

## Perspective

# Will You Still Treat Me When I'm 64? Care of the Older Adult With HIV Infection

*HIV infection is associated with chronic immune activation that is superimposed on immunologic senescence in older adults, resulting in the acquisition of age-related diseases at younger ages. The incidence of coronary artery disease is higher among HIV-infected persons than uninfected individuals matched for age and sex. HIV infection and its treatment have been associated with premature bone loss. Lung, hepatic, and anal cancers occur at younger ages in persons with HIV infection. HIV-infected patients are living longer, and proper attention to the management of comorbidities in this population is essential. This article summarizes an IAS–USA continuing education webinar presented by Howard Libman, MD, in January 2015.*

**Keywords:** HIV, aging, age-related diseases, coronary artery disease, bone loss, cancer, mortality

Aging is characterized by progressive physiologic changes associated with increased susceptibility to many diseases. It is influenced by genetic factors, lifestyle, and environmental exposures. In general, aging is associated with loss of the physiologic reserves needed to cope with challenges to homeostasis, and all organ systems are affected to some degree. With regard to specific systems, it is difficult to determine the impact of age alone on the cardiovascular system, as there is an increased risk of hypertension, diabetes mellitus, obesity, and sedentary behavior with aging. Aging is also associated with a greater probability of fracture related to decreased bone mass and an increased risk of falling, and there is slowing of repair once fracture occurs. Bone mass declines by approximately 0.5% per year in older adults not infected with HIV.

Aging is accompanied by decrements in immune function, contributing to increased risk of infections, malignancies, and autoimmune disorders. The ability of B- and T-cell lymphocytes to generate responses to new antigens and vaccinations is diminished, there is decreased production

of interleukin (IL)-2 and IL-2 receptors, thymic involution occurs, and the cytokine profile is consistent with a chronic, low-level inflammatory state.

The molecular basis of aging reflects the fact that natural selection does not play a role in preserving beneficial genes in later life, and some genes that provide benefit in early life may be detrimental with aging. There has been a variable effect of caloric restriction in prolonging life in laboratory animals. However, shortening of telomeres (the nucleoprotein end caps of chromosomes) increases the vulnerability of aging cells to DNA damage and dysregulation.

## HIV and Aging

HIV infection, even when controlled, in older adults is associated with chronic immune activation superimposed on immunologic senescence. In the setting of IL-2 downregulation and thymic dysfunction, older HIV-infected individuals may have delayed immune reconstitution. Chronic immune activation has been shown to result in accelerated aging of T cells, and it is unclear if these changes are reversed by antiretroviral therapy.<sup>1</sup>

Since the 1980s, an increasing percentage of HIV-infected patients are living longer, with approximately 30% now aged 50 years or older.<sup>2</sup> In 2012,

17.1% of newly diagnosed cases of HIV infection and 25.6% of newly diagnosed cases of AIDS were in adults aged 50 years or older.<sup>2</sup> Sexual contact among men who have sex with men is the most common mode of HIV transmission among older men, and heterosexual sexual contact is the most common mode of transition among older women.<sup>2</sup> Older persons may have acquired HIV infection later in life, may have more advanced HIV infection at the time of diagnosis, and may be at increased risk of acquiring opportunistic infections or of transmitting HIV infection to others. Immunologic response to antiretroviral therapy is less robust in this population. Although adherence to antiretroviral therapy is generally good, older individuals may be at increased risk for drug toxicity owing to age-related changes in pharmacokinetics.

Among 12,196 HIV-infected, treatment-naïve individuals in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) who initiated antiretroviral therapy, CD4+ cell counts after 24 months of therapy were diminished as age increased, starting at age 40 years, but viral suppression was not affected.<sup>3</sup> In another prospective study that evaluated treatment outcomes in 3015 HIV-infected individuals, of whom 401 were older than 50 years, clinical progression to an AIDS-defining illness was more common in older individuals despite better virologic control (hazard ratio [HR], 1.52; 95% confidence interval [CI], 1.2–2.0).<sup>3,4</sup>

With regard to adherence to antiretroviral therapy, the literature suggests an up to 95% adherence rate among older HIV-infected individuals. In a meta-analysis, older age reduced the risk of nonadherence by 27% (relative risk [RR], 0.72; 95% CI, 0.64–0.82).<sup>5</sup> In other studies, older age was associated with a significantly reduced risk of nonadherence in both the short term

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(RR, 0.75; 95% CI, 0.64-0.87) and the long term (RR, 0.65; 95% CI, 0.50-0.85).<sup>5</sup>

Among HIV-infected individuals taking protease inhibitors, a higher rate of adverse events was reported in those older than 60 years than in those younger than 40 years (64% and 35%, respectively).<sup>6</sup> In a study of 508 treatment-naïve patients, antiretroviral regimen changes owing to toxicity were associated with older age.<sup>7</sup> This increased risk of adverse events may reflect age-related decreases in renal and hepatic function and in serum albumin level, and changes in the cytochrome P450 enzyme system.

