

I. INTRODUCTION

Information about HIV-infected women over the age of 50 and their treatment is limited because few studies have targeted this gender and age group. However, some generalizations have been observed in clinical studies, including the following:

- Before the use of antiretroviral therapy (ART), older age was a predictor for an increased rate of disease progression to AIDS and death.^{1,2} The age factor can be mitigated by appropriate treatment with ART.^{3,4}
- HIV-related symptoms and side effects of HIV-related medications may be difficult to distinguish from common age-related comorbidities, such as anemia, wasting, dyspnea on exertion, rheumatologic disorders,⁵ dementia, osteoporosis, lipid abnormalities, and insulin resistance.
- Because of the increased incidence of malignancy in HIV-infected adults⁶ and the increased incidence and association of some malignancies with aging, clinicians need to be vigilant for vulvar and cervical neoplasia (see *Anogenital Neoplasia*) and ovarian, breast, and uterine cancer in older women.

This chapter discusses prevalence and identification of HIV in women over the age of 50, primary health care for HIV-infected older women, the implications of initiating ART and/or hormone replacement therapy (HRT), and the psychosocial issues that may affect older women living with HIV infection. The medical care for HIV-infected menopausal women and women over the age of 50 also includes the same elements of routine medical care that are appropriate for HIV-infected persons in general (see the [Adult Treatment](#) guidelines).

II. IDENTIFICATION AND PREVENTION OF HIV IN OLDER WOMEN

The number of older women with HIV infection is expected to increase for two reasons: 1) the rate and incidence of new infections in this age group are increasing,⁷ and 2) women already in care for HIV infection are expected to live longer due to improved ART and other treatment advances.

A. Risk Assessment and Risk-Reduction Counseling

RECOMMENDATION:

Clinicians should discuss sexual and other risk behaviors and HIV prevention education at routine clinical visits for all HIV-infected women, regardless of age.

Women of all ages who are sexually active should receive risk-reduction counseling and education to prevent HIV transmission.^{8,9} The need to discuss sexual risk behaviors with older women is supported by the following data. In New York State during 2007, women over the age of 50 comprised:

- 278 of 1,251 women with all new HIV diagnoses (22%)
- 124 of 435 women with new late* HIV diagnoses (29%)
- 320 of 1,313 women with new AIDS diagnoses (25%)
- 3,694 of 14,679 women living with HIV (25%)
- 7,534 of 21,530 women living with AIDS (35%)

* AIDS within 1 year of HIV diagnosis

Healthcare providers may be reluctant to discuss HIV risk behaviors with older women because it is assumed that these women are not sexually active or have conservative behaviors. Many older women do not perceive themselves as being at risk and may be uncomfortable inquiring about HIV infection. Women of all ages should receive risk assessments and risk-reduction counseling to prevent HIV transmission.⁸

Risk-reduction counseling for the prevention of STI and HIV transmission should include use of condoms. Some older women may not want to use condoms because they experience vaginal irritation from dryness due to atrophic vaginitis, which can occur with decreasing hormone levels during menopause. However, condom use may be particularly important for these patients because atrophic vaginitis may increase mucosal viral transmission of HIV.¹⁰

Key Point:

Use of water-based lubricants and treatment with vaginal estrogen preparations, which are considered safe and effective, can decrease the discomfort that some older women may experience with condom use.¹¹

B. Identification of Acute Retroviral Syndrome and New Diagnoses in Older Women

RECOMMENDATION:

Clinicians should consider acute retroviral syndrome in the differential diagnosis for older women who present with flu-like illnesses.

Older women may present with symptoms of acute retroviral syndrome, which may be dismissed as being associated with other age-related conditions, such as menopause or diabetes. Because the risk for new HIV infection in women over the age of 50 is often underestimated, clinicians need to be vigilant for older women who present in primary care with the acute retroviral syndrome. HIV should be part of the differential diagnosis for flu-like illnesses, and HIV testing should be performed. For recommendations on testing for acute HIV infection and management of patients with acute HIV infection, see [Diagnosis and Management of Acute HIV Infection](#).

III. ROUTINE PRIMARY HEALTHCARE RECOMMENDATIONS FOR OLDER HIV-INFECTED WOMEN

Although many clinicians focus primarily on the complexities of managing HIV disease, general primary care guidelines for older women should also be implemented, including age-specific screening (see Table 1).

