Original Article

Excess cancer prevalence in men with HIV: A nationwide analysis of Medicaid data

Siran M. Koroukian, PhD [iD] [1,2]; Guangjin Zhou, PhD[1]; Suparna M. Navale, MS, MPH[3]; Nicholas K. Schiltz, PhD [iD] [4];
Uriel Kim, PhD [iD] [1,2,5]; Johnie Rose, MD, PhD[2,5,6]; Gregory S. Cooper, MD, MA[7,8,9];
Scott Emory Moore, PhD, APRN, AGPCNP-BC[4]; Laura J. Mintz, MD, PhD[9,10]; Ann K. Avery, MD[9,11];
Sudipto Mukherjee, MD, PhD, MPH[12,13]; and Sarah C. Markt, ScD, MPH [iD] [1,2]

BACKGROUND: Cancer is one of the most common comorbidities in men living with HIV (MLWH). However, little is known about the MLWH subgroups with the highest cancer burden to which cancer prevention efforts should be targeted. Because Medicaid is the most important source of insurance for MLWH, we evaluated the excess cancer prevalence in MLWH on Medicaid relative to their non-HIV counterparts. **METHODS:** In this cross-sectional study using 2012 Medicaid Analytic eXtract data nationwide, we flagged the presence of HIV, 13 types of cancer, symptomatic HIV, and viral coinfections using codes from the *International Classification of Diseases, Ninth Revision, Clinical Modification*. The study population included individuals administratively noted to be of male sex (men), aged 18 to 64 years, with (n = 82,495) or without (n = 7,302,523) HIV. We developed log-binomial models with cancer as the outcome stratified by symptomatic status, age, and race/ethnicity. **RESULTS:** Cancer prevalence was higher in MLWH than in men without HIV (adjusted prevalence ratio [APR], 1.84; 95% confidence interval [CI], 1.78-1.90) and was higher among those with symptomatic HIV (APR, 2.74; 95% CI, 2.52-2.97) than among those with asymptomatic HIV (APR, 1.73; 95% CI, 1.67-1.79). The highest APRs were observed for anal cancer in younger men, both in the symptomatic and asymptomatic groups: APR, 312.97; 95% CI, 210.27-465.84, and APR, 482.26; 95% CI, 390.67-595.32, respectively. In race/ethnicity strata, the highest APRs were among Hispanic men for anal cancer (APR, 198.53; 95% CI, 144.54-272.68) and for lymphoma (APR, 9.10; 95% CI, 7.80-10.63). **CONCLUSIONS:** Given the Medicaid program's role in insuring MLWH, the current findings highlight the importance of the program's efforts to promote healthy behaviors and vaccination against human papillomavirus in all children and adolescents and to provide individualized cancer screening for MLWH. *Cancer* 2022;0:1-9. © 2022 American Cancer Society.

KEYWORDS: anal cancer, cancer prevalence, epidemiology, Medicaid, men with HIV.

INTRODUCTION

Despite stabilization of the annual number of incident HIV cases, the prevalence of HIV in the United States has increased dramatically, largely as a result of the introduction of highly active antiretroviral therapy and improved longevity in people living with HIV (PLWH).[1] Recent estimates indicate that nearly 1.2 million adolescents and adults in the United States are living with HIV.[2] Nonetheless, the life expectancy of PLWH has never returned to that of the general population,[2] in great part because of the high comorbidity burden in PLWH.[2,3]

Among the most common comorbidities affecting PLWH are non–AIDS-defining cancers, such as lung, head and neck, and anal cancers, which are associated with significant morbidity and mortality.[4-8] A previous study demonstrated that non–AIDS-defining cancer was the leading non-AIDS cause of death in PLWH,[9] responsible for 10-17% of deaths in PLWH.[10,11] Although the cancer burden in the United States is expected to increase as the population ages,[12] it may affect PLWH more acutely because they are generally diagnosed with cancer 10 to 20 years earlier than people without

HIV.[13,14] This is caused in part by premature aging,[15] compromised immune function, and a high prevalence of non-HIV cancer risk factors (eg, smoking and coinfection by oncogenic viruses, such as human papillomavirus [HPV]).[16]

HIV disproportionately affects persons of color, men who have sex with men, transgender women, those who inject drugs, and those with lower socioeconomic status.[17] Medicaid is the most important source of health insurance for PLWH, providing coverage for 40% of PLWH in 2018.[18] This large representation of PLWH in Medicaid underscores the importance of evaluating their health care needs, including their needs for cancer prevention and control.

In this study, we measured the excess prevalence of various cancers in PLWH compared with the general population using 100% Medicaid data from all 50 states and the District of Columbia. We hypothesized that HIV status would be associated with excess cancer prevalence, especially in men with symptomatic HIV. We further hypothesized that excess prevalence would vary across age and race/ethnicity subgroups of men living with HIV (MLWH) who were on Medicaid. We focused on individuals administratively noted to be male (which includes cisgender men and some transgender individuals) to provide a more in-depth analysis by anatomic cancer site, given differences in the prevalence of HPV-related conditions (eg, anogenital warts and anal cancer) between men and women with HIV.[19] We also focused on individuals in the 18-64 age group, given the demographic makeup of the Medicaid population.

MATERIALS AND METHODS

In this cross-sectional study, we evaluated the excess prevalence of cancer in men with and without HIV using 100% Medicaid Analytic eXtract (MAX) files covering all 50 states and the District of Columbia. Our study year was 2012, which was the most recent year for which national MAX data were available at the time the study was initiated. This study was approved by the Institutional Review Board (protocol 2017-1817) and the Centers for Medicare & Medicaid Services (Data Use Agreement 2017-51352).

