

HIV and the Older Person

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Key Considerations and Recommendations When Caring for Older People With HIV

- Diagnosis of HIV at a later stage of disease is more common among older people. Early diagnosis and treatment of HIV and counseling to prevent secondary HIV transmission remain important in the clinical care of older people with HIV.
- Antiretroviral therapy (ART) is recommended for all people with HIV **(AI)**. ART is especially important for older individuals because they have a greater risk of serious non-AIDS complications and potentially a blunted immunologic response to ART.
- Compared to people without HIV, people with HIV have a twofold higher risk of developing atherosclerotic cardiovascular disease (ASCVD), and their age at incident ASCVD diagnosis is about a decade younger. In addition to current American Heart Association (AHA)/American College of Cardiology (ACC)/Multisociety Guidelines, the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends initiating at least a moderate-intensity statin in people with HIV aged 40 to 75 years who have 10-year ASCVD risk estimates of 5% to <20% **(AI)**. See [Statin Therapy in People With HIV](#) for the Panel's additional recommendations on the use of statin therapy as primary prevention for people with HIV.
- Polypharmacy is common in older people with HIV, and all drugs, supplements, and herbal treatments should be assessed regularly for appropriateness, potential for adverse effects, proper dosing, and drug interactions **(AIII)**.
- Potential for drug–drug interactions between antiretroviral drugs and concomitant medications (including statins, supplements, and herbal medicines) should be assessed regularly, especially before a new ART regimen or concomitant medication is started. In this context, it is also important to inquire and counsel about the use of non-daily medications, including long-acting injectables and as-needed medications.
- Adverse drug events from ART and concomitant drugs may occur more frequently in older people with HIV than in younger individuals with HIV. Therefore, the bone, kidney, metabolic, cardiovascular, cognitive, and liver health of older individuals with HIV should be monitored closely.
- HIV infection is associated with immunologic aging and systemic inflammation, which may contribute to the development of comorbidities across multiple organ systems as well as aging phenotypes like frailty. HIV experts, primary care providers, and other specialists should work together to optimize the medical care of older people with HIV, including adhering to treatment and prevention guidelines for different medical comorbidities.
- Age-related decline in neurocognitive function is faster in people with HIV compared to those without. Cognitive impairment in people with HIV—with manifestations including problems with memory, attention, and executive function—is associated with reduced adherence to therapy and poorer health outcomes, including increased risk of death. For people with progressive cognitive impairment, referral to a specialist (e.g., neurologist, neuropsychologist, geriatrician) for evaluation, testing, and management may be warranted **(BIII)**.
- Mental health disorders, including an increased risk of anxiety and depression, are a concern among aging people with HIV. Screening for depression and management of mental health issues are important when caring for older people with HIV.
- Given that the burden of aging-related diseases is significantly higher among people with HIV than in the general population, additional medical and social services may be required to effectively manage both HIV and comorbid conditions.

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 or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Introduction

Effective antiretroviral therapy (ART) has increased survival in people with HIV¹⁻⁴, resulting in an increasing number of older people with HIV. In the United States in 2022, the proportion of people newly diagnosed with HIV aged ≥55 years was 9%, according to the [Centers for Disease Control and Prevention \(CDC\)](#). Among people with HIV in 2022, 38% were aged ≥55 years, 13.2% were aged ≥65 years, and these proportions are expected to increase steadily.⁵ The difference in life expectancy between people with HIV and the general population has significantly narrowed since the use of effective ART and is now estimated to be 5 years or fewer for those with CD4 T lymphocyte (CD4) cell count >500/μL after initiating ART.³ However, the difference in mortality rates increases significantly with advancing age. While there has been a large reduction in AIDS-related mortality with effective ART, noninfectious comorbidities and complications, including atherosclerotic cardiovascular diseases (ASCVD) and non-AIDS malignancies, now account for a growing proportion of the causes of death among people with HIV.^{2,3,6,7}

