AIDS Care: Psychological and Socio-medical Aspects of AIDS/HIV

Trends in cancer diagnoses and survival among persons with AIDS in a high HIV prevalence urban area

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Trends in cancer diagnoses and survival among persons with AIDS in a high HIV prevalence urban area

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Washington, DC (DC), has among the highest AIDS prevalence and cancer incidence in the USA. This study compared cancer diagnoses and survival among AIDS cases with AIDS-defining cancers (ADCs) to those with non-AIDS-defining cancers (NADCs) in DC from 1996 to 2006. Survival by cancer type and time period was also examined for 300 individuals diagnosed with AIDS who developed cancer; 49% of AIDS cases developed an ADC. ADC cases were younger at both AIDS and cancer diagnosis and had significantly lower median CD4 counts at AIDS diagnosis than NADC cases. The most frequent cancers were non-Hodgkin lymphoma (NHL; 44% of ADC), Kaposi's sarcoma (40% of ADC), and lung cancer (20% of NADC). There was no significant difference in distribution of cancers when comparing ADCs to NADCs, or over time (1996–2001 vs. 2002–2006). Survival among NHL, oral cavity, and lung cancer cases was 0.4, 0.8, and 0.3 years, respectively; the risk of death was approximately two times higher for each of these cancers when compared to other cancers. Given the high burden of cancer and HIV in DC, early highly active antiretroviral therapy initiation, routine cancer screening, and risk reduction through behavioral modification should be emphasized to prevent cancer among HIV-infected persons.

Keywords: HIV; AIDS; cancer; survival; mortality

Introduction

Since highly active antiretroviral therapy (HAART) was introduced in the mid-1990s, the natural progression of HIV has been altered with prolonged survival and reduced risk of opportunistic infections. In the USA, HIV-related mortality decreased significantly between the pre- and post-HAART eras (Moore & Chaisson, 1999; Palella et al., 1998, 2006). Consequently, improvements in survival have resulted in more opportunity for HIV-infected persons to develop diseases requiring longer latency periods, including selected cancers (Hessol et al., 2007; Simard & Engels, 2010).

AIDS-defining cancers (ADCs) include Kaposi's sarcoma (KS), non-Hodgkin lymphoma (NHL), and cervical cancer. In the post-HAART era, the incidences of KS and NHL decreased (Centers for Disease Control and Prevention, 1992; Engels, Pfeiffer, et al., 2006), yet the incidences of non-AIDS-defining cancers (NADCs), such as liver, oral, and lung cancers, among HIV-infected individuals remained constant (Shiels et al., 2011) or increased (Bower, Palmieri, & Dhillon, 2006; Engels, Pfeiffer, et al., 2006; Patel et al., 2008; Powles et al.,

2009). Interest in understanding the role of NADCs that are increasingly observed among HIV-infected persons allows researchers to focus on the mechanisms of cancer etiology among this particularly vulnerable population.

The District of Columbia (DC) has one of the highest AIDS case rates in the USA (Centers for Disease Control and Prevention, 2013). The DC Department of Health (DC DOH) began confidential name-based AIDS surveillance in 1985 and code-based HIV surveillance in 2001 (District of Columbia Department of Health, 2006). In 2007, as per Centers for Disease Control and Prevention guidance (Gerberding, 2005), the DC DOH transitioned to an integrated HIV/AIDS surveillance system, including confidential name-based HIV reporting. By December 2012, routinely collected surveillance data revealed DC's HIV prevalence to be approximately 2.5% (District of Columbia Department of Health, 2014). The HIV epidemic in DC is both complex and generalized, affecting blacks, men who have sex with men (MSM), and high-risk heterosexuals in all geographic areas of the city (District of Columbia Department of Health, 2012; Magnus et al., 2009, 2010).

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In addition to a high HIV prevalence, DC also has a high cancer burden, with extremely high cancer mortality. As of 2008, DC had the eighth highest cancer mortality rate in the USA among population-based cancer registries reporting to the North American Association of Cancer Registries (Vargas, Rogers, & Pearson-Fields, 2012). Between 2005 and 2008, NADCs accounted for 4.6–8.3% of deaths among HIV cases in DC (Centers for Disease Control and Prevention, 2008). Disparities in cancer incidence and mortality in DC likely result from inequalities in health-care access (Centers for Disease Control and Prevention, 2008; District of Columbia Department of Health, 2012; Jemal et al., 2009).

