

# What Does Aging with HIV Mean for Nursing Homes?

*This editorial comments on the article by Miller et al.*

Worldwide, more people are living, and aging, with human immunodeficiency virus (HIV) than ever before.<sup>1</sup> Combination antiretroviral therapy (ART) has changed HIV infection from a rapidly fatal disease to a chronic condition with an extended life expectancy. The North American AIDS Cohort Collaboration (NA-ACCORD) contributed Figure 1 that demonstrates the changing age demographic among men and women living and dying with HIV infection from 2001 through 2016. Of note, in 2001, 25.6% of HIV deaths occurred among those 50 years of age or older. By 2016, this proportion doubled. Further, this phenomenon is not unique to North America. By 2030, 73% of people living with HIV in Europe are projected to be 50 years of age or older.<sup>2</sup>

Despite these trends, few studies have described the impact of aging with HIV on nursing home utilization. One study, published in the current issue of this journal, focused on long-stay nursing home residents from 2001 to 2010 and compared HIV-infected with uninfected residents. "Nursing Home Residents by HIV Status: Characteristics, Dementia Diagnoses, and Antipsychotic Use" by Susan C. Miller and colleagues used population-based Medicaid and Minimum Data Set data from 14 states with the highest HIV prevalence and found that the prevalence of long-stay residents (>89 d) with HIV increased 71% from 2001 to 2010.<sup>3</sup> In the highest prevalence states of New Jersey, Louisiana, Florida, New York, and Maryland, the absolute proportion of nursing home residents living with HIV exceeded 2% by late 2008. If these trends have continued, nearly 4% of long-stay nursing home residents in these states are now people living with HIV (PLWH). Compared with long-stay nursing home residents without HIV infection, PLWH were 10 to 20 years younger, and dementia was more common in younger residents (among residents older than 65 years, 20% HIV-positive patients had dementia vs 16% uninfected).

Miller et al also found a greater use of antipsychotics among younger HIV-infected residents compared with younger uninfected residents. The fact that PLWH in nursing homes may be more likely to receive a potentially inappropriate medication (PIM) such as an antipsychotic, is concerning. The harmful effects of PIMs may be intensified among those aging with HIV. Those aging with HIV have greater levels of physiologic injury reflected in poorer liver, renal, and bone

marrow function,<sup>4,6</sup> making them more susceptible to adverse events associated with polypharmacy.

Of note, antiretroviral medications (ARVs) have important neurocognitive side effects and drug interactions. Among younger subjects, in the HIV-CAUSAL collaboration, a higher CNS Penetration Effectiveness score of the ARVs was associated with a 74% increased risk for dementia.<sup>7</sup> Specific ARVs were associated with adverse neuropsychological events and neurocognitive impairment.<sup>8</sup> Nucleoside reverse transcriptase inhibitors may lead to mitochondrial toxicity of neurons that can then cause neuropathy, psychosis, depression, and mania.<sup>8</sup> Nonnucleoside reverse transcriptase inhibitors, most notably efavirenz, are also associated with adverse central nervous system drug effects including sleep disturbances, vivid dreams, depression, and cognitive impairments.<sup>9</sup> These side effects and drug interactions have not been well studied among older PLWH.