TABLE 1 ROUTINE PRIMARY HEALTHCARE RECOMMENDATIONS FOR OLDER HIV-INFECTED WOMEN^a	
Procedure	Frequency
Gynecological evaluation	At baseline and annually and as indicated for ongoing problems. This examination should include direct visualization of the vulva, vagina, and cervix, and a bimanual pelvic examination that includes a digital rectal examination.
Cytologic screening	<ul style="list-style-type: none"> • Cervical Pap tests <ul style="list-style-type: none"> ○ Baseline and then 6 months after baseline; repeat annually, as long as results are normal ○ Abnormal Pap tests results should be repeated every 3 to 6 months until two successive normal Pap tests are reported^b • Anal Pap tests <ul style="list-style-type: none"> ○ Baseline and annually for women with a history of anogenital condyloma or abnormal cervical/vulvar histology
Post-hysterectomy cervical screening ^c	Annual cervical Pap test when: <ul style="list-style-type: none"> • Hysterectomy was performed because of high-grade dysplasia, HPV-related anogenital dysplasia of the cervix, or carcinoma • A supracervical hysterectomy (uterus removed and cervix left in place) was performed • The reason for the hysterectomy cannot be determined by patient self-report or other means • Any cervical tissue remains
STI screening	<ul style="list-style-type: none"> • RPR or VDRL for syphilis with verification of positive test by confirmatory FTA-Abs or TP-PA <ul style="list-style-type: none"> ○ Baseline and at least annually; every 3 months for patients with ongoing high-risk behavior • Gonorrhea and chlamydia^{d,e} <ul style="list-style-type: none"> ○ Baseline and at least annually
Mammography	Annually, starting at age 40 ^f
Bone mineral densities	Baseline at menopause and after 50. The frequency thereafter has not been determined ^g

^a Routine immunizations can be found in the [Immunizations](#) chapter; routine diagnostic screening tests can be found in [Primary Care Approach to the HIV-Infected Patient](#)

^b Colposcopy should be performed for women with abnormal Pap tests. Follow-up would then vary on a case-by-case basis. Women with cervical HSIL should be referred for high-resolution anoscopy.

^c Annual Pap tests are not recommended for HIV-infected women who have undergone a total hysterectomy for reasons not related to cervical abnormalities.

^d All sites of exposure are screened. For specific recommendations regarding the types of assays used, refer to [Gonococcal and Chlamydial Infections](#) in [Management of STIs in HIV-Infected Patients](#)

^e For women with one of the following: recent STI, multiple sexual partners, a new sexual partner, or a sexual partner with symptoms of an STI.

^f American Cancer Society (ACS), available at: <http://caonline.amcancersoc.org/cgi/reprint/53/3/141>

However, the optimal age of initiation for breast screening and the intervals for mammography are still being studied. See *Breast Health in HIV-Infected Women*, for cancer screening guidelines from other organizations.

^g National Osteoporosis Foundation, available at: www.nof.org

IV. USE OF ART IN THE OLDER HIV-INFECTED WOMAN

RECOMMENDATION:

Clinicians should follow standard guidelines for initiation of ART in older women (see [Adult Antiretroviral Therapy](#)).

A. Benefits of ART

Initiating treatment with ART at appropriate CD4 counts and viral load thresholds may be especially important in HIV-infected people over the age of 50 because there is evidence that they progress more quickly and have a lower potential for immune restoration.^{12,13} Appropriate treatment with ART may mitigate some negative effects of aging with HIV infection, such as cognitive decline.¹⁴

B. Risks of ART

Risks of initiating ART include metabolic complications, such as lipid disorders, insulin resistance and diabetes, altered body fat distribution, and, consequently, a higher risk of cardiovascular disease. These antiretroviral-related complications can be difficult to diagnose and manage in older patients who may have the same, age-related, pre-existent metabolic abnormalities.

Another potential risk of ART includes bone loss, although the relationship among HIV infection, ART, and bone loss in women remains unclear.^{15,16} Components of ART, in particular NRTIs and PIs, have been associated with a decrease in bone density. However, some evidence does exist for higher bone density in women exposed to nevirapine.¹⁷ Multiple factors contribute to the development of osteopenia/osteoporosis in HIV-infected women, including age, heredity, and HIV infection itself.