Given the high rate of HIV/AIDS, the generalization of the epidemic, and the increased cancer risk in DC, this study sought to assess cancer burden among AIDS cases in DC. As part of the national HIV/AIDS Cancer Match Study (HACM; National Cancer Institute, 2013), this study linked DC's AIDS and cancer registries for cases diagnosed and reported between 1996 and 2006. Through the linkage, we described and compared the demographic and clinical characteristics of AIDS cases with no cancer to those with cancer. Cancers were characterized as ADCs or NADCs. We also compared the distribution of cancers and survival rates among AIDS cases with cancer during the early (1996–2001) vs. late HAART (2002–2006) periods. Previous studies have documented the significant impact of HAART on these indicators since 1996; however, few have focused on the early 2000s, which brought the approval of new antiretroviral (ARV) medications, availability of rapid HIV diagnostic technologies, and expansion of HIV testing and treatment guidelines.

Methods

AIDS cases were identified through routine surveillance data collected between 1985 and 2008 by the DC DOH HIV/AIDS, Hepatitis, STD and TB Administration. Confidential name-based reporting of HIV cases was not mandated until November 2006 in DC; thus, HIV cases were excluded from this analysis. AIDS cases were matched with cancer cases reported to the DC DOH Cancer Registry (DCCR) from 1996 to 2006. Both registries were limited to include only persons diagnosed with AIDS or cancer who were DC residents at the time of their diagnosis. There were 26,578 AIDS cases in the DC HIV/AIDS Reporting System (HARS) database and 33,109 cancer cases in the DCCR during this period.

In accord with HACM methodology, a probabilistic matching algorithm was used to link the two registries by name, social security number, sex, birth/death dates, and race (National Cancer Institute, 2013). Authorized personnel manually reviewed the matches to ensure linkage accuracy. The matched data-set contained 8800 cases diagnosed with AIDS between 1996 and 2006. Non-invasive cancers were excluded from the analysis; basal and squamous cell skin cancers are not collected by the registry. For individuals with more than one cancer, only the first cancer case was included. Subsequent primaries in the same individual were not analyzed. Cases were included if cancer occurred from 4 to 60 months post-AIDS diagnosis, allowing examination of cancer incidence over approximately 5 years for a cohort defined at AIDS onset (Engels, 2008).

Demographic variables included age, sex, race, mode of transmission, insurance status, CD4 counts at AIDS diagnosis, and birthplace. Race was categorized as non-Hispanic white, non-Hispanic black, and Hispanic; individuals of other races were excluded. CD4 count at AIDS diagnosis was based on the most recent CD4 count recorded between 6 months pre- and 3 months post-AIDS diagnosis, in order to capture the CD4 measurement closest to cancer diagnosis.

Chi-square analysis or Wilcoxon rank sum tests were used to compare demographic variables across groups. Demographic variables were also summarized by ADC and most common NADC types. Cancer types were summarized and data were stratified into two time periods: 1996–2001 and 2002–2006. Chi-square analysis was used to compare the effect of HAART availability on the distribution of cancer types. We used 2001 as the cut-off for the early HAART period, as code-based HIV surveillance reporting began in DC during this year (District of Columbia Department of Health, 2006), which likely improved surveillance for both HIV and AIDS cases and enabled earlier disease detection (District of Columbia Department of Health, 2012). In addition during this time period, rapid diagnostic tests that could detect HIV quicker became available resulting in improved diagnosis (US Food and Drug Administration, 2009). Additionally, the ARV treatment medication pipeline expanded significantly with increasing availability of new classes of ARVs and the availability of combination and once-a-day dosing regimens (US Food and Drug Administration, 2009); all of which changed the course of HIV treatment.