The discussion in this section of the guidelines refers to individuals aged ≥50 years as older people with HIV. Many older people with HIV have had HIV for years or decades; therefore, accumulating disease risk associated with longstanding HIV disease itself and/or exposure to antiretroviral (ARV) medications (including prior use of older ART regimens with greater toxicity in some cases) should be considered. Specifically, HIV may affect the biology of aging, possibly resulting in earlier manifestations of morbidities generally associated with more advanced age. As a result, older people with HIV may suffer from aging-related illnesses earlier and at higher rates than those without HIV, and will require more non-ART medications than younger people, which may complicate HIV clinical care.^{8,9,10}

It is also important to consider distinct issues for people who are diagnosed with and/or acquire HIV at older ages. For example, older adults may have an increased risk of acquisition and transmission of HIV, in part as a consequence of reduced mucosal and immunologic defenses and changes in risk related-behaviors (e.g., decrease in condom use because of less concern about pregnancy or more high-risk sexual activity with increased use of erectile dysfunction drugs).^{11,12} In addition, HIV screening among older adults remains low because they are generally perceived to be at low risk of acquiring HIV. The sections below review important considerations for the diagnosis and treatment of HIV among older people, as well as the potential clinical implications for people now living to older ages with longstanding HIV disease.

HIV Screening and Diagnosis in the Older Person

Older people with HIV (aged ≥55 years) are significantly more likely to meet the case definition of AIDS at HIV diagnosis than people aged <55 years (threshold defined by CDC surveillance data).¹³ Also, older adults appear to have lower CD4 counts at seroconversion and steeper CD4 count decline over time¹⁴ and tend to present to care with significantly lower CD4 counts.^{15,16} Therefore, education, preventive measures (including pre-exposure prophylaxis or PrEP), and routine screening of asymptomatic older adults for HIV should be emphasized,¹⁷ as well as considering HIV infection in the medical evaluation of older adults.

Antiretroviral Therapy in the Older Person With HIV

Importance of Prompt Initiation of Antiretroviral Therapy After HIV Diagnosis

ART is recommended for all individuals with HIV (AI; see [Initiation of Antiretroviral Therapy](#)). Early treatment may be particularly important in older adults because of blunted immune recovery and

increased risk of serious non-AIDS events in this population.^{18,19} However, ART-associated CD4 cell recovery in older adults is generally slower and lower in magnitude than in younger people,²⁰⁻²³ suggesting that early diagnosis and treatment may result in better immunologic response and possibly improved clinical outcomes. In a modeling study based on data from an observational cohort, the beneficial effects of early ART were projected to be greatest in the oldest age group (people aged 45 to 65 years).²⁴ The benefits of early ART initiation were further demonstrated in an analysis of HIV cohorts from Europe and the Americas showing a lower all-cause and non-AIDS mortality with immediate ART initiation in people aged 50 to 70 years.²⁵ More definitive information was provided by the START study, which randomized ARV treatment-naïve participants with CD4 counts >500 cells/mm³ to either immediate ART or deferred ART until CD4 count dropped below 350 cells/mm³. The highest absolute risk reduction of serious AIDS and non-AIDS events associated with immediate ART was found in participants aged 50 years or older.²⁶ All older people with HIV should be informed that maintaining a plasma HIV RNA (viral load) at <200 copies/mL with ART improves overall health and prevents sexual transmission of HIV (see the [Treatment as Prevention](#) section).

