

The Influence of Race and Comorbidity on the Timely Initiation of Antiretroviral Therapy Among Older Persons Living With HIV/AIDS

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Current trends in the epidemiology of HIV in the United States indicate that older persons (≥ 50 years) are a burgeoning population affected by HIV.¹ The Centers for Disease Control and Prevention estimated that in 2009, older persons constituted 33% of all people living with HIV/AIDS (PLWHA).² Emerging data project that by 2020, half of all PLWHA will be aged 50 years or older.² Within this age group, persons aged between 50 and 64 years account for the majority (89%) of all HIV diagnoses.¹ As seen in the national data, racial/ethnic, gender, and regional disparities also exist in the HIV disease burden among older persons.^{1,3} Older African Americans and Hispanics are, respectively, 13 and 5 times more likely to receive an HIV diagnosis than are White Americans, and men are more likely to be diagnosed than are women.¹ The southern United States is disproportionately burdened by HIV cases occurring in this age group.^{1,3} Surveillance reports showed that the southern United States accounted for the greatest number of HIV cases among all older persons in 2010.^{1,3}

Besides the increased survival of PLWHA, various explanations have been offered for the HIV prevalence among older people in the United States. Older persons are more likely to underestimate their personal risk for contracting HIV and other sexually transmitted infections because they assume that HIV is an infection primarily affecting younger persons.^{4,5} Older women may also be more inclined to engage in unprotected sexual intercourse because of the minimal risk of pregnancy^{6,7} even though they are at increased risk for HIV during penetration because of the vaginal and cervical thinning that occurs during menopause.^{7,8} Ageism and stigma surrounding HIV testing in this age group^{7,9,10} as well as a failure of health care providers to inquire about and

Objectives. We examined whether the timely initiation of antiretroviral therapy (ART) differed by race and comorbidity among older (≥ 50 years) people living with HIV/AIDS (PLWHA).

Methods. We conducted frequency and descriptive statistics analysis to characterize our sample, which we drew from 2005–2007 Medicaid claims data from 14 states. We employed univariate and multivariable Cox regression analyses to evaluate the relationship between race, comorbidity, and timely ART initiation (≤ 90 days post-HIV/AIDS diagnosis).

Results. Approximately half of the participants did not commence ART promptly. After we adjusted for covariates, we found that older PLWHA who reported a comorbidity were 40% (95% confidence interval = 0.26, 0.61) as likely to commence ART promptly. We found no racial differences in the timely initiation of ART among older PLWHA.

Conclusions. Comorbidities affect timely ART initiation in older PLWHA. Older PLWHA may benefit from integrating and coordinating HIV care with care for other comorbidities and the development of ART treatment guidelines specific to older PLWHA. Consistent Medicaid coverage helps ensure consistent access to HIV treatment and care and may eliminate racial disparities in timely ART initiation among older PLWHA. (*Am J Public Health.* 2014;104:e135–e141. doi: 10.2105/AJPH.2014.302227)

provide information on safe sex to this population are other reasons for the high HIV infection rates.⁷ Other factors include greater avenues for sexual activity such as Internet dating sites that target older persons¹¹ and the increased availability of drugs for erectile dysfunction,^{2,7} both of which facilitate sexual partnerships among this age group. Lastly, older persons are too often left out of HIV prevention efforts, as the majority of HIV prevention programs target younger persons, African Americans, and men who have sex with men.^{12,13}

Antiretroviral therapy (ART) has significantly changed the clinical course of HIV and enabled the long-term survival of PLWHA. However, older PLWHA are more likely to rapidly progress to AIDS and have shorter survival times than are younger persons, although they are more likely to be ART adherent.^{14–17} Among persons aged 50 years or

older, African Americans and other minorities are also more likely to be diagnosed with HIV late in the course of the disease, contributing to disparities in HIV survival and mortality even with ART.^{1,2} Immune senescence^{18,19} and comorbidities^{20,21} are other factors unique to older PLWHA that may play a role in the clinical course of HIV. Studies have shown that older PLWHA have a less robust immunological response to ART, because of either diminished thymic function that occurs with aging or lower CD4 counts at baseline.^{18,19,22}