See [Long-Term Complications of Antiretroviral Therapy](#) for more detailed information on metabolic complications in the setting of HIV infection.

C. Adverse Drug Reactions and Drug-Drug Interactions

RECOMMENDATION:

Clinicians should assess for signs or symptoms of adverse reactions, drug-drug interactions, and cumulative side effects when patients are receiving multiple types or classes of medications for comorbidities and/or HIV.

The risk for drug interactions and/or serious toxicities increases with the number of medications a patient is taking, the age of the patient, the severity of the disease being treated, and the presence of renal and hepatic dysfunction. Older HIV-infected women frequently will have all of these risk factors and will be at increased risk for iatrogenic harm. Older people may have altered metabolism, which can impact pharmacokinetics and contribute to antiretroviral toxicities and drug interactions.

Drug interactions with antiretroviral medications, particularly PIs, have become an increasingly complex challenge for clinicians treating HIV-infected patients. Antiretroviral medications are known to interact with major classes of drugs that are commonly used to treat older patients, such as antidepressants, anticonvulsants, lipid-lowering agents, and many antibiotics and antifungals. Clinicians need to be aware of drugs that are associated with clinically significant drug interactions with antiretroviral medications in order to avoid the use of these drugs or to monitor patients for virologic failure or toxicity.

V. HORMONE REPLACEMENT THERAPY (HRT) IN HIV-INFECTED WOMEN

RECOMMENDATIONS:

Clinicians should refer HIV-infected women experiencing severe symptoms of menopause to a clinician experienced in the most current management of menopausal symptoms. An individualized risk/benefit analysis of the use of HRT should be performed regardless of whether or not the woman is receiving ART.

Clinicians should discuss with HIV-infected women the benefits of exercise, weight control, improved nutrition, including calcium supplementation, and smoking cessation for the prevention of osteoporosis and coronary heart disease.

Menopause occurs at different ages for women. In general, women undergo menopause between the ages of 40 and 50. Signs and symptoms of menopause before the age of 40 is considered premature menopause.

HRT is no longer the standard of care for relief of menopausal symptoms. Recent studies have shown limited benefit for the prevention of cardiovascular risk. Therefore, if used, HRT should be used at the lowest effective doses for the shortest time possible for relief of menopausal symptoms.¹⁸

A. Guidelines for HRT

Guidelines for prescribing HRT are shown in Table 2.

TABLE 2 GUIDELINES FOR PRESCRIBING HORMONE REPLACEMENT THERAPY (HRT)
<ul style="list-style-type: none"> • Provide HRT for the shortest possible time at the lowest effective doses • Consult with the patient at least once a year about HRT therapy, working toward successfully discontinuing the use of HRT • Recommend regular breast cancer screening <ul style="list-style-type: none"> ▪ Annual clinical breast examinations ▪ Annual mammograms for women ≥ 40*
<p>* The optimal age of initiation for breast screening and the intervals for mammography are still being studied. See <i>Breast Health in HIV-Infected Women</i>, for more detailed information.</p>

Clinicians can also refer to the following organizations for updated guidelines:

- American College of Obstetricians and Gynecologists (ACOG) Committee Opinion: www.ncbi.nlm.nih.gov/pubmed/18978127
- US Preventive Services Task Force: www.uspreventiveservicestaskforce.org/uspstf/uspspmho.htm
- North American Menopause Society: www.menopause.org/PSht10.pdf

B. Alternatives to HRT

Safe and well-established alternatives to HRT are available for the prevention of coronary heart disease and osteoporosis. In addition, alternatives to HRT are available for treatment of symptoms of menopause but have not been shown to be as effective as HRT (see Table 3). Clinicians should remind women of the protective effects of exercise; weight control; improved nutrition, including calcium supplementation; and smoking cessation.

