as going to bed and waking up at a set time • Avoid activities that are otherwise performed outside of the bedroom, such as working • Avoid stimulating activities before bedtime, such as watching television or browsing the Internet

2. Pharmacologic Treatment

RECOMMENDATION:

Medications that have narrow therapeutic ranges and potential for abuse, including barbiturates, choral hydrate, and meprobamate, should not be used as first-line agents for treating insomnia.

The medications described below are commonly used to treat insomnia. Barbiturates, choral hydrate, and meprobamate were previously prescribed to treat insomnia; however, because of their narrow therapeutic windows and potential for abuse, they are no longer drugs of choice. All of these drugs should be prescribed with caution because patients may develop tolerance within a short period of time, and withdrawal symptoms may be severe.

Sedative/Hypnotic Agents

Pharmacologic therapy with benzodiazepines has been used successfully to treat insomnia. Benzodiazepines with long half-lives, such as flurazepam, may be most beneficial for use in patients whose insomnia is associated with anxiety. However, some primary care clinicians are wary of prescribing this class of agents because of the addiction potential and the residual drowsiness patients may experience the following day. Temazepam (Restoril) has been used with success and has an intermediate half-life. Although protease inhibitors (PIs) may prolong the

duration of many benzodiazepines because of inhibition CYP3A4 enzyme activity, resulting in excessive daytime somnolence, this effect does not apply to temazepam, which is metabolized by glucuronidation.

The newer hypnotic agents, zaleplon (Sonata), zolpidem (Ambien), and eszopiclone (Lunesta), are benzodiazepine receptor agonists with shorter half-lives and are not likely to result in the day-after drowsiness. They may have decreased addiction potential compared with older agents. Patients can be educated about using hypnotics on an as-needed basis rather than nightly; it is easier for patients to discontinue a drug that they are not taking every day. The inhibition of CYP3A4 enzyme activity by PIs is also a concern when prescribing benzodiazepine receptor agonists, particularly eszopiclone.

Refer to [*Interactions Between HIV-Related Medications And Psychotropic Medications: Indications And Contraindications.*](#)

Antidepressants

RECOMMENDATIONS:

Clinicians who prescribe tricyclic antidepressants to induce sleep should obtain routine blood levels in patients receiving long-term treatment. Assessment of blood levels may not be necessary for patients without liver disease who are receiving low doses of these agents.

Clinicians should perform a routine electrocardiogram before prescribing tricyclic antidepressants and should not prescribe this class of drugs to patients with cardiac conduction problems.

Antidepressants have been used to induce sleep.

- *Trazodone* can promote sleep and is widely used for this purpose. However, trazodone levels are increased by PIs, especially when they are boosted; therefore, lower doses should be used in patients receiving PIs. Trazodone may cause priapism, but the incidence is low.
- *Tricyclic antidepressants* are beneficial but have longer half-lives than short-acting hypnotic agents, and potential adverse effects include cardiac dysrhythmias and pulmonary complications. A routine electrocardiogram should be performed before prescribing tricyclics, and this class of drugs should not be prescribed to patients with cardiac conduction problems. However, tricyclic antidepressants also have characteristics that may benefit some patients, including treatment of chronic pain, promotion of weight gain, and reduction of diarrhea. Routine blood levels of tricyclic antidepressants should be obtained in patients receiving long-term treatment. However, assessment of blood levels may not be necessary for patients without liver disease who are receiving low doses of these agents (e.g., 10 to 25 mg/day amitriptyline, nortriptyline, doxepin, or desipramine).

The SSRI antidepressants are not sufficiently sedating to be used as sleeping agents.

Antihistamines

While many clinicians continue to prescribe antihistamines for sleep, side effects that should be taken into consideration include the following:

- Daytime drowsiness
- Diminished daytime cognitive abilities
- Uncomfortable anticholinergic effects

Melatonin and Melatonin-Agonist Drugs

RECOMMENDATION:

Clinicians should advise patients of the potential side effects, particularly severe hypersensitivity reactions such as anaphylaxis and angioedema, of melatonin and melatonin-agonist therapy.

