



## Review Article

### Aging with HIV: Triumphs and Challenges

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#### Abstract

The HIV population is aging. Antiretroviral therapy has significantly improved the life expectancy of people living with HIV, which is now approaching that of the general population. However, older adults with HIV are at a greater risk of developing comorbidities and experiencing polypharmacy, and they tend to encounter these challenges at a younger age. There is an ongoing need to adapt healthcare infrastructure and public health policies to address the complex needs of the aging HIV population.

**Keywords:** Aging; Comorbidity; HIV; Polypharmacy; Prevention; Women

#### Abbreviations

HIV: Human Immunodeficiency Virus  
AIDS: Acquired Immunodeficiency Syndrome  
PLWH: People Living With HIV  
LTS: Long Term Survivors  
CYPP450: Cytochrome P450  
LTC: Long-term Care

#### Introduction

HIV care has gone through an amazing transformation over the past 30 years. What was once a terminal diagnosis can now be managed as a chronic condition. People are living with HIV longer than ever before as treatment regimens become more effective, tolerable and initiated earlier in the disease progress at higher CD4 counts.

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Today nearly half of People Living With HIV (PLWH) in North America are over the age 50 [1,2], with rising numbers of older adults living with HIV around the world [3]. As we celebrate this changing demographic, it is important to acknowledge the challenges faced by this aging population and adapt our clinical and public health practices accordingly.

#### Diversity Among Older Adults with HIV

Firstly, it is important to recognize that older adults with HIV represent a diverse population of individuals that may face unique challenges related to their physical and mental health. For example, Long Term Survivors (LTS), individuals who were diagnosed with HIV before effective antiretroviral therapy became available [4], received some of the earliest HIV therapies, exposing them to significant toxicities and increasing their risk of developing chronic conditions such as lipodystrophy, diabetes, peripheral neuropathy and metabolic syndrome. Many LTS have experienced immense psychosocial trauma related to receiving a diagnosis that was once considered a death sentence, losing friends and loved ones to the condition, facing years of stigma, poverty, food insecurity and social isolation [5]. Providing trauma-informed care in a multidisciplinary setting may be of particular benefit for this group.

In contrast, there are also a substantial proportion of older adults with a recent HIV diagnosis. In 2018, people over the age of 50 accounted for 22.5% of new HIV diagnoses in Canada [1] and similarly in the United States, 1 in 6 new diagnoses in 2017 were among those over age 50 [2]. These numbers include individuals that recently acquired HIV as well as those that were recently tested but acquired the infection earlier. Individuals with delayed diagnosis have more advanced immune dysregulation at the time of presentation and are at greater risk of presenting with opportunistic infections and comorbidities related to chronic uncontrolled HIV infection. On the other hand, older adults with recently acquired HIV infection may have relatively preserved immune systems but require more guidance in terms of access to HIV resources and community supports. Finally, the mode of HIV transmission might carry additional information about the social aspects of an individual's diagnosis and journey, such as experiences related to sexual identity, drug use or sex work. Undoubtedly, it is important to recognize the multifaceted needs of older adults with HIV and have an appreciation for their varied backgrounds.

#### Delayed HIV Diagnosis in Older Adults and Women

Older adults are more likely to have unrecognized HIV infection for many years and subsequently be diagnosed as inpatients, at lower CD4 counts and at more advanced stages of HIV infection relative to younger adults [6,7]. Women are particularly at increased risk of being diagnosed late in their illness and are less likely to be tested in the outpatient setting [8]. Delayed diagnosis in women and older adults reflects low perceived risk of HIV infection among patients and their healthcare providers. Late treatment initiation is especially detrimental in the aging population. In 2015, a large international

randomised controlled trial showed a clear morbidity and mortality benefit to early treatment initiation at high baseline CD4 counts, compared to delaying treatment until CD4 count drops below 350, across age groups [9]. However, rates of AIDS-defining illnesses, serious non-AIDS illnesses (including cardiovascular disease, end-stage renal and liver disease and non-AIDS cancers) and death were disproportionately higher in older adults if treatment was delayed. Absolute risk reduction was greatest in the >50 age group with the lowest number needed to treat to prevent an adverse clinical event, demonstrating that older adults benefit the most from early recognition and treatment of HIV infection. These findings contributed to a change in practice, which now emphasizes early treatment initiation, at high CD4 counts. Unrecognized infection in older adults prevents them from benefiting from this treatment approach. Improving risk factor recognition along with implementation of routine HIV screening are therefore of great importance to improve survival and reduce morbidity in this population.

### **Increasing Life Expectancy but not Comorbidity-Free Years**

The life expectancy of PLWH continues to increase and is approaching that of the general population. In North America, total life expectancy at age 20 increased from 56.1 years in 2000-2002 to 71.4 years in 2006-2007 among PLWH [10]. In contrast, life expectancy in the general population in Canada in 2007 was 80.5, and 78 in the United States [11,12]. The life expectancy gap relative to the general population narrowed further to just 3.4 years in 2014-2016 in an American cohort of PLWH with early treatment initiation [13]. Although people are living longer with HIV, they tend to spend a substantially greater number of years dealing with chronic conditions with fewer healthy years free of comorbidities. On average, PLWH developed common medical comorbidities 16 years earlier than those in the general population [13]. This number has not improved since early 2000's or with implementation of early treatment strategies.

