Original Article

Disparities in Cancer Treatment Among Patients Infected With the Human Immunodeficiency Virus

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BACKGROUND: Patients with cancer who are infected with the human immunodeficiency virus (HIV) are less likely to receive cancer treatment compared with HIV-uninfected individuals. However, to the authors' knowledge, the impact of insurance status and comorbidities is unknown. **METHODS:** Data from the National Cancer Data Base were used to study nonelderly adults diagnosed with several common cancers from 2003 to 2011. Cancer treatment was defined as chemotherapy, surgery, radiotherapy, or any combination during the first course of treatment. Multivariate logistic regression was used to examine associations between HIV status and lack of cancer treatment, and identify predictors for lack of treatment among HIV-infected patients. **RESULTS:** A total of 10,265 HIV-infected and 2,219,232 HIV-uninfected cases were included. In multivariate analysis, HIV-infected patients with cancer were found to be more likely to lack cancer treatment for cancers of the head and neck (adjusted odds ratio [aOR], 1.48; 95% confidence interval [95% CI], 1.09-2.01), upper gastrointestinal tract (aOR, 2.62; 95% CI, 2.04-3.37), colorectum (aOR, 1.70; 95% CI, 1.17-2.48), lung (aOR, 2.46; 95% CI, 2.19-2.76), breast (aOR, 2.14; 95% CI, 1.16-3.98), cervix (aOR, 2.81; 95% CI, 1.77-4.45), prostate (aOR, 2.16; 95% CI, 1.69-2.76), Hodgkin lymphoma (aOR, 1.92; 95% CI, 1.66-2.22), and diffuse large B-cell lymphoma (aOR, 1.82; 95% CI, 1.65-2.00). Predictors of a lack of cancer treatment among HIV-infected individuals varied by tumor type (solid tumor vs lymphoma), but black race and a lack of private insurance were found to be predictors for both groups. **CONCLUSIONS:** In the United States, HIV-infected patients with cancer appear to be less likely to receive cancer treatment regardless of insurance and comorbidities. To the authors' knowledge, the current study is the largest study of cancer treatment in HIV-infected patients with cancer in the United States and provides evidence of cancer treatment disparities even after controlling for differences with regard to insurance status and comorbidities. Further work should focus on addressing differential cancer treatment. ***Cancer*** **2016;000:000-000**. © *2016 American Cancer Society.*

KEYWORDS: access to cancer treatment, acquired immunodeficiency syndrome (AIDS)-defining cancer, cancer treatment disparities, health services research, human immunodeficiency virus (HIV)-associated cancer.

INTRODUCTION

Cancer is an increasingly common cause of morbidity and mortality among individuals infected with the human immunodeficiency virus (HIV). In the United States, cancer incidence rates in this population have changed since the introduction of highly active antiretroviral therapy (HAART). The number of acquired immunodeficiency syndrome (AIDS)-defining cancers has decreased and the number of non-AIDS defining cancers has increased with the growth and aging of the HIV population.[1,2] Cancer is now the second most common cause of death among HIV-infected individuals.[3]

HIV-infected patients with cancer have lower overall survival compared with HIV-uninfected individuals.[4] Although this may in part be related to deaths from AIDS-related complications, a recent population-based study found higher cancer-specific mortality among HIV-infected versus HIV-uninfected patients with cancer.[5] Lack of appropriate cancer treatment may contribute to worse cancer-specific mortality. In a prior study of cancer treatment in HIV-infected patients with lung cancer in Texas, we found that HIV-infected patients were less likely to receive treatment than HIV-uninfected individuals.[6] Furthermore, there was a suggestion that this treatment disparity contributed to the lower survival observed in the HIV-infected cases. A second, larger, population-based study examining cancer treatment in

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Additional supporting information may be found in the online version of this article.

DOI: 10.1002/cncr.30052, **Received:** February 8, 2016; **Revised:** March 20, 2016; **Accepted:** March 24, 2016, **Published online** Month 00, 2016 in Wiley Online Library (wileyonlinelibrary.com)

HIV-infected patients with several common cancers in 3 US states again demonstrated significant differences in cancer treatment rates between HIV-infected and HIV-uninfected individuals.[7]

Although to our knowledge these studies were the first to highlight the widespread disparity in cancer treatment in HIV-infected individuals, an important limitation is that they did not account for differences in medical comorbidities and insurance status. HIV-infected individuals frequently have other illnesses, and patients with significant comorbid disease may not be candidates for standard cancer therapy.[8] Similarly, insurance status also plays an important role in access to and delivery of cancer treatment.[9] HIV-infected patients in the United States are more likely to be uninsured or underinsured compared with the HIV-uninfected population, which could be a major contributing factor.[10,11]

In the current study, we used data from the National Cancer Data Base (NCDB), including information regarding insurance status and medical comorbidities, to assess differences in cancer treatment rates between HIV-infected and HIV-uninfected individuals for 10 common cancers. Our aim was to determine the impact of insurance status and medical comorbidities on cancer treatment disparities in the US HIV-infected population. To our knowledge, this is also the largest study to date examining differences in the receipt of cancer treatment by HIV status in the United States.