TABLE 3 ALTERNATIVES TO HORMONE REPLACEMENT THERAPY	
Signs or Symptoms	Alternative Treatment
Hot flashes*/menopause symptom alleviation	<ul style="list-style-type: none"> • Paroxetine • Gabapentin • Clonidine
Vaginal dryness/ atrophy	<ul style="list-style-type: none"> • Water-based lubricants and vaginal estrogen preparations
Prevention or treatment of osteoporosis	<ul style="list-style-type: none"> • Alendronate sodium, risendronate, raloxifene, calcitonin • Smoking cessation • Decreased alcohol consumption • Increased physical activity • Calcium and vitamin D supplementation and correction of malnutrition
* References 19 and 20.	

C. HRT Interactions with Antiretroviral Medications

RECOMMENDATION:

Because amprenavir and fosamprenavir levels are reduced with ethinyl estradiol and norethindrone use, they should not be used with hormone replacement therapy.

No significant interactions between HRT and antiretroviral medications have been documented. However, studies of combined hormonal oral contraceptives show a 20% decrease in amprenavir (and presumably fosamprenavir) levels. Data also show that some antiretroviral medications reduce the AUC for estradiol in oral contraceptives. However, there is no current recommendation to increase the doses of estrogen in HRT while receiving ART. In addition, risks for cardiovascular disease and the questionable benefit of HRT in decreasing osteoporosis in menopause have limited the use of HRT in all women.

VI. MENTAL HEALTH AND SUBSTANCE USE

RECOMMENDATIONS:

Clinicians should perform a mental health assessment at baseline and at least annually.

The assessment should include the following components (I):

- **Cognitive impairment, depression, anxiety, posttraumatic stress disorder, suicidal/violent ideation, and alcohol and substance use**
- **Sleep habits and appetite assessment**
- **Psychiatric history, including psychotropic medications**
- **Psychosocial assessment, including domestic violence, housing status, and presence of social support**

Clinicians should refer patients to appropriate mental health and substance use treatment providers when indicated. (II)

Clinicians should incorporate selected brief screening instruments in the patient assessment. These instruments should be tailored for optimal use at initial, annual, and interim visits. The chosen screening instruments should be adjusted for the patient's mental health or substance use history.

Key Point:

Depressive symptoms and negative life events have been associated with symptoms of menopause in HIV-infected women.

Depression affects as many as 20% of the HIV-infected population,²¹ and stress and depression have been reported among older women with HIV infection. Many of these women experience increased stress from limited healthcare services, lack of resources, and caring for others as well as themselves. In addition, older women are often omitted from research and educational programs. Mental health interventions, including the use of antidepressants, may provide a quality-of-life benefit for HIV-infected women who suffer from depressive symptoms.²²

Unmet needs for mental health services, substance use treatment, and social services may inhibit effective adherence and treatment for HIV.²³ For some patients, referrals for these services may be necessary. For additional information, see the [Mental Health](#) and [Substance Use Guidelines](#) at www.hivguidelines.org

VII. SEXUAL DYSFUNCTION

RECOMMENDATION:

Clinicians should assess older HIV-infected women for sexual dysfunction and/or decreased libido; testosterone supplementation should not be used for treating these conditions.

Clinicians caring for HIV-infected older women have noted that decreased libido is a common complaint affecting quality of life. The lack of clinical trials on effective therapy for women has meant that clinicians are addressing a complicated issue with little scientific guidance. There are no data supporting the efficacy of testosterone use for the management of sexual dysfunction or decreased libido associated with menopause and/or HIV. Because the side effects, safety, and efficacy of long-term use of testosterone currently are not known, testosterone supplementation is not advised. However, decreased libido caused by depression or other psychosocial stressors should be considered and may be treatable.

