Non-AIDS comorbidity burden differs by sex, race, and insurance type in aging adults in HIV care

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Objective: To understand the epidemiology of non-AIDS-related chronic comorbidities (NACMs) among aging persons with HIV (PWH).

Design: Prospective multicenter observational study to assess, in an age-stratified fashion, number and types of NACMs by demographic and HIV factors.

Methods: Eligible participants were seen during 1 January 1997 to 30 June 2015, followed for more than 5 years, received antiretroviral therapy (ART), and virally suppressed (HIV viral load <200 copies/ml ≥75% of observation time). Age was stratified (18–40, 41–50, 51–60, ≥61 years). NACMs included cardiovascular disease, cancer, hypertension, diabetes, dyslipidemia, arthritis, viral hepatitis, anemia, and psychiatric illness.

Results: Of 1540 patients, 1247 (81%) were men, 406 (26%) non-Hispanic blacks (NHB), 183 (12%) Hispanics/Latinos, 575 (37%) with public insurance, 939 (61%) MSM, and 125 (8%) with injection drug use history. By age strata 18–40, 41–50, 51–60, and at least 61 years, there were 180, 502, 560, and 298 patients, respectively. Median HIV Outpatient Study observation was 10.8 years (range: min-max = 5.0–18.5). Mean number of NACMs increased with older age category (1.4, 2.1, 3.0, and 3.9, respectively; $P < 0.001$), as did prevalence of most NACMs ($P < 0.001$). Age-related differences in NACM numbers were primarily due to anemia, hepatitis C virus infection, and diabetes. Differences (all $P < 0.05$) in NACM number existed by sex (women >men, 3.9 vs. 3.4), race/ethnicity (NHB >non-NHB, 3.8 vs. 3.4), and insurance status (public >private, 4.3 vs. 3.1).

Conclusions: Age-related increases existed in prevalence and number of NACMs, with disproportionate burden among women, NHBs, and the publicly insured. These groups should be targeted for screening and prevention strategies aimed at NACM reduction.

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Introduction

The Centers for Disease Control and Prevention (CDC) estimate that nearly half of persons living with HIV in the United States are currently older than 50 years of age [1], a result of reduced mortality rates reflecting timely use of virally suppressive combination antiretroviral therapy (ART). Among ART-treated adults, non-AIDS-related chronic comorbidities (NACMs) account for the majority of deaths and the preponderance of morbidity [2,3].

Existing epidemiologic data suggest that persons living with HIV are diagnosed with NACMs at substantially younger ages than their HIV-uninfected counterparts, possibly by up to a decade or more [4,5]. This phenomenon may be related to at least two issues: persons living with HIV more frequently have risk factors for many NACMs, such as tobacco smoking, dyslipidemia, insulin resistance, chronic hepatitis C virus (HCV) or hepatitis B virus (HBV) infection, recreational substance use, obesity, poverty, and mental illness [6–16]; HIV infection, even among ART-treated and virologically suppressed persons, is associated with chronically elevated levels of systemic inflammation, immune dysregulation, and hypercoagulability [17–20]. Indeed, existing data suggest that current routine, well health screening strategies developed in the general population, such as for cardiovascular disease or bone fracture risk, may be inadequate for persons living with HIV [21,22].

Further characterization of the epidemiology of NACMs among aging persons living with HIV is needed to optimize clinical care and to plan effective health screening strategies in this population. In this analysis, we evaluated prevalence of multiple NACMs, by age and other demographic characteristics, in a large, diverse population of adults with HIV receiving ART.

Methods

The HIV Outpatient Study

The HIV Outpatient Study (HOPS) is an ongoing, open, prospective cohort study of over 10 000 adults with HIV (aged 18 years and over) seen in HIV-specialty clinics since 1993 [23]. The nine clinics included in the present analyses are located in six US cities: Tampa, Florida; Washington, District of Columbia; Denver, Colorado (three sites); Chicago, Illinois (two sites); Stony Brook, New York; and Philadelphia, Pennsylvania. The HOPS protocol has been approved and renewed annually by each participating institution's ethical review board, including the CDC. All study participants have provided written informed consent. All HOPS clinicians have extensive experience treating HIV-infected patients. Information was abstracted from outpatient charts and/or electronic medical records at each visit, entered electronically by trained staff, compiled centrally, reviewed, and cleaned before being analyzed. Abstracted information included: demographic characteristics, risk factors for HIV infection, diagnoses, prescribed medications, laboratory values [including $CD4^+$ T-lymphocyte cell counts/μl ($CD4^+$) and plasma HIV-RNA levels (viral loads)], mortality, and hospitalization records (primarily from discharge summaries).

