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HIV and Ageing: Improving Quantity and Quality of Life

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Abstract

Purpose of Review—Evidence-based strategies are needed to address the growing complexity of care of those ageing with HIV so that as life expectancy is extended, quality of life is also enhanced.

Recent Findings—Modifiable contributing factors to the quantity and quality of life in adults ageing with HIV include: burden of harmful health behaviours, injury from HIV infection, HIV treatment toxicity, and general burden of age-associated comorbidities. In turn, these factors contribute to geriatric syndromes including multimorbidity and polypharmacy, physiologic frailty, falls and fragility fractures, and cognitive dysfunction, which further compromise the quality of life long before they lead to mortality.

Summary—Viral suppression of human immunodeficiency virus (HIV) with combination antiviral therapy (cART) has led to increasing longevity but has not enabled a complete return to health among ageing HIV-infected individuals (HIV+). As adults age with HIV, the role of HIV itself and associated inflammation, effects of exposure to antiretroviral agents, the high prevalence of modifiable risk factors for age-associated conditions (e.g. smoking), and the effects of other viral coinfections are all influencing the health trajectory of persons ageing with HIV. We must move from the simplistic notion of HIV becoming a “chronic controllable illness” to understanding the continually evolving “treated” history of HIV infection with the burden of age-associated conditions and geriatric syndromes in the context of an altered and ageing immune system.

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Conflict of Interest

Dr. Justice reports no conflict of interest. Dr. Reiss through his institution has received independent scientific grant support from Gilead Sciences, Inc., Janssen Pharmaceuticals Inc, Merck & Co, Bristol-Myers Squibb and ViiV Healthcare; he has served on scientific advisory board for Gilead Sciences, Inc.; he serves on data safety monitoring committee for Janssen Pharmaceuticals Inc; chaired a scientific symposium by ViiV Healthcare, for which his institution has received remuneration. Dr. Keri Althoff has served on scientific advisory boards for Gilead Sciences, Inc. Dr Mikaela Smit received consultancy fees from Gilead Science to present at the Advisory Board and HIV team meeting, and is receiving through her institution scientific grant support from Gilead Science.

Keywords

HIV; ageing; multimorbidity; patient centered care; polypharmacy

INTRODUCTION

Where ever effective antiretroviral therapy (ART) is available, people are ageing with HIV. The median age of HIV-infected adults has passed 50 years in the United States, and Canada, Australia and most of Europe are close behind. Similar trends are emerging in Latin America, the Caribbean, Sub-Saharan Africa, Asia, the Middle East, and North Africa.[1] Nevertheless, HIV-infected adults ≥50 years of age with suppressed HIV-1 RNA and free of AIDS-defining illnesses or comorbidities experience a shorter life expectancy than uninfected individuals.[2,3] Modifiable contributing factors to the quantity and quality of life in adults ageing with HIV likely include: burden of harmful health behaviours, injury from HIV infection, HIV treatment toxicity, and general burden of age-associated comorbidities. In turn, these factors contribute to geriatric syndromes including multimorbidity and polypharmacy, physiologic frailty, falls and fragility fractures, and cognitive dysfunction, which further compromise quality of life long before they lead to mortality. Evidence-based strategies are needed to address the growing complexity of care of those ageing with HIV so that life expectancy can be extended and quality of life can be preserved.

FACTORS INFLUENCING AGEING WITH HIV

Although adults ageing with HIV are subject to the same risk factors for age-related diseases and conditions as uninfected adults, they differ in prevalence of harmful health behaviours. They also experience ongoing HIV-associated inflammation and immune activation[4] and adverse effects of chronic exposure to ART likely leading to excess organ system injury.[5] The extent to which this excess is expressed in cellular ageing, including cellular senescence, mitochondrial dysfunction, telomere attrition, and epigenetic alteration remains an area of active research.[6,7]

