Cancer Treatment Disparities in HIV-Infected Individuals in the United States

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ABSTRACT

Purpose

HIV-infected individuals with cancer have worse survival rates compared with their HIV-uninfected counterparts. One explanation may be differing cancer treatment; however, few studies have examined this.

Patients and Methods

We used HIV and cancer registry data from Connecticut, Michigan, and Texas to study adults diagnosed with non-Hodgkin's lymphoma, Hodgkin's lymphoma, or cervical, lung, anal, prostate, colorectal, or breast cancers from 1996 to 2010. We used logistic regression to examine associations between HIV status and cancer treatment, adjusted for cancer stage and demographic covariates. For a subset of local-stage cancers, we used logistic regression to assess the relationship between HIV status and standard treatment modality. We identified predictors of cancer treatment among individuals with both HIV and cancer.

Results

We evaluated 3,045 HIV-infected patients with cancer and 1,087,648 patients with cancer without HIV infection. A significantly higher proportion of HIV-infected individuals did not receive cancer treatment for diffuse large B-cell lymphoma (DLBCL; adjusted odds ratio [aOR], 1.67; 95% CI, 1.41 to 1.99), lung cancer (aOR, 2.18; 95% CI, 1.80 to 2.64), Hodgkin's lymphoma (aOR, 1.77; 95% CI, 1.33 to 2.37), prostate cancer (aOR, 1.79; 95% CI, 1.31 to 2.46), and colorectal cancer (aOR, 2.27; 95% CI, 1.38 to 3.72). HIV infection was associated with a lack of standard treatment modality for local-stage DLBCL (aOR, 2.02; 95% CI, 1.50 to 2.72), non-small-cell lung cancer (aOR, 2.43; 95% CI, 1.46 to 4.03), and colon cancer (aOR, 4.77; 95% CI, 1.76 to 12.96). Among HIV-infected individuals, factors independently associated with lack of cancer treatment included low CD4 count, male sex with injection drug use as mode of HIV exposure, age 45 to 64 years, black race, and distant or unknown cancer stage.

Conclusion

HIV-infected individuals are less likely to receive treatment for some cancers than uninfected people, which may affect survival rates.

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INTRODUCTION

Before the widespread adoption of highly active antiretroviral therapy (HAART), cancers in HIV-infected individuals were largely malignancies related to severe immunosuppression (ie, AIDS-defining cancers), namely Kaposi's sarcoma, non-Hodgkin's lymphoma, and cervical cancer.¹⁻⁶ The availability of HAART since 1996 has prolonged the survival of HIV-infected individuals.⁷ While the incidence of AIDS-defining malignancies has decreased, there has been a rise in the incidence of non-AIDS-defining cancers (NADCs), in part owing to an aging HIV population.^{2,4-6,8-11} Death as a result of NADCs is an increasingly important cause of mortality in people with HIV infection.^{12,13}

HIV-infected people with cancer have worse survival rates compared with their HIV-uninfected counterparts.¹⁴ This high mortality is partly owing to death as a result of AIDS-related complications, but additional proposed explanations for the disparity in survival rates include advanced stage at cancer diagnosis, biologically aggressive cancer phenotype because of immune dysregulation, and decreased efficacy or increased toxicity from cancer therapy.¹⁴⁻¹⁶

Another possible explanation for the poor survival rates after cancer diagnosis is that HIV-infected people may not receive appropriate cancer treatment. In a prior study of patients with lung cancer in Texas, we found that HIV-infected people with lung cancer were less likely to receive cancer treatment

than those uninfected with HIV, and this disparity may have been associated with a survival decrement.¹⁷ Evidence-based guidelines for the management of HIV-infected patients with cancer are lacking for most NADCs, because patients with HIV are typically excluded from cancer clinical trials. Lack of guidelines may lead to undertreatment of HIV-infected patients with cancer, particularly if cancer treatment is perceived as having lower efficacy or higher toxicity.

In our current study, we use linked data from HIV and cancer registries in three US states to assess the receipt of cancer treatment among HIV-infected individuals compared with that received by HIV-uninfected individuals. We also examine predictors of treatment among HIV-infected people with cancer.