Additional clinical characteristics of HIV infection in older persons include acquiring age-related diseases at younger ages than uninfected persons. Neurocognitive dysfunction, some non-AIDS-defining cancers, and a wide range of pulmonary diseases are also more prevalent in older HIV-infected individuals. It is hypothesized that increased immune activation and long-term chronic inflammation contribute to premature aging in this population.

With regard to premature aging, a case-control study involving 2854 HIV-infected patients and 8562 uninfected controls treated at Modena University in Italy from 2002 to 2009 examined noninfectious comorbidities, including cardiovascular disease (CVD), hypertension, diabetes, bone fractures, and renal failure.<sup>8</sup> Independent predictors of polypathology ( $P < .001$ ) included older age (odds ratio [OR], 1.11), male sex (OR, 1.77), CD4+ cell count nadir below 200/ $\mu$ L (OR, 4.46), and duration of antiretroviral therapy (OR, 1.01). The prevalence of polypathology among HIV-infected patients aged 41 years to 50 years was similar to that among uninfected participants aged 51 years to 60 years, suggesting that comorbidities occur in HIV-infected individuals approximately 10 years earlier than in their uninfected counterparts.

With regard to cognitive dysfunction, epidemiologic findings indicate that older age is a risk factor for HIV-associated dementia, although there have been few studies in this regard.

In a longitudinal study comparing 106 HIV-infected individuals older than 50 years with 96 HIV-infected individuals aged 20 years to 39 years, with multivariate analysis there was a 3-fold higher risk of dementia in the older group after adjusting for race, education level, presence of depression, substance use, antiretroviral therapy status, CD4+ cell count, and viral load.<sup>9</sup>

With regard to malignancy risk, data from observational studies have suggested that lung, hepatic, and anal cancers occur at younger ages in HIV-infected adults than in uninfected adults. In an analysis of age at diagnosis of non-AIDS-defining cancer using data from 15 HIV and cancer registry databases in the United States, which included data on 212,055 persons with AIDS, lung and anal cancers were found to occur earlier in persons with AIDS than in persons without AIDS (median age 50 years and 54 years, respectively;  $P < .001$ ) than in the general population.<sup>10</sup>

In an analysis of 33,420 HIV-infected individuals and 66,840 uninfected controls matched for age, sex, race, and ethnicity in the Veterans Aging Cohort Study, chronic obstructive pulmonary disease, lung cancer, pulmonary hypertension, and pulmonary fibrosis were more frequent among the HIV-infected individuals.<sup>11</sup>

### CVD and Risk Factors

Traditional risk factors for coronary artery disease (CAD) are male sex, increasing age, higher low-density lipoprotein (LDL) cholesterol level, lower high-density lipoprotein (HDL) cholesterol level, hypertension, diabetes mellitus, obesity, cigarette smoking, and a family history of premature CAD. Modifiable traditional risk factors in HIV-infected persons should be identified and managed effectively.

The incidence of CAD is higher in HIV-infected individuals than in uninfected individuals matched for age and sex, with studies showing increases in both subclinical atherosclerosis (eg, carotid intima media thickness) and clinical endpoints (eg, acute myocardial infarction [MI]). HIV infection is

associated with increased soluble and cellular markers of inflammation, endothelial dysfunction, and altered coagulation, all of which contribute to risk of CVD. The degree to which HIV infection itself, antiretroviral therapy, and other risk factors contribute to increased risk of CVD in HIV-infected patients remains unknown; however, there is a high prevalence of traditional risk factors in this population. With regard to antiretroviral therapy, protease inhibitors appear to be associated with higher risk of CAD, and some data suggest that the nucleoside analogue reverse transcriptase inhibitor (nRTI) abacavir and the nonnucleoside analogue reverse transcriptase inhibitor efavirenz also increase risk. However, discontinuation of antiretroviral therapy is also associated with higher risk of CAD.

Available data suggest a 50% increased risk of acute MI among middle-aged or older HIV-infected individuals compared with uninfected individuals of the same age. For example, an analysis of patients followed from 2003 to 2009 in the Veterans Aging Cohort Study assessed risk of acute MI among those with no CVD at baseline after adjusting for sex, race, ethnicity, hypertension, diabetes, hyperlipidemia, smoking status, hepatitis C virus infection, body mass index, renal disease, anemia, substance use, CD4+ cell count, viral load, and antiretroviral therapy status. The incidence rate ratio (IRR) of MI was significantly higher in HIV-infected individuals than in uninfected individuals, among those aged 40 years to 49 years (IRR, 1.34; 95% CI, 1.04-1.72), those aged 50 years to 59 years (IRR, 1.80; 95% CI, 1.47-2.11), and those aged 60 years to 69 years (IRR, 1.53; 95% CI, 1.03-2.26).<sup>12</sup>

Management of hypertension in HIV-infected individuals is similar to that in uninfected individuals. Hypertension is defined as having a blood pressure reading greater than or equal to 140/90 mm Hg at 3 separate visits over a period of 1 week or more. In the absence of a history of or a physical exam indicating secondary hypertension, baseline evaluation should include testing of renal function and

potassium level, a urinalysis, and an electrocardiogram. Approaches to non-pharmacologic management of hypertension include modest salt restriction, increased physical activity, and weight reduction. Initial drug therapy should consist of a thiazide diuretic, an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker, or a calcium channel blocker in most patients. For individuals with blood pressure readings of more than 20/10 mm Hg above goal, an ACE inhibitor or angiotensin receptor blocker plus a calcium channel blocker is recommended. There are no important drug interactions between antiretroviral drugs and those commonly used to treat hypertension.

