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.[1,2,3,4] The changing of the HIV epidemic to increasing 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 living 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.

Epidemiology of HIV in Older Persons

Among people with diagnosed HIV at year end 2018 in the United States, 51% were 50 years of age or older (Figure 1) and those 50 to 54 years of age comprised 15% of all persons living with diagnosed HIV.[5] In 2018, among all adults and adolescents newly diagnosed with HIV, 17% were 50 years of age or older (Figure 2).[5] 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 (Figure 3).[5]

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.[6,7,8,9] 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.[10,11,12]

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.[9,13,14,15,16] 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.[17] 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.[18]

**HIV Aging Consensus Project**

To address the complexities of managing older persons with HIV, the HIV Aging Consensus Project, a collaborative report produced by the American Academy of HIV Medicine, the AIDS Community Research Initiative of America, and the American Geriatrics Society, advances a new paradigm of coordinated, patient-centered HIV care that strives to maximize functional status and improve quality of life for those individuals with HIV living into their fifth decade and beyond.[19,20,21]
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.[14] With accelerated aging, an age-related comorbid condition could occur at an earlier age in persons with HIV compared to those without HIV (Figure 4). 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 (Figure 5). 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 (Figure 6).[14] 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.[22,23]

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 infection who are taking antiretroviral therapy.[13,22,24] 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).[10,13,25] 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.[26] 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.[26]

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.[6,14] 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.[6] 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.[6] 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.
CD4 Cell Counts in Older Persons with HIV

In 2018, among persons 55 years of age or older newly diagnosed with HIV, 35.2% had stage 3 HIV infection (AIDS) at the time of diagnosis (based on CD4 count less than 200 cells/mm$^3$ or 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 7). These data are consistent with a report from 2007 that showed a median CD4 count of only 266 cells/mm$^3$ at diagnosis for adults over age 50.[27] The potential importance of a low CD4 count at diagnosis is compounded by the relatively attenuated CD4 cell reconstitution with antiretroviral therapy in older adults, particularly those with advanced immunosuppression at baseline.

- **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.[29]
- **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$^3$ in the first two years of antiretroviral therapy.[30]
- **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$^3$ or 200 cells/mm$^3$ compared with younger adults.[31]
- **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 increased probability of clinical progression to AIDS events or death.[32]

Taken together, these data suggest that (1) older persons with HIV are diagnosed with lower CD4 cell counts, (2) older persons with HIV have poorer CD4 cell count recovery with antiretroviral therapy, and (3) older persons starting on antiretroviral therapy have worse outcomes than younger persons.
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.[33] 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 lack of need for pregnancy prevention and a low perception of risk of acquiring HIV and other sexually transmitted infections.[34, 35, 36] 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.[20] 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.[20]

Awareness of HIV Diagnosis

Available CDC surveillance data estimates that more than 90% of persons with HIV who are 55 years of age or older had a known HIV diagnosis; this high fraction of diagnosed HIV contrasted with a much lower fraction of diagnosed HIV in younger persons (Figure 8).[37]
Antiretroviral Therapy in the Older Patient with HIV

Initiating Antiretroviral Therapy in Persons Older than Age 50

The Adult and Adolescent ARV Guidelines recommend initiating antiretroviral treatment in all persons with HIV, including persons 50 years of age and older, regardless of the CD4 cell count.[34] There are multiple reasons to justify starting antiretroviral therapy in all persons with HIV who are older than 50 years of age:

1. Older persons with HIV have greater risk of developing non-AIDS complications than younger persons with HIV,
2. Older persons with HIV often have a blunted immunologic response to antiretroviral therapy,
3. Chronic HIV may cause accelerated development of comorbid conditions that are common in older persons,
4. Persons older than 50 years may have significant risk of HIV transmission due to unfavorable changes in mucosal surfaces and infrequent use of condoms (due to lack of concern for pregnancy).
5. Antiretroviral therapy substantially reduces mortality in older persons with HIV.[38,39,40,41] As suggested by findings from the Strategies for the Management of Antiretroviral Therapy (SMART) trial, the mortality benefit conferred by antiretroviral therapy was in large part due to the prevention of cardiovascular, renal, and hepatic events (and not just due to the prevention of AIDS-related events), a finding particularly important with older persons.[42]

