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Excess Clinical Comorbidity Among HIV-Infected Patients Accessing Primary Care in US Community Health Centers

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Abstract

Objectives: As the life expectancy of people infected with human immunodeficiency virus (HIV) infection has increased, the spectrum of illness has evolved. We evaluated whether people living with HIV accessing primary care in US community health centers had higher morbidity compared with HIV-uninfected patients receiving care at the same sites.

Methods: We compared data from electronic health records for 12 837 HIV-infected and 227 012 HIV-uninfected patients to evaluate the relative prevalence of diabetes mellitus, hypertension, chronic kidney disease, dyslipidemia, and malignancies by HIV serostatus. We used multivariable logistic regression to evaluate differences. Participants were patients aged ≥18 who were followed for ≥3 years (from January 2006 to December 2016) in 1 of 17 community health centers belonging to the Community Health Applied Research Network.

Results: Nearly two-thirds of HIV-infected and HIV-uninfected patients lived in poverty. Compared with HIV-uninfected patients, HIV-infected patients were significantly more likely to be diagnosed and/or treated for diabetes (odds ratio [OR] = 1.18; 95% confidence interval [CI], 1.22-1.41), hypertension (OR = 1.38; 95% CI, 1.31-1.46), dyslipidemia (OR = 2.30; 95% CI, 2.17-2.43), chronic kidney disease (OR = 4.75; 95% CI, 4.23-5.34), lymphomas (OR = 4.02; 95% CI, 2.86-5.67), cancers related to human papillomavirus (OR = 5.05; 95% CI, 3.77-6.78), or other cancers (OR = 1.25; 95% CI, 1.10-1.42). The prevalence of stroke was higher among HIV-infected patients (OR = 1.32; 95% CI, 1.06-1.63) than among HIV-uninfected patients, but the prevalence of myocardial infarction or coronary artery disease did not differ between the 2 groups.

Conclusions: As HIV-infected patients live longer, the increasing burden of noncommunicable diseases may complicate their clinical management, requiring primary care providers to be trained in chronic disease management for this population.

Keywords

HIV, diabetes, hypertension, kidney disease, cancer

With the advent of highly active antiretroviral therapy, people who are infected with human immunodeficiency virus (HIV) are living longer, particularly now that the newer medications are better tolerated than the original medications.[1,2] Life expectancy has also increased dramatically. An HIV-infected adult aged 20 who became infected in 2016 can expect to live 53 additional years compared with a 20-year-old diagnosed 30 years ago, who was likely to die within a decade.[3] Projections from a Dutch national database suggest that the median age of HIV-infected patients will increase to 57 years by 2030, with 39% of HIV-infected patients being aged ≥60.[4] Despite the increased longevity,

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concerns have been raised that HIV disease and its treatment might accentuate and accelerate the onset of noncommunicable morbidities.[5] HIV-infected people have high rates of atherosclerosis, diabetes, chronic kidney disease, and several malignancies in studies conducted at academic research centers.[6-9] Multiple factors might explain the excess morbidity, including the long-term effects of HIV-induced immune dysregulation and inflammation, behavioral risks (eg, tobacco and other substance use), and the potential long-term effects of antiretroviral medication.[10]

Because recent data suggest that earlier initiation of treatment is associated with decreased morbidity and mortality, the use of highly active antiretroviral therapy is increasingly common.[11] Almost all studies assessing HIV morbidity have used samples of patients from specialty clinics at teaching hospitals, rather than community-based samples, raising questions about generalizability of the findings.[12]

To date, no studies of chronic HIV infection have been conducted in safety-net community health centers in the United States, where disenfranchised patients may have multiple risk factors for other common conditions. Studies of HIV-infected patients in the Veterans Administration system have provided important insights about the changing spectrum of HIV disease in a racially and ethnically diverse sample but may not be generalizable to community-based samples.[13] The more than 9000 Federally Qualified Health Centers play an increasingly pivotal role in ensuring health care access to 25 million primary care patients. Our study is particularly important because community health center patients tend to be poorer and are more likely to come from racial/ethnic minority communities than those who access care in private settings.[14] We evaluated whether the prevalence of selected conditions (diabetes mellitus, hypertension, chronic kidney disease, dyslipidemia, atherosclerotic disease, and cancer) was higher among HIV-infected patients than among HIV-uninfected patients receiving primary care at community health centers in a geographically diverse sample.

Methods

The Community Health Applied Research Network was established by the Health Resources and Services Administration in 2011; it consists of 17 community health centers in 9 states (Arizona, California, Hawaii, Illinois, Maryland, Massachusetts, New York, Oregon, and South Carolina) and a common database of more than 1 million patients, with electronic health record data from 2006 until the present.[15] Electronic health record systems allow health care researchers to analyze large clinical data sets in a standardized manner. To better understand the population health implications of the Affordable Care Act, the Health Resources & Services Administration funded the Community Health Applied Research Network to develop a common database of key clinical data elements from community health centers across the United States. The Community Health Applied Research Network Data Coordinating Center is based at the Kaiser Permanente Center for Health Research in Portland, Oregon. We analyzed clinical data and sociodemographic characteristics of 12 837 HIV-infected adults and 227 012 HIV-uninfected locally matched adults aged $\geq$18 who accessed care at 1 of the 17 community health centers for $\geq$3 years (defined as $\geq$2 clinic visits between 2006 and 2014).