Management of diabetes is also similar in HIV-infected and uninfected persons. Diagnosis of diabetes is often based on a glycated hemoglobin (HgbA1c) value of at least 6.5%. Treatment goals include prevention of symptomatic hyperglycemia and vascular complications, with a target HgbA1c value of less than or equal to 7.0%. Non-pharmacologic management consists of weight reduction through dietary modification and increased physical activity. Initial drug therapy generally consists of metformin with a sulfonylurea (eg, glipizide). Metformin may cause lactic acidemia (as do some older nRTIs). There are no other important drug interactions between antiretroviral drugs and those commonly used to treat diabetes. Of note, diabetes and HIV infection have a particularly detrimental effect on renal function.<sup>13</sup>

Cigarette smoking is more common among HIV-infected individuals than the general population, and HIV-infected smokers are less likely to quit.<sup>14</sup> However, there is no evidence that specific smoking cessation interventions are more or less effective. A combination of behavioral interventions and pharmacologic therapy to encourage smoking cessation generally works better than either method alone. Drug options include nicotine replacement therapies (eg, patches, gum, or lozenges), bupropion, and varenicline, and may be used alone or in combination. There are no important

drug interactions between antiretroviral drugs and those commonly used for smoking cessation.

For hyperlipidemia in the general population, a desirable total cholesterol level is less than 200 mg/dL and a desirable LDL cholesterol level is less than 130 mg/dL. Epidemiologic studies show a graded relationship between total cholesterol level and CAD risk. Patients with clinical atherosclerosis or a combination of factors resulting in a greater than 20% 10-year risk of a new cardiovascular event may benefit substantially from statin therapy. Patients without clinical atherosclerosis may have a lesser absolute benefit from statin treatment. The relative risk reduction rate with statin therapy in most studies has been between 20% and 30%.

Two widely used CVD risk calculators are the Framingham risk calculator and the newer American College of Cardiology/American Heart Association risk calculator.<sup>15,16</sup> Each calculates a 10-year risk of MI and provides a threshold for initiating statin therapy. However, it remains unclear how best to incorporate the risk posed by HIV infection and its treatments into these risk calculations.

Dyslipidemia is common among HIV-infected individuals taking antiretroviral therapy, and it may be isolated or seen in combination with other features of lipodystrophy. HIV-infected persons should be evaluated and treated for dyslipidemia in a similar fashion to uninfected persons. CVD risk factors should be assessed when designing an initial antiretroviral regimen. For individuals who are at risk for CVD, protease inhibitors (with the possible exception of atazanavir) and abacavir should be avoided. Protease inhibitors, particularly ritonavir, increase most statin levels. Concurrent use of simvastatin or lovastatin with protease inhibitors and cobicistat is contraindicated. Pravastatin (except with darunavir), atorvastatin, and rosuvastatin may be used as alternatives. It is prudent to start a statin at a low dose and to monitor liver function and creatine phosphokinase level during treatment.

To screen for CVD, HIV-infected individuals should have fasting glucose or HgbA1c measured every 6 months to 12 months, a fasting lipid profile completed every 6 months to 12 months, and regular blood pressure measurements. To assess for body fat maldistribution, a patient self-report should be taken and body weight measured at each visit, with periodic anthropometric measurements of skinfold, waist, and hip. A 1-time ultrasound for abdominal aortic aneurysm is recommended for men aged 65 years to 75 years with a history of smoking. Preventive treatment includes aspirin for prevention of CAD in men aged 45 years to 79 years and for prevention of cerebrovascular disease in women aged 55 years to 79 years when risk of atherosclerosis outweighs risk of gastrointestinal bleeding.

### Premature Bone Loss

Osteopenia, osteoporosis, and pathologic fractures have been described in the context of HIV infection. Osteoporosis may present with fractures of vertebrae, forearms, or hips. HIV infection itself, use of tenofovir or protease inhibitors, alterations in metabolism of vitamin D, and lactic acidemia related to use of older nRTIs may be contributing factors to premature bone loss. Immobility, cigarette smoking, excessive alcohol use, chronic renal disease, hypogonadism, hyperparathyroidism, hyperthyroidism, and steroid use accentuate bone loss. The optimal use of bone densitometry as a screening test for HIV-infected individuals is uncertain. Calcium and vitamin D supplements should be given to high-risk patients, and regular exercise and smoking cessation should be advised.

