Curr Treat Options Infect Dis (2019) 11:388–400
DOI 10.1007/s40506-019-00204-6

HIV Medicine (C Yoon, Section Editor)

Special Topics in the Care of Older People with HIV

Tessa del Carmen, MD[1]
Carrie Johnston, MD[2]
Chelsie Burchett, MA[1]
Eugenia L. Siegler, MD[1,*]

Address
[*,1]Division of Geriatrics and Palliative Medicine, Weill Cornell Medicine, New York, NY, USA
Email: cmd9008@med.cornell.edu
[2]Division of Infectious Diseases, Weill Cornell Medicine/New York Presbyterian Hospital, New York, NY, USA

Published online: 8 November 2019

This article is part of the Topical Collection on *HIV Medicine*

Keywords Aging · Geriatric syndromes · Women's health · Comprehensive geriatric assessment · Stigma · HIV

Abstract

Purpose of review Antiretroviral therapy has enabled many people with HIV to live long lives with their infection, but the literature suggests that long-term survivors are developing comorbidities and aging-related syndromes at earlier ages than their non-infected counterparts. In addition, there is evidence of sex-based differences in comorbidity risk.
Recent findings How to best care for people aging with HIV is not known, but the tools of comprehensive geriatric assessment can identify people at risk for decline. Newer antiretroviral therapies offer promise of fewer side effects and drug interactions. We will also discuss special needs of women aging with HIV.
Summary People with HIV and their providers are often unprepared to confront issues of aging, and each clinical program must develop methods to assess older patients and manage age-related complications and syndromes.

Introduction

Demographics

Effective antiretroviral therapy has enabled people to live with HIV; as a result, the population with HIV is aging, and the proportion people with HIV who are older is increasing and will continue to do so [1]. In the USA, the Centers for Disease Control and Prevention reported that at the end of 2016, 48% of people living with HIV (PLWH) in the USA were 50 years of age and

older [2]. In New York City, almost one-fourth of PLWH in 2017 were 60 and older [3]. That older people with HIV (OPH) are able to live long, productive lives is a remarkable achievement, but people with HIV likely experience advanced aging [4], even at the cellular level. Compared to their HIV-negative counterparts, OPH have greater levels of multimorbidity [5, 6], polypharmacy [7], aging-related syndromes like frailty [8, 9], and behavioral health concerns like depression [10]; frailty in particular has been associated with poorer outcomes [11].

Although people 60 and older account for approximately 5% of new infections with HIV each year in the USA [2], the majority of OPH are long-term survivors; it may be difficult for providers who have cared for their patients for decades to see age-related changes in a patient who has been aging along with them. Many HIV providers may lack geriatric training and may not know how to care for their patients as they develop age-related complications.

Each clinical program must determine how to adapt care to meet the needs of OPH in their practice. This review begins a geriatric perspective of the older patient with HIV and then describes approaches to select issues germane to this population. It is not focused on specific comorbidities; it aims to supplement existing guidelines.

Approach to the older person with HIV

Recognizing and addressing the added stigma of aging

According to the Centers for Disease Control and Prevention, HIV disproportionately affects racial and ethnic minorities [12]. OPH can experience intersectional stigma, that is, multiple simultaneous characteristics that are devalued [13], as they face the new stigma associated with age [14]. How OPH perceive stigma of aging depends upon sex, ethnicity, HIV risk factors, and social supports [15]. Similarly, the effect of stigma on health also depends on a multiplicity of factors [16]. For example, a recent study from the WHIS cohort suggested that internalized stigma contributes to non-adherence through loneliness and depression—more so for minority women than others [17].

While providers may not be able to reduce societal stigma, they can learn from their patients about the different ways in which OPH experience stigma to help mitigate existing disparities in their care [18•]. Addressing aging, along with other psychosocial factors, can help identify coping strategies. One way to explore the impact of aging is to ask the patient directly: Have you thought of yourself as aging? How can I help you as you grow older with HIV?

Adopting a geriatric approach

Practices must adapt to meet the needs of people aging with HIV, but geriatric care can be overwhelming, and it is difficult to know where to start. Geriatric specialists share the domains of primary care with their colleagues, but frame their priorities differently, using what are termed the "5 Ms": "Mind, Mobility, Medications, Multicomplexity, and Matters Most to Me" [19]. This different perspective can be illustrated in the geriatric approach to management of people who have multiple chronic illnesses especially in the setting of HIV. Protocols or guidelines for individual comorbidities may lead to conflicting or burdensome recommendations when multiple comorbidities and functional impairment are present. The goal is balance:

(1) Is the patient as functional, mobile, and pain-free as possible?

(2) Do disease management choices reflect the patient's priorities?

(3) Is the patient taking the correct dose of the correct medications? Can inappropriate polypharmacy be avoided?

(4) Has the patient's mental health (both affective and cognitive) been optimized?

Implementing geriatric assessment

How to improve care for OPH in a busy clinical setting is a challenge many practices face. We have addressed this problem in an academic HIV practice [20] as have others [21], by embedding geriatricians who use comprehensive geriatric assessment to evaluate the OPH and offer suggestions about management to their primary care clinicians. This is only one model of care for OPH. Others, which are currently in operation or under development, include nurse-led geriatric assessment or pre-clinical screening for age-related syndromes and comorbidities [21].

