Caring for Older Adults with the Human Immunodeficiency Virus

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Increasing proportions of older adults are living with the human immunodeficiency virus (HIV). It is estimated that more than 50% of individuals with HIV in the United States are aged 50 and older. Part of this group consists of individuals who have aged with chronic HIV infection, but a large proportion also results from new HIV diagnosis, with approximately 17% of new HIV diagnoses in 2013 occurring in individuals aged 50 and older. Although many of the recommendations on management of HIV infection are not age-specific, individuals with HIV aged 50 and older differ from their younger counterparts in many aspects, including immune response to antiretroviral therapy, multimorbidity, antiretroviral toxicities, and diagnostic considerations. This article outline these differences, offers a strategy on how to care for this unique population, and provides special considerations for problem-based management of individuals with HIV aged 50 and older. **J Am Geriatr Soc 2016.**

Key words: HIV; aging; multimorbidity

The prevalence of human immunodeficiency virus (HIV) infection in the older population is increasing for two reasons: persons with known HIV infection are living longer, and newly acquired infections continue to occur in older people. Currently, more than half of all people living with HIV in the United States are aged 50 and older,[1] and approximately 17% of new HIV diagnoses occur in people aged 50 and older.[2]

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DOI: 10.1111/jgs.14584

The most common mode of HIV transmission in adults aged 50 and older is through sexual contact.[3] In men, male-to-male sexual contact is the most common transmission risk,[2] whereas heterosexual contact is the most common in women. This may be due to a false sense of security among older adults, who view sexually transmitted infections (STIs) as a condition of the young and may forgo safe-sex practices based on this perception.[4] They may also forgo barrier contraceptives when unwanted pregnancy is no longer a concern. Even though sexual exposure is the most common mode of HIV transmission in individuals with HIV aged 50 and older, safer-sex behavioral campaigns have not been inclusive of older adults,[5] and the Centers for Disease Control and Prevention (CDC) recommends routine screening for HIV only up to the age of 64.[6] Injection drug use also remains a significant risk factor for transmission of HIV in older adults.[7]

ACCELERATED OR ACCENTUATED AGING IN OLDER ADULTS WITH HIV

For many years, there has been a debate surrounding how HIV infection affects the aging process: Acceleration (causing the development of certain age-associated comorbidities at an earlier age) or accentuation (increasing certain age-associated comorbidities at any given age). These age-associated comorbidities include conditions such as coronary artery disease, cerebrovascular disease, osteoporotic fractures, dementia, and frailty. Although traditional lifestyle risk factors such as smoking are more-prevalent in individuals with HIV, statistical adjustment for these traditional risk factors did not seem to affect the prevalence of some age-associated comorbidities, suggesting that HIV infection may have an independent effect on increasing multimorbidity.[8]

Current evidence seems inconclusive but suggests that the answer may depend on the types of clinical outcomes examined. For example, a few studies have suggested that the prevalence of frailty phenotype[9] and gait speed decline[10] may be accelerated in individuals with HIV. On the contrary, two other studies[11,12] showed that, although the HIV-infected population had higher excess and relative rates of age-associated comorbidities such as cardiovascular diseases and chronic kidney disease, they did not occur significantly earlier after diagnosis of HIV or the start of

0002-8614/16/$15.00

antiretroviral therapy (ART) than in uninfected controls, suggesting a model of accentuated rather than accelerated aging. It is likely that more research on the basic science and the person-centered clinical outcomes of aging with chronic HIV infection is needed before firm conclusions can be made.

PATHOLOGICAL DIFFERENCES BETWEEN HIV-INFECTED OLDER ADULTS AND THEIR YOUNGER COUNTERPARTS

Immune Response to ART

Despite successful viral suppression with ART, older adults have less-robust immunological recovery than their younger counterparts, with associated greater mortality.[13] Research has shown that HIV infection and the process of aging produce inflammation and immune activation, which is more pronounced in individuals with HIV than in uninfected counterparts of the same age despite effective ART. This process, sometimes called "inflammaging," includes an increase in the number of CD8 T-cells, a shift in the balance of T-regulatory responses, and a generalized chronic inflammatory state associated with various cytokines, including interleukin-6, tumor necrosis factor alpha, and transforming growth factor beta.[14] This excessive immune activation and inflammation has been shown to hinder CD4 T-cell immune reconstitution and promote disease progression in individuals with HIV. Consequently, early HIV diagnosis and treatment in older adults with HIV are of great importance.