Data Source

The MAX database consists of: 1) the Personal Summary file, which we used to retrieve individuals' demographics and months of enrollment in Medicaid during the study year, as well as the US Census Divisions; and 2) claims files, including Inpatient and Other Therapy files for care received in inpatient and outpatient hospital and noninstitutional care settings.

Study Population

Our study population included 7,385,018 men, as defined by sex documented in their Medicaid record, 18-64 years of age, after excluding individuals who were identified in the following categories: 1) those with Kaposi sarcoma and non-Hodgkin lymphoma, given a potential overlap with the conditions we used to identify symptomatic MLWH (see Supporting Table 1); 2) individuals dually enrolled in Medicare and Medicaid because of potentially incomplete claims data; 3) those who only had exclusively premium claims (or *Recipient Indicator "2"*, which had no valid diagnosis codes; and 4) those who had neither State Children's Health Insurance Program enrollment months nor Medicaid enrollment months (*Recipient Indicator "9"*).

Key Variables of Interest

By using the MAX files from each state, we created binary variables for HIV status and for 13 common cancers based on the presence of relevant *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis codes listed in the Agency for Healthcare Research and Quality Software Tools, including the Clinical Classification Software[20] (see Supporting Table 2). For each diagnosis, we required at least 1 occurrence in the Inpatient file or 2 more separate occurrences in the Other Therapy file, at least 30 days apart. The 13 cancer types included cancer of the head/neck, esophagus, stomach, colon, rectum, anus, liver and intrahepatic bile duct, pancreas, prostate, bronchus/lung, and other respiratory and intrathoracic organs as well as lymphoma and leukemia. The presence of cancer (all cancers combined and by type) was our outcome of interest, and HIV status was our main independent variable. Individuals with multiple cancers were included in each cancer site analysis.

Other independent variables included individuals' age in 2012 (aged 18-44 and 45-64 years) and race/ethnicity (White, Black, Hispanic [including Hispanic or Latino and 1 or more race(s)], Asian, American Indian or Alaskan Native, Native Hawaiian or Other Pacific Islander, More than one race, and Unknown or missing). Given this categorization of the race/ethnicity variable, we assumed that all those not grouped in the Hispanic category were of non-Hispanic ethnicity. We dichotomized age at 44 years based on the age distribution of the cancers with the highest excess prevalence—anal

cancer and lymphoma—in men with and without HIV (see Supporting Fig. 1A-C). We chose these categorizations of age given the limited sample size for men with HIV and cancer. In addition, our models accounted for the US Census Divisions (New England, Mid-Atlantic, East North Central, West North Central, South Atlantic, East South Central, West South Central, Mountain, and Pacific).[21] Finally, to account for a greater opportunity to capture the diagnoses of interest in individuals with longer periods of enrollment in Medicaid, we included a continuous variable reflecting the total number of months of enrollment in Medicaid during 2012.

To leverage the richness of Medicaid claims data, we used all available claims data to further identify individuals with HIV as either symptomatic or asymptomatic, in the presence or absence of diagnosis codes indicating the presence of opportunistic infections and AIDS-related symptoms, as a proxy for compromised immune status. We also flagged coinfections by hepatitis B (HBV) or hepatitis C virus (HCV) and/or HPV (for relevant diagnosis codes, see Supporting Table 1).

Statistical Analysis

We estimated prevalence ratios by HIV status using log-binomial models but resorted to log-Poisson regression models when the models failed to converge.[22] We calculated the prevalence ratio for cancer overall and for specific cancers. In each model, HIV status was the main independent variable. Other independent variables included age, race/ethnicity, US Census Division, enrollment months, and coinfection by HBV/HCV (in models for liver cancer) or HPV (in models for head/neck, rectal, and anal cancers). When combining different cancer types, we accounted for coinfections by including a binary variable indicating the presence of HBV, HCV, and/ or HPV. We did not adjust for coinfections in the models for lymphoma.

We set our level of statistical significance at $\alpha <$ .05. However, given the large size of our study population, we focused our attention on the clinical meaningfulness of the findings and the varying magnitudes of adjusted prevalence ratios (APRs) across the comparison groups.

To examine effect modifications, we stratified our analysis by HIV symptomatic status and, further, by age group and race/ethnicity, focusing on the most common cancers: rectal and anal cancers and lymphomas. To address the small numbers in our stratified analysis by race/ethnicity (see Supporting Table 3), we presented our data for non-Hispanic Whites, non-Hispanic Blacks,

Hispanics, and All Others. The latter category aggregated data for all other race categories to allow for more stability in our models.

Finally, we note the following additional analyses: First, to ensure that we captured claims for all Medicaid beneficiaries, regardless of their enrollment in managed care, we conducted extensive analyses on the patterns of missingness of diagnosis codes in claims data. We excluded Medicaid/Medicare dually eligible individuals and those with *Recipient Indicator "2"* (recipient only had premium payment claims; ie, no health care service claims) or *Recipient Indicator "9"* (recipient was not enrolled in a State Children's Health Insurance Program or Medicaid for any months during the study period). We included enrollment and claims data for all other Medicaid beneficiaries, including nonusers. Although we detected no systematic missingness for diagnosis codes among Medicaid beneficiaries who had claims or encounter data in our final study population, we note that managed care encounters may be less complete than fee-for-service claims.[23] Second, we conducted sensitivity analysis to examine excess prevalence after including MLWH who had Kaposi sarcoma and certain AIDS-defining lymphomas in the symptomatic group. The results did not change in any meaningful way (data not shown).