Comorbidities such as coronary artery disease; diabetes mellitus; hypertension; dyslipidemia; bone, liver, and kidney disease; chronic respiratory disorders; cancers; and psychiatric and neurocognitive conditions are common among older persons.^{23,24} HIV is also associated with increased prevalence of these comorbidities.²⁴ Comorbidities are more prevalent among older persons,

especially older PLWHA, than they are among younger populations.^{2,20,21,25} Comorbidities can complicate and accelerate the HIV disease process, manifesting as frailty, organ and functional impairment, and increased likelihood of hospitalization and death.^{2,24–26} The increased prevalence of comorbidities may impact the clinical management of HIV/AIDS.^{20,21} These comorbidities may interfere with the timing of ART initiation, disrupt ART metabolism, or require drug treatment that may interact with ART, complicating HIV/AIDS disease treatment and survivability.^{20,21} However, research on the influence of comorbidities on ART receipt and initiation among older PLWHA is sparse, with the findings of 1 study showing that comorbidities did not influence ART receipt.²⁷

Research examining the correlates of ART initiation or receipt has focused mainly on racial disparities in age-diverse populations.^{28–38} Although older PLWHA represent the growing face of HIV, are at higher risk for HIV disease progression, and have comorbidities that are likely to influence treatment decisions in this population, research examining the interaction of aging, race, and ART receipt and initiation is lacking. Because of this, we sought to determine the influence of race and comorbidity on the timely initiation of ART among older persons. We hypothesized that African Americans and persons with comorbidities would report delayed ART initiation.

METHODS

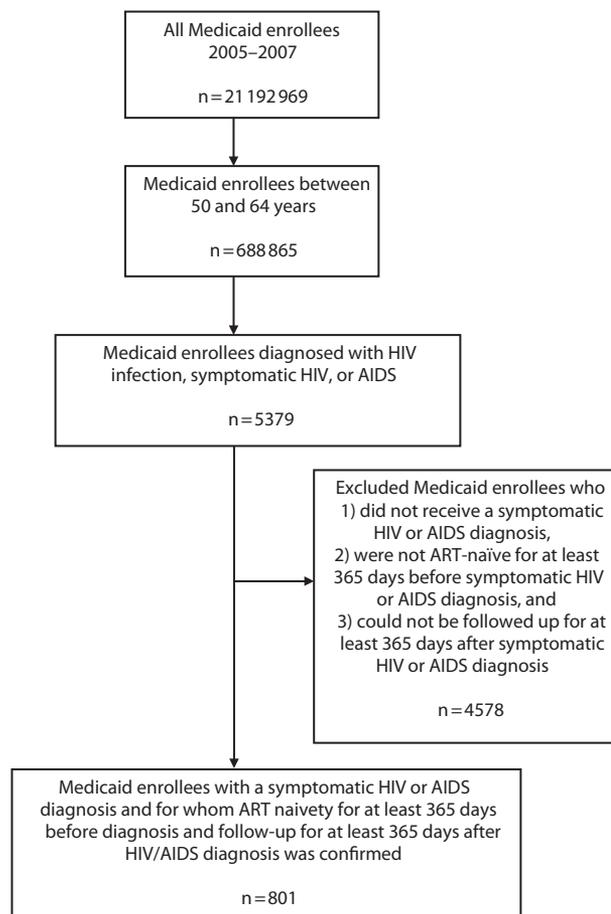
We used a retrospective cohort design with a study population that we abstracted from Medicaid claims data from 14 US states (Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, Missouri, North Carolina, South Carolina, Tennessee, Texas, and Virginia) between January 1, 2005, and December 31, 2007. Persons from these states account for approximately one third of all US Medicaid enrollees and about half of all African American Medicaid enrollees in the United States.³⁹ These states, mostly in the southern United States, also account for the greatest burden of HIV among older people.¹ Medicaid is also the largest source of health coverage for PLWHA.⁴⁰ We used Medicaid Analytic eXtract files, which are individual-level

data files on health care utilization and include personal summary (demographic and enrollment data), inpatient, outpatient, pharmacy, and long-term care files for all enrollees in each state for each calendar year.

