

Dementias Among Older Males and Females in the U.S. Medicare System With and Without HIV

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Background: Despite the growing concern that people with HIV (PWH) will experience a disproportionate burden of dementia as they age, very few studies have examined the sex-specific prevalence of dementia, including Alzheimer disease and related dementias (AD/ADRD) among older PWH versus people without HIV (PWOH) using large national samples.

Methods: We constructed successive cross-sectional cohorts including all PWH aged 65+ years from U.S. Medicare enrollees and PWOH in a 5% national sample of Medicare data from 2007 to 2019. All AD/ADRD cases were identified by ICD-9-CM/ICD-10-CM diagnosis codes. Prevalence of AD/ADRD was calculated for

each calendar year by sex–age strata. Generalized estimating equations were used to assess factors associated with dementia and calculate the adjusted prevalence.

Results: PWH had a higher prevalence of AD/ADRD, which increased over time compared with PWOH, especially among female beneficiaries and with increasing age. For example, among those aged 80+ years, the prevalence increased from 2007 to 2019 (females with HIV: 31.4%–44.1%; females without HIV: 27.4%–29.9%; males with HIV: 26.2%–33.3%; males without HIV: 21.0%–23.5%). After adjustment for demographics and comorbidities, the differences in dementia burden by HIV status remained, especially among older age groups.

Conclusions: Older Medicare enrollees with HIV had an increased dementia burden over time compared with those without HIV, especially women and older subjects. This underscores the need to develop tailored clinical practice guidelines that facilitate the integration of dementia and comorbidity screening, evaluation, and management into the routine primary care of aging PWH.

Key Words: HIV, dementia, prevalence, aging, sex differences

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INTRODUCTION

Safe and effective combination antiretroviral therapy (ART) has prolonged life expectancy in people with HIV (PWH).¹ PWH 50+ years comprise more than half of all adults with HIV in the U.S., with those 65+ years showing the greatest growth.² Cognitive decline is more common in PWH than in people without HIV (PWOH). Studies have found that 20%–50% of PWH have at least mild neurocognitive impairment, even when they are taking suppressive ART.^{3–8}

Dementia is a major neurocognitive disorder that manifests as impairment in thinking, executive function, learning, social cognition, memory, language, and other cognitive functions severe enough to interfere with daily activities.⁹ Aging is the primary risk factor for dementia in the general population. The prevalence of Alzheimer disease (AD) and AD-related dementias (ADRD) doubles for every 5-year interval beyond age 65.¹⁰ Many aging-related comorbidities contributing to cognitive decline—such as cardiovascular disease, hypertension, diabetes mellitus, stroke, and depression—are more prevalent in PWH.^{11–14} Other risk factors, including substance use, low education, social isolation, and sedentary lifestyle, are also more common in PWH.¹⁵ In addition, PWH are exposed to

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HIV-related biomechanisms of neurologic change, including a persistent state of low-grade inflammation,^{16,17} cumulative exposure to ART,^{18–21} and increased aging-related comorbidities,^{11–14} which may augment the progression of dementia. These factors increase the concern that PWH will experience a disproportionate burden of dementia as they age.

Very few studies have examined trends in the prevalence of dementia among older PWH compared with PWOH using large national samples. One recent study examined 13,296 older PWH on ART and demographically similar PWOH who received care at Kaiser Permanente healthcare systems between 2000 and 2016. Although both groups experienced increases in dementia prevalence, the overall prevalence of dementia was higher among PWH.²² The model adjusted for a selected set of comorbidities focusing on cardiovascular disease risk factors and depression. No sex-stratified data were provided.

Compared with men, AD/ADRD disproportionately affects older women^{23,24} and cognitive decline is also faster among women.²⁵ The biological underlying mechanisms, mixed pathology, clinical presentation, and risk factors for dementia all differ by sex.^{24,26–28} Factors related to female reproductive history influence AD/ADRD risk and the disease experience.^{29,30} Considering and accounting for sex differences in AD/ADRD research is critical to clinical practice and research.

The objective of this study was to evaluate the trend of AD/ADRD prevalence by sex in older U.S. Medicare enrollees with and without HIV, and further to examine the factors associated with AD/ADRD prevalence and the effect of HIV on time trends and sex differences. We hypothesize that the prevalence of AD/ADRD is higher and increasing among PWH, especially women, after adjusting for demographics and comorbidities. Understanding the trends and associated factors of dementia in this population will help guide the screening and management of dementia among older PWH and inform policymakers regarding the optimal distribution of health care resources.