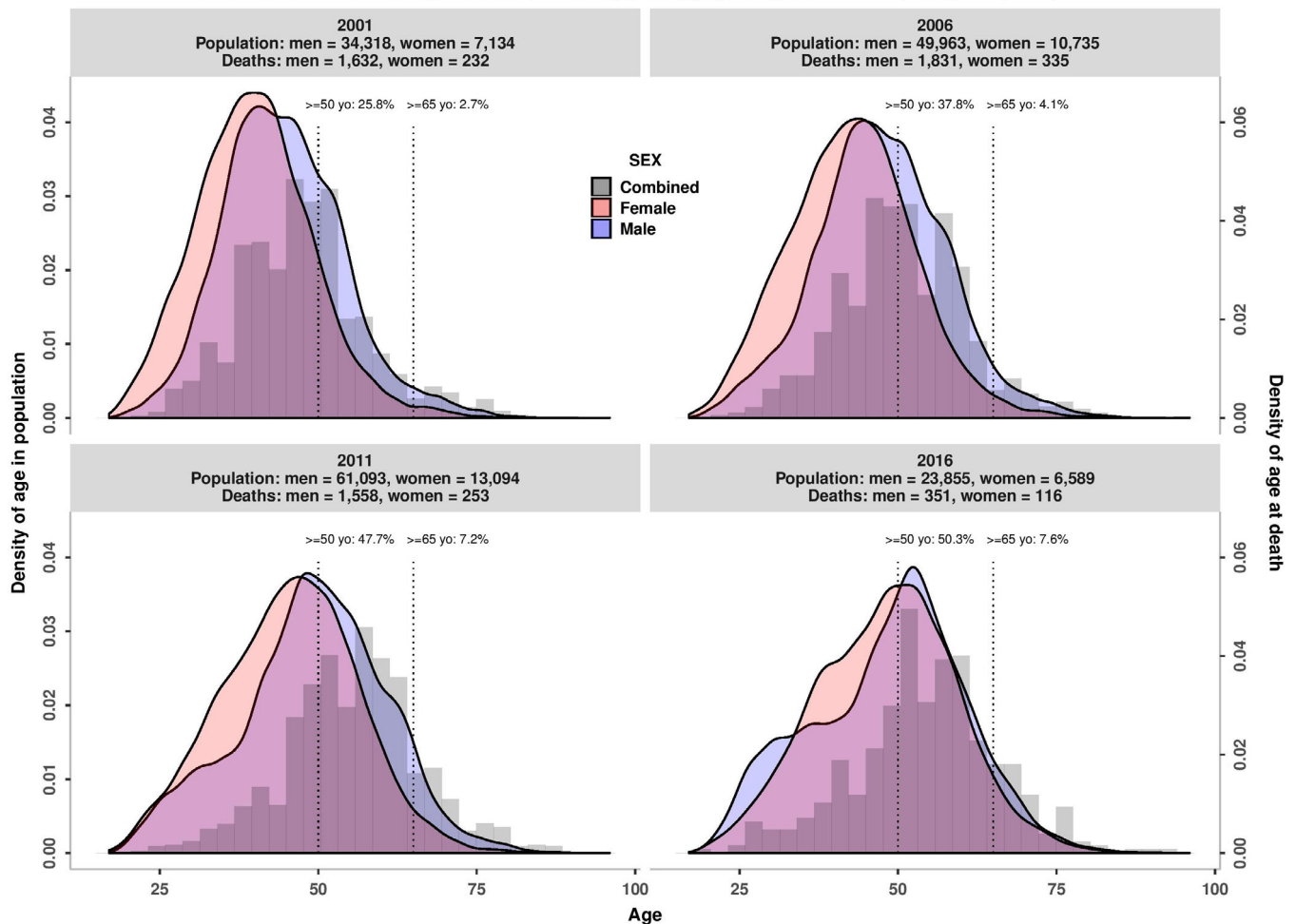
A recent complementary analysis to that of Miller et al used data on Medicare-eligible PLWH and focused on new nursing home admissions among PLWH, comparing admissions from 1998 to 2000 with those from 2011 to 2013.<sup>10</sup> Comparing the two time intervals, recent admissions of PLWH were 16 years older (60 vs 44 y), had twice the prevalence of viral hepatitis (16% vs 8%) and more anemia (31% vs 25%) but had less pneumonia (11% vs 14%) and less than half as much dementia (9% vs 21%). Taken together, these studies suggest that the proportion of PLWH admitted to and experiencing extended nursing home admissions is growing, that the difference in age at admission among PLWH and those without is narrowing, and that the profile of disease may differ in important ways by HIV status.