Choice of Antiretroviral Regimens in the Older Person With HIV

The choice of ARV regimen for an older person with HIV should be informed by a comprehensive review of the person's other medical conditions and medications (including non-prescription drugs, supplements, and herbal treatments), and results from cumulative genotypic resistance testing. The What to Start section ([Table 7](#)) of these guidelines provides guidance on selecting an ARV regimen based on a person's characteristics and specific clinical conditions (e.g., kidney disease, elevated risk for cardiovascular disease [CVD], osteoporosis). In older people with HIV and reduced renal function, dosage adjustment of nucleoside reverse transcriptase inhibitors (NRTIs) may be necessary (see [Appendix B](#)). In addition, ARV regimen selection may be influenced by potential interactions between ARV medications and drugs used concomitantly to manage comorbidities (see the [Liverpool HIV Drug Interaction Checker](#)). Adults aged >50 years should be monitored for ART effectiveness and safety as similarly recommended for other populations with HIV (see [Table 3](#)); however, in older people, special attention should be paid to the greater potential for adverse effects of ART on renal, liver, cardiovascular, central nervous system, metabolic, and bone health (see [Table 20](#)). A meta-analysis confirmed that people with HIV have a 1.5-fold higher risk of fragility-related fracture and a fourfold higher risk of hip fracture. The increased risk is not completely explained by differences in bone mineral density (BMD) alone, indicating there may be differences due to bone microarchitecture or other HIV-related factors contributing to the marked fracture risk. ART regimens that contain tenofovir disoproxil fumarate (TDF),²⁷ boosted protease inhibitors (PIs), or both are associated with a significantly greater loss of BMD, with or without osteoporosis, compared to regimens containing other NRTIs and integrase strand transfer inhibitors (INSTIs).²⁸⁻³¹ Abacavir (ABC), NRTI-sparing regimens, and tenofovir alafenamide (TAF) may be considered as alternatives to the use of TDF in older individuals who may be at risk of nephrotoxicity, osteopenia, or osteoporosis; however, with ABC, the benefit should be balanced with its potential for increasing the risk of CVD (see [What to Start](#)). The long-acting (LA) injectable combination of cabotegravir (CAB) and rilpivirine (RPV) is also an option for ART among older people with HIV, with the same considerations as for all people with HIV (see [Optimizing Antiretroviral Therapy in the Setting of Viral Suppression](#)).

Antiretroviral Efficacy and Safety Considerations in the Older Person With HIV

The efficacy, pharmacokinetics (PK), adverse effects, and drug interaction potentials of ART in older adults have not been studied systematically. Data from clinical trials of second-generation INSTIs (dolutegravir [DTG] and bictegravir),³² two-drug regimens (DTG/lamivudine),³³ and LA CAB/RPV

have shown similar virologic efficacy, safety, and tolerability between participants >50 years of age and those aged 50 and younger.³⁴

Hepatic metabolism and renal elimination are the major routes of drug clearance, including the clearance of ARV drugs. Both liver and kidney functions decrease with age and may result in impaired drug elimination and increased drug exposure.³⁵ Most clinical trials have included only a small proportion of participants aged >50 years, and current ARV dosing recommendations are based on PK and pharmacodynamic data derived from participants with normal organ function. Because it is not known whether drug accumulation in older people may lead to greater incidence and severity of adverse effects than in younger people, therapy in older people requires close monitoring and heightened awareness of drug-related adverse effects, especially in those with hepatic or renal impairment.

Adherence Concerns

Suboptimal adherence to ART is the most common cause of treatment failure. Although most older people with HIV are able to achieve viral suppression with a single-tablet regimen, some people who have a long history of ART may have acquired drug resistance, thus requiring more complex multiple-pill regimens. Complex dosing requirements, high pill burden, polypharmacy, inability to access medications because of cost or availability, limited health literacy (including misunderstanding of instructions), depression, substance use, frailty, and neurocognitive impairment are among the key reasons for nonadherence and should be regularly assessed and managed (see [Adherence to the Continuum of Care](#)).³⁶⁻³⁸ Although some of the factors associated with nonadherence may be more prevalent in older people with HIV, older people have demonstrated better adherence to ART than younger people in some studies.³⁹⁻⁴¹ Severe menopausal symptoms are also associated with reduced adherence to ART, which increases the risk of drug resistance and adverse HIV-related health outcomes in menopausal women, highlighting the importance of managing these symptoms among women with HIV.^{42,43} To facilitate ART adherence, it may be useful to discontinue unnecessary non-HIV medications, simplify ART regimens, and apply evidence-based behavioral approaches including the use of adherence aids such as pillboxes or daily calendars, and support from family members and friends (see [Adherence to the Continuum of Care](#)). LA dosing options, such as LA CAB/RPV, may ease pill burden and adherence concerns for some older adults (see [Optimizing Antiretroviral Therapy](#)).