MATERIALS AND METHODS

We identified adults aged ≥18 years diagnosed with their first cancer between 2003 and 2011 from the NCDB. The NCDB is a hospital-based cancer registry that is sponsored by the American College of Surgeons and the American Cancer Society, collecting data from >1500 facilities accredited by the American College of Surgeons Commission on Cancer. It captures approximately 70% of newly diagnosed cancer cases in the United States. We included the 10 most common cancers observed among HIV-infected patients in the NCDB: cancers of the head and neck (oral cavity, pharynx, and larynx), upper gastrointestinal tract (pancreas, stomach, and esophagus), colorectum, anus, lung, female breast, cervix, and prostate; Hodgkin lymphoma; and diffuse large B-cell lymphoma (DLBCL). We focused on DLBCL instead of all non-Hodgkin lymphomas because cancer treatment differs by non-Hodgkin lymphoma subtype and DLBCL is the most common subtype in HIV-infected individuals. We chose 2003 as the starting year for the current study because the NCDB began collecting comorbidity data in this year using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis codes.

HIV status was ascertained from reported comorbidities using the ICD-9-CM diagnosis codes (04200-04400, 07953, or V08). For patients with lymphoma, HIV status also was reported through a Collaborative Staging site-specific factor. Because we focused on insurance status as an important contributor to receipt of cancer treatment, we excluded patients aged ≥65 years, nearly all of whom would have been Medicare-eligible by virtue of age, but we included individuals aged <65 years who had Medicare as a result of medical disability or end-stage renal disease. We further excluded patients with missing sex (618 patients) or missing treatment information (9,535 patients). A total of 2,229,497 patients with cancer were included in the analyses.

Cancer sites were determined as per the Surveillance, Epidemiology, and End Results (SEER) cancer statistics review using *International Classification of Diseases for Oncology, 3rd Edition* (ICD-O-3) site and histology codes.[12] Cancer stage was summarized based on American Joint Committee on Cancer staging.[13] Patient characteristics included age at diagnosis, sex, race/ethnicity, insurance status, comorbidity score, census region, and year of cancer diagnosis. Insurance status was based on the patient's primary payer/insurance carrier at the time of the initial diagnosis and/or treatment. HIV/AIDS is 1 of 15 non-cancer comorbid conditions in the Charlson-Deyo comorbidity score,[14] and therefore we recalculated the comorbidity score excluding HIV/AIDS to derive a modified Charlson-Deyo comorbidity score independent of HIV infection to reflect non-HIV-related disease burden.

The first course of cancer treatment was ascertained for DLBCL and Hodgkin lymphoma as chemotherapy, radiotherapy, or a combination of both. For all other cancer sites, cancer treatment was defined as surgery, radiotherapy, chemotherapy, or any combination of these therapies. Sensitivity analyses were performed to include hormone therapy for breast and prostate cancers, immunotherapy for lymphomas, and palliative care for all cancer types. Given the generally high rates of cancer treatment overall, we framed our analyses in terms of lack of cancer treatment.

Statistical Analysis

Pearson chi-square tests were used to compare demographic and clinical characteristics between HIV-infected and HIV-uninfected patients. For each cancer site, multivariate logistic regression analysis was used to assess the

relationship between HIV status and lack of cancer treatment, adjusted for demographic and clinical covariates. Because active surveillance is a treatment option for patients with low-risk prostate cancer, we performed a sensitivity analysis to examine the association between HIV and lack of cancer treatment for patients with stage II to IV prostate cancers only. We performed further analysis to examine the association between HIV status and lack of cancer treatment among privately insured patients. Finally, we performed a sensitivity analysis excluding patients who refused cancer treatment as reported to the NCDB.

