Dementia incidence and prevalence in older adults with HIV: a 23-year retrospective cohort study

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Objective: To compare dementia incidence and prevalence by HIV status, race/ethnicity, and sex.

Design: A retrospective cohort, 2000–2023.

Methods: Adults with HIV aged at least 50 years and 1 : 20 matched individuals without HIV from Kaiser Permanente, a U.S. healthcare system, were included. Dementia diagnoses were identified via electronic health records. We estimated rates of incident dementia diagnoses and prevalence, overall and by time period (2000–2004, 2005–2009···2020–2023) using Poisson regression, and assessed trends using Joinpoint regression. Covariate-adjusted rate ratios compared dementia by HIV status, with sub-analyses stratified by race/ethnicity and sex.

Results: Among 24 762 people with HIV and 494 963 people without HIV (86.9% men, 45.5% White, 23.1% Black, 20.3% Hispanic), incident dementia diagnoses declined from 2000 to 2023 in both people with and without HIV (-7.68 and -2.70% per period, respectively). Overall, the incidence of dementia diagnosis was higher in people with HIV (adjusted incidence rate ratio [aIRR]=1.72, 95% CI=1.59–1.85). In the most recent period (2020–2023), this difference was not statistically significant (aIRR=1.16, 95% CI=0.99–1.35), partly due to increases in diagnoses among people without HIV during this period. Dementia prevalence remained higher in people with HIV, overall (adjusted prevalence ratio [aPR]=1.71, 95% CI=1.61–1.82) and in 2020–2023 (aPR=1.59, 95% CI=1.46–1.73), with similar patterns by race/ethnicity and sex.

Conclusion: Incident dementia diagnoses have declined in people with HIV and are approaching those of people without HIV, with consistent trends across demographic subgroups. However, prevalence remains elevated, likely reflecting excess risk from earlier years. These findings highlight the need for sustained attention to cognitive health and the integration of dementia-related services in HIV care.

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Introduction

In the U.S. and globally, age-related cognitive decline is of increasing concern in the aging HIV population. People with HIV are known to experience a greater burden of cognitive impairments compared to the general population [1–4]. Recent studies also suggest an elevated risk of age-associated dementia among people with HIV, even among those on effective antiretroviral therapy (ART) [5–8], which could cause substantial health burden for both individuals and healthcare systems. Contributing factors include comorbidities that affect vascular health, behavioral factors such as substance use, and persistent HIV reservoirs–all of which may adversely impact neurocognition and accentuate brain aging [9–12].

Despite growing recognition of the potential impacts of age-associated dementia in this population, limited evidence exists on how dementia burden among people with HIV compares to that of the general population. Further, no prior study has characterized the epidemiology of age-associated dementia among people with HIV by race and ethnicity. In the general population, the overall frequency of dementia is projected to triple within the next 3 decades due to population aging, becoming a leading driver of morbidity and healthcare expenditures [13]. Given the disproportionately higher dementia risk among people with HIV, understanding dementia epidemiology in this population will be critical to prepare for future healthcare demands.

To contribute knowledge on the burden of dementia in the aging HIV population, we assembled a diverse cohort of adults with HIV and demographically matched comparators without HIV from three integrated healthcare systems in the United States. In this study, we describe our initial analyses of incident dementia diagnoses and prevalence, overall and stratified by race/ethnicity and sex.

Materials and methods

Study setting

The study was conducted within Kaiser Permanente (KP) integrated health systems across three U.S. regions–Northern California (KPNC), Southern California (KPSC), and the Mid-Atlantic States (KPMAS; includes Maryland, Virginia, and Washington, District of Columbia, USA). KP provides comprehensive medical, diagnostic, pharmacy, and HIV care services. ART prescriptions can be filled directly through KP pharmacies. The study protocol was approved by the KPNC Institutional Review Board.

Cohort development and matching

The study period was January 1, 2000, to December 31, 2023. Individuals were eligible for inclusion if they were aged at least 50 years and had at least 1 year of continuous KP health plan enrollment, allowing enrollment gaps up to 90 days. People with HIV were identified using KP's regional HIV registries, which capture all known cases of HIV/AIDS using laboratory data, pharmacy records, and International Classification of Diseases (ICD)-coded diagnoses. A comparator group of people *without* HIV infection included individuals from the KP patient population not listed in the HIV registries and presumed to be HIV-uninfected.