Comprehensive geriatric assessment (CGA), as its name implies, encompasses a broad range of biopsychosocial domains. Table 1 lists the basic components and their definitions. Instruments to measure these components are available in the literature or online. An HIV and Aging Toolkit with links to instruments and references [22] is available through the Northeast Caribbean AIDS Education and Training Center (http://necaaetc.org). Because links frequently change, the website provides access to annual updates of the toolkit [23].

Table 1. Components of comprehensive geriatric assessment

Component	Description
Basic activities of daily living (BADL)	Fundamental functions like dressing, bathing, grooming, toileting
Instrumental activity of daily living (IADL)	More advanced functions like managing medications and finances, cooking, using the phone
Overall health status	Patient's assessment of their health; whether they are in pain and how pain affects their life
Cognition	Global assessment of intellectual functions such as memory, concentration, vocabulary, calculation, abstraction, executive function
Mental health	Can include screens for depression, anxiety, PTSD, loneliness
Nutrition/muscle mass/bone health	Underweight or overweight; recent changes in weight, presence of sarcopenia; fracture risk, food insecurity
Social supports/living situation	Financial status; family and/or other relationships; risk of domestic abuse, including elder mistreatment; accessibility of home
Multimorbidity	Chronic illnesses as a group—how the illnesses and their treatments interact
Medications	Appropriateness of each medication; ensuring comorbidities are adequately addressed and treated
Frailty	State of vulnerability; can be assessed by evaluating it phenotypically (assessing for weight loss, fatigue, weakness, etc.) or by measuring the impact of accumulation of "deficits"
Advance directives	Documentation of decision maker (in case of incapacity) as well as instructions. Generally state-based.
Mobility	Gait speed, stability, risk of falling

Reconfiguring a practice to care for geriatric HIV patients is a complex process, and there are many factors to consider, including patient needs, staff training, availability of geriatricians, workflow, billing, and institutional support [20].

Even in the absence of providers with geriatric or gerontologic expertise, CGA principles can and should be adopted into an existing practice. The first step is determining what is practicable. A thorough CGA is the gold standard but may take an hour or more and requires a clinician who has the necessary skill and time; a clinical practice may lack access to a geriatric specialist or the financial support. Instead, the practice can begin by establishing priorities and devote resources to screening and assessment for the domain it considers most important. Here are some examples:

- The practice may wish to screen for *frailty* to identify those patients who are at greatest risk of poor outcomes [24]; staff can choose a validated tool and establish a protocol for referral. The VACS calculator [25] is another excellent prognostic tool and could be generated directly from the EHR using readily available data (https://vacs.med.yale.edu/calculator/IC).
- Staff may note many patients walking more slowly and using assistive devices, and they may want to improve their patients' *mobility*. New evidence-based guidelines can provide strategies for increasing physical activity in a clinical population [26••].
- More patients are expressing concerns about memory and wish evaluation of their *cognitive status*. Hakkers' group provides a case study for implementation of a screening protocol [27].

Irrespective of domain, in addition to determining which screens to use, the practice must decide whom to screen, who will do the screening, and what the outcome of the screen will be. The choice of the screen(s) is less important than getting started; the addition of even one assessment can help the practice develop an awareness of how their patients are aging.

Attending to symptom burden

Geriatric care also emphasizes advance directives and symptom control. Pain management and palliative care, although relevant for people with HIV of all ages, take high priority for OPH. Chronic pain is associated with poorer health outcomes in PWH [28], and ART adherence rates are lower in people with untreated pain [29]; effective treatment of pain is part of comprehensive care of PWH. Palliative care can ameliorate overwhelming symptom burden at any stage of illness. The 2017 Infectious Disease Society of America (IDSA) guidelines [30] recommend consultation with palliative care when caring for PLH of all ages with chronic pain, in addition to non-pain symptoms at the end of life; palliative care consultation can also include psychosocial and spiritual support [31].

Recommendations

- Clinical programs for people with HIV must prepare to screen for and take care of aging-related problems.

- Comprehensive geriatric assessment is the gold standard for evaluating older people. Consider collaboration with a local geriatrician or gerontologic nurse practitioner who would be sensitive to the needs of people with HIV.
- Any practice can begin to screen for cognitive loss, fall risk, and other aging-related complications with readily available assessment tools.
- Screening protocols should include types of patients to be targeted, when screening should take place and by whom, and referrals or other outcomes of the screening.
- Palliative care and discussions of advanced directives should be incorporated as part of the 5 M's of geriatric care.

Deciding to rock the boat: antiretroviral regimen changes in older patients

Managing antiretroviral medications (ARVs) in OPH can be complex; there are often co-morbid conditions that require multiple medications, increasing the risk of drug-drug interactions [32]. The physiologic changes associated with aging, including reduced lean body mass, decreased renal and hepatic function, and decreased gastrointestinal transit, can alter drug metabolism and increase OPH risk for higher effective drug levels and side effects. In addition, age-related decreases in blood flow to the liver, liver mass, and drug-metabolizing enzyme content have the potential to decrease the hepatic clearance of drugs [33, 34]. Special care and attention should be given to medication side effects in older patients, given potential for sub-optimal drug metabolism.