Optimizing Antiretroviral Therapy in Older People With HIV

Given the greater incidence of comorbidities, non-AIDS complications, and frailty among older people with HIV, switching one or more ARVs in an HIV regimen may be necessary to minimize toxicities, drug–drug interactions, or to reduce pill burden.³⁸ Expert guidance now recommends bone density monitoring in men aged ≥50 years and postmenopausal women and suggests switching from TDF or boosted PIs to other ARVs (such as TAF or INSTIs, respectively) in older people at high risk for fragility fractures.⁴⁴ Given the high prevalence and faster progression of chronic kidney disease (CKD) in aging people with HIV—likely from a combination of HIV, ART, and non-HIV risk factors—development of CKD must be closely monitored in an older person on ART.^{45,46} [Table 7](#) provides guidance for ARV drugs to use based on selected clinical scenarios, including comorbidities.

Polypharmacy in Older People With HIV

People with HIV and aging-associated comorbidities may require additional pharmacologic interventions that can complicate therapeutic management.⁸ In addition to taking medications to manage HIV and comorbid conditions, many older people with HIV are also taking medications to relieve discomfort (e.g., pain medications, sedatives) or to manage adverse effects of medications

(e.g., anti-emetics). Older individuals may also self-medicate with over-the-counter medicines or supplements.

Polypharmacy is more common in older people with HIV than similarly aged people in the general population.^{8,47,48} Among people with HIV aged ≥ 65 years, it is predicted that the prevalence of comorbidities and polypharmacy rose with increasing age and duration of HIV infection.^{49,50} In the Swiss HIV Cohort Study, the prevalence of polypharmacy and inappropriate prescribing in people aged ≥ 75 was 66% and 67%, respectively.⁵¹

In people aging with HIV, the effects of polypharmacy, including the use of drugs that affect neurocognitive function, can contribute to serious adverse outcomes, such as serious falls and fractures, delirium, hospitalization (including intensive care unit admissions), and death.⁵²⁻⁵⁷ Polypharmacy may also increase the likelihood of adverse consequences such as medication errors (by prescribers or prescription recipients), medication nonadherence, additive drug toxicities, and drug–drug interactions. Older people with HIV are probably at an even greater risk of polypharmacy-related adverse consequences than younger or similarly aged people without HIV. When evaluating any new clinical concern or laboratory abnormality in people with HIV, especially in older people, clinicians should always consider the possible role of adverse drug reactions from both ARV drugs and other concomitantly administered medications.

Drug–Drug Interaction Concerns

Interactions between ARV drugs and concomitant medications, supplements, and herbal treatments can occur and can be easily overlooked by prescribers.⁵⁸ Potential drug–drug interactions can occur between ARV and non-ARV medications, as well as between non-ARV medications.^{48,59} The available drug interaction information on ARV agents is derived primarily from PK studies performed in small numbers of relatively young participants with normal organ function who do not have HIV (see the [Liverpool HIV Drug Interaction Checker](#)). Data from these studies provide clinicians with a basis to assess whether a significant interaction may exist. However, the magnitude of an interaction may be greater in older than in younger people with HIV; therefore, it is important for clinicians to remain vigilant to assess for potential drug–drug interactions given the high prevalence of polypharmacy in older people with HIV. The risk of significant drug–drug interactions appears to be higher with PI-based or non-nucleoside reverse transcriptase inhibitors-based ART than with INSTI-based ART, although there are some important interactions with INSTIs that should be recognized and managed (including with polyvalent cations that are frequently taken as supplements).⁶⁰⁻⁶²

Hormonal therapies may be taken to alleviate symptoms of menopause or for other medical indications. Although data on drug–drug interactions between hormonal therapies and ART are limited, existing data suggest little to no impact of hormonal therapies on the efficacy of some ART.⁶³⁻⁶⁵

HIV and Immunologic Aging

Chronic HIV infection is associated with elevated soluble markers of immune activation and inflammation, as well as cellular phenotypes indicative of T cell and myeloid cell activation, even after HIV RNA levels are suppressed with ART.⁶⁶ The levels of inflammation and immune activation also increase with age and age-associated diseases.⁶⁷ In this context, the combined effects of HIV and advancing age on chronic inflammation have implications for risk from a broad spectrum of diseases.^{68,69}