People with and without HIV were matched on age (±1 year), race/ethnicity, sex, prior duration of KP health plan enrollment, and calendar year of cohort entry. The matching process was completed using predefined match criteria and rules. The target match ratio was 1 : 20 (people with HIV to people without HIV). Given that aging is a primary risk factor for dementia, special care was taken to achieve close age matching. Race/ethnicity categories included Hispanic (any race), Non-Hispanic Asian (including Native Hawaiian and Pacific Islander), non-Hispanic Black, non-Hispanic White, and Other (including Native American and people of multiple or unknown race/ethnicity). People with HIV could be included in the comparator group prior to their HIV diagnosis and were censored on date of HIV diagnosis. The final cohort comprised 24 762 people with HIV, including 24 726 people with HIV (99.9%) matched to 20 comparators and 36 people with HIV (0.01%) matched to fewer than 20 comparators.

Follow-up

For analyses of incident dementia diagnoses, participants were followed until the earliest occurrence of a dementia diagnosis, death, health plan disenrollment, or the study end date (December 31, 2023). For analyses of dementia prevalence, follow-up ended at the earliest of death, health plan disenrollment, or study end. Individuals with a dementia diagnosis at or before baseline (i.e., cohort entry) were excluded from incidence analyses but included in prevalence analyses. Individuals who were diagnosed with incident dementia during the study period remained prevalent cases until the end of follow-up.

Data collection

Electronic health record (EHR) and HIV registry data were collected across the three participating KP health systems. EHR data included information on medical diagnoses, laboratory results, prescription medication fills, healthcare utilization, and insurance coverage. These data are maintained in a virtual data warehouse with standardized formats, which facilitated data pooling and harmonization across regions.

Dementia was identified using ICD codes (Supplemental Table 1, http://links.lww.com/QAD/D749) previously confirmed in a KP study to have comparable positive predictive value in people with and without HIV (93 and

97%, respectively; $P = 0.21$) [6]. These ICD codes included diagnoses of Alzheimer's disease, vascular dementia, Parkinson's dementia, dementia with Lewy bodies, frontotemporal dementia, and other or unspecified dementias. For the current study, new ICD-10-CM codes adopted in KP health systems in 2022 were mapped to existing dementia categories to ensure consistent classification across the study period [14]. Because the study period included the COVID-19 pandemic time period, the case definition also incorporated dementia diagnoses made during telehealth encounters. Incident dementia diagnoses were defined as the first recorded dementia diagnosis of any type.

Covariates included sociodemographic factors (age, sex, race/ethnicity, Census-based neighborhood-level education), ICD-coded diagnoses of comorbidities (cardiovascular disease, cerebrovascular disease, diabetes mellitus, dyslipidemia, hypertension, depression, substance use disorders), and patient-reported smoking status (Supplemental Table 1, http://links.lww.com/QAD/D749). Administrative data captured insurance type (commercial, Medicare, Medicaid, Affordable Care Act, charitable care) and number of healthcare encounters in the year before baseline (a proxy for healthcare engagement). For people with HIV, data included $CD4^+$ cell counts, HIV RNA levels, date of first recorded HIV diagnosis, and ART prescription fills.

Statistical analyses

Incident dementia diagnoses and dementia prevalence were evaluated by HIV status, race/ethnicity, and sex for the full study period (i.e., 2000–2023) and within five time periods (i.e., 2000–2004, 2005–2009, 2010–2014, 2015–2019, 2020–2023).

First, rates of incident dementia diagnoses and prevalence were estimated for people with and without HIV within each period using Poisson regression. To adjust for demographic shifts over time, rates were standardized to the age and sex distribution of the total study population (people with and without HIV combined) in the first period (2000–2004). Trends in standardized incidence rate (sIR) were evaluated by calculating average percentage change in sIR per period using Joinpoint regression, which identifies inflection points in population-level trends by fitting linear segments to the data (Joinpoint Regression Program, version 5.3.0) [15]. The best-fitting and simplest model was selected using a sequence of permutation tests with Monte Carlo sampling and Bonferroni correction for multiple testing. Pairwise comparability tests assessed whether trends in dementia incidence and prevalence differed by HIV status.

Next, we compared incident dementia diagnoses and prevalence by HIV status, overall and within individual time periods, using rate ratios from unadjusted and covariate-adjusted Poisson regression models. Adjusted models included terms for sociodemographics (sex, attained age, race/ethnicity, neighborhood-level education), comorbidities (cardiovascular disease, cerebrovascular disease, diabetes, dyslipidemia, hypertension, depression, substance use disorders), smoking history, and healthcare utilization (KP region, insurance type, and number of healthcare encounters in the year before baseline).