Currently, most standard initial antiretroviral therapy regimens consist of three medications, with antiretrovirals (ARV) from at least two different drug classes, aimed to prevent the development of drug-resistant HIV [35•]. Advances in medication regimens and understanding of drug resistance patterns make it possible to consider switching from an initial or current effective regimen (once HIV viremia is suppressed) to a simpler alternative regimen. This option is especially valuable when considering polypharmacy, pill burden, drug-drug interactions, medication side effects, and cost [35•].

For OPH on nucleoside reverse transcriptase inhibitor (NRTI) medications, dose adjustment is often required as renal function decreases. Due to their adverse effects on bone, changing from tenofovir disoproxil fumarate (TDF) and boosted protease inhibitors is recommended for older patients at risk for frailty and bone fracture [32]. Within-class and between-class switches are often effective in maintaining viral suppression in the absence of viral resistance to a new medication.

Other options to simplify ARV regimens include switching to a one pill per day co-formulated tablet containing either three or two active ARV medications. While single tablet ARV co-formulations offer patients the ease of one pill per day dosing, not all tablets are equivalent; some contain pharmacologic boosters (ritonavir or cobicistat) that are the highest risk for drug-drug interactions. Since the advent of the first co-formulated tablet in 2006, many others have followed suit in the form of three drug regimens [36]. More recently, the SWORD-1 and SWORD-2 studies have

demonstrated effective control of HIV in patients who are virally suppressed with a single tablet two-drug regimen consisting of dolutegravir and rilpivirine [37•]. The momentum of two-drug regimens has continued through evaluation of dolutegravir and lamivudine as *initial* therapy in the GEMINI-1 and GEMINI-2 trials, with promising non-inferiority phase 2 study results compared to dolutegravir, TDF and emtricitabine combination ARV [38] and its recent approval as a single tablet regimen in ART-naïve adults without resistance in the US.

Even with comprehensive guideline recommendations, clinicians must consider many factors when selecting an ARV regimen, including medication potency, presence of HIV resistance mutations, drug-drug interactions, patient co-morbidities, and ease of dosing. A prospective cohort study of OPH (median age 70 years) found a high prevalence of non-conventional ARV regimens, suggesting that HIV providers must often tailor ARV regimens to individual patient's needs. Approximately two-thirds of the patients in this cohort were on a conventional three-drug regimen; the final third was divided between predominantly dual-therapy regimens (25% of total), and a small proportion of individuals on monotherapy (6.5% of total) or "mega-ART" with more than three drugs (1.6%) [39].

Clinical trials evaluating the role of long-acting intramuscular injection ARV drug regimens are an area of active interest. The ATLAS and FLAIR trials investigate the role of intramuscular injection cabotegravir and rilpivirine as a monthly injection in treatment-experienced [40] and treatment-naïve [41] individuals, respectively. The FLAIR trial initiates therapy with an oral integrase inhibitor based three-drug single tablet regimen as per standard of care, then after viral suppression assesses monthly intramuscular cabotegravir and rilpivirine for maintenance of viral suppression. While both trials showed promising non-inferiority results at preliminary data review at 48 weeks [42, 43], it should be noted that median age of participants ranged from 34 to 42 in these studies, and therefore, pharmacodynamics have not been fully evaluated in OPH.

In summary, optimizing medication regimens can include deprescribing or changing medications of all types, including ARVs, as polypharmacy can be associated with significant drug side effects that may outweigh clinical benefit [44].

Recommendations

- Recent advances in ARV regimens offer opportunities to switch an effective regimen to an alternative regimen in some situations that is simpler and/or safer, while still maintaining viral suppression.
- Regularly assess OPH medication regimens, with the goal of reducing pill burden and/or dosing frequency, increasing tolerability, and decreasing drug-drug interactions.
- A full review of the patient's ARV treatment history, past ARV-associated toxicities, and resistance testing results is needed to determine which

medication switches are appropriate.
- New drug combinations including de-escalation and novel methods of drug delivery are actively undergoing study at this time; however, their application in OPH warrants further study.

Recognizing the needs of older women with HIV

At the end of 2016, there were more than 235,000 women with HIV in the USA [2]. In New York City, women represented 26.5% of all PLH, and 18.3% of new HIV diagnoses. More than 58% of women with HIV in NYC are 50 and older and more than 90% are African-American or Latina [3]. Women with HIV deserve special attention; they report worse health-related quality of life [45, 46] and experience greater HIV-related morbidity than men [47]. Evidence is now emerging that WLH are more vulnerable to cognitive impairment, cardiovascular disease, and bone disease compared to their HIV-negative counterparts [48, 49, 50, 51]. Recognizing these differences and identifying risk factors can help health care providers optimize treatment and preventive care.