Response to Antiretroviral Treatment in Older Persons

Multiple studies have shown that older individuals have less robust CD4 count responses to antiretroviral therapy than younger individuals.[30,31,40,41,43] In contrast to these blunted CD4 responses, older persons with HIV achieve equivalent or superior virologic responses to antiretroviral therapy when compared with younger persons with HIV.[38,39,40] 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.[41] These findings, however, were not replicated in the NA-ACCORD Study, possibly because patients in this study, across all age groups, had good adherence.[30] 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 9).[44]

Selection of Antiretroviral Regimens in Older Persons

The Adult and Adolescent ARV Guidelines recommend the same regimens for older adults with HIV as for younger persons with HIV.[34] 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.[34]

Drug Interactions and Polypharmacy

The Adult and Adolescent ARV Guidelines include tables that provide important information about drug interactions between antiretroviral medications and other medications.[45] 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.[20,46] 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.\[^{47}\] Not surprisingly, older individuals with HIV are more likely than younger persons with HIV to take multiple medications.\[^{48,49,50}\] 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.\[^{34}\]

**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.\[^{20}\] 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.\[^{20}\] The HIV renal guidelines indicate that the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation is another acceptable option for calculating creatinine clearance.\[^{51}\]
Common Comorbid Conditions in Older Persons with HIV

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. Normal aging is associated with a gradual decline in physiological reserve, but in frailty syndrome, the decline is accelerated. Typical clinical presentations of frailty include extreme fatigue, recurrent infections, falls, delirium, or fluctuating disability. Experts on aging have quantitatively defined frailty as the presence of three or more of the following five parameters:

1. Unintentional weight loss,
2. Self-reported exhaustion,
3. Low energy expenditure,
4. Slow gait speed, and
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. 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. 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.

Cardiovascular Disease

Cardiovascular disease is of special concern for adults with HIV as a preponderance of evidence shows that adults with HIV have a 1.5- to 2-fold greater risk of cardiovascular disease than the general population. 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. 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. This increased risk is mediated by several factors:

- Traditional risk factors (age, dyslipidemia, obesity, and smoking),
- Metabolic alterations related to some antiretroviral regimens (insulin resistance and dyslipidemia), and
- Nontraditional factors linked to HIV itself, including 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
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.[20, 51] 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.[51] 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.[51] The HIV Medical Association (HIVMA) 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.[51]

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 age 50 and older had osteoporosis, and 28 to 45% had decreased bone density at the lumbar spine or hip.[66] Lower bone density and higher fracture rates are found among adults with HIV compared with the general population without HIV, and fracture prevalence increases disproportionally with age in both men and women with HIV.[67, 68] This increased risk of osteoporosis and fracture has been largely explained by lower body weight, smoking, and vitamin D deficiency, but HIV-related factors may play a role, such as direct HIV-1 infection of osteoclasts and reduced bone mineral density from use of tenofovir DF.[67, 69, 70, 71, 72, 73] Management of osteopenia and osteoporosis is the same for persons with HIV as for those without HIV, though prescribers should note that calcium-containing antacids may impair absorption of atazanavir, rilpivirine, and integrase strand transfer inhibitors (INSTIs). Thus, calcium-containing antacids should be administered according to the dosing instructions in the relevant antiretroviral medication package inserts; in some instances, such as with once daily raltegravir 1200 mg, antacids should not be coadministered with the antiretroviral medication under any circumstances.

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% and hypogonadism-related symptoms may negatively impact quality of life by causing fatigue, depression, impaired concentration, sleep disturbance, and decreased libido.[74] 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.[75] The HIVMA/IDSA Primary Care Guidance recommend 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.[65] Testosterone replacement may be considered for persons with symptomatic hypogonadism; individuals receiving testosterone replacement therapy should be reevaluated in conjunction with following 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.[76]