METHODS

Data Source

We used Medicare data from 100% of beneficiaries with an HIV diagnosis and a 5% national sample of Medicare enrollees without an HIV diagnosis anytime in 2007–2019 from all 50 U.S. states and the District of Columbia (DC) through access to the Centers for Medicare and Medicaid Services Virtual Research Data Center. Data were integrated from the Master Beneficiary Summary Files. The Master Beneficiary Summary Files contain demographic and enrollment information about beneficiaries enrolled in Medicare during a calendar year, such as date of birth, sex, race/ethnicity, date of death, state, Medicaid Dual Eligibility, original entitlement for Medicare, and monthly coverage. The Chronic Conditions Data Warehouse (CCW) includes indicators of 62 chronic conditions, such as first ever occurrence date and flags of conditions in the calendar year based on

algorithms requiring a multiple year look-back period. This study was approved by the University of Texas Medical Branch at the Galveston Institutional Review Board (IRB # 20–0275). A Data Use Agreement was established with the Centers for Medicare and Medicaid Services before all data analysis.

Cohort Identification and Study Measures

We constructed successive cross-sectional cohorts for PWH and PWOH for each calendar year, including individuals ≥ 65 in the calendar year and with 3 years of fee-for-service (FFS) coverage (Medicare parts A and B with no Health Maintenance Organization enrollment). We created 8 strata based on age at the end of the calendar year (65–69, 70–74, 75–79, 80+ years) and sex (male, female) (see Table 1, Supplemental Digital Content, <http://links.lww.com/QAI/C31>, Supplemental Digital Content for flow chart of cohort construction).

All diseases/conditions—such as HIV infection, AD/ADRD events, and comorbidities—were identified using physician diagnosis by International Classification of Diseases 9th and 10th Revision, Clinical Modification (ICD-9-CM/ICD-10-CM) codes based on CCW criteria.³¹ CCW uses combinations of inpatient claims and other nondrug claims of any service type during a reference period: for example, 2 years for HIV, 3 years for AD/ADRD, and 1 year for depression. Those who met the claims criteria were defined as having the condition. The primary outcome for this study was the occurrence of a physician clinical diagnosis of AD/ADRD including AD, vascular, frontotemporal, and unspecified dementia (see Table 2, Supplemental Digital Content, <http://links.lww.com/QAI/C31>, Supplemental Digital Content for CCW AD/ADRD diagnosis codes and algorithm specification). Earlier and recent validation studies using the Aging Demographics and Memory Study clinical assessments within the broader Health and Retirement Study have demonstrated that, with 3 years of data from the physician supplier and hospital outpatient claims files, investigators were able to correctly identify ~87% of patients with dementia using ICD-9-CM dementia codes^{32,33} and that ICD-10-CM codes for dementia diagnosis showed good discrimination, with an area under the curve of 0.86.³⁴ We classified individual comorbidities relevant to dementia risk including psychiatric disorders, alcohol use disorders, tobacco use disorders, drug/opioid abuse disorder, hypertension, diabetes, cardiovascular disease, viral hepatitis, other liver conditions, stroke/transient ischemic attack, head injury, fibromyalgia/chronic pain/fatigue, obesity, visual impairment, hearing impairment, and other (see Table 3, Supplemental Digital Content, <http://links.lww.com/QAI/C31>, Supplemental Digital Content for classification of comorbidities).^{35,36} The number of other relevant comorbidities was categorized (0, 1, 2, 3, 4, and 5+).

Other variables of interest included race (White, Black, Hispanic, Other/Unknown), original entitlement for Medicare enrollment (disabled, older age), and the time-varying covariates of Medicare-Medicaid dual eligibility

status (Yes, No) and U.S. Census region (Northeast, South, Midwest, West). Observations with unknown region were excluded in multivariable analysis.