PATIENTS AND METHODS

The HIV/AIDS Cancer Match Study is a [population-based study](#) that links 14 US HIV registries (that participate in the enhanced HIV/AIDS Reporting System) and cancer registries.¹⁸ A probabilistic algorithm is used to match records between HIV and cancer registries; following the linkage, investigators retain only anonymized data. Our current study was restricted to patients with cancer from Connecticut, Michigan, and Texas because cancer treatment data were available in these registries and were included in the linked data files. Institutional review boards at the Connecticut, Michigan, and Texas registries approved the study.

Patients with cancer were identified in the cancer registries, and their HIV status at the time of cancer diagnosis was ascertained using the linked HIV registry data. From the cancer registries, we included adults who were at least 18 years old, diagnosed between 1996 and 2010 with AIDS-defining malignancies (ie, non-Hodgkin's lymphoma and cervical cancer) and common NADCs (ie, Hodgkin's lymphoma, and lung, anal, prostate, colorectal, and breast cancers). To ensure reporting of both HIV and AIDS, we restricted our study period by state to the years in which reporting of both HIV and AIDS was mandatory, specifically, 2002 to 2010 for Connecticut, 1996 to 2010 for Michigan, and 1997 to 2009 for Texas. Because of the rarity of Kaposi's sarcoma among HIV-uninfected individuals, and the possibility that many unlinked cases of Kaposi's sarcoma would have unreported HIV infection, we omitted this cancer from our study. We also excluded liver cancer, because first-line treatment for liver cancer commonly includes modalities (eg, radiofrequency ablation or chemoembolization) that are not captured by cancer registries. Within non-Hodgkin's lymphoma, we restricted analyses to diffuse large B-cell lymphoma (DLBCL), because this histologic subtype comprises the majority of HIV-infected cancer cases, and several other histologic subtypes of non-Hodgkin's lymphoma do not require upfront cancer treatment.

The cancer registries provided data on the first course of cancer treatment. For all cancers except lymphoma, we defined cancer treatment as surgery, radiation, chemotherapy, or any combination of these therapies administered as first course. For DLBCL and Hodgkin's lymphoma, cancer treatment was defined as chemotherapy (including rituximab for DLBCL), radiation, or both administered as first course. In [sensitivity analyses](#) for prostate and breast cancer, hormone therapy was included. In a sensitivity analysis for DLBCL, additional types of immune therapy (eg, radioimmunotherapy) were included. We also defined a standard treatment modality variable for local-stage DLBCL, non-small-cell lung cancer (NSCLC), and cervical, colon (excluding rectum), and breast cancers, based on the treatment modality (surgery, radiation, or chemotherapy) required for curative intent according to National Comprehensive Cancer Network guidelines.¹⁹ We chose to focus on early-stage cancer because treatment paradigms are more readily defined and curability is highest.

Using χ^2 tests, we compared HIV-infected and HIV-uninfected patients with cancer by cancer type, cancer stage (local, regional, and distant based on Surveillance, Epidemiology, and End Results summary staging²⁰), and demographic characteristics (sex, age at cancer diagnosis, race/ethnicity, year of cancer diagnosis, and US state). For each cancer type, we used logistic regres-

sion to assess the relationship between HIV status and cancer treatment, adjusted for cancer stage, sex, age at cancer diagnosis (< 45 years, 45 to 64 years, and $\geq$ 65 years), race/ethnicity, year of cancer diagnosis, and US state. We performed a separate analysis restricted to patients whose cancers were diagnosed from 2006 to 2010 to examine treatment patterns in the most recent time period. We repeated this analysis for local-stage cancer to assess the relationship between HIV status and receipt of the standard treatment modality. Because the majority of patients with cancer received treatment, we focus on the proportion of patients who were untreated.

We also used logistic regression to assess predictors of cancer treatment among HIV-infected patients with cancer. These analyses considered all cancers together and included adjustment for cancer type. In addition to demographic characteristics and cancer stage, we examined CD4 T-lymphocyte (CD4) counts at the time point nearest to and preceding cancer diagnosis as well as mode of HIV transmission. We describe HIV viral load results for patients, but owing to a large amount of missing data, these values were not examined in relation to cancer treatment. HIV stage (HIV without AIDS ν AIDS) was not included in the adjusted model because of strong collinearity with CD4 count.

Adjusted odds ratios (ORs) with 95% CIs are reported for all analyses. Stata Statistical Software version 12.1 (College Station, TX) was used.