We used the Community Health Applied Research Network database to evaluate the prevalence of diabetes, hypertension, coronary artery disease, myocardial infarction, stroke, dyslipidemia, chronic kidney disease, lymphomas, human papillomavirus (HPV)–related cancers, or other cancers in HIV-infected patients and HIV-uninfected patients. The Data Coordinating Center developed a standardized structured query language relational database schema and a data dictionary to ensure consistency across analyses.[15] We reviewed the data sources for each clinical condition and developed operational definitions (Table 1). We determined HIV status by using recorded *International Classification of Diseases, Ninth Revision* (ICD-9)[16] diagnosis codes and laboratory results. For the diagnosis of diabetes, we used ICD-9 diagnosis codes, medications, and laboratory values; for hypertension, we used medications or ICD-9 diagnosis codes along with blood pressure measurements to inform the diagnosis. For the diagnosis of dyslipidemia, we used lipid-lowering medications and blood lipid results. For chronic kidney disease, we used creatinine clearance to inform the definition. For the diagnoses of cancers, we used ICD-9 diagnosis codes.

Statistical Analyses

We used descriptive statistics to examine the characteristics of each group. In addition to computing the unadjusted prevalence of each comorbid condition, we computed the estimated marginal prevalence and compared the rates of each condition between groups by using multilevel logistic regression with Stata (version 13.2)[18] to account for the clustering of patients within community health centers and to control for confounding of other variables that may account for any relationship between HIV status and these outcomes.[19-21] These variables included age (nonlinear), race/ethnicity, and sex (male, female, transgender) as independent variables in the models. For the diabetes outcome, an additional model included body mass index (BMI) as an independent variable. Inferential tests for the regression coefficients are based on the z statistic; we evaluated all tests at a 2-tailed alpha level of .05 and reported 95% confidence intervals (CIs).

Data collection for this study was approved by the institutional review boards of the Data Coordinating Center at the Kaiser Permanente Center for Health Research, Portland, Oregon, and the 4 participating Research Nodes based at Fenway Health, Boston, Massachusetts; Association of Asian Pacific Community Health Organizations, San Leandro, California; Alliance of Chicago Community

Table 1. Operational definitions of clinical comorbid chronic conditions among adult patients seeking services at community health centers, Community Health Applied Research Network database, January 2006-2016

Clinical Condition	Operational Definition[a]
HIV	• ≥2 visits with HIV-related ICD-9 diagnoses (042 795.71, V08) separated by at least 30 days, or • A positive HIV-specific laboratory test, or • Kaposi's sarcoma for patients aged >60
Diabetes	• Use of insulin or oral antihyperglycemic agent,[b] or • ≥1 HbA1c ≥6.5%, or • A visit or problem list diagnosis on ≥2 visits
Hypertension	• A visit or problem list diagnosis of hypertension AND the presence of any antihypertensive medication defines pharmacologically treated hypertension, or • A visit or problem list diagnosis of hypertension AND the average of ≥2 systolic blood pressure measurements ≥140 mm Hg or diastolic blood pressure measurements ≥90 mm Hg (>7 days apart)
Chronic kidney disease	• eGFR <60 mL/min/1.73 m^2 for ≥3 months (2 values >90 days apart without an intervening normal value)
Dyslipidemia	• Use of a lipid-lowering medication, or • Any of the following laboratory abnormalities: low-density lipoprotein ≥130 mg/dL; high-density lipoprotein ≤30 mg/dL for men or ≤40 mg/dL for women, or • Total cholesterol ≥200 mg/dL, or • Triglycerides ≥200 mg/dL
Coronary artery disease, myocardial infarction, or stroke	• A visit or problem list diagnosis of coronary artery disease, myocardial infarction, or stroke
Cancers	• A visit or problem list diagnosis of cancer • Cancers were then separated into HPV-associated cancer, lymphomas, and all other cancers. Patients with HIV-specific cancers (Burkitt's tumor or lymphoma for all patients and Kaposi's sarcoma for patients aged >60) were removed from the analysis.

Abbreviations: eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; HIV, human immunodeficiency virus; HPV, human papillomavirus; ICD-9, *International Classification of Diseases, Ninth Revision*.[16]

[a]Data source for original clinical definitions: Centers for AIDS Research Network of Integrated Clinical Systems.[17]

[b]Not valid if medication dispensed was metformin, any thiazolidinedione, or exenatide, and none of the other criteria were met.

Health Services, Chicago, Illinois; and OCHIN, Inc, Portland, Oregon.

Results

The study sample included 239 849 eligible community health center primary care patients, of whom 86 220 (35.9%) were male, 37 182 (15.5%) were non-Hispanic black, and 48 434 (20.2%) were Hispanic; the mean age was 41 (Table 2). Most patients for whom income information was available (n = 156 376, 65.2%) were living below twice the federal poverty level, 8031 (5.1%) of whom were HIV infected. On average, HIV-infected patients tended to be young, male, non-Hispanic white, and insured and to have a history of cigarette smoking ($P < .001$ for all). HIV-infected patients varied by sex: 27.8% of female, 70.0% of male, and 2.2% of transgender patients were HIV infected. The prevalence of hepatitis C infection, alcohol use, or substance use disorders was significantly higher among HIV-infected patients than among HIV-uninfected patients.

HIV-infected patients tended to have more medical visits (mean, 11.7 per year) than HIV-uninfected patients (mean, 6.5 per year), but both groups accessed primary care regularly. HIV-infected patients appeared to have generally controlled infection (ie, CD4 count >500 cells/mm^3), with a mean and median most recent CD4 count of 604 and 572 cells/mm^3, respectively. Plasma HIV ribonucleic acid testing was available for 59.2% of HIV-infected patients at their most recent visit, and it was undetectable for 73.2% of HIV-infected patients.