Statistical Analysis

All analyses were performed by stratifying age at each calendar year and sex (total of 8 strata). We first calculated the crude prevalence of AD/ADRD for each calendar year by HIV status. All individuals who reached 65 years in the calendar year and had at least 3 years of FFS coverage were included in the denominator. Those who met claims criteria for AD/ADRD and had sufficient FFS coverage were included in the numerator. Therefore, one individual may contribute multiple times over years across the age categories. We then examined the factors associated with the odds of AD/ADRD and whether the time trend differed between PWH and PWOH using generalized estimating equation (GEE) models with binomial distribution, logit link function, and an AR(1) working correlation structure. The GEE models included HIV diagnosis, calendar year as a categorical variable, and HIV-year interaction, adjusted for continuous age and other demographic variables and comorbidity classes. Because of significant HIV-year interactions, we present results further stratifying HIV status within the age–sex stratum. We estimated the adjusted prevalence of AD/ADRD by year and report the association between covariates and outcome using odds ratios (OR) and their 95% confidence intervals (CI). We further explored the interactions between HIV status and each demographic and comorbidity variable. The *P*-values were adjusted using the false discover rate (FDR). All tests were two-sided with a significance level of 0.05. All analyses were performed using SAS version 9.4 (SAS Inc., Cary, NC).

RESULTS

Demographics

We identified 87,216 PWH and 2,289,831 PWOH contributing at least a one-year assessment of AD/ADRD, with average person-years of 4.7 and 6.4, respectively (see Table 1, Supplemental Digital Content, <http://links.lww.com/QAI/C31>, Supplemental Digital Content for flow chart of cohort construction). In the overall sample, 55.6% of beneficiaries were women. The mean age at first entering the cohort was 73.3 (SD 8.1) years. More PWH were men compared with PWOH (65.7% vs. 43.6%). PWH were younger on average than PWOH, especially among men. The mean age (SD) was 70.0 (5.7), 72.8 (7.7), 72.6 (6.7), and 74.0 (7.8) years for men with HIV, women with HIV, men without HIV, and women without HIV, respectively. There were more Black beneficiaries among male and female PWH than among PWOH (30.7%, 37.1%, 7.6%, and 8.4%, respectively).

We observed a growing aging population among PWH, especially among men, which doubled over the span of 13 years, whereas the size of the PWOH cohort was relatively stable from 2007 to 2019 (Table 1). Demographic characteristics were similar between 2009 and 2019 for PWOH

(Table 1). Among women with HIV, the proportion of Black beneficiaries grew (23.4% vs. 38.8%) and that of Hispanic beneficiaries shrank (10.8% vs. 5.3%) from 2007 to 2019. There was also a large increase in the proportion of PWH with disabled/end-stage renal disease (ESRD) as the original Medicare entitlement in both men (29.6% vs. 44.9%) and women (21.4% vs. 40.6%). The increase in the number of comorbidities over time was more pronounced in PWH and women, especially for psychiatric disorders, tobacco/drug/opioid use disorders, viral hepatitis/liver diseases, pain/fatigue, and obesity (Fig. 1).

Crude Prevalence of Alzheimer Disease and AD-Related Dementias

We identified 26,887 and 608,141 AD/ADRD-prevalent cases in all years among PWH and PWOH, respectively. Both male and female PWH had a significantly higher overall prevalence of AD/ADRD across all years (males with HIV: 26.4%, 95% CI: 26.0% to 26.7%; females with HIV: 39.4%, 95% CI: 38.9% to 40.0%) compared with PWOH (males: 22.9%, 95% CI: 22.8% to 23.0%; females: 29.4%, 95% CI: 29.3% to 29.8%), with larger differences among women (Fig. 2A). The gap between PWH and PWOH showed an increasing trend over time, was more prominent in women, and increased with age (Fig. 2A). For example, among those aged 80+ years, the prevalence increased from 2007 to 2019 from 26.2% (95% CI: 24.3% to 28.0%) to 33.3% (95% CI: 31.9% to 34.7%) in men and from 31.4% (95% CI: 29.6% to 33.1%) to 44.1% (95% CI: 42.6% to 45.6%) in women with HIV, compared with 21.0% (95% CI: 20.8% to 21.2%) to 23.5% (95% CI: 23.3% to 23.7%) in male PWOH and 27.4% (95% CI: 27.2% to 27.5%) to 29.9% (95% CI: 29.7% to 30.1%) in female PWOH.

GEE Analysis

The GEE models estimate the adjusted odds of AD/ADRD, which is the ratio of the adjusted probability that AD/ADRD occurs to the probability that AD/ADRD does not occur. The probability is adjusted for differential demographic and comorbidity characteristics between groups within each of the 8 strata at that stratum’s mean profile of each characteristic. To translate the odds to a more clinically interpretable scale, we presented the adjusted probability (ie, adjusted prevalence) of AD/ADRD. The highly significant HIV-year interactions typically result in nonparallel curves on the probability scale. For example, in Figure 2D, the interaction *P*-value is 0.002 for women aged 80 and above. This means that the probability curves shown in Figure 2B diverge over time between PWH and PWOH for this stratum.