For this analysis, we selected HOPS participants who received continuous care for at least 5 years, from 1 January 1997 to 30 June 2015, to ensure sufficient time to observe the relevant comorbidities while in HOPS care. We required their HIV infection to be well controlled, as defined by receiving ART for at least 75% of the observation time and having a suppressed HIV viral load (<200 copies/ml) for at least 75% of the time receiving ART. We assessed the frequency of 11 chronic comorbidities by age category at the participant's last HOPS visit using a cross-sectional study design.

Outcome measures

We evaluated 11 NACMs: cardiovascular disease, cancer, hypertension, diabetes, dyslipidemia, HBV or HCV infection, chronic kidney disease, chronic anemia, psychiatric illness, and chronic joint disease/fracture.

Comorbidities were defined based on diagnoses, laboratory measurements, and treatments documented in the patient medical record (see Appendix A in the Supplemental Digital Content for detailed definitions, http://links.lww.com/QAD/B523). If a comorbidity was documented at any time while under HOPS observation, it was considered to be ongoing at the time of last observation.

Independent (predictor) variables

The HIV transmission risk group was defined using the following hierarchy: persons who inject drugs (PWID); then gay, bisexual, and other MSM; and persons whose only self-reported risk was heterosexual contact. Health insurance payor was based on self-report at time closest to the end of observation. BMI was calculated based on the most recent height and weight measurements. $CD4^+$ cell count values analyzed were those closest to 6 months prior or 3 months after ART initiation. History of having ever smoked tobacco was established based on chart review.

Statistical analyses

Wilcoxon rank-sum tests for continuous variables, Yates-corrected chi-square test for categorical variables, or Mantel-Haenszel chi-square tests for trend across age groups for ordinal variables were used to compare patient characteristics by age category at observation end. We calculated the mean number of comorbidities recorded (of the 11 chronic conditions considered) per participant, both overall and according to race/ethnicity, sex, HIV transmission risk group, and payor, and 95% confidence

intervals (CIs) assuming a binomial distribution. We compared overall NACM prevalence and that for each chronic disease across age strata using the Cochran–Armitage trend test. We visualized multimorbidity (≥2 simultaneous comorbidities) by age group. We then explored the association of sociodemographic characteristics with the number of comorbid conditions using a modified Poisson approach to estimate relative risks (prevalence ratios) and 95% CIs in both univariate and multivariable models. Logistic regression analyses were used to determine demographic factors associated with specific comorbidity outcomes, with final models utilizing manual backward selection. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, North Carolina, USA).

Results

Among 10 671 HOPS participants, 3002 had at least 5 continuous years of observation between 1 January 1997 and 30 June 2015, and received care at a HOPS site. Of those persons, 2334 received ART for at least 75% of observed follow-up, and 1540 were virally suppressed for at least 75% of the time while receiving ART (Supplemental Figure one in the Supplemental Digital Content, http://links.lww.com/QAD/B523).

The 1540 included participants were classified into age groups based on their age at their last HOPS observation, with the largest groups being aged 41–50 years and 51–60 years (Table 1). Older age groups had more non-Hispanic

Table 1. Characteristics of participants by age group, the HIV Outpatient Study, 1997–2015, United States ($N = 1540$).