Weight gain after ART initiation

While HIV-infected adults tend to be less obese than uninfected adults,[8] the prevalence of obesity has increased over time, and is associated with the ageing HIV-infected population, earlier ART start and increasingly widespread ART coverage.[9,10] Weight gain following ART has been well documented[10,11], with increase in body mass index amongst HIV-positive patients in the first year on ART surpassing that of demographically-matched uninfected comparators.[10,11] This weight gain is likely due in part to decreased metabolic demand from ART-induced viral suppression coupled with ART-induced fat accumulation and potential changes to appetite.[12] However, weight gain after ART should be avoided among those who are overweight or obese as it is not independently associated with improved survival.[11] Further, ART-associated weight gain is associated with incident cardiovascular disease (CVD), diabetes and higher waist circumference and lower hip circumference may mediate the association between HIV and frailty in HIV-infected adults.[13,14]

Increased visceral adipose tissue (VAT) is particularly problematic. Even with current ART medications, VAT increases by 25–35% in the two years following ART initiation.[15] Elevated VAT and peripheral lipoatrophy are associated with CVD risk and risk between VAT and CVD is higher in HIV-infected compared to uninfected adults irrespective of VAT-level.[16] Further, renin-angiotensin-aldosterone system activation associated with VAT accumulation contributes to insulin resistance in HIV infection,[17] which likely contributes to the excess risk of diabetes associated with weight gain after ART initiation (Herrin).

Further, although information on short-term risk of side effects is required for antiretroviral drug licensing, longer-term effects must be evaluated once a drug is in clinical use. Certain antiretroviral drugs may contribute to the risk of comorbidites via related toxicity and metabolic pathway activation. For example, abacavir and some protease inhibitors (PIs) have been associated with cardiovascular risk,[18] PIs have also been associated with insulin resistance and diabetes.[19,20]

Harmful health behaviours

Smoking, alcohol, and substance abuse all represent modifiable risk factors for comorbidities. HIV-infected adults on ART in Europe and the United States may lose more life years through smoking than through HIV.[21] Alcohol is associated with an excess risk of physiologic frailty and mortality among HIV-infected compared with uninfected adults, even at low levels.[22] Further, HIV-infected adults are not exempt from the epidemic of opioid abuse which is being fueled by a growing abundance of opioid prescriptions, and is a particular problem in the United States.[23] Opioid-associated mortality is higher in older compared to younger adults, irrespective of HIV status.[24] The paper by Kathy Petoumenous et al in this issue outlines the association between HIV, substance abuse and survival in more detail.

COMORBIDITIES: AGE- AND HIV-ASSOCIATED NON-AIDS CONDITIONS

Among those ageing with HIV, increased life expectancy has been accompanied by dramatic decreases in AIDS-related morbidity and mortality and an excess burden of comorbidities compared with uninfected demographically similar adults.[25–28] The TEMPRANO and START trials have demonstrated that immediate ART initiation can reduce the incidence of comorbidities compared to deferred treatment initiation, pointing to the role of long-term immune activation and inflammation.[29,30] Of note, while those with HIV are at greater risk of comorbidites across age strata and while certain cellular markers may suggest more rapid “ageing,” comorbid events do not appear to occur dramatically earlier.[26,31] In fact, and perhaps even more worrisome, differences in risk may grow with age.[26]

Cardiovascular disease (CVD)

The risk of myocardial infarction (MI), for example, is 1.5- to 2-fold higher among HIV-infected adults without any major CVD risk factor than uninfected adults, and even higher amongst those with HIV and CVD risk factors;[25,32] it is possible that the relative risk of MI is changing over time in HIV-infected adults.[33] ill Detectable HIV-1 RNA has been associated with CVD in HIV-infected adults.[34] Risk prediction models for CVD specific to