Because demographic and clinical characteristics between HIV-infected and HIV-uninfected patients are known to be different, a sensitivity analysis was performed using propensity score (PS) with a 10:1 matching method. For each cancer case, we calculated the propensity of being infected with HIV based on demographic and tumor characteristics. We divided up the PSs into deciles across the full range of values and randomly selected 10 HIV-uninfected patients for each HIV-infected patient from each decile as the PS-matched subgroup. Covariate balance was checked before and after PS matching.

Finally, we used multivariate logistic regression to identify factors predictive of lack of cancer treatment among HIV-infected patients. These analyses were stratified by tumor type: solid tumors (cancers of the head and neck, lung, upper gastrointestinal tract, colorectum, anus, prostate, breast, and cervix) and lymphomas (DLBCL and Hodgkin lymphoma). We chose to stratify the analysis by cancer type because lymphomas represent a unique entity in terms of management and prognosis. Because pairwise tests are influenced by the choice of the reference groups, we presented the *P* value of global trend tests for heterogeneity and trends instead of individual *P* values. Statistical analyses were performed using SAS statistical software (version 9.3; SAS Institute Inc, Cary, NC).

RESULTS

Demographic and clinical characteristics of the patients with cancer included in the current study are shown in Table 1. The final cohort consisted of 10,265 HIV-infected patients and 2,219,232 HIV-uninfected patients. Several significant differences were noted between the 2 groups. HIV-infected patients were more likely to be young (median age, 47 years vs 55 years in the HIV-uninfected group), male (77.0% vs 47.6%), non-Hispanic black (41.1% vs 13.2%), and Hispanic (14.0% vs 5.7%). A greater percentage of HIV-infected patients had Medicaid (32.2% vs 10.1%), Medicare (19.6% vs 8.4%), or no insurance (10.3% vs 5.9%) compared with HIV-uninfected cases, the majority of whom had private insurance (72.5%). Although the majority of patients had a modified Charlson-Deyo comorbidity score of 0, the HIV-infected group had a higher percentage with a score >0 compared with the HIV-uninfected patients (23.5% vs 17.9%).

Among HIV-infected patients, the most common cancer types were DLBCL (42.1%), Hodgkin lymphoma (16.8%), and lung cancer (13.8%), versus breast (30.7%), prostate (20.4%), and lung (15.9%) cancer among HIV-uninfected patients (Table 1). A higher percentage of HIV-infected patients had stage IV cancer at the time of diagnosis (37.2% vs 18.9% in the HIV-uninfected group), whereas a higher percentage of HIV-uninfected patients were diagnosed with stage I or II cancers (57.2% vs 33.2% in the HIV-infected group).

Table 2 compares cancer treatment between HIV-infected and HIV uninfected cases. Anal cancer was the only cancer type for which treatment rates did not appear to differ significantly between HIV-infected and HIV-uninfected patients. For all other cancers, HIV-infected individuals were significantly more likely to be untreated for cancer, with adjusted odds ratios (aORs) ranging from 1.48 (95% confidence interval [CI], 1.09-2.01) for head and neck cancer to 2.81 (95% CI, 1.77-4.45) for cervical cancer (Table 2). The results were similar in a sensitivity analysis including hormone therapy as the first course of treatment for breast cancer (aOR, 2.04; 95% CI, 1.01-4.12) and prostate cancer (aOR, 1.88; 95% CI, 1.43-2.48). In a sensitivity analysis including immune therapy as the first course of treatment, the results were similar for Hodgkin lymphoma (aOR, 1.92; 95% CI, 1.66-2.23) and DLBCL (aOR, 1.84; 95% CI, 1.67-2.02). The aORs did not change appreciably when palliative care was included as the first course of treatment for all cancers. In an analysis limited to patients with stage II to IV prostate cancers, HIV was associated with a lack of cancer treatment (aOR, 1.91; 95% CI, 1.39-2.63). The results also did not change appreciably when patients refusing cancer treatment were excluded from the analyses.

Table 3 compares lack of cancer treatment among privately insured HIV-infected and HIV-uninfected individuals. Similar to all HIV-infected patients, HIV-infected individuals who were privately insured were found to be significantly more likely to be untreated for cancers of the upper gastrointestinal tract, colorectum, lung, breast, prostate, Hodgkin lymphoma, and DLBCL compared with HIV-uninfected privately insured patients. Differences were not found to be significant for cancers of the head and neck, anus, and cervix.