Characteristics at observation end unless otherwise specified[a]	Age at end of observation (years)					
n (%) or median (IQR)	Overall ($n = 1540$)	18–40 ($n = 180$)	41–50 ($n = 502$)	51–60 ($n = 560$)	≥61 ($n = 298$)	*P* value[b]
Sex at birth						0.17
Female	293 (19.0)	41 (22.8)	103 (20.5)	103 (18.4)	46 (15.4)	
Male	1,247 (81.0)	139 (77.2)	399 (79.5)	457 (81.6)	252 (84.6)	
Race/ethnicity						0.017
Non-Hispanic/Latino white	900 (58.4)	82 (45.6)	299 (59.6)	332 (59.3)	187 (62.8)	
Non-Hispanic/Latino black	406 (26.4)	55 (30.6)	127 (25.3)	152 (27.1)	72 (24.2)	
Hispanic/Latino	183 (11.9)	35 (19.4)	58 (11.6)	61 (10.9)	29 (9.7)	
Other/unknown race/ethnicity	51 (3.3)	8 (4.4)	18 (3.6)	15 (2.7)	10 (3.4)	
HIV transmission risk group						0.009
MSM	939 (61.0)	115 (63.9)	317 (63.1)	338 (60.4)	169 (56.7)	
Heterosexual	375 (24.4)	47 (26.1)	120 (23.9)	136 (24.3)	72 (24.2)	
PWID	125 (8.1)	4 (2.2)	30 (6.0)	54 (9.6)	37 (12.4)	
Other/unknown	101 (6.6)	14 (7.8)	35 (7.0)	32 (5.7)	20 (6.7)	
Payor						<0.001
Private	846 (54.9)	119 (66.1)	312 (62.2)	307 (54.8)	108 (36.2)	
Public	575 (37.3)	49 (27.2)	144 (28.7)	216 (38.6)	166 (55.7)	
Self-pay/none	75 (4.9)	10 (5.6)	30 (6.0)	23 (4.1)	12 (4.0)	
Other/unknown	44 (2.9)	2 (1.1)	16 (3.2)	14 (2.5)	12 (4.0)	
AIDS status	951 (61.8)	80 (44.4)	284 (56.6)	362 (64.6)	225 (75.5)	<0.001
BMI (kg/m^2)						<0.001
<18.5	37 (2.4)	1 (0.6)	10 (2.0)	12 (2.1)	14 (4.7)	
18.5–24.9	608 (39.5)	77 (42.8)	178 (35.5)	201 (35.9)	152 (51.0)	
25.0–29.9	521 (33.8)	58 (32.2)	184 (36.7)	195 (34.8)	84 (28.2)	
≥30	365 (23.7)	44 (24.4)	128 (25.5)	148 (26.4)	45 (15.1)	
Unknown	9 (0.6)	0 (0.0)	2 (0.4)	4 (0.7)	3 (1.0)	
$CD4^+$ cell count at ART initiation[c]						0.28
<50	158 (10.9)	15 (8.4)	54 (11.7)	58 (11.0)	31 (11.0)	
50–199	211 (14.6)	22 (12.3)	68 (14.8)	79 (15.0)	42 (14.8)	
200–349	235 (16.2)	40 (22.4)	77 (16.7)	79 (15.0)	39 (13.8)	
350–499	190 (13.1)	36 (20.1)	69 (15.0)	52 (9.9)	33 (11.7)	
≥500	136 (9.4)	19 (10.6)	47 (10.2)	48 (9.1)	22 (7.8)	
Unknown	518 (35.8)	47 (26.3)	146 (31.7)	209 (39.8)	116 (41.0)	
Median (IQR)	263 (96–404)	316 (187–405)	260 (101–413)	248 (84–407)	247 (77–392)	0.08
Smoker, current/prior	820 (53.2)	81 (45.0)	255 (50.8)	317 (56.6)	167 (56.0)	0.022
Years since HIV diagnosis, median (IQR)	15.4 (10.4–21.0)	9.0 (7.1–12.6)	14.0 (10.0–18.6)	17.4 (11.9–23.0)	19.3 (14.3–25.0)	<0.001
Years ART use, median (IQR)	13.6 (8.7–18.2)	7.9 (6.3–11.1)	12.2 (8.6–15.9)	15.8 (10.0–19.1)	17.4 (12.5–20.5)	<0.001
Years observation, median (IQR)	10.9 (7.5–15.0)	7.5 (6.3–9.7)	10.1 (7.3–13.6)	12.0 (8.0–16.2)	13.8 (10.1–17.8)	<0.001

ART, antiretroviral therapy; IQR, interquartile range; PWID, person who inject drugs.
[a]End of observation was defined as the earliest of the dates of death, last contact with HIV provider, or 30 June 2015.
[b]Wilcoxon rank-sum tests for continuous variables, Yates-corrected chi-square test for categorical variables, or Mantel-Haenszel chi-square tests for trend across age groups for ordinal variables.
[c]Closest value to date of ART-initiation documented six months prior through three months post-index date among those with ART initiation date known [1448 out of 1540 participants (94.0%)].