Finally, we conducted stratified analyses by race/ethnicity (Black, Hispanic, White) and by sex (male, female). For race-stratified and sex-stratified trend analyses, sIRs were standardized to the respective subgroup's age and sex distribution in the first period (e.g., to examine trends among White study participants, rates were standardized to the age and sex distribution of White study participants in the first period). There was an insufficient number of dementia cases among Asian participants to conduct race-stratified analyses by period; therefore, incidence and prevalence among people of Asian race were evaluated only for the overall study period. Individuals of Other or unknown race/ethnicity were excluded from race-stratified analyses. Differences in the association of HIV with dementia incidence and prevalence by demographic subgroup were evaluated in covariate-adjusted Poisson models with interaction terms for HIV*race/ethnicity and HIV*sex.

To account for the potential effects of suboptimal HIV control, which could increase dementia risk among people with HIV, we repeated all models in sensitivity analyses excluding individuals who did not have at least one ART prescription fill in the year prior to baseline or who had detectable HIV RNA (>200 copies/ml) at baseline. To assess the potential impact of prior immunosuppression, we repeated analyses excluding individuals with a baseline nadir $CD4^+$ cell count less than 200 cells/μl. HIV viral suppression during follow-up was examined descriptively but was not included as a time-updated covariate in the models due to the potential bidirectional relationship between cognitive impairment and HIV control. Finally, we conducted a descriptive comparison of dementia types (e.g., Alzheimer's disease, vascular dementia) by HIV status at incident diagnosis and among prevalent cases in the most recent time period (2020–2023). Analyses were conducted using Stata 19.5 (College Station, Texas, USA).

Results

The study included 24 762 people with HIV and a matched cohort of 494 963 people without HIV (Table 1). People with and without HIV were similar on the matching factors of age, sex, race/ethnicity, and prior duration of KP enrollment. The median age at baseline was 50.8 years in people with HIV (interquartile range [IQR] = 50.0–56.1; range = 50.0–91.6) and 51.8 years in people without HIV (IQR = 50.8–56.3, range = 50.0–93.0). Participants were

Table 1. Characteristics of study population at baseline.

Characteristic	People with HIV $N=24762$ *n* (%)	People without HIV $N=494963$ *n* (%)
Age, median years (IQR, range)[a]	50.8 [50.0–56.1, 50.0–91.6))	51.8 (50.8–56.3, 50.0–93.0)
Male[a]	21513 (86.9)	430021 (86.9)
Race/ethnicity[a]		
White, non-Hispanic	11257 (45.5)	225140 (45.5)
Black, non-Hispanic	5713 (23.1)	114244 (23.1)
Hispanic	5029 (20.3)	100579 (20.3)
Asian, non-Hispanic	949 (3.8)	18962 (3.8)
Other or unknown	1814 (7.3)	36038 (7.3)
Lower neighborhood-level education[b]	4196 (16.9)	94813 (19.2)
Insurance type		
Commercial	18528 (74.8)	421887 (85.2)
Medicare	3592 (14.5)	36121 (7.3)
Medicaid	1168 (4.7)	14574 (2.9)
Other or unknown	1474 (6.0)	22381 (4.5)
Duration of health plan enrollment[a]		
1 year	10540 (42.6)	210428 (42.6)
2 years	1280 (5.2)	25777 (5.2)
3–4 years	3270 (13.2)	65396 (13.2)
5–9 years	4039 (16.3)	80758 (16.3)
≥10 years	5633 (22.7)	112604 (22.7)
Cardiovascular disease	1468 (5.9)	26316 (5.3)
Cerebrovascular disease	768 (3.1)	10741 (2.2)
Diabetes mellitus	3170 (12.8)	71820 (14.5)
Dyslipidemia	11213 (45.3)	193253 (39.0)
Hypertension	8103 (32.7)	163,308 (33.0)
Depression	6543 (26.4)	48676 (9.8)
Substance use disorder	3474 (14.0)	31383 (6.3)
History of smoking	9119 (36.8)	131742 (26.6)
Number of healthcare encounters in prior year, median (IQR, range)	5 (3–10, 0–320)	2 (1–5, 0-366
Preexisting dementia diagnosis	367 (1.48)	2378 (0.48)

IQR, interquartile range.
[a]People with and without HIV were matched on age (±1 year), sex, race/ethnicity, duration of health plan enrollment at baseline, and calendar year of study inclusion.
[b]Lower neighborhood-level education was defined as ≥25% of the population in the patient's Census block group having less than a 12th grade level education.