The prevalence of all clinical conditions of interest was significantly higher in HIV-infected patients than in HIV-uninfected patients in the unadjusted analyses, except for cardiac conditions (Table 3). Hypertension was most common in HIV-infected compared with HIV-uninfected patients (43.7% vs 35.9%, $P < .001$), followed by dyslipidemia (42.9% vs 41.5%, $P < .001$). The least prevalent condition was HPV-associated malignancy (cervix, vulvar, rectal, oropharyngeal), which was diagnosed in 0.8% of HIV-infected versus 0.3% of HIV-uninfected patients ($P < .001$). The prevalence of cancers not associated with HIV or HPV was also greater among HIV-infected patients than among HIV-uninfected patients. Although the absolute numbers of lymphomas and HPV-associated cancers were lower than numbers of other cancers, their relative prevalence was greater among HIV-infected patients than among HIV-uninfected patients ($P < .001$ for all comparisons). Although strokes were uncommon (1.1% of the entire sample), they were more common among HIV-infected patients than among HIV-uninfected patients ($P = .002$), but the

Table 2. Sociodemographic characteristics of HIV-infected and HIV-uninfected adult patients seen in community health centers, Community Health Applied Research Network database, 2006-2014[a]

Characteristic	All Patients	HIV-Infected Patients	HIV-Uninfected Patients	Adjusted *P* Value[b]
Total no.	239 849	12 837	227 012	<.001
Mean (SD) age at first encounter, y	41.0 (15.3)	40.3 (11.8)	41.1 (15.5)	
Age at first encounter, no. (%)				<.001
18-24	39 626 (16.5)	1402 (10.9)	38 224 (16.8)	
25-34	55 185 (23.0)	2696 (21.0)	52 489 (23.1)	
35-44	48 424 (20.2)	4009 (31.2)	44 415 (19.6)	
45-54	47 536 (19.8)	3324 (25.9)	44 212 (19.5)	
55-64	30 986 (12.9)	1132 (8.8)	29 854 (13.2)	
≥65	18 092 (7.5)	274 (2.1)	17 818 (7.8)	
Sex, no. (%)				<.001
Female	152 443 (63.6)	3567 (27.8)	148 876 (65.6)	
Male	86 220 (35.9)	8984 (70.0)	77 236 (34.0)	
Transgender	1182 (0.5)	286 (2.2)	896 (0.4)	
Unknown	4 (0.0)	0	4 (0.0)	
Race/ethnicity, no. (%)				.92
Hispanic	48 434 (20.2)	1788 (13.9)	46 646 (20.5)	
Non-Hispanic white	82 556 (34.4)	7170 (55.9)	75 386 (33.2)	
Non-Hispanic black	37 182 (15.5)	2955 (23.0)	34 227 (15.1)	
Non-Hispanic other	7635 (3.2)	668 (5.2)	6967 (3.1)	
Non-Hispanic Asian/Pacific Islander	61 862 (25.8)	212 (1.7)	61 650 (27.2)	
Unknown	2180 (0.9)	44 (0.3)	2136 (0.9)	
Insurance status at or near index, no. (%)				.93
Uninsured	79 310 (33.1)	2209 (17.2)	77 101 (34.0)	
Insured	156 863 (65.4)	10 514 (81.9)	146 349 (64.5)	
Unknown	3676 (1.5)	114 (0.9)	3562 (1.6)	
FPL status at or near index, no. (%)				<.001
≤200% FPL	156 376 (65.2)	8031 (62.6)	148 345 (65.3)	
>200% FPL	21 912 (9.1)	1375 (10.7)	20 537 (9.0)	
Unknown	61 561 (25.7)	3431 (26.7)	58 130 (25.6)	
Patient has ever smoked, no. (%)				<.001
Yes	79 851 (33.3)	6176 (48.1)	73 675 (32.5)	
No	103 732 (43.2)	3843 (29.9)	99 889 (44.0)	
Unknown	56 266 (23.5)	2818 (22.0)	53 448 (23.5)	

Abbreviations: FPL, federal poverty level; HIV, human immunodeficiency virus.
[a]Data source: Community Health Applied Research Network Data Warehouse version 3, May 2016.[15]
[b]*P* values are based on analyses that adjust for the intraclass correlation of patients nested within clinics using mixed effects logistic regression models.

relative prevalence of myocardial infarction and coronary artery disease did not differ between the 2 groups.

After adjusting for the quadratic and linear effect of age plus race and sex, and the frequency of primary care visits, HIV-infected patients were significantly more likely than HIV-uninfected patients to have diabetes, whether or not adjusting for BMI (OR = 1.31; 95% CI, 1.22-1.41); to be diagnosed and/or treated for hypertension (OR = 1.38; 95% CI, 1.31-1.46); and to have chronic kidney disease (OR = 4.75; 95% CI, 4.23-5.34) (Table 3). Dyslipidemia was also more prevalent among HIV-infected patients than among HIV-uninfected patients (OR = 2.30; 95% CI, 2.17-2.43). Additionally, HIV-infected patients were more likely than HIV-uninfected patients to be diagnosed with lymphomas (OR = 4.02; 95% CI, 2.86-5.67), HPV-related cancers (OR = 5.05; 95% CI, 3.77-6.78), and other cancers (OR = 1.25; 95% CI, 1.10-1.42) ($P < .001$ for all comparisons). Although HIV-infected patients did not differ from HIV-uninfected patients in their prevalence of myocardial infarction or coronary artery disease, they were more likely to have a stroke (OR = 1.32; 95% CI, 1.06-1.63).

Discussion

During the past 2 decades, HIV has been transformed from an untreatable immunodeficiency usually resulting in death from opportunistic infections and neoplasms to a chronic manageable infection, often requiring only 1 well-tolerated pill per day.[22] As the life expectancy of HIV-infected people has increased,[23] their spectrum of illnesses has evolved.[24] We found higher rates of diabetes, hypertension, chronic kidney disease, stroke, and several cancers in HIV-infected patients accessing primary care at community health centers than among HIV-uninfected patients. Our study is the first to document excess morbidities among HIV-infected patients accessing care in safety-net community health centers.