HIV-infected adults, such as the D:A:D CVD risk model, take into account HIV-related risk factors (e.g. CD4 count and ART regimens) and have demonstrated superior risk prediction of myocardial infarction compared to the Framingham and ATP3 risk scores, both developed in the general population.[35,36] The 2013 American College of Cardiology/American Heart Association atherosclerotic CVD (ASCVD) risk prediction model however, which was developed in the general population and is used to determine likelihood of benefit from statin treatment, has recently been shown to be a better model for discriminating those with high and low risk compared to the D:A:D model.[36] However, the ASCVD model suffers from issues with calibration when applied to HIV-infected adults, resulting in underestimates of high CVD risk and underutilization of statins.[37] A new clinical trial, REPRIEVE (Randomized Trial to Prevent Vascular Events in HIV), will test the impact of pitavastatin on primary prevention of CVD among people with HIV at low to moderate *a priori* CVD risk.[38]

Cancer

Non-AIDS cancers are now the leading cause of death among HIV-infected individuals in care[27] and a major source of morbidity for people ageing with HIV. Virally associated cancers, including hepatocellular, anal, oropharyngeal, cervical cancer, and Hodgkin's lymphoma, represent a significant burden of disease among those ageing with HIV. Anal cancer remains high, particularly in men-who-have-sex-with-men, and is linked to infection with human papillomavirus and possibly time on PI-based regimens.[39,40] The new multi-centre trial, ANCHOR, will help determine if treatment of pre-cancerous lesions among those with HIV can prevent anal cancer from developing.[41] In addition, age-related cancers increasingly contribute to cancer burden among those with HIV.[42] HIV-infected adults have a disproportionate burden of lung cancer, and HIV has been found to be an independent risk factor for lung cancer after adjustment for smoking and other risk factors.[43]

Liver Disease

Risk of liver disease is elevated among HIV-infected adults without viral hepatitis. The risk of hepatocellular cancer, a major form of cancer among those with HIV, only occurs among those with pre-existing liver fibrosis and most typically, advanced fibrosis or cirrhosis. ART medications can exacerbate liver injury through multiple mechanisms including metabolic host-mediated injury (tipranavir), hypersensitivity (abacavir and nevirapine), and mitochondrial toxicity (didanosine, stavudine, and zidovudine).[44]

Additionally, the odds of having hepatitis C virus (HCV) infection are six time higher in people living with HIV than in those without HIV.[45] Co-infection with HCV has a synergistic effect on liver injury leading to more rapid progression of cirrhosis which is slowed, but not neutralized, after ART initiation.[46] Highly effective direct-acting antivirals for HCV[47] may slow progression of fibrosis but the impact of direct-acting antivirals on the long-term risk of hepatocellular carcinoma remains to be established. The paper by Klein et al in this issue outlines the association between HIV and HCV in more detail. Co-infection with hepatitis B is also relatively common, especially in Asia. Its effects in association with HIV are less well understood, but may be contributing to the risk of hepatocellular cancer.

Renal insufficiency

Renal insufficiency, a major risk factor for drug toxicity and CVD, is a contra-indication for several antiretroviral drugs, including tenofovir disoproxil fumarate. Renal insufficiency is likely multifactorial including decreasing renal function with age, greater genetic susceptibility to renal disease among those of African descent and renal toxicity related to long-term use of ART. Tenofovir alafenamide, which has demonstrated similar efficacy in suppressing HIV but an improved renal safety profile compared to tenofovir disoproxil fumarate, may help preserve renal function but will need to be evaluated in long-term studies.[48] Finally, lower CD4 cell counts are associated with a greater risk of renal disease progression and ART (excluding tenofovir disoproxil fumarate) appears to ameliorate some of this risk.[49,50]

Pulmonary disease

Lung diseases associated with HIV after accounting for smoking include pulmonary hypertension, bacterial pneumonia, and Chronic Obstructive Pulmonory Disease (COPD).[51] Infection with HIV, especially with lower CD4 cell count, is an independent risk factor for acute exacerbations of COPD,[52] and is also associated with reduced diffusing capacity.[53] While a relatively rare event in the general population, pulmonary arterial hypertension occurs 1,000-fold more commonly among those with HIV for reasons that are not well understood. Lung disease in HIV has a major impact on symptom burden, functional status, and frailty.[54,55] Vaccination may be an important part of resilient ageing in those ageing with HIV; pneumococcal vaccination of those with HIV infection offers protection against pneumonia.