A contributing factor to the early development of aging-related diseases among people with HIV has been posited to be the effect of HIV on immunologic aging. In addition to higher levels of immune activation, aging is associated with a higher frequency of cellular senescence as well as impaired

immune responses and surveillance.⁷⁰ HIV infection is associated with higher frequencies of T cell phenotypes characteristic of immunosenescence, as well as phenotypes reflective of highly differentiated or activated states.⁷¹⁻⁷⁴ Higher frequencies of senescent T cells are then associated with a greater risk for such comorbidities as CVD. In addition, the degree of CD4 T cell recovery after ART initiation is diminished among people ≥ 50 years old versus younger people with HIV.^{75,76} This impaired T cell recovery with advancing age may then have functional consequences, as people with HIV demonstrate reduced immune responses to vaccination, as well as impaired control of copathogens such as cytomegalovirus (CMV).⁷⁷⁻⁷⁹ The persistence of impaired or ineffective immune response toward copathogens then contributes to ongoing chronic immune activation (e.g., CMV-specific responses),⁷⁸ as well as the increased risk of both AIDS and non-AIDS-defining cancers that are driven by pro-oncogenic viruses (e.g., human papillomavirus [HPV]- and Epstein-Barr virus [EBV]-related cancers).⁸⁰

Immunologic aging in the context of HIV also entails chromosomal and genetic changes. Whether a consequence of untreated HIV viremia, direct toxicity from ARV drugs, or both, people with HIV have been shown to have shorter leukocyte chromosome telomere length, itself a marker of poor health and mortality.⁸¹⁻⁸³ DNA methylation is an epigenetic alteration that occurs at a predictable rate with advancing age, predicts lifespan, and increases in the setting of chronic HIV disease.⁸⁴⁻⁸⁷ Finally, a genetic mechanism that may more directly link immunologic aging to comorbid disease risk is clonal hematopoiesis, which entails an age-related expansion of somatic gene mutations among leukocytes (also referred to as age-related clonal hematopoiesis or ARCH). Clonal hematopoiesis is more common among people with HIV, and the degree of difference with people without HIV may be more pronounced with advancing age^{88,89} and in people with low nadir CD4 counts.^{90,91} Several of the leukocyte gene mutations characteristic of clonal hematopoiesis lead to dysregulation of inflammatory pathways, which is then associated with higher levels of inflammatory markers and ASCVD.⁹²⁻⁹⁴ In summary, clonal hematopoiesis is an example of HIV disease influencing age-related genetic somatic mutations that may contribute to ongoing systemic inflammation and associated disease risk among older people with HIV.

Disease-modifying pharmacologic interventions targeting immunologic aging are an area of active study within geroscience, but none are currently recommended specifically for older people with HIV with the exception of statin therapy as primary prevention of ASCVD risk (see Atherosclerotic Cardiovascular Disease in the Older Person With HIV below and [Statin Therapy in People With HIV](#)).

Morbidity, Mortality, and Non-AIDS Complications Among Older People With HIV

The clinical implications of greater immunologic aging and persistent inflammation can manifest in any organ system, diminishing the health span of older people with HIV. The frailty phenotype—defined clinically as a decrease in muscle mass, weight, physical strength, energy, and physical activity—represents an important example of an age-related syndrome that occurs with greater frequency and at earlier ages among people with HIV and is associated with a broad spectrum of adverse effects and disease risk. Specifically, frailty among people with HIV has been associated with incident CVD, diabetes mellitus, recurrent falls and fractures, lower quality of life, cognitive impairment, hospitalization, and mortality.⁹⁵⁻¹⁰⁴ The frailty phenotype remains incompletely characterized among older people with HIV and identifying effective treatment strategies is an important priority for clinical management. However, pharmacologic and non-pharmacologic interventions addressing frailty among people with HIV have been proposed and have the potential to significantly impact their quality of life and survival.^{105,106}

Although the life expectancy of people with HIV is approaching that of people without HIV, the incidence and prevalence of age-associated comorbidities in people with HIV are increasing.^{107,108}

The age-related comorbidity burden is significantly higher in people with HIV compared to the age-matched general population.⁸ These predictions differ by comorbidity and by demographic factors—including race, ethnicity, age, sex, and HIV transmission mode—displaying substantial disparities for some populations.