The prevalence of noncommunicable diseases among HIV-infected people has implications for clinical care and

Table 3. Unadjusted prevalence, estimated marginal prevalence, and odds ratios of clinical conditions among HIV-infected and HIV-uninfected adult patients seen in community health centers, Community Health Applied Research Network database, 2006-2014[a]

	HIV-Infected Patients (n = 12 837)		HIV-Uninfected Patients (n = 227 012)		
Condition	Unadjusted Prevalence, No. (%)	Estimated Marginal Prevalence, %[b]	Unadjusted Prevalence, No. (%)	Estimated Marginal Prevalence, %[b]	OR (95% CI)[c]
Diabetes	2249 (17.5)[d]	19.8	36 799 (16.2)	16.5	1.31 (1.22-1.41)
Chronic kidney disease	613 (4.8)[d]	14.3	10 675 (4.7)	5.9	4.75 (4.23-5.34)
Hypertension	5604 (43.7)[d]	44.2	81 489 (35.9)	39.1	1.38 (1.31-1.46)
Dyslipidemia	5505 (42.9)[d]	56.1	94 192 (41.5)	41.6	2.30 (2.17-2.43)
HPV-related cancer	104 (0.8)[d]	1.1	576 (0.3)	0.2	5.05 (3.77-6.78)
Lymphoma	69 (0.5)[d]	0.5	303 (0.1)	0.1	4.02 (2.86-5.67)
Other cancer	491 (3.8)[d]	3.6	6980 (3.1)	2.9	1.25 (1.10-1.42)
Stroke	184 (1.4)[d]	1.5	2502 (1.1)	1.2	1.32 (1.06-1.63)
Myocardial infarction	51 (0.4)	0.5	858 (0.4)	0.4	1.06 (0.73-1.54)
Coronary artery disease	79 (0.6)	1.1	2369 (1.0)	0.9	1.30 (0.95-1.77)
	HIV-Infected Patients, No. (%) (n = 12 837)		HIV-Uninfected Patients, No. (%) (n = 227 012)		
Condition	Unadjusted Prevalence, No. (%)	Estimated Marginal Prevalence[b] (95% CI)	Unadjusted Prevalence, No. (%)	Estimated Marginal Prevalence[b] (95% CI)	*P* Value
Diabetes	2249 (17.5)	.187 (.146-.229)	36 799 (16.2)	.149 (.115-.183)	<.001
Chronic kidney disease	613 (4.8)	.076 (.031-.122)	10 675 (4.7)	.031 (.012-.050)	<.001
Hypertension	5604 (43.7)	.478 (.418-.538)	81 489 (35.9)	.366 (.311-.421)	<.001
Dyslipidemia	5505 (42.9)	.375 (.312-.438)	94 192 (41.5)	.607 (.542-.672)	<.001
HPV-related cancer	104 (0.8)	.010 (.006-.014)	576 (0.3)	.002 (.001-.003)	<.001
Lymphoma	69 (0.5)	.006 (.004-.008)	303 (0.1)	.001 (.001-.001)	<.001
Other cancer	491 (3.8)	.035 (.028-.043)	6980 (3.1)	.027 (.021-.032)	<.001
Stroke	184 (1.4)	.013 (.009-.017)	2505 (1.1)	.009 (.007-.012)	.002
Myocardial infarction	51 (0.4)	.004 (.002-.006)	858 (0.4)	.003 (.002-.004)	.18
Coronary artery disease	79 (0.6)	.008 (.004-.012)	2369 (1.0)	.006 (.003-.009)	.04

Abbreviations: HIV, human immunodeficiency virus; HPV, human papillomavirus; OR, odds ratio.

[a]Data source: Community Health Applied Research Network Data Warehouse version 3, May 2016.[15]

[b]The estimated marginal prevalence represents average prevalence after adjusting for covariates and accounting for the random effect of clinic (ie, the clustering of patients within a clinic).

[c]Multilevel logistic regression models controlled for age, race/ethnicity, and sex and accounted for clustering of patients within community health centers. Models also considered body mass index as well as opioid use, hepatitis C virus infection, and alcohol use.

[d]$P \leq .002$ comparing unadjusted prevalences of HIV-infected vs HIV-uninfected patients.

health care resources. One reason that HIV-infected people develop age-related morbidities at a faster rate than HIV-uninfected people may be the cumulative effects of long-standing inflammation caused by responding to a chronic viral infection, particularly among those who initiated highly active antiretroviral therapy when symptomatic.[25] Even those who initiate treatment promptly after being diagnosed with HIV do not fully recover immunologically, because the destruction of immune reserve occurs immediately after HIV infection is established. The earliest major cellular depletion is of gut-associated lymphoid tissue, making an HIV-infected person less capable than an HIV-uninfected person of limiting the circulation of gastrointestinal bacterial products that stimulate chronic immune activation.[26] Subclinical immunodeficiency may be associated with decreased immune surveillance, resulting in an increased risk of neoplasia, particularly from virally associated cancers, such as HPV-related tumors (cervical, vulvar, anal, and oropharyngeal malignancies), or Epstein-Barr virus–associated lymphomas (particularly Burkitt's lymphoma and central nervous system lymphomas).[27] In addition to enduring decades of chronic inflammation, HIV-infected people who have been infected for more than a decade are likely to have taken medications that can cause chronic morbidity. Some of the earlier drugs that aging HIV-infected patients with long-standing infection took included stavudine, which could result in hyperglycemia and progression to diabetes.[28] Among the most commonly used contemporary antiretroviral medications is tenofovir disiproxil fumarate, which is associated with nephrotoxicity, particularly among those with preexisting risk factors, such as untreated hypertension or diabetes.