We used SAS version 9.4 for UNIX (SAS Institute, Inc) for data processing and analysis and the ggplot2 (package in R Studio, version 1.3.1093) environment to generate the forest plots for APRs.

RESULTS

Our study population included 82,495 MLWH and 7,302,523 men without HIV. Table 1 details their distribution by demographics, coinfections, and type of cancer. Compared with men without HIV, a higher percentage of MLWH were in the 45-64 age group (59.79% vs 29.84%), were non-Hispanic Black men (48.62% vs 19.36%), or presented with cancer (5.06% vs 1.32%). The age distribution for men with anal cancer, lymphoma, and all other cancers is provided in Supporting Figure 1A-C. For both anal cancer and lymphoma, the median age was younger among MLWH than among men without HIV (54 vs 45 years and 50 vs 47 years, respectively). For all other types of cancer, however, the median age was comparable between the 2 groups (56 vs 54 years, respectively).

Among men with HIV, 8.78% were identified with symptomatic HIV. Compared with MLWH in the

TABLE 1. Distribution of the Study Population by HIV Symptomatic Status, Demographics, and Cancer Type

	No. (% of Total)			
Variable of interest	Men With HIV and Symptoms	Men With HIV but Without Symptoms	Men With HIV	Men Without HIV
Age, y				
18-44	3274 (45.18)	29,898 (39.73)	33,172 (40.21)	5,123,299 (70.16)
45-64	3973 (54.82)	45,350 (60.27)	49,323 (59.79)	2,179,224 (29.84)
Race/Ethnicity				
Non-Hispanic White	1382 (19.07)	17,591 (23.38)	18,973 (23.00)	3,013,360 (41.26)
Non-Hispanic Black	3736 (51.55)	36,373 (48.34)	40,109 (48.62)	1,413,808 (19.36)
Hispanic	1324 (18.27)	13,791 (18.33)	15,115 (18.32)	1,752,108 (23.99)
Asian	79 (1.09)	851 (1.13)	930 (1.13)	356,002 (4.88)
American Indian or Alaskan Native	27 (0.37)	368 (0.49)	395 (0.48)	89,728 (1.23)
Native Hawaiian or other Pacific Islander	26 (0.36)	247 (0.33)	273 (0.33)	66,780 (0.91)
More than one race	32 (0.44)	376 (0.50)	408 (0.49)	30,395 (0.42)
Unknown or missing	641 (8.85)	5651 (7.51)	6292 (7.63)	580,342 (7.95)
Total	7247 (100)	75,248 (100)	82,495 (100)	7,302,523 (100)
Coinfections				
Hepatitis B virus	458 (6.32)	2561 (3.40)	3019 (3.66)	24,492 (0.34)
Hepatitis C virus	1400 (19.32)	12,004 (15.95)	13,404 (16.25)	108,895 (1.49)
Human papillomavirus	306 (4.22)	2738 (3.64)	3044 (3.69)	35,638 (0.49)
Cancer types				
Head/neck	59 (0.81)	288 (0.38)	347 (0.42)	15,400 (0.21)
Esophagus	21 (0.29)	56 (0.07)	77 (0.09)	3804 (0.05)
Stomach	11 (0.15)	50 (0.07)	61 (0.07)	3661 (0.05)
Colon	29 (0.40)	221 (0.29)	250 (0.30)	13,342 (0.18)
Rectum	43 (0.59)	313 (0.42)	356 (0.43)	7752 (0.11)
Anus	98 (1.35)	1193 (1.59)	1291 (1.56)	908 (0.01)
Liver and intrahepatic bile duct	58 (0.80)	282 (0.37)	340 (0.41)	8352 (0.11)
Pancreas	11 (0.15)	58 (0.08)	69 (0.08)	3396 (0.05)
Bronchus/lung	94 (1.30)	388 (0.52)	482 (0.58)	19,320 (0.26)
Other respiratory and intrathoracic	**	<11	23 (0.03)	1073 (0.01)
Prostate	42 (0.58)	424 (0.56)	466 (0.56)	18,164 (0.25)
Leukemia	32 (0.44)	114 (0.15)	146 (0.18)	8254 (0.11)
Lymphoma[a]	209 (2.88)	779 (1.04)	988 (1.20)	9460 (0.13)
All cancers[b]	585 (8.07)	3592 (4.77)	4177 (5.06)	96,096 (1.32)

[a]These were non–AIDS-defining lymphomas only.

[b]Individuals with more than one cancer were included in each cancer site analysis. Therefore the cells for *All Cancers* do not represent the sum of the cells for each cancer type.

Cell < 11 was masked in accordance with Centers for Medicare & Medicaid Services Privacy Rules.

**Cell was masked to prevent the reader from deriving the small cell in the corresponding row.

asymptomatic group, a larger percentage of MLWH in the symptomatic group were aged 18 to 44 years (45.18% vs 39.73%). However, with few exceptions (those with More than one race or with unknown/missing race), the distribution by race/ethnicity was comparable between symptomatic and asymptomatic MLWH. With regard to cancer prevalence, however, a higher percentage of symptomatic than asymptomatic MLWH presented with cancer during 2012 (8.07% vs 4.77%). In the 2 groups, lymphoma and rectal and anal cancers represented 59.83% and 63.61% of all cancers, respectively.