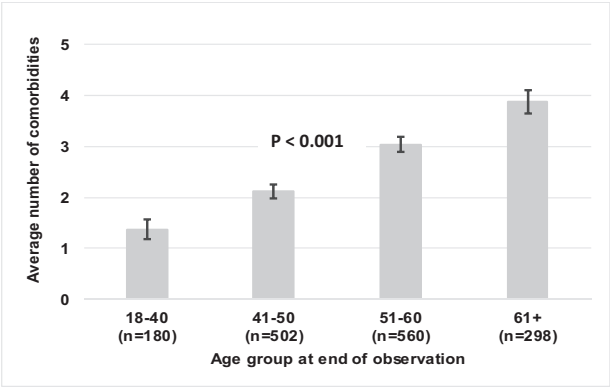

Fig. 1. Average number of NACM with 95% confidence intervals, the HIV Outpatient Study (HOPS), 1997–2015 United States ($N = 1540$). NACM, non-AIDS-related chronic comorbidity.

whites (NHW) vs. non-Hispanic blacks (NHBs) and Hispanics/Latinos ($P = 0.017$), and had more PWID participants ($P = 0.009$). Older participants were more likely to have public insurance, have a history of an AIDS diagnosis, and to have lower BMIs than their younger counterparts; older participants were also more likely to be current or prior smokers, and to have been diagnosed with HIV for a greater length of time ($P < 0.05$ for all).

Number of comorbidities and associated factors

The mean number of comorbidities increased with advancing age, with 1.4 (95% CI 1.19–1.56) observed among persons in the 18–40-year age group, compared to other age groups which averaged 2.1, 3.0, and 3.9 comorbidities, respectively ($P < 0.001$ for trend; Fig. 1). In univariate analyses, greater observed mean numbers of comorbidities by age stratum were driven primarily by differences in specific NACMs: anemia, HCV, and diabetes (Fig. 2 in the manuscript and Appendix B in the Supplemental Digital Content, http://links.lww.com/QAD/B523). There were significant differences in mean numbers of comorbidities by race/ethnicity (blacks > nonblacks, 3.0 vs. 2.6), sex (women > men, 3.1 vs. 2.6), and payor (public > private insurance, 3.6 vs. 2.1; $P < 0.01$ for all; Table 2 in the manuscript Supplemental Figure 2 and Appendix C in the Supplemental Digital Content, http://links.lww.com/QAD/B523).

Prevalence of non-AIDS comorbidities and multimorbidity

Overall, the most common comorbidities were psychiatric disorders (54.2%), dyslipidemia (46.0%), hypertension (40.4%), and chronic kidney disease (26.0%). The prevalence of each comorbidity significantly increased with advancing age, except for hepatitis B virus infection and psychiatric disorders (Fig. 2 in the manuscript and Appendix B in the Supplemental Digital Content,