Through routine programmatic activities, vital status was ascertained through DCCR linkage with the DC Vital Records' electronic death certificate files (eDCF) and through HARS linkage with the eDCF and the Social Security Administration's Death Master File. Survival time was calculated from time of cancer diagnosis to death from all causes or the end of calendar year 2006. Median survival time and 24-month and 5-year survival were summarized. Kaplan–Meier methods and the log-rank test were used to conduct unadjusted survival analyses comparing survival between ADC and NADC cases and between early and later HAART

periods within the major cancer types and overall. We compared risk of death by cancer types using unadjusted and adjusted Cox proportional hazards regression models, with the other cancer group serving as the reference group. Adjusted models included sex, race/ethnicity, health insurance status, mode of transmission, CD4 category, early vs. later HAART era, cancer type (ADC vs. NADC), age at cancer diagnosis, and age at AIDS diagnosis. SAS version 9.2 was used for all analyses. All reported *p*-values were two-sided with a cut-off of $p \leq 0.05$.

Results

Description of people with AIDS, with and without cancer

Between 1996 and 2006, 8800 DC residents were diagnosed with AIDS; 8500 had no cancer diagnosis during the study time period (Table 1). Among the AIDS cases without cancer, 71% were male, 86% were black, and 70% were diagnosed with AIDS between 30 and 49 years of age (median age = 40 years). HIV was most commonly transmitted via MSM (32%), injection drug use (IDU; 26%), and heterosexual contact (23%). The CD4 count at AIDS diagnosis was <200 cells/ µL in 73% of AIDS cases without cancer (median CD4 count = 114 cells/µL). The only statistically significant difference between AIDS cases with cancer and those without was that AIDS-only cases were significantly younger at AIDS diagnosis (AIDS-only median age at AIDS diagnosis = 40.2 years vs. AIDS with cancer = 41.8 years; $p = 0.015$).

ADCs vs. NADC cases

After matching the DCCR to HARS, 300 individuals (3.4%) with AIDS were identified as having cancer. There were approximately as many ADCs ($n = 146$) as

Table 1. Demographic characteristics of AIDS cases with and without cancer, Washington, DC, 1996–2006.

Categorical variables	AIDS without cancer ($n = 8500$) Median	All cancers ($n = 300$) Median	ADC ($n = 146$) Median	NADCs ($n = 154$) Median	Cancer vs. no cancer *p*-value[a]	ADC vs. NADC *p*-value[b]
Median age at AIDS diagnosis (in years)	40.2	41.8	37.8	46.2	0.0025	<0.0001
Median age at cancer diagnosis (in years)	–	45.0	40.0	50.0	–	<0.0001
Median years from AIDS diagnosis to cancer diagnosis	–	2.17	1.75	2.46	–	0.01
Median CD4 at AIDS diagnosis (cells/µL)	114	102	86	130	0.78	0.025
	N (%)	*N* (%)	*N* (%)	*N* (%)		
Sex						
Male	5998 (70.6)	223 (74.3)	106 (72.6)	117 (76.0)	0.16	0.50
Female	2502 (29.4)	77 (25.7)	40 (27.4)	37 (24)		
Race/ethnicity						
Non-Hispanic white	855 (10.1)	33 (11.0)	18 (12.3)	15 (9.7)	0.32	0.54
Non-Hispanic black	7270 (85.5)	259 (86.3)	123 (84.2)	136 (88.3)		
Hispanic	375 (4.4)	8 (2.7)	5 (3.4)	3 (1.9)		
Mode of transmission						
MSM	2681 (31.5)	114 (38.0)	61 (41.8)	53 (34.4)	0.20	0.51
IDU	2198 (25.9)	77 (25.7)	33 (22.6)	44 (28.6)		
MSM/IDU	316 (3.7)	11 (3.7)	6 (4.1)	5 (3.2)		
Heterosexual	1975 (23.2)	56 (18.7)	26 (17.8)	30 (19.5)		
NIR[c]	1235 (14.5)	40 (13.3)	20 (13.7)	20 (13.0)		
Other[d]	95 (1.1)	2 (0.07)	0 (0.0)	2 (1.3)		
Insurance status						
Private	2302 (27.1)	94 (31.3)	46 (31.5)	48 (31.2)	0.19	0.93
Public	4097 (48.2)	131 (43.7)	67 (45.8)	64 (41.6)		
None	976 (11.5)	37 (12.3)	18 (12.3)	19 (12.3)		
Missing/unknown	1125 (13.2)	38 (12.7)	15 (10.3)	23 (14.9)		
Place of birth						
USA	8102 (95.3)	288 (96.0)	138 (94.5)	150 (97.4)	0.82	0.17
Non-USA	303 (3.6)	10 (3.3)	7 (4.8)	3 (1.9)		

