

# HIV in Older Adults

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Module 6: [Key Populations](#)

Lesson 4: [HIV in Older Adults](#)

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## Background

### Aging Population in the HIV Epidemic

With the advent of potent antiretroviral therapies, the life expectancy of individuals with HIV has increased dramatically, resulting in an HIV epidemic with an aging population. Life expectancy among persons with HIV who receive antiretroviral treatment now approaches that of the general population ([Figure 1](#)).[\[1,2,3\]](#) The shift of the HIV epidemic to increasingly involve older persons highlights several health care needs: (1) medical care systems with the capacity to provide clinical services for a large cohort of older persons with HIV, (2) active screening programs to detect HIV in older persons, and (3) implementation of strategies to prevent forward transmission of HIV from older persons.

### HIV and the Aging Process

The impact of HIV on aging is not entirely clear. With the benefit of antiretroviral therapy, most persons with HIV live healthy and long lives, whereas others struggle with multiple comorbidities that negatively impact their quality of life. Many comorbid medical conditions, such as cardiovascular disease, diabetes, renal disease, and cancer, occur frequently in older persons with HIV.[\[4,5,6,7\]](#) These HIV-associated non-AIDS conditions are likely the manifestation of an interplay of factors, including chronic inflammation, immune senescence, microbial translocation, and changes in the gut microbiome, all of which may contribute to accelerated aging and an increased overall burden of disease in the population with HIV.[\[8,9,10\]](#)

### Complexity of Managing Older Persons with HIV

As the population of older persons with HIV in the United States increases, the evaluation and management of comorbid conditions that often occur with aging takes on a larger role in HIV clinical care. Further, most studies have shown that persons with chronic HIV experience elevated risk (and possibly earlier onset) of medical comorbid conditions, including liver disease, cardiovascular disease, diabetes, non-AIDS malignancies, kidney disease, osteoporosis, neurocognitive impairment, and frailty.[\[7,11,12,13,14\]](#) In one analysis involving United States veterans with HIV, 53% of persons aged 50 to 59 years had at least one comorbid medical disease, and this number increased to 66% in persons 60 years of age and older.[\[15\]](#) As a result of comorbidities, many older persons with HIV take multiple non-antiretroviral medications. Thus, older persons with HIV often require a particularly high intensity of medical care, as they generally have an increased prevalence of comorbid medical conditions and often have polypharmacy.[\[16\]](#)

## Accelerated versus Accentuated Aging

### Concept of Accelerated versus Accentuated Aging

Older persons with HIV clearly have a higher prevalence of noninfectious comorbidities than age-matched persons without HIV, but it is unclear whether this results from HIV-related accelerated aging via pathways common to the aging process or whether HIV serves as an additive factor for a wide range of conditions that accentuate the aging process ([Figure 2](#)).[\[12\]](#) With accelerated aging, an age-related comorbid condition could occur at an earlier age in persons with HIV compared to those without HIV. With accentuated aging, an age-related comorbid condition could occur more commonly (at a higher rate) at all ages in persons with HIV compared to those without HIV. In addition, it is possible that both accelerated and accentuated aging could exist, whereby conditions could develop at both an earlier stage and at a higher rate.[\[12\]](#) Further, higher prevalence rates of comorbid conditions, such as smoking, drug use, and viral hepatitis, in persons with HIV may confound studies examining the impact of HIV on aging.[\[17,18\]](#)

### Accelerated Aging in Persons with HIV

The concept that HIV causes premature or accelerated aging is plausible, yet unproven. This concept emerged from studies that show comorbid conditions affect persons with HIV at a younger age than persons without HIV, even among those individuals with HIV who are taking antiretroviral therapy.[\[11,17,19\]](#) Investigators have observed that adults with HIV have immune profiles that mimic those found in older adults who do not have HIV, leading to the hypothesis that HIV-related immune dysfunction and inflammation are responsible for early aging of the immune system (immunosenescence).[\[8,11,20\]](#) In a study of biomarkers of innate immunity in persons with HIV (with and without detectable HIV RNA levels) and persons without HIV, the individuals with HIV who had detectable HIV RNA levels showed levels of age-related monocyte activation biomarkers that were comparable to persons without HIV who were 12 years older.[\[21\]](#) This effect was less pronounced in the subset of persons with HIV who had undetectable HIV RNA levels—their markers corresponded to those seen in controls without HIV who were 4 years older.[\[21\]](#)

### Accentuated Aging in Persons with HIV

In contrast to the accelerated aging paradigm, where comorbid conditions develop at an earlier age, the accentuated aging hypothesis postulates that the risk of comorbidities in adults with HIV is elevated at every age relative to those adults without HIV.[\[4,12\]](#) Results from a nested study in the Veterans Aging Cohort Study (VACS) confirmed that adults with HIV are at increased risk for myocardial infarction, end-stage renal disease, and non-AIDS-defining malignancies, but these outcomes occur at similar ages in adults with or without HIV; in this study as in others, traditional risk factors (smoking, dyslipidemia, oncogenic viral infections, male sex, Black race, low socioeconomic status, high blood pressure) conferred a similar or greater magnitude of risk for aging-associated diseases than did HIV.[\[4\]](#) Thus, a paradigm of “accentuated aging” is emerging, whereby it is believed the risk of comorbidities is higher at every age relative to the risk in adults without HIV.[\[4\]](#) It will be important to follow additional studies that evaluate accelerated (premature) versus accentuated aging, as findings may have implications for screening and other disease prevention strategies.

## Epidemiology of HIV in Older Persons

### Age of Persons Living with Diagnosed HIV

The Centers for Disease Control and Prevention (CDC) reports on the number of persons diagnosed with HIV in the United States, which includes all persons who have been diagnosed with HIV and are still living, regardless of when the diagnosis of HIV was made.[\[22\]](#) At year-end 2021, there were 1,072,267 persons diagnosed with HIV in the United States. Among those diagnosed with HIV, 53.3% were 50 years of age and older ([Figure 3](#)).[\[22\]](#) During the past 20 years, there has been a gradually increasing aging population of persons with HIV in the United States, which clearly reflects that people on suppressive antiretroviral therapy are surviving much longer and are not dying from AIDS-related complications.

### Age of Persons with New HIV Diagnoses

The CDC also reports on the number of new HIV diagnoses each year and this reflects individuals with a new positive HIV test during the year, but the individual may have acquired HIV long before the diagnosis of HIV was made. Of the 35,769 adults and adolescents newly diagnosed with HIV diagnoses during 2021, persons 50 years of age and older accounted for 16.3% of these new diagnoses ([Figure 4](#)).[\[22\]](#) In addition, the new HIV diagnoses rate (persons diagnosed with HIV per 100,000 population) was lower in persons 50 years of age than in younger age groups.[\[22\]](#)

### Relationship Between Age and HIV Stage at Time of HIV Diagnosis

In 2021, among persons 55 years of age or older newly diagnosed with HIV, 34.1% had stage 3 HIV infection (AIDS) at the time of diagnosis (based on a CD4 count less than 200 cells/mm<sup>3</sup>, a CD4 percentage less than 14%, or an AIDS-defining clinical condition); this proportion of older individuals with AIDS at diagnosis was much higher than with newly diagnosed younger adults ([Figure 5](#)).[\[23\]](#) These data, which show that older persons with HIV are diagnosed with a lower CD4 cell count, have major importance when considering the relatively attenuated CD4 cell reconstitution with antiretroviral therapy in older adults, particularly those with advanced immunosuppression.[\[24,25\]](#)

# Screening and Detection of HIV in Older Adults

## HIV Screening Guidelines

The Centers for Disease Control and Prevention (CDC) recommends that all individuals ages 13 to 64 be tested for HIV at least once and more often if there are ongoing risks for HIV acquisition.<sup>[26]</sup> The CDC screening guidelines do not recommend routine HIV testing for persons 65 years of age and older, though many individuals in the age group continue to be sexually active. Indeed, national surveys have shown high rates of sexual activity in these older adults, but low rates of condom use due to a lack of need for pregnancy prevention and a low perception of the risk of acquiring HIV and other sexually transmitted infections.<sup>[27,28,29]</sup> Erectile dysfunction medications have enabled many older men to remain sexually active when they might not otherwise. For older women, age-related changes that lead to vaginal dryness can increase HIV acquisition risk.<sup>[30]</sup> Major barriers to HIV screening in the elderly include lack of knowledge about HIV in this population and underestimation of HIV risk by medical providers who often assume their elderly patients are not sexually active.<sup>[30]</sup>

## Awareness of HIV Diagnosis

Available CDC surveillance data estimates that fewer than 10% of persons with HIV who are 55 years of age or older have undiagnosed HIV; this low fraction of undiagnosed HIV contrasted with a much higher fraction of undiagnosed HIV in younger age groups ([Figure 6](#)).<sup>[31]</sup>