RESULTS

Characteristics of Participants With Cancer

Table 1 lists characteristics of HIV-infected and HIV-uninfected patients with cancer (HIV-infected, $n = 3,045$; HIV-uninfected $n = 1,087,648$). Among HIV-infected participants, DLBCL, lung, and anal cancers were the most common cancer diagnoses, whereas in HIV-uninfected participants, prostate, breast, and lung cancers were the most common. A greater proportion of HIV-infected participants had distant (36.5% ν 18.0%) or unknown (13.4% ν 9.2%) cancer stage at the time of diagnosis. Compared with the HIV-uninfected cancer participants, a greater proportion of HIV-infected patients were men (80.1% ν 51.4%) and younger (median age, 46 ν 66 years). HIV-infected participants were more likely to be non-Hispanic black (40.3% ν 11.6%) or Hispanic (17.0% ν 8.6%). A greater proportion of HIV-infected participants were diagnosed with cancer in the later calendar years (during 2006-2010; 41.7% ν 34.5%), largely because of a rising proportion of NADCs over time.

Among HIV-infected participants, the majority (88.5%) had a previous diagnosis of AIDS. Median CD4 count before cancer diagnosis was 144 cells/ μ L (CD4 count data were available for 80.2% of participants at a median of 25 months before diagnosis), and median viral load before cancer diagnosis was 38,000 copies/mL (viral load data were available for 35.3% of participants at a median of 5 months before diagnosis).

Association of HIV Status and Lack of Cancer Treatment

Table 2 lists a comparison of cancer treatment for HIV-infected and HIV-uninfected patients with cancer. Anal cancer was the only cancer for which the proportions of participants who did not receive cancer treatment were virtually identical whether they were infected with HIV or not (8.3% ν 8.1%; adjusted OR, 1.01; 95% CI, 0.68 to 1.50). DLBCL, lung cancer, Hodgkin's lymphoma, prostate cancer, and colorectal cancer all showed a significantly higher proportion of participants with HIV who did not receive cancer treatment compared with HIV-uninfected participants (DLBCL: adjusted OR, 1.67; 95% CI, 1.41 to 1.99; lung cancer: adjusted OR, 2.18; 95% CI, 1.80 to 2.64;

Table 1. Patients With Cancer in Connecticut, Michigan, and Texas (1996-2010) by HIV Infection Status

Characteristic	With HIV		Without HIV		P
	No. of Participants (n = 3,045)	%	No. of Participants (n = 1,087,648)	%	
Cancer type					< .001
DLBCL	1,054	34.6	26,065	2.4	
Cervix	121	4.0	20,677	1.9	
Lung	581	19.1	260,652	24.0	
Anus	487	16.0	6,558	0.6	
Hodgkin's lymphoma	300	9.9	11,065	1.0	
Prostate	233	7.6	290,549	26.7	
Colorectum	161	5.3	195,156	17.9	
Breast	108	3.5	276,926	25.5	
Cancer stage					< .001
Local	929	30.5	530,171	48.7	
Regional	597	19.6	262,277	24.1	
Distant	1,111	36.5	195,309	18.0	
Unknown	408	13.4	99,891	9.2	
Sex					< .001
Male	2,439	80.1	559,517	51.4	
Female	606	19.9	528,131	48.6	
Age at cancer diagnosis, years					< .001
< 45	1,343	44.1	72,667	6.7	
45-64	1,525	50.1	407,060	37.4	
≥ 65	177	5.8	607,921	55.9	
Race/ethnicity					< .001
Non-Hispanic white	1,272	41.8	836,586	76.9	
Non-Hispanic black	1,227	40.3	125,986	11.6	
Hispanic	516	17.0	94,036	8.6	
Other	13	0.4	11,651	1.1	
Unknown	17	0.5	19,389	1.8	
Cancer diagnosis year					< .001
1996-2000	685	22.5	308,127	28.3	
2001-2005	1,090	35.8	404,598	37.2	
2006-2010	1,270	41.7	374,923	34.5	
State					< .001
Connecticut	350	11.5	92,218	8.5	
Michigan	687	22.6	426,015	39.2	
Texas	2,008	65.9	569,415	52.3	

Abbreviation: DLBCL, diffuse large B-cell lymphoma.