86.9% male, 45.5% White, 23.1% Black, 20.3% Hispanic, 3.8% Asian, and 7.3% other or unknown ethnicity. At baseline, people with HIV had a median duration of 3.0 years of prior KP enrollment (IQR = 1.0–9.0, range = 1.0–61.0), and people without HIV had a median of 3.0 years of prior KP enrollment (IQR = 1.0–9.0, range = 1.0–75.0). Among people with HIV, 70.3% had HIV RNA levels less than 200 copies/ml at baseline, 48.1% had $CD4^+$ cell counts at least 500 cells/μl, and 82.2% had an ART prescription fill in the past year. The median duration of known HIV infection at baseline was 10.6 years (IQR = 2.9–18.1, range = 0–43.9), and 26.3% had a prior nadir $CD4^+$ cell count less than 200 cells/μl.

Incident dementia diagnoses

At baseline, 367 people with HIV and 2,378 people without HIV had preexisting dementia diagnoses and were excluded from incidence analyses, resulting in a cohort of 24395 people with HIV and 492585 people without HIV for analyses of incident dementia. Median duration of follow-up was 5.0 years (IQR=2.08–9.95, range 0.003–24.0) for people with HIV and 4.87 years (IQR=1.91–9.89, range 0.003–24.0) for people without HIV.

During follow-up, 819 incident dementia diagnoses occurred among people with HIV, and 9428 cases occurred among people without HIV. Telehealth encounters for initial dementia diagnosis became more common during the COVID-19 pandemic, but few diagnoses were made without subsequent in-person follow-up. Only 18 of the 819 people with HIV (2.2%) and 165 of the 9428 people without HIV (1.8%) did not have an in-person visit after their telehealth diagnosis. Among people with HIV, reasons for censoring other than incident dementia were health plan disenrollment ($n=10741$; 44.0%), end of the study ($n=10476$; 42.9%), and death ($n=2359$; 9.7%). Among people without HIV, reasons for censoring were health plan disenrollment (n = 251346; 51.0%), end of the study ($n=204728$; 41.6%), death ($n=26654$; 5.4%), and incident HIV diagnosis ($n=429$; 0.0009%).

From 2000 to 2023, the age-sex- sIR of dementia declined in both groups but remained consistently higher among people with HIV in every time period. Among people with HIV, the sIR declined from 11.08 cases per 1000 person-years (95% confidence period [CI] 9.34, 13.06) in 2000–2004 to an sIR of 2.29 (1.89, 2.74) in

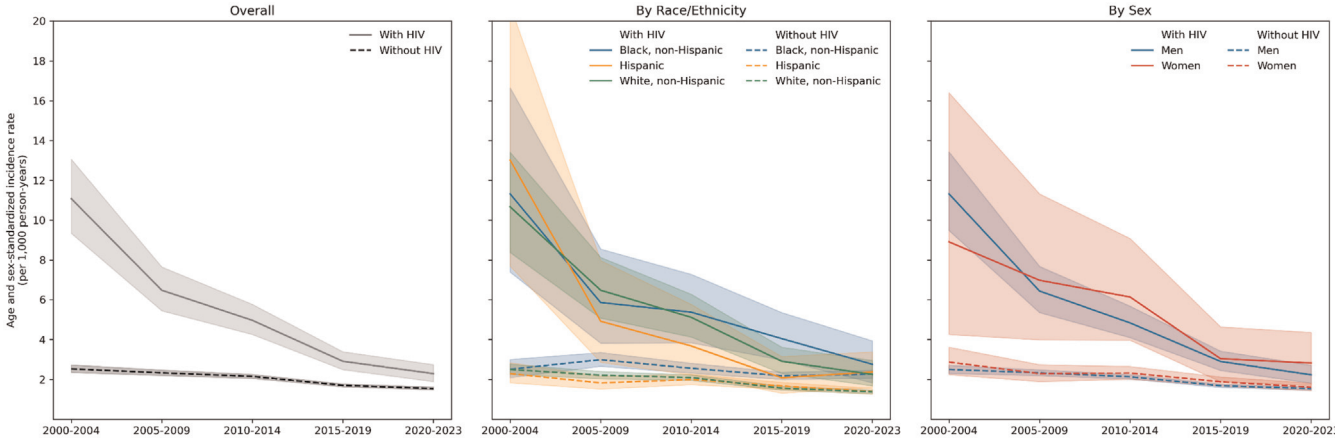

Fig. 1. Incidence of dementia by HIV status, overall, by race/ethnicity, and by sex: Kaiser Permanente, 2000–2023. Incidence estimates were standardized to the age and sex distribution in the time period 2000–2004.