# Antiretroviral Therapy in the Older Patient with HIV

## Initiating Antiretroviral Therapy in Persons Older than Age 50

The Adult and Adolescent ART Guidelines recommend initiating antiretroviral treatment in all persons with HIV, including persons 50 years of age and older, regardless of the CD4 cell count.<sup>[27]</sup> There are multiple reasons to justify starting antiretroviral therapy in all persons with HIV who are older than 50 years of age:

- Older persons with HIV have a greater risk of developing non-AIDS complications than younger persons with HIV.
- Older persons with HIV often have a blunted immunologic response to antiretroviral therapy.
- Chronic HIV may cause accelerated development of comorbid conditions that are common in older persons.
- Persons older than 50 years may have a significant risk of HIV transmission due to unfavorable changes in mucosal surfaces and infrequent use of condoms (due to lack of concern for pregnancy).
- Antiretroviral therapy substantially reduces AIDS-related and non-AIDS-related mortality in older persons with HIV.<sup>[32,33,34,35]</sup>

## Selection of Antiretroviral Regimens in Older Persons

The Adult and Adolescent ART Guidelines recommend the same regimens for older adults with HIV as for younger persons with HIV.<sup>[27,36]</sup> Unfortunately, most antiretroviral therapy trials have included only a small proportion of persons older than 50 years, and there are no unique guidelines for initial regimens or monitoring while on antiretroviral therapy for older adults with HIV. Since older persons have higher rates of comorbid medical conditions, such as renal or liver disease, some experts have advocated closer monitoring for antiretroviral therapy side effects, drug toxicity, and adverse interactions with other disease-related medications.<sup>[27]</sup>

### Table 1. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

#### Recommended Initial Regimens for Most People with HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use. Choice of antiretroviral therapy during pregnancy should be guided by recommendations from the Perinatal Guidelines.	
For people who do NOT have a history of long-acting cabotegravir use as HIV PrEP, the following regimens are recommended:	
<b>INSTI + 2 NRTIs:</b> <ul style="list-style-type: none"> <li>• Bictegravir-tenofovir alafenamide-emtricitabine (AI)</li> <li>• Dolutegravir plus (tenofovir alafenamide or tenofovir DF)<sup>a</sup> plus (emtricitabine or lamivudine) (AI)</li> </ul>	
<b>INSTI + 1 NRTI</b> <ul style="list-style-type: none"> <li>• Dolutegravir-lamivudine (AI)—except for individuals with HIV RNA &gt;500,000 copies/mL, HBV coinfection, or when antiretroviral therapy is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available</li> </ul>	
For people with HIV and a history of using long-acting cabotegravir as HIV PrEP, integrase genotypic drug resistance testing should be done before the start of antiretroviral therapy. If treatment is begun prior to the results of genotypic testing, the following regimen is recommended:	
<b>Boosted PI + 2 NRTIs:</b>	

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use. Choice of antiretroviral therapy during pregnancy should be guided by recommendations from the Perinatal Guidelines.	
<ul style="list-style-type: none"> <li>Darunavir (boosted with cobicistat or ritonavir) plus (tenofovir alafenamide or tenofovir DF)<sup>a</sup> plus (emtricitabine or lamivudine)—pending the results of the genotype test (AIII).</li> </ul>	
<p><b>Abbreviations:</b> INSTI = integrase strand transfer inhibitor; NRTI = nucleoside reverse transcriptase inhibitor</p> <p><sup>a</sup>Tenofovir alafenamide and tenofovir DF are two forms of tenofovir approved by the FDA. Tenofovir alafenamide has fewer bone and kidney toxicities than tenofovir DF, whereas tenofovir DF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.</p> <p>Rating of Recommendations: A = Strong; B = Moderate; C = Weak</p> <p>Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion</p>	

Source:

- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. What to Start. Initial Combination Antiretroviral Regimens for People With HIV. September 12, 2024. [[HIV.gov](https://www.hiv.gov)]

## Virologic Response to Antiretroviral Treatment in Older Persons

Older persons with HIV achieve equivalent or superior virologic responses to antiretroviral therapy when compared with younger persons with HIV.[32,33,34] In a retrospective cohort study involving 5,000 adults with HIV starting antiretroviral therapy, investigators reported higher rates of suppressed HIV RNA levels in persons older than 50 years than in persons younger than 50 years, which was explained by better adherence in the older patients.[35] These findings, however, were not replicated in the NA-ACCORD Study, possibly because patients in this study, across all age groups, had good adherence.[24] In CDC surveillance data that examined the HIV Care Continuum according to age group, persons in the older age groups had the highest levels of HIV RNA suppression (Figure 7).[23]

## Immunologic Recovery in Older Persons with HIV

Multiple studies have shown that older individuals have less robust CD4 count responses to antiretroviral therapy than younger individuals.[24,25,34,35,37] The following summarizes data from several key studies related to immunologic recovery in older persons with HIV after starting antiretroviral therapy.

- European COHERE:** Data from the large multicohort European COHERE study found poorer immunological responses in older adults compared with younger adults during the first three years of antiretroviral therapy.[38]
- NA-ACCORD:** The North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) found that older adults were less likely than younger adults to have a CD4 increase of at least 100 cells/mm<sup>3</sup> in the first two years of antiretroviral therapy.[24]
- Euro SIDA:** In the EuroSIDA cohort study, older adults had lower median CD4 cell increases, lower maximum CD4 cell counts, and were less likely to achieve a CD4 increase of at least 100 cells/mm<sup>3</sup> or 200 cells/mm<sup>3</sup> compared with younger adults.[25]
- ART Cohort Collaboration:** In the ART Cohort Collaboration, investigators analyzed 13 cohort

studies involving 12,574 persons with HIV who started combination antiretroviral therapy and found that age 50 years and older was associated with an increased probability of clinical progression to AIDS events or death.[39]

## **Drug Interactions and Polypharmacy**

The Adult and Adolescent ART Guidelines include tables that provide important information about drug interactions between antiretroviral medications and other medications.[40] Any antiretroviral regimen that includes either ritonavir or cobicistat can potentially cause significant interactions with other medications. Other antiretroviral medications can also cause significant drug interactions. Antiretroviral medication drug interactions are particularly an issue in older individuals with HIV who frequently take multiple medications in addition to antiretroviral therapy. Further, the high prevalence of multiple comorbid medical conditions among older persons with HIV heightens the likelihood of polypharmacy.[30,41] In one study, 82% of adults with HIV took at least one additional medication, and 58% took more than five, and these numbers were higher than for persons without HIV.[42] Not surprisingly, older individuals with HIV are more likely than younger persons with HIV to take multiple medications.[43,44,45] Furthermore, older adults are more likely to have renal or hepatic impairment that can impact metabolism and elimination of medications, so close monitoring is advised.[27]

## **Strategies to Reduce Medication-Related Toxicity in Older Patients**

Strategies to help reduce the risk of drug interactions and toxicity include using a pharmacy that has an integrated computer system, performing a formalized annual drug review and reconciliation of patient medication lists, and adjusting medication doses, as appropriate, in persons with renal or hepatic dysfunction.[30] Some expert panels recommend using the Cockcroft-Gault equation to estimate creatinine clearance for determining renal dosage adjustments of medications; although this equation is not as accurate in older persons, it is the method most widely used to estimate renal function in package inserts and in renal dosing charts.[30] The HIV renal guidelines indicate that the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation is another acceptable option for calculating creatinine clearance.[46]

## Common Comorbid Conditions in Older Persons with HIV

The following summarizes some of the more common comorbid conditions that occur in older persons with HIV, with an emphasis on conditions frequently seen that have high clinical importance.

### Cancer

As persons with HIV live longer with effective antiretroviral therapy, more are developing non-AIDS malignancies, such as colorectal cancer and lung cancer, and these malignancies are increasingly a cause of death.[\[18,47,48\]](#) A retrospective review of 13 cohorts participating in the Antiretroviral Therapy Cohort Collaboration (ART-CC) between 1996 and 2006 showed that non-AIDS malignancies were the most frequent cause of death, occurring in 11.8% of subjects.[\[30,49\]](#) The large Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study also found that non-AIDS-related malignancies were responsible for a large share of the mortality burden.[\[50\]](#) Both the ART-CC and D:A:D studies, as well as the SMART trial, showed that increasing age is strongly associated with an increased risk of non-AIDS malignancies.[\[30\]](#) The shifting spectrum of cancer in the HIV population underscores the importance of incorporating standardized cancer surveillance practices in the care of persons with HIV, especially as they get older.