Figure 1 presents the age-adjusted and race/ethnicity adjusted prevalence ratios (APRs) before stratifying by age and race/ethnicity. For both the symptomatic and asymptomatic groups combined and for all cancers, the APR was 1.84 (95% confidence interval [CI], 1.78-1.90), indicating that the prevalence of cancer was nearly twice as high in MLWH than in men without HIV. However, the APR was markedly higher in symptomatic MLWH than in asymptomatic MLWH (APR, 2.74 [95% CI, 2.52-2.97] and 1.73 [95% CI, 1.67-1.79], respectively). The highest APR was observed for anal cancer (APR, 42.64 [95% CI, 34.15-53.24] in symptomatic MLWH and 70.43 [95% CI, 63.77-77.82] in asymptomatic MLWH), followed by lymphoma (APR, 14.56 [95% CI, 12.71-16.68] and 5.14 [95% CI, 4.76-5.54] in symptomatic and asymptomatic MLWH, respectively). Other cancers for which we observed excess prevalence included esophageal cancer (APR, 3.63; 95% CI, 2.36-5.57) and
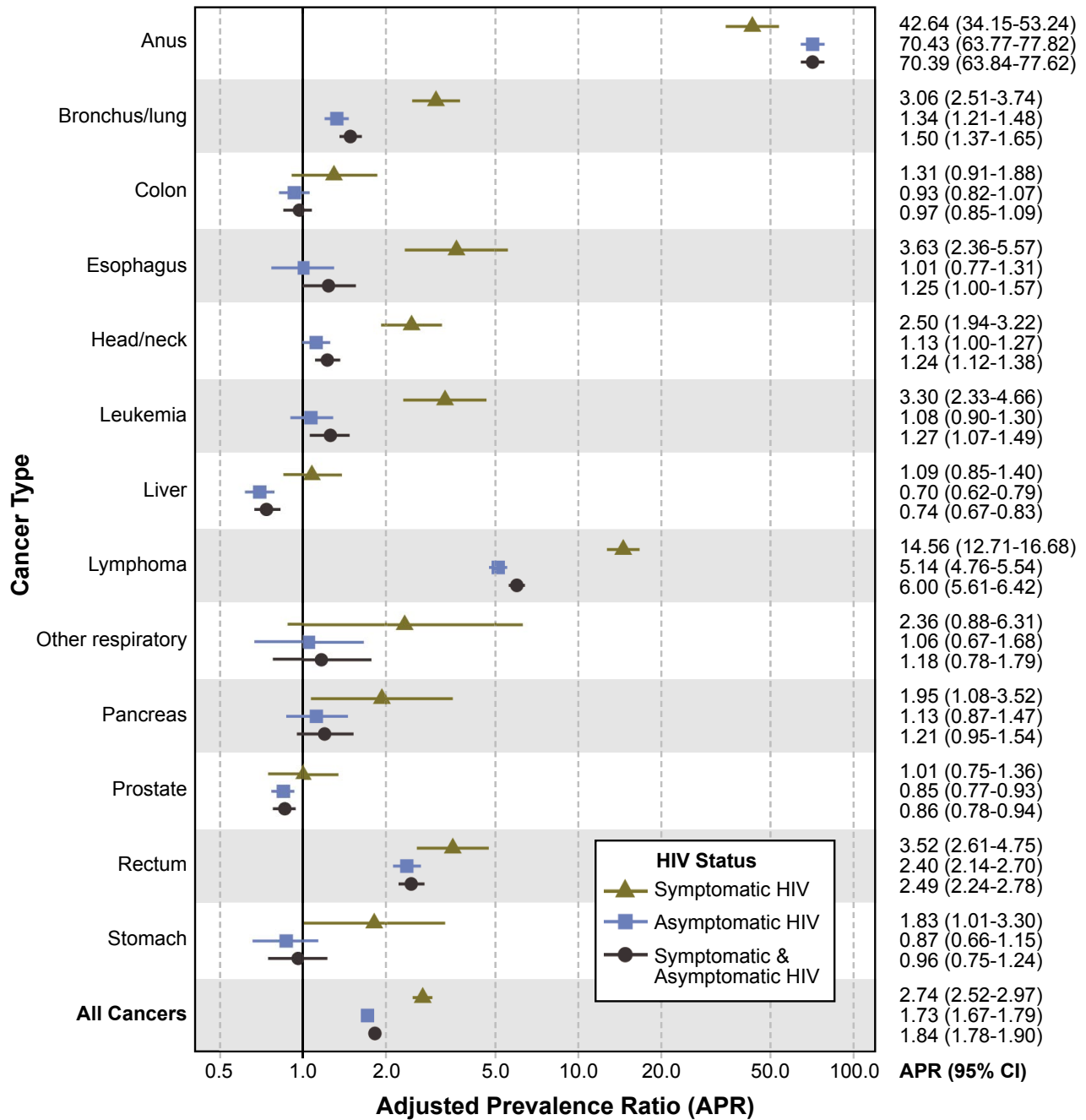
FIGURE 1. Age-adjusted and race/ethnicity-adjusted prevalence ratios and 95% CIs are shown for various types of cancer stratified by HIV symptomatic status. The x-axis is on a logarithmic scale. For all adjusted prevalence ratios (APRs), the reference category is men without HIV. APRs for which the 95% confidence interval (CI) crosses 1.0 are not statistically significant at $P < .05$. Models were adjusted for age, race/ethnicity, US Census Divisions, months of enrollment in Medicaid during 2012, and coinfections for hepatitis B virus (HBV), hepatitis C virus (HCV), and human papillomavirus (HPV). Models for liver cancer were adjusted for HBV/HCV status, whereas models for head/neck, rectal, and anal cancers were adjusted for HPV status. Models for all other cancers and all cancers combined were adjusted for the presence of any coinfection (HBV/HCV and/or HPV). Models for lymphoma did not adjust for coinfections.