REFERENCES

1. Phillips AN, Lee CA, Elford J, et al. More rapid progression to AIDS in older HIV-infected people: The role of CD4+ T-cell counts. *J Acquir Immune Defic Syndr* 1991;4:970-975. [[PubMed](#)]
2. Adler WH, Baskar PV, Chrest FJ, et al. HIV infection and aging: Mechanisms to explain the accelerated rate of progression in the older patient. *Mech Ageing Dev* 1997;96:137-155. [[PubMed](#)]
3. Cuzin L, Delpierre C, Gerard S, et al. Immunological and clinical responses to highly active antiretroviral therapy in patients with HIV infection aged >50 years. *Clin Infect Dis* 2007;45:654-657. [[PubMed](#)]
4. Casau NC. Perspective on HIV infection and aging: Emerging research on the horizon. *Clin Infect Dis* 2005;41:855-863. [[PubMed](#)]
5. Casado E, Olive A, Holgado S, et al. Musculoskeletal manifestations in patients positive for human immunodeficiency virus: Correlation with CD4 count. *J Rheumatol* 2001;28:802-804. [[PubMed](#)]
6. Gallagher B, Wang Z, Schymura M, et al. Cancer incidence in New York State Acquired Immunodeficiency Syndrome Patients. *Amer J Epi* 2001;154:544-556. [[PubMed](#)]
7. Centers for Disease Control and Prevention. Division of HIV/AIDS Prevention. United States HIV&AIDS Statistics by Age. HIV/AIDS Surveillance Report. Available at: <http://www.cdc.gov/hiv/topics/surveillance/resources/reports/index.htm>
8. Lieberman R. HIV in older Americans: An epidemiologic perspective. *J Midwifery Womens Health* 2000;45:176-182. Review. [[PubMed](#)]
9. Golub SA, Tomassilli JC, Pantalone DW, et al. Prevalence and correlates of sexual behavior and risk management among HIV-positive adults over 50. *Sex Transm Dis* 2010;37:615-620.
10. Dwyer JM, Penny R, Gatenby PA, et al. Susceptibility of postmenopausal women to infection with HIV during vaginal intercourse. *Med J Aust* 1990;153:299.
11. The North American Menopause Society. The role of local vaginal estrogen for treatment of vaginal atrophy in postmenopausal women: 2007 position statement of The North American Menopause Society. *Menopause* 2007;14:355-356. [[PubMed](#)]
12. Lederman MM, McKinnis R, Kelleher D, et al. Cellular restoration in HIV infected persons treated with abacavir and a protease inhibitor: Age inversely predicts naive CD4 cell count increase. *AIDS* 2000;14:2635-2642. [[PubMed](#)]
13. Belanger F, Meyer L, Carre N, et al. Influence of age at infection on human immunodeficiency virus disease progression to different clinical endpoints: The SEROCO cohort (1988-1994). The Seroco Study Group. *Int J Epidemiol* 1997;26:1340-1345. [[PubMed](#)]
14. Vance DE, Burrage JW. Promoting successful cognitive aging in adults with HIV: Strategies for intervention. *J Gerontol Nurs* 2006;32:34-41. [[PubMed](#)]
15. Glesby MJ. Bone disorders in human immunodeficiency virus infection. *Clin Infect Dis* 2003;37(Suppl):S91-S95. Review. [[PubMed](#)]

16. Dolan SE, Huang JS, Killilea KM, et al. Reduced bone density in HIV-infected women. *AIDS* 2004;18:475-483. [[PubMed](#)]
17. Anastos K, et al. The association of bone mineral density with HIV infection and antiretroviral treatment in women. Eleventh Conference on Retroviruses and Opportunistic Infections, San Francisco, Abstract 744, 2004.
18. The North American Menopause Society. Estrogen and progestogen use in peri- and postmenopausal women: March 2007 position statement of The North American Menopause Society. *Menopause* 2007;14:168-182. [[PubMed](#)]
19. Nelson HD, Vesco KK, Haney E, et al. Nonhormonal therapies for menopausal hot flashes: Systematic review and meta-analysis. *JAMA* 2006;295:2057-2071. [[PubMed](#)]
20. Tice JA, Grady D. Alternatives to estrogen for treatment of hot flashes: Are they effective and safe? *JAMA* 2006;295:2076-2078. [[PubMed](#)]
21. Komiti A, Judd F, Grech P, et al. Depression in people living with HIV/AIDS attending primary care and outpatient clinics. *Aust N Z J Psychiatry* 2003;37:70-77. [[PubMed](#)]
22. Miller SA, Santoro N, Lo Y, et al. Menopause symptoms in HIV-infected and drug-using women. *Menopause* 2005;12:348-356. [[PubMed](#)]
23. Cook JA, Grey D, Burke J, et al. Depressive symptoms and AIDS-related mortality among a multi-site cohort of HIV-positive women. *Am J Public Health* 2004;94:1133-1140. [[PubMed](#)]