These initial studies on nursing home use among PLWH make valuable contributions but only begin to address the myriad medical, psychological, social, and societal issues surrounding HIV care in nursing homes. Aging with HIV is not just like aging without HIV. Liver and kidney disease are more common in PLWH in nursing homes than in uninfected individuals.<sup>10</sup> Many common forms of cancer including lung, anal, lymphoma, and hepatocellular cancer are more common among those aging with HIV.<sup>11</sup> The proportion of PLWH who develop end-stage diseases requiring transplant, dialysis, surgery, repeated rounds of chemotherapy, and/or radiation is likely to grow, and long-term placement for these levels of care may be particularly challenging.

Controlling for age, PLWH experience more intense levels of chronic inflammation, microbial translocation,

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**Figure:** Histograms depicting the changing age distribution in HIV care (primary y axis, blue and red curves) and the distribution of the age at death (secondary y axis, gray bars), NA-ACCORD, 2001, 2006, 2011, 2016



Participants in the observed histograms had =1 CD4 or HIV RNA measurement in the calendar year depicted to be included

**Figure 1.** Histograms depicting the changing age distribution of adults in HIV care (primary y-axis, men = blue and women = red) and the distribution of the age at death (secondary y-axis, gray bars), NA-ACCORD, 2001, 2006, 2011, and 2016. Blue-shaded histograms, corresponding to the primary y-axis, represent distribution of men by age for each observation year; pink-shaded histograms, corresponding to the primary y-axis, represent distribution of women by age for each observation year. Gray bars represent age at death corresponding to the secondary y-axis. yo, years old.

hypercoagulability, and immune dysfunction than their uninfected counterparts.<sup>12</sup> As a result of the sociodemographic factors and behaviors that put them at risk of HIV infection and as a result of the virus and its treatment, they experience multimorbidity, polypharmacy, and physiologic frailty earlier,<sup>13</sup> and they are more susceptible to its harms than uninfected counterparts.<sup>6</sup> In addition, many older individuals with HIV continue to feel stigmatized and suffer discrimination in settings less familiar with HIV and its modern care.<sup>14-16</sup> This may be particularly true in the nursing home setting where PLWH will continue to be a minority. Stigma can substantially limit engagement in medical care, adherence to ART, and quality of life among those aging with HIV infection. It may also prove a barrier to nursing home admission.

In addition, palliative medicine principles are essential to sustaining quality of life during aging. Providers and people aging with HIV need to consider how best to approach treatment preferences.<sup>17</sup> For PLWH in resource-poor areas, physical

symptom burden may be similar to that experienced by patients living with cancer and requires careful symptom assessment and management. In all settings, person-centered care should address spiritual needs and psychological suffering.

Finally, end-of-life planning is a topic that needs to be revisited in the era of effective ART therapy for HIV infection. Using data from the International Place of Death Study that included 11 countries, most PLWH die in the hospital and, compared with patients with cancer, PLWH are more likely to die in a nursing home (PLWH = 0.9-17.0% vs cancer = 1.0-10.8%).<sup>18</sup> It is reasonable to assume that many of these individuals would prefer to die in more familiar settings, surrounded by those with whom they have had extended, meaningful relationships. That requires more accurate prognostic assessment than can be achieved with CD4 cell count, HIV-1 RNA copies, and age. Using a wider set of physiologic measures,<sup>19,20</sup> it is possible to identify individuals nearing the end of life in the current treatment era.

In sum, much remains to be done if people with HIV are to be allowed to age with grace and dignity. Studies such as the one by Miller et al are a start. Let's get to work.

