

Achieving the fourth 90: healthy aging for people living with HIV

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The availability of potent antiretroviral therapy (ART) has transformed the HIV epidemic, changing HIV disease from a fatal illness to a chronic, manageable condition. In higher income countries, life expectancy for people living with HIV (PLWH) has increased substantially, nearing that of the general population [1–7], and similar gains have been seen in some parts of sub-Saharan Africa, the area of the world most impacted by HIV [2,4,8–12]. Although access to ART is far from universal, substantial progress has been made in reaching the UNAIDS 90–90–90 targets, that is, that 90% of all PLWH in a community or a country are aware of their status, 90% of those aware have initiated ART, and 90% of those on ART achieve durable viral suppression. [13,14]. The median age of PLWH is expected to increase as the scale-up of HIV treatment continues, with more and more PLWH garnering the survival benefits from treatment. Older adults are also at risk of HIV acquisition and they are rarely prioritized for HIV prevention or testing efforts. The resultant ‘greying of the HIV epidemic’ raises important questions regarding understanding the effect of aging on PLWH, the effect of HIV infection on the aging process, and optimal approaches to HIV prevention among older individuals (Table 1). Thus, a critical priority is to aim for healthy aging among PLWH, an achievement that some have called ‘the 4th 90’.

There is a growing body of work focused on HIV and aging; however, only a minority is from the low and middle-income countries (LMIC) that have the highest burden of HIV. In this article, we provide an overview of

HIV among older PLWH and highlight the need for further research to better understand the interaction between HIV and aging in LMIC.

Older people living with HIV

The number of older PLWH (age ≥ 50 years) is predicted to increase by 47% to 6.9 million by 2020 [15]. Despite a growing body of research on HIV and aging in high-income countries, little is known about the intersection of HIV and aging in LMIC, especially in sub-Saharan Africa, which accounted for 62% of newly diagnosed infections among older PLWH in 2016 [16]. Among PLWH in sub-Saharan Africa, 15% are aged at least 50 years, and modeling predicts that by 2040 this proportion will increase to 27% and the number of older PLWH will increase to 9.1 million [17].

Unfortunately, until recently, most population-based HIV prevalence surveys in sub-Saharan Africa have not included older adults, limiting the accuracy of estimates in this age group. Surveys that have included older adults have found a HIV prevalence ranging from 5% among those aged 50–64 years in Kenya, to 13% among those aged 50–54 years in South Africa; in Swaziland, prevalence was 6.4% among adults aged at least 50 years and 13% in men and 7% in women aged 60–64 [18]. A population-based survey in Rwanda that included individuals up to age 59 years found a higher HIV

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Table 1. HIV prevention and care continuum: challenges for older individuals in low and middle-income countries.

Social/behavioral	Structural	Biological/physiological
Perception of low risk	Providers unaware of HIV risk among older individuals	Suboptimal immunological response to antiretroviral drugs
Low rates of HIV testing	Limited availability of tailored HIV prevention and treatment services	Some antiretroviral drugs may increase risk of some noncommunicable conditions
Low rates of condom use	Lack of access to services for non-HIV conditions	Increased risk of co-morbid conditions (e.g. hypertension, cancer)
Adherence challenges	Limited mobility hinders access to services	Increased risk of polypharmacy with risk of nonadherence, adverse events and drug–drug interactions
Continued engagement in risky behaviors	Increased risk of poverty	
Lack of social support		

prevalence for most of the older age groups compared with younger age groups [19]. A recent review of data from 40 Demographic Health Surveys (DHS) conducted in 27 sub-Saharan African countries from 2003 to 2012 found that HIV prevalence in adults aged 45–59 years was higher than in the overall adult population for most countries, except for the Democratic Republic of Congo, Ethiopia, Mozambique, Sierra Leone, and Swaziland [20]. In Cameroon, Kenya, Lesotho, Malawi, Niger, and Tanzania, the HIV prevalence in the older age group was above the population average in the most recent survey. Of note, some surveys only included adults up to age 49. The 2015–2018 Population HIV Impact Assessments (PHIAs) being conducted in 15 countries in sub-Saharan African countries and Haiti will include older adults and will shed important light on HIV-related parameters in this population (<http://phia.icap.columbia.edu/>). Age disaggregated results from the first three country surveys, from Malawi, Zambia, and Zimbabwe show that HIV prevalence tends to be higher among those aged at least 50 years compared with those aged 15–49 years [21–23].

Comorbid conditions among older people living with HIV

Older PLWH face many of the same health challenges as older individuals in the general population, although the impact of aging may be greater among PLWH. Studies in high-income countries have found that HIV is associated with increased frailty, osteoporotic bone fractures, diabetes, and myocardial infarction [24–27]. Conditions such as diabetes, cardiovascular disease, bone fractures, non-AIDS-defining malignancies, liver disease, and renal failure along with multimorbidity have also been identified at younger ages in PLWH compared with HIV-uninfected adults [28,29].