Hodgkin's lymphoma: adjusted OR, 1.77; 95% CI, 1.33 to 2.37; prostate cancer: adjusted OR, 1.79; 95% CI, 1.31 to 2.46; colorectal cancer: adjusted OR, 2.27; 95% CI, 1.38 to 3.72). Though the proportion of participants who were not treated seemed to be the same for HIV-infected and HIV-uninfected DLBCL participants, after adjustment, HIV-infected participants were more likely to be untreated for cancer. This difference largely reflects the fact that HIV-infected participants were younger than HIV-uninfected participants, because adjustment for age alone had a substantial effect on the odds ratio (not shown). Associations for cervical (adjusted OR, 1.60; 95% CI, 0.87 to 2.95) and breast cancer (adjusted OR, 1.81; 95% CI, 0.87 to 3.77) were not statistically significant. In an analysis restricted to participants with cancer who were diagnosed from 2006 to 2010, the associations were largely similar, with the exception of anal cancer, for which HIV-infected participants were more likely to be treated than HIV-uninfected participants (Table 2). In a sensitivity analysis including

hormone therapy as first course of treatment, the results were similar for prostate cancer (adjusted OR, 1.65; 95% CI, 1.19 to 2.31) and breast cancer (adjusted OR, 1.73; 95% CI, 0.81 to 3.71). In a sensitivity analysis including immune therapy as first course of treatment for DLBCL, the results were similar (adjusted OR, 1.65; 95% CI, 1.39 to 1.97).

Table 3 lists the results of an analysis restricted to local-stage cancers for which the standard treatment modality is aimed at cure. HIV infection was associated with greater lack of standard cancer treatment for local-stage DLBCL (adjusted OR, 2.02; 95% CI, 1.50 to 2.72), lung cancer (adjusted OR, 2.43; 95% CI, 1.46 to 4.03), and colon cancer (adjusted OR, 4.77; 95% CI, 1.76 to 12.96). HIV infection was not significantly associated with a lack of the standard treatment modality for local-stage cervical (adjusted OR, 1.30; 95% CI, 0.39 to 4.29) and breast cancer (adjusted OR, 1.38; 95% CI, 0.58 to 3.29).

Predictors of Lack of Cancer Treatment in HIV-Infected Participants

Among HIV-infected participants with cancer (Table 4), distant and unknown stages were associated with a lack of treatment, whereas regional stage was associated with greater levels of treatment, compared with local-stage disease. Men with intravenous drug use as the mode of HIV exposure were more likely to be untreated (compared with men who were exposed to HIV via sex with men; adjusted OR, 1.58; 95% CI, 1.16 to 2.15). Associations between other risk groups and lack of cancer treatment were not significant. Individuals 45 to 64 years old were more likely to be untreated (adjusted OR, 1.30; 95% CI, 1.04 to 1.63) compared with younger patients, as were non-Hispanic black participants versus non-Hispanic white participants (adjusted OR, 1.27; 95% CI, 1.01 to 1.60).

Individuals with CD4 counts lower than or equal to the median (median, 144 cells/ μ L) were more likely to be untreated for cancer compared with those whose CD4 counts were higher than the median (adjusted OR, 1.50; 95% CI, 1.21 to 1.86). In addition, people with AIDS were more likely to be untreated than participants with HIV infection but not AIDS (univariable OR, 1.36; 95% CI, 1.01 to 1.84).

DISCUSSION

In three US states, HIV-infected participants with cancer were less frequently treated for cancer than their HIV-uninfected counterparts for several common cancer types (DLBCL, Hodgkin's lymphoma, and lung, prostate, and colorectal cancers). A disparity was also seen in the most recent calendar years (2006 to 2010) and for receipt of the standard treatment modality for local-stage DLBCL, non-small-cell lung cancer, and colon cancer. Among HIV-infected participants, factors independently associated with a lack of treatment included low CD4 count, male sex with intravenous drug use as mode of HIV transmission, older age, black race, and distant or unknown cancer stage.