Menopause

Menopause, the permanent cessation of menstruation resulting from the loss of ovarian follicular activity, is recognized after 12 consecutive months of amenorrhea [52]. HIV-positive women may experience menopause earlier than women without HIV, which may predispose them to earlier onset (compared to non-HIV cohorts) of diseases whose risk increases after menopause [53, 54]. Generalized symptoms such as fatigue, joint pains, and mood disorders commonly seen in HIV may be components of menopause [51]. Menopause affects aging in women, and HIV can accelerate these changes [51]. In addition to causing menopausal symptoms, the significant drop in estrogen levels is the catalyst for increased morbidity secondary to the changes in post-menopausal cardiovascular, microvascular, skeletal, and immune systems [49, 51]. Although each woman's needs must be assessed individually, guidelines from the Infectious Disease Society of America (IDSA) do not recommend the *routine* use of hormone replacement therapy for the treatment of menopause [54], as many antiretroviral medications interact with estrogen and progesterone [55]. Non-hormone therapy interventions for symptoms of menopause include serotonin-specific receptor inhibitors and gabapentin to treat hot flashes [55].

Cardiovascular disease

People with HIV have a higher risk of cardiovascular disease than their uninfected counterparts [56]. Chronic low-grade inflammation and persistent immune activation are felt to be major mechanisms [49]. In addition to being an independent risk factor for CVD, HIV is associated with increased hypercoagulability, dyslipidemia, and microvascular dysfunction, and certain ART regimens as well may increase risks of developing CVD [49, 57, 58]. Women living with HIV are at elevated risk compared to their non-HIV counterparts for cardiac morbidity such as congestive heart failure and ischemic heart disease [57]. WLH

are also higher risk for ischemic strokes [57, 58]. Addressing negative health behaviors like smoking and inactivity is an essential part of health promotion. IDSA guidelines suggest checking a fasting lipid profile and hemoglobin a1c at initiation of ART and within 1–3 months of starting ART [54, 57], but for women at high risk, imaging tests for ischemic heart disease may be more beneficial than exercise tolerance testing because of the lower predictive value and reliability in women compared to men [56]. Functional, rather than anatomic imaging modalities may be more sensitive, given the higher prevalence of microvascular disease in women [59].

Cognitive changes

Women with HIV may be more vulnerable to cognitive impairment compared to HIV-negative women and HIV-positive men [49, 51, 58, 60, 61••]. HIV crosses the blood-brain barrier and infects perivascular macrophages and microglia; with the advent of ART, HIV-associated dementia has declined, but milder HIV-associated neurocognitive disorders are still prevalent [49] despite viral suppression [27]. OPH are also at risk for vascular neurocognitive disorders because of other traditional factors as microvascular changes, cardiovascular disease, and metabolic syndromes [62], in addition to age-related neurodegenerative diseases [63]. Another concern is the potential of synergistic adverse side effects of medications such as anticholinergics and opioids that may impair cognition [48]. Women, in particular, may be at higher risk for cognitive impairment given a greater susceptibility to ischemic stroke compared to their uninfected counterparts; of note, this stroke risk may be somewhat mitigated by longer duration of ARV [64•]. With this knowledge, clinicians should be more cognizant of the prevention and treatment of risk factors of cognitive impairment in OWH. As physical activity may be protective against cognitive impairment in women [65], interventions to increase physical activity should be addressed at an early age [65] and added to medical management.

Bone health

Women and men both are affected by bone loss in aging, but the onset of menopause causes an acceleration of bone loss and increased risk of fractures in women [50]. PLH in the first 2 years of ART have bone changes similar to women without HIV undergoing menopause [50]. As WLH age and experience menopause, their risk of fractures will increase [66]. A recent Italian study documented that bone mineral density decreases twice as quickly in HIV-infected woman than in HIV-infected men [67]. There is a 2–3-fold higher prevalence of fractures in WLH older than 50 years compared to the general population [68]. The risk for developing osteoporosis is likely multifactorial, comprising lifestyle risk factors like smoking as well as HIV-related conditions like nutritional deficiencies and ART-related side effects [50, 69]. HIV itself increases osteoclastic activity and decreases bone formation while elevated tumor necrosis factor levels propel osteoclast-mediated bone resorption [69].

The FRAX assessment tool [70] is often used to assess risk, but it has been found to underestimate fracture risk in PLWH [66, 71] and should be supplemented by identification of clinical risk factors for bone loss

and fractures. Current recommendations are to screen all postmenopausal WLH and HIV-infected men starting at 50 years of age or who are at high risk of fragility fractures due to a history of low trauma fractures, chronic steroid use of more than 3 months, clinical hypogonadism, malabsorption, inflammatory bowel disease, or primary hyperparathyroidism. Dual-energy x-ray absorptiometry should be used for screening (when available) and should be repeated every 2–5 years if the initial test indicates low risk [54, 69, 72]. Pharmacologic treatment is indicated in patients with low BMD (*t* score below – 2.5) or with a history of low trauma vertebral or hip fracture [73]. The Swiss guidelines [71] also recommend intervention when the patient's 10-year FRAX fracture risk exceeds the guideline's age-based fracture threshold.

Recommendations

- Menopause may present at younger ages in women with HIV. Awareness of the physiologic changes associated with it and the increased risk of osteoporosis and cardiovascular disease that occur after menopause can help providers address diseases earlier to maximize treatment and improve outcomes.
- Women with HIV appear to be at higher risk for cognitive impairment and may benefit from early screening; attention to pharmacologic, metabolic, and vascular risk factors may mitigate some of the contributing factors to cognitive decline.