### Cardiovascular Disease

Cardiovascular disease is of special concern for adults with HIV as evidence shows that adults with HIV have an increased risk of cardiovascular disease compared to the general population, with this relative increased risk typically estimated at about 1.5- to 2-fold.[\[51,52,53\]](#) A Kaiser observational study of more than 4,000 patients demonstrated that adults with HIV had higher rates of both myocardial infarction and hospitalization for coronary heart disease compared to similar-aged adults without HIV.[\[54\]](#) The Veterans Aging Cohort Study, which involved nearly 90,000 veterans, also showed a higher risk of myocardial infarction risk among veterans with HIV compared to veterans without HIV, and this difference was observed across multiple decades of age ([Figure 8](#)).[\[51\]](#) This increased risk is mediated by several factors: [\[52,55,56\]](#)

- Traditional risk factors (age, dyslipidemia, obesity, and smoking)
- Metabolic alterations related to some antiretroviral regimens (insulin resistance and dyslipidemia)
- Nontraditional factors linked to HIV itself, such as immune activation, inflammation, and immunosuppression

No HIV-specific guidelines exist for evaluating or managing cardiovascular risk factors, so medical providers should, in most instances, follow the guidelines established for the general population. In older adults with HIV, assessment and management of cardiovascular risk factors is extremely important, and some experts have suggested that risk calculators likely underestimate the risk of cardiovascular disease in persons with HIV.

### Diabetes Mellitus

Diabetes mellitus is an expanding epidemic in the aging population in the United States, with approximately 29% of all adults 65 years of age and older meeting the criteria for diabetes.[\[57\]](#) In general, persons with HIV and diabetes should be managed according to the American Diabetic Association (ADA) guidelines for older adults.[\[58\]](#) For older adults with few coexisting chronic illnesses, intact cognitive function, and good functional status, the target HbA1c should be less than 7.0-7.5%.[\[58,59\]](#) For older adults with coexisting chronic illnesses, cognitive impairment, or functional dependence, the target HbA1c should be less than 8.0-8.5%, especially if they have a life expectancy of less than 5 years or are at high risk for hypoglycemia or drug interactions.[\[30,58\]](#)

### Frailty

Most experts conceptually define frailty as a state of increased vulnerability of older adults to have a sudden



change in health status after a stressor event, such that a relatively small event may cause a disproportionate decline in health status.[60] Normal aging is associated with a gradual decline in physiological reserve, but in frailty syndrome, the decline is accelerated.[60] Typical clinical presentations of frailty include extreme fatigue, recurrent infections, falls, delirium, or fluctuating disability.[61] Experts on aging have quantitatively defined frailty as the presence of three or more of the following five parameters:[61]

1. Unintentional weight loss
2. Self-reported exhaustion
3. Low energy expenditure
4. Slow gait speed
5. Weak grip strength

Several studies have shown that individuals with HIV are more likely to suffer from frailty syndrome than individuals without HIV, and they are more likely to develop frailty at a younger age.[62,63,64] A cross-sectional study of 445 adults with HIV in an outpatient setting identified various risk factors for frailty syndrome, including prior opportunistic infections, more advanced immune suppression, and a higher number of comorbid conditions.[62] A review on this topic cited multiple factors that predispose adults with HIV to frailty, including longer time since HIV diagnosis, low current CD4 cell count, low nadir CD4 cell count, detectable plasma HIV RNA levels, low or high body mass index, hepatitis C virus infection, diabetes, kidney disease, and longer duration of antiretroviral therapy.[65]

## Neurocognitive Disorders

Cognitive disorders, including dementia, are widespread in the general population in the United States. Age is the major factor that predicts the development of dementia, with the prevalence nearly doubling every 10 years after age 60.[66] Overall, adults with HIV have poorer cognitive performance than adults without HIV.[67] Several studies in persons with HIV have identified multiple risk factors for neurocognitive decline: older age, low nadir CD4 cell count, detectable plasma HIV RNA levels, previous central nervous system injury, and comorbidities, such as hypertension, viral hepatitis, and substance use disorder.[30,68] Screening for cognitive impairment should be incorporated into the routine care of older persons with HIV. Brief, validated, clinic-based instruments for assessing cognitive status include the Montreal Cognitive Assessment (MoCA) and the [International HIV Dementia Scale](#); these tests, however, are not sensitive for the diagnosis of HAND, especially milder stages of HAND.[69,70,71] Persons with HIV who have abnormal screening results should be referred for formal neuropsychiatric testing, which is required to make a diagnosis of HAND. It is important to recognize that older individuals with HIV also are at risk for Alzheimer's disease and cerebrovascular disease.[30] Treatable causes of neurocognitive disorders, such as substance use disorders, medication-related effects, thyroid disease, vitamin B12 deficiency, syphilis, opportunistic infections, tumor, and depression, should be identified and addressed.

## Osteoporosis

Decreased bone mineral density is a common problem among older individuals in the general population; between 2013 and 2014, 6 to 11% of persons in the United States 50 years of age and older had osteoporosis, and 28 to 45% had decreased bone density at the lumbar spine or hip.[72] Studies performed earlier in the HIV epidemic have shown lower bone density and higher fracture rates in adults with HIV compared to adults without HIV, with an increased fracture prevalence disproportionate to age in both men and women with HIV.[73,74,75] In the current antiretroviral era, it is unclear if testosterone deficiency occurs at a higher frequency in men with HIV who are receiving suppressive antiretroviral therapy. In persons with HIV, increased risk of osteoporosis and fracture has been associated with lower body weight, smoking, vitamin D deficiency, and use of tenofovir DF.[74,76,77,78,79,80] Most experts avoid tenofovir DF in persons with increased risk for osteoporosis, and some avoid tenofovir DF in older patients in general. Persons with HIV and osteoporosis who receive calcium-containing antacids should be counseled regarding potential

interactions with antiretroviral medications, particularly when administering with oral integrase strand transfer inhibitors (INSTIs).

## Renal Disease

As in the general population, chronic kidney disease in adults with HIV contributes significantly to the risk of cardiovascular disease, frailty, and all-cause mortality.[30,46] The estimated prevalence of chronic kidney disease ranges from 5 to 10% among adults with HIV in North America, and the prevalence of albuminuria is estimated to be 2- to 5-fold higher among persons with HIV compared to those without HIV.[46] Older age is an important predictor of chronic kidney disease in adults with HIV; other factors include use of tenofovir DF, female sex, diabetes, hypertension, hepatitis C infection, injection drug use, history of acute kidney injury, lower CD4 cell count, and higher HIV RNA levels.[46] The HIV Medical Association/Infectious Diseases Society of America (HIVMA/IDSA) has provided a comprehensive Clinical Practice Guideline for the Management of Chronic Kidney Disease in Patients Infected with HIV that addresses the scope of the problem of renal disease among persons with HIV and provides management recommendations.[46]

## Testosterone Deficiency

Hypogonadism becomes more common as men age. In adult men with HIV, hypogonadism is more likely to occur and may occur at a younger age than in men without HIV. The prevalence of hypogonadism among men with HIV who are 50 years of age or older may be as high as 32%, though these estimates are based on older data.[81] Hypogonadism-related symptoms may negatively impact the quality of life by causing fatigue, depression, impaired concentration, sleep disturbance, and decreased libido.[81] Hypogonadism may also contribute to decreases in muscle mass, body hair, and bone mineral density. In addition, a recent retrospective analysis of 1,359 men with HIV showed a bidirectional association between low serum testosterone and multimorbidity syndrome, frailty, and HIV-associated non-AIDS comorbidities.[82] The HIVMA/IDSA Primary Care Guidance recommends testing for testosterone deficiency in men with any of the following: decreased libido, erectile dysfunction, reduced bone mass (or low-trauma fractures), hot flashes, or sweats; testing should also be considered in persons with less specific symptoms, such as fatigue and depression.[83] Testosterone replacement may be considered for persons with symptomatic hypogonadism; individuals receiving testosterone replacement therapy should be reevaluated in conjunction with follow-up testosterone levels to see if they have improved clinically. Persons receiving testosterone therapy should be counseled about increased risk of prostate cancer—testosterone should not be offered to men with prostate cancer or high risk of prostate cancer. The impact of testosterone replacement therapy on cardiovascular disease is not clear.[84]

# Life Expectancy, Age of Death, and Advanced Care Planning

## Life Expectancy

Following the widespread use of potent combination antiretroviral therapy, the life expectancy of persons with HIV has dramatically increased.[2,3,85] Investigators in the NA-ACCORD examined the life expectancy among persons diagnosed with HIV in the United States and Canada during the years 2000 through 2007 and estimated that a person diagnosed with HIV at age 20 would be expected to live into their early 70s if they received effective antiretroviral therapy.[1] Subsequent studies have shown similar findings, with continued gains in survival.[2,85] As would be expected, with increasing longevity among persons with HIV who receive antiretroviral therapy, most individuals who die with HIV in the United States are older than 50 at the time of death. In the CDC HIV surveillance data, among all the deaths in the United States in 2021 for persons diagnosed with HIV, approximately 73% occurred in persons 50 years of age and older (Figure 9).[22] These death statistics underscore the dramatic shift from the earlier years of the HIV epidemic, where most deaths occurred in persons younger than 40 years of age.