Numerous provider-level factors may contribute to lower treatment rates for HIV-infected patients with cancer. The absence of specific treatment guidelines for HIV-infected patients with cancer may allow provider perceptions of HIV-infected patients to influence decisions to recommend treatment. Providers may perceive HIV-infected patients as having lower performance status, lower efficacy of cancer treatment, or a lower threshold for cancer treatment toxicity,

Table 2. Association of HIV Infection With Lack of Cancer Treatment

Cancer Type	All Years 1996-2010						Analysis Restricted to Years 2006-2010					
	HIV Infected and Without Cancer Treatment		HIV Uninfected and Without Cancer Treatment		Adjusted Odds Ratio	95% CI*	HIV Infected and Without Cancer Treatment		HIV Uninfected and Without Cancer Treatment		Adjusted Odds Ratio	95% CI†
	No. of Participants	%	No. of Participants	%			No. of Participants	%	No. of Participants	%		
DLBCL	207	23.0	5,157	23.4	1.67	1.41 to 1.99	70	21.7	2,071	24.2	1.40	1.05 to 1.87
Cervix	14	12.7	1,585	8.6	1.60	0.87 to 2.95	5	16.7	639	10.4	1.77	0.62 to 5.02
Lung	181	34.9	53,323	24.1	2.18	1.80 to 2.64	90	39.5	22,644	27.5	2.23	1.70 to 2.95
Anus	38	8.3	481	8.1	1.01	0.68 to 1.50	16	7.0	252	10.3	0.55	0.30 to 0.99
Hodgkin's lymphoma	75	29.3	1,839	20.2	1.77	1.33 to 2.37	30	28.9	699	20.6	1.84	1.16 to 2.91
Prostate	63	30.6	52,579	20.8	1.79	1.31 to 2.46	38	28.2	22,880	24.2	1.53	1.03 to 2.27
Colorectum	23	14.7	12,868	7.2	2.27	1.38 to 3.72	13	16.1	5,474	8.8	2.01	1.00 to 4.04
Breast	9	9.0	12,067	4.7	1.81	0.87 to 3.77	3	6.5	6,768	7.2	0.89	0.26 to 2.99

NOTE. Percentages of HIV-uninfected and HIV-infected participants with missing treatment data (who were excluded from analysis) were 7.7% and 5.3% for surgery, 18.4% and 13.2% for radiotherapy, 14.3% and 10.3% for chemotherapy, and 11.0% and 9.7%, respectively, for the composite treatment variable.

Abbreviation: DLBCL, diffuse large B-cell lymphoma.

*Odds ratios are adjusted for cancer stage, sex, age at diagnosis, race/ethnicity, year of cancer diagnosis, and state.

†Odds ratios are adjusted for cancer stage, sex, age at diagnosis, race/ethnicity, and state.

compared with HIV-uninfected patients. Treatment of anal cancer, for which guidelines for HIV-infected patients are available, did not differ by HIV status; in fact, HIV-infected patients were more likely to be treated than HIV-uninfected patients in the most recent calendar period (Table 2). Although HIV-infected people were more likely to present with distant or unknown stages of cancer, the difference in stage did not explain the lower rates of cancer treatment, as the associations between HIV infection and lack of treatment were apparent in adjusted models (Table 2).

In the absence of guidelines, another major issue is that the published data addressing cancer treatment in HIV-infected patients vary in their extent and quality. Clinical trial data are available to inform management of HIV-infected patients with DLBCL and anal cancer, but not other NADCs.²¹⁻²⁵ Before the introduction of HAART, use of standard-dose chemotherapy for lymphomas was associated with substantial toxicity and frequent opportunistic infections.^{26,27} However, since the advent of HAART and hematopoietic

growth factors, full-dose chemotherapy can be administered safely to HIV-infected patients with lymphoma, leading to improved cancer survival rates.²⁸⁻³¹ For other cancers, HIV-infected patients have generally been excluded from clinical trials, so randomized trial data regarding treatment outcomes are largely unavailable.³² Nonetheless, retrospective studies and case reports from the HAART era suggest comparable treatment toxicity with standard therapy.³³⁻⁴³ Despite the availability of modern retrospective data, the disparity in cancer treatment was apparent even when restricting our analysis to patients with cancer who were diagnosed from 2006 to 2010 (Table 2). This suggests that although access to cancer care may have improved over time, there is still a higher likelihood of lack of treatment for HIV-infected people in the most recent calendar period.