GEE analysis showed significant HIV-year interactions among 5 of the 8 age-by-sex strata, which indicates that the change in adjusted prevalence of AD/ADRD over time differed between PWH and PWOH (Fig. 2D). Among PWOH, the covariate-adjusted AD/ADRD prevalence remained stable over time, except for the oldest group (80+), which showed an increasing trend, especially among women

TABLE 1. Demographic Shift Over Time Among PWH and PWOH by Sex

	PWOH								PWH							
	Male				Female				Male				Female			
	2007		2019		2007		2019		2007		2019		2007		2019	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Total	471,634	100	505,493	100	671,432	100	665,466	100	12,636	100	29,481	100	9457	100	13,273	100
Age group (yr)																
65–69	73,570	15.6	83,991	16.6	83,389	12.4	100,017	15.0	3881	30.7	11,013	37.4	1881	19.9	3623	27.3
70–74	134,112	28.4	162,135	32.1	159,860	23.8	197,231	29.6	4020	31.8	9445	32.0	2633	27.8	3302	24.9
75–79	111,482	23.6	113,574	22.5	148,283	22.1	139,249	20.9	2553	20.2	4833	16.4	2130	22.5	2297	17.3
80+	152,470	32.3	145,793	28.8	279,900	41.7	228,969	34.4	2182	17.3	4190	14.2	2813	29.8	4051	30.5
Race/ethnicity																
White	419,354	88.9	432,275	85.5	591,166	88.1	573,359	86.2	8526	67.5	18,902	64.1	5989	63.3	6886	51.9
Black	30,756	6.5	32,619	6.5	50,942	7.6	47,414	7.1	3039	24.1	8012	27.2	2208	23.4	5145	38.8
Hispanic	7274	1.5	6961	1.4	10,150	1.5	9412	1.4	758	6.0	1062	3.6	1022	10.8	701	5.3
Other/unknown	14,250	3.0	33,638	6.7	19,174	2.9	35,281	5.3	313	2.5	1505	5.1	238	2.5	541	4.1
Current medicare and medicaid dual coverage																
No	420,014	89.1	457,598	90.5	544,473	81.1	573,432	86.2	8230	65.1	18,833	63.9	5309	56.1	6749	50.9
Yes	51,620	10.9	47,895	9.5	126,959	18.9	92,034	13.8	4406	34.9	10,648	36.1	4148	43.9	6524	49.2
Current U.S. census region																
Unknown	2969	0.6	2391	0.5	3420	0.5	2524	0.4	93	0.7	150	0.5	56	0.6	91	0.7
Northeast	118,631	25.2	111,707	22.1	171,961	25.6	148,038	22.3	1798	14.2	3774	12.8	1386	14.7	1858	14.0
South	182,450	38.7	199,938	39.6	258,818	38.6	265,057	39.8	5702	45.1	11,967	40.6	5022	53.1	6242	47.0
Midwest	87,215	18.5	87,436	17.3	133,283	19.9	121,310	18.2	2740	21.7	7003	23.8	1819	19.2	3241	24.4
West	80,369	17.0	104,021	20.6	103,950	15.5	128,537	19.3	2303	18.2	6587	22.3	1174	12.4	1841	13.9
Original Medicare eligibility																
Disabled/ESRD	54,164	11.5	65,495	13.0	51,190	7.6	65,463	9.8	3743	29.6	13,236	44.9	2020	21.4	5382	40.6
Old age	417,470	88.5	439,998	87.0	620,242	92.4	600,003	90.2	8893	70.4	16,245	55.1	7437	78.6	7891	59.5

ESRD: end-stage renal disease.

(Fig. 2B). Women with HIV had a higher adjusted prevalence of AD/ADRD in all age categories and the increasing trend was more pronounced in those age 75+, reflecting differential trends between women with and without HIV, statistically shown as significant HIV-year interactions ($P = 0.01$ and 0.002 respectively in Fig. 2D). Despite the higher prevalence of AD/ADRD in women with HIV <75 years old, the change in AD/ADRD over time was statistically not different compared with women without HIV (Figs. 2C, D). Although smaller differences in the adjusted prevalence were observed among men (Figs. 2C, D), those with HIV who were 80 years and older had a higher adjusted prevalence of AD/ADRD, which increased faster than in men without HIV (Fig. 2B).