2020–2023 (Fig. 1; Supplemental Table 2, http://links.lww.com/QAD/D749). Among people without HIV, the sIR declined from 2.53 (2.35, 2.73) to 1.54 (1.48, 1.62) over the same time periods. The average percentage decrease in sIR per period was greater among people with HIV (-7.68, 95% CI = -8.82, -6.56) than among people without HIV (-2.70, 95% CI = -3.91, -1.24), $P < 0.001$.

In trend analyses stratified by race/ethnicity, declining dementia incidence was observed across all racial/ethnic groups, regardless of HIV status (Fig. 1; Supplemental Table 2, http://links.lww.com/QAD/D749). Among Hispanic people with HIV, however, the sIR increased modestly in the final time period–from an sIR of 2.08 (1.31, 3.15) in 2015–2019 to an sIR of 2.37 (1.60, 3.38) in 2020–2023, though this was not statistically significant and case numbers were small (23 dementia cases in 2015–2019 and 33 dementia cases in 2020–2023). This trend was not observed in any other racial/ethnic group. In trend analyses stratified by sex, dementia incidence declined consistently across all time periods for both men and women.

Across the full study period, incident dementia diagnoses were more common among people with HIV than people without HIV (adjusted incidence rate ratio [aIRR] = 1.72, 95% CI = 1.59–1.85), even after adjustment for sociodemographics, comorbidities, substance use, and healthcare utilization (Table 2). This elevated incidence decreased over time–from an aIRR of 3.80 (3.16, 4.62) in 2000–2004 to an aIRR of 1.16 (0.99, 1.35) in 2020–2023 (Table 2). Results were consistent by race/ethnicity and sex (Table 2, interaction p values: HIV*race = 0.29, HIV*sex = 0.54).

Dementia prevalence

From 2000 to 2023, dementia prevalence was higher among people with HIV in all periods but declined over time whereas dementia prevalence among people without HIV remained relatively stable. Among people with HIV, the age-sex-standardized prevalence rate (sPR) declined from 48.54 cases per 1000 persons (95% CI = 42.40–55.32) in 2000–2004 to 25.78 (23.26, 28.46) in 2020–2023 (data not shown in tables). Among people without HIV, sPR was 11.53 (10.85, 12.24) in 2000–2004 and 10.98 (10.63, 11.35) in 2020–2023. The average percentage change in sPR per period was greater among people with HIV (-3.46, 95% CI = -5.01, -1.78) than among people without HIV (-0.93, 95% CI = -3.19, 1.98). In analyses stratified by race/ethnicity and sex, results were similar.

Over the full study period, dementia prevalence was greater among people with HIV (adjusted prevalence ratio [aPR] = 1.71 (1.61–1.82), Supplemental Table 3, http://links.lww.com/QAD/D749). Dementia prevalence was also greater among people with HIV within individual time periods (Supplemental Table 3, http://links.lww.com/QAD/D749). In the most recent time period (2020–2023), dementia prevalence was 38.31 cases per 1000 persons (95% CI = 35.42–41.43) among people with HIV and 23.10 (22.57, 23.64) among people without HIV (Fig. 2; unadjusted PR = 1.66, 95% CI=1.53–1.80); after adjustment for covariates, prevalence remained significantly higher among people with HIV in this period (aPR=1.59, 95% CI=1.46, 1.73; Supplemental Table 3, http://links.lww.com/QAD/D749).

In analyses stratified by race/ethnicity and sex, the higher dementia prevalence among people with HIV was observed across all subgroups (Fig. 2, interaction *P* values: HIV*race=0.12, HIV*sex=0.73).

Sensitivity analyses

Sensitivity analyses excluding people with detectable HIV RNA at baseline or no ART at baseline, and excluding individuals with history of low nadir $CD4^+$ at baseline, resulted in attenuated incidence and prevalence ratios but

Table 2. Incidence rate ratios comparing dementia in people with and without HIV, overall, by race/ethnicity, and by sex: Kaiser Permanente, 2000–2023.