An additional reason for lower rates of cancer treatment could be that providers may have limited experience treating patients with HIV infection, or may not practice in a setting where dual management by oncologists and HIV specialists is possible. Treatment can be clinically

Table 3. Association of HIV With Lack of Standard Cancer Treatment Modality For Local-Stage Cancers

Cancer Type	Standard Treatment Modality*	No. of Participants With HIV	No. of Participants Without HIV	HIV Infected and Not Receiving Standard Treatment		HIV Uninfected and Not Receiving Standard Treatment		Adjusted Odds Ratio	95% CI†
				No. of Participants	%	No. of Participants	%		
DLBCL	Chemotherapy	213	6,280	93	43.7	2,251	35.8	2.02	1.50 to 2.72
Cervix	Surgery or radiotherapy	51	9,543	3	6.4	440	4.7	1.30	0.39 to 4.29
NSCLC	Surgery or radiotherapy	72	41,614	24	33.3	7,700	18.5	2.43	1.46 to 4.03
Colon	Surgery	24	48,140	5	20.8	2,204	4.6	4.77	1.76 to 12.96
Breast	Surgery	54	155,843	6	11.1	7,516	4.8	1.38	0.58 to 3.29

NOTE. Percentages of HIV-uninfected and HIV-infected participants with missing treatment data (who were excluded from analysis) were 11.2% and 8.6% for chemotherapy and DLBCL, 6.0% and 0% for surgery and cervical cancer, 17.4% and 11.8% for radiation and cervical cancer, 7.5% and 3.8% for surgery and NSCLC, 17.2% and 7.6% for radiation and NSCLC, 5.6% and 0% for surgery and colon cancer, and 5.2% and 0% for surgery and breast cancer, respectively.

Abbreviations: DLBCL, diffuse large B-cell lymphoma; NSCLC, non-small-cell lung cancer.

*Standard treatment modality is defined as the treatment modality (surgery, radiotherapy, or chemotherapy) required as part of a curative treatment approach for local-stage cancer as defined by the National Comprehensive Cancer Network guidelines.¹⁹ In the case of NSCLC and cervical cancer, surgery or radiotherapy may be offered as part of a curative approach for local-stage disease.

†Odds ratios are adjusted for sex, age at diagnosis, race/ethnicity, year of cancer diagnosis, and state.

Table 4. Predictors of Lack of Cancer Treatment Among Participants With HIV Infection

Characteristic	HIV Infected and Not Receiving Cancer Treatment		HIV Infected and Receiving Cancer Treatment		Adjusted Odds Ratio	95% CI*
	No. of Participants	%	No. of Participants	%		
Cancer stage						
Local	150	17.6	703	82.4	1	
Regional	68	12.5	478	87.5	0.65	0.47 to 0.91
Distant	283	28.4	715	71.6	1.40	1.07 to 1.84
Unknown	109	35.5	198	64.5	2.83	2.04 to 3.92
Sex and mode						
Male MSM	247	19.8	1002	80.2	1	
Male heterosexual	49	28.8	121	71.2	1.25	0.84 to 1.84
Male IVDU	103	32.5	214	67.5	1.58	1.16 to 2.15
Male MSM/IVDU	38	22.0	135	78.0	1.06	0.71 to 1.60
Male other	72	28.6	180	71.4	1.30	0.93 to 1.81
Female heterosexual	40	17.6	187	82.4	1.07	0.70 to 1.64
Female IVDU	35	19.4	145	80.6	0.98	0.62 to 1.54
Female other	26	19.1	110	80.9	1.05	0.64 to 1.73
Age at cancer diagnosis, years						
< 45	218	18.7	946	81.3	1	
45-64	348	25.2	1,034	74.8	1.30	1.04 to 1.63
≥ 65	44	27.8	114	72.2	1.35	0.87 to 2.09
Race/ethnicity						
Non-Hispanic white	220	19.7	899	80.3	1	
Non-Hispanic black	288	26.1	817	73.9	1.27	1.01 to 1.60
Hispanic	94	20.8	359	79.2	1.01	0.75 to 1.35
Other	4	36.4	7	63.6	1.70	0.45 to 6.49
Unknown	4	25.0	12	75.0	1.78	0.52 to 6.10
CD4 count						
> Median†	272	27.1	733	72.9	1	
≤ Median	242	20.8	920	79.2	1.50	1.21 to 1.86
Missing	96	17.9	441	82.1	0.89	0.67 to 1.19

NOTE. Results are for all participants with cancer combined.
Abbreviations: IVDU, intravenous drug use; MSM, men who have sex with men.
*Multivariable odds ratios derived from a model that includes all of the variables shown, with additional adjustment for state, diagnosis year, and cancer type.
†Median CD4 count was 144 cells/ μ L.