leukemia (APR, 3.30; 95% CI, 2.33-4.66) in the symptomatic group only, and rectal cancer (APR, 3.52 [95% CI, 2.61-4.75] and 2.40 [95% CI, 2.14-2.70]) in the

symptomatic and asymptomatic groups, respectively. For liver cancer, however, we noted comparable prevalence in the symptomatic group (APR, 1.09; 95% CI, 0.85-1.40)

TABLE 2. Adjusted Prevalence Ratios and 95% Confidence Intervals for Select Cancers by HIV Symptomatic Status and Age

Cancer Type	APR (95% CI)[a]		
	Symptomatic HIV	Asymptomatic HIV	Symptomatic and Asymptomatic Combined
Younger age group: 18-44 y			
Anus	312.97 (210.27-465.84)	482.26 (390.67-595.32)	480.28 (390.27-591.04)
Rectum	16.78 (9.67-29.11)	11.55 (9.04-14.77)	12.10 (9.63-15.21)
Lymphoma	31.73 (25.64-39.26)	13.85 (12.27-15.63)	16.42 (14.75-18.29)
All other cancers	4.98 (3.82-6.48)	1.97 (1.70-2.30)	2.30 (2.02-2.63)
All cancers combined	13.28 (11.45-15.42)	8.82 (8.23-9.45)	9.38 (8.80-10.01)
Older age group: 45-64 y			
Anus	24.08 (17.70-32.76)	36.71 (32.66-41.25)	36.18 (32.27-40.57)
Rectum	2.57 (1.80-3.68)	1.90 (1.67-2.17)	1.95 (1.73-2.21)
Lymphoma	6.82 (5.67-8.21)	3.74 (3.41-4.12)	4.29 (3.93-4.67)
All other cancers	1.31 (1.16-1.47)	0.81 (0.77-0.85)	0.85 (0.81-0.89)
All cancers combined	1.83 (1.66-2.02)	1.24 (1.19-1.29)	1.30 (1.25-1.35)

Abbreviations: APR, adjusted prevalence ratio; CI, confidence interval.
[a]APRs obtained from log-binomial models were stratified by symptomatic status and age. Models were adjusted for race/ethnicity, US Census Division, and months of enrollment in Medicaid during 2012. Models for head/neck, rectal, and anal cancers were adjusted for the presence of human papillomavirus status. Models for all other cancers and all cancers combined were adjusted for the presence of any coinfection (hepatitis B virus/hepatitis C virus and/or human papillomavirus). Models for lymphoma were not adjusted for coinfections.

TABLE 3. Age-Adjusted Prevalence Ratios and 95% Confidence Intervals for Select Cancers by HIV Symptomatic Status and Race/Ethnicity

Cancer Type	APR (95% CI)[a]		
	Symptomatic HIV	Asymptomatic HIV	Symptomatic and Asymptomatic Combined
Non-Hispanic White			
Anus	37.37 (26.31-53.10)	54.92 (47.63-63.33)	55.36 (48.17-63.61)
Rectum	4.76 (2.88-7.87)	2.89 (2.40-3.48)	3.03 (2.54-3.60)
Lymphoma	14.92 (11.22-19.83)	5.27 (4.60-6.05)	5.96 (5.26-6.76)
All other cancers	1.76 (1.39-2.23)	1.03 (0.94-1.13)	1.09 (1.00-1.19)
All cancers combined	3.11 (2.63-3.69)	2.04 (1.92-2.17)	2.13 (2.01-2.26)
Non-Hispanic Black			
Anus	44.02 (29.92-64.77)	62.72 (51.10-76.98)	63.65 (52.04-77.86)
Rectum	3.35 (2.17-5.16)	2.02 (1.67-2.44)	2.13 (1.79-2.54)
Lymphoma	12.05 (9.85-14.75)	4.12 (3.65-4.64)	4.92 (4.42-5.48)
All other cancers	1.66 (1.42-1.93)	0.89 (0.83-0.96)	0.97 (0.91-1.04)
All cancers combined	2.61 (2.32-2.93)	1.47 (1.40-1.56)	1.59 (1.51-1.67)
Hispanic			
Anus	87.38 (48.22-158.35)	207.37 (149.91-286.85)	198.53 (144.54-272.68)
Rectum	4.05 (1.82-9.02)	2.50 (1.82-3.44)	2.63 (1.95-3.55)
Lymphoma	26.03 (19.67-34.45)	7.43 (6.24-8.83)	9.10 (7.80-10.63)
All other cancers	2.10 (1.62-2.73)	0.88 (0.77-1.01)	0.99 (0.88-1.12)
All cancers combined	3.78 (3.13-4.56)	2.06 (1.89-2.25)	2.25 (2.07-2.44)
All Others			
Anus	28.97 (13.32-62.99)	91.78 (70.75-119.06)	87.32 (67.48-112.99)
Rectum	**[b]	2.23 (1.57-3.18)	2.07 (1.47-2.94)
Lymphoma	11.08 (6.90-17.79)	6.34 (5.08-7.91)	6.86 (5.59-8.41)
All other cancers	1.05 (0.69-1.60)	0.85 (0.73-1.00)	0.87 (0.75-1.02)
All cancers combined	1.78 (1.31-2.42)	1.89 (1.70-2.10)	1.89 (1.71-2.08)