Conclusion

Optimal clinical care of older people with HIV necessitates more than attention to viral load and specific comorbidities; it requires a frame of reference that includes attention to the 5 Ms of geriatrics: Mind, Mobility, Medications, Multicomplexity, and "Matters Most to Me." Comprehensive geriatric assessment can be performed by trained providers in the clinic or as consultation, but HIV clinical programs can start a program for older patients by focusing on one or a few domains. Women's health also deserves special attention, as women with HIV appear to be more susceptible to comorbidities like bone disease and cognitive impairment. Risk mitigation and screening should begin at younger ages.

Compliance with Ethical Standards

Conflict of Interest

Dr. Siegler has received salary support for an investigator-initiated study from Gilead Sciences, Inc.
Drs. Johnston and Del Carmen and Ms. Burchett declare that they have no conflicts of interest.
Dr. Johnston has grant support from NIH/NIAID T32 AI007613.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Smit M, Brinkman K, Geerlings S, Smit C, Thyagarajan K, van Sighem A, et al. Future challenges for clinical care of an ageing population infected with HIV: a modelling study. Lancet Infect Dis. 2015;15(7):810–8.
2. Centers for Disease Control and Prevention. HIV Surveillance Report 2017 [Internet]. 2018 [cited 2019 Feb 13] p. 129. Report No.: Volume 29. Available from: http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html.
3. HIV Epidemiology and Field Services Program. 2017 HIV Surveillance Annual Report [Internet]. New York, NY: New York City Department of Health and Mental Hygiene; 2018. [cited 2019 Feb 13] p. 20. Available from: https://www1.nyc.gov/assets/doh/downloads/pdf/dires/hiv-surveillance-annualreport-2017.pdf.
4. De Francesco D, Wit FW, Bürkle A, Oehlke S, Kootstra NA, Winston A, et al. Do people living with HIV experience greater age advancement than their HIV-negative counterparts? AIDS. 2019;33(2):259.
5. Schouten J, Wit FW, Stolte IG, Kootstra NA, van der Valk M, Geerlings SE, 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(12):1787–97.
6. Kong AM, Pozen A, Anastos K, Kelvin EA, Nash D. Non-HIV Comorbid Conditions and Polypharmacy Among People Living with HIV Age 65 or Older Compared with HIV-Negative Individuals Age 65 or Older in the United States: A Retrospective Claims-Based Analysis. AIDS Patient Care STDs. 2019;33(3):93–103.
7. Guaraldi G, Malagoli A, Calcagno A, Mussi C, Celesia BM, Carli F, et al. The increasing burden and complexity of multi-morbidity and polypharmacy in geriatric HIV patients: a cross sectional study of people aged 65 – 74 years and more than 75 years. BMC Geriatr. 2018;18(1):99.
8. Greene M, Justice AC, Covinsky KE. Assessment of geriatric syndromes and physical function in people living with HIV. Virulence. 2017;8(5):586–98.
9. Greene M, Covinsky KEM, Valcour V, Miao YM, Madamba JB. Lampiris HM#, et al. Geriatric Syndromes in Older HIV-Infected Adults. J Acquir Immune Defic Syndr. 2015;69(2):161–7.
10. Do AN, Rosenberg ES, Sullivan PS, Beer L, Strine TW, Schulden JD, et al. Excess burden of depression among HIV-infected persons receiving medical care in the united states: data from the medical monitoring project and the behavioral risk factor surveillance system. PLoS One. 2014;9(3):e928423.
11. Kelly SG, Wu K, Tassiopoulos K, Erlandson KM, Koletar SL, Palella FJ. Frailty Is an Independent Risk Factor for Mortality, Cardiovascular Disease, Bone Disease, and Diabetes Among Aging Adults With Human Immunodeficiency Virus. Clin Infect Dis. 2019; 27;69(8):1370–1376. Available from: https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciy1101/5258114. Accessed 29 Dec 2019
12. The White House Office of National AIDS Policy. National HIV/AIDS Strategy for The United States: Updated to 2020. 2015;74. https://files.hiv.gov/s3fs-public/nhas-update.pdf. Accessed 11 May 2019
13. Earnshaw VA, Bogart LM, Dovidio JF, Williams DR. Stigma and Racial/Ethnic HIV Disparities: Moving Toward Resilience. Am Psychol. 2013;68(4):225–36.
14. Emlet CA. "You're Awfully Old to Have This Disease": Experiences of Stigma and Ageism in Adults 50 Years and Older Living With HIV/AIDS. The Gerontologist. 2006;46(6):781–90.
15. Shen MJ, Freeman R, Karpiak S, Brennan-Ing M, Seidel L, Siegler EL. The intersectionality of stigmas among key populations of older adults affected by HIV: a thematic analysis. Clin Gerontol. 2018;0(ja):1–13.
16. Palar K, Frongillo EA, Escobar J, Sheira LA, Wilson TE, Adedimeji A, et al. Food Insecurity, Internalized Stigma, and Depressive Symptoms Among Women Living with HIV in the United States. AIDS Behav. 2018;22(12):3869–78.
17. Turan B, Smith W, Cohen MH, Wilson TE, Adimora AA, Merenstein D, et al. Mechanisms for the Negative Effects of Internalized HIV-Related Stigma on Antiretroviral Therapy Adherence in Women: The Mediating Roles of Social Isolation and Depression. J Acquir Immune Defic Syndr. 2016;72(2):198–205.
18.• Stangl AL, Earnshaw VA, Logie CH, van Brakel W, C. Simbayi L, Barré I, et al. The Health Stigma and Discrimination Framework: a global, crosscutting framework to inform research, intervention development, and policy on health-related stigmas. BMC Med. 2019;17(1):31

Recognizing the importance of better addressing health related stigmas, the Health Stigma and Discrimination Framework was developed to enhance methods for research and policy.