## Advanced Care Planning

Earlier in the HIV epidemic, prior to the availability of potent combination antiretroviral therapy, advanced care planning was routinely incorporated into HIV care.[30] Now that patients are leading longer, healthier lives, advanced care planning is often overlooked and underutilized.[86] Experts recommend that clinicians caring for older adults with HIV discuss end-of-life issues with these individuals and encourage them to designate a durable power of attorney for health care, as well as to complete an advance health care directive, such as the state-specific Physicians Orders for Life Sustaining Treatment (POLST) forms.[30]

## Summary Points

- Approximately 53% of all persons with diagnosed HIV in the United States are 50 years of age or older.
- Current CDC guidelines recommend routine HIV screening for persons aged 13 through 64 years but do not address HIV screening for persons 65 years of age and older.
- Persons who are older than 50 years of age tend to underestimate HIV risk acquisition.
- Older persons with HIV have higher rates of comorbid conditions than persons without HIV, and many older persons with HIV have multimorbidity that requires taking many non-antiretroviral medications.
- The Adult and Adolescent ART Guidelines recommend initiating antiretroviral therapy in all persons with HIV, including persons with HIV who are 50 years of age and older, regardless of CD4 cell count or HIV RNA level.
- Recommended antiretroviral therapy regimens for older persons with HIV are the same as for younger patients.
- When compared with younger individuals with HIV, older persons with HIV have equally good, if not better, rates of virologic suppression.
- Older adults with HIV have a less robust immune response to antiretroviral therapy than younger adults.
- Many of the common age-related, non-AIDS conditions play a major role in the clinical management of older persons with HIV.
- Clinicians caring for older persons with HIV should encourage them to designate a durable power of attorney for health care and complete an advance health care directive.

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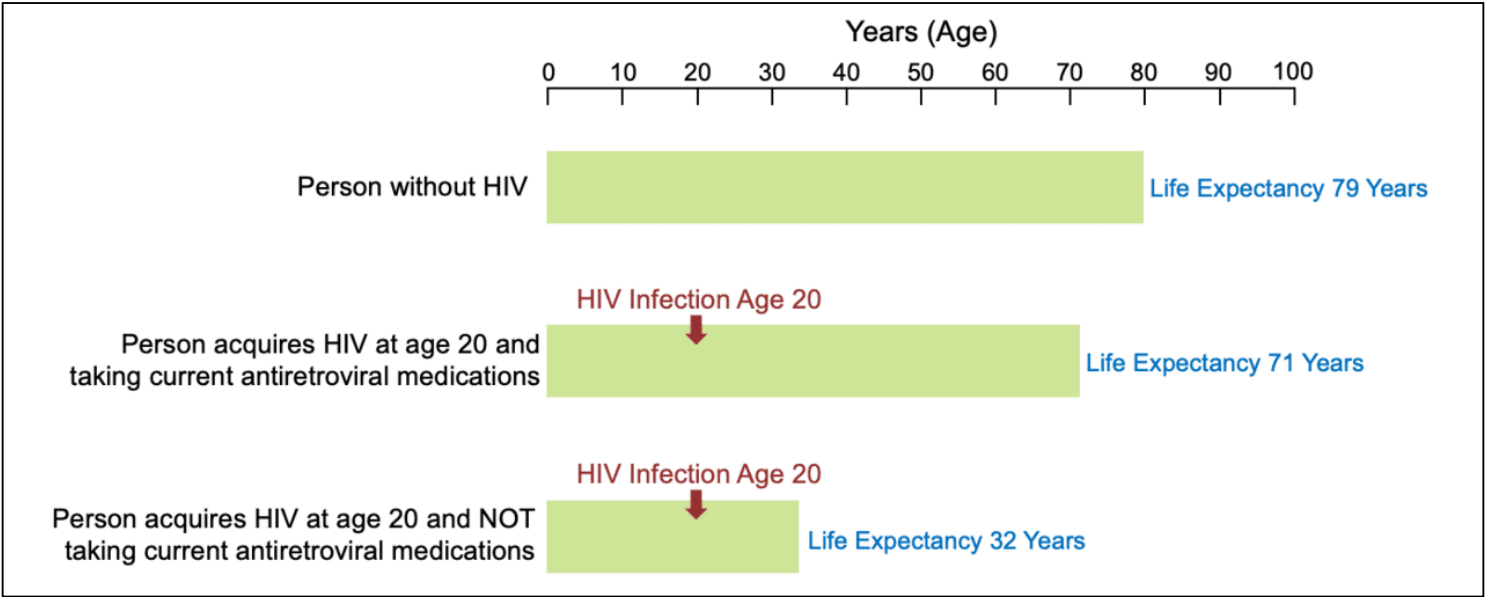
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# Figures

**Figure 1 Life Expectancy of Persons with HIV**

This illustration shows that young individuals with HIV can have a nearly normal life expectancy if they take current antiretroviral medications.

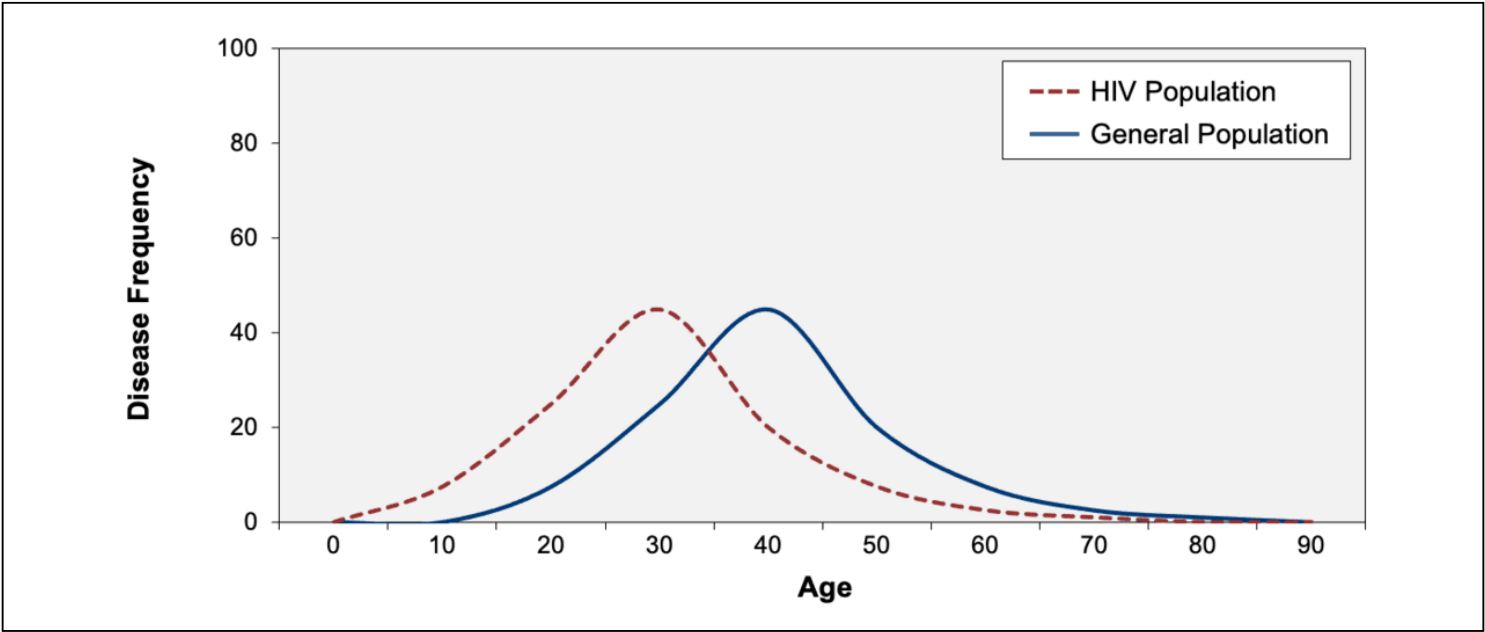
Source: Samji H, Cescon A, Hogg RS, et al. Closing the gap: increases in life expectancy among treated HIV-positive individuals in the United States and Canada. PLoS One. 2013;8:e81355.