Greater Multimorbidity

Older adults with HIV are at greater risk of multimorbidity,[8] defined as the development of multiple chronic conditions that do not simply coexist but together interact to worsen health outcomes. Older adults with HIV have higher burdens of cardiovascular, metabolic, pulmonary, renal, bone, and malignant diseases.[8] For example, individuals with HIV are at greater risk of strokes and acute myocardial infarction.[15] It is likely that factors related to lifestyle common in individuals with HIV and chronic HIV infection, such as ART toxicity and polypharmacy, microbial translocation, and changes in inflammation and immune activation, contribute to multimorbidity,[16] with longer duration of severe immunodeficiency (CD4 count <200 cells/μL) correlating with higher comorbidity burden.[8]

Multimorbidity has important ramifications for health outcomes. It is associated with self-reported poor health, declines in self-rated health status, and greater mortality (adjusted odds ratio = 11.87, 95% confidence interval = 5.72–24.62).[17] With increasing disease burden, individuals with HIV with multimorbidity are also at risk of fragmentation of or contradictions in care plans because of involvement of multiple clinicians in multiple settings.[18]

Antiretroviral Toxicities

Older adults with HIV may have toxicities related to ART caused by age-related changes in physiology and increased multimorbidity. Physiologically, older adults have age-related declines in renal and hepatic function, the primary metabolic pathways for drug detoxification. Moreover, many individuals have comorbidities that alter drug metabolism (e.g., hepatitis C coinfection causing liver dysfunction) or necessitate multiple medications that increase the likelihood of drug–drug and drug–disease interactions.

Current guidelines recommend that all individuals with HIV be treated with ART, regardless of CD4 count. The recommended ART regimens are listed in Table 1, with multiple combinations available in once-daily dosing tablet forms (Table 2).

Integrase strand transfer inhibitors (INSTIs) have among the fewest side effects and drug interactions of all the antiretroviral medications, and the current International Antiviral Society-USA guidelines recommend only INSTI as the anchor drug in ART.[19] Boosted protease inhibitors are less favored for the initial treatment of HIV. They may cause considerable drug–drug interactions because they are potent CYP3A inhibitors and may increase serum lipids and lipodystrophy.

Nucleoside reverse transcriptase inhibitors continue to be components of a complete antiretroviral regimen. The major toxicities include renal and bone (tenofovir disoproxil fumarate) and cardiovascular (abacavir). A list of the common side effects and drug interactions is shown in Table S1. A newer formulation of tenofovir, tenofovir alafenamide, has been shown to have much less renal and bone toxicity.[20] Because cardiovascular events have been linked to abacavir use, it should be avoided when possible.

DIAGNOSTIC CONSIDERATIONS

Prior research has found that healthcare professionals often underestimate the level of sexual activity of older adults and their risk of STI exposure.[4] Moreover, many symptoms of early HIV infection mimic those of aging and may be difficult for practitioners to differentiate. Symptoms of acute HIV infection such as headache, loss of energy, loss of appetite, influenza-like symptoms, and weight loss are common in older adults, and a myriad of conditions associated with old age, such as malignancy and frailty, can cause them.

With inaccurate perception of HIV exposure risk and symptom mimicry, underdiagnosis and late diagnosis of HIV infection are common in older adults.[4] Late diagnosis is associated with delayed treatment, impaired response to ART, greater morbidity and mortality, lost opportunity to prevent onward transmission, and greater healthcare costs.[21] As a result, it is essential that clinicians maintain a high suspicion and routinely screen older adults for HIV, regardless of risk perception. Although CDC guidelines recommend routine screening up to the age of 64,[6] the rationale or research evidence for this age cutoff was not included, and continued screening in older adults should be considered, because risk perception may be inaccurate in this population. Based on cost-effectiveness, providers may consider risk-based testing[22] or screening up to age 75 if individuals are sexually active, and the prevalence of HIV in the population is greater than 1%.[23] They should also routinely ask about risk factors related to HIV infection, including sexual behaviors and substance use. Future

Table 1. Current Antiretroviral Guidelines for Initiation of Treatment

Class	Department of Health and Human Services	International Antiviral Society-USA	European AIDS Clinical Society
Integrase strand transfer inhibitors	DTG/ABC/3TC DTG + TDF/FTC or TAF/FTC EVG/COBI/TDF/FTC EVG/COBI/TAF/TFC RAL + TDF/FTC or TAF/FTC	DTG/ABC/3TC DTG + TAF/FTC EVG/COBI/TAF/FTC RAL + TAF/FTC	DTG/ABC/3TC DTG + TDF/FTC EVG/COBI/TDF/FTC RAL + TDF/FTC
Boosted protease inhibitors	DRV + RTV + TDF/FTC or TAF/FTC		DRV + RTV + TDF/FTC
Nonnucleoside reverse transcriptase inhibitors			RPV/TDF/FTC

DTG = dolutegravir; ABC = abacavir; 3TC = lamivudine; TDF = tenofovir disoproxil fumarate; FTC = emtricitabine; TAF = tenofovir alafenamide; EVG = elvitegravir; COBI = cobicistat; RAL = raltegravir; DRV = darunavir; RTV = ritonavir; RPV = rilpivirine.