	People with HIV		People without HIV		Incidence rate ratio (95% CI)	
	Cases	Person-years	Cases	Person-years	Unadjusted	Adjusted[a]
Full cohort without dementia diagnosis at baseline					*N* = 24 395	*N* = 492 585
2000–2004	143	13 081	680	267 704	4.30 (3.59, 5.15)	3.80 (3.13, 4.62)
2005–2009	140	21 540	1148	443 251	2.51 (2.11, 2.99)	2.28 (1.89, 2.75)
2010–2014	178	33 413	1845	667 943	1.93 (1.65, 2.25)	1.88 (1.60, 2.20)
2015–2019	187	49 569	2621	976 159	1.41 (1.21, 1.63)	1.57 (1.35, 1.83)
2020–2023	171	48 382	3134	9 420 340	1.06 (0.91, 1.24)	1.16 (0.99, 1.35)
All periods combined	819	165 985	9428	3 297 097	1.73 (1.61, 1.85)	1.72 (1.59–1.85)
By race/ethnicity						
Black, non-Hispanic					*N* = 5627	*N* = 113 505
2000–2004	26	2310	122	48 503	4.48 (2.93, 6.85)	4.73 (2.91, 7.69)
2005–2009	26	4443	300	91 302	1.78 (1.19, 2.66)	1.60 (1.04, 2.48)
2010–2014	44	7310	498	149 727	1.81 (1.33, 2.46)	1.83 (1.33, 2.51)
2015–2019	60	11 194	777	225 145	1.55 (1.19, 2.02)	1.70 (1.31, 2.21)
2020–2023	47	11 481	980	228 687	0.96 (0.71, 1.28)	1.03 (0.77, 1.38)
All periods combined	203	36 737	2,677	743 364	1.53 (1.33, 1.77)	1.55 (1.34–1.80)
Hispanic					*N* = 4971	*N* = 100 217
2000–2004	21	1804	84	36,411	5.05 (3.1, 8.12)	4.63 (2.77, 7.74)
2005–2009	17	3480	133	68 590	2.52 (1.52, 4.18)	2.73 (1.64, 4.53)
2010–2014	21	6002	242	110 023	1.59 (1.02, 2.49)	1.47 (0.91, 2.38)
2015–2019	23	10 291	371	188 330	1.13 (0.74, 1.73)	1.23 (0.79, 1.93)
2020–2023	33	11 028	419	199 258	1.42 (1.00, 2.03)	1.48 (1.01, 2.15)
All periods combined	115	32 605	1249	602 612	1.70 (1.41, 2.06)	1.71 (1.40–2.09)
White, non-Hispanic					*N* = 11 068	*N* = 224 070
2000–2004	74	7058	365	145 558	4.18 (3.26, 5.37)	3.59 (2.74, 4.69)
2005–2009	74	11 379	584	235 456	2.62 (2.06, 3.34)	2.28 (1.76, 2.95)
2010–2014	95	17 639	967	355 061	1.98 (1.60, 2.44)	1.84 (1.48, 2.28)
2015–2019	92	24 526	1305	490 284	1.41 (1.14, 1.74)	1.60 (1.29, 1.98)
2020–2023	83	21 764	1543	432 853	1.07 (0.86, 1.33)	1.21 (0.96, 1.51)
All periods combined	418	82 366	4764	1 659 211	1.77 (1.60, 1.95)	1.74 (1.57–1.93)
By sex						
Men					*N* = 21 202	*N* = 428 033
2000–2004	133	11 847	608	242 840	4.48 (3.72, 5.41)	4.07 (3.25, 4.98)
2005–2009	124	19 250	1028	395 700	2.48 (2.06, 2.99)	2.26 (1.86, 2.76)
2010–2014	153	29 666	1624	589 031	1.87 (1.58, 2.21)	1.80 (1.51, 2.14)
2015–2019	164	43 718	2280	853 740	1.40 (1.20, 1.65)	1.61 (1.37, 1.89)
2020–2023	146	41 895	2684	808 246	1.05 (0.88, 1.24)	1.18 (1.00, 1.40)
All periods combined	720	146 376	8224	2 889 557	1.73 (1.60, 1.86)	1.73 (1.60–1.87)
Women					*N* = 3193	*N* = 64 552
2000–2004	10	1234	72	24 864	2.80 (1.45, 5.42)	2.13 (0.98, 4.64)
2005–2009	16	2290	120	47 552	2.77 (1.64, 4.66)	2.51 (1.48, 4.27)
2010–2014	25	3748	221	78 911	2.38 (1.57, 3.61)	2.38 (1.53, 3.70)
2015–2019	23	5851	341	122 420	1.41 (0.93, 2.15)	1.40 (0.91, 2.17)
2020–2023	25	6487	450	133 793	1.15 (0.77, 1.71)	1.06 (0.69, 1.63)
All periods combined	99	19 609	1204	407 540	1.71 (1.39, 2.09)	1.59 (1.28–1.98)

[a]Adjusted for attained age, sex, race/ethnicity, neighborhood-level education, cardiovascular disease, cerebrovascular disease, diabetes, dyslipidemia, hypertension, depression, substance use disorders, ever smoking, KP region, insurance type, and number of healthcare encounters in the year before baseline.

similar overall patterns across time periods (Supplemental Tables 4 and 5, http://links.lww.com/QAD/D749).