**Figure 2 (Image Series) - Models of Aging in Persons with HIV (Image Series) - Figure 2 (Image Series) - Models of Aging in Persons with HIV**  
**Image 2A: Model of Accelerated Aging**

This conceptual graphic illustrates accelerated HIV aging, in which age-associated comorbidities occur at an earlier age in persons with HIV than in the general population, but these comorbidities occur at roughly the same frequency (or rate) in persons with HIV and in the general population. Typical age-associated comorbidities include cardiovascular disease, cancer, diabetes, liver disease, frailty, and neurocognitive impairment.

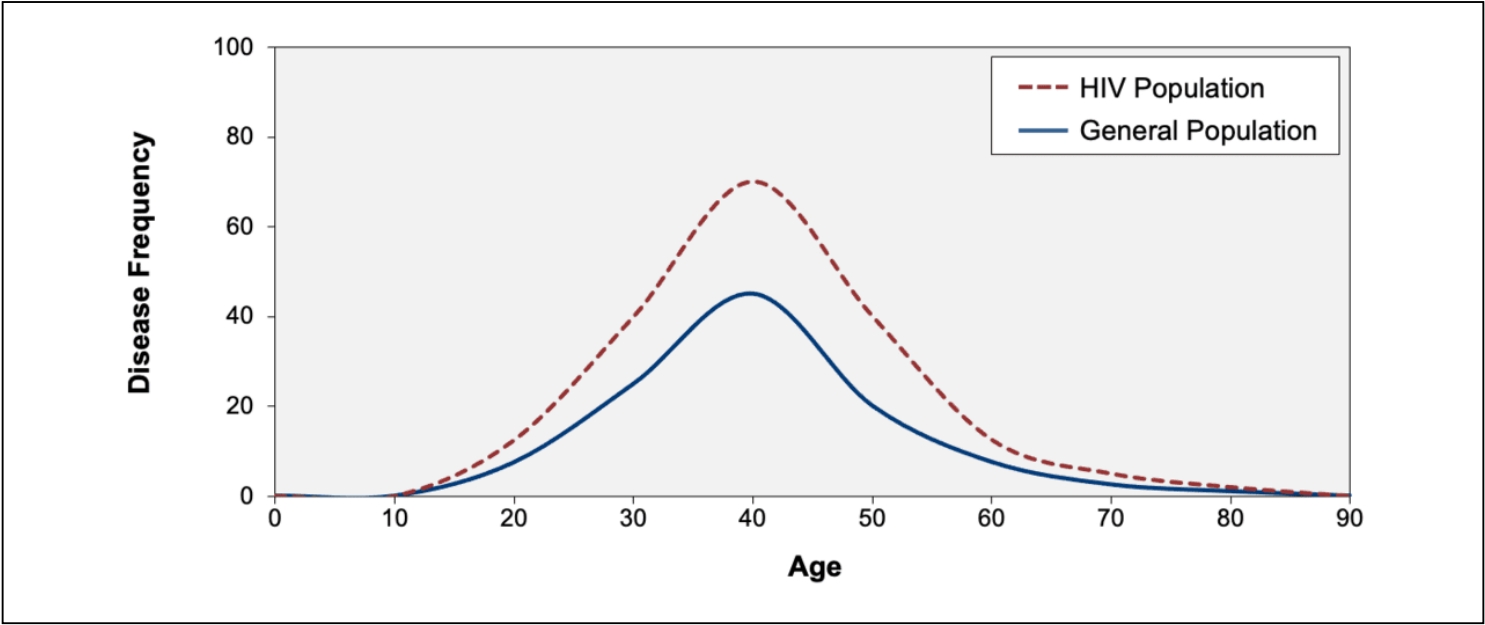
Source: Image based on model from: Pathai S, Bajillan H, Landay AL, High KP. Is HIV a model of accelerated or accentuated aging? J Gerontol A Biol Sci Med Sci. 2014;69:833-42.



**Figure 2 (Image Series) - Models of Aging in Persons with HIV**  
**Image 2B: Model of Accentuated Aging**

This conceptual graphic illustrates accentuated HIV aging, in which age-associated comorbidities occur at a significantly higher frequency (or rate) in persons with HIV when compared with persons in the general population, but at roughly the same age. Typical age-associated comorbidities include cardiovascular disease, cancer, diabetes, liver disease, frailty, and neurocognitive impairment.

Source: Image based on model from: Pathai S, Bajillan H, Landay AL, High KP. Is HIV a model of accelerated or accentuated aging? J Gerontol A Biol Sci Med Sci. 2014;69:833-42.

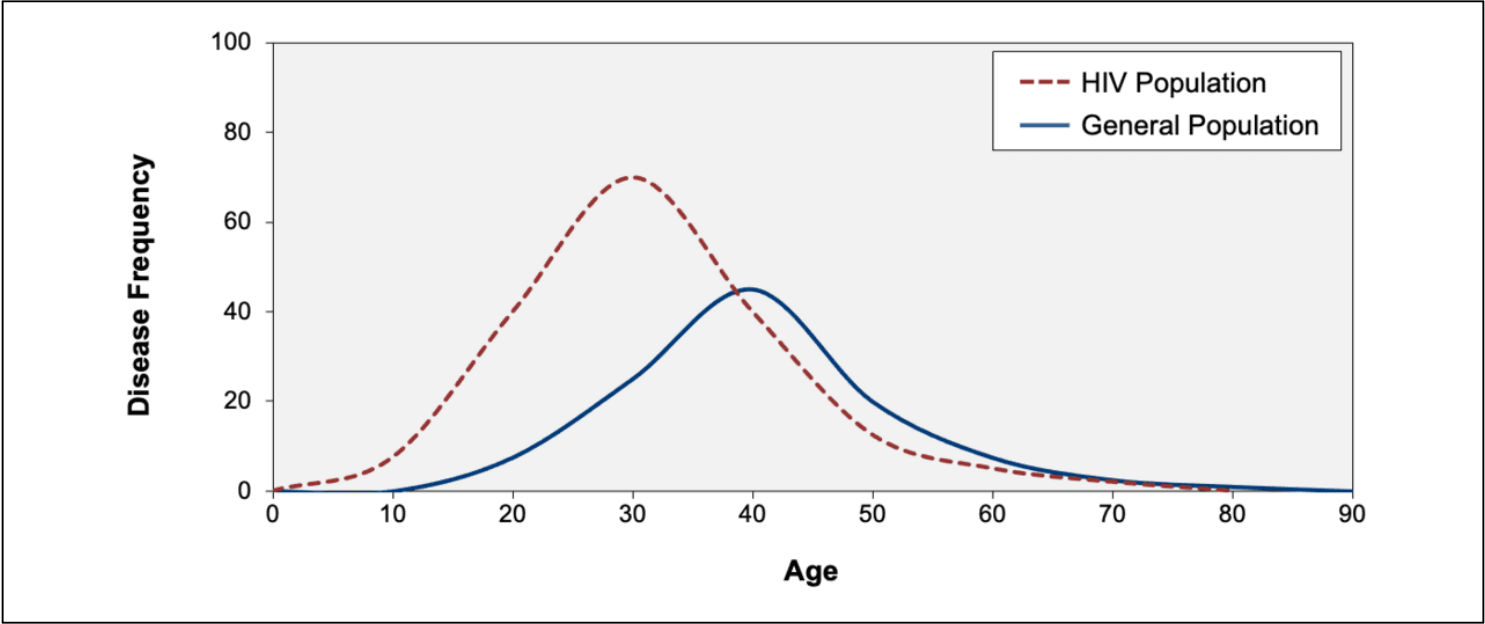




**Figure 2 (Image Series) - Models of Aging in Persons with HIV**  
**Image 2C: Model of Accelerated and Accentuated Aging**

This conceptual graphic illustrates combined accelerated and accentuated HIV aging, in which age-associated comorbidities occur at a significantly earlier age and at a significantly higher frequency (or rate) in persons with HIV when compared with persons in the general population. Typical age-associated comorbidities include cardiovascular disease, cancer, diabetes, liver disease, frailty, and neurocognitive impairment.