Table 2. Available Once-Daily Dosing Antiretroviral Regimens

Regimen	Composition
EFV/FTC/TDF	NNRTI + 2 NRTI
RPV/FTC/TDF	NNRTI + 2 NRTI
RPV/FTC/TAF	NNRTI + 2 NRTI
EVG/COBI/FTC/TDF	INSTI + booster + 2 NRTI
EVG/COBI/FTC/TAF	INSTI + booster + 2 NRTI
DTG/3TC/ABC	INSTI + 2 NRTI

EFV = efavirenz; FTC = emtricitabine; TDF = tenofovir disoproxil fumarate; RPV = rilpivirine; TAF = tenofovir alafenamide; EVG = elvitegravir; COBI = cobicistat; DTG = dolutegravir; 3TC = lamivudine; ABC = abacavir; NNRTI = nonnucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; INSTI = integrase strand transfer inhibitor.

research should explore diagnostic yields of testing algorithms developed specifically for individuals with HIV aged 65 and older, because evidence in this age group is limited, and transmission patterns may differ from those in younger individuals with HIV.

MANAGEMENT STRATEGY FOR THE CARE OF OLDER ADULTS WITH HIV

Each older adult with HIV is a unique and complex individual. They cannot be described fully using one-dimensional classifications, such as chronological age or single disease entities. Aging occurs at different rates in different individuals and within the same individual in different organs, resulting in different aging phenotypes that chronological age alone cannot predict. In addition, viewing individuals with HIV from a single disease perspective ignores the importance of multimorbidity and the often multifactorial nature of their diseases. Most importantly, different individuals have different goals and preferences. Consequently, applying disease-centric guidelines uniformly to every individual without taking into account aging phenotypes, multimorbidity, or individual preference ignores the unique care needs of each individual and may increase treatment burden without improvements in mortality or quality of life.

Understanding that not all 50-year-old individuals with HIV should be approached the same way, clinicians may use the Veterans Aging Cohort Study (VACS) Index[24] to distinguish between those who are aging well and those who may appear phenotypically older than their chronological age. The VACS Index creates a score consisting of preassigned points for age, routinely monitored indicators of HIV disease, and general indicators of organ system injury. It has been shown to assist clinician assessment of severity of illness[25] and predict cause-specific and all-cause mortality.[24] Based on prognosis predicted using the VACS index, clinicians can elicit individual preferences, identify diseases and risk factors that affect these goals, calculate the likely effects and lag time to benefit of various disease-centric guidelines on these goals, and use this information to prioritize interventions and guide shared decision-making with individuals and caregivers.[18] Indices of frailty or measures of physical function may also be used, because they have been shown to correlate with advanced HIV disease[26] and mortality.[27]

SPECIAL CONSIDERATIONS FOR PROBLEM-BASED MANAGEMENT OF INDIVIDUALS WITH HIV AGED 50 AND OLDER

This section outlines problem-based practice guidelines specific to individuals with HIV aged 50 and older that should be considered in addition to usual HIV care in younger individuals, although because research on appropriate disease management specific to individuals with HIV aged 50 and older is limited, much of current problem-based clinical guidelines for this population extrapolate data from guidelines for uninfected adults of the same age. It is likely that, as more individuals with HIV age, and older adults with HIV become better represented in research trials, future problem-based guidelines for this population will need to be adjusted.

Immunizations

Live attenuated varicella vaccination, which has been approved in adults aged 50 and older without HIV can be given to adults with HIV without evidence of immunity with CD4 counts of 200 cells/μL or greater,[28] because no vaccine-strain varicella zoster virus infection has been documented in individuals with HIV with CD4 counts above this threshold.[29]

Although the CDC has no recommendation on zoster vaccine in individuals with HIV aged 60 and older with a CD4 count of 200 cells/μL or greater, it may be reasonable to vaccinate this group of individuals according to the Infectious Disease Society of America (IDSA) recommendation.[30]

A recent study showed superior immunogenicity in adults aged 65 and older who received high-dose inactivated influenza vaccine (IIV) than in those who received standard dosing. Similar results were shown in a small clinical trial of individuals with HIV aged 18 and older.[31] The CDC recommends high-dose IIV as an equivalent option to standard-dose IIV in adults aged 65 and older regardless of HIV status.[28] Live influenza vaccine should not be used in individuals with HIV.