Clinicians should be familiar with doses and potential adverse reactions associated with melatonin therapy, including over-the-counter preparations. The melatonin agonist ramelteon (Rozerem), the first of a new class of melatonin agonists to receive FDA approval, has been approved for the treatment of insomnia and may have some advantages over sedative/hypnotic agents with regard to dependence and overuse. However, patients should be cautioned about potentially severe adverse reactions, including hypersensitivity reactions such as anaphylaxis and angioedema. Importantly, long-term interactions with ARV agents are unknown at this time.

V. PAIN

A. Assessment and Diagnosis

RECOMMENDATIONS:

Clinicians should have a heightened awareness of pain among HIV-infected patients and should ask patients about pain at each visit.

Clinicians should assess for fatigue and mental health disorders in patients with chronic pain.

Pain is a complex phenomenon that includes both a sensory component and a component of psychological distress. Pain can be described in a variety of ways (see Table 4), and careful diagnostic evaluation results in better treatment and outcomes.

TABLE 4 DESCRIPTIONS OF PAIN	
Acute nociceptive pain*	Typically constant, well-localized, and either sharp or stabbing or dull and cramping, depending on the area and injury involved
Chronic pain syndromes	Involve more complex sensations and descriptions but can mimic any of the sensations associated with acute pain
Neuropathic pain*	Characteristically burning, tingling, lancinating, or electric-like

* Sometimes pain is a mixture of nociceptive and neuropathic factors.

The experience of pain cannot be easily separated from either the mental health or the physical state of the patient. Pain is often associated with fatigue, anxiety, sleep disorders, changes in appetite, and depressive symptoms, and HIV-infected patients are at increased risk for certain painful conditions, such as neuropathy. Social environments, cultural backgrounds, and psychological and emotional pain contribute to the manner in which people perceive and cope with physical pain. In addition, pain prevalence in injection drug users (IDUs) may be different from that in non-IDUs.⁹ Current or former IDUs may have lower pain tolerance, or higher tolerance to analgesics, than non-IDUs.

Possible medical etiologies are assessed first and, once excluded, are followed by assessment for mental health and substance use etiologies (see Table 5).

TABLE 5
DIFFERENTIAL DIAGNOSIS FOR PATIENTS WITH PAIN

Medical Etiologies	
<ul style="list-style-type: none"> • HIV progression 	Severity of pain, its distribution, and its effect on quality of life all increase as HIV progresses; declining CD4 cell counts are directly related to the likelihood of developing pain syndromes ¹⁰
<ul style="list-style-type: none"> • Diabetes 	Diabetes can cause or contribute to neuropathic and nociceptive pain
<ul style="list-style-type: none"> • Opportunistic infections 	Herpes simplex virus or varicella zoster virus can cause or contribute to neuropathic and nociceptive pain
<ul style="list-style-type: none"> • Postherpetic neuralgia 	A fairly common problem in patients who have had advanced HIV; the condition usually has many of the features of other neuropathic pain syndromes, with burning and prickly sensations in combination with pain
<ul style="list-style-type: none"> • Complications of the peripheral or central nervous system 	Injury or malfunction in the peripheral or central nervous system, such as those resulting from tumors or scar tissue, can cause inflammation or compression of nerves
Mental Health Etiologies	
<ul style="list-style-type: none"> • Depression 	Pain is often a presenting symptom of depression and is more likely to persist in patients with depression; depressed patients often have a lower threshold for pain
<ul style="list-style-type: none"> • Post-traumatic stress disorder and anxiety disorders 	A substantial proportion of people living with HIV/AIDS have symptoms of post-traumatic stress disorder (PTSD) or another anxiety disorder. Patients with PTSD symptoms report greater pain severity and greater disturbance of affect and interference with performance of daily function than those without this disorder. ¹¹ Any anxiety disorder can lower the threshold for pain
<ul style="list-style-type: none"> • Substance use 	Substance use may contribute to the development of pain and inability to tolerate pain, as well as to the development of mental health disorders; in turn, patients with pain may develop substance use problems or dependence on prescribed analgesics
<ul style="list-style-type: none"> • Psychosocial problems 	<ul style="list-style-type: none"> ○ Stressful living conditions or family crises (e.g., loss of a job, the death of a loved one) ○ Domestic violence ○ Daily activities that cause pain, including employment responsibilities that may cause or exacerbate pain