The effect of antiretroviral therapy on cases of osteoporotic fracture that occurred after diagnosis of HIV infection in a case registry from 1988 to 2009 was examined in a multivariate analysis adjusted for race, age, tobacco use, diabetes, body mass index, and presence of hepatitis C virus infection, and in a second multivariate analysis adjusted for all of the foregoing factors plus concomitant exposure to antiretroviral



**Table 1.** HIV Primary Care Recommendations From the HIV Medicine Association of the Infectious Diseases Society of America

Intervention	Recommendation	Comments
Blood pressure check	Perform annually for all individuals	None
Digital rectal examination	Consider annually for all individuals	Inspect for anal warts and malignancies in all patients, and for prostate abnormalities in men
Ophthalmologic examination	Perform a dilated examination every 6 mo-12 mo for individuals with CD4+ cell counts <50/ $\mu$ L	A tonometry test is advised every 2 y-3 y in all those aged $\geq$ 50 y
Depression screening	Perform annually for all individuals	Use a conventional mental health interview or standardized test
Measurement of fasting glucose and HgbA1c	Perform every 6 mo-12 mo for all individuals	Consider testing 1 mo-3 mo after initiation or modification of antiretroviral therapy. Measurement of HgbA1c may be used for screening; consider a threshold cutoff of 5.8%. HgbA1c measurement should be performed every 6 mo for those with diabetes mellitus
Fasting lipid profile	Perform every 6 mo-12 mo for all individuals	Consider testing 1 mo-3 mo after initiation or modification of antiretroviral therapy
Syphilis serology	Perform annually for individuals at risk for STIs	More frequent testing may be indicated for patients at high risk for STIs
Gonorrhea and chlamydia testing	Perform annually for patients at risk for STIs	More frequent testing may be indicated for patients at high risk for STIs. Repeat testing after 3 mo if results are positive
Hepatitis C virus testing	Perform annually for at-risk patients (eg, injection drug users and men who have sex with men)	More frequent testing may be indicated for patients at high risk, especially if serum transaminase levels are increased
Trichomoniasis testing	Perform annually for all women	Repeat testing after 3 mo if result is positive
TB skin test or interferon-gamma release assay	Perform at baseline and annually for patients at risk for TB	No need to repeat for patients with a prior positive TB skin test result; additional TB testing may be indicated depending on potential exposure
Colorectal cancer screening	Perform at age 50 y for asymptomatic individuals at average risk	More frequent testing is indicated for patients with a history of adenomatous polyps; testing at an earlier age may be considered for patients with a strong family history of colon cancer
Mammography	Perform annually for all women aged $\geq$ 50 y	Some experts advise starting at age 40 y based on assessment of individual risks/benefits
Cervical Papanicolaou testing	Perform annually for all women after 2 normal Papanicolaou test results documented during the first year after diagnosis of HIV infection	None
Bone densitometry	Perform baseline exam for postmenopausal women and men aged $\geq$ 50 y	Detection of premature bone loss requires periodic monitoring thereafter; risk factors include white race, small body habitus, sedentary lifestyle, cigarette smoking, alcohol use, phenytoin use, corticosteroid use, hyperparathyroidism, vitamin D deficiency, thyroid disease, and hypogonadism
Abdominal ultrasonography	Perform once for men aged 65 y-75 y who have ever smoked	Screening test for abdominal aortic aneurysm
Patient education	Address regularly for all patients	May include information on sexual behavior, alcohol and drug counseling, diet, weight reduction, smoking cessation, and seat belt use

Abbreviations: HgbA1c, glycated hemoglobin; STI, sexually transmitted infection; TB, tuberculosis. Adapted from Aberg et al.<sup>18</sup>

therapy.<sup>17</sup> Among 56,660 individuals evaluated, tenofovir use was associated with an osteoporotic fracture HR of 1.06 (95% CI, 0.99-1.12) in the first multivariate analysis and of 1.06 (95% CI, 0.99-1.14) in the second multivariate analysis. Among 32,439 patients taking potent antiretroviral therapy, the association of tenofovir use with osteoporotic fracture became significant, with a yearly HR of 1.13 (95% CI, 1.05-1.21;  $P = .001$ ) in the first multivariate analysis and of 1.12 (95% CI, 1.03-1.21;  $P = .011$ ) in the second multivariate analysis. Exposure to boosted