Individuals with HIV aged 19 and older should receive 13-valent pneumococcal conjugate vaccine (PCV13) and 23-valent pneumococcal polysaccharide vaccine (PPSV23), but the interval between the two types of vaccine and the number of doses needed differ in individuals with HIV aged 65 and older. In pneumococcal vaccine–naïve persons, PCV13 should be given first, followed by PPSV23 at least 8 weeks after. In persons who previously received PPSV23 at age 65 and older, only PCV13 should be given, at least 1 year after the prior dose of PPSV23. In persons who previously received PPSV23 before age 65, PCV13 should be given at least 1 year after the prior dose of PPSV23, followed by a second dose of PPSV23 at least 5 years after the prior dose of PPSV23[32] (Table 3).

Table 3. Recommended Immunizations for Individuals with the Human Immunodeficiency Virus Aged 50 and Older

Vaccine	CD4 Count <200 Cells/μL	CD4 Count ≥200 Cells/μL	Comments
IIV	Yes	Yes	According to Centers for Disease Control and Prevention, high-dose equivalent to standard-dose IIV
Tdap and Td	Yes	Yes	Tdap once, then Td every 10 years
Zoster	No	No recommendation	Probably safe if CD4 > 200
Measles, mumps, rubella	No	If indicated	1–2 doses if indicated
Varicella	No	If indicated	2 doses if no evidence of immunity
PCV13 and PPSV23	Yes	Yes	Give PCV13 first, then PPSV23 8 weeks later
Hepatitis A	If indicated	If indicated	2 doses
Hepatitis B	Yes	Yes	3 doses

Adapted from Kim DK, Bridges CB, Harriman KH. Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older: United States, 2016. Ann Intern Med 2016;164:184–194.

IIV = inactivated influenza vaccine; Td = tetanus-diphtheria; Tdap = tetanus-diphtheria-pertussis; PCV = pneumococcal conjugate vaccine; PPSV23 = pneumococcal polysaccharide vaccine.

Age-Related Sexual Changes

Older adults with HIV may experience menopause and hypogonadism, resulting in age-related sexual changes that affect sexual function and behaviors. For example, menopause may result in vaginal dryness, and freedom from unwanted pregnancy and the need for contraception may lead to lack of barrier protection and greater risk of STIs. Consequently, providers should routinely ask about sexual history and symptoms and provide safe-sex counseling for older adults and their partners at every visit, because risk perception can be misleading in this population.

Although it is unclear whether age of onset of menopause differs between individuals with HIV and their uninfected counterparts, it is suspected that the transition through menopause for individuals with HIV differs.[33] First, HIV-related effects such as chronic inflammation may lead to ovarian dysfunction, resulting in altered natural history and symptoms of menopause in individuals with HIV. Moreover, the effect of estrogen depletion may compound the already-greater risk of dyslipidemia, cardiovascular disease, and osteoporosis in this population. Last, symptoms of menopause may be difficult to distinguish from those of other chronic illnesses in older adults with HIV, with research showing that providers and individuals themselves underrecognize menopausal symptoms.[33] Treatment options according to the IDSA guideline[30] are similar to uninfected individuals, with hormone replacement therapy recommended in women with severe menopausal symptoms but only for a limited period of time and at the lowest effective dose.

Hypogonadism is common and occurs prematurely in men with HIV.[34] Diagnosis is challenging because symptoms of hypogonadism may overlap with those of other chronic illnesses commonly found in older adults with HIV. According to the IDSA guidelines,[30] morning serum testosterone level may be assessed in older men with HIV with low libido, erectile dysfunction, low bone mass or low-trauma fractures, hot flashes, or sweats. Low levels should be confirmed with repeat testing. Free testosterone measurement should be considered because of changes in sex hormone–binding globulin with aging. Treatment options are similar to those in uninfected individuals.

Hypertension

Goal blood pressure for elderly adults without HIV is controversial and presents a challenge for clinicians, with even less evidence to guide management in the population with HIV.

The Systolic Blood Pressure Intervention Trial (SPRINT) evaluated a subgroup of ambulatory uninfected adults aged 75 and older and demonstrated that a systolic blood pressure (SBP) target of less than 120 mmHg resulted in lower rates of cardiovascular events and death from any cause than a target of less than 140 mmHg.[35] There was no substantial difference in major adverse events, with only slightly higher rates of hypotension, syncope, and acute changes in renal function.[36] Nevertheless, the study was limited in multiple areas. First, it excluded individuals with diabetes mellitus, heart failure, prior stroke, and postural decrease in blood pressure.