TABLE 1. Characteristics of HIV-Infected and HIV-Uninfected Patients With Cancer, 2003 to 2011

Characteristic	HIV-Infected Patients No. (%)	HIV-Uninfected Patients No. (%)	*P*
Total	10,265 (100.0)	2,219,232 (100.0)	
Age at cancer diagnosis, y			<.001
18-44	4142 (40.3)	317,103 (14.3)	
45-54	3971 (38.7)	718,752 (32.4)	
55-64	2152 (21.0)	1,183,377 (53.3)	
Sex			<.001
Male	7904 (77.0)	1,055,566 (47.6)	
Female	2361 (23.0)	1,163,666 (52.4)	
Race/ethnicity			<.001
Non-Hispanic white	3877 (37.8)	1,534,804 (69.1)	
Non-Hispanic black	4221 (41.1)	291,763 (13.2)	
Hispanic	1433 (14.0)	125,727 (5.7)	
Other	134 (1.3)	70,824 (3.2)	
Unknown	600 (5.8)	196,114 (8.8)	
Insurance status			<.001
Private	3641 (35.5)	1,609,611 (72.5)	
Medicaid[a]	3309 (32.2)	224,715 (10.1)	
Medicare	2009 (19.6)	185,705 (8.4)	
Uninsured	1061 (10.3)	131,212 (5.9)	
Unknown	245 (2.4)	67,989 (3.1)	
Modified Charlson-Deyo comorbidity score[b]			<.001
0	7835 (76.5)	1,822,795 (82.1)	
1	1654 (16.1)	307,999 (13.9)	
≥2	758 (7.4)	88,438 (4.0)	
Census region			<.001
Northeast	2439 (23.8)	450,097 (20.3)	
South	4647 (45.3)	855,841 (38.6)	
Midwest	1531 (14.9)	565,324 (25.5)	
West	1615 (15.7)	339,938 (15.3)	
Unknown	33 (0.3)	8032 (0.4)	
Y of cancer diagnosis			<.001
2003-2005	2711 (26.4)	691,397 (31.2)	
2006-2008	3774 (36.8)	762,049 (34.3)	
2009-2011	3780 (36.8)	765,786 (34.5)	
Cancer type			<.001
Head and neck	502 (4.9)	146,101 (6.6)	
Upper GI	288 (2.8)	144,732 (6.5)	
Colorectum	353 (3.4)	278,914 (12.6)	
Anus	807 (7.9)	17,776 (0.8)	
Lung	1420 (13.8)	353,156 (15.9)	
Breast	226 (2.2)	680,632 (30.7)	
Cervix	196 (1.9)	64,505 (2.9)	
Prostate	429 (4.2)	453,912 (20.4)	
Hodgkin lymphoma	1727 (16.8)	34,436 (1.6)	
DLBCL	4317 (42.1)	45,068 (2.0)	
AJCC cancer stage			<.001
I	1679 (16.4)	530,442 (23.9)	
II	1729 (16.8)	738,558 (33.3)	
III	1855 (18.1)	379,057 (17.1)	
IV	3822 (37.2)	420,232 (18.9)	
Unknown	1180 (11.5)	150,943 (6.8)	

Abbreviations: AJCC, American Joint Committee on Cancer; DLBCL, diffuse large B-cell lymphoma; GI, gastrointestinal; HIV, human immunodeficiency virus.
[a] This category includes Medicaid as well as other forms of governmental insurance, including Bureau of Indian Affairs and Public Health Service.
[b] There are 15 non-cancer diseases, each with an associated weight, included in calculating the Charlson-Deyo comorbidity index: myocardial infarction (weight, 1), congestive heart failure (weight, 1), peripheral vascular disease (weight, 1), cerebrovascular disease (weight, 1), dementia (weight, 1), chronic pulmonary disease (weight, 1), peptic ulcer (weight, 1), mild liver disease (weight, 1), diabetes (weight, 1), diabetes with complications (weight, 2), hemiplegia or paraplegia (weight, 2), renal disease (weight, 2), moderate or severe liver disease (weight, 3), and human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) (weight, 6). The Charlson-Deyo comorbidity index is then calculated by the weighed sum of the diseases indicated by *International Classification of Diseases, Ninth Revision* (ICD-9) codes. In the current study, because the entire study cohort was comprised of patients with cancer with or without HIV/AIDS, the comorbidity index was recalculated excluding "HIV/AIDS."