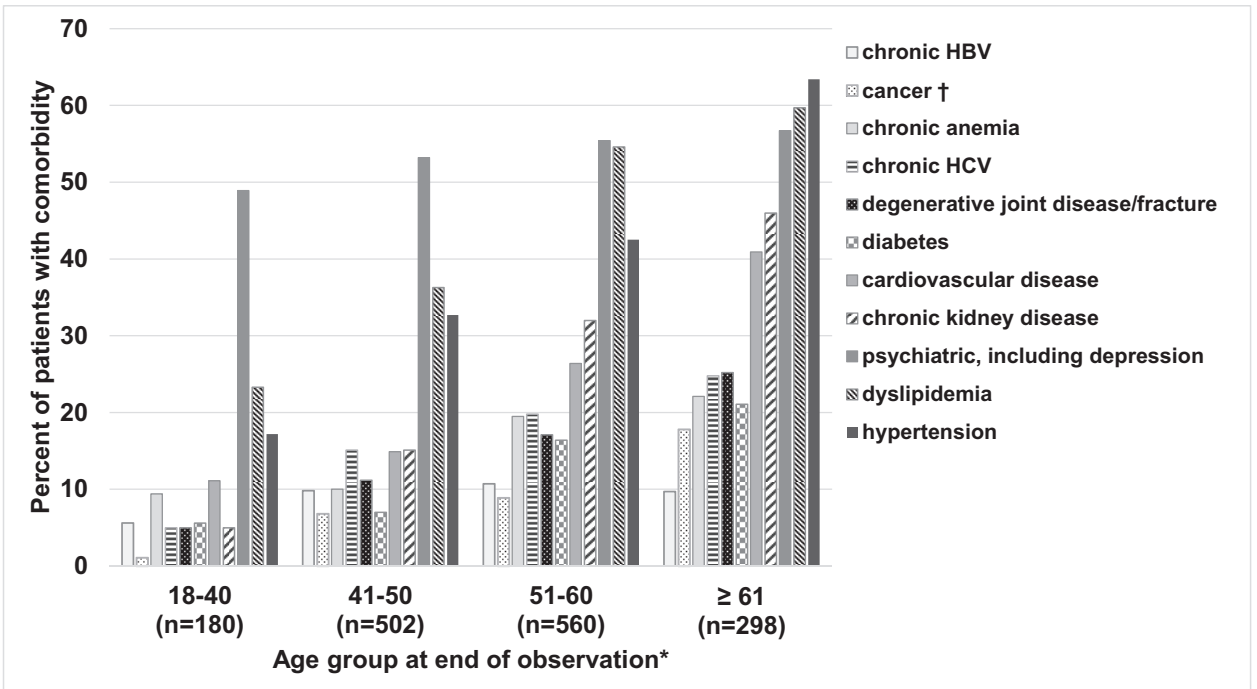

Fig. 2. Percentage of patients with comorbidities at end of observation, the HIV Outpatient Study, 1997–2015 United States ($N = 1540$). *Earliest of death, last HIV provider contact, or 30 June 2015. †Excluding skin cancers but including malignant melanoma. Note: All Cochran-Armitage *P*-values for trend for each condition across age groups were < 0.05, indicating significant increases by age, except for psychiatric illness and chronic HBV infection. HBV, hepatitis B virus; HCV, hepatitis C virus.

Table 2. Factors associated with having a greater number of NACMs, the HIV Outpatient Study, 1997–2015, United States ($N = 1540$).

Independent variables	Univariate		Multivariable	
At observation end	RR (95% CI)	*P* value	aRR (95% CI)	*P* value
Age group (years)				
18–40	Referent		Referent	
41–50	1.09 (0.97–1.24)	0.14	1.20 (1.06–1.36)	0.003
51–60	1.30 (1.15–1.46)	<0.001	1.49 (1.32–1.69)	<0.001
≥ 61	1.42 (1.26–1.61)	<0.001	1.62 (1.42–1.85)	<0.001
Sex at birth				
Female	1.10 (1.03–1.18)	0.006	0.91 (0.83–1.00)	0.046
Male	Referent		Referent	
Race/ethnicity				
Non-Hispanic/Latino black	1.19 (1.12–1.27)	< 0.001	0.99 (0.92–1.06)	0.72
All other	Referent		Referent	
HIV transmission risk group				
MSM	Referent		Referent	
Heterosexual	1.24 (1.16–1.33)	<0.001	1.12 (1.02–1.22)	0.018
PWID	1.52 (1.39–1.66)	<0.001	1.32 (1.19–1.46)	<0.001
Other/unknown	1.33 (1.18–1.48)	<0.001	1.18 (1.05–1.33)	0.007
Payor				
Private	Referent		Referent	
Public	1.48 (1.40–1.57)	<0.001	1.37 (1.28–1.47)	<0.001
Self-pay/none	1.15 (1.00–1.31)	0.045	1.20 (1.05–1.37)	0.008
Other/unknown	1.02 (0.86–1.21)	0.81	1.04 (0.87–1.24)	0.65
BMI (kg/m^2)				
<18.5	1.15 (0.97–1.37)	0.11	1.00 (0.84–1.19)	0.99
18.5–24.9	Referent		Referent	
25.0–29.9	1.00 (0.94–1.07)	0.94	1.05 (0.98–1.12)	0.18
≥30	1.14 (1.06–1.22)	<0.001	1.14 (1.06–1.23)	<0.001
Unknown	1.21 (0.86–1.69)	0.27	1.08 (0.77–1.51)	0.66
Current or prior smoker				
Yes	1.15 (1.09–1.22)	<0.001	1.07 (1.01–1.14)	0.017
No	Referent		Referent	
$CD4^+$ cell count (cells/μl), nadir				
<50	1.20 (1.06–1.35)	0.004	1.07 (0.94–1.21)	0.30
50–199	1.22 (1.09–1.38)	<0.001	1.09 (0.97–1.23)	0.15
200–349	1.02 (0.90–1.15)	0.77	0.98 (0.87–1.11)	0.78
350–499	1.05 (0.92–1.19)	0.50	1.03 (0.90–1.17)	0.67
≥500	Referent		Referent	
Calendar period of observation end				
2002–2006	1.45 (1.30–1.63)	<0.001	1.37 (1.21–1.54)	<0.001
2007–2011	1.15 (1.04–1.26)	0.004	1.14 (1.04–1.26)	0.005
2012–2014	1.02 (0.95–1.10)	0.57	1.03 (0.95–1.11)	0.49
2015	Referent		Referent	

aRR, adjusted risk ratio; ART, antiretroviral therapy; CI, confidence interval; NACM, non-AIDS-related chronic comorbidities; PWID, person who inject drugs; RR, risk ratio.

http://links.lww.com/QAD/B523). The Venn diagram in Supplemental Fig. 3 (http://links.lww.com/QAD/B523) depicts the overlap in occurrence of comorbidities (i.e. number of persons simultaneously having 1, 2, or all 3, of the more common comorbidities) stratified by age group. There was substantial co-occurrence of dyslipidemia and hypertension regardless of age group, and chronic kidney disease became increasingly more common with advancing age among persons with dyslipidemia and/or hypertension.