Patient Selection and Measures

To be eligible for the study, participants had to (1) be aged between 50 and 64 years, (2) receive a diagnosis of symptomatic HIV or AIDS to be ART-eligible, and (3) be enrolled for at least 365 days before HIV/AIDS diagnosis to determine ART naïveté (medical records indicating no prior ART use) and 365 days after HIV/AIDS diagnosis to determine time to ART initiation. We excluded participants who did not meet all inclusion criteria. We selected participants aged between 50 and

64 years because most (89%) HIV/AIDS diagnoses occur in this age subgroup, and we wanted to minimize the number of dual eligible (Medicaid and Medicare) participants. Medicaid claims data do not include CD4 counts, so we limited study participants to those who had claims for symptomatic HIV disease or AIDS (*International Classification of Diseases, Ninth Revision, Clinical Modification*⁴¹ code O42). We used the date of symptomatic HIV or AIDS diagnosis as our index date because the clinical guidelines at the time the data were collected recommended ART initiation upon receiving either diagnoses.⁴² Figure 1 illustrates the participant selection criteria we used in this study. Of the approximately 21 million Medicaid enrollees from the 14 states in 2006, 688 865 were aged



Note. ART = antiretroviral therapy.

FIGURE 1—Flow diagram showing participant selection: Medicaid claims data, United States, 2005–2007.

between 50 and 64 years. Of this number, 5379 received a diagnosis of HIV/AIDS and 801 met our inclusion criteria.

The independent variables were race (White, African American, and other races) and comorbidity (yes and no) at time of HIV/AIDS diagnosis. We included gender (male and female), residential status (urban and rural), age, and state of residence as covariates. We measured age as a continuous variable. We categorized participants who identified as non-White or non-African American as other because of their small sample size.

We used the Elixhauser Comorbidity Index⁴³ to measure non-HIV-related comorbid medical conditions, using an algorithm developed by Quan et al.,⁴⁴ and categorized them into 2 groups on the basis of whether any comorbidity was reported (0 = no; ≥ 1 = yes). We determined residential status, a covariate, by merging the Medicaid Analytic eXtract data with county-level data from the Area Resource File—a health data resource that includes a compilation of publicly available data such as population, environmental characteristics, and geographical descriptors (urban

vs rural).⁴⁵ We included gender, residential status, and age as covariates because of their role as conceptual confounders in ART receipt and initiation,³³ and we included state of residence because of the varying state Medicaid eligibility criteria. Georgia was the reference state because it has one of the highest numbers and rates of persons living with a diagnosis of HIV.⁴⁶ Our outcome variable of interest was time to initiation of ART. We measured time to initiation of ART as a continuous variable (in days) and as a dichotomized variable (≤ 90 days or > 90 days). We chose this time point because of its use as a benchmark in determining early or late engagement in HIV care⁴⁷ and its use in previous research.^{48,49}

Analysis

We conducted frequencies and descriptive statistics to characterize the sample overall and by race. We employed the χ^2 test and analysis of variance to determine the association between race and categorical (gender, urban vs rural status, and comorbid status) and continuous (age) variables, respectively.

We used the Kruskal–Wallis test to evaluate whether time to ART initiation varied by race.