The pattern of association between comorbidities and AD/ADRD was generally similar in PWH and PWOH among the age–sex strata (Fig. 3). The test for comorbidity–HIV interactions showed a modifying effect of HIV on the association between some comorbidities and AD/ADRD, such as psychiatric disorders and alcohol/drug/opioid use disorders (see Table 4, Supplemental Digital Content, <http://links.lww.com/QAI/C31>, Supplemental Digital Content for P -values of interactions). Among all comorbidities, the top 5 conditions associated with AD/ADRD were psychiatric

disorders, head injury, stroke/transient ischemic attack, alcohol abuse disorder, and cardiovascular diseases in PWH and PWOH. Particularly, for psychiatric disorders, the ORs (95% CI) ranged from 1.61 (1.55–1.67) to 2.26 (2.14–2.37) and 1.61 (1.60–1.62) to 2.52 (2.45–2.59) for PWH and PWOH respectively, with stronger associations in younger age groups and among women.

DISCUSSION

This study found that PWH had a higher prevalence of AD/ADRD, which increased over time compared with PWOH, especially among female beneficiaries. The differences between PWH and PWOH largely decreased after adjustment for demographics and comorbidities. However, differences in dementia burden remained, especially among older age groups. We also found a spectrum of comorbidities associated with AD/ADRD, with psychiatric disorders the most prominent among these.

Given that older age is the main risk factor for dementia, the prolonged life expectancy among PWH will contribute to an increase in the prevalence of AD/ADRD in this population. Our findings are generally consistent with the recent study that showed overall increases in dementia

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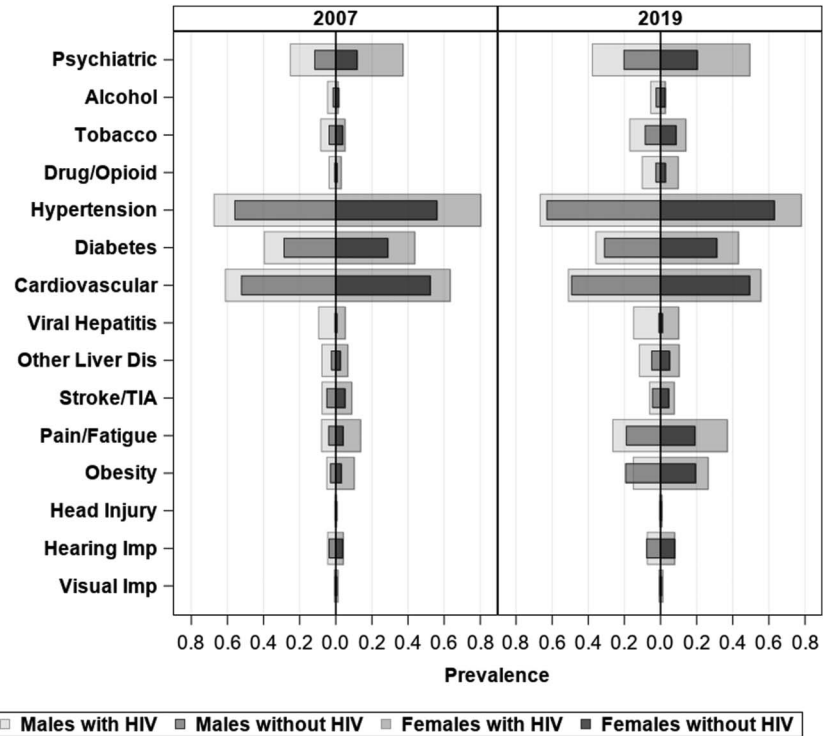


FIGURE 1. Increased crude prevalence of comorbidity over time among PWH and PWOH by sex. TIA, transient ischemic attack.

prevalence over time.²² In contrast to our study, that study included PWH 50 years and older (mean age 54 years at baseline) among members of Kaiser Permanente health plans in Northern California, Southern California, and the Mid-Atlantic (Maryland, Virginia, Washington DC). That study compared HIV cases with frequency-matched controls and further adjusted for a selected set of comorbidities. The study found that the overall prevalence of dementia was higher among PWH in 2000–2016 [adjusted prevalence ratio 1.86, 95% CI: 1.70 to 2.04] and also in 2015–2016 (adjusted prevalence ratio 1.75, 95% CI: 1.56 to 1.97).²² Our study targeted an older population (≥ 65 years) and included Medicare beneficiaries from all U.S. states and DC. Thus, our analyses extend these findings to a much larger, more contemporary, older, national and rapidly growing population of PWH. Because of the expected high impact of age and sex on dementia prevalence, we examined the trend and associated factors by stratifying by age (in 5-year increments) and sex. We adopted the multivariable adjustment approach within each stratum and controlled for continuous age, other demographic variables, and a wide range of conditions. This process allowed us to account more effectively for differential age and sex effects and provide more specific information for the subgroups.