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## REFERENCES

- Wandeler G, Johnson LF, Egger M. Trends in life expectancy of HIV-positive adults on antiretroviral therapy across the globe: comparisons with general population. *Curr Opin HIV AIDS*. 2016;11(5):492-500.
- Smit M, Brinkman K, Geerlings S, et al. Future challenges for clinical care of an ageing population infected with HIV: a modelling study. *Lancet Infect Dis*. 2015;15(7):810-818.
- Miller SC, Daiello LA, Shireman TI, Wilson IB. Nursing home residents by HIV status: characteristics, dementia diagnoses, and antipsychotic use. *J Am Geriatr Soc*. 2018; <https://doi.org/10.1111/jgs.15949>.
- Akgun KM, Tate JP, Crothers K, et al. An adapted frailty-related phenotype and the VACS index as predictors of hospitalization and mortality in HIV-infected and uninfected individuals. *J Acquir Immune Defic Syndr*. 2014;67(4):397-404.
- Hotton AL, Weber KM, Hershov RC, et al. Prevalence and predictors of hospitalizations among HIV-infected and at-risk HIV-uninfected women. *J Acquir Immune Defic Syndr*. 2017;75(2):e27-e35.
- Justice AC, Gordon KS, Skanderson M, et al. Nonantiretroviral polypharmacy and adverse health outcomes among HIV-infected and uninfected individuals. *AIDS*. 2018;32(6):739-749.
- Caniglia EC, Cain LE, Justice A, et al. Antiretroviral penetration into the CNS and incidence of AIDS-defining neurologic conditions. *Neurology*. 2014;83(2):134-141.
- Treisman GJ, Soudry O. Neuropsychiatric effects of HIV antiviral medications. *Drug Saf*. 2016;39(10):945-957.
- Ciccarelli N, Fabbiani M, Di Giambenedetto S, et al. Efavirenz associated with cognitive disorders in otherwise asymptomatic HIV-infected patients. *Neurology*. 2011;76(16):1403-1409.
- Olivieri-Mui B, McGuire J, Cahill S, Griffith J, Briesacher B. People living with HIV in U.S. nursing homes in the fourth decade of the epidemic. *J Assoc Nurses AIDS Care*. 2019;30(1):20-34.
- Park LS, Tate JP, Sigel K, et al. Association of viral suppression with lower AIDS-defining and non-AIDS-defining cancer incidence in HIV-infected veterans: a prospective cohort study. *Ann Intern Med*. 2018;169:87-96.
- Althoff KN, Smit M, Reiss P, Justice AC. HIV and ageing: improving quantity and quality of life. *Curr Opin HIV AIDS*. 2016;11(5):527-536.
- High KP, Brennan-Ing M, Clifford DB, et al. HIV and aging: state of knowledge and areas of critical need for research. A report to the NIH office of AIDS research by the HIV and aging working group. *J Acquir Immune Defic Syndr*. 2012;60(Suppl 1):S1-S18.
- Katz IT, Ryu AE, Onuegbu AG, et al. Impact of HIV-related stigma on treatment adherence: systematic review and meta-synthesis. *J Int AIDS Soc*. 2013; 16(3 Suppl 2):18640.
- Stringer KL, Turan B, McCormick L, et al. HIV-related stigma among healthcare providers in the Deep South. *AIDS Behav*. 2016;20(1):115-125.
- Schuster MA, Collins R, Cunningham WE, et al. Perceived discrimination in clinical care in a nationally representative sample of HIV-infected adults receiving health care. *J Gen Intern Med*. 2005;20(9):807-813.
- Harding R. Palliative care as an essential component of the HIV care continuum. *Lancet HIV*. 2018;5(9):e524-e530.
- Harding R, Marchetti S, Onwuteaka-Philipsen BD, et al. Place of death for people with HIV: a population-level comparison of eleven countries across three continents using death certificate data. *BMC Infect Dis*. 2018;18(1):55.
- 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;33:903-912.
- Tate JP, Justice AC, Hughes MD, et al. An internationally generalizable risk index for mortality after one year of antiretroviral therapy. *AIDS*. 2013;27(4):563-572.