To exclude possible confounding from the covariate differences between HIV-infected and HIV-uninfected individuals, a PS-matched subgroup of HIV-uninfected cases was selected to perform sensitivity analyses. After PS matching, the distribution of the covariates was more balanced (see online Supporting Information Table 1 and

TABLE 2. Lack of Cancer Treatment in HIV-Infected Patients Compared With HIV-Uninfected Patients

Cancer Type	Total No. of HIV-Infected Patients	HIV-Infected Patients Not Receiving Cancer Treatment No. (%)	Total No. of HIV-Uninfected Patients	HIV-Uninfected Patients Not Receiving Cancer Treatment No. (%)	Adjusted OR (95% CI)[a]	*P*
Head and neck	502	47 (9.4)	146,101	7465 (5.1)	1.48 (1.09-2.01)	.013
Upper GI	288	126 (43.8)	144,732	26,565 (18.4)	2.62 (2.04-3.37)	<.001
Colorectum	353	35 (9.9)	278,914	10,604 (3.8)	1.70 (1.17-2.48)	.006
Anus	807	39 (4.8)	17,776	558 (3.1)	1.20 (0.83-1.71)	.333
Lung	1420	464 (32.7)	353,156	48,095 (13.6)	2.46 (2.19-2.76)	<.001
Breast	226	13 (5.8)	680,632	10,852 (1.6)	2.14 (1.16-3.98)	.015
Cervix	196	23 (11.7)	64,505	2371 (3.7)	2.81 (1.77-4.45)	<.001
Prostate	429	103 (24.0)	453,912	32,726 (7.2)	2.16 (1.69-2.76)	<.001
Hodgkin lymphoma	1,727	295 (17.1)	34,436	2724 (7.9)	1.92 (1.66-2.22)	<.001
DLBCL	4317	769 (17.8)	45,068	4168 (9.3)	1.82 (1.65-2.00)	<.001

Abbreviations: 95% CI, 95% confidence interval; DLBCL, diffuse large B-cell lymphoma; GI, gastrointestinal; HIV, human immunodeficiency virus; OR, odds ratio.
[a] ORs were adjusted for age at diagnosis, sex, race/ethnicity, insurance status, modified Charlson-Deyo comorbidity score, census region, cancer diagnosis year, and cancer stage.

TABLE 3. Lack of Cancer Treatment In HIV-Infected and HIV-Uninfected Patients Among Privately Insured Cases

Cancer Type	Total No. of HIV-Infected Patients	HIV-Infected Patients Not Receiving Cancer Treatment No. (%)	Total No. of HIV-Uninfected Patients	HIV-Uninfected Patients Not Receiving Cancer Treatment No. (%)	Adjusted OR (95% CI)[a]	*P*
Head and neck	122	5 (4.1)	88,704	3258 (3.7)	1.15 (0.47-2.84)	.759
Upper GI	75	26 (34.7)	93,786	13,543 (14.4)	3.61 (2.17-6.03)	<.001
Colorectum	115	8 (7.0)	200,129	5347 (2.7)	2.24 (1.05-4.77)	.036
Anus	247	5 (2.0)	11,272	297 (2.6)	0.74 (0.29-1.85)	.514
Lung	334	76 (22.8)	205,698	20,358 (9.9)	2.47 (1.89-3.22)	<.001
Breast	67	4 (6.0)	542,008	6016 (1.1)	4.24 (1.36-13.17)	.013
Cervix	37	3 (8.1)	36,711	924 (2.5)	2.73 (0.80-9.29)	.108
Prostate	181	30 (16.6)	375,288	21,510 (5.7)	2.25 (1.48-3.42)	<.001
Hodgkin lymphoma	739	116 (15.7)	24,718	1872 (7.6)	1.87 (1.50-2.33)	<.001
DLBCL	1724	222 (12.9)	31,297	2574 (8.2)	1.57 (1.34-1.84)	<.001

Abbreviations: 95% CI, 95% confidence interval; DLBCL, diffuse large B-cell lymphoma; GI, gastrointestinal; HIV, human immunodeficiency virus; OR, odds ratio.
[a] ORs are adjusted for age at diagnosis, sex, race/ethnicity, modified Charlson-Deyo comorbidity score, census region, cancer diagnosis year, and cancer stage.

online Supporting Information Fig. 1). Similar to the findings among the unmatched subjects, HIV-infected cases in the PS-matched subcohort were still significantly more likely to be untreated at all cancer sites, with the exception of anal cancer (see online Supporting Information Table 2). Among privately insured PS-matched patients, the results were similar to the unmatched analysis (see online Supporting Information Table 3).