Modeled associations of factors associated with having more comorbidities

In univariate analyses, we found that older age, female sex, and NHB race/ethnicity were each positively and significantly associated with having a greater number of comorbidities (Table 2). We observed greater mean numbers of comorbidities among heterosexuals and PWID (compared with MSM), persons with public insurance or self-pay/no insurance (compared with persons with private insurance), those who were obese (compared with those having normal BMI), and those followed in earlier calendar periods. In multivariable analyses (Table 2), factors significantly associated with having a greater number of NACMs included older age, having a history of injection drug use (IDU), BMI at least 25.0, having public insurance, and earlier calendar period (2002–2006).

Univariate analyses of the associations between demographic, behavioural, and clinical factors with specific comorbidities are shown in Supplemental Table 2 in the Supplemental Digital Content (http://links.lww.com/QAD/B523). In parsimonious multivariable logistic regression models of factors associated with specific

Table 3. Parsimonious logistic regression models of factors associated with comorbid outcomes, the HIV Outpatient Study, 1997–2015 United States ($N = 1540$).

Demographic characteristics at observation end	Comorbidities: odds ratio (95% confidence interval)					
	Anemia ($n = 242$)	Psychiatric conditions ($n = 834$)	Hypertension ($n = 986$)	Diabetes ($n = 302$)	Chronic kidney disease ($n = 401$)	Cardiovascular disease ($n = 365$)
Age in years						
≤30	Referent[a]		Referent	Referent[a]	Referent[a]	Referent[a]
31–40	Referent[a]		1.62 (0.64–4.11)	Referent[a]	Referent[a]	Referent[a]
41–50	0.96 (0.51–1.81)		2.64 (1.08–6.45)	1.50 (0.82–2.75)	3.36 (1.64–6.87)	1.23 (0.72–2.09)
51–60	2.02 (1.10–3.73)		5.16 (2.11–12.62)	2.52 (1.40–4.55)	8.89 (4.42–17.86)	2.28 (1.36–3.82)
≥61	2.13 (1.10–4.12)		10.35 (4.0–26.17)	3.22 (1.72–6.02)	14.41 (7.05–29.46)	4.07 (2.35–7.05)
Sex at birth						
Women	3.03 (2.14–4.28)	1.49 (1.11–2.00)	0.54 (0.40–0.74)			
Men	Referent	Referent	Referent			
Race/ethnicity						
Non-Hispanic/Latino black	2.59 (1.88–3.58)	0.65 (0.50–0.84)	1.36 (1.03–1.80)		0.58 (0.43–0.78)	
All other	Referent	Referent	Referent		Referent	
Payor						
Public or no insurance	2.21 (1.58–3.10)	2.75 (2.19–3.45)	1.82 (1.42–2.32)	2.12 (1.62–2.78)	1.89 (1.46–2.45)	1.40 (1.09–1.80)
Private insurance	Referent	Referent	Referent	Referent	Referent	Referent
BMI						
≥30 (kg/m^2)			2.44 (1.83–3.26)	2.43 (1.82–3.24)		1.43 (1.08–1.90)
<30 (kg/m^2)			Referent	Referent		Referent
Current or prior smoker						
Yes		1.54 (1.25–1.91)			0.66 (0.51–0.84)	
No		Referent			Referent	
CD4$^+$ cell count (cells/μl), nadir						
<50	7.67 (2.89–20.41)					
50–199	6.11 (2.32–16.08)					
200–349	4.16 (1.56–11.11)					
350–499	2.59 (0.91–7.35)					
≥500	Referent					
Years follow-up	1.04 (1.01–1.08)			1.07 (1.03–1.10)		1.05 (1.02–1.08)
Calendar period of observation end						
2002–2006						
2007–2011						
2012–2014						
2015						