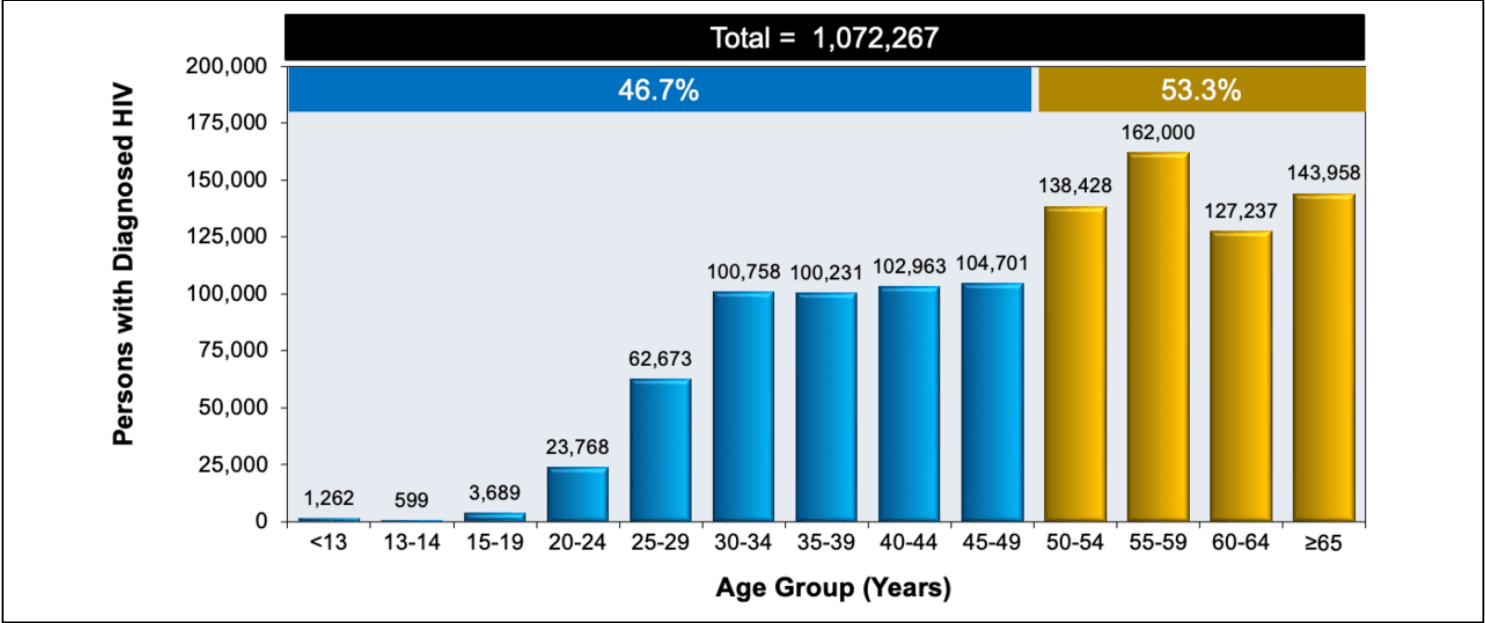
Source: Image based on model from: Pathai S, Bajillan H, Landay AL, High KP. Is HIV a model of accelerated or accentuated aging? J Gerontol A Biol Sci Med Sci. 2014;69:833-42.



**Figure 3 Persons with Diagnosed HIV in the United States, by Age Group, Year-End 2021**

At year-end 2021, more than 50% of persons living with diagnosed HIV in the United States were at least 50 years of age.

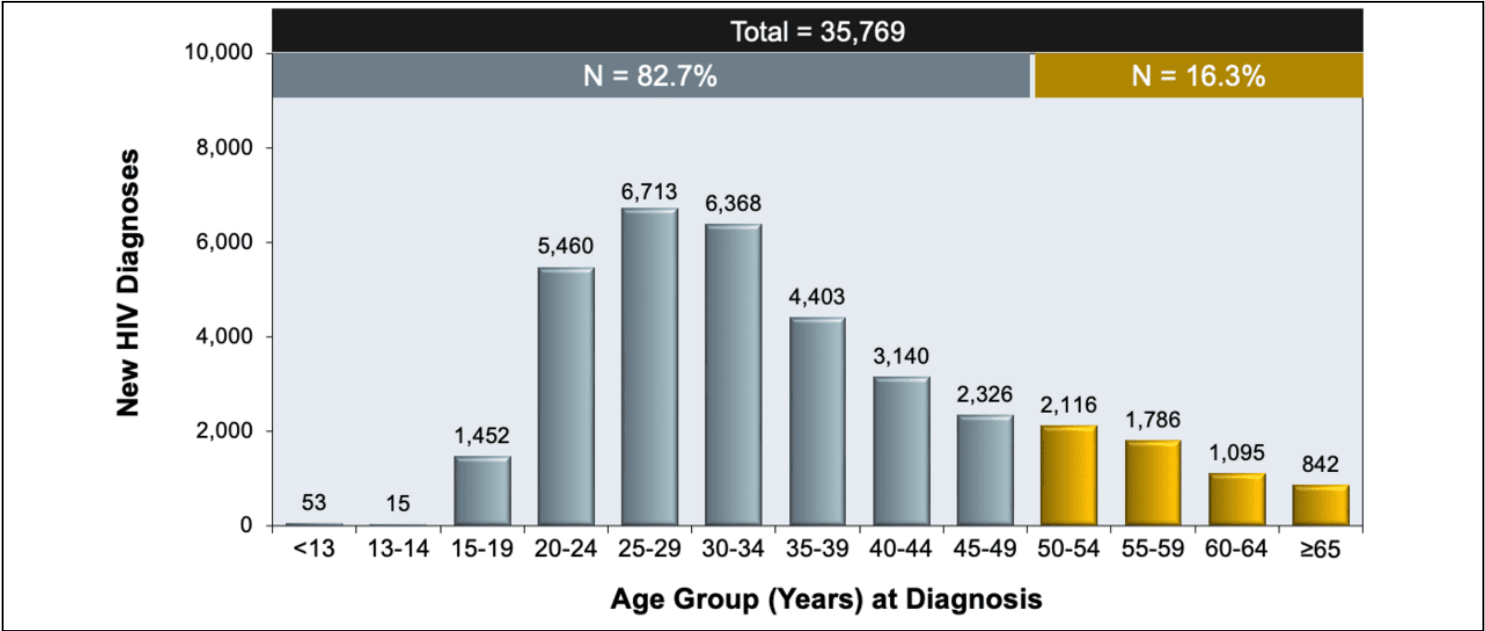
Source: Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas, 2021. HIV Surveillance Report, 2021; vol. 34. Published May 2023.



**Figure 4 New Diagnoses of HIV in the United States by Age Group at Time of Diagnosis, 2021**

In 2021 persons 50 years of age and older comprised 16.3% of new HIV diagnoses in the United States.

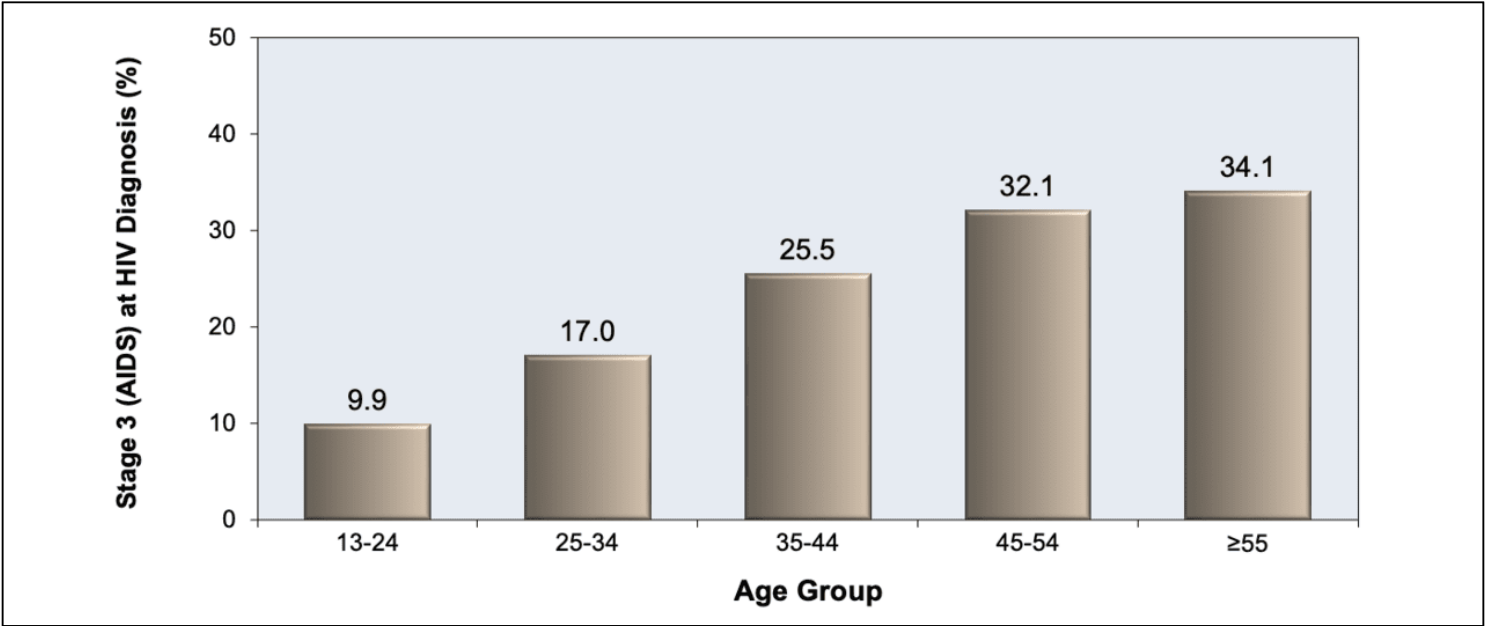
Source: Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas, 2021. HIV Surveillance Report, 2021; vol. 34. Published May 2023.