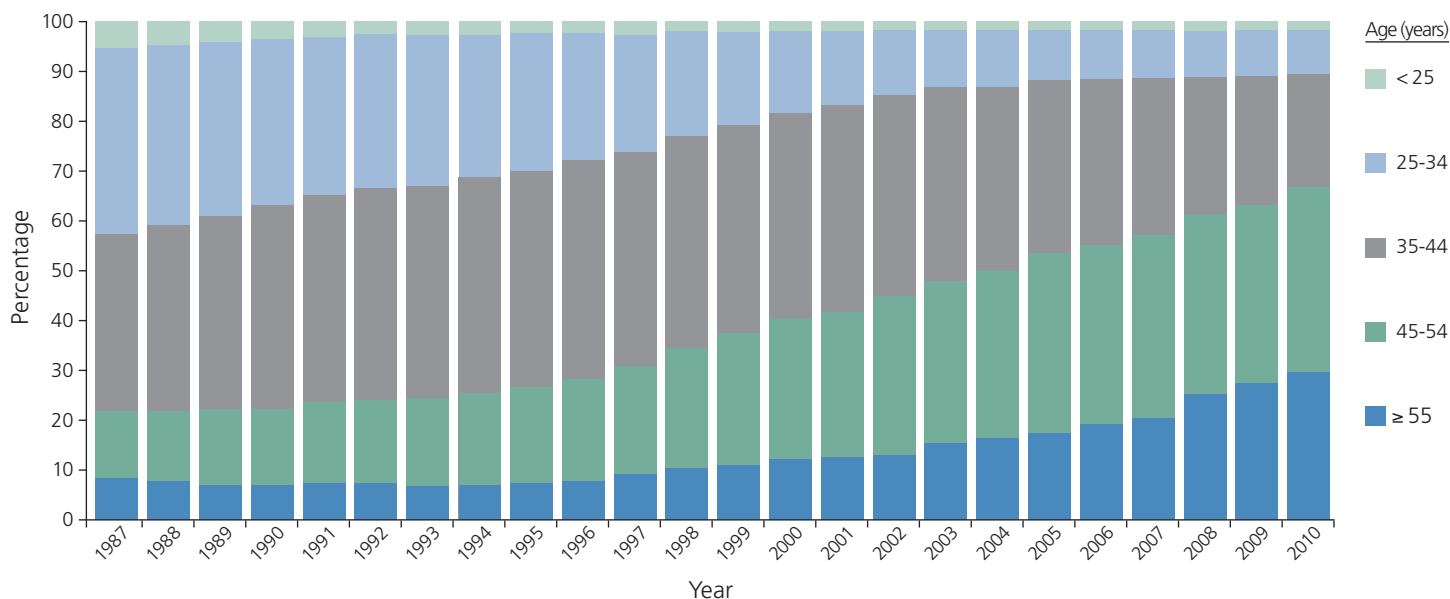
protease inhibitors was associated with a significant HR of 1.08 (95% CI, 1.01-1.15;  $P = .026$ ) in the first multivariate analysis and a nonsignificant HR of 1.05 (95% CI, 0.97-1.13;  $P = .237$ ) in the second multivariate analysis. Among protease inhibitors, the fixed-dose combination of lopinavir and ritonavir was associated with a borderline significant HR of 1.09 (95% CI, 1.00-1.20;  $P = .051$ ) in the second multivariate analysis.

Current HIV primary care guidelines from the HIV Medicine Association of the Infectious Diseases Society of

America (IDSA) recommend bone densitometry screening for men aged 50 years or older and for postmenopausal women.<sup>18</sup> Radiography or magnetic resonance imaging for avascular necrosis of the hips should be performed for symptomatic patients only.

## Immunizations

Live attenuated vaccines should be avoided in HIV-infected individuals with low CD4+ cell counts, unless the benefits clearly outweigh risks. Vaccines are generally more immunogenic in



**Figure 1.** Changes in distribution of deaths attributable to HIV infection in the United States, by age group, from 1987 to 2010. Adapted from Centers for Disease Control and Prevention.<sup>23</sup>

individuals with higher CD4+ cell counts and lower viral loads and should be delayed pending immune reconstitution after initiating antiretroviral therapy when appropriate. Immunologic response to vaccines should be assessed when possible.

HIV-infected individuals are at increased risk for serious pneumococcal infections, including pneumonia and bacteremia. This increased risk may result from altered antibody production, leading to decreased opsonization. It is now recommended that previously unvaccinated individuals receive the 13-valent pneumococcal conjugate vaccine followed by the 23-valent polysaccharide vaccine at least 8 weeks later, with a second dose of the 23-valent vaccine 5 years later. For those who have previously received the 23-valent vaccine, the 13-valent vaccine should be given at least 1 year after the last 23-valent vaccine dose. For those who require additional doses of the 23-valent vaccine, the first dose should be given no sooner than 8 weeks after the 13-valent vaccine dose and at least 5 years after most recent 23-valent vaccine dose.<sup>19</sup>

HIV-infected individuals may also be at increased risk for complications of influenza, although there are limited data in this regard. It is currently

recommended that all HIV-infected individuals receive an inactivated seasonal flu vaccine.<sup>20</sup> Live (intranasal) preparations of influenza vaccines should not be used for HIV-infected individuals.