Dementia types

At incident diagnosis, unspecified dementia was the most common dementia diagnosis in both people with and without HIV (44.0 and 42.8%, respectively), followed by other specified dementia and vascular dementia. Alzheimer's disease comprised a smaller proportion of incident diagnoses among people with HIV (1.7%) compared with people without HIV (8.5%). Patterns were similar for prevalent cases (Supplemental Table 6, http://links.lww.com/QAD/D749).

Discussion

Incident dementia diagnoses among people with HIV have declined and are converging with rates observed in demographically matched peers without HIV. Encouragingly, this downward trend was observed across all race/ethnicity and sex subgroups of people with HIV. However, dementia prevalence remains elevated – 38.31 cases per 1000 persons in the recent period (2020–2023) – with consistently elevated rates across all demographic subgroups, likely reflecting higher cumulative risk from earlier years. Therefore, dementia screening and care will need to remain a continued focus in HIV primary care for years to come.

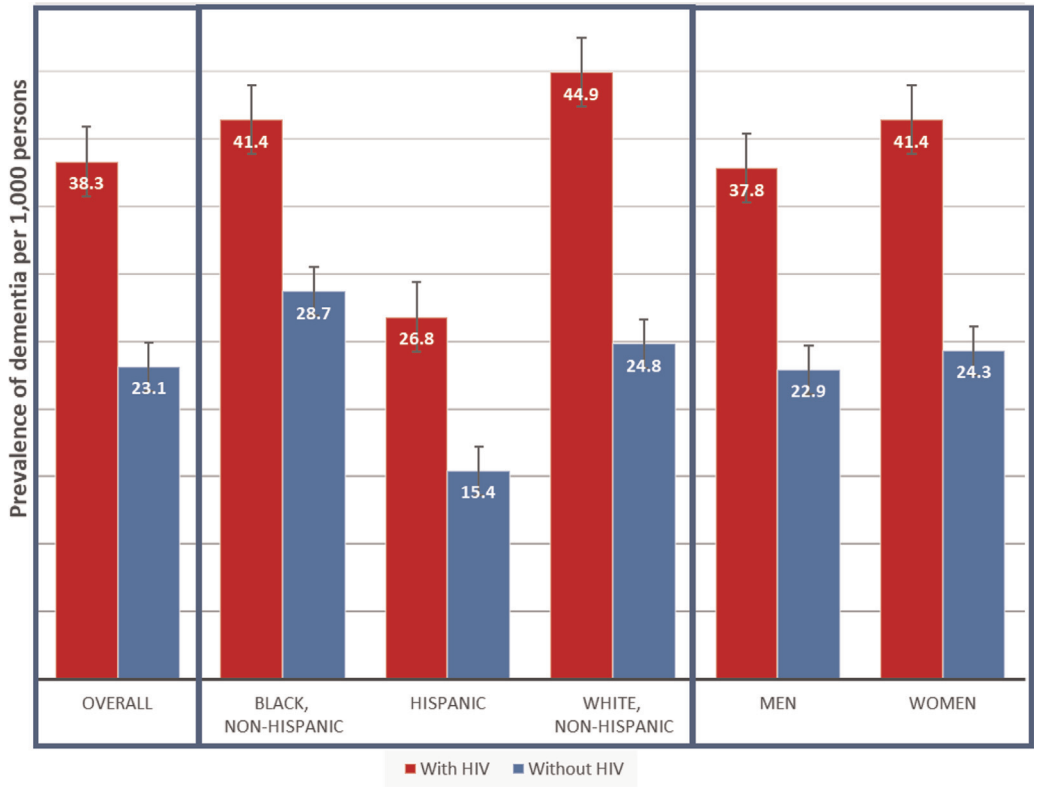

Fig. 2. Prevalence of dementia in 2020–2023 period in people with HIV and demographically matched people without HIV, overall, by race/ethnicity, and by sex.

This study helps fill a critical knowledge gap by describing the burden of dementia among people with HIV by race/ethnicity and sex, an important step in understanding cognitive health in an aging and increasingly diverse HIV population. While declining trends in dementia incidence were generally consistent across demographic subgroups, a modest increase among Hispanic individuals with HIV during 2020–2023 warrants further investigation, especially given Centers for Disease Control (CDC) projections that Hispanic populations will face the largest increases in dementia incidence in coming years [16]. In terms of dementia prevalence, people with HIV had a significantly higher burden of dementia across all racial/ethnic groups, highlighting the need to integrate HIV-specific considerations into broader aging care strategies. Given that people with HIV often experience social isolation and have fewer informal caregiving options, adapting existing HIV and dementia care infrastructure to meet increasing demands could support more inclusive care and positively impact the wellbeing of people aging with HIV [17,18]. Ensuring equitable access to dementia and HIV-related services will also be vital, particularly for racial and ethnic minority populations who often experience poorer dementia and HIV health outcomes [19–22].