We conducted univariate and multivariable Cox proportional hazards regression analyses to examine the influence of race and comorbidity on time to initiation of ART. We estimated the unadjusted and adjusted hazard ratio (HR) for timely ART initiation and set a 2-tailed level of statistical significance at .05. We calculated a Kaplan–Meir survival curve to estimate the cumulative probability of ART initiation by race and comorbidity. We conducted all analyses with SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

Table 1 describes the characteristics of our study sample overall and by race. Our sample was predominantly (75.0%) African American; Whites made up 15.9%. The remainder (9.1%) included all other races combined (Asian, non-Hispanic White, and Native American). Of all study participants, 54.9% were male, 83.3% of participants resided in urban areas, and 8.5% reported at least 1

TABLE 1—Demographic Characteristics of Older People Living With HIV/AIDS Enrolled in Medicaid (n = 801) by Race: Medicaid Claims Data, United States, 2005–2007

Variable	Total, No. (%), Mean ±SD, or Median (Q1, Q3)	African American, Total, No. (%), Mean ±SD, or Median (Q1, Q3)	White, Total, No. (%), Mean ±SD, or Median (Q1, Q3)	Other, Total, No. (%), Mean ±SD, or Median (Q1, Q3)	P
Total	801 (100.0)	601 (75.0)	127 (15.9)	73 (9.1)	
Comorbidity ^a					
Yes	68 (8.5)	54 (9.0)	6 (4.7)	8 (11.0)	.21
No	733 (91.5)	547 (91.0)	121 (95.3)	65 (89.0)	
Gender ^a					
Female	361 (45.1)	279 (46.4)	48 (37.8)	34 (46.6)	.19
Male	440 (54.9)	322 (53.6)	79 (62.2)	39 (53.5)	
Residential status ^a					
Urban	667 (83.3)	513 (85.4)	102 (80.3)	52 (71.2)	<.01
Rural	134 (16.7)	88 (14.6)	25 (19.7)	21 (28.8)	
Age, ^b y	54.5 ±3.7	54.6 ±3.7	54.2 ±3.6	54.4 ±3.9	.52
Timely ART initiation ^a					
Yes, ≤ 90 d	397 (49.6)	289 (48.1)	64 (50.4)	44 (60.3)	.18
No, > 90 d	404 (50.4)	312 (51.9)	63 (49.6)	29 (39.7)	
Time to ART initiation, ^c d	96 (13, 365)	114 (13, 365)	66 (15, 365)	28 (7, 365)	.16

Note. ART = antiretroviral therapy; Q = quartile.

^a χ^2 test.

^bAnalysis of variance.

^cKruskal–Wallis test.

comorbid condition. The mean age of our study sample was 54.5 years. Only half of our ART-eligible participants initiated ART promptly (≤ 90 days). The median duration to ART initiation was 96 days overall but 114 days for African Americans, the longest duration of all racial groups. There were no significant differences in comorbid status, gender, age, and median time to initiate ART by race. However, African Americans were significantly more likely to report urban residence ($P < .01$).

Table 2 shows the unadjusted and adjusted HR of the univariate and multivariable Cox regression models. Race was not independently associated with time to initiation of ART in the univariate analysis, but comorbidity was. Participants who reported a comorbidity were significantly less likely to initiate ART promptly (HR = 0.43; 95% confidence interval [CI] = 0.29, 0.66; $P < .01$) than were participants who did not. Other covariates, including gender, residential status, age, and state of residence were not associated with prompt ART initiation. After we adjusted for covariates, there were still no differences in timely ART initiation by race but comorbidity remained significantly associated with timely ART initiation (HR = 0.40; 95% CI = 0.26, 0.61; $P < .01$).

ART-eligible participants without any comorbidity were 2.5 times as likely to initiate ART promptly upon receiving a diagnosis of HIV/AIDS. The covariates were not significantly associated with time to initiate ART. The Kaplan–Meier survival curve showed no racial differences in the ART initiation rate (Figure 2). Figure 3 illustrates the Kaplan–Meier survival curve, showing that older PLWHA without any comorbidity initiated ART at a more rapid rate than did older PLWHA with a comorbidity.