**Figure 5 Percentage of Persons with Stage 3 (AIDS) at the Time of HIV Diagnosis, by Age Group, 2021**

This graph shows that the likelihood of having stage 3 HIV at the time of HIV diagnosis increases with age.

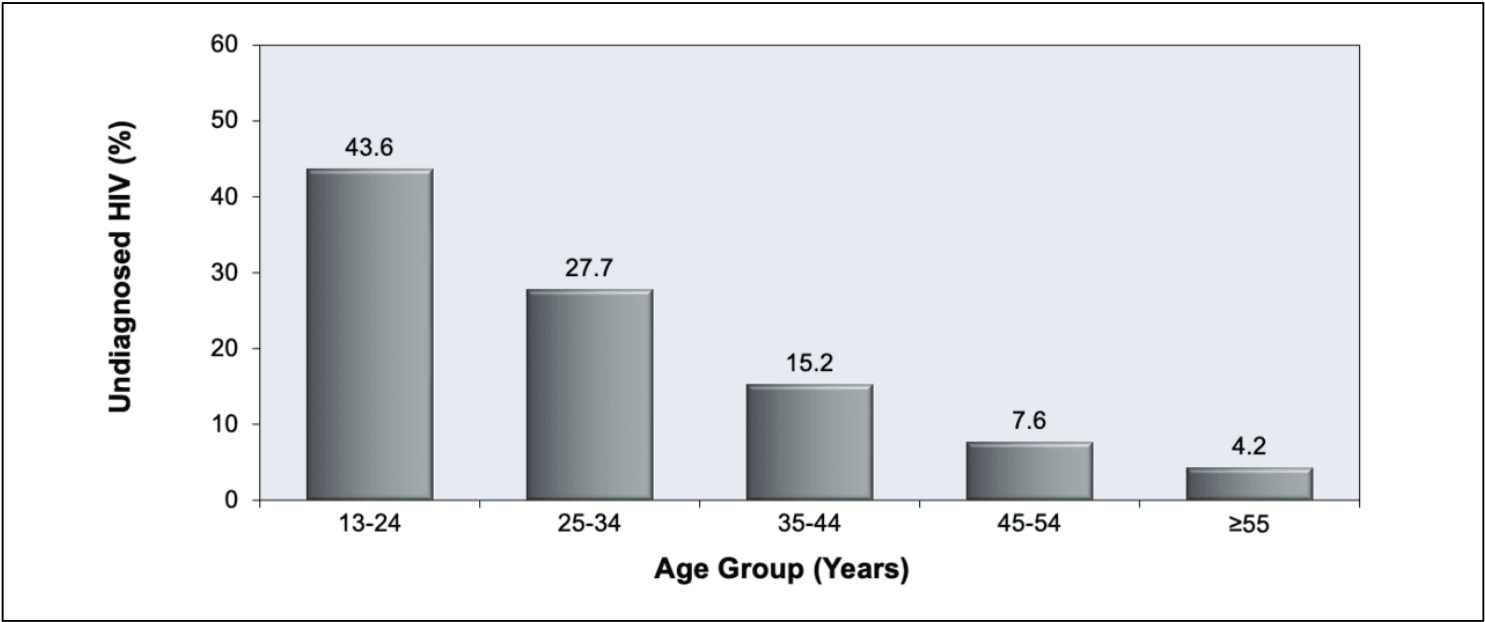
Source: Centers for Disease Control and Prevention. Monitoring Selected National HIV Prevention and Care Objectives by Using HIV Surveillance Data United States and 6 Dependent Areas, 2021. HIV Surveillance Supplemental Report. 2023;28(No. 4). Published May 2023.



**Figure 6 Persons with Undiagnosed HIV, by Age Group, United States, 2021**

This graphic shows percentage of people in the United States who have undiagnosed HIV. In general, the percentage of persons with undiagnosed HIV decreases with age.

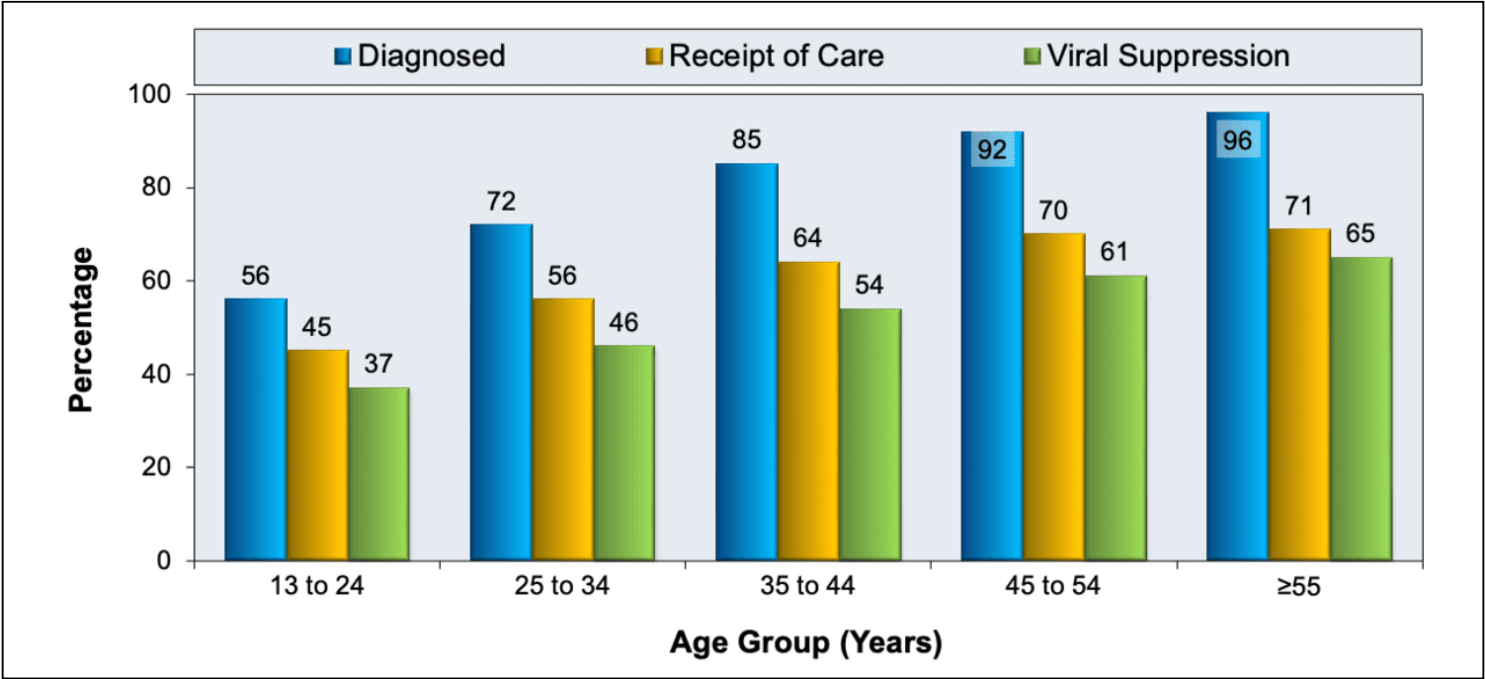
Source: Centers for Disease Control and Prevention. Estimated HIV Incidence and Prevalence in the United States, 2017–2021. HIV Surveillance Supplemental Report. 2023;28(3). Published May 2023.



**Figure 7 Persons with Diagnosed or Undiagnosed HIV in HIV Care Continuum Outcomes, by Age, United States, 2021**

In the HIV Care Continuum, persons in the older age groups (45 and older) had the highest levels of HIV RNA suppression.