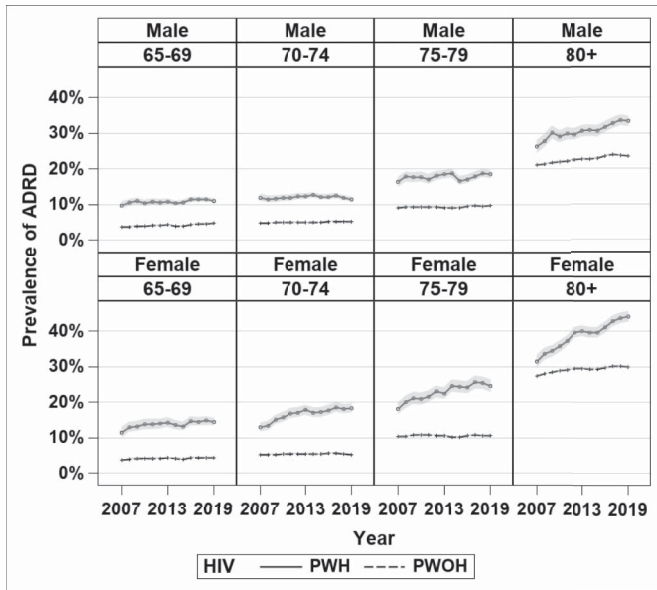
Within each age stratum, we found that PWH had a higher burden of dementia, which increased faster compared to PWOH, in men and women. The oldest groups were most affected, especially among women. These findings were confounded or moderated by differential demographic and comorbid characteristics and reflect the fact that older PWH increasingly develop age-related comorbidities and psychiatric disorders that affect cognitive function and are often more

common in women. Alcohol/drug/opioid use disorders were also more common in PWH and increased over time. After adjusting for demographic factors and comorbidities, the differences between PWH and PWOH decreased in all strata, although significant gaps remained among those 80 years and older. That the gaps between PWH and PWOH were larger in women than in men for all age strata suggests that the excessive burden of AD/ADR in women with HIV cannot be accounted by differences in demographics and comorbidities. We also found that many age-related comorbidities were highly associated with dementia among PWH. Compared to PWOH, the lower OR (ie, smaller relative measure) in PWH reflects the observation that there were higher odds of AD/ADR among PWH without a particular comorbidity.

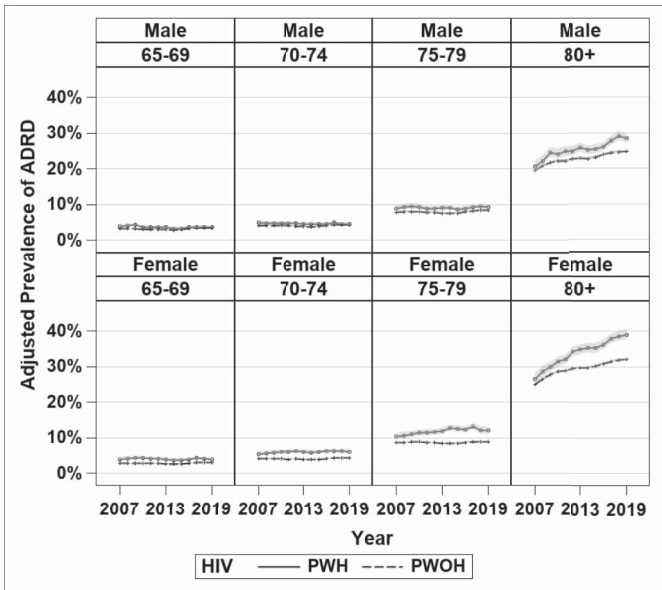
The strong association between psychiatric disorders (eg, depression) and AD/ADR may be explained by several reasons. Depression can impair cognitive function leading to a “pseudodementia” presentation.³⁷ Loneliness, social isolation and heavy alcohol use,^{38,39} major psychosocial consequences of depression, and especially prominent among PWH, are risk factors for dementia.³⁵ Depression and cognitive impairment may also represent the same underlying pathologic process, perhaps because of direct and indirect effects of HIV replication in the central nervous system (CNS).⁴⁰ Toxoplasmosis is a common CNS infection in PWH⁴¹ and some studies have demonstrated negative effects of latent toxoplasmosis on mental health⁴² and dementia.⁴³