Table 4 shows predictors of a lack of cancer treatment among HIV-infected individuals by tumor type (solid tumor vs lymphoma). Patients of black race and with Medicaid, Medicare, or no insurance were more likely to be untreated for cancer, regardless of tumor type. Other predictive factors varied between solid tumors and lymphomas. Advanced stage at the time of cancer diagnosis (stage IV) was found to be associated with a lack of cancer treatment for solid tumors (aOR, 2.60 [95% CI, 1.93-3.51] compared with stage I), but associated with the receipt of treatment for lymphomas (aOR, 0.70; 95% CI, 0.58-0.85). Higher modified Charlson-Deyo comorbidity scores of 1 or 2 were found to be predictors of a lack of cancer treatment among HIV-infected patients with lymphoma, but were not predictors in patients with solid tumors. Older age was associated with a lack of treatment for both lymphomas and solid tumors, although this was statistically significant only for lymphomas.

TABLE 4. Predictors of Lack of Cancer Treatment Among HIV-Infected Patients

Characteristic	HIV-Infected Patients Not Receiving Cancer Treatment Row %	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]	*P*
Solid Tumors				
Age at cancer diagnosis, y				.076[b]
18-44	14.1	1	1	
45-54	20.9	1.62 (1.31-2.00)	1.21 (0.95-1.54)	
55-64	23.5	1.88 (1.51-2.34)	1.29 (0.99-1.68)	
Sex				.153
Male	20.1	1	1	
Female	20.2	1.01 (0.85-1.20)	1.17 (0.94-1.46)	
Race/ethnicity				.003
Non-Hispanic white	15.3	1	1	
Non-Hispanic black	24.2	1.77 (1.49-2.10)	1.42 (1.16-1.73)	
Hispanic	16.4	1.09 (0.80-1.48)	0.98 (0.69-1.39)	
Other	7.5	0.45 (0.14-1.47)	0.61 (0.18-2.11)	
Unknown	24.2	1.76 (1.27-2.44)	1.44 (0.99-2.09)	
Insurance status				<.001
Private	13.3	1	1	
Medicaid[c]	23.7	2.00 (1.63-2.46)	1.75 (1.39-2.20)	
Medicare	20.4	1.66 (1.33-2.08)	1.59 (1.24-2.02)	
Uninsured	26.1	2.30 (1.71-3.10)	1.99 (1.42-2.78)	
Unknown	30.7	2.87 (1.63-5.06)	2.27 (1.20-4.30)	
Modified Charlson-Deyo comorbidity score				.188[b]
0	18.7	1	1	
1	21.7	1.20 (1.00-1.44)	0.97 (0.79-1.19)	
≥2	26.7	1.58 (1.25-2.01)	1.26 (0.96-1.66)	
AJCC cancer stage				<.001
I	10.4	1	1	
II	9.8	0.93 (0.67-1.29)	0.70 (0.48-1.01)	
III	12.4	1.21 (0.88-1.67)	1.02 (0.73-1.44)	
IV	32.1	4.06 (3.09-5.34)	2.60 (1.93-3.51)	
Unknown	35.1	4.64 (3.37-6.39)	3.89 (2.74-5.53)	
Lymphomas				
Age at cancer diagnosis, y				.001[b]
18-44	16.1	1	1	
45-54	19.3	1.25 (1.08-1.44)	1.29 (1.11-1.50)	
55-64	19.4	1.25 (1.03-1.53)	1.30 (1.05-1.60)	
Sex				.607
Male	17.6	1	1	
Female	17.6	1.00 (0.85-1.17)	0.96 (0.81-1.14)	
Race/ethnicity				<.001
Non-Hispanic white	14.7	1	1	
Non-Hispanic black	20.5	1.50 (1.29-1.75)	1.42 (1.20-1.67)	
Hispanic	17.3	1.22 (1.00-1.48)	1.09 (0.89-1.34)	
Other	19.2	1.38 (0.81-2.33)	1.28 (0.75-2.20)	
Unknown	19.2	1.38 (1.04-1.84)	1.49 (1.11-2.00)	
Insurance status				<.001
Private	13.7	1	1	
Medicaid[c]	18.7	1.45 (1.23-1.71)	1.40 (1.18-1.66)	
Medicare	20.8	1.65 (1.35-2.02)	1.49 (1.21-1.83)	
Uninsured	22.8	1.86 (1.51-2.29)	1.78 (1.43-2.21)	
Unknown	23.0	1.87 (1.30-2.69)	1.78 (1.23-2.60)	
Modified Charlson-Deyo comorbidity score				<.001[b]
0	16.6	1	1	