**Neurocognitive Disorders**

Cognitive disorders, including dementia, are widespread in the general population in the United States. Age is the major factor that predicts development of dementia, with the prevalence nearly doubling every 10 years after age 60.[77] Overall, adults with HIV have poorer cognitive performance than adults without HIV.[78] The CHARTER Study, an observational study performed in the era of potent combination antiretroviral therapy, reported rare prevalence of profound neurocognitive impairment (HIV-associated dementia), but a high prevalence (52%) of milder neurocognitive impairment, generally referred to as HIV-associated neurocognitive disorders (HAND); this study did not have age restrictions.[79] 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.[20,79] 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.[80,81,82] 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 have risk for Alzheimer’s disease and cerebrovascular disease.[20] Treatable causes of neurocognitive disorder, such as substance use disorders, medication-related effects, thyroid disease, vitamin B12 deficiency, syphilis, opportunistic infections, tumor, and depression should be identified and addressed.

**Cancer**

As persons with HIV live longer with effective antiretroviral therapy, more are developing non-AIDS malignancies, such as hepatocellular carcinoma, colorectal cancer, and lung cancer, and these malignancies are increasingly a cause of death.[23,83,84] 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.[2,20] 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.[85] 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.[20] 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.
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.[1,3,4,86] 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.[3,4] 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 2017 for persons diagnosed with HIV, approximately 71% occurred in persons 50 years of age and older (Figure 11) and the death rate among persons with diagnosed HIV was highest in persons 50 through 64 years of age (Figure 12).[87] These death statistics underscore the dramatic shift from the earlier years of the HIV epidemic where most deaths occurred in persons younger than age 40 years.

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.[20] Now that patients are leading longer, healthier lives, advanced care planning is often overlooked and underutilized.[88] 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 healthcare directive, such as the state-specific Physicians Orders for Life Sustaining Treatment (POLST) forms.[20]
Summary Points

- Approximately 50% of all persons with 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 ARV 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.
- Older adults with HIV have a less robust immune response to antiretroviral therapy than younger adults despite equally good, if not better, rates of virologic suppression.
- 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 healthcare directive.
Citations


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By year-end 2018, 50.6% of persons living with diagnosed HIV in the United States were at least 50 years of age.

In 2018 persons 50 years of age and older comprised 16.6% of new HIV diagnoses in the United States. Note, the number of new HIV diagnoses is not equivalent to the number of new HIV infections that occurred that year (HIV incidence), as persons could have acquired HIV long before testing positive and being diagnosed in 2018.

In 2018, the rate of new HIV diagnoses in persons 50 years of age and older were significantly lower than in persons 20 through 49 years of age; these rates of new HIV diagnoses are not equivalent to the rate of new HIV infections (HIV incidence rate), as persons could have acquired HIV long before testing positive and being diagnosed in 2018.

Figure 4 Model of Accelerated Aging in Persons with HIV

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.

**Figure 5 Model of Accentuated Aging in Persons with HIV**

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.

Figure 6 Model of Accelerated and Accentuated Aging in Persons with HIV

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.

Figure 7 Percentage of Persons with Stage 3 (AIDS) at the Time of HIV Diagnosis, by Age Group 2018

This graph shows that the likelihood of having stage 3 HIV at the time of HIV diagnosis increases with age. Stage 4 HIV (AIDS) was defined as a CD4 count less than 200 cells/mm$^3$, a CD4 percentage less than 14, or an AIDS-defining opportunistic infection.

Figure 8 Proportion of Persons Living with HIV in the United States who have Diagnosed HIV in 2018

This graphic shows the HIV diagnosed fraction among different age groups. The HIV diagnosed fraction represents the percentage of persons with HIV in the United States who have a known HIV diagnosis divided by estimated total number of persons with HIV in the United States. In general, the HIV diagnosed fraction increases with age.

Figure 9 Persons Living with Diagnosed or Undiagnosed HIV Infection HIV Care Continuum Outcomes, by Age, 2016—United States

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

Figure 10 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.

Figure 11 Deaths in Persons with Diagnosed HIV Infection in United States, by Age Group, Year End 2017

Notably, 70.9% of the deaths that occurred in 2017 among persons diagnosed with HIV in the United States involved persons 50 years of age and older.

The 2017 death rate of persons living with diagnosed HIV in the United States (deaths per 100,000 population) was highest in persons 50 through 64 years of age.