After accounting for demographics and comorbidities, PWH still had excess risks that differed among subgroups, which could be explained by unmeasured factors, such as HIV clinical factors (disease stage, treatment), education, and

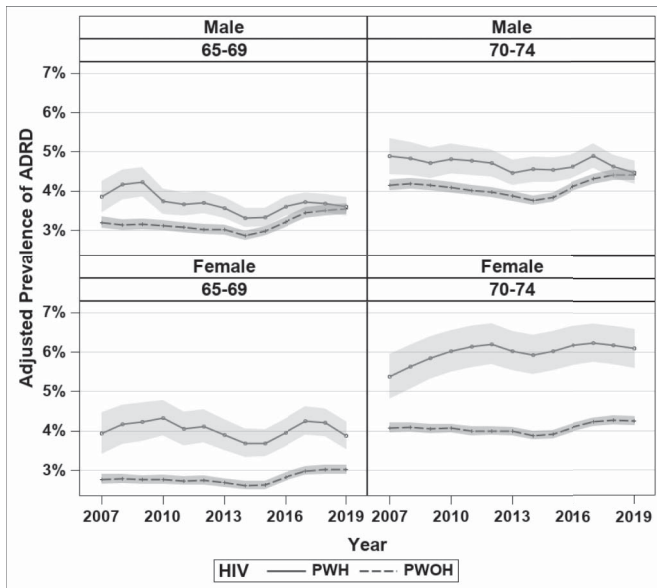
A) Crude prevalence



B) Adjusted prevalence



C) Adjusted prevalence (<75 years old)



D) p-values for HIV by year interactions

Sex	Age	p-value
Male	65-69	0.003
Male	70-74	0.02
Male	75-79	0.62
Male	80+	0.02
Female	65-69	0.59
Female	70-74	0.79
Female	75-79	0.01
Female	80+	0.002

Note: P-values are for the significance of the comparison of the adjusted prevalences of PWH and PWOH shown in Figures 2B and 2C over time. Stratified GEE models include HIV, year, HIV by year interactions and adjust for continuous age, race, Medicare & Medicaid dual coverage, U.S. census region, original entitlement for Medicare.

FIGURE 2. Prevalence of AD/DRD. AD/DRD, Alzheimer disease (AD)/AD-related dementias (ADR).

social support. CD4 nadir is a predictor of HIV neurocognitive impairment and initiation of ART as early as possible may reduce the risk of developing HIV-associated neurocognitive disorders.⁴⁴ In contrast, it is possible that long-term exposure to certain ART drugs may cause chronic CNS toxicity.⁴⁵⁻⁴⁷ For example, a clinicopathologic study of PWH demonstrated that darunavir or ritonavir use was associated with higher likelihood of cerebral degenerative changes, such as neuronal phospho-tau lesions and marked microgliosis in the putamen.⁴⁶ Human herpes viruses are another possible contributor to excessive risk in PWH.^{48,49} Further studies are needed to investigate these factors.

This study has several limitations. We focused on the overall dementia burden over time and adopted a consecutive cross-sectional study design; thus, the results demonstrate association rather than causation. Further studies are needed to evaluate the incidence of dementia and investigate factors that affect the development of dementia. Although we used a validated method to identify AD/ADR in claims data, the accuracy and completeness of Medicare claims to identify patients with dementia is not perfect.²⁸⁻³⁰ The sensitivity and specificity of Medicare claims is reported to be 0.85 and 0.89 for AD/ADR.³² Also, because most dementias are mixed,^{26,50} especially at later ages, and it is challenging to classify them