Demographic Characteristics at observation end	Comorbidities: odds ratio (95% confidence interval)				
	Dyslipidemia ($n = 989$)	Cancer ($n = 139$)	Degenerative joint disease/fracture ($n = 171$)	HBV, chronic ($n = 148$)	HCV, chronic ($n = 270$)
Age in years					
≤30	Referent	Referent[a]	Referent[a]		Referent[a]
31–40	1.18 (0.46–2.98)	Referent[a]	Referent[a]		Referent[a]
41–50	1.49 (0.61–3.64)	6.25 (1.48–26.38)	1.95 (0.80–4.76)		3.44 (1.67–7.10)
51–60	2.67 (1.09–6.56)	8.60 (2.06–35.98)	3.87 (1.65–9.10)		4.66 (2.28–9.54)
≥61	3.84 (1.51–9.72)	18.59 (4.43–78.05)	4.93 (2.06–11.83)		5.20 (2.48–10.90)
Sex					
Women	0.65 (0.48–0.86)			0.58 (0.36–0.94)	
Men	Referent			Referent	
Race/ethnicity					
Non-Hispanic/Latino black	0.56 (0.43–0.73)			2.43 (1.67–3.52)	1.66 (1.22–2.25)
All other	Referent			Referent	Referent
Payor					
Public or no insurance			2.18 (1.54–3.08)		2.70 (1.99–3.64)
Private insurance			Referent		Referent
BMI					
≥30 (kg/m^2)	2.18 (1.64–2.89)				0.70 (0.50–0.99)
<30 (kg/m^2)	referent				Referent
Current or prior smoker					
Yes				1.73 (1.22–2.47)	1.51 (1.14–2.00)
No				Referent	Referent
CD4$^+$ cell count (cells/μl), nadir					
<50		3.33 (1.27–8.76)		3.20 (1.21–8.42)	
50–199		2.57 (0.99–6.66)		2.42 (0.93–6.27)	
200–349		1.46 (0.54–3.92)		2.61 (1.00–6.77)	
350–499		1.48 (0.53–4.18)		1.44 (0.51–4.06)	
≥500		Referent		Referent	
Years follow-up	1.10 (1.06–1.13)			1.05 (1.00–1.09)	
Calendar period of observation end					
2002–2006		2.17 (1.21–3.92)	0.35 (0.14–0.88)		2.22 (1.37–3.60)
2007–2011		1.69 (0.99–2.89)	0.39 (0.19–0.80)		1.32 (0.84–2.05)
2012–2014		0.99 (0.62–1.59)	0.66 (0.44–1.01)		1.01 (0.70–1.43)
2015		Referent	Referent		Referent

Note: Backward selection was used to create the final multivariable models.
[a]There were less than five participants 30 years or younger with anemia, diabetes, CKD, CVD, cancer, joint disease, HBV and HCV, r respectively, so the lowest two age categories were combined.

comorbidities (Table 3), women had greater odds of psychiatric conditions and anemia than men, but lower odds of hypertension; NHBs had greater odds of anemia, hypertension, and chronic viral hepatitis, but lower odds of dyslipidemia, chronic kidney disease, and psychiatric illness than nonblacks; publicly insured persons had greater odds of anemia, psychiatric conditions, hypertension, diabetes, chronic kidney disease, cardiovascular disease, degenerative joint disease, and chronic HCV infection than other payor groups ($P < 0.05$ for all). These associations were generally consistent with findings in fully adjusted logistic regression models (Supplemental Table 2 in the Supplemental Digital Content, http://links.lww.com/QAD/B523).

Discussion

In this large, prospectively-followed, diverse group of ART-treated adults with HIV who received continuous care and had well controlled viremia on ART, we observed age-related increases in the prevalence of important NACMs and in the presence of multimorbidity. There were more NACMs among older participants (particularly over the age of 50 years), women, NHBs, publicly insured persons, persons with greater BMI, and persons with a history of injection drug use. In fully adjusted regression models, although sex and race/ethnicity were nonsignificant, the increased NACM burden persisted for persons with public insurance, with greater BMI, and with heterosexual or IDU HIV risk. In addition, with advancing age, we observed increasing overlap in the percentage of participants with at least two of the three most common nonpsychiatric NACMs we studied: hypertension, dyslipidemia, and chronic kidney disease.

Furthermore, specific NACMs appeared to account for observed discordances in overall NACM burden by medical insurance type and by participant demographics. Of note, many of these demographic-based differences in specific disease occurrence mirror observations that have been made in the general US population: [24–26] women were more likely to have diagnoses of psychiatric conditions and anemia than men; blacks had greater likelihood of anemia and hypertension than nonblacks; publicly insured persons had more anemia, psychiatric conditions, hypertension, diabetes, chronic kidney disease, and cardiovascular disease than persons in other payor groups.