Data from insured adults suggest that people with HIV spend approximately 15 years more of their lifespan with one or more major comorbidities when compared to people without HIV; this difference is reduced but persists (at approximately 10 years) for people who initiate ART at a CD4 count of >500 cells/mm³.¹⁰⁹ A simulation modeling study projected that by 2030, 45% of people with HIV on ART would be living with two or more physical comorbidities and 64% with at least one mental health comorbidity.¹¹⁰

Non-AIDS–Defining Complications and Comorbidities in the Older Person With HIV

Non-AIDS comorbid conditions constitute an increasing proportion of morbidity and mortality among people with HIV.^{3,111} Heart disease and cancer are the leading causes of death in older people with HIV in the United States. Similarly, other non-AIDS events, such as cognitive impairment and liver disease, have also emerged as major causes of morbidity and mortality in people with HIV receiving effective ART. The prevalence of multimorbidity among people with HIV has increased in the past decade,¹¹² with hypertension and hypercholesterolemia being the most common comorbidities.¹¹³

Three groups of factors likely contribute to this burden of noncommunicable diseases among people with HIV: (1) an over-representation of traditional risk factors in this population, especially higher rates of smoking, diabetes, and dyslipidemia; (2) HIV-associated chronic inflammation and immune activation, which are not completely abated by suppressive ART; and (3) possible cardiometabolic complications of some ARV drugs.¹¹⁴⁻¹²²

As the life expectancy of people with HIV increases with ART, more women with HIV are experiencing menopause. Although menopause may occur earlier in women with HIV than in women in the general population,¹²³ early menopause may also be a consequence of smoking, depression, substance use disorder, and other psychosocial factors that are disproportionately present in women with HIV.¹²⁴ Also, HIV might compound menopause-related metabolic changes. For instance, HIV infection and menopausal stage were independent predictors of lower BMD and had an additive effect on lumbar spine and total hip BMD.¹²⁵

HIV-specific primary care guidelines have been developed and are available for clinicians caring for people with HIV, especially for older people with HIV.^{126,127} Additional specific guidelines have also been developed for the evaluation and management of the following specific comorbidities in people with HIV: bone health,⁴⁴ kidney disease,¹²⁸ and secondary prevention for ASCVD.¹²⁹ In addition, the following guidelines recently developed for the general population can be applied to older people with HIV: management of hypertension¹³⁰, hyperglycemia¹³¹, and hyperlipidemia.¹³² However, it is important to note that the recommendations in many of these guidelines have not all been validated in the context of HIV disease. For instance, cardiovascular risk prediction functions developed for the general population likely underestimate the risk in people with HIV.^{129,133} Findings of the Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) study have provided significant insight into the potential role of statins in the prevention of major adverse cardiovascular events in people with HIV. See [Statin Therapy in People With HIV](#) for recommendations from the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) on statin therapy as primary prevention of ASCVD among people with HIV. Further analyses of the REPRIEVE data will likely yield additional insights into their benefits (and potential risks) in people with HIV, as well as differences in the predictive value of risk equation scores in demographic subsets of study participants.

Atherosclerotic Cardiovascular Disease in the Older Person With HIV

When compared to people without HIV, data from several studies have shown that people with HIV have about a twofold higher risk of developing ASCVD, and their age at incident ASCVD diagnosis is about a decade younger.^{108,109,134,135} ASCVD risk prediction tools used for the general population tend to underestimate risk among people with HIV.^{133,136} Data also suggest that the relative increase in ASCVD risk is greater among women with HIV than among age-matched men with HIV when compared to people without HIV.^{137,138} Factors influencing ASCVD risk among people with HIV include both higher prevalence of traditional cardiometabolic risk factors and ongoing systemic inflammation associated with HIV,^{114,137} even in individuals with viral suppression while on ART. In addition, structural barriers and health disparities in screening and treatment of ASCVD risk factors likely also contribute to excess ASCVD risk among people with HIV in the United States.^{139,140}