[a]Tests comparing all cancers to AIDS noncancer population; [b]Tests comparing ADC to NADC population; [c]NIR, no identified risk; [d]Includes hemophilia, blood transfusion, perinatal exposure missing/unknown values that were not included in statistical comparisons.

NADCs (n = 154). As shown in Table 1, differences in age at AIDS and cancer diagnosis between the ADC and NADC groups were statistically significantly different. NADC cases were older at AIDS (46.2 vs. 37.8; $p <$ 0.0001) and cancer (50.0 vs. 40.0; $p <$ 0.0001) diagnosis than ADC cases. NADCs also had a significantly longer median time from AIDS to cancer diagnosis (2.5 years vs. 1.8 years; p = 0.01) and a significantly higher median CD4 count at AIDS diagnosis (130 vs. 86 cells/µL; p = 0.025) vs. ADC cases.

Cancer types

Table 2 shows the distribution of ADCs and NADCs comparing early and later HAART eras. Although not statistically significant, ADCs accounted for a slightly higher percentage of all cancer cases in the late vs. early HAART period (56% vs. 45%; p = 0.11). ADC cases were mostly KS (40%) and NHL (44%). The most common NADCs were lung cancer (20%), HL (8%), anal cancer (8%), and prostate cancer (7%). There were no significant changes in the distribution of ADCs or NADCs over time. However, while the proportion of lung and other cancers decreased, the proportion of anal and oral cancers approximately doubled among NADCs from the early to late post-HAART eras.

Table 3 displays the demographic characteristics of ADC cases and the most common NADC cases. KS cases were youngest at AIDS diagnosis while lung cancer cases were oldest (median 33.8 years vs. 48.5

years). A similar pattern was true for median age at cancer diagnosis. The median time from AIDS to cancer diagnosis was longest for anal cancer cases (3.3 years). Median CD4 count at AIDS diagnosis was lowest among KS cases (67 cells/µL) and highest among anal cancer cases (188 cells/µL). KS occurred in a notably higher proportion of male cases (93%), compared to the other cancers. Mode of transmission was predominantly MSM among anal cancer cases (85%), compared to NHL (41%) and lung cancer (13%).

Survival after cancer diagnosis

Table 4 presents survival after cancer diagnosis. NHL, lung, and oral cavity cancers had the shortest median survival times (<1 year), while KS, cervical cancer, HL, and breast cancer had the longest (4.6, 5.2, 5.6, and 7.7 years, respectively). Twenty-four-month survival was highest among prostate (88.9%), breast (85.7%), cervical (80.1%), and anal (76.2%) cancer cases. Five-year survival was highest among prostate (66.7%), colorectal (65.3%), and cervical (64.1%) cancer cases and lowest among those with oral cavity cancers with no one surviving at 5 years. There was no statistical difference in survival time following cancer diagnosis in ADCs vs. NADCs (log-rank test p-value = 0.85; Figure 1). Cox proportional hazards regression models indicated that ADC cases experienced a similar risk of death after controlling for previously mentioned covariates (HR = 1.10; 95% CI: 00.76, 1.60).

Table 2. Type of cancer by period of diagnosis.