DISCUSSION

Older PLWHA are the changing face of HIV in the United States but have received less focused attention as a public health priority. Correspondingly, there is limited research examining deficits in prompt ART initiation by race and comorbidity despite their respective importance and prevalence in this population. Our data are among the first to demonstrate the influence of these factors on the timely initiation of ART among older PLWHA. We hypothesized that African Americans and participants with comorbidities would not initiate ART promptly. Contrary to our hypothesis,

the results of our study did not demonstrate any racial disparities in the prompt initiation of ART in our study sample. Our inability to detect racial disparities in this study could be attributed to numerous factors. Because our sample was drawn from Medicaid claims data, all study participants had consistent health insurance coverage and presumably the same level of health care access during the study period (2005–2007). Consequently, persons with barriers to accessing care, persons who disengaged from care during the study period, uninsured and underinsured persons, and other vulnerable groups (most of which include disproportionate minority representation) were underestimated or excluded from the study sample. The consistent source of health care in this population before HIV infection may have also facilitated health literacy, trust in health care providers, and motivation to commence treatment, consequently mitigating racial disparities in timely ART initiation in this study sample. Additionally, because Medicaid data contain only claims information, we could not include and control for key social determinants of health such as income, educational level, and employment status, all of which drive racial disparities.⁵⁰

Although no study to our knowledge has examined racial disparities in ART initiation or receipt among older persons exclusively, many studies have examined racial disparities in ART initiation and receipt on age-diverse populations with mixed findings. Consistent with our findings, some previous studies did not demonstrate racial differences in ART receipt or initiation^{28,31,32,51,52} and about half of ART-eligible persons commenced ART promptly.⁵² However, other studies have identified racial disparities in ART receipt or initiation, noting that African Americans and non-Whites were less likely than were Whites to initiate or receive ART.^{29,33–37} Most of the participants in the aforementioned studies were younger than 50 years. Our study therefore contributes to the existing literature on aging and HIV by examining the influence of race on the timely initiation of ART initiation among older PLWHA.

The findings also suggest that consistent access to HIV care, facilitated by Medicaid and other HIV/AIDS discretionary programs, may mitigate racial disparities in ART initiation. For

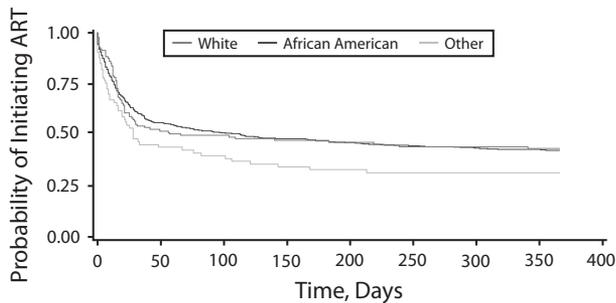
TABLE 2—Univariate (Unadjusted) and Multivariable (Adjusted) Cox Regression Models Showing Relationship Between Variables and Timely Antiretroviral Therapy Initiation Among Older People Living With HIV/AIDS: Medicaid Claims Data, 2005–2007

Variable	Unadjusted HR (95% CI)	Adjusted HR ^a (95% CI)
Race		
White (Ref)	1.00	1.00
African American	1.01 (0.78, 1.30)	0.98 (0.76, 1.28)
Other	1.40 (0.98, 2.02)	1.19 (0.82, 1.74)
Comorbidity		
No (Ref)	1.00	1.00
Yes	0.43* (0.29, 0.66)	0.40* (0.26, 0.61)
Gender		
Female (Ref)	1.00	1.00
Male	1.05 (0.88, 1.26)	1.13 (0.94, 1.37)
Residential status		
Urban (Ref)	1.00	1.00
Rural	1.13 (0.89, 1.44)	1.13 (0.87, 1.48)
Age	1.01 (0.98, 1.03)	1.01 (0.99, 1.04)

Note. CI = confidence interval; HR = hazard ratio.