Several large cohort studies that tracked acute and chronic disease among HIV-infected people and documented

substantial morbidity primarily followed patients receiving care in tertiary research centers. Our study found a high rate of hypertension (more than one-third of HIV-infected patients). The Women's Interagency HIV Study reported that HIV-infected women at baseline had a prevalence of hypertension of 26%, which is similar to the prevalence among demographically matched HIV-uninfected women.[28] Factors associated with hypertension include increasing age, African American race, smoking, low education levels, and obesity (BMI >30 kg/m^2) and, in HIV-infected patients, particularly those using protease inhibitors, an increased likelihood of metabolic syndrome.[29] More recent data suggest that hypertension rates increased among HIV-infected patients between 2003 and 2013, with the highest prevalence found among Medicare recipients (65.1%; who would tend to be older) compared with those who used commercial insurance (25.0%).[30] The higher prevalence of hypertension in HIV-infected Community Health Applied Research Network patients compared with locally selected HIV-uninfected controls is notable, given that they tended to be younger and were less likely to be African American than patients followed in other cohort studies.[27-29]

Rates of insulin resistance appear to be higher in HIV-infected people than in HIV-uninfected people.[31-33] The Multicenter AIDS Cohort Study found that HIV-infected men using antiretroviral therapy had approximately a 5-fold increase in risk of diabetes compared with HIV-uninfected controls and that antiretroviral therapy use conferred a 2-fold to 3-fold increased risk of hyperglycemia compared with HIV-infected, untreated controls.[31] Hepatitis C coinfection, which is common in HIV infection and was more prevalent among HIV-infected patients in this Community Health Applied Research Network sample compared with HIV-uninfected patients in this sample, is an independent risk factor for developing diabetes.[34-37] The increased rates of opiate use disorder among HIV-infected patients in our cohort may reflect higher rates of injection drug use as the mechanism for the higher prevalence of hepatitis C. HIV-uninfected patients who are obese or have excess abdominal fat have a higher risk of developing diabetes than the general US population.[38] The higher risk of diabetes among HIV-infected patients than among HIV-uninfected patients in our study was particularly notable given the large number of HIV-uninfected Asian Pacific Islanders who received primary care in several of the participating Community Health Applied Research Network community health centers and who would have a greater genetic predisposition to glucose intolerance.[39] The propensity toward diabetes for HIV-infected patients was robust; it persisted even after adjustment for BMI.

Our study found significant excess risk of chronic kidney disease among HIV-infected patients, also noted in other studies.[40-42] The reasons for the excess renal morbidity in HIV-infected patients include HIV disease itself, as well as several of the medications used to treat HIV, particularly tenofovir disiproxil fumarate, one of the most common treatments.[43] The increasing age of HIV-infected patients also contributes to renal morbidity; rates of chronic kidney disease are <1% in patients aged <40 and increase to >6% among patients aged >60.[44] The excess risk for chronic kidney disease in HIV-infected patients was particularly high among younger patients: a relative risk of 4.6 in those aged <40, but a nonsignificant difference among those aged >60 (ie, aging HIV-uninfected patients acquire chronic kidney disease from many other causes).[45] The North American AIDS Cohort Collaboration on Research and Design found that race was also independently associated with chronic kidney disease among HIV-infected people; black HIV-infected patients had a 46% increased risk of progressive chronic kidney disease than white HIV-infected patients.[46] The results of our study also underscore the need to carefully control for potential confounders, such as race and age, because the prevalence of chronic kidney disease was only slightly higher among HIV-infected patients, but the difference in ORs was much greater. In this community-based sample, the finding of excess chronic kidney disease in HIV-infected patients was particularly striking, given that HIV-infected patients tended to be younger and were less likely to be from a racial/ethnic minority group than other community health center patients, highlighting the importance of adjusted analyses.

Lipid abnormalities are common among HIV-infected people and are seen in both untreated people and those using highly active antiretroviral therapy.[47-50] In our study, both HIV-infected patients and HIV-uninfected patients frequently took medication for dyslipidemia and/or had a laboratory test indicating dyslipidemia (ie, elevated plasma low-density lipoprotein cholesterol or triglyceride levels). Severe dyslipidemia in HIV-infected patients—hypertriglyceridemia in particular—is increased in patients who use protease inhibitors, especially ritonavir-containing regimens.[51] The effect of various antiretroviral medications on lipids varies considerably. Recent recommendations for initial highly active antiretroviral therapy regimens included initiating treatment with 2 nucleoside reverse transcriptase inhibitors and an integrase strand transfer inhibitor,[51] regimens that are less likely to cause dyslipidemia in patients without other risk factors than previously recommended options. The high prevalence of dyslipidemia in HIV-infected patients and HIV-uninfected patients in this sample may reflect that this condition is increasingly common in the general population but may also suggest that most patients accessing primary care services in safety-net community health centers could benefit from lifestyle interventions that might decrease their risk of complications from untreated dyslipidemia (eg, exercise, diet, and medication).

HIV-infected patients have been known to be at increased risk for malignancies associated with immunodeficiency since the beginning of the epidemic, although the spectrum has changed in the current era of highly active antiretroviral therapy.[52] In recent years, the prevalence of Kaposi's sarcoma and central nervous system lymphomas has declined, whereas the prevalence of Hodgkins and non-Hodgkins lymphoma has increased.[53] The rates of other cancers have also

increased, particularly liver, anal, laryngeal, and lung cancers.[54-56] The increased prevalence of liver cancer may reflect the high rates of chronic hepatitis B and hepatitis C infection in HIV-infected patients, and the increasing rate of anal cancer may reflect high levels of concomitant oncogenic HPV infection. The high rates of lung cancer may reflect excess rates of cigarette smoking among HIV-infected patients,[55-59] and rates of laryngeal cancer may be affected by both excess smoking and HPV exposure. In the Community Health Applied Research Network population, lymphomas and HPV-related cancers were much more prevalent among HIV-infected patients than among HIV-uninfected patients, consistent with other epidemiological studies, but excess risk for other cancers was also seen. Thus, astute clinicians will need to be alert for a wide range of oncogenic outcomes as their HIV-infected patients age.