Depression

An estimated 13% of HIV-infected adults experience major depression.[56] Depression has been linked to reduced retention in care[57] and reduced cognitive performance.[58] Traditionally, depression has been associated with stigma in HIV-infected populations.[59] In the geriatric population additional triggers for depression may include social isolation and additional stresses, such as ill health and stress caused by the loss of a loved one. A recent study showed significant discrepancy in physician perception and self-reported depressive symptoms and called for mandatory depression screening in all HIV-infected adults.[60] Measuring depression is challenging, with many options for screening, diagnosis, and rating symptoms and the need to account for cultural considerations. Bipolar disorders and schizophrenia may interact with depression. Depressive symptoms in people with HIV with bipolar disorder have been associated with poor psychotropic medication adherence.[61] Both bipolar disorder and schizophrenia have also been linked to poor adherence to ART in HIV-infected adults.[62] Some ART medications may also contribute; there remains controversy concerning efavirenz and suicide with a recent analysis suggesting a two-fold increased risk.[63]

GERIATRIC SYNDROMES

The increased burden of comorbidities in adults ageing with HIV requires a shift in the HIV care paradigm from targeted disease-specific management to a holistic, geriatrics-based,

approach (Figure 1). The goal in geriatric care is not exclusively one of extending survival. It is instead focused on also maintaining quality of life for as long as possible. Geriatric syndromes are characterized by multifaceted aetiologies and recursive associations; for example, multimorbidity leads to polypharmacy. Polypharmacy can lead to declines in neurocognitive performance, which can contribute to falls and fragility fractures causing pain, additional psychoactive medication, and increased polypharmacy.

Multimorbidity and polypharmacy

Multimorbidity and polypharmacy go hand-in-hand. Multimorbidity, defined as "multiple, potentially interacting, medical and psychiatric conditions," is a geriatrics-rooted concept with applicability to ageing with HIV.[64] Multimorbidity is typically measured as a count of the number of comorbid conditions, which makes multimorbidity a function of the number of conditions considered.[64] Multimorbidity is both a result of risk factors for individual HIV and age-related conditions, as well as the propensity for one condition to increase the risk of others. As the number of conditions increases, so does the proportion of individuals taking multiple medications (polypharmacy). Patients on 5 or more medications experience a significant number of medication-related adverse effects.[65] Among HIV-infected individuals 50 years or older with access to care, polypharmacy is becoming the norm in North America.[66–68] Approximately a third of long-term HIV-infected adults in Canada are taking 5 or more medications.[66] In contrast, in the Netherlands only 5% of all patients in care are taking 3 or more medications in addition to ART and these proportions increase with age[64] and will likely increase with time.[67] Opioid and benzodiazepine medications are particularly problematic and confer an independent association with mortality after adjustment for severity of illness and for number of chronic medications.[69]

A recent modelling study forecasts that multi-morbidity amongst HIV-infected adults in Europe will increase to 84% by 2030, with 54% using multiple medications, and CVD contributing the largest burden.[67] Harms of multimorbidity and polypharmacy include: 1) complicated drug interactions (with other drugs and with alcohol and substance use), 2) a potential decrease in ART adherence due to confusion of medication dosing and timing and/or medication fatigue, 3) cumulative toxicity, 4) mortality and 5) expense. Successful management of multimorbidity and polypharmacy will be vital for future HIV care. A proposed framework for managing polypharmacy in people ageing with HIV includes 1) an annual medication reconciliation, 2) assessment of tobacco, alcohol, and substance use, 3) a risk and benefit assessment and ranking of medications, and 4) prioritization with patient input.[68] As a result of multimorbidity and polypharmacy, ageing HIV-infected adults are likely to suffer from the geriatric syndromes discussed below.