Cancer type	Total (N = 300) N (%)	Year of diagnosis[a]		p-value[b]
		"Early HAART" 1996–2001 (N = 220) N (%)	"Later HAART" 2002–2006 (N = 80) N (%)	
ADCs	146 (49)	101 (46)	45 (56)	0.78
KS	59 (40)	39 (39)	20 (44)	
NHL	64 (44)	46 (46)	18 (40)	
Cervical	23 (16)	16 (16)	7 (16)	
NADCs	154 (51)	119 (54)	35 (44)	0.084
Anal	13 (8)	8 (7)	5 (14)	
Breast	7 (5)	4 (3)	3 (9)	
Colorectal	16 (6)	15 (13)	1 (2)	
HL	13 (8)	7 (6)	6 (17)	
Lung	30 (20)	25 (21)	5 (14)	
Oral cavity	9 (6)	6 (5)	3 (9)	
Prostate	11 (7)	8 (7)	3 (9)	
Other[c]	55 (22)	46 (39)	9 (26)	

[a]Total percentages may be greater than 100 due to rounding; [b]χ^2 tests comparing cancers in early to later HAART era; [c]Other cancers: Unspecified (12); Larynx (7); Kidney (7); Bone and soft tissue (5); Female genital (4); Esophagus (3); Liver (3); Pancreas (3); Male genital (3); Bladder (2); Brain (2); Melanoma (2); Gallbladder (1); Thyroid (1).

Table 3. Demographic characteristics of ADC cases and most common NADC cases by cancer type.

	ADCs			NADCs		
	KS (*N* = 59)	NHL (*N* = 64)	Cervical (*N* = 23)	Anal (*N* = 13)	HL (*N* = 13)	Lung (*N* = 30)
Continuous variables	Median	Median	Median	Median	Median	Median
Age at AIDS diagnosis	33.8	41.5	39.6	43.4	43.1	48.5
Age at cancer diagnosis	36.0	44.5	41.0	48.0	45.0	51.5
Years from AIDS diagnosis to cancer diagnosis	1.2	2.2	2.5	3.3	1.2	2.4
CD4 at AIDS diagnosis (cells/μL)	67	100	91	188	133	95
Categorical variables	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)
Sex						
Male	55 (93.2)	55 (70.7)	0 (0)	13 (100)	117 (76.0)	20 (66.7)
Female	4 (6.8)	13 (20.3)	23 (100)	0 (0)	37 (24.0)	10 (33.3)
Race/ethnicity						
Non-Hispanic white	9 (15.3)	9 (14.1)	0 (0)	5 (38.5)	2 (15.4)	1 (3.3)
Non-Hispanic black	48 (81.4)	53 (82.8)	22 (95.7)	7 (53.9)	11 (84.6)	29 (96.7)
Hispanic	2 (3.3)	2 (3.1)	1 (4.3)	1 (7.7)	0 (0)	0 (0)
Mode of transmission						
MSM	35 (59.3)	26 (40.6)	0 (0)	11 (84.6)	8 (61.5)	4 (13.3)
IDU	5 (8.5)	15 (23.4)	13 (56.5)	0 (0)	2 (15.4)	15 (50.0)
MSM/IDU	4 (6.8)	2 (3.1)	0 (0)	1 (7.7)	0 (0)	1 (3.3)
Heterosexual	11 (18.6)	8 (12.5)	7 (30.4)	1 (7.7)	1 (7.7)	5 (13.7)
NIR[a]	4 (6.8)	13 (20.3)	3 (13.0)	0 (0)	2 (15.4)	4 (13.3)
Other[b]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.3)

[a]NIR, no identified risk for infection; [b]Includes hemophilia, blood transfusion, and perinatal exposure.

Table 4. Median and 24-month survival after cancer diagnosis by cancer type.