Strengths and Limitations

This study had several strengths. First, our study was unique in that it compared common clinical morbidities among a large sample of HIV-infected patients and HIV-uninfected patients receiving their primary care in Federally Qualified Health Centers. With the passage of the Affordable Care Act, an increasing number of medically complex patients will obtain their care at community health centers; as such, our findings should be relevant for the clinical management of a large segment of the HIV-infected population in care. The study also demonstrated higher rates of hypertension, diabetes, chronic kidney disease, dyslipidemia, and cancers among HIV-infected patients than among HIV-uninfected patients receiving care at Community Health Applied Research Network community health centers. Moreover, the absolute rates of all of these conditions were high among HIV-infected patients accessing care in community health centers; for example, more than 40% had hypertension and dyslipidemia, and almost 20% had diabetes. Thus, primary care community health center providers will need to be attentive to the need for routine management of comorbid conditions in medically complex HIV-infected patients.[51] Another strength of this study was the geographic and racial/ethnic diversity of the population; the study involved an underserved population usually not included in similar research despite its large size and importance, and the carefully defined outcomes applied equivalently to both HIV-infected and HIV-uninfected community health center patients.

This study also had several limitations. First, it was not feasible to account for when HIV or the other clinical conditions first occurred; thus, it was not possible to infer that HIV causes excess morbidity. However, we evaluated a relatively large HIV-infected population accessing primary care outside of tertiary centers, and we had comparable electronic health data available for the HIV-uninfected population. Some of the operational diagnoses may have overestimated certain conditions because they relied on medication lists. For example, a patient receiving a statin might not have dyslipidemia but could be at high risk of developing the condition, and the medication was being used prophylactically. Another potential bias was differential detection bias related to the nonrandom likelihood that patients with some conditions were more likely to have more frequent clinic visits than others (eg, HIV-infected patients and/or patients with diabetes). This potential bias could result in more disease detection in these groups than among HIV-uninfected controls without diabetes. HIV-infected patients had almost twice as many visits each year than HIV-uninfected patients, which could lead to ascertainment biases; however, both groups were in regular care, with the HIV-uninfected group having about 6 clinic visits per year. The analysis attempted to control for this ascertainment bias, but given that some community health center patients might receive some of their services outside of their primary care site (eg, through the Veterans Administration or in specialty care centers), the ability to track all health care use was limited.

Conclusions

Our study has implications for the long-term management of HIV-infected patients in primary care, given the high prevalence of common clinical morbidities detected in this large, diverse sample with tens of thousands of years of follow-up. As HIV-infected people age, an increasing number of treatable noncommunicable diseases may give rise to issues related to polypharmacy.[60] The management of non-HIV and antiretroviral treatment regimens will increasingly complicate the primary care of HIV-infected people. To date, although guidelines on how best to clinically manage HIV-infected people with other chronic noncommunicable diseases are available,[61] further research is needed to define best practices, as well as the optimal combination of treatment regimens and behavioral interventions to optimize preventive behaviors. From a health-systems perspective, appropriate health care delivery models that are diverse in medical expertise, including gerontologists, cardiologists, endocrinologists, oncologists, and nephrologists, in addition to HIV care providers, will be fundamental to the care of HIV-infected people. Future studies are needed to inform the development of sensible care guidelines to identify which models best meet the needs of HIV-infected people and to bring these intersecting issues to the forefront of the research agenda for aging HIV-infected people.

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References

1. Samji H, Cescon A, Hogg RS, et al. Closing the gap: increases in life expectancy among treated HIV-positive individuals in the United States and Canada. *PLoS One*. 2013;8(12):e81355.
2. Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas, 2013. *HIV Surveill Rep*. 2013;25:1-82.
3. Marcus JL, Chao CR, Leyden WA, et al. Narrowing the gap in life expectancy for HIV-infected and HIV-uninfected individuals with access to care. *J Acquir Immune Defic Syndr*. 2016; 73(1):39-46.
4. Smit M, Brinkman K, Geerlings S, et al. Future challenges for clinical care of an ageing population infected with HIV: a modelling study. *Lancet Infect Dis*. 2015;15(7):810-818.
5. Shiels MS, Pfeiffer RM, Engels EA. Age at cancer diagnosis among persons with AIDS in the United States. *Ann Intern Med*. 2010;153(7):452-460.
6. Althoff KN, Gange SJ. A critical epidemiological review of cardiovascular disease risk in HIV-infected adults: the importance of the HIV-uninfected comparison group, confounding, and competing risks. *HIV Med*. 2013;14(3):191-192.
7. Althoff KN, McGinnis KA, Wyatt CM, et al. Comparison of risk and age at diagnosis of myocardial infarction, end-stage renal disease, and non-AIDS-defining cancer in HIV-infected versus uninfected adults. *Clin Infect Dis*. 2015;60(4):627-638.
8. Brown TT, Cole SR, Li X, et al. Antiretroviral therapy and the prevalence and incidence of diabetes mellitus in the multicenter AIDS Cohort Study. *Arch Intern Med*. 2005;165(10): 1179-1184.
9. Schouten J, Wit FW, Stolte IG, et al. Cross-sectional comparison of the prevalence of age-associated comorbidities and their risk factors between HIV-infected and uninfected individuals: the AGEhIV Cohort Study. *Clin Infect Dis*. 2014;59(12): 1787-1797.
10. Deeks SG, Phillips AN. HIV infection, antiretroviral treatment, ageing, and non-AIDS related morbidity. *BMJ*. 2009;338: a3172.
11. Lundgren JD, Babiker AG, Gordin F, et al. Initiation of antiretroviral therapy in early asymptomatic HIV infection. *N Engl J Med*. 2015;337(9):795-807.
12. Wong C, Althoff K, Gange SJ. Identifying the appropriate comparison group for HIV-infected individuals. *Curr Opin HIV AIDS*. 2014;9(4):379-385.
13. Rajeevan N, Niehoff KM, Charpentier P, et al. Utilizing patient data from the Veterans Administration electronic health record