The [2018 American Heart Association \(AHA\)/American College of Cardiology \(ACC\)/Multisociety Guidelines](#) provide recommendations on the use of statins as primary prevention based on risk stratification using estimates of 10-year ASCVD risk from the pooled cohort equations.^{141,142} In the general population, statin therapy is recommended for all people at high 10-year ASCVD risk (defined as $\geq 20\%$). Recent findings from the REPRIEVE trial have provided evidence for the use of statin therapy as primary prevention for people with HIV at low-to-intermediate ASCVD risk (i.e., $< 20\%$). REPRIEVE, a large randomized controlled trial among people with HIV aged 40 to 75 years who were receiving ART, showed that when compared to placebo, pitavastatin 4 mg daily was associated with a 35% reduction in major adverse cardiovascular events over a median follow-up duration of 5 years.¹⁴³ Results from REPRIEVE informed the Panel's recommendation on the use of at least moderate-intensity statin therapy as primary prevention among people with HIV of age 40 to 75 years, with a stronger recommendation for those with ASCVD risk score $\geq 5\%$ who will have a higher absolute benefit from statin therapy. See [Statin Therapy in People With HIV](#) for the Panel's full recommendations on statin therapy.

Neurocognitive Impairment in the Older Person With HIV

Cognitive impairment in people with HIV can manifest as difficulty with memory, attention, speed of information processing, and executive and motor functions. Studies that use neuropsychological testing to define categories of impaired cognition—termed HIV-associated neurocognitive disorder (HAND)—find that up to 30% of people with HIV on virally suppressive ART meet these research-based criteria¹⁴⁴, although these categories have not been validated for use in clinical practice. Research studies also demonstrate a steeper decline in performance on neuropsychological tests with advancing age in individuals with HIV compared to those without HIV over the same age range.¹⁴⁵ Although viral persistence and chronic brain inflammation can contribute, cognitive impairment is multifactorial in people with HIV. It is not solely HIV-associated, but also influenced by factors related to comorbidities, including polypharmacy, mood disorders, vascular disease, social isolation, stress, and independent neurodegenerative conditions.¹⁴⁶⁻¹⁵¹ Hormonal shifts that occur with aging may contribute to neurocognitive impairment, and these changes may manifest as unique differences in clinical manifestations by sex.¹⁵² Finally, the risk of neurodegenerative disease rises with increasing age independent of HIV, and diagnosis of Alzheimer's disease or other forms of progressive dementia in older people with HIV is now an important clinical concern.¹⁵³

Cognitive impairment carries potentially detrimental clinical consequences for aging people with HIV. In a prospective observational study, cognitive impairment was predictive of a lower likelihood of retention in care among older people.¹⁵⁴ Cognitive impairment is also associated with reduced adherence to therapy¹⁵⁵ and poorer health outcomes including increased mortality.¹⁵⁶ Given the importance of cognitive health, screening for neurocognitive impairment is important, though optimal primary care-based screening methods remain unclear. Initial screening with questions about

symptoms of memory loss, slowness, and poor attention can help to guide the need for referral to a specialist (e.g., neurologist, neuropsychologist, or geriatrician).^{157,158} Though such questions can be useful in identifying cognitive impairment, a positive response to these questions is not necessarily specific to impairment related to HIV.¹⁵⁹ Of note, people with substantial impairment may not have enough insight into their condition to answer the questions, and input from a partner or family member corroborating the impaired person's cognitive history may enhance the validity of the assessment. No brief cognitive screening test has been clearly shown to be sensitive or specific for cognitive impairment in HIV; the frequently used Mini-Mental State Exam does not typically capture executive function impairment, which is the main manifestation of subtle cognitive impairment in people with HIV.¹⁶⁰ The Montreal Cognitive Assessment may be more sensitive but is not specific. A lower threshold than the original cut-off score of 26 on the Montreal Cognitive Assessment is likely more optimal for HAND screening, as it lowers false positive rates and improves diagnostic accuracy.¹⁶¹ If a person has persistent concerns over time, has symptoms corroborated by an acquaintance, or has progressively worsening symptoms, referral to a neurologist for evaluation and management or to a neuropsychologist for formal neuropsychological testing may be warranted **(BIII)**.¹⁶⁰