The reasons for the elevated risk of noncommunicable diseases (NCDs) among PLWH are not entirely understood but increased inflammation because of HIV replication, increased cellular senescence, and the metabolic effect associated with certain antiretroviral

drugs may all play a role [30–32]. It is also not clear if HIV accelerates NCD risk (i.e. at the time of HIV infection, the risk of NCDs increases at a faster rate than that in the general population), accentuates HIV risk (i.e. there is a one-time increase in the risk NCDs at the time of HIV infection but no difference in the year-to-year increase in risk), or has both effects [33].

Studies on the association between aging and HIV have had inconsistent findings. This may be because of the fact that PLWH in certain settings having higher rates of chronic disease risk factors such as substance use (smoking, alcohol, drug use) and co-infections (cytomegalovirus, hepatitis B and C viruses), as well as characteristics such as homelessness and social isolation that hinder access to health-related services compared with those without HIV infection [30,32,34]. Even when some of these factors are taken into account, residual confounding likely exists.

The Veterans Aging Cohort Study found that HIV-infected veterans had a higher risk than HIV-uninfected veterans of myocardial infarction, end-stage renal disease, and non-AIDS-defining cancer, but these outcomes occurred at similar ages in demographically comparable HIV-uninfected veterans suggesting that HIV did not accelerate aging [35]. A multicohort study comparing age at diagnosis of cancer among PLWH versus the general population found that after adjusting for cancer risk factors, the median age at diagnosis was lower among PLWH for lung, anal, oral cavity/pharynx, and kidney cancers and myeloma but not for other cancers [36]. However, a cohort of HIV-infected and comparable HIV-uninfected participants aged at least 45 from the Netherlands found that PLWH had a significantly higher mean number of age-associated NCDs with rates of hypertension, myocardial infarction, peripheral arterial disease, and impaired renal function significantly higher among PLWH; associations with HIV infection remained significant in adjusted models [37].

In settings with high ART coverage, non-AIDS related conditions have become increasingly important causes of morbidity and mortality among PLWH [38]. A recent multicohort study that included PLWH from Europe,

USA, and Australia found that the percentage of deaths attributable to non-AIDS-related cancers increased between 1999–2000 and 2009–2011 [39].

It is important to note that research findings from higher income settings may not apply to resource-constrained settings. Co-occurrence of other acute and chronic infections may differ, as may the prevalence of substance use and other risk factors. In addition, individuals in low-income countries have more limited access to NCD risk reduction interventions and care during their lives, whereas HIV-related stigma in such settings may lead to delays in diagnosis and initiation of ART. Older women and key populations with HIV infection also face unique challenges associated with aging and may require tailored services; however, few aging-related studies have focused on these groups especially in lower income settings [15].

Inflammation is thought to play an important role in aging and is associated with co-infection with cytomegalovirus, hepatitis B and C viruses, malaria, and *Mycobacterium tuberculosis*, which may result in persistent inflammation even when HIV is well controlled [40]. The prevalence of these infections may be different in higher income versus lower income settings. A recent review article found a pooled prevalence of cytomegalovirus (CMV) infection in Africa of 94.8% among asymptomatic HIV-positive adults compared with 81.8% among HIV-negative adults [41]. Additionally, the African region has a high prevalence of chronic hepatitis B infection at 6.1%, only second in the world to the Western Pacific Region at 6.2% [42].

There is also limited information on NCD risk factors among both PLWH as well as among the general population in lower income settings. Generally, smoking rates are lower in sub-Saharan Africa compared with other parts of the world [43]. However, even with this lower background rate of smoking, there is some evidence that risk factors may be higher in PLWH than in uninfected persons in sub-Saharan Africa, as is noted in wealthier countries. For example, a recent study found that among PLWH attending a clinic in South Africa, 52% of men and 13% of women were smokers, which is higher than in the general population in South Africa (men: 31.9%, women: 7.0%) [44]. Obesity, another NCD risk factor, is a growing problem worldwide including in sub-Saharan Africa [45] and although historically being underweight was the largest concern for PLWH, with effective HIV treatment, high rates of overweight and obesity have been reported [46,47].

Studies in South Africa have found that older PLWH had weaker grip strength compared with similarly aged HIV-uninfected adults [48] and that biological markers of aging were increased in the former group [49]. In a study from Uganda among older PLWH on ART, similar health and functional status were reported among older individuals with and without HIV infection when controlling for

other variables, with the exception of reported lower BMI among PLWH [50]. Another study in Uganda of older PLWH and older HIV-uninfected adults found that PLWH were more likely to have chronic obstructive pulmonary disease (COPD) and eye problems (except for those aged 60–69 years) though diabetes and angina were more prevalent in the HIV-uninfected participants [51]. The latter study also found that no difference existed between PLWH and HIV-uninfected participants in having one or more chronic conditions or in disability scores. A recent large study conducted in South Africa found that PLWH persons over 40 years were less likely to have hypertension, diabetes, or be overweight or obese and to have multiple cardiometabolic disease comorbidities compared with HIV-negative persons [52]. However, adjusted analyses were not presented in the latter study. Mixed findings to date from studies conducted in sub-Saharan Africa may also be because of systematic differences between PLWH and HIV-uninfected populations that result in residual confounding.