Cancer type	Died *N* (%)	Median survival time (in years)	24-month survival (standard error)	5-year survival (standard error)	Unadjusted HR (95% CI)	Adjusted HR[a] (95% CI)
KS (*n* = 59)	27 (46)	4.6	57.8 (6.8)	48.4 (7.2)	0.70 (0.42, 1.12)	0.70 (0.34, 1.41)
NHL (*n* = 64)	47 (73)	0.4	34.0 (6.2)	17.1 (6.1)	**1.58 (1.01, 2.48)**	**2.05 (1.11, 3.79)**
Cervical (*n* = 23)	5 (22)	5.2	80.1 (9.0)	64.1 (16.0)	**0.27 (0.11, 0.70)**	**0.23 (0.06, 0.83)**
Anal (*n* = 23)	3 (39)	3.1	76.2 (14.8)	19.1 (16.9)	0.56 (0.22, 1.44)	1.10 (0.39, 3.12)
Breast (*n* = 7)	2 (29)	7.7	58.7 (13.2)	42.8 (31.0)	0.34 (0.08, 1.43)	0.35 (0.08, 1.64)
Colorectal (*n* = 16)	4 (25)	3.1	73.4 (11.6)	65.3 (12.9)	**0.37 (0.14, 0.94)**	**0.48 (0.05, 0.65)**
HL (*n* = 13)	9 (73)	5.6	67.7 (13.4)	45.1 (20.5)	0.60 (0.24, 1.55)	0.60 (0.17, 2.17)
Lung (*n* = 30)	26 (87)	0.3	14.4 (6.6)	10.8 (5.9)	**2.19 (1.30, 3.67)**	**2.48 (1.20, 5.16)**
Oral cavity (*n* = 9)	7 (78)	0.8	16.9 (41.4)	0	1.69 (0.74, 3.83)	2.23 (0.73, 6.76)
Prostate (*n* = 11)	2 (18)	2.9	88.9 (10.5)	66.7 (20.8)	**0.22 (0.05, 0.93)**	0.24 (0.05, 1.05)
Other (*n* = 55)	33 (60)	1.6	47.0 (6.8)	40.3 (7.1)	1.00	1.00

[a]Adjusted for age at AIDS diagnosis, age at cancer diagnosis, sex, race/ethnicity, HAART period (early vs. late), mode of transmission, CD4 count at AIDS diagnosis, health insurance, and cancer group (ADC vs. NADC). Statistically significant hazard ratios are bolded.

In the adjusted model, NHL and lung cases were significantly more likely to die compared to other cancers (NHL HR: 2.05; lung HR 2.48). After adjusting for covariates, the risk of death for cervical cancer remained significantly lower (adjusted HR = 0.23; 95% CI: 0.06, 0.83). There were no significant differences in overall survival or by individual cancer type when comparing early and later HAART eras (adjusted HR = 1.30; 95% CI: 0.75, 2.26) and survival at 24 months or 5 years (data not shown).

Discussion

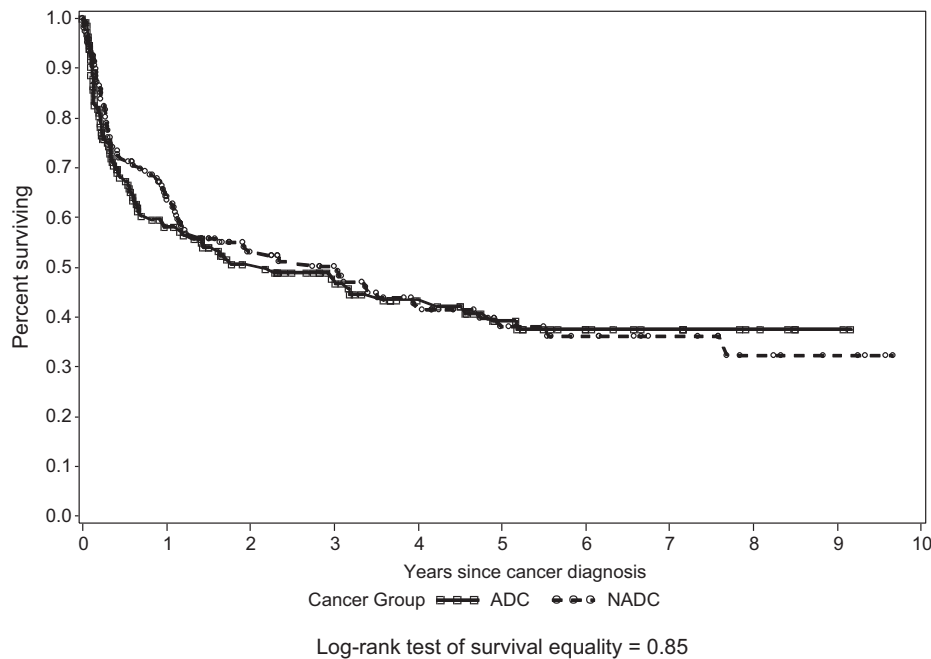Despite high HIV/AIDS prevalence and cancer incidence in DC, a relatively low proportion of AIDS patients

Figure 1. Year of survival time from cancer diagnosis to death, 1996–2006, District of Columbia (*n* = 300).