B. Management

RECOMMENDATION:

Clinicians should consider referring patients with chronic pain to a pain management specialist or consider consulting with a specialist during management.

Acute pain associated with immediate injury is usually handled with direct antinociceptive treatments, including narcotics and antiinflammatory drugs. Chronic pain, which is often associated with psychological and functional morbidity, may require more complex and multidisciplinary approaches. Despite the importance of pain management, chronic pain remains undertreated in the HIV-infected population.¹² Clinicians report lack of knowledge, inadequate availability of pain management specialists, and concerns about prescribing opioids and possible drug abuse as major obstacles to improved pain management. Although limited studies exist, some evidence suggests that non-white race, fewer years of education, greater numbers of physical symptoms, and greater psychological distress are independent factors associated with inadequate pain management. Furthermore, it is often difficult for patients living in predominantly non-white neighborhoods to fill prescriptions for opioids.¹³

1. Patient Response to Pharmacologic Pain Treatment

Experts in pain management have established definitions of dependence, tolerance, and pseudoaddiction to describe patients' responses to pain treatment (see Table 6).¹⁴ These definitions can assist clinicians in understanding patients' behavior in response to treatment and to determine whether changes to patients' treatment should be made accordingly. Importantly, the definitions in Table 6 are different from those established by the *Diagnostic and Statistical Manual IV*, which describes the terms tolerance and dependence in the context of intoxication and substance abuse.

TABLE 6 PATIENT RESPONSES TO PAIN MEDICATION	
Dependence	<ul style="list-style-type: none">• Does <i>not</i> refer to a disorder• Refers to the situation in which there has been enough exposure to a substance that its abrupt cessation would lead to a withdrawal syndrome• Occurs in relation to many classes of drugs, including opioids and certain antihypertensives and antidepressants
Tolerance	<ul style="list-style-type: none">• Is <i>not</i> used to characterize addiction• Indicates the need for a higher dose of drug to maintain the same level of effect• Is common to many classes of drugs and may or may not signal a progression of underlying disease
Pseudoaddiction	<ul style="list-style-type: none">• Occurs when medical staff interpret the attempts of patients to obtain analgesics as addictive behaviors when the behavior is actually a consequence of untreated or undertreated pain¹⁵

When a patient exhibits drug-seeking behavior, the minimal differential diagnosis includes dependence, tolerance, pseudoaddiction, psychiatric comorbidity, addiction, and criminal intent. Distinction among these entities by a psychiatrist or by a clinician with experience in identifying underlying causes of drug-seeking behavior will enable the primary care clinician to respond appropriately to such behavior.

2. Pain, Fatigue, and Depression

RECOMMENDATION:

Clinicians should refer patients to a psychiatrist when there is concern that an active mental health disorder is complicating the management of pain.

Pain is often accompanied by fatigue and depression, and these conditions can sustain one another and complicate treatment.^{16,17} In patients with depression, the presence of chronic pain increases the severity of the physical symptoms of depression (including fatigue and insomnia), the duration of depressive episodes, and the frequency of recurring depressive episodes.¹⁸ Although most studies have evaluated the relationship of pain and depression, pain may also be related to other psychiatric disorders, such as PTSD and anxiety disorders. In patients with comorbid PTSD and chronic pain, it is likely that several factors mutually maintain the PTSD and the chronic pain, so that treating one in isolation from the other will be less effective than addressing both.