to support web-based clinical decision support: informatics challenges and issues from three clinical domains. *BMC Med Inform Decis Mak*. 2017;17(1):111.
14. National Association of Community Health Centers. About our health centers. http://www.nachc.org/about-our-health-centers. Accessed October 12, 2017.
15. Laws R, Gillespie S, Puro J, et al. The Community Health Applied Research Network (CHARN) data warehouse: a resource for patient-centered outcomes research and quality improvement in underserved, safety net populations. *eGEMS (Wash DC)*. 2014;2(3):1097.
16. Centers for Disease Control and Prevention. International classification of diseases, ninth revision (ICD-9). https://www.cdc.gov/nchs/icd/icd9.htm. Accessed October 26, 2017.
17. Kitahata MM, Rodriguez B, Haubrich R, et al. Cohort profile: the Centers for AIDS Research Network of Integrated Clinical Systems. *Int J Epidemiol*. 2008;37(5):948-955.
18. StataCorp. *Stata Release 13.2* [computer program]. College Station, TX: StataCorp; 2013.
19. Bryk AS, Raudenbush SW. *Hierarchical Linear Models: Applications and Data Analysis Methods*. Thousand Oaks, CA: SAGE; 1992.
20. Hox JJ. *Multilevel Analysis: Techniques and Applications*. Mahwah, NJ: Lawrence Erlbaum Associates; 2002.
21. Snijders TAB, Bosker RJ. *Multilevel Analysis: An Introduction to Basic and Advanced Multilevel Modeling*. Thousand Oaks, CA: SAGE; 1999.
22. US Department of Health and Human Services. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-treatment-guidelines/0. Published 2016. Accessed March 25, 2016.
23. Written statement of Dr. Ronald O. Valdiserri, Deputy Assistant Secretary for Health, Infectious Diseases, Office of HIV/AIDS & Infectious Disease Policy, U.S. Department of Health & Human Services to the United States Senate Special Committee on Aging. http://www.aging.senate.gov/imo/media/doc/01_Valdisseri_9_18_13.pdf. Published 2013. Accessed September 5, 2016.
24. High KP, Brennan-Ing M, Clifford DB, et al. HIV and aging: state of knowledge and areas of critical need for research. A report to the NIH Office of AIDS Research by the HIV and Aging Working Group. *J Acquir Immune Defic Syndr*. 2012;60(suppl 1):S1-S18.
25. Deeks SG. HIV infection, inflammation, immunosenescence, and aging. *Annu Rev Med*. 2011;62:141-155.
26. Brenchley JM, Price DA, Schacker TW, et al. Microbial translocation is a cause of systemic immune activation in chronic HIV infection. *Nat Med*. 2006;12(12):1365-1371.
27. Mitsuyasu RT. Non-AIDS-defining malignancies in HIV. *Top HIV Med*. 2008;16(4):117-121.
28. Khalsa A, Karim R, Mack WJ, et al. Correlates of prevalent hypertension in a large cohort of HIV-infected women: women's interagency HIV study. *AIDS*. 2007;21(18):2539-2541.
29. Sattler FR, Qian D, Louie S, et al. Elevated blood pressure in subjects with lipodystrophy. *AIDS*. 2001;15(15):2001-2010.
30. Meyer N, Gallant JE, Hsue P, Song X. Comorbidities of patients with human immunodeficiency virus (HIV) in the USA—a longitudinal analysis of prevalent HIV patients over 11 years. Paper presented at: Joint 55th Interscience Conference on Antimicrobial Agents and Chemotherapy and 28th International Congress of Chemotherapy Meeting; September 17-21, 2015; San Diego, CA.
31. Brown T, Cole SR, Li X, Kingsley LA, Palella F, Riddler SA. Prevalence and incidence of pre-diabetes and diabetes in the Multicenter AIDS Cohort Study. Paper presented at: Conference on Retroviruses and Opportunistic Infections; February 8-11, 2004; San Francisco, CA.
32. Rasmussen LD, Mathiesen ER, Kronborg G, Pedersen C, Gerstoft J, Obel N. Risk of diabetes mellitus in persons with and without HIV: a Danish nationwide population-based cohort study. *PLoS One*. 2012;7(9):e44575.
33. Monroe AK, Glesby MJ, Brown TT. Diagnosing and managing diabetes in HIV-infected patients: current concepts. *Clin Infect Dis*. 2014;60(3):453-462.
34. Currier J, Boyd F, Kawabata H, Dezil C, Burtcel B, Hodder S. Diabetes mellitus in HIV infected individuals. Paper presented at: Conference on Retroviruses and Opportunistic Infections; February 24-28, 2002; Seattle, WA.
35. De Wit S, Sabin CA, Weber R, et al. Incidence and risk factors for new-onset diabetes in HIV-infected patients: the data collection on adverse events of anti-HIV drugs (D: A: D) study. *Diabetes Care*. 2008;31(6):1224-1229.
36. Mehta S, Moore RD, Graham NM. Potential factors affecting adherence with HIV therapy. *AIDS*. 1997;11(14):1665-1670.
37. Wang CS, Wang ST, Yao WJ, Chang TT, Chou P. Community-based study of hepatitis C virus infection and type 2 diabetes: an association affected by age and hepatitis severity status. *Am J Epidemiol*. 2003;158(12):1154-1160.
38. Pouliot MC, Després JP, Lemieux S, et al. Waist circumference and abdominal sagittal diameter: best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. *Am J Cardiol*. 1994;73(7):460-468.
39. Karter AJ, Schillinger D, Adams AS, et al. Elevated rates of diabetes in Pacific Islanders and Asian subgroups: The Diabetes Study of Northern California (DISTANCE). *Diabetes Care*. 2013;36(3):574-579.
40. Wong C, Gange SJ, Horberg MA, et al. Age-related morbidities among HIV-infected adults from 2000 to 2010. Paper presented at: Conference on Retroviruses and Opportunistic Infections; February 23-26, 2015; Seattle, WA.
41. Abraham AG, Althoff KN, Jing Y, et al. End-stage renal disease among HIV-infected adults in North America. *Clin Infect Dis*. 2015;60(6):941-949.
42. Mocroft A, Kirk O, Reiss P, et al. Estimated glomerular filtration rate, chronic kidney disease and antiretroviral drug use in HIV-positive patients. *AIDS*. 2010;24(11):1667-1678.
43. Choi AI, Li Y, Parikh C, Volberding PA, Shlipak MG. Long-term clinical consequences of acute kidney injury in the HIV-infected. *Kidney Int*. 2010;78(5):478-485.