Homebound and institutionalized individuals were also excluded. With greater risk of frailty and multimorbidity in older adults with HIV, it is unclear whether or how these results should be applied, although with greater risk of metabolic diseases, stroke, and acute myocardial infarction in individuals with HIV with high blood pressure,[15] it could be argued that strict blood pressure control is especially warranted in older adults with HIV. Second, mean SBP achieved in the target group was 123 mmHg, suggesting that cardiovascular benefits can perhaps still be achieved at goals greater than 120 mmHg.[36]

Current hypertension guidelines for individuals without HIV have not taken SPRINT results into account, and there are no specific hypertension goals for individuals with HIV. The Eighth Joint National Committee recommends a blood pressure goal of less than 150/90 mmHg in adults aged 60 and older with hypertension and less than 140/90 mmHg for all adults with hypertension and diabetes mellitus or nondiabetic chronic kidney disease.[37] Based on the recent SPRINT results, providers may consider a stepwise approach, beginning with a SBP goal of less than 140 mmHg. If this is achieved without adverse effects, a lower SBP goal of less than 130 mmHg may be considered.[36]

Diabetes

Although primary care guidelines for the management of persons infected with HIV from the IDSA did not include age-specific glycemic goals for individuals with HIV, the American Academy of HIV Medicine and the American Geriatrics Society recommend a target glycosylated hemoglobin (HbA1c) of 8% for older adults with HIV with frailty, with less than a 5-year life expectancy, at high risk of hypoglycemia, or at high risk of polypharmacy.[38] This recommendation mirrors the guideline on standards of medical care in diabetes mellitus from the American Diabetes Association.[39] HbA1c may underestimate average blood glucose because of high red blood cell turnover in individuals with HIV, and new-onset or worsening diabetes mellitus may result from interactions between corticosteroid use (including nasal sprays or inhalers) and certain ART such as protease inhibitors boosted with ritonavir or cobicistat.

Osteoporosis

Certain lifestyle and HIV-related factors put individuals with HIV at higher risk of osteoporosis, including smoking, alcohol abuse, glucocorticoid therapy, low physical activity, immune dysfunction, persistent inflammation, and side effects of antiretroviral medications. Viral suppression should be achieved with ART, and modifiable risk factors should be addressed. For example, a switch from tenofovir disoproxil fumarate to tenofovir alafenamide[20] or supplementation with vitamin D plus calcium[40] may help reduce bone loss in individuals with HIV.

The IDSA recommends baseline bone densitometry (DXA) screening for osteoporosis in postmenopausal women and in men aged 50 and older with HIV.[30] Bisphosphonates may be considered as first-line treatment, with a follow-up DXA 1 year after to monitor response to therapy.

Malignancy

As with the general population, age is a risk factor for multiple types of malignancies in individuals with HIV. In addition to cancer screening unrelated to acquired immunodeficiency syndrome (AIDS) such as mammography annually in women with HIV aged 50 and older and colorectal cancer screening in individuals with HIV aged 50 and older with average risk and greater than 10-year life expectancy, older adults with HIV should continue to be screened for AIDS-related malignancies. According to the IDSA, cervical Papanicolaou tests should be performed in women with HIV at initiation of care, at 6 months, and then annually thereafter if results are normal. Men who have sex with men, women with a history of receptive anal intercourse or abnormal cervical Papanicolaou test results, and all individuals with HIV with genital warts should receive anal Papanicolaou tests annually. Although individuals with HIV are at greater risk of lung cancer, the current IDSA guidelines do not address this, and providers may adopt a screening strategy similar to that in the general population. Future research on cancer screening in individuals with should avoid recommendations focusing on age cutoff and build risk and cost-effectiveness models that incorporate aging phenotype, life expectancy, and care preferences in a whole-person approach.

Neurocognitive Disorders

Cognitive impairment in individuals with HIV is associated with older age and lifestyle and HIV-related risk factors. Individuals with HIV are susceptible to HIV-associated neurocognitive disorders (HAND) and other causes of cognitive impairment common individuals without HIV, such as Alzheimer's and vascular dementia. The absence of higher cortical dysfunction such as aphasia, agnosia, or apraxia helps distinguish HAND from Alzheimer's dementia, and background hypertension or episodes of lacunar strokes may indicate vascular dementia instead of HAND.

Neither the CDC nor the IDSA offers guidelines on HIV-associated neurocognitive impairment, although the European AIDS Clinical Society guideline provides an algorithm for its diagnosis and management.[41] For symptomatic persons without obvious confounding conditions, depression should be evaluated and treated. If problems persist, brain magnetic resonance imaging and cerebrospinal fluid (CSF) examination should be performed to exclude other causes of cognitive impairment. Individuals diagnosed with HAND should start ART if they are not already on a regimen or have ART optimized if CSF viral escape is detected.

Age is also a risk factor for peripheral neuropathy. As a result, pain should be considered the fifth vital sign and should be assessed at every visit. Trials of symptomatic and disease-modifying treatments for HIV-associated distal symmetric polyneuropathy have had limited success, and the Food and Drug Administration has not approved any treatments at this time.