TABLE 4. *Continued*

Characteristic	Lymphomas			
	HIV-Infected Patients Not Receiving Cancer Treatment Row %	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]	*P*
1	20.1	1.27 (1.04-1.54)	1.27 (1.04-1.56)	
≥2	26.9	1.85 (1.44-2.37)	1.80 (1.39-2.33)	
AJCC cancer stage				<.001
I	21.5	1	1	
II	11.9	0.49 (0.38-0.64)	0.51 (0.39-0.66)	
III	12.4	0.52 (0.41-0.66)	0.51 (0.04-0.65)	
IV	16.5	0.72 (0.60-0.87)	0.70 (0.58-0.85)	
Unknown	28.9	1.48 (1.20-1.84)	1.47 (1.18-1.83)	

Abbreviations: 95% CI, 95% confidence interval; AJCC, American Joint Committee on Cancer; HIV, human immunodeficiency virus; OR, odds ratio.
[a] ORs were adjusted for age at diagnosis, sex, race/ethnicity, insurance status, modified Charlson-Deyo comorbidity score, cancer stage, and (not shown) census region, cancer type, and cancer diagnosis year.
[b] Trend tests.
[c] This category includes Medicaid as well as other forms of governmental insurance, including the Bureau of Indian Affairs and Public Health Service.

DISCUSSION

Two prior studies have demonstrated differences in the receipt of cancer treatment between HIV-infected and HIV-uninfected individuals,[6,7] but they did not account for comorbidities and insurance status, both of which are known to affect receipt of cancer treatment. Taking these 2 factors into consideration, we found that HIV-infected patients with cancer were still less likely to receive cancer treatment for nearly all common cancer types compared with HIV-uninfected individuals. These disparities persisted among privately insured patients. Among HIV-infected individuals, black race and Medicaid, Medicare, and no insurance were associated with a lack of treatment for both solid tumors and lymphomas.

Although survival from HIV has improved greatly in the antiretroviral era,[15] HIV-infected individuals may be at an increased risk of developing comorbid conditions due to viral co-infections, diseases of aging such as cardiovascular disease, and toxicity from antiretroviral medications.[16] In addition, HIV-infected individuals are more likely to engage in adverse health behaviors such as smoking and intravenous drug use.[17] A higher number and severity of comorbidities influence candidacy for cancer treatments.[8] In the current study, we observed that HIV-infected individuals had a significantly higher modified Charlson-Deyo comorbidity score compared with HIV-uninfected individuals (Table 1). However, the difference in comorbidity did not account for the lack of cancer treatment in HIV-infected individuals because the associations were observed even after controlling for modified Charlson-Deyo comorbidity scores (Table 2).

Similarly, insurance status is an important predictor of the receipt of cancer treatment in the general population. A recent study of nonelderly adults in the SEER database found that patients with Medicaid or no insurance were significantly more likely to present with advanced stage cancer, less likely to receive cancer treatment, and had worse survival.[9] HIV-infected patients in the United States are frequently uninsured or underinsured.[10,11] In the current study cohort, we noted that a much higher percentage of nonelderly HIV-infected individuals with cancer had Medicaid (32.2% vs 10.1% for HIV-uninfected individuals), Medicare (19.6% vs 8.4%), or no insurance (10.3% vs 5.9%). Only 35.5% of the HIV-infected individuals had private insurance compared with 72.5% of HIV-uninfected individuals. Improved access to cancer treatment is urgently needed, not only for uninsured patients but also for those with Medicaid and Medicare. However, these differences in insurance status did not fully account for the observed cancer treatment disparity because we demonstrated associations between HIV and a lack of cancer treatment even when insurance status was included as a covariate (Table 2). Furthermore, in the analyses restricted to privately insured patients, the associations between HIV infection and lack of cancer treatment remained apparent for most cancers. These findings together suggest that comorbidities and insurance status alone do not explain the treatment disparity observed in prior studies.