(3.4%) develop cancer, 49% of whom develop an ADC. Regardless of cancer status, most AIDS cases in our sample were male, non-Hispanic black, and infected through MSM or IDU. These demographics, including the overall older age distribution, are consistent with the demographics of DC's HIV-infected population (District of Columbia Department of Health, 2012) and those of the national HACM cohort (Shiels et al., 2011). AIDS cases with cancer were demographically similar to those without, except that AIDS-only cases were significantly younger at AIDS diagnosis. Further, the demographic distributions of patients with HL, anal, and lung cancer are consistent with those previously documented (Hessol et al., 2007).

The relatively even distribution of NADCs and ADCs observed highlights the changing distribution of cancer among AIDS cases. Previous studies have found higher distributions of ADCs ranging from 70% to 90% (Hessol et al., 2007; Spagnuolo et al., 2012). More recent cohort studies have documented higher proportions of NADCs, likely due to prolonged survival (Hessol et al., 2007; Shiels et al., 2011). The younger median age among ADCs vs. NADCs is also consistent with previously published studies (Spagnuolo et al., 2012) and is likely explained by the increased risk of many cancers that comes with advancing age, regardless of HIV status (Long, Engels, Moore, & Gebo, 2008). Further, the significantly lower CD4 count at AIDS diagnosis observed among ADCs vs. NADCs is perhaps related to the finding that degree of immunosuppression is associated with risk of developing an ADC (Barbaro

& Barbarini, 2007; Biggar, Chaturvedi, Goedert, & Engels, & HIV/AIDS Cancer Match Study, 2007; Clifford et al., 2005; Patel et al., 2008).

Among AIDS cases in DC, the most commonly observed cancers were KS and NHL. This indicates that, despite HAART's impact and the decreased incidences of these cancers, these ADCs persist as AIDS-defining illnesses (Engels et al., 2008; Long et al., 2008; Spano et al., 2008). Consistent with previous studies, this cohort's most commonly diagnosed NADCs included lung cancer, HL, anal cancer, and prostate cancer, as these cancers are considered less associated with the degree of HIV immunosuppression than ADCs (Frisch, Biggar, Engels, Goedert, & AIDS-Cancer Match Registry Study Group, 2001). Diagnoses of lung cancer may be related to tobacco use; up to 85% of HIV-infected persons in the USA report ever smoking (Clifford et al., 2012; Giordano & Kramer, 2005; Tesoriero, Gieryic, Carrascal, & Lavigne, 2010), although HIV likely amplifies tobacco's effects on carcinogenesis (Chaturvedi et al., 2007; Engels, 2008; Engels, Brock, et al., 2006; Kirk et al., 2007; Shebl, Engels, Goedert, & Chaturvedi, 2010). With diagnoses doubling over the time periods analyzed, HL became one of the five most common NADCs among DC AIDS cases, echoing a trend documented in the greater US population (Biggar et al., 2006; Cinti, Gandhi, & Riddell, 2008). The increasing frequency of prostate cancer observed in this study may relate to its general prevalence, the predominance of black men in this cohort, and the aging cohort of HIV cases (Shiels, Goedert, Moore, Platz, & Engels,

2010). Finally, the increased proportion of anal cancers in the late vs. early post-HAART eras may be related to prolonged survival among AIDS cases, which allows time for progression of anal lesions to cancer (Simard, Pfeiffer, & Engels, 2010).