### **Comorbidities among PLWH**

PLWH are at a substantially increased risk relative to the general population of developing medical comorbidities, including cardiovascular disease, diabetes, renal failure and liver disease, and they are more likely to experience polypharmacy and drug-drug interactions [14-16]. The difference in risk increases as people age. Co-infection with cytomegalovirus seems to be an independent risk factor for developing non-AIDS defining comorbidities, especially cardiovascular and cerebrovascular diseases [17]. Prevalence of osteopenia and osteoporosis is also substantially higher among PLWH with greater risk of bone fracture across age groups [14,18]. Certain cancers are more prevalent among PLWH, including AIDS-defining (i.e., Kaposi's sarcoma, non-Hodgkin's lymphoma, cervical cancer) and non-AIDS defining cancers (i.e., Hodgkin's lymphoma, lung, liver, anal and oropharyngeal cancers) [19,20]. With advancing age and time since HIV diagnosis, cancer burden shifts from AIDS-defining to non-AIDS defining cancers [19]. This change is a reflection of HIV treatment initiation and recovery of the CD4 count, coupled with prolonged exposure to risk factors, such as smoking, alcohol consumption and co-infections with human papillomavirus and Hepatitis C virus. Smoking is highly prevalent among PLWH (>50% report active smoking), with rates that are three times that of the general population [21,22]. People with HIV are also less likely

to quit smoking [21], contributing substantially to development of comorbid disease.

In order to reduce the burden related to co-morbidities commonly experienced by PLWH, routine screening and utilization of preventative strategies is required. These should include assessments of blood pressure, glycemic control, lipids profile, renal function and cancer screening, along with testing for co-infections and vaccination. Smoking cessation programs are critical to address the large burden of tobacco dependence in this population. An approach that combines behavioural and pharmacological treatments to facilitate smoking cessation has been found to be more successful than standalone interventions and should be integrated into routine HIV care [22,23].

Finally, comorbidity management must implement careful medication review to avoid potential drug-drug interactions. As people age with HIV, they are more likely to be taking medications in addition to anti-retroviral therapy, such as cardiovascular medications, lipid-lowering agents, antiplatelets, anticoagulants, acid-lowering medications and hypoglycemics, as well as psychoactive medications and analgesics [24,25]. Many anti-retroviral agents are metabolized through the Cytochrome P450 (CYP450) enzyme system [24]. They can also exert bidirectional effects on CYP450 isoenzymes, potentially resulting in increased or decreased metabolism of many commonly prescribed medications. On the other hand, medications that impact absorption or metabolism of anti-retroviral agents can impact treatment efficacy. Given the complex nature of these interactions and increased potential for toxicities, clinicians need to routinely screen for drug-drug interactions with guidance from online resources [26] or a pharmacist with experience in HIV treatment.

### **Women's Health**

Women aging with HIV may encounter some additional challenges. For example, they may experience menopause at an earlier age relative to the general population and experience a higher burden of symptoms and metabolic changes associated with menopause [27-29]. In particular, psychological and vasomotor symptoms have been reported to be more common in women living with HIV [29]. As women with HIV transition through menopause, they face higher rates of osteoporosis, cardiovascular and cerebral vascular disease and impaired lipid and glucose metabolism [30,31]. Furthermore, symptoms related to HIV infection or its treatment can be mistaken for menopause, such as night-sweats, sleep disturbances, menstrual cycle irregularities or vaginal dryness [27]. Conditions associated with HIV infection, including tuberculosis and lymphoma, can present with symptoms similar to menopause and should be considered in the right clinical context. Finally, it is important for clinicians to recognize that as women age, they may be at an elevated risk for HIV transmission due to thinning of the vaginal and cervical mucosa with menopause, immunological changes in the cervix, and reduced condom use when contraception is no longer a concern [32,33].

### **Geriatric Syndromes**

Geriatric syndromes are multifactorial conditions used to identify vulnerable older adults and include conditions such as falls, frailty, functional and cognitive impairment [34]. Traditional risk factors for developing geriatric syndromes include psychosocial factors such as social isolation and substance use, as well as medical factors including multimorbidity, polypharmacy and chronic inflammation -

factors that are common in the aging HIV population. Consequently, geriatric syndromes among PLWH have been reported to occur at the same rates but several years earlier than in the general population [34]. Lower nadir CD4 count was associated with increased risk of developing geriatric syndromes, revealing a potential target for intervention unique to PLWH in addition to traditional risk factor modification. As the aging HIV population grows, we need to consider how to deliver comprehensive care to this population, including assessment, prevention and management of geriatric syndromes.

### Long-Term Healthcare Facilities

PLWH currently represent a small proportion of individuals living in Long-Term Care (LTC) or complex continuing care facilities, however, as the HIV population ages these numbers are expected to increase [35]. In general, healthcare providers working in these facilities have little experience caring for PLWH. It has been recognized that managing comorbidities, mental health issues and polypharmacy among PLWH entering LTC facilities may be especially challenging and services will need to be adapted to address the needs of this population [36]. Furthermore, issues of stigma can be amplified as individuals enter LTC facilities. Many will experience anticipated and enacted stigma as they reveal their HIV status while trying to create new social networks, negatively affecting their psychological well-being and contributing to increased social isolation [37]. Institutional policies that empower PLWH to maintain their existing social supports, which are often informal and fragile, as they enter LTC, can be protective against the effects of stigma [36,38]. There are ongoing efforts to educate LTC providers about the unique needs of PLWH and the expected progression of illness, with the goal of promoting compassionate and informed care for this population [39].

### Conclusion

People are living longer with HIV but they tend to develop medical comorbidities earlier and more frequently than those in the general population, resulting in fewer healthy years. Delayed treatment initiation is especially detrimental in the aging HIV population and therefore early detection needs to be prioritized through screening. As people age, preventative care and risk factor modification become integral components of HIV care in addition to management of geriatric syndromes.

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### Conflicts of Interest

The authors declare no conflicts of interest.

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