There are other factors that may contribute to the observed disparities in the receipt of cancer treatment by HIV status. HIV-infected patients with cancer have historically been excluded from cancer clinical trials, thereby

limiting the applicability of clinical trial results for this population.[18] Furthermore, cancer treatment guidelines specific to HIV-infected patients are not available for most cancer types, which may contribute to treatment disparities. The management of anal cancer in HIV-infected patients is well studied and documented in clinical guidelines,[19] and it is notable that this was the only cancer for which differences in cancer treatment by HIV status were not observed herein. Lack of experience treating HIV-infected patients with cancer also may play a role. In a survey study of US medical and radiation oncologists, physicians were less likely to offer cancer treatment to HIV-infected individuals if they had concerns about the efficacy or toxicity of treatment, and were more likely to offer treatment if they were comfortable discussing side effects and prognosis.[20] The majority of respondents believed that currently existing cancer management guidelines were insufficient for the management of HIV-infected patients, and a very small number discussed cancer management with their patients' HIV specialists. Furthermore, HIV-infected patients may avoid or not adhere to cancer treatment due to the psychosocial and economic challenges associated with the dual management of cancer and HIV.[21] Substance abuse may complicate cancer treatment adherence,[22,23] although rates of smoking, drinking, and intravenous drug use were not ascertained in the current study.

Among HIV-infected individuals, black race was associated with a lack of cancer treatment, a finding previously described in the general cancer population.[24] Advanced cancer stage was associated with a lack of cancer treatment for solid tumors but not lymphomas. This may reflect differences in overall prognosis and cancer-specific survival between patients with advanced stage solid tumors and advanced lymphomas.[13] For lymphomas, advancing age was found to be significantly associated with a lack of cancer treatment, a finding that is consistent with prior studies in the general cancer population.[25,26] Modified Charlson-Deyo comorbidity scores of 1 and 2 also were found to be significantly associated with a lack of cancer treatment for lymphomas, which may reflect concerns regarding the systemic effects of chemotherapy, the mainstay of treatment for lymphomas, even for early-stage disease. In contrast, early-stage solid tumors are often treated with surgery and/or radiotherapy, both of which are local therapies that may be more readily delivered to patients with comorbidities; however, we did not aim to capture differences in treatment type in the current study.

The strengths of the current study include the large number of HIV-infected patients with cancer in the NCDB, covering 70% of the total incidence cancer cases in the United States. In addition, we focused on nonelderly patients in the modern era of HIV treatment, and the demographic characteristics of the patients with cancer in the current study largely mirror the US HIV population.[27] Although we made multiple comparisons, many of the associations demonstrated herein were highly significant, making chance an unlikely explanation.

There are several important limitations, as well. First, we did not have data regarding HIV severity, CD4 count, or receipt of HAART, which may influence candidacy for cancer treatment. Second, the Charlson-Deyo comorbidity score (excluding HIV) was calculated based on a maximum of 10 reported comorbidities; therefore, underascertainment of comorbidities is possible and may disproportionately affect the HIV-infected group. In addition, the severity of these comorbidities is not reported to the NCDB and also may differ by HIV status. We also note that the total number of cases was small for some cancers in the analyses of privately insured patients. Finally, it is likely that there was some underascertainment of outpatient cancer treatment data within the NCDB, and therefore we may have overestimated the percentage of patients who lacked cancer treatment; however, we would not expect major differences in ascertainment by HIV status.

The results of the current study indicate that HIV-infected adults diagnosed with any of 9 common cancers were less likely to receive cancer treatment than their HIV-uninfected counterparts, even after controlling for comorbidities and insurance status. These results were obtained for HIV-infected patients in the modern era of HIV treatment, and the disparity was observed among patients with private insurance. These findings suggest that cancer care providers and policy makers need to devote special attention to the HIV-infected patient population to understand and address the factors driving differential cancer treatment, which may include lack of management guidelines and clinical trial data. Cancer treatment not only extends survival from cancer, but also can improve quality of life, even for patients with advanced stage disease.[19] The observed disparity is of particular importance given the extended survival of HIV-infected patients treated with antiretroviral therapy and the rising number of cancer cases.

FUNDING SUPPORT

Chun Chieh Lin, Xuesong Han, and Ahmedin Jemal were supported by the American Cancer Society Intramural Research

Department. Eric A. Engels was supported by the intramural research program of the National Cancer Institute.

CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

AUTHOR CONTRIBUTIONS

Gita Suneja: Conceptualization, methodology, investigation, writing-original draft, writing-review and editing, visualization, and project administration. **Chun Chieh Lin**: Conceptualization, methodology, software, formal analysis, investigation, resources, data curation, writing-original draft, writing-review and editing, visualization, and project administration. **Edgar P. Simard**: Conceptualization, writing-review and editing, and visualization. **Xuesong Han**: Conceptualization, writing-review and editing, and visualization. **Eric A. Engels**: Conceptualization, methodology, investigation, writing-review and editing, visualization, supervision, and project administration. **Ahmedin Jemal**: Conceptualization, methodology, investigation, resources, data curation, writing-review and editing, visualization, supervision, and project administration.

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