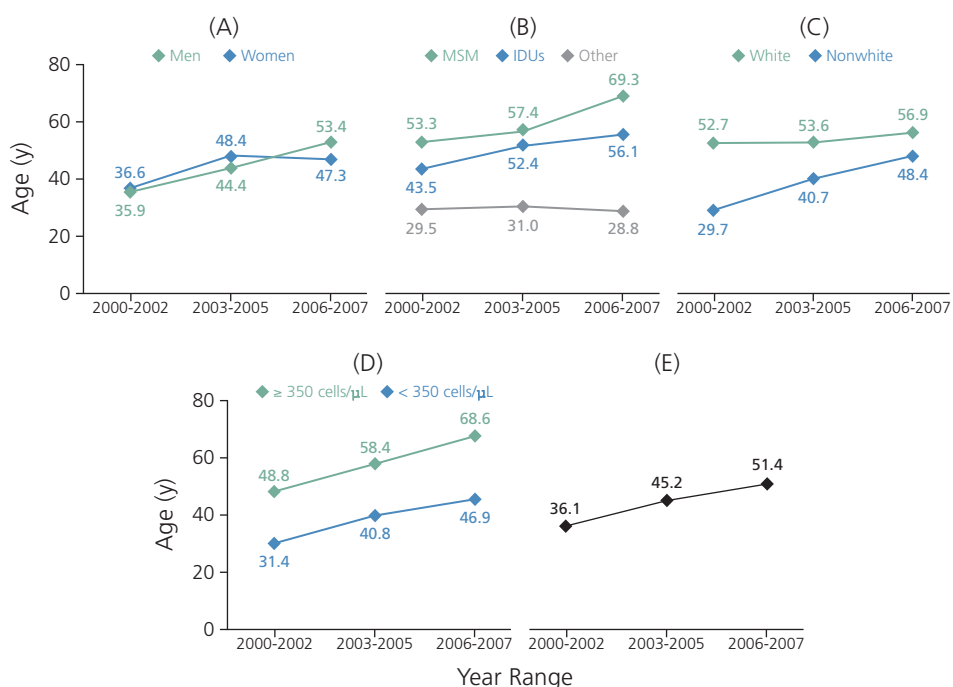
The zoster vaccine may be considered for some HIV-infected patients aged 60 years or older. In a study of 395 patients on stable antiretroviral therapy who had CD4+ cell counts greater than 200/ $\mu$ L and were randomly assigned to receive 2 doses of zoster vaccine or placebo, antibody titers were increased in vaccine recipients at 24 weeks, with no substantial difference in frequency of zoster cases between the 2 groups; the only substantial difference in safety was a higher incidence of local reactions in those who received vaccine instead of placebo.<sup>21</sup>

### Other Aspects of Routine Health Care

A summary of routine health care maintenance assessments from current IDSA HIV primary care guidelines can be seen in Table 1.<sup>18</sup> Annual screening for depression in all individuals is now recommended by the US Preventive Services Task Force (USPSTF) via conventional mental health interview or a variety of standardized tests.<sup>22</sup> However,

screening should only be done in settings in which interventions for depression (ie, pharmacotherapy and care from a mental health professional) are available.

USPSTF recommendations for cancer screening include the following. For breast cancer, biannual mammography for women aged 50 years to 74 years is recommended, with individualized screening recommended for younger women. For cervical cancer, annual Papanicolaou testing is recommended for women after documentation of 2 normal Papanicolaou test results; the role of human papillomavirus testing for HIV-infected women is unclear. For colon cancer, a colonoscopy every 10 years starting at age 50 years is recommended, with earlier and more frequent screening performed for patients with a history of polyps or inflammatory bowel disease. For prostate cancer, annual digital exams for men aged 50 years to 74 years should be considered; prostate-specific antigen testing is no longer recommended for most men, but a conversation with the patient about potential benefits and risks is appropriate. Annual screening for chlamydia, gonorrhea, and syphilis is recommended for adults who are at ongoing risk for sexually transmitted diseases. Annual purified protein



**Figure 2.** Midpoint life expectancy estimates for individuals diagnosed with HIV infection at age 20 years, by sex (A), transmission group (B), race (C), CD4+ cell count at time of initiation of antiretroviral therapy (D), and overall (E). IDUs indicates injection drug users; MSM, men who have sex with men. Adapted from Samji et al.<sup>25</sup>

derivative or interferon-gamma release testing is recommended for adults at ongoing risk for tuberculosis infection.<sup>18</sup>

## Mortality

As individuals with HIV infection are living longer with the use of potent antiretroviral therapy, an increasing proportion of deaths related to HIV infection have occurred in older age groups. However, as of 2010, there was still a higher proportion of deaths related to HIV infection among individuals aged 45 years to 54 years than among those aged 55 years or older (Figure 1).<sup>23</sup>