challenging because of drug interactions between antineoplastics and antiretrovirals, and the potential increase in immunosuppression from chemotherapy or radiation.⁴⁴⁻⁴⁶ In the United Kingdom, a study showing improved cancer outcomes in HIV patients treated at experienced centers has led to the recommendation that patients with HIV and cancer be referred to centers where multidisciplinary care is readily accessible.^{47,48}

For prostate cancer, some patients may elect to defer treatment for an extended period of monitoring (ie, active surveillance), which may contribute to low treatment rates. Observation may be warranted for low-risk prostate cancers (defined as patients with local stage, Gleason score ≤ 6 , and serum prostate-specific antigen ≤ 10), particularly in older patients with limited life expectancy.⁴⁹ However, among untreated participants with prostate cancer in our study, a larger proportion of those with HIV infection were younger than 65 years compared with HIV-uninfected participants (74.6% v 27.5%). Indeed, among HIV-infected participants with prostate cancer who did not receive cancer treatment, only 20.6% had both local-stage disease and were 65 years or older, suggesting that active surveillance does not completely explain the lack of treatment. Also, the disparity in treatment of HIV-infected participants persisted in a sensitivity analysis in which we included hormonal therapy as an option for prostate cancer treatment.

The lack of cancer treatment in HIV-infected participants with local-stage DLBCL, non-small-cell lung cancer, and colon cancer is particularly concerning given the curative potential of treatment for early-stage cancer. Treatment for early-stage cancer can prevent recurrence and prolong disease-free and overall survival rates.⁵⁰⁻⁵² This issue has increased in importance with the improved overall survival rates of HIV-infected people. Indeed, among HIV-infected people with cancer, the rate of death as a result of cancer has declined over time, but those cancer deaths represent a growing fraction of all deaths.⁵³

Among HIV-infected patients with cancer, predictors of a lack of treatment included distant or unknown cancer stage, male sex with intravenous drug use as the mode of HIV exposure, and lower CD4 counts. These associations may reflect the presence of comorbid illnesses, lower performance status, or worse perceived prognosis by clinicians. Intravenous drug use may be associated with nonadherence to prescribed cancer treatment. Older age and non-Hispanic black race are also associated with lack of cancer treatment, a finding previously demonstrated in the general cancer population.^{54,55} HIV-infected patients may also elect to forgo cancer treatment because of a fear of toxicity, inadequate understanding of the benefit of cancer treatment, or the burden of dual management of cancer and HIV.

The strengths of our study include its large size and population-based comparison of HIV-infected and HIV-uninfected participants. The demographic characteristics of the participants in our study mirror the underlying demographics of the HIV-infected population in the United States (ie, young age and large proportions of men, non-Hispanic black individuals, and Hispanics).^{56,57} Our study also has several limitations. First, data regarding performance status and medical comorbidities were not available, and these factors affect candidacy for cancer treatment. The National Comprehensive Cancer Network guidelines used for our analysis of cancer treatment disparities in early-stage cancers suggest using performance status to inform treatment decision-making. Second, we did not have data on socioeconomic status and insurance coverage, which can affect access to or referral for cancer treatment. In addition, cancer registries recorded only the first course of treatment, defined as treatment commenced within 6 months of diagnosis. Treatments initiated more than 6 months after cancer diagnosis were not recorded in Michigan and Connecticut. Furthermore, underascertainment of cancer treatment, particularly for ambulatory services such as chemotherapy and radiotherapy administration, may explain the high rates of nontreatment, although we would not expect a difference in underascertainment by HIV status. Finally, CD4 count and viral loads were not available for all HIV-infected participants, and the majority of those data available were not recorded at the most relevant time point (ie, concurrent with cancer diagnosis).

In conclusion, we found that HIV-infected people with cancer were less likely to be treated than HIV-uninfected people with the

same cancers. This adverse association was present in the most recent calendar years and for a subset of local-stage cancers for which cure is achievable with appropriate treatment. Cancer clinical trials should enroll HIV-infected participants, and cancer management guidelines should incorporate recommendations for HIV-infected patients, particularly as survival rates from HIV improve and cancer becomes an increasingly important cause of mortality in the HIV-infected population.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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GLOSSARY TERMS

population-based study: a study in which the patients are drawn from a defined population in a manner that is representative of the source population studied. Such a design can avoid bias arising from the selective factors that guide affected individuals to a particular medical facility, allowing for greater generalizability of the findings.

sensitivity analyses: analyses that evaluate the impact of missing data and possible differences in interval assessments.

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