Abbreviations: APR, adjusted prevalence ratio; CI, confidence interval.
[a]APRs obtained from log-binomial models were stratified by symptomatic status and race/ethnicity. All models were adjusted for age, US Census Division, and months of enrollment in Medicaid during 2012. Models for head/neck, rectal, and anal cancers were adjusted for human papillomavirus status. Models for all other cancers and all cancers combined were adjusted for the presence of any coinfection (hepatitis B virus/hepatitis C virus and/or human papillomavirus). Models for lymphoma were not adjusted for coinfections.
[b]The number of cases was too small for Poisson models to converge or to yield robust APR.

and lower prevalence in the asymptomatic group (APR, 0.70; 95% CI, 0.62-0.79) after adjusting for HBV/HCV coinfections in the multivariable models.

The APRs stratified by age and symptomatic status presented in Table 2 showed a significant effect modification by age. For all cancers combined, the APR was

9.38 (95% CI, 8.80-10.01) in the younger age group but 1.30 (95% CI, 1.25-1.35) in the older age group, indicating that, compared with men without HIV, the prevalence of cancer was over 9 times greater in MLWH in the younger age group but 1.3 times higher in the older age group. In addition, the APR was considerably higher in the symptomatic group than in the asymptomatic group (APR, 13.28 [95% CI, 11.45-15.42] vs 8.82 [95% CI, 8.23-9.45], respectively, in the younger age group; and APR, 1.83 [95% CI, 1.66-2.02] vs 1.24 [95% CI, 1.19-1.29], respectively, in the older age group).

Among specific cancers, the highest APR was for anal cancer in both age groups: It was nearly 500 in the younger age group (APR, 480.28; 95% CI, 390.27-591.04), which was markedly more than that observed in the older age group (APR, 36.18; 95% CI, 32.27-40.57). In addition, in the younger age group, the APR for anal cancer was higher in the asymptomatic group (APR, 482.26; 95% CI, 390.67-595.32) than in the symptomatic group (APR, 312.97; 95% CI, 210.27-465.84), but it was somewhat lower for rectal cancer in the asymptomatic group (APR, 11.55; 95% CI, 9.04-14.77) than in the symptomatic group (APR, 16.78; 95% CI, 9.67-29.11). For lymphoma, the APR was 16.42 (95% CI, 14.75-18.29) and 4.29 (95% CI, 3.93-4.67) in the younger and older age groups, respectively. In both age groups, the APR for lymphoma was considerably higher in the symptomatic group than in the asymptomatic group.

Table 3 presents the age-adjusted APRs for select cancers by HIV symptomatic status and race/ethnicity. For all cancers and for the symptomatic and asymptomatic groups combined, the highest and lowest APRs were observed among Hispanic men (APR, 2.25; 95% CI, 2.07-2.44) and non-Hispanic Black men (APR, 1.59; 95% CI, 1.51-1.67). In addition, with a few exceptions (eg, for anal cancer), we observed higher APRs in the symptomatic group than in the asymptomatic group. Among those in the All Others category, the APRs were similar in the symptomatic groups (APR, 1.78; 95% CI, 1.31-2.42) and the asymptomatic groups (APR, 1.89; 95% CI, 1.70-2.10).

For cancer-specific APRs, we noted considerable variations in the APRs across race/ethnicity categories and by symptomatic status. For both the symptomatic and asymptomatic groups combined, the highest APRs for anal cancer and for lymphoma were observed among Hispanic men (APR, 198.53 [95% CI, 144.54-272.68] and 9.10 [95% CI, 7.80-10.63], respectively).

Conversely, the lowest APRs for anal cancer and for lymphoma were observed in non-Hispanic White men (APR, 55.36; 95% CI, 48.17-63.61) and non-Hispanic Black men (APR, 4.92; 95% CI, 4.42-5.48), respectively.

DISCUSSION

Using national Medicaid data, we observed an excess prevalence of cancer among MLWH, particularly for anal cancer, rectal cancer, and lymphoma. Overall, cancer prevalence was nearly twice as high in MLWH than in men without HIV enrolled on Medicaid. However, the excess prevalence was markedly higher in younger MLWH than in older MLWH, attesting to the younger ages at cancer diagnosis in people with HIV.[13] Consistent with previous studies, the prevalence of anal cancer was higher among MLWH compared with their non-HIV counterparts, and this association was stronger in the younger age group[13,14] (nearly 500 times higher in the younger age group vs 36 times higher in the older age group). These findings suggest that the burden of anal cancer is of much greater magnitude than previously described in PLWH, although most prior studies have reported hazard or risk ratios rather than prevalence ratios, as we do in this study.[14,24,25]

Our findings also showed variations in excess cancer prevalence by HIV symptomatic status and across cancer sites. MLWH experienced higher cancer prevalence than men without HIV for most cancer types, whether they were in the symptomatic or asymptomatic groups. With the exception of anal cancer, however, the magnitude of APRs was considerably smaller in asymptomatic MLWH than in symptomatic MLWH, attesting to the higher cancer burden in symptomatic MLWH.