Polypharmacy

Older adults with HIV are at greater risk of polypharmacy,[42] defined as taking medications that are inappropriate for the individual's medical condition, using medications that cause adverse drug events, or using incorrect dosing for the condition. Polypharmacy in older adults with HIV is more prevalent because of greater multimorbidity, multiple HIV-related factors affecting cytochrome P450 isoenzymes and renal function, and underrepresentation of older adults with HIV in pharmacokinetic studies. Polypharmacy in individuals with HIV may contribute to medication fatigue, nonadherence to ART, falls, and poor medication quality prescribing.[42]

To avoid polypharmacy, a medication review is recommended at every visit and a medication reconciliation annually.[38] Routine use of an up-to-date electronic resource such as Epocrates, Lexi-Comp, and www.hiv-druginteractions.org will help clinicians monitor the array of drug–drug interactions and needed dose modifications based on renal or hepatic function,[43] although changes to ART can be complex, and only providers with adequate expertise should make them. Although the Chronic Kidney Disease Epidemiology Collaboration glomerular filtration rate estimate is the most accurate for use in individuals with HIV on stable ART,[44] the Cockcroft-Gault calculated creatinine clearance remains the standard of care for medication dosing. Last, individuals should be encouraged to use a single pharmacy, preferably specializing in HIV with an integrated computer network.

Alcohol and Substance Abuse

Substance use disorders are more common in individuals with HIV, in younger and older populations alike.[45] Consequently, providers should routinely screen for alcohol and substance use in older adults with HIV,[30] because risk perception is often inaccurate in this population. Although specific research on the effects of substance use in elderly adults with HIV is limited, evidence in younger cohorts suggests deleterious outcomes including poor medication adherence, end-organ damage, risky sexual activity, psychiatric comorbidities, adverse social consequences such as criminal activity or homelessness, malignancy, cognitive impairment with resulting injuries such as falls and fractures, and overall mortality.

Special considerations may be given to the increasing legalization of marijuana in the United States, because it is likely that this will present challenges to HIV providers. Beneficial effects of marijuana in individuals with HIV may include better mood, less anxiety, improved appetite, less nausea, and less pain,[46] although smoking marijuana may cause cough, phlegm production, wheezing, and airflow obstruction.[47] Of particular concern in older adults with HIV, smoking marijuana may also lead to greater risk of lung cancer[48] and impaired cognition.[49] Researchers and policy-makers must therefore provide clear evidence and guidelines, especially in elderly individuals with HIV, before legalization causes unintended adverse effects in this vulnerable population.

Despite limited evidence of effective interventions for substance abuse disorders in elderly adults with HIV, providers may explore brief, targeted counseling combined with pharmacotherapy, because most medication options are deemed safe in the setting of ART.[45]

Advance Care Planning

With greater risk of neurocognitive impairment and debility from multimorbidity, advance care planning is essential in older adults with HIV. Without appropriate documentation of a surrogate decision-maker for health care and finances, decisions regarding emergence or end-of-life care may be legally deferred to estranged family members who are unaware of the individual's preferences or HIV status.[50] Although there are no specific guidelines for individuals with HIV, the U.S. Department of Health and Human Services recommends advance care planning in all individuals with chronic life-limiting illness or anyone aged 55 and older regardless of health status.

CONCLUSION

An increasing proportion of older adults is living with HIV, and these adults differ from their younger counterparts in many ways, including risk of late or underdiagnosis, impaired immunological recovery, differing antiretroviral toxicities, and greater multimorbidity. Each older adult with HIV is a unique and complex individual, and disease-centric guidelines should not be applied the same way in every individual. The geriatrics approach of caring for the whole person should guide management of diseases in older adults with HIV, incorporating aging phenotypes, interactions with multimorbidity, and individual preferences into person-centered care plans. The VACS Index may be used to identify aging phenotypes and can provide useful prognostic information to help providers prioritize interventions and guide shared decision-making with individuals and caregivers.

ACKNOWLEDGMENTS

Conflict of Interest: Jonathan Appelbaum serves as a continuing medical education speaker for Clinical Care Options and Healthmatters CME and serves on the advisory board for Gilead, Janssen, and Merck.

Author Contributions: All authors: data acquisition, preparation of manuscript.

Sponsor's Role: This article received no funding, and there are no sponsor's roles to report.

REFERENCES

1. Brooks JT, Buchacz K, Gebo KA et al. HIV infection and older Americans: The public health perspective. Am J Public Health 2012;102:1516–1526.
2. Centers for Disease Control and Prevention. HIV Surveillance Report, 2014; vol. 26 [on-line]. Available at http://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-us.pdf Accessed July 20, 2016.
3. Centers for Disease Control and Prevention. Diagnoses of HIV Infection Among Adults Aged 50 Years and Older in the United States and Dependent Areas, 2007–2010. HIV Surveillance Supplemental Report 2013;18 (No. 3) [on-line]. Available at http://www.cdc.gov/hiv/topics/surveillance/resources/reports/#supplemental Accessed October 18, 2015.
4. Pilowsky DJ, Wu LT. Sexual risk behaviors and HIV risk among Americans aged 50 years or older: A review. Subst Abuse Rehabil 2015;6:51–60.