Declining dementia incidence may be due to improved ART and better management of vascular risk factors common in people with HIV, such as cardiovascular disease, hypertension, and smoking [23–25]. However, maintaining consistent HIV viral suppression can be challenging, particularly in older populations where cognitive decline may impair ART adherence. In our cohort, 95.4% of individuals with detectable viral load at baseline had at least one subsequent episode of detectable viral load, and 23.2% of those with undetectable baseline viral load later experienced viral rebound, which could reflect the bidirectional relationship between HIV control and cognition.

Since our study period overlapped with the COVID-19 pandemic, changes in healthcare utilization may have influenced dementia recognition and diagnoses, impacting dementia estimates in the final years of our study. For instance, emerging knowledge about the neurologic effects of COVID-19 infection could have increased rates of cognitive screening [26–28]. Additionally, differential COVID-19-related mortality among people with dementia, or in the overall population of older adults may have affected observed incidence, though whether this varied by HIV status is unknown [29,30]. Continued monitoring of postpandemic trends will be needed to assess whether the observed convergence of dementia incidence persists and whether it varies by HIV status or demographic subgroup.

Although our study population was predominantly male (86%), dementia prevalence was higher among women,

regardless of HIV status, consistent with general population studies [31,32]. As the HIV population continues to age, factors that contribute to dementia risk among women, including menopausal transitions, hormone replacement therapy [33–37], and life-course adversity affecting cognitive reserve [32,38,39], may widen differences in dementia prevalence by sex. Understanding how these factors interact with HIV is an important area for future research.

This study had several limitations. First, dementia diagnoses were identified using ICD codes from routine clinical data, which could be influenced by changes in diagnostic practice and coding over time. Matching of people with and without HIV by year of cohort entry, along with mapping ICD codes to consistent dementia categories across the study period, would likely have minimized the impact of these cohort effects. Also, these data would capture patterns of care generally seen in clinical practice. Second, small numbers of dementia cases among Asian participants limited our ability to conduct stratified analyses or examine temporal trends in this group, an issue also present in other studies [32,40,41]. Further, underdiagnosis of dementia has been reported across racial and ethnic groups, including Asian, Black, and Hispanic populations, due to a combination of cultural, linguistic, and healthcare-related factors [40,42–46]. In our study, low case counts among Asian participants may reflect these broader patterns as well as cultural norms around aging specific to this population [41,43,47,48]. Third, analyses may have been affected by residual confounding from dementia risk factors not routinely recorded in the EHR, such as physical activity levels and environmental exposures. Fourth, models were adjusted for neighborhood-level education as a proxy for individual-level educational attainment, which may not fully capture the influence of education on dementia risk. Finally, although we report dementia types descriptively, models comparing incidence and prevalence by HIV status were not stratified by type. However, though dementia types may differ in etiology and trajectory, clinical care needs would largely overlap; therefore, our conclusions regarding the importance of high-quality dementia care would still be applicable.

This study also had notable strengths. KP serves a large population of older adults with HIV in an integrated healthcare setting and is broadly representative of the racial and ethnic diversity of the underlying community [49]. By harmonizing 23 years of KP EHR and HIV registry data across three U.S. regions, we assembled a demographically diverse study population suitable for both race-stratified and sex-stratified analyses. People with HIV had stable access to ART, and ART uptake was high (82% at baseline), reducing potential confounding effects of suboptimally treated HIV. In addition, our inclusion of a matched comparator group of people without HIV from the same healthcare setting enabled robust comparisons of dementia burden and helped account for potential differences in dementia diagnosis due to differential access to care. The ability to adjust for individual-level comorbidities and healthcare utilization further strengthened our estimates. Finally, because this study was conducted within integrated health systems our findings may generalize to other insured populations with similar access to care.

Conclusion

This study offers one of the most comprehensive longitudinal assessments of dementia among people with HIV in the modern ART era. The decline in incident dementia diagnoses is an encouraging trend that may reflect improved HIV treatment and care. However, the persistently higher prevalence underscores the need for sustained attention to cognitive health and integration of dementia-related services into HIV care.

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Conflicts of interest

The authors declare no conflicts of interest.

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