To our knowledge, this is the first national study to examine excess cancer prevalence in MLWH enrolled on Medicaid by symptomatic status. In the absence of conditions like opportunistic infections, asymptomatic HIV status suggests viral suppression and a relatively healthy immune system. Although it has been demonstrated that viral suppression contributes to cancer prevention,[26] the lower APRs in the asymptomatic group in our study should be interpreted with caution because these findings pertain to Medicaid beneficiaries and not to the general population. Because Medicaid is a safety-net program, individuals who seek to enroll in Medicaid not only have low incomes but also present with complex mental and physical health care needs

and/or the diagnosis of a catastrophic illness, such as cancer. Hence, we hypothesize that, rather than a decreased risk of developing cancer, the lower cancer prevalence in asymptomatic MLWH for most cancers likely reflects that men in this group may not have the complex health care needs that would prompt them to enroll in Medicaid, except when they are diagnosed with certain cancers. To test this hypothesis, future studies should compare the co-occurrence of mental and physical chronic conditions in MLWH enrolled on Medicaid by symptomatic status.

This is also the first study, to our knowledge, using nationwide Medicaid data to study excess prevalence for cancers other than those associated with HPV. Because there are additional risk factors (eg, smoking and non-HPV coinfections) that increase the risk of cancer in PLWH,[27,28] our findings highlight the importance of individualized education and cancer screening, depending on the risk factors present in each individual with HIV,[29] as well as a proactive stance by the Medicaid program to promote HPV vaccination in all children and adolescents. Because screening for anal cancer remains controversial and because the current study is cross-sectional (rather than prospective) in nature, we are unable to recommend screening for anal cancer. For lymphoma, although there is no screening, improved access to health care allows for timely evaluation of symptoms, diagnostic evaluation, and treatment initiation.

Our findings should be interpreted in light of the following limitations. First, given our use of administrative data, the demographic variables (age, race/ethnicity, and sex) are as documented in the administrative records. Hence, we assumed that the sex variable in the Medicaid database was the individual's sex assigned at birth, thus our study population primarily included individuals assigned male sex at birth. Second, we did not have any reliable measures in claims data on behavioral health and risk factors, including smoking, alcohol consumption, or sexual behaviors. Given the very large magnitude in many of our APRs, however, it is unlikely that including these risk factors in our models would have completely explained the observed associations. Third, our method to identify the presence of cancer in Medicaid beneficiaries relied exclusively on diagnosis codes in claims data. Absent additional data from cancer registries, we were unable to ascertain cancer incident/prevalent status or age at cancer diagnosis. Finally, we note that these results reflect data from 2012. Since then, Medicaid enrollment increased substantially as a result of the Medicaid expansion in 2014, then declined in the years from 2017 to 2019,[30]

and increased again in fiscal year 2021.[31] Going forward, it will be important to examine whether these changes have had any effect on the patterns of cancer burden in Medicaid-insured MLWH observed in the current study. Regardless, a major component of today's Medicaid population consists of people with low incomes defined by pre-expansion eligibility criteria and people with slightly higher income levels in the expanded eligibility group. In the absence of substantial secular trends, it is reasonable to assume that the patterns reported herein will remain in the Medicaid population and that our findings are still highly relevant today. We also suggest the need for subsequent work in the development of targeted prevention measures.

In conclusion, cancer is a significant source of morbidity and mortality among PLWH, and the burden of cancer will likely increase in the future as this population ages. Medicaid plays a key role in insuring PLWH, a role that has only increased since the passage of the Affordable Care Act and postpandemic. Our findings call for a proactive stance by Medicaid to adopt a multipronged approach, to not only improve HIV-specific care but also to promote individualized cancer screening and more widespread HPV vaccination in children and adolescents.

CONFLICT OF INTEREST DISCLOSURES

AUTHOR CONTRIBUTIONS

Siran M. Koroukian: Conceptualization, data curation, formal analysis, funding acquisition, investigation, project administration, resources, software, supervision, validation, visualization, writing–original draft, and writing–review and editing. **Guangjin Zhou:** Conceptualization, data curation, formal analysis, resources, software, validation, visualization, writing–original draft, and writing–review and editing. **Suparna M. Navale:** Conceptualization, data curation, formal analysis, resources, software, and writing–review and editing. **Nicholas K. Schiltz:** Conceptualization, formal analysis, and writing–review and editing. **Uriel Kim:** Conceptualization, writing–original draft, data visualization, and writing–review and editing. **Johnie Rose:** Conceptualization and writing–review and editing.