Beyond screening and referral to specialists in neurology, neuropsychology, or geriatrics, an approach to cognitive impairment in aging people with HIV should involve assessing and correcting reversible and treatable factors that contribute to cognitive symptoms, as well as directly addressing modifiable risk factors. Reversible and treatable factors that may contribute to cognitive symptoms include hypothyroidism, low vitamin B12 levels, syphilis, sleep apnea, and cerebrovascular disease.¹⁶² Hearing impairment, diabetes, obesity, hypertension, depression, smoking, alcohol or substance use, and limited physical and social activity have been identified as significant modifiable risk factors for dementia in people without HIV.¹⁶³ Given the prevalence of many of these risk factors in older people with HIV, careful attention to their prevention or amelioration is an important component of primary care and cognitive care in aging people with HIV. Finally, the [U.S. Preventive Service Task Force](#) now recommends screening older adults (>65 years) for depression.¹⁶⁴

Mental Health Concerns in the Older Person With HIV

Mental health-related problems are a growing concern in aging people with HIV, though little is known about their prevalence and consequences in this population specifically. In a study that compared a cohort of individuals aged >60 years with HIV to a historical control group of healthy older people, a heightened risk of mood disorders including anxiety and depression was noted among people with HIV.¹⁶⁵ Social isolation combined with depression is particularly common among older adults with HIV and, in addition to its direct effects on morbidity and mortality, it may contribute to poor medication adherence and retention in care.^{166,167} The risk of suicide remains greater in people with HIV than in the general population, though increasing age might not further heighten the risk.¹⁶⁸ In one analysis of a multicenter observational study in France, suicide emerged as the second-highest cause of death among virologically suppressed people with HIV on ART.¹⁶⁹ Screening for depression and management of mental health issues are critical aspects of HIV primary care; guidelines for people with HIV, as well as for aging individuals without HIV, recommend behavioral approaches including individual psychotherapy, cognitive behavioral therapy, group therapy, and often pharmacological treatment.¹⁶⁹ When resources are available, integrated care models with routine screening by health care support staff, review by primary providers, and referral to on-site mental health specialists are likely to be the most effective approaches in vulnerable aging populations.

Health Care Utilization and Cost Sharing

The substantially increased burden of age-related comorbidities among people aging with HIV, including CVD, CKD, neurocognitive disease, and fractures, can lead to increased healthcare

utilization and higher costs.¹⁷⁰ Out-of-pocket health care expenses (e.g., copayments, deductibles), loss of employment, and other financial-related factors can cause temporary interruptions in treatment, including ART, which should be avoided whenever possible (see [Cost Considerations and Antiretroviral Therapy](#) for more information). The increased life expectancy and higher prevalence of chronic complications in aging populations with HIV can place greater demands upon HIV services¹⁷¹ and require a focused approach to prioritize modifiable health-related problems. Facilitating continued access to health care, including access to insurance-covered care and medications, is essential to minimize treatment interruptions; clinical outcomes can improve with additional multidisciplinary services to manage concomitant chronic disorders and assist with overcoming structural barriers to care. See the Ryan White HIV/AIDS Program's [Available Care & Services](#) page for additional information.

End-of-Life Issues, Including Palliative Care and Interruption of ART

As with all aging people, it is important to discuss living wills, advance directives, and long-term care planning. Palliative care and hospice should be discussed with a person-centered approach that incorporates the person's family situation and cultural, religious, and personal values, among other factors.^{172,173}

Few data exist on the use of ART in people with debilitating chronic, severe, or non-AIDS terminal conditions.^{174,175} Discontinuation of ART usually results in rebound viremia and a decline in CD4 count; an acute retroviral syndrome has also been reported after abrupt ART discontinuation. For these reasons, most clinicians would continue ART if there are no significant adverse reactions to the ARV drugs. In cases where ART negatively affects quality of life, the decision to continue therapy should be made together with the affected person and/or family members after a discussion of the risks and benefits of continuing or stopping ART.

References

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