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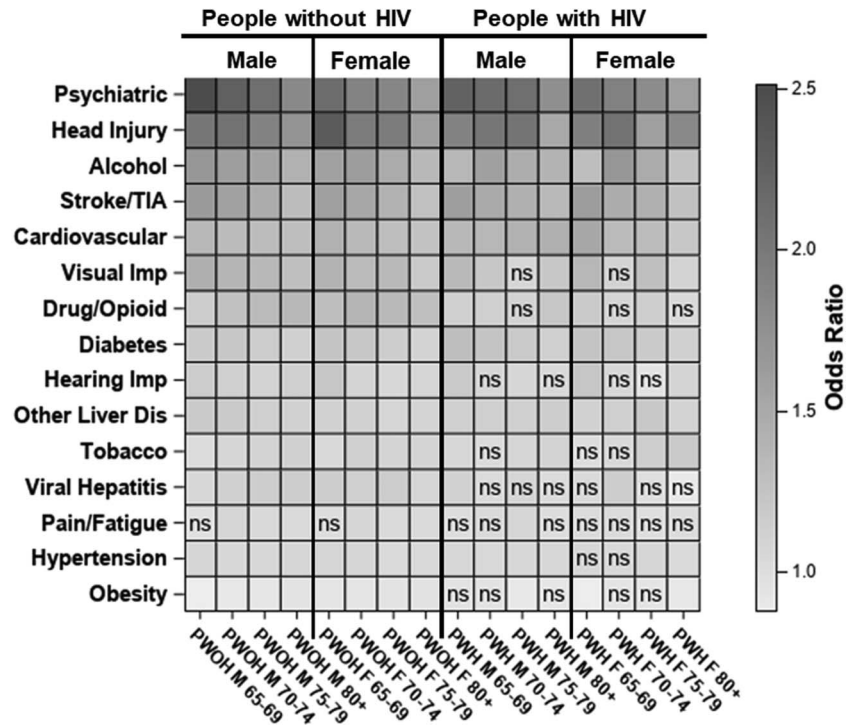


FIGURE 3. Association between comorbidities and AD/ADRD among PWH and PWOH by sex and age strata. AD/ADRD, Alzheimer disease (AD)/AD-related dementias (ADRD); NS, not significant ($P \geq 0.05$); TIA, transient ischemic attack; darker gradients indicate stronger association.

into distinct categories based on the clinical diagnosis codes alone, our analyses considered all types of dementia together including AD and AD-related dementia. Therefore, the analysis could not study Alzheimer disease itself. Furthermore, the population of patients with dementia may differ from the population of those given a diagnosis of dementia by their physicians. We studied the latter, which underrepresents individuals with early or milder dementia and those with poor access to medical care.⁵¹ The pathogenesis of AD may differ in PWH. For example, the appearance of amyloid burden and association between the apolipoprotein E and AD in general populations were not observed in some studies of PWH.^{52,53} Also, a recent study examined biomarkers of age-related neurodegeneration in the CSF in relation to neurocognitive impairment in older PWH. Poorer neurocognitive performance was associated with higher CSF tTau, a marker of age-related neuronal injury, but not with biomarkers of amyloid metabolism.⁵⁴ Furthermore, a small cases series demonstrated the complexity of AD diagnosis among older PWH.⁵⁵ Finally, the data available were collected for processing claims, with no detailed clinical, psychological, or behavioral information, so these factors cannot be accounted for in this analysis.

Strengths of the present study included using data from 100% of older PWH and a 5% national sample of PWOH enrolled in the U.S. Medicare program. Data extended up to 13 years with recent data included. The large sample size made it possible to evaluate temporal trends, observe interactions, and conduct stratified analysis. We examined the time trend of prevalent dementia and a spectrum of comorbidities associated with dementia among 8 age–sex strata, then compared these between older PWH and PWOH, which was beyond the scope of previous studies.

These results are generalizable to the older FFS Medicare population and have important implications for the management and treatment of dementia among patients with HIV. Given the increasingly high burden of dementia among older Medicare enrollees with HIV, enhanced regular screening for dementia among PWH and comprehensive management of dementia are indicated. The significantly higher burden of dementia among women with HIV and older age subgroups highlights the necessity of closely monitoring treatment and supporting engagement in the care of these vulnerable patients. In addition, early treatment of comorbidities, especially psychiatric disorders, alcohol and drug use disorders, and cardiovascular diseases in PWH is critical, given the additional risk of dementia in this population. Implementing these strategies will not only extend the lifespan of PWH, but also improve their healthspan and quality of life.⁵⁶

In conclusion, older Medicare enrollees with HIV had an increased dementia burden over time compared with those without HIV, especially women and older subjects. Age-related comorbidities—especially psychiatric disorders, which are more prominent in women—were strongly associated with this trend. These findings underscore the need to develop clinical practice guidelines that facilitate the integration of dementia and comorbidity screening, evaluation, and management into the routine primary care of aging PWH.

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