REFERENCES

1. Friedman EE, Duffus WA. Chronic health conditions in Medicare beneficiaries 65 years old, and older with HIV infection. *AIDS*. 2016;30:2529-2536.
2. Marcus JL, Leyden WA, Alexeeff SE, et al. Comparison of overall and comorbidity-free life expectancy between insured adults with and without HIV infection, 2000-2016. *JAMA Netw Open*. 2020;3:e207954.
3. Hogg RS, Eyawo O, Collins AB, et al. Health-adjusted life expectancy in HIV-positive and HIV-negative men and women in British Columbia, Canada: a population-based observational cohort study. *Lancet HIV*. 2017;4:e270-e276.
4. Thrift AP, Chiao EY. Are non-HIV malignancies increased in the HIV-infected population? *Curr Infect Dis Rep*. 2018;20:22.
5. Chichetto NE, Polanka BM, So-Armah KA, et al. Contribution of behavioral health factors to non-AIDS-related comorbidities: an updated review. *Curr HIV/AIDS Rep*. 2020;17:354-372.
6. Brickman C, Palefsky JM. Cancer in the HIV-infected host: epidemiology and pathogenesis in the antiretroviral era. *Curr HIV/AIDS Rep*. 2015;12:388-396.
7. Webel AR, Schexnayder J, Cioe PA, Zuniga JA. A review of chronic comorbities in adults living with HIV: state of the science. *J Assoc Nurses AIDS Care*. 2021;32:322-346.
8. Farahani M, Mulinder H, Farahani A, Marlink R. Prevalence and distribution of non-AIDS causes of death among HIV-infected individuals receiving antiretroviral therapy: a systematic review and meta-analysis. *Int J STD AIDS*. 2017;28:636-650.
9. Smith CJ, Ryom L, Weber R, et al. Trends in underlying causes of death in people with HIV from 1999 to 2011 (D:A:D): a multicohort collaboration. *Lancet*. 2014;384:241-248.
10. Engels EA, Yanik EL, Wheeler W, et al. Cancer-attributable mortality among people with treated human immunodeficiency virus infection in North America. *Clin Infect Dis*. 2017;65:636-643.
11. Horner MJ, Shiels MS, Pfeiffer RM, Engels EA. Deaths attributable to cancer in the US HIV population during 2001-2015. *Clin Infect Dis*. 2022;72:e224-e231.
12. Yang HY, Beymer MR, Suen SC. Chronic disease onset among people living with HIV and AIDS in a large private insurance claims dataset. *Sci Rep*. 2019;9:18514.
13. Wang CC, Silverberg MJ, Abrams DI. Non-AIDS–defining malignancies in the HIV-infected population. *Curr Infect Dis Rep*. 2014;16:406.
14. Ye Y, Burkholder GA, Mukherjee A, et al. A 12-year retrospective evaluation of anal pre-cancerous lesions and cancer in people living with HIV-1 infection in the Southeastern U.S. *Infect Agent Cancer*. 2021;16:14.
15. Nasi M, De Biasi S, Gibellini L, et al. Ageing and inflammation in patients with HIV infection. *Clin Exp Immunol*. 2017;187:44-52.
16. Dubrow R, Silverberg MJ, Park LS, Crothers K, Justice AC. HIV infection, aging, and immune function: implications for cancer risk and prevention. *Curr Opin Oncol*. 2012;24:506-516.
17. Centers for Disease Control and Prevention (CDC). Social determinants of health among adults with diagnosed HIV infection, 2018. HIV Surveillance Supplemental Report 2020;25(no. 3). CDC; 2020. Accessed March 7, 2021. https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-supplemental-report-2020-vol25-no3.pdf
18. Kates J, Dawson L, Horn TH, et al. Insurance coverage and financing landscape for HIV treatment and prevention in the USA. *Lancet*. 2021;397:1127-1138.
19. Ye Y, Burkholder GA, Wiener HW, et al. Comorbidities associated with HPV infection among people living with HIV-1 in the southeastern US: a retrospective clinical cohort study. *BMC Infect Dis*. 2020;20:144.
20. Agency for Healthcare Research and Quality (AHRQ). Clinical Classification Software-DIAGNOSES. AHRQ; 2016. Accessed February 3, 2018. https://www.hcup-us.ahrq.gov/toolssoftware/ccs/AppendixASingleDX.txt
21. US Census Bureau. 2010 Census Regions and Divisions of the United States. US Census Bureau; 2018. Accessed April 8, 2021. https://www.census.gov/geographies/reference-maps/2010/geo/2010-census-regions-and-divisions-of-the-united-states.html
22. Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. *Am J Epidemiol*. 2005;162:199-200.
23. Bradley CJ, Stevens JL, Enewold L, Warren JL. Stage and mortality of low-income patients with cancer: evidence from SEER-Medicaid. *Cancer*. 2021;127:229-238.
24. Silverberg MJ, Lau B, Justice AC, et al. Risk of anal cancer in HIV-infected and HIV-uninfected individuals in North America. *Clin Infect Dis*. 2012;54:1026-1034.
25. Michaud JM, Zhang T, Shireman TI, Lee Y, Wilson IB. Hazard of cervical, oropharyngeal, and anal cancers in HIV-infected and HIV-uninfected Medicaid beneficiaries. *Cancer Epidemiol Biomarkers Prev*. 2020;29:1447-1457.
26. Park LS, Tate JP, Sigel K, et al. Association of viral suppression with lower AIDS-defining and non-AIDS-defining cancer incidence in HIV-infected veterans: a prospective cohort study. *Ann Intern Med*. 2018;169:87-96.
27. Park LS, Hernandez-Ramirez RU, Silverberg MJ, Crothers K, Dubrow R. Prevalence of non-HIV cancer risk factors in persons living with HIV/AIDS: a meta-analysis. *AIDS*. 2016;30:273-291.
28. Satre DD, Levine-Hall T, Sterling SA, et al. The relationship of smoking and unhealthy alcohol use to the HIV care continuum among people with HIV in an integrated health care system. *Drug Alcohol Depend*. 2021;219:108481.
29. Hessol NA, Strickler HD. Cancer risk in people living with HIV. *Lancet HIV*. 2017;4:e477-e479.
30. Kaiser Family Foundation. Analysis of Recent Declines in Medicaid and CHIP Enrollment. Kaiser Family Foundation; 2019. Accessed July 27, 2021. https://www.kff.org/medicaid/fact-sheet/analysis-of-recent-declines-in-medicaid-and-chip-enrollment/
31. Kaiser Family Foundation. Medicaid Enrollment & Spending Growth: FY 2021 & 2022. Accessed March 03, 2022. https://www.kff.org/medicaid/issue-brief/medicaid-enrollment-spending-growth-fy-2021-2022/