Available data on mortality trends include those from the D:A:D (Data Collection on Adverse Events of Anti-HIV Drugs) study, which has been ongoing since 1999. There have been 3909 deaths observed in the study among 49,731 patients followed up through 2011, and the overall crude mortality rate is 12.7 per 1000 person-years, although it decreased from 16.9 per 1000 person-years to 9.6 per 1000 person-years over the follow-up period. Twenty-

nine percent of deaths were attributable to AIDS-related causes, 15% to non-AIDS-related cancers, 13% to liver disease, and 11% to CVD. Over the course of follow-up, the proportion of deaths attributable to AIDS-related events has decreased from 34% to 22% and the proportion attributable to non-AIDS-defining malignancies has increased from 9% to 23%.<sup>24</sup>

Figure 2 shows how projected life expectancy increased among individuals with HIV infection between the periods from 2000 to 2002 and 2006 to 2007.<sup>25</sup> Overall, life expectancy for an individual diagnosed with HIV infection at age 20 years has increased from 36 years to 51 years. There are differences in projected life expectancy based on sex, transmission group, and race, and according to CD4+ cell count at initiation of antiretroviral therapy. However, many HIV-infected individuals are expected to live 70 years or more.

## Summary

Aging is characterized by progressive physiologic changes associated with

an increased susceptibility to many diseases. HIV infection, even when controlled, is associated with chronic immune activation that is superimposed on immunologic senescence in older adults. Older persons may be diagnosed later and may have more advanced HIV infection at the time of diagnosis, and there is a less robust immunologic response to antiretroviral therapy in this population. HIV-infected individuals generally acquire age-related diseases at younger chronologic ages than the general population, and it is hypothesized that increased immune activation and long-term chronic inflammation contribute to such premature aging.

Lung, hepatic, and anal cancers occur at younger ages in HIV-infected adults than in uninfected adults. The incidence of CAD is higher among HIV-infected individuals than among uninfected individuals matched for age and sex. Results of CAD risk calculation should be interpreted in the context of this increased risk. HIV infection and its treatments have been associated with premature bone loss. Age-related immunizations and screening tests for cancers and other conditions should be addressed. Mortality in HIV-infected persons has decreased substantially over the past 2 decades, with non-AIDS-related conditions now accounting for the majority of deaths.

*Presented by Dr Libman in January 2015. First draft prepared from transcripts by Matthew Stenger. Reviewed and edited by Dr Libman in June 2015.*

*Financial affiliations in the past 12 months: Dr Libman has intellectual property rights licensed by UpToDate.*

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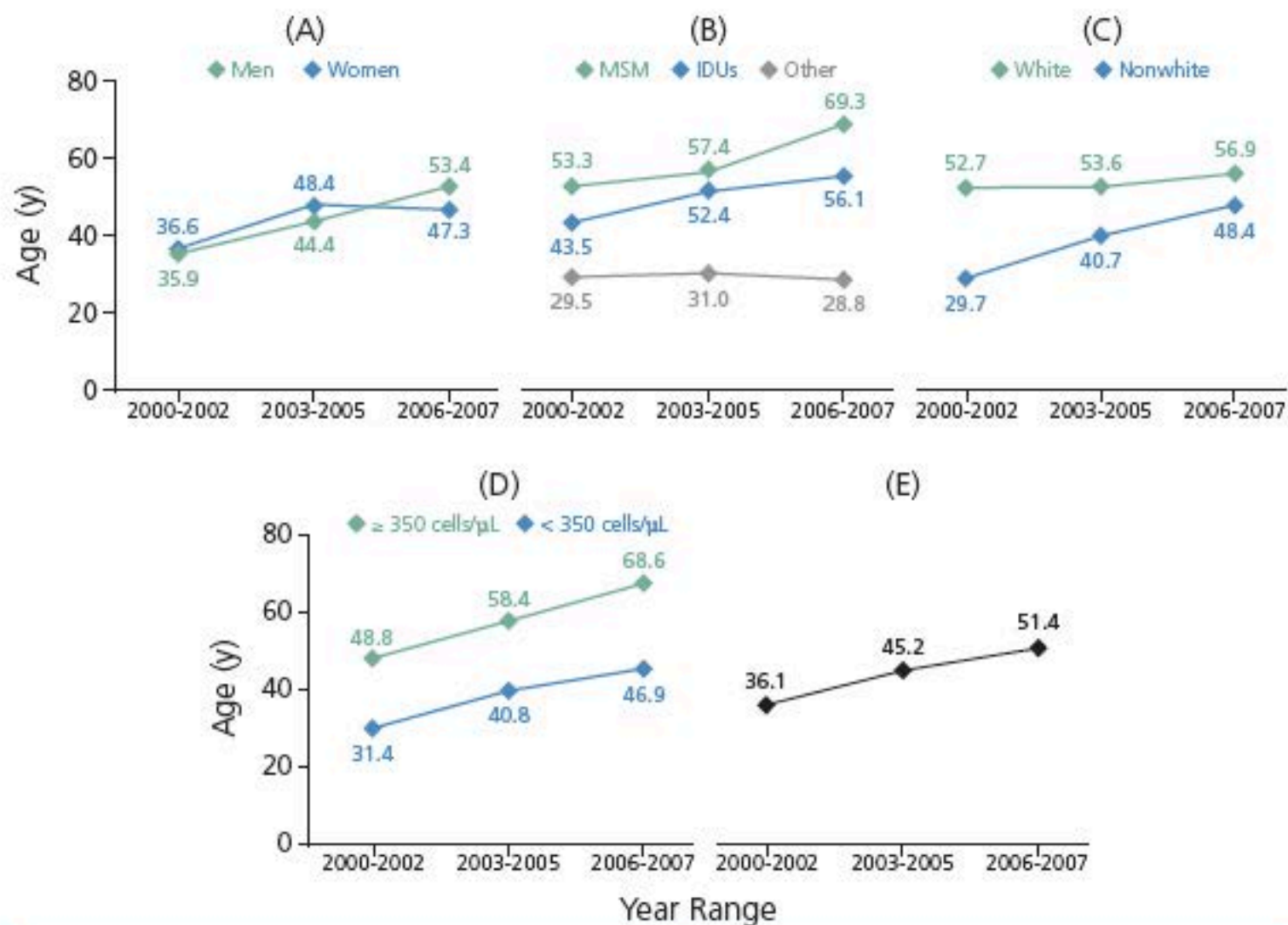