44. Goulet JL, Fultz SL, Rimland D, et al. Aging and infectious diseases: do patterns of comorbidity vary by HIV status, age, and HIV severity? *Clin Infect Dis*. 2007;45(12): 1593-1601.
45. Lucas GM, Lau B, Atta MG, Fine DM, Keruly J, Moore RD. Chronic kidney disease incidence, and progression to end-stage renal disease, in HIV-infected individuals: a tale of two races. *J Infect Dis*. 2008;197(11):1548-1557.
46. Gange SJ, Kitahata MM, Saag MS, et al. Cohort profile: the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). *Int J Epidemiol*. 2007;36(2): 294-301.
47. Lakka HM, Laaksonen DE, Lakka TA, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA*. 2002;288(21):2709-2716.
48. Deedwania PC, Thomas NC, Brar K. Metabolic syndrome is highly prevalent in patients with coronary artery disease. *J Am Coll Cardiol*. 2003;41(6):267.
49. Dubé MP, Stein JH, Aberg JA, et al. Guidelines for the evaluation and management of dyslipidemia in human immunodeficiency virus (HIV)-infected adults receiving antiretroviral therapy: recommendations of the HIV Medical Association of the Infectious Diseases Society of America and the Adult AIDS Clinical Trials Group. *Clin Infect Dis*. 2003;37(5):613-627.
50. Grunfeld C, Pang M, Doerrler W, Shigenaga JK, Jensen P, Feingold KR. Lipids, lipoproteins, triglyceride clearance, and cytokines in human immunodeficiency virus infection and the acquired immunodeficiency syndrome. *J Clin Endocrinol Metab*. 1992;74(5):1045-1052.
51. Sanne I, Piliero P, Squires K, Thiry A, Schnittman S; AI424-007 Clinical Trial Group. Results of a phase 2 clinical trial at 48 weeks (AI424-007): a dose-ranging, safety, and efficacy comparative trial of atazanavir at three doses in combination with didanosine and stavudine in antiretroviral-naive subjects. *J Acquir Immune Defic Syndr*. 2003;32(1):18-29.
52. Bonnet F, Lewden C, May T, et al. Malignancy-related causes of death in human immunodeficiency virus-infected patients in the era of highly active antiretroviral therapy. *Cancer*. 2004; 101(2):317-324.
53. Yanik EL, Katki HA, Engels EA. High cancer risk among the HIV-infected elderly in the United States. Paper presented at: Conference on Retroviruses and Opportunistic Infections; February 23-26, 2015; Seattle, WA.
54. Engels EA, Biggar RJ, Hall HI, et al. Cancer risk in people infected with human immunodeficiency virus in the United States. *Int J Cancer*. 2008;123(1):187-194.
55. Patel P, Hanson DL, Sullivan PS, et al. Incidence of types of cancer among HIV-infected persons compared with the general population in the United States, 1992-2003. *Ann Intern Med*. 2008;148(10):728-736.
56. Robbins HA, Pfeiffer RM, Shiels MS, Li J, Hall HI, Engels EA. Excess cancers among HIV-infected people in the United States. *J Natl Cancer Inst*. 2015;107(4):dju503.
57. Niaura R, Shadel WG, Morrow K, Tashima K, Flanigan T, Abrams DB. Human immunodeficiency virus infection, AIDS, and smoking cessation: the time is now. *Clin Infect Dis*. 2000; 31(3):808-812.
58. Gritz ER, Vidrine DJ, Lazev AB, Amick BC III, Arduino RC. Smoking behavior in a low-income multiethnic HIV/AIDS population. *Nicotine Tob Res*. 2004;6(1):71-77.
59. Mamary EM, Bahrs D, Martinez S. Cigarette smoking and the desire to quit among individuals living with HIV. *AIDS Patient Care STDS*. 2002;16(1):39-42.
60. Krentz HB, Gill MJ. The impact of non-antiretroviral polypharmacy on the continuity of antiretroviral therapy (ART) among HIV patients. *AIDS Patient Care STDS*. 2016;30(1):11-17.
61. Aberg JA, Gallant JE, Ghanem KG, Emmanuel P, Zingman BS, Horberg MA. Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. 2014;58(1):1-10.