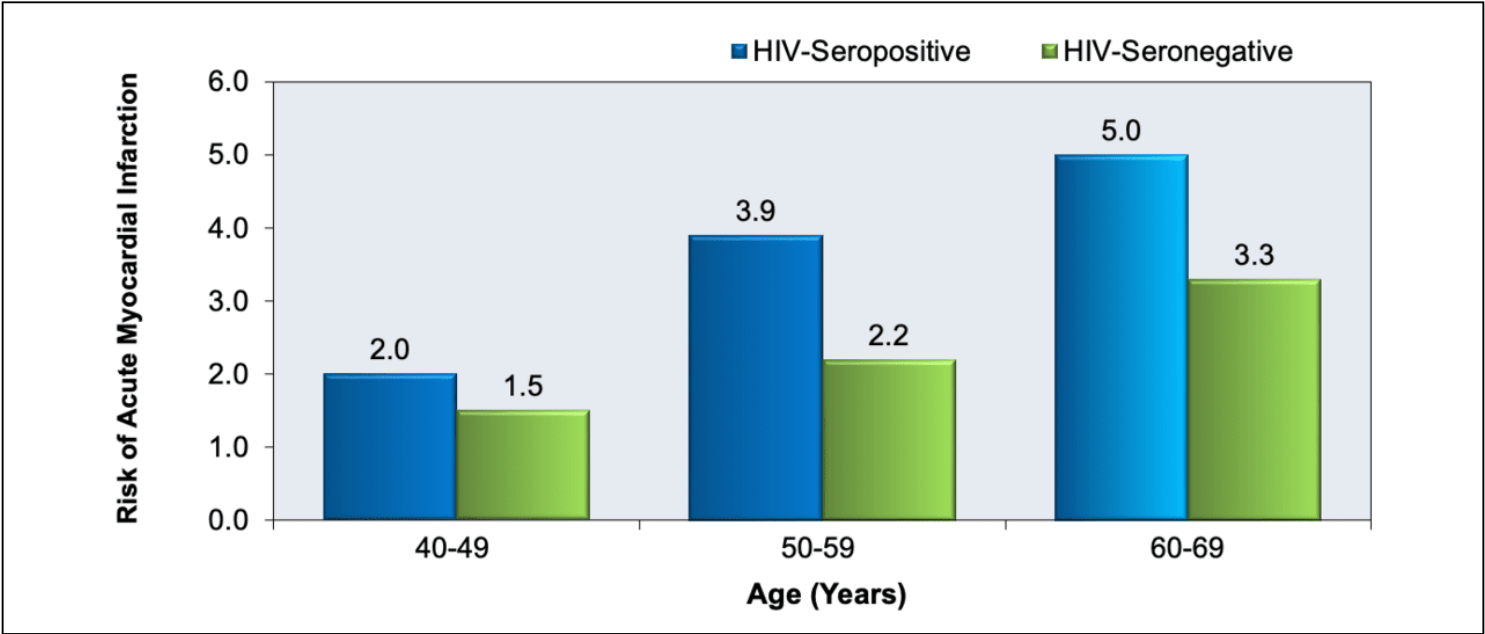
Source: Centers for Disease Control and Prevention. Monitoring Selected National HIV Prevention and Care Objectives by Using HIV Surveillance Data—United States and 6 Dependent Areas, 2021. HIV Surveillance Supplemental Report. 2023;28(No. 4). Published May 2023.



**Figure 8 Risk of Acute Myocardial Infarction Based on HIV Status and Age**

This graph is based on data from 82,459 participants in the Veterans Aging Cohort Study (Virtual Cohort) from April 1, 2003 through December 31, 2009. Persons with HIV clearly had a higher risk of developing acute myocardial infarction and this risk was seen across multiple decades of age.

Source: Freiberg MS, Chang CC, Kuller LH, et al. HIV infection and the risk of acute myocardial infarction. JAMA Intern Med. 2013;173:614-22.



**Figure 9 Deaths in Persons with Diagnosed HIV, by Age Group, United States, Year-End 2021**

Notably, 73.3% of the deaths that occurred in 2021 among persons diagnosed with HIV in the United States involved persons 50 years of age and older.

Source: Centers for Disease Control and Prevention. Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas, 2018 (Preliminary). HIV Surveillance Report, 2019; vol. 30:1-129. Published November 2019.

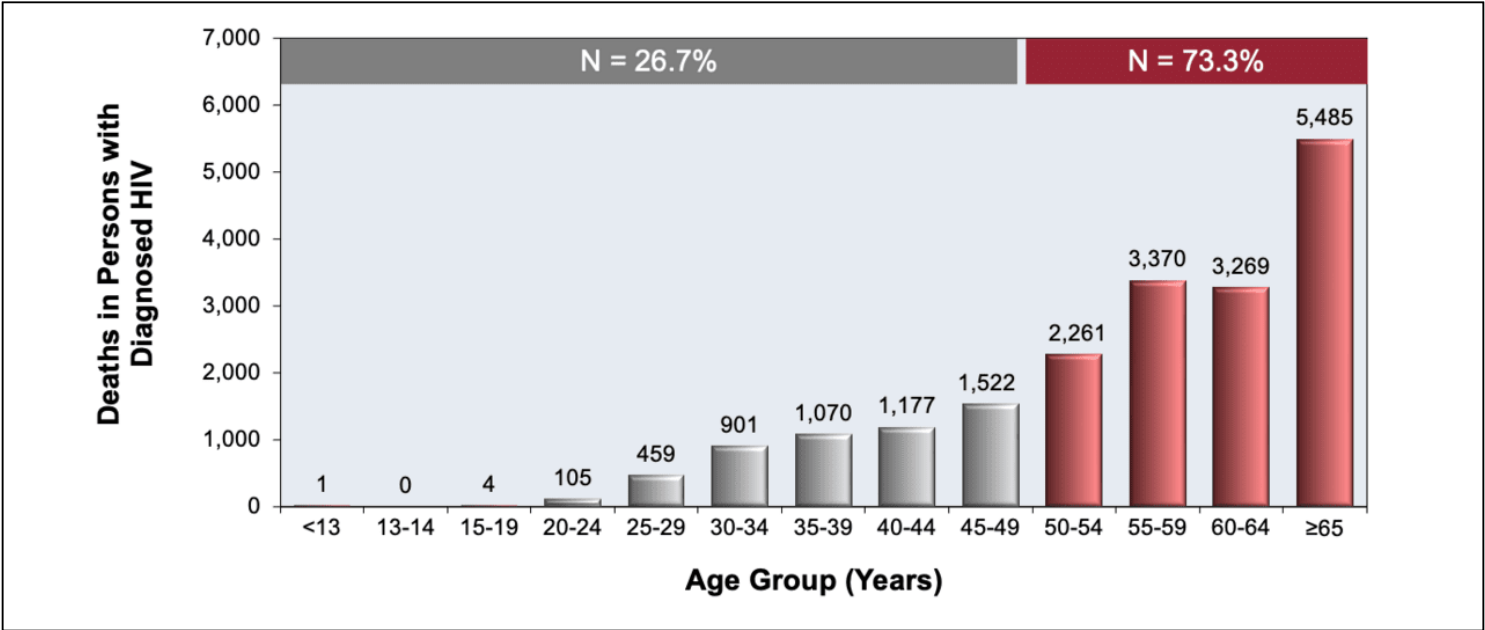




Table 1. **Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV**

### Recommended Initial Regimens for Most People with HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use. Choice of antiretroviral therapy during pregnancy should be guided by recommendations from the Perinatal Guidelines.

For people who do NOT have a history of long-acting cabotegravir use as HIV PrEP, the following regimens are recommended:

#### INSTI + 2 NRTIs:

- Bictegravir-tenofovir alafenamide-emtricitabine (AI)
- Dolutegravir plus (tenofovir alafenamide or tenofovir DF)<sup>a</sup> plus (emtricitabine or lamivudine) (AI)

#### INSTI + 1 NRTI

- Dolutegravir-lamivudine (AI)—except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or when antiretroviral therapy is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

For people with HIV and a history of using long-acting cabotegravir as HIV PrEP, integrase genotypic drug resistance testing should be done before the start of antiretroviral therapy. If treatment is begun prior to the results of genotypic testing, the following regimen is recommended:

#### Boosted PI + 2 NRTIs:

- Darunavir (boosted with cobicistat or ritonavir) plus (tenofovir alafenamide or tenofovir DF)<sup>a</sup> plus (emtricitabine or lamivudine)—pending the results of the genotype test (AIII).

**Abbreviations:** INSTI = integrase strand transfer inhibitor; NRTI = nucleoside reverse transcriptase inhibitor

<sup>a</sup>Tenofovir alafenamide and tenofovir DF are two forms of tenofovir approved by the FDA. Tenofovir alafenamide has fewer bone and kidney toxicities than tenofovir DF, whereas tenofovir DF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

Rating of Recommendations: A = Strong; B = Moderate; C = Weak

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion

Source:

- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. What to Start. Initial Combination Antiretroviral Regimens for People With HIV. September 12, 2024. [[HIV.gov](https://www.hiv.gov)]