For additional information regarding depression, see [Depression and Mania in Patients With HIV/AIDS](#); for post-traumatic stress disorder, see [Trauma and Post-Traumatic Stress Disorder in Patients With HIV/AIDS](#).

3. Pain in Substance Users

RECOMMENDATION:

Clinicians should not deny patients treatment of pain because of a history of addiction.

A multidisciplinary approach should be used for the management of pain in patients with comorbid substance use and mental health disorders. Pain is often undertreated in this population, and it can be particularly difficult to treat in the primary care setting, which often does not provide mental health services or substance use treatment services. Management of pain in HIV-infected substance users is further complicated by the possibility that these patients may require higher doses of medications for the pain to be alleviated. Clinicians also need to be aware of the possibility of the pain medicine being used or distributed illicitly.

For a detailed discussion regarding the treatment of pain in HIV-infected substance user, see the Substance Use Guidelines [Pain in the HIV-Infected Substance User](#)

VI. FATIGUE

A. Assessment and Diagnosis

RECOMMENDATION:

Clinicians should maintain a high level of suspicion for depression in patients presenting with fatigue.

Fatigue is a frequent and distressing symptom for people with HIV infection. The prevalence of fatigue among outpatients with HIV may be as high as 37%.¹⁹ Fatigue is generally multifactorial and can accompany other symptoms, such as pain, weight gain, and sexual dysfunction. In HIV-infected patients, fatigue is strongly associated with clinical AIDS and hemoglobin levels ≤ 12 g/dL.¹⁹ Fatigue is both predictive and a consequence of depression.²⁰ In a study of primary care patients from the general population, approximately 40% of patients suffering from fatigue had a past diagnosis of depression or anxiety disorder, with 17.2% receiving a current diagnosis of major depression.²¹

Possible medical, medication-related, and mental health etiologies for fatigue are listed in Table 7.

TABLE 7	
DIFFERENTIAL DIAGNOSIS FOR PATIENTS PRESENTING WITH FATIGUE	
Medical Etiologies	<ul style="list-style-type: none"> • Infections, especially: <ul style="list-style-type: none"> ○ Chronic viral hepatitis ○ Mononucleosis ○ Cytomegalovirus ○ Extrapulmonary mycobacterium tuberculosis ○ <i>M. avium</i> complex • Malignancies • Neurologic disorders including multiple sclerosis and stroke • Systemic/metabolic/endocrinologic disorders <ul style="list-style-type: none"> ○ Electrolyte imbalance ○ HIV-associated neuropathy ○ Type 2 diabetes ○ Anemia ○ Endocrine disorders including hypothyroidism and hypogonadism ○ Connective tissue disorders ○ Obesity and nutritional deficiencies ○ Major organ impairment or failure • Disrupted sleep, including sleep apnea • Pregnancy and menopause
HIV-Related Medications	<ul style="list-style-type: none"> • Zidovudine and other nucleoside analogs • PIs • Ganciclovir • Trimethoprim-sulfamethoxazole (TMP-SMX) • Interferon
Mental Health Etiologies	<ul style="list-style-type: none"> • Affective disorders, especially major depression and dysthymia • Anxiety disorders • Somatoform disorders • Substance use

B. Management

RECOMMENDATION:

Clinicians should use caution when prescribing psychostimulants for fatigue.

If fatigue is not related to depression, psychostimulants may offer some benefit in managing severe HIV-related fatigue. Psychostimulants may also be used to treat fatigue associated with a variety of medical and psychiatric conditions, such as hepatitis C virus, medication-related depression, HIV dementia, and pain. However, psychostimulants should be prescribed with caution. Modafinil, a non-amphetamine-derived psychostimulant, has demonstrated efficacy in some patients with HIV-related fatigue and may have less abuse potential than traditional psychostimulants.²²

Fatigue related to sleep apnea may require treatment with continuous positive airway pressure (CPAP). Evaluation of sleep in a laboratory is often required for such a diagnosis.