**Table 1.** HIV Primary Care Recommendations From the HIV Medicine Association of the Infectious Diseases Society of America

Intervention	Recommendation	Comments
Blood pressure check	Perform annually for all individuals	None
Digital rectal examination	Consider annually for all individuals	Inspect for anal warts and malignancies in all patients, and for prostate abnormalities in men
Ophthalmologic examination	Perform a dilated examination every 6 mo-12 mo for individuals with CD4+ cell counts <50/ $\mu$ L	A tonometry test is advised every 2 y-3 y in all those aged $\geq$ 50 y
Depression screening	Perform annually for all individuals	Use a conventional mental health interview or standardized test
Measurement of fasting glucose and HgbA1c	Perform every 6 mo-12 mo for all individuals	Consider testing 1 mo-3 mo after initiation or modification of antiretroviral therapy. Measurement of HgbA1c may be used for screening; consider a threshold cutoff of 5.8%. HgbA1c measurement should be performed every 6 mo for those with diabetes mellitus
Fasting lipid profile	Perform every 6 mo-12 mo for all individuals	Consider testing 1 mo-3 mo after initiation or modification of antiretroviral therapy
Syphilis serology	Perform annually for individuals at risk for STIs	More frequent testing may be indicated for patients at high risk for STIs
Gonorrhea and chlamydia testing	Perform annually for patients at risk for STIs	More frequent testing may be indicated for patients at high risk for STIs. Repeat testing after 3 mo if results are positive
Hepatitis C virus testing	Perform annually for at-risk patients (eg, injection drug users and men who have sex with men)	More frequent testing may be indicated for patients at high risk, especially if serum transaminase levels are increased
Trichomoniasis testing	Perform annually for all women	Repeat testing after 3 mo if result is positive
TB skin test or interferon-gamma release assay	Perform at baseline and annually for patients at risk for TB	No need to repeat for patients with a prior positive TB skin test result; additional TB testing may be indicated depending on potential exposure
Colorectal cancer screening	Perform at age 50 y for asymptomatic individuals at average risk	More frequent testing is indicated for patients with a history of adenomatous polyps; testing at an earlier age may be considered for patients with a strong family history of colon cancer
Mammography	Perform annually for all women aged $\geq$ 50 y	Some experts advise starting at age 40 y based on assessment of individual risks/benefits
Cervical Papanicolaou testing	Perform annually for all women after 2 normal Papanicolaou test results documented during the first year after diagnosis of HIV infection	None
Bone densitometry	Perform baseline exam for postmenopausal women and men aged $\geq$ 50 y	Detection of premature bone loss requires periodic monitoring thereafter; risk factors include white race, small body habitus, sedentary lifestyle, cigarette smoking, alcohol use, phenytoin use, corticosteroid use, hyperparathyroidism, vitamin D deficiency, thyroid disease, and hypogonadism
Abdominal ultrasonography	Perform once for men aged 65 y-75 y who have ever smoked	Screening test for abdominal aortic aneurysm
Patient education	Address regularly for all patients	May include information on sexual behavior, alcohol and drug counseling, diet, weight reduction, smoking cessation, and seat belt use

Abbreviations: HgbA1c, glycated hemoglobin; STI, sexually transmitted infection; TB, tuberculosis. Adapted from Aberg et al.<sup>18</sup>





**Figure 2.** Midpoint life expectancy estimates for individuals diagnosed with HIV infection at age 20 years, by sex (A), transmission group (B), race (C), CD4+ cell count at time of initiation of antiretroviral therapy (D), and overall (E). IDUs indicates injection drug users; MSM, men who have sex with men. Adapted from Samji et al.<sup>25</sup>