HIV and non-HIV disease management in older people living with HIV

Management of HIV and other health conditions can be more complex in older PLWH [53]. ART side effects may be more severe, and ART may exacerbate or increase the risk of other conditions such as kidney disease, declines in bone mineral density and bone fracture, symptomatic peripheral neuropathy, and cardiovascular disease including myocardial infarction [54,55]. In addition, older PLWH are likely to already have comorbid conditions such as cardiovascular, renal, and liver disease, which has the potential to complicate the management of HIV disease because of challenges related to polypharmacy and drug–drug interactions [56,57]. Although ART adherence is generally better among older PLWH, cognitive impairment associated with aging may affect adherence [56,58]. Furthermore, upon initiating HIV treatment, older adults do not experience the same magnitude in CD4⁺ cell count recovery as younger adults, thus leading to their continued vulnerability to various complications – a finding noted repeatedly in both higher income settings [59,60] and in studies from sub-Saharan Africa [61–67]. This is compounded by the finding that delayed ART initiation has been associated more strongly with mortality in older compared with younger adults [68].

Despite the rapidly increasing prevalence of NCDs in lower income countries [69], their health systems are often not optimized to deliver chronic care, and the resources needed to screen, diagnose, and manage NCDs and other non-AIDS related conditions relevant to older PLWH are frequently limited [70]. Extending the lessons learned from the successful scale-up of HIV services to

NCD programs may accelerate the creation of effective NCD services for both PLWH and the general population. Examples include the use of a public health approach to NCD program design, focusing on evidence-based algorithmic management to enable task shifting to nonphysician clinicians, and to simplify the procurement of medications and laboratory supplies [70–72]. Other lessons from HIV programs include the need for systematic outreach to communities to increase demand for NCD services, clinician training, provision of psychosocial support to enhance adherence to medications and retention in care, and the use of simple monitoring and evaluation indicators to measure performance along the cascade from diagnosis to effective treatment [73]. It is increasingly clear that integration of routine NCD screening, prevention, and treatment services into HIV programs is an effective way to identify and treat PLWH with NCDs [74].

Risk of HIV acquisition among older individuals

Although older adults continue to be at risk for HIV acquisition, with evidence of ongoing sexual activity and low condom use [75–80], the lack of awareness by healthcare providers of HIV risk among this age group limits their access to HIV testing and prevention interventions, thus increasing the likelihood of unrecognized HIV infection [81,82]. Even though opt-out HIV testing is recommended in the United States for all patients in healthcare settings, very few (<5%) older adults report receiving a HIV test [83] and testing rates are lower compared to younger adults, even at venues where HIV prevalence is relatively high, such as needle exchange sites and sexually transmitted infection clinics [84]. The same findings have been noted in sub-Saharan Africa [85]. A recent systematic review found that behavioral interventions to reduce HIV risk among older adults were lacking [77]. Major challenges to providing HIV education for older adults include the following: ageism among health professionals, reluctance among older adults to discuss sexuality, and misconceptions among older adults about their own HIV risk [86].

There are few studies that assessed HIV incidence among older adults in sub-Saharan Africa and only one with data from the last 5 years in the context of ART scale-up. One open cohort study from Zimbabwe conducted from 1998 to 2011 found an incidence of 0.708 per 100 person-years in adults at least 45 years of age, with high rate among men compared with women (1.03 versus 0.57) [79]. A study conducted in South Africa from 2006 to 2008 found that HIV incidence among adults aged at least 50 years was 0.5 (95% CI 0.3–1.0) per 100 person-years, with rates not significantly higher in men compared with

women (0.9 versus 0.4 per 100 person-years) [87]. A recently published nationally representative survey from Rwanda found that HIV incidence was higher among individuals between 36 and 45 years of age compared with those between 16 and 25 years of age [19].

Conclusion

Populations around the world are aging, with associated societal, economic, and health challenges [88,89]. Unfortunately, older PLWH face unique challenges in accessing the services they need (Table 1). In lower income countries, many of which will be bearing the largest burden of aging PLWH, more research is needed on HIV disease among older individuals. Cohort studies that include a sufficient number of older PLWH from these settings are needed to examine the interaction of HIV and aging over their life course. Surveillance and surveys should also include sufficient number of older PLWH to enable accurate estimates of HIV prevalence and incidence. Additionally, program data should be disaggregated by age and sex, enabling routine reporting on older PLWH.

HIV programs should also ensure that older PLWH have access to non-HIV clinical services and to appropriate supportive services responsive to their needs. Lastly, HIV prevention efforts must not overlook older adults and should acknowledge their sexuality and their needs for tailored prevention messages, tools, and services. Only with such concerted efforts can the global community do justice to the needs of older PLWH and protect older individuals from acquiring HIV infection. Now is the opportune time to embark on vigorous efforts to confront this threat, to ensure that older individuals with HIV can live long and healthy lives into older age, and to end the threat of HIV in this population.

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Conflicts of interest

There are no conflicts of interest.

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