When fatigue is related to hypogonadism, replacement therapy with testosterone, either through biweekly injections or gel preparations, has been shown to be safe and effective in testosterone-deficient HIV-infected men. Dehydroepiandrosterone (DHEA) or testosterone replacement therapy has been studied in women,^{23,24} but safety and efficacy have not been established.

VII. APPETITE AND WEIGHT LOSS

A. Assessment and Diagnosis

RECOMMENDATION:

Clinicians should refer patients with depression that is associated with significant weight loss, anorexia symptoms, and psychomotor retardation for psychiatric evaluation.

Malnutrition and being underweight affect quality of life and place HIV-infected people at risk for increased morbidity and mortality. Depression can be associated with anorexia, weight loss, and psychomotor retardation. These patients should be referred as soon as possible for psychiatric evaluation.

Table 8 provides some medical and mental health etiologies associated with weight loss.

TABLE 8	
DIFFERENTIAL DIAGNOSIS FOR PATIENTS WITH APPETITE AND WEIGHT LOSS	
Medical Etiologies	
• Dietary restrictions	Suboptimal caloric intake can result from medication side effects, gastrointestinal conditions, or poor dental health
• Malignancy	Patients with cancer, particularly advanced cancer, often present with weight loss and anorexia
• Hypogonadism	Androgen insufficiency often occurs in HIV-infected men and women and results in weight loss in association with loss of both lean body mass and bone mineral density ^{25,26}
Mental Health Etiologies	
• Depression, mania, and anxiety disorders	These disorders can cause either an increase or a decrease in appetite and may be associated with weight change
• Substance use	Substance use, particularly methamphetamine, cocaine, and heroin use, can be associated with decreased appetite and weight loss
• Eating disorders	<ul style="list-style-type: none"> ○ Anorexia nervosa ○ Bulimia nervosa*

* Bulimia nervosa can also be associated with weight gain.

B. Management

Poor appetite and inadequate caloric intake can lead to increased side effects from ARV therapies, which can lead to poor adherence. Additionally, weight redistribution or abnormal redistribution of body fat can occur with ARV treatment. Patients experiencing disfigurement attributable to ARV therapy are at risk for developing depressive symptoms.²⁷

A registered dietician can work with patients to prescribe an acceptable nutritional plan. Nutritional supplements may benefit patients who are unable to consume enough food to meet daily caloric requirements. The use of anabolic steroids or dronabinol may help alleviate wasting in HIV-infected patients. Inpatient parenteral nutritional therapy may be necessary in extreme cases. Weight loss attributable to hypogonadism may be alleviated by hormone replacement therapy.

Refer to the Clinical Guidelines for the Treatment of HIV-Infected Adults: [*General Nutrition, Weight Loss, and Wasting Syndrome*](#).

VIII. SEXUAL DYSFUNCTION

A. Assessment and Diagnosis

RECOMMENDATIONS:

Clinicians should assess for sexual dysfunction in HIV-infected patients by inquiring about types, patterns, and frequency of sexual behaviors.

Clinicians should attempt to distinguish between the potential psychological and biological factors of sexual dysfunction.

Clinicians should refer patients with potentially dangerous sexual behavior to mental health services or a program with appropriate expertise when possible.

Sexual dysfunction is a complex issue for many clinicians treating HIV-infected patients. Management considerations involve not only treatment of the symptoms and improvement of patients' sexual health but also behavioral counseling to ensure that patients practice safe sex, particularly effective barrier protection, to avoid HIV transmission. Assessment for sexual dysfunction can enable detection of medical, mental health, psychosocial, and substance use disorders associated with sexual dysfunction.

The potential factors for sexual dysfunction can be classified into those that are biological and psychological (see Table 9). However, in the majority of cases, a combination of psychological and biological factors is responsible for sexual dysfunction.