5. Kirkman L, Kenny A, Fox C. Evidence of absence: Midlife and older adult sexual health policy in Australia. Sex Res Social Policy 2013;10:135–148.
6. Centers for Disease Control and Prevention. Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings [on-line]. Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm Accessed October 18, 2015.
7. Skalski LM, Sikkema KJ, Heckman TG. Coping styles and illicit drug use in older adults with HIV/AIDS. Psychol Addict Behav 2013;27:1050–1058.
8. Schouten J, Wit FW, Stolte IG et al. Cross-sectional comparison of the prevalence of age-associated comorbidities and their risk factors between HIV-infected and uninfected individuals: The AGEhIV cohort study. Clin Infect Dis 2014;59:1787–1797.
9. Desqulbet L, Jacobson L, Fried L et al. HIV-1 infection is associated with an earlier occurrence of a phenotype related to frailty. J Gerontol A Biol Sci Med Sci 2007;62A:1279–1286.
10. Schrack JA, Althoff KN, Jacobson LP et al. Accelerated longitudinal gait speed decline in HIV-infected older men. J Acquir Immune Defic Syndr 2015;70:370–376.
11. Althoff KN, McGinnis KA, Wyatt CM et al. Comparison of risk and age at diagnosis of myocardial infarction, end-stage renal disease, and non-AIDS-defining cancer in HIV-infected versus uninfected adults. Clin Infect Dis 2015;60:627–638.
12. Rasmussen LD, May MT, Kronborg G et al. Time trends for risk of severe age-related diseases in individuals with and without HIV infection in Denmark: A nationwide population-based cohort study. Lancet HIV 2015;2:e288–e298.
13. Semeere AS, Lwanga I, Sempa J et al. Mortality and immunological recovery among older adults on antiretroviral therapy at a large urban HIV clinic in Kampala, Uganda. J Acquir Immune Defic Syndr 2014;67:382–389.
14. Hunt P, Cao HL, Muzoora C et al. Impact of $CD8^+$ T cell activation on $CD4^+$ T cell recovery and mortality in HIV-infected Ugandans initiating antiretroviral therapy. AIDS 2011;25:2123–2131.
15. Armah K, Chang CC, Baker JV et al. Prehypertension, hypertension, and the risk of acute myocardial infarction in HIV-infected and -uninfected veterans. Clin Infect Dis 2014;58:121–129.
16. Deeks SG, Tracy R, Douek DC. Systemic effects of inflammation on health during chronic HIV infection. Immunity 2013;39:633–645.
17. Koroukian SM, Warner DF, Owusu C et al. Multimorbidity redefined: Prospective health outcomes and the cumulative effect of co-occurring conditions. Prev Chronic Dis 2015;12:E55.
18. Tinetti ME, Fried TR, Boyd CM. Designing health care for the most common chronic condition—multimorbidity. JAMA 2012;307:2493–2494.
19. Gunthard HF, Saag MS, Benson CA et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults. JAMA 2016;316:191–210.
20. Sax PE, Wohl D, Yin MT et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate, coformulated with elvitegravir, cobicistat, and emtricitabine, for initial treatment of HIV-1 infection: Two randomised, double-blind, phase 3, non-inferiority trials. Lancet 2015;385:2606–2615.
21. British HIV Association. UK National Guidelines for HIV Testing [on-line]. Available at http://www.bhiva.org/guidelines.aspx Accessed September 15, 2016.
22. Goetz M, Hoang T, Kan V et al. Rates and predictors of newly diagnosed HIV infection among veterans receiving routine once-per-lifetime HIV testing in the Veterans Health Administration. J Acquir Immune Defic Syndr 2015;69:544–550.
23. Qaseem A, Snow V, Shekelle P et al. Screening for HIV in health care settings: A guidance statement from the American College of Physicians and HIV Medicine Association. Ann Intern Med 2009;150:125–131.
24. Justice AC, Modur S, Tate JP et al. Predictive accuracy of the Veterans Aging Cohort Study Index for mortality with HIV infection: A North American cross cohort analysis. J Acquir Immune Defic Syndr 2013;62:149–163.
25. Justice AC, Tate JP, Brown ST et al. Can the Veterans Aging Cohort Study Index improve clinical judgment for both HIV infected and uninfected veterans? J Gen Intern Med 2013;28:S39–S39.
26. Oursler K, Goulet J, Crystal S et al. Association of age and comorbidity with physical function in HIV-infected and uninfected patients: Results from the Veterans Aging Cohort Study. AIDS Patient Care STDs 2011;26:13–20.
27. Piggott DA, Muzaale A, Mehta SH et al. Frailty, HIV infection, and mortality in an aging cohort of injection drug users. PLoS ONE 2013;8:e54910.