Functional decline

Decline in physical performance can be reflected in slow gait speed and weak grip strength, both of which appear to be predictors of disability, morbidity and mortality in the general population. Faster rate of decline and an increased risk for slow gait speed have been observed among HIV-infected compared to uninfected men.[70] Functional impairment, including gait speed and grip strength, has been associated with low muscle mass and loss of

bone density in those ageing with HIV.[71] Increased physical activity are recommended for reducing functional impairment among those ageing with HIV.[72]

Cognitive dysfunction

Cognitive dysfunction in HIV is multifaceted in nature and dysfunction is estimated to effect as many as half of HIV-infected adults.[73] Contributing factors associated with cognitive dysfunction may include HIV itself including serious immune-deficiency, on-going substance use, neurocognitively active medications, depression, and multimorbidity.[74,75] Changes in brain structure have been correlated with cognitive impairment in HIV-infected adults,[73] with a recent study in suppressed HIV-infected and uninfected adults showing that microstructural abnormalities were more common in HIV-infected adults.[76] Most recently, a novel high-resolution subcortical shape analysis technique was found to be more sensitive to associations between brain volume and CD4 counts as well as neurocognitive scores over traditional whole volume subcortical analyses.[77] As people age with HIV beyond 65 years of age we will likely see substantially more cognitive dysfunction with consequence for HIV care, including lower adherence to ART[78] and reduced retention.[57,58] Alzheimer's disease and vascular dementia will likely play an increasing role.

Frailty

Frailty, another geriatric syndrome, is commonly defined as a loss of physiologic reserve and increased vulnerability to negative health outcomes. Many recent studies have shown an increased prevalence of frailty in HIV-infected compared with uninfected adults.[14,79] Frailty has commonly been measured using the Fried criteria (≥3 of the following criteria: weakness, slowness, unintentional weight loss, exhaustion, and low physical activity), which were developed and validated in a general population sample age 80 years or older,[80] and there is controversy regarding how to operationalize this definition among people ageing with HIV. [79]

Alternative measures of frailty include the Rockwood index and the Veterans Aging Cohort Study (VACS) Index (http:vacs.med.yale.edu). While the former is based on accumulation of deficits, and has not been widely applied amongst ageing adults with HIV[81] the VACS Index was developed specifically for HIV-infected adults and is based on an accumulation of physiologic deficits. The VACS Index incorporates age and biomarkers specific for HIV and for liver, renal, and bone marrow disease. Further, the VACS Index has been associated with physiologic frailty,[82–84] cognitive performance,[74] functional status,[85] hospitalizations,[86] and inflammatory markers [87,88] and reproducibly estimates the probability of all-cause mortality among HIV infected individuals.[89,90] The VACS Index is also a good predictor of cardiovascular mortality and can improve clinical assessment of mortality risk even when all the component measures are available.[91,92] It is increasingly used in HIV clinical settings to guide decision-making as to the frequency of medical follow-up, clinical risk assessment and end of life planning.

Falls and fractures

Falls and fractures are important health outcomes that have been linked to multimorbidity, polypharmacy, functional impairment, CVD, diabetes, HCV co-infection, and tenofovir

disoproxil fumarate use.[82,93–96] Markers of HIV-infection (CD4 count, viral load), however, have not been associated with falls.[727270] Interestingly, the perception of balance has been associated with falls in HIV-infected men.[97] Alcohol and other substance use likely contribute substantially to risk of falls and fractures. Proton pump inhibitors, a commonly used medication to reduce gastric acid production, have negative effects on bone health (and have also been linked to an increased risk of chronic kidney disease).[98] A single infusion of zoledronic acid, a long-acting bisphosphonate for the treatment of osteoporosis, at ART initiation was shown to prevent ART-induced bone loss.[99] However, the long-term effects of bisphosphonates, the first-line therapy for low bone mineral density, as well as the impact of calcium and vitamin D supplementation to prevent bone disease, are unknown in HIV-infected adults.