19. Tinetti M, Huang A, Molnar F. The Geriatrics 5M's: A New Way of Communicating What We Do. J Am Geriatr Soc. 2017;65(9):2115–5.
20. Singh HK, Del Carmen T, Freeman R, Glesby MJ, Siegler EL. From One Syndrome to Many: Incorporating Geriatric Consultation into HIV Care. Clin Infect Dis. 2017;65(3):501–6.
21. Greene ML, Tan JY, Weiser SD, Christopoulos K, Shiels M, O'Hollaren A, et al. Patient and provider perceptions of a comprehensive care program for HIV-positive adults over 50 years of age: The formation of the Golden Compass HIV and aging care program in San Francisco. PLoS One. 2018;13(12):e0208486.
22. Siegler EL. Care of People Aging with HIV: Northeast/Caribbean AETC Toolkit, V.4 [Internet]: Northeast Caribbean AIDS Education and Training Center Program; 2018. Available from: https://necaaetc.org/file/949/download?token=qf8-RrNg.
23. NECA AETC Clinical Support Tools [Internet]. 2019 [cited 2019 Mar 3]. Available from: https://necaaetc.org/content/clinical-support-tools.
24. Walston J, Buta B, Xue Q-L. Frailty Screening and Interventions: Considerations for Clinical Practice. Clin Geriatr Med. 2018;34(1):25–38.
25. Tate JP, Sterne JAC, Justice AC. Improved discrimination of mortality with Veterans Aging Cohort Study (vacs) Index 2.0 in Hiv-positive individuals. AIDS. 2019;33(5):903–12.
26.•• Montoya JL, Jankowski CM, O'Brien KK, Webel AR, Oursler KK, Henry BL, et al. Evidence-informed practical recommendations for increasing physical activity among persons living with HIV. AIDS. 2019;33(6):931–9
This review reinforces the central role increasing physical activity plays in the health of people with HIV.
27. Hakkers CS, Kraaijenhof JM, van Oers-Hazelzet EB, Visser-Meily AJMA, Hoepelman AIM, Arends JE, et al. HIV and Cognitive Impairment in Clinical Practice: The Evaluation of a Stepwise Screening Protocol in Relation to Clinical Outcomes and Management. AIDS Patient Care STDs. 2017;31(9):363–9.
28. Jiao JM, So E, Jebakumar J, George MC, Simpson DM, Robinson-Papp J. Chronic pain disorders in HIV primary care: clinical characteristics and association with healthcare utilization. Pain. 2016;157(4):931.
29. Uebelacker LA, Weisberg RB, Herman DS, Bailey GL, Pinkston MM, Stein MD. Chronic pain in HIV-infected patients: relationship to depression, substance use, and mental health and pain treatment. Pain Med. 2015;16(10):1870–81.
30. Bruce RD, Merlin J, Lum PJ, Ahmed E, Alexander C, Corbett AH, et al. 2017 HIVMA of IDSA Clinical Practice Guideline for the Management of Chronic Pain in Patients Living With HIV. Clin Infect Dis. 2017;65(10):e1–37.
31. Slomka J, Prince-Paul M, Webel A, Daly BJ. Palliative care, hospice, and advance care planning: Views of people living with HIV and other chronic conditions. J Assoc Nurses AIDS Care. 2016;27(4):476–84.
32. Guaraldi G, Pintassilgo I, Milic J, Mussini C. Managing antiretroviral therapy in the elderly HIV patient. Expert Rev Clin Pharmacol. 2018;11(12):1171–81.
33. McLachlan AJ, Pont LG. Drug metabolism in older people–a key consideration in achieving optimal outcomes with medicines. J Gerontol A Biol Sci Med Sci. 2012;67(2):175–80.
34. Le Couteur DG, Fraser R, Hilmer S, Rivory LP, McLean AJ. The hepatic sinusoid in aging and cirrhosis: effects on hepatic substrate disposition and drug clearance. Clin Pharmacokinet. 2005;44(2):187–200.
35.• Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents [Internet]. US Department of Health and Human Services; 2013. Available from: http://aidsinfo.nih.gov/contentfiles/lvguidelines/aa_recommendations.pdf.
The DHHS Guidelines includes a section about HIV in Older Adults under the category of "HIV in Specific Populations".
36. Food and Drug Administration. FDA Approves the First Once-a-Day Three-Drug Combination Tablet for Treatment of HIV-1 News [Internet]. AIDSinfo. [cited 2019 May 8]. Available from: https://aidsinfo.nih.gov/news/769/fda-approves-the-first-once-a-day-three-drug-combination-tablet-for-treatment-of-hiv-1.
37.• Llibre JM, Hung C-C, Brinson C, Castelli F, Girard P-M, Kahl LP, et al. Efficacy, safety, and tolerability of dolutegravir-rilpivirine for the maintenance of virological suppression in adults with HIV-1: phase 3, randomised, non-inferiority SWORD-1 and SWORD-2 studies. Lancet. 2018;391(10123):839–849.
This study demonstrates non-inferiority of a novel two drug regimen to maintain viral suppression in individuals with suppressed viremia on a stable ARV regimen.
38. Cahn P, Madero JS, Arribas JR, Antinori A, Ortiz R, Clarke AE, et al. Dolutegravir plus lamivudine versus dolutegravir plus tenofovir disoproxil fumarate and emtricitabine in antiretroviral-naive adults with HIV-1 infection (GEMINI-1 and GEMINI-2): week 48 results from two multicentre, double-blind, randomised, non-inferiority, phase 3 trials. Lancet. 2019;393(10167):143–55.
39. Nozza S, Malagoli A, Maia L, Calcagno A, Focà E, De Socio G, et al. Antiretroviral therapy in geriatric HIV patients: the GEPPO cohort study. J Antimicrob Chemother. 2017;72(10):2879–86.
40. Study Evaluating the Efficacy, Safety, and Tolerability of Switching to Long-acting Cabotegravir Plus Long-acting Rilpivirine From Current Antiretroviral Regimen in Virologically Suppressed HIV-1-infected Adults - Full Text View - ClinicalTrials.gov [Internet]. Clinical Trials.gov. [cited 2019 Mar 13]. Available from: https://clinicaltrials.gov/ct2/show/NCT02951052.
41. Study to Evaluate the Efficacy, Safety, and Tolerability of Long-acting Intramuscular Cabotegravir and Rilpivirine for Maintenance of Virologic Suppression Following Switch From an Integrase Inhibitor in HIV-1