^aAdjusted for state

* $P < .01$.

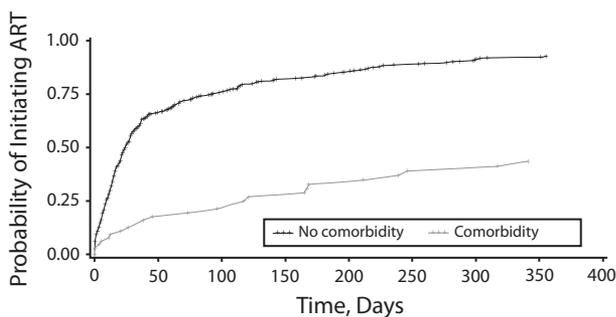


Note. ART = antiretroviral therapy.

FIGURE 2—Kaplan-Meier estimate of time to antiretroviral therapy initiation by race: Medicaid claims data, United States, 2005-2007.

example, a recent study on Medicaid enrollees who had consistent access to HIV care over time has demonstrated the absence of disparities between African Americans and Whites in ART receipt.⁵² Another study, by Moore et al., also attributed the absence of racial disparities in ART receipt in their study to consistent access to HIV care facilitated by the Ryan White Program.²⁸ Similarly, a study using participants in the US Military HIV Natural History Study, who had consistent access to HIV care, also noted the absence of racial disparities in ART initiation.⁵¹ Because of these findings, the decision by many states—particularly southern states with large racial/ethnic minority populations and high rates of HIV/AIDS—not to expand Medicaid and the uncertainty surrounding the future of the Ryan White Program will likely limit access to consistent HIV care and may hinder efforts at eliminating racial disparities in Medicaid nonexpansion states.⁵⁴

Another key finding was that older PLWHA with at least 1 comorbidity were more likely to report delayed ART initiation. This finding may be because of the risk of aggravating an existing organ dysfunction^{55,56} or concerns related to drug-drug (ART and comorbid medication) interaction.^{57,58} For example, tenofovir and emtricitabine, both HIV medications, are directly nephrotoxic and may worsen renal impairment.^{55,56} Atazanavir, another HIV medication, reduces the potency of warfarin, a blood thinner used in patients with atrial fibrillation,⁵⁷ whereas proton-pump inhibitors used in patients with gastroesophageal reflux disease decreases the absorption of atazanavir, hindering its effectiveness.⁵⁸ There are also no controlled data on the pharmacodynamics and pharmacokinetics of ART among older PLWHA; nor are there established treatment guidelines or recommendations for older PLWHA, especially those with comorbidities.⁴² All these factors may make health care providers



Note. ART = antiretroviral therapy.

FIGURE 3—Kaplan-Meier estimate of time to antiretroviral therapy initiation by comorbidity: Medicaid claims data, United States, 2005-2007.

reluctant to commence HIV treatment, resulting in delayed ART initiation among older PLWHA.

Because of the increase in comorbidities as people age, older PLWHA may receive care from multiple providers for their comorbidities (e.g., nephrologist, endocrinologist, cardiologist) in addition to their HIV care. Failure to integrate and coordinate medical care and medication history—a challenge across many aspects of the health care system—can lead to gaps and delays in care, including delayed ART initiation. Psychiatric comorbidities such as depression may also negatively affect the readiness and motivation of treatment-eligible patients to promptly commence ART.^{59,60} Comorbidities may therefore drive delayed ART initiation and, consequently, shorter survival times and elevated mortality among older PLWHA.