28. Centers for Disease Control and Prevention. Recommended adult immunization schedule: United States, 2010. Ann Intern Med 2010;152:36–39.
29. Shafran SD. Live attenuated herpes zoster vaccine for HIV-infected adults. HIV Med 2016;17:305–310.
30. Aberg JA, Gallant JE, Ghanem KG et al. Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV medicine association of the Infectious Diseases Society of America. Clin Infect Dis 2014;58:e1.
31. McKittrick N, Frank I, Jacobson JM et al. Improved immunogenicity with high-dose seasonal influenza vaccine in HIV-infected persons: A single-center, parallel, randomized trial. Ann Intern Med 2013;158:19–26.
32. Centers for Disease Control and Prevention. Intervals between PCV13 and PPSV23 vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP) [on-line]. Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6434a4.htm Accessed July 21, 2016.
33. Tariq S, Anderson J, Burns F et al. The menopause transition in women living with HIV: Current evidence and future avenues of research. J Virus Erad 2016;2:114–116.
34. Rochira V, Guaraldi G. Hypogonadism in the HIV-infected man. Endocrinol Metab Clin North Am 2014;43:709–730.
35. Williamson JD, Supiano MA, Applegate WB et al. Intensive vs standard blood pressure control and cardiovascular disease outcomes in adults aged ≥75 years: A randomized clinical trial. JAMA 2016;315:2673–2682.
36. Chobanian A. SPRINT results in older patients: How low to go? JAMA 2016;315:2669–2670.
37. James PA, Oparil S, Carter BL et al. 2014 Evidence-based guideline for the management of high blood pressure in adults: Report from the panel members appointed to the Eighth Joint National Committee (JNC8). JAMA 2014;311:507–520.
38. American Academy of HIV Medicine. Recommended Treatment Strategies for Clinicians Managing Older Patients with HIV [on-line]. Available at http://aahivm.org/Upload_Module/upload/HIV%20and%20Aging/Aging%20report%20working%20document%20FINAL%2012.1.pdf Accessed October 18, 2015.
39. American Diabetes Association. Standards of medical care in diabetes—2015 abridged for primary care providers. Clin Diabetes 2015;33:97–111.
40. Overton ET, Chan ES, Btown TT et al. High-dose vitamin D and calcium attenuates bone loss with antiretroviral therapy initiation: A prospective, randomized placebo-controlled trial for bone health in HIV-infected individuals. Ann Intern Med 2015;162:815–824.
41. European AIDS Clinical Society. Guidelines Version 7.1 [on-line]. Available at http://www.eacsociety.org/files/guidelines-7.1-english.pdf Accessed October 18, 2015.
42. Edelman E, Gordon K, Glover J et al. The next therapeutic challenge in HIV: Polypharmacy. Drugs Aging 2013;30:613–628.
43. Pau A, Boyd S. Recognition and management of significant drug interactions in HIV patients—challenges in using available data to guide therapy. Clin Pharmacol Ther 2010;88:712–719.
44. Vrouenraets SM, Fux CA, Wit FW et al. A comparison of measured and estimated glomerular filtration rate in successfully treated HIV-patients with preserved renal function. Clin Nephrol 2012;77:311–320.
45. Edelman EJ, Tetrault JM, Fiellin DA. Substance use in older HIV-infected patients. Curr Opin HIV AIDS 2014;9:317–324.
46. Prentiss D, Power R, Balmas G et al. Patterns of marijuana use among patients with HIV/AIDS followed in a public health care setting. J Acquir Immune Defic Syndr 2004;35:38–45.
47. Pletcher MJ, Vittinghoff E, Kalhan R et al. Association between marijuana exposure and pulmonary function over 20 years. JAMA 2012;307:173–181.
48. Callaghan RC, Alleback PAS. Marijuana use and risk of lung cancer: A 40-year cohort study. Cancer Causes Control 2012;24:1811–1820.
49. Meier MH, Caspi A, Ambler A et al. Persistent cannabis users show neuropsychological decline from childhood to midlife. Proc Natl Acad Sci USA 2012;109:E2657–E2664.
50. Sangarlangkarn A, Merlin JS, Tucker RO et al. Advance care planning and HIV infection in the era of antiretroviral therapy: A review. Top Antivir Med 2016;23:174–180.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1. Common Antiretroviral Medications with Associated Toxicities and Drug Interactions.

Table S2. Routine Healthcare Maintenance in Individuals with the Human Immunodeficiency Virus Aged 50 and Older.