Infected Therapy Naive Participants - Full Text View - ClinicalTrials.gov [Internet]. ClinicalTrials.gov. [cited 2019 May 8]. Available from: https://clinicaltrials.gov/ct2/show/NCT02938520.

42. Swindells S, Andrade-Villanueva J, Richmond G, Rizzardini G, Baumgarten A, Masia MDM, et al. Long-acting cabotegravir + rilpivirine as maintenance therapy: ATLAS week 48 results | CROI Conference [Internet]. [cited 2019 May 8]. Available from: http://www.croiconference.org/sessions/long-acting-cabotegravir-rilpivirine-maintenance-therapy-atlas-week-48-results.
43. Orkin C, Arasteh K, Hernández-Mora MG, Pokrovsky V, Overton ET, Girard P-M, et al. Long-acting cabotegravir + rilpivirine for HIV maintenance: FLAIR week 48 results | CROI Conference [Internet]. [cited 2019 May 8]. Available from: http://www.croiconference.org/sessions/long-acting-cabotegravir-rilpivirine-hiv-maintenance-flair-week-48-results.
44. Scott I, Hilmer S, Reeve E, Potter K, Le Couteur D, Rigby D, et al. Reducing Inappropriate Polypharmacy: The Process of Deprescribing. JAMA Intern Med. 2015;175(5):827–34.
45. Catalan J, Tuffrey V, Ridge D, Rosenfeld D. HALL (HIV and Later Life) Team. What influences quality of life in older people living with HIV? AIDS Res Ther. 2017;14:22.
46. Mrus JM, Williams PL, Tsevat J, Cohn SE, Wu AW. Gender differences in health-related quality of life in patients with HIV/AIDS. Qual Life Res. 2005;14(2):479–91.
47. Blackstock OJ, Tate JP, Akgün KM, Crystal S, Duggal M, Edelman EJ, et al. Sex Disparities in Overall Burden of Disease Among HIV-Infected Individuals in the Veterans Affairs Healthcare System. J Gen Intern Med. 2013;28(Suppl 2):577–82.
48. Rubin LH, Radtke KK, Eum S, Tamraz B, Kumanan KN, Springer G, et al. Cognitive Burden of Common Non-antiretroviral Medications in HIV-Infected Women. JAIDS J Acquir Immune Defic Syndr. 2018;79(1):83.
49. Monsuez J-J, Belin C, Bouchaud O. Microvascular Function in Aging Among Women Living with HIV. Curr HIV/AIDS Rep. 2016;13(6):392–8.
50. Weitzmann MN, Ofotokun I, Titanji K, Sharma A, Yin MT. Bone Loss Among Women Living with HIV. Curr HIV/AIDS Rep. 2016;13(6):367–73.
51. Schnall R, Jia H, Olender S, Gradilla M, Reame N. In people living with HIV (PLWH), menopause (natural or surgical) contributes to the greater symptom burden in women: results from an online US survey. Menopause. 2018;25(7):744–52.
52. Utian WH. The International Menopause Society menopause-related terminology definitions. Climacteric. 1999;2(4):284–6.
53. Andany N, Kennedy VL, Aden M, Loutfy M. Perspectives on menopause and women with HIV [Internet]. International Journal of Women's Health. 2016; 11;8:1-22 Available from: https://www.dovepress.com/perspectives-on-menopause-and-women-with-hiv-peer-reviewed-fulltext-article-IJWH. Accessed 9 May 2019
54. Aberg JA, Gallant JE, Ghanem KG, Emmanuel P, Zingman BS, Horberg MA, 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(1):1–10.
55. Womack J, Brandt C, Justice A. Primary Care of Women Aging with HIV. J Midwif Women's Health. 2015;60(2):146–57.
56. Volpe M, Uglietti A, Castagna A, Mussini C, Marchetti G, Bellagamba R, et al. Cardiovascular disease in women with HIV-1 infection. Int J Cardiol. 2017;241:50–6.
57. Womack JA, Chang C-CH, So-Armah KA, Charles A, Baker Jason V, Brown Sheldon T, et al. HIV Infection and Cardiovascular Disease in Women. J Am Heart Assoc. 3(5):e001035.
58. Stone L, Looby SE, Zanni MV. Cardiovascular Disease Risk among Women Living with HIV in North America & Europe. Curr Opin HIV AIDS. 2017;12(6):585–93.
59. Bairey Merz CN, Shaw LJ, Reis SE, Bittner V, Kelsey SF, Olson M, et al. Insights From the NHLBI-Sponsored Women's Ischemia Syndrome Evaluation (WISE) Study: Part II: Gender Differences in Presentation, Diagnosis, and Outcome With Regard to Gender-Based Pathophysiology of Atherosclerosis and Macrovascular and Microvascular Coronary Disease. J Am Coll Cardiol. 2006;47(3, Supplement):S21–9.
60. Rubin LH, Maki PM, Springer G, Benning L, Anastos K, Gustafson D, et al. Cognitive trajectories over 4 years among HIV-infected women with optimal viral suppression. Neurology. 2017;89(15):1594–603.
61.•• •• Maki PM, Rubin LH, Springer G, Seaberg EC, Sacktor N, Miller EN, et al. Differences in Cognitive Function Between Women and Men With HIV. JAIDS J Acquir Immune Defic Syndr.. 2018;79(1):101