Our findings indicate that as the incidence and prevalence of HIV/AIDS among older people continues to grow, the impact of comorbidities on HIV treatment warrants additional attention. This might suggest the need for improved integration and coordination of care and medication prescription practices among all health care providers, similar to patient-centered medical homes or accountable care organizations to harmonize the management of HIV/AIDS and comorbidities without undermining HIV treatment efficacy.⁵⁴ Other services such as check-in appointments to allow dose adjustments and evaluate drug tolerance and medication substitution should also be incorporated into the routine health care of older PLWHA on ART. Leverage of electronic health records both within and across practices to ensure that older PLWHA initiate ART in a timely manner and are retained in care is critical to the optimal management of HIV/AIDS and other comorbidities. Finally, incorporating nonmedical modalities such as lifestyle modifications (e.g., exercise, healthy diet, and alcohol and smoking cessation) into the concurrent management of comorbidities in older PLWHA on ART in lieu of medications when applicable may prove beneficial.

Strengths and Limitations

As with any study, ours was subject to limitations. First, our data did not allow us to control for clinical indicators such as CD4 count and viral load, both of which may influence ART

initiation. Second, our data precluded us from controlling for variables such as income, educational level, employment status, HIV/AIDS stigma, mode of transmission, substance use, and stressful life events, variables that affect ART initiation and receipt.^{31,34,61,62} Additionally, because we used Medicaid claims data, we underrepresented older PLWHA who were uninsured or underinsured and those who had alternate insurance coverage. Finally, we used Medicaid claims data from enrollees in predominantly southern states, so our sample is not nationally representative. Persons receiving Medicaid must meet eligibility criteria, which is set by each state and therefore restricts Medicaid enrollees to certain categories of people. Thus, our sample may be neither representative of nor generalizable to all older PLWHA.

Despite these limitations, our study has its strengths. Our study is among the few that have examined factors influencing the timely initiation of ART in older PLWHA. Because most of the participants in our study were diagnosed with HIV/AIDS as older persons, we could determine ART naïveté and control for the aging cohort effect on our outcome.⁶³ Our study design was a retrospective, not cross-sectional, cohort study, which enabled us to establish temporal trends (from time of diagnosis and comorbidity to ART initiation) and conduct time-to-event analysis rather than associations. Finally, because we used Medicaid claims data, patients and health care providers were unaware that this information would be used for research, reducing the likelihood of reporter bias.

Conclusions

Our findings suggest that comorbidities affect timely ART initiation in older PLWHA. There were no disparities in ART initiation by race. Understanding that HIV tends to be diagnosed at a later disease stage in older persons and that only half of our study participants received ART promptly, it is critical that strategies to support prompt ART initiation be developed to prevent incident HIV infections, halt rapid clinical progression, and improve long-term survival.⁶⁴ To meet the challenges of the HIV epidemic and meet the objectives of the National HIV/AIDS Strategy,⁶⁵ HIV treatment and prevention efforts should include a targeted

focus on older adults. Health care providers should inquire about risk factors for HIV in older patients, promptly link older PLWHA to HIV care, and maintain coordinated care with specialty providers, especially for patients with comorbid conditions.

Emphasizing healthy lifestyle modifications and scheduling follow-up appointments to evaluate and manage concurrent comorbidities, drug tolerance, and drug adjustments are equally important. It is essential that older PLWHA with comorbidities receive coordinated care without undermining ART efficacy and timeliness. To this end, specific treatment guidelines for older persons are required. Finally, we call for further research to better understand the impact of aging on HIV and HIV treatment and to develop HIV/AIDS education and prevention interventions that target older persons. ■

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Contributors

W. E. Abara originated the study, developed the research question, and drafted the article. L. Smith assisted in drafting the article. S. Zhang ran data analyses. A. J. Fairchild and H. J. Heiman reviewed drafts of the article. G. Rust provided expertise in Medicaid data analysis, helped refine the research question, and reviewed a draft of the article.

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Human Participant Protection

This research was conducted with approval of the institutional review board of the Morehouse School of

Medicine, which also waived the requirement for individual informed consent.

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