Patients experiencing more complex problems, such as significant difficulties within a relationship, substance use, history of a traumatic sexual experience or abuse, or severe depression and anxiety disorders, may require referral for mental health services. Patients with persistent patterns of compulsive sexual behavior that have an addictive quality may develop a high frequency of risky behaviors and may need specialized treatment for this problem.

TABLE 9
BIOLOGICAL AND PSYCHOLOGICAL FACTORS ASSOCIATED WITH SEXUAL DYSFUNCTION

Biological Factors	
<ul style="list-style-type: none"> • Metabolic 	<ul style="list-style-type: none"> ○ Hyperglycemia/diabetes ○ Lipodystrophy
<ul style="list-style-type: none"> • Endocrine 	<ul style="list-style-type: none"> ○ Hypogonadism ○ Hyperthyroidism ○ Hypothyroidism ○ Hyperprolactinemia
<ul style="list-style-type: none"> • Neurologic 	<ul style="list-style-type: none"> ○ Central nervous system interference, including that induced by antidepressants ○ Spinal cord injury ○ Peripheral neuropathy
<ul style="list-style-type: none"> • Cardiovascular 	<ul style="list-style-type: none"> ○ Atherosclerosis ○ Hypertension ○ Dyslipidemia
<ul style="list-style-type: none"> • Infection 	<ul style="list-style-type: none"> ○ Pelvic inflammatory disease ○ Balanitis/vulvovaginitis
<ul style="list-style-type: none"> • Iatrogenic 	<ul style="list-style-type: none"> ○ Medication-related ○ Medication interactions ○ Radiotherapy ○ Surgical
Psychological Factors	
<ul style="list-style-type: none"> • Traumatic sexual experience or abuse • Poor sex education • Psychosocial barriers to healthful living • Substance use • Depression • Anxiety • Reaction to lipodystrophy • Relationship problems • Loss of partner • Performance anxiety • Diminished libido • Poor communication skills • Fear of transmitting HIV • Fear of superinfection with treatment-resistant HIV or infection with another STI 	

B. Management

RECOMMENDATION:

Clinicians should establish a treatment plan for sexual dysfunction after determining the patient's specific symptoms and/or any known underlying factors.

The treatment of sexual dysfunction in HIV-infected patients is based on the specific symptoms and/or any known underlying factors.

Lifestyle changes, including quitting smoking, losing excess weight, and increasing physical activity may help some people overcome sexual dysfunction. Consideration of changing medications for certain medical conditions may also be appropriate.

Hypogonadism is a common cause of not only sexual dysfunction but also low mood, fatigue, and weight loss in HIV-infected men and women. Replacement therapy with testosterone may be beneficial in men. Testosterone has been used in women, but its safety and efficacy have not been established. Low estrogen levels in women can result in too little lubrication, vaginal epithelial atrophy, and dyspareunia. After consideration of the potential risks and benefits, limited estrogen replacement therapy, particularly in the form of estrogen vaginal gel, may provide relief from these symptoms. Commercial, water-based vaginal lubricants also may ameliorate the symptoms of vaginal atrophy and painful sex.

In men, premature ejaculation can be treated with SSRIs and/or sex therapy. However, SSRIs and many other psychotropic medications have side effects that can interfere with sexual function.

For erectile dysfunction (ED), the phosphodiesterase inhibitors sildenafil citrate (Viagra), vardenafil hydrochloride (Levitra), and tadalafil (Cialis) may be considered. However, their effects on cardiovascular function require careful assessment of patients' cardiovascular risk. Contraindications for these medications include concomitant treatment with nitrate-based drugs, hypotension, cardiovascular risk factors, and severe hepatic and renal impairment. Special consideration is required for patients receiving treatment with α -blockers because of the risk of a sudden decrease in blood pressure when the drugs are taken within a short time of one another (within approximately 4 hours). Dosing considerations are also necessary when ED medications are used with ARV therapy.

Refer to the Clinical Guidelines for the Treatment of HIV-Infected Adults: [HIV Drug-Drug Interactions: Erectile Dysfunction Drugs](#).

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