This provocative study provides evidence that women with HIV are more vulnerable to HIV related cognitive dysfunction than their male counterparts.

62. Cysique LA, Brew BJ. Vascular cognitive impairment and HIV-associated neurocognitive disorder: a new paradigm. J Neurovirol [Internet]. 2019 [cited 2019 Jan 18]; Available from: https://doi.org/10.1007/s13365-018-0706-5
63. Sacktor N. Changing clinical phenotypes of HIV-associated neurocognitive disorders. J Neurovirol. 2018;24(2):141–5.
64.• Chow FC, Regan S, Zanni MV, Looby SE, Bushnell CD, Meigs JB, et al. Elevated ischemic stroke risk among women living with HIV infection. AIDS. 2018;32(1):59

This study identified where HIV modifies the impact of sex specific risk factors on stroke risk in women with HIV.

65. Chow FC, Makanjuola A, Wu K, Berzins B, Kim K-YA, Ogunniyi A, et al. Physical Activity Is Associated With Lower Odds of Cognitive Impairment in Women but

Not Men Living With Human Immunodeficiency Virus Infection. J Infect Dis. 2019;219(2):264–74.
66. Sharma A, Shi Q, Hoover DR, Tien PC, Plankey MW, Cohen MH, et al. Frailty predicts fractures among women with and at-risk for HIV. AIDS. 2019;33(3):455–63.
67. Erlandson KM, Lake JE, Sim M, Falutz J, Prado CM, Domingues da Silva AR, et al. Bone Mineral Density Declines Twice as Quickly Among HIV-Infected Women Compared With Men. J Acquir Immune Defic Syndr. 2018;77(3):288–94.
68. Triant VA, Brown TT, Lee H, Grinspoon SK. Fracture prevalence among human immunodeficiency virus (HIV)-infected versus non-HIV-infected patients in a large U.S. healthcare system. J Clin Endocrinol Metab. 2008;93(9):3499–504.
69. McComsey GA, Tebas P, Shane E, Yin MT, Overton ET, Huang JS, et al. Bone Disease in HIV Infection: A Practical Review and Recommendations for HIV Care Providers. Clin Infect Dis. 2010;51(8):937–46.
70. Kanis JA on behalf of the World Health Organization Scientific Group. Assessment of osteoporosis at the primary health-care level. Technical Report. [Internet]. UK: World Health Organization Collaborating Centre for Metabolic Bone Diseases, University of Sheffield; 2007. [cited 2019 May 11]. Available from: www.who.int/chp/topics/rheumatic/en/index.html
71. Biver E, Calmy A, Aubry-Rozier B, Birkhäuser M, Bischoff-Ferrari HA, Ferrari S, et al. Diagnosis, prevention, and treatment of bone fragility in people living with HIV: a position statement from the Swiss Association against Osteoporosis. Osteoporos Int. 2019;39(5):1125–35.
72. Cejtin HE. Care of the human immunodeficiency virus–infected menopausal woman. Am J Obstet Gynecol. 2012;207(2):87–93.
73. Brown TT, Hoy J, Borderi M, Guaraldi G, Renjifo B, Vescini F, et al. Recommendations for Evaluation and Management of Bone Disease in HIV. Clin Infect Dis. 2015;60(8):1242–51.

Publisher's Note