CONCLUSION

As disease patterns become more complex among those ageing with HIV, HIV care will need to carefully consider how to appropriately prioritize prevention, screening and treatment (see Text Box and Figure 1) and clinical research will need to embrace the complexity of ageing with HIV (see Text Box and Figure 1) to maintain a high quality of life while continuing to extend survival.

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Key Points

- Ageing with HIV is characterized by multimorbidity and polypharmacy, which is strongly influenced by chronic infection with HIV.
- Many factors influence quality and quantity of life in this group, HIV-1 RNA suppression is the first therapeutic goal, but many other management issues follow.
- Attention to mental health, geriatric syndromes, maintaining physical activity, and avoiding excess weight gain after ART are advised.

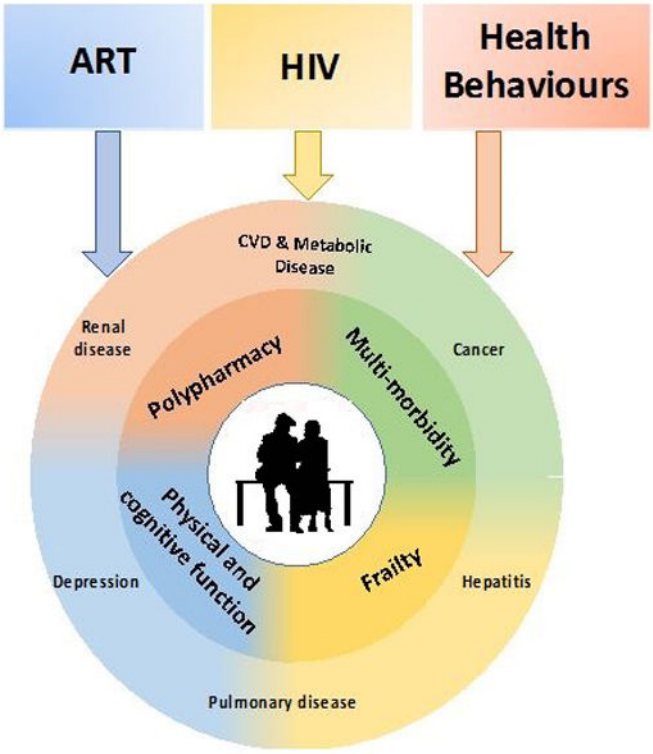

Figure 1.

Moving from standard care of ageing HIV-positive patients to care that incorporates key geriatric principles. The boxes illustrate elements amongst HIV-positive patients that may further contribute to disease and condition in ageing. Within the circle are the levels of clinical/medical elements that patients may suffer from as they age with HIV.

Depiction of the complexities of aging with HIV and caring for this population.

Table 1

Integrated Care for those Aging with HIV

To ensure improved survival and quality of life for those ageing with HIV, we recommend integrating the following principles into HIV care:

- **Earlier HIV diagnosis and treatment.** Early initiation of treatment is thought to reduce HIV-related inflammation, as reflected by current guidelines. HIV screening, including screening in older populations, is needed to identify unknown infection and initiate ART.
- **Earlier HCV diagnosis and treatment.** Due to the impact of HCV on HIV disease trajectory, diagnosis of HCV and treatment using direct acting antivirals for HCV viral eradication is important for successful ageing with HIV.
- **Screening for and treatment of comorbidities**. It will be important to ensure regular screening of HIV-infected individuals for comorbidities with important clinical impact including metabolic syndrome, organ system disease, and cancer.
- **Proactively manage weight gain after ART initiation.** Weight gain after successful ART is inevitable if eating and exercise habits remain unchanged. Weight gain after ART initiation among those who are overweight or obese confers no survival advantage and increases risk of diabetes and metabolic disease. Normal weight patients initiating ART should be advised to gain no more than 7–10 pounds and overweight or obese patients should avoid weight gain. Nutritional counselling once HIV-1 RNA is suppressed may be helpful.
- **Emphasize the importance of physical activity.** Physical activity is not only needed to control weight, but also to build and maintain muscle mass for physical function and falls prevention, and improve cognition and mental health. In consultation with a physical therapist, consider providing the patient with an “exercise prescription” using resources readily available to the patient.
- **Eliminate substance use.** Treatment for substance use and relapse should be a top priority. Tobacco and alcohol use are major risk factors for many age-related diseases. Smoking cessation, alcohol and substance use treatment programs will be increasingly important means of preserving health in HIV-infected individuals. Treatment for alcohol and opioid abuse and smoking cessation programs for younger HIV-infected adults are needed to preserve health at older ages.
- **Actively manage polypharmacy.** Regular medication reconciliation with identification of potentially inappropriate medications is essential as those with HIV age to avoid drug fatigue, serious interactions, hospitalisation, and early mortality. Opioid prescription management will be critical to mitigating the effect of this epidemic on ageing with HIV.
- **Use tools to know when to intervene.** Various calculators and indexes exist which can be used in HIV care. The VACS Index, for example, can facilitate monitoring the overall health of HIV infected individuals, help inform intervals of follow up, and alert provider and patient to changes in the patient’s physiologic frailty that may require closer monitoring, a change in management, or a move to an assisted living facility or hospice.
- **Preparing care facilities for HIV-infected adults:** We must ensure an HIV-knowledgeable workforce in assisted living facilities and hospices that serve the general population.
- **End of life planning.** Many ageing HIV infected individuals will require end of life support, with facilities and providers trained in the care of those with HIV-infection.
- **Testing and adaptation of models of care.** Whether HIV clinics continue to be the medical home for adults ageing with HIV, or primary care teams step in to help manage the increasing complexity of care, patient-centered care, focused on the patient’s personal goals for quality of life, should be adapted and override an exclusive focus on survival.

Table 2

Research Recommendations

If we are to optimize care for those aging with HIV infection, we need substantially more information from studies that span the continuum from basic science to observational research to operations research to clinical trials. Questions that need to be addressed include:

- What are the conditions that drive morbidity and mortality for those aging with HIV?
  - How can we effective adapt and implement interventions that have worked for these conditions outside of HIV?
  - What systems of care are best suited to this task?
- What are the conditions for which those aging with HIV experience excess risk and why?
  - Are underlying mechanisms, or the balance of contributing mechanisms, for these conditions different for those aging with HIV than for those aging without HIV?
  - Do differences in mechanism or the balance of contributing mechanisms justify a different clinical approach?
  - What can these differences teach us more generally about the mechanisms behind these conditions in those aging without HIV?
- How does prolonged immune dysfunction interact with multiple chronic viral infections to lead to increased risk of virally-associated diseases?
  - Will HIV infected individuals successfully treated for HCV infection still experience higher rates of cirrhosis and hepatocellular cancer?
  - How can we more effectively treat HBV to avoid hepatocellular cancer?
- How do we characterize the phenotype(s) of aging with HIV so that we can provide the most appropriate packages of care services (monitoring, screening and treatment)? Modelling will provide important tools to develop tailored and evidence-based service integration and policy changes.

Table 3

Online Resources

The following are resources for additional information relevant to aging well with HIV and caring for those aging with HIV.

- The European AIDS Clinical Society and the US Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescences provides guidelines on HIV treatment, including prevention and management of co-morbidities in HIV infected individuals http://www.eacsociety.org/ https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/277/hiv-and-the-older-patient
- The Veteran Aging Cohort Study Index (VACS Index) http://medicine.yale.edu/intmed/vacs/welcome/vacsindexinfo.aspxv
- The Graying of AIDS project collates stories and accounts of survivors or adults who contracted HIV at older age, and provides resources on aging with HIV. http://www.grayingofaids.org/#
- JUSTRI is a training and resource initiative with a guide to ageing well with HIV. http://justri.org/about-us/about-justri/