Factors that may have contributed to or accounted for our central findings, that is, differences in age-associated NACM burden by demographics and insurance type, are diverse, numerous, and, for the most part, not measurable directly from our medical abstraction database. These include uptake of and maintenance of healthy behaviors, access to medical care, screening for and preventive measures aimed at NACM early detection and risk management, and timeliness of initiation of NACM-specific treatments. Extent of use of other preventive and well health measures that can mitigate the risk of some NACMs (e.g. diabetes and hypertension) such as smoking cessation, weight reduction, and systematic physical activity likewise could not be directly ascertained from our data. Nevertheless, factors associated with overall health in the general population that have been linked to having public (vs. nonpublic) insurance have been described and most often involve overall healthcare access, timeliness of care delivery including preventive care, and poverty [26–29].

Our observation of age-related increasing overlap in the percentage of participants with at least two of three of our most common nonpsychiatric NACMs (hypertension, dyslipidemia, and chronic kidney disease) suggests an age-related NACM phenotype among ART-treated persons with HIV. This phenotype involves specific NACMs with common or overlapping etiologic risks, some commonality of pathophysiologic mechanisms, and constitutes convergent risks for other NACMs. For example, hypertension is a known risk factor for chronic kidney disease; dyslipidemia is associated with insulin resistance, which is a risk for chronic kidney disease; hypertension and diabetes are both associated with obesity; all 3 NACMs comprise independent risks for increased cardiovascular disease [30–34]. However, we did note some counterintuitive findings, including the apparent protective effect of NHB race on dyslipidemia and CKD; precise reasons accounting for these findings were not apparent, but may have reflected differences between NHB and non-Black participants who were not related to race/ethnicity and for which we could not readily account.

We sought specifically to evaluate the effect of other-than-HIV factors on the prevalence of NACMs in studied patients. For this reason, we chose to study ART-treated participants who, overall, had good HIV control (virologically suppressed $\geq$75% of the time under observation). Other work has demonstrated that HIV infection, even when well controlled, is associated with chronic elevations (compared to HIV-uninfected persons) in systemic levels of inflammation, immune dysregulation, and hypercoagulabilty [17–20]; these factors affect the overall health risk and correlate with mortality risk as well as risk for cardiovascular events, non-AIDS-defining cancers, and kidney disease among persons with HIV [35,36], but were not measured in our cohort. In this analysis, we found fewer associations between NACMs and $CD4^+$ nadir (our best proxy for duration of HIV infection), and did not examine the use of specific ART regimens or drugs; however, based on existing body of HOPS [37,38] and other HIV cohorts research [39,40], we do not believe ART drugs constitute principal determinants of NACM risk.

Regarding associations between ART use and NACMs, we were limited in our ability to evaluate the complex relationships between specific ART types used and risks for specific NACMs. The evaluation of these often-nuanced relationships is beyond the scope of this study and requires accounting for changes in types of ART used by individual patients over time.

Other limitations to our findings exist and include the fact that our data were routinely collected via medical record abstraction, and there was considerable variability in the timing of participant healthcare visits. Furthermore, we had no information on additional risk factors and potential confounders for the associations with some demographic covariates, including hard data regarding participant socioeconomic status, outpatient healthcare encounters outside of the primary care site, housing and job stability, and nutritional status, among others. The NACMs in our study were defined based on combinations of diagnoses, treatments, and laboratory results (see Appendix A), and detection of some may have depended on the intensity of screening (e.g. HCV, cancer, etc.). For example, anemia was determined by presence of a diagnosis code as recorded by the clinicians at individual HOPS sites, but diagnoses of anemia were not adjudicated centrally using a uniform definition based upon laboratory data. Hence the definitions of anemia may have varied slightly from HOPS site to HOPS site. We were unable to disaggregate treated and untreated NACM conditions.

As ART-treated persons with HIV age, the main determinants of overall health and survival are less likely to be directly related to HIV virologic control and immunodeficiency than to the long-term consequences of age-related chronic comorbid illnesses. Our study demonstrates that discordances in NACM prevalence exist by race, sex, and type of medical insurance, and that many of these differences increase with advancing age. Our findings highlight the need for clinicians to consider demographic, healthcare coverage, and social determinants of health in the routine primary care of persons with HIV; such factors may ultimately inform healthcare delivery systems, including interventions aimed at screening for and preempting of important age-related NACMs.

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Conflicts of interest

F.J.P. has been a consultant and /or on the Speakers' Bureau for Gilead Sciences, Janssen Pharmaceuticals, Merck and Co. and ViiV

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