The proportion of cervical cancer cases observed in this study (16%) is higher than in other HACM sites (Shiels et al., 2011) and may be explained by the historically high cervical cancer incidence rates in DC and the increasing proportion of HIV-infected women over time. Between 2006 and 2010, the cervical cancer incidence rate in DC was 9.3 cases per 100,000, which is comparable to rates in demographically similar urban areas. The rate was 7.4 cases in Fulton County, which includes Atlanta, 9.7 cases in Wayne County, which includes Detroit, and 10.0 cases in Baltimore City (National Cancer Institute, 2009). Cervical cancer incidence rates in both DC and the USA have declined in recent years, and a similar trend may be observed among HIV-infected women in the future (Centers for Disease Control and Prevention, 2010; National Cancer Institute, 2009). Preliminary studies of the HPV vaccine in HIV-infected persons show safety and immunogenicity among men and women (Kahn et al., 2013; Wilkin et al., 2010), and vaccination, which is currently recommended for certain populations of HIV-infected persons, may assist in cancer prevention (US Department of Health and Human Services, 2009).

There were no significant changes in the distribution of ADCs and NADCs between early and later HAART eras, despite a decrease in the overall number of cancers, the increasing availability of HAART, and improved diagnostic tests. Furthermore, consistent with previous studies (Long et al., 2008), our analysis identified no significant differences in survival among cancer cases over time. Other studies examining the impact of HAART availability on survival concluded that improvements in survival were variable with respect to cancer type (Fordyce, Singh, Nash, Gallagher, & Forlenza, 2002; Hessol et al., 2007; Spagnuolo et al., 2012). Studies conducted in San Francisco (Hessol et al., 2007) and New York (Fordyce et al., 2002) examined the impact of HAART on cancer survival among adults living with AIDS. Both found that the impact on survival was not uniform over time, though the study in New York observed substantially fewer improvements among persons with ADCs. In contrast, a study in Italy (Spagnuolo et al., 2012) found that, although survival for ADCs (NHL and KS) improved, overall there was similar survival among ADCs and NADCs in the pre- and post-HAART eras.

Although differences in survival were not observed over time in this study, survival by cancer type showed that lung, oral cavity, and NHL had the poorest prognoses, with median survival of less than a year.

The poorer survival rate among NHL cases contrasts to those in the literature, which show improved survival for HIV cases on HAART (Diamond, Taylor, Im, Miradi, & Anton-Culver, 2006; Fordyce et al., 2002; Hessol et al., 2007; Robotin et al., 2004). Given these suboptimal survival rates, DC HIV providers should collaborate with oncologists to treat NHL early and aggressively and improve oral cancer screening efforts.

Our study has several noteworthy limitations. First, DC transitioned from code- to name-based confidential HIV surveillance in 2006. Thus, data on HIV-only cases were unavailable at the time of the linkage. Given this limitation, we used the most complete and recent data available at the time of this analysis. Based on more recent surveillance reports published by the DC DOH, it appears as though our findings remain relevant with opportunistic illnesses, ADCs, and NADCs contributing to as many as 50% of deaths among HIV cases in DC between 2008 and 2012 (District of Columbia Department of Health, 2014). Future linkages to include HIV-only cases are already under way and will increase the linkage's completeness and provide further data to understand HIV progression as it relates to cancer development. Additionally, since the data were limited to follow up through 2006, this additional linkage will help to obtain a more complete picture of the development of cancer among persons with HIV or AIDS in Washington, DC. Second, although both registries collected useful demographic and HIV risk factor data, neither routinely collects information about cancer risk, such as access to care and screenings, and exposure to viral infections. Information on smoking exposure was not included in this data-set, as more than 35% of it was missing from the DCCR when the linkage was conducted. Furthermore, at the time of the linkage, the HARS registry was not routinely collecting data on ARV use. Last, survival analysis was based on death from all causes, rather than on deaths from a specific cancer and/or AIDS, thereby increasing the number of deaths observed. However, this bias is nondifferential and equally affects both groups. Despite these limitations, this analysis adds to the scientific literature by describing the epidemiologic characteristics of an urban area in which the drivers of the HIV epidemic are mixed, with both MSM and heterosexual sexual contact as leading modes of transmission, and in an area where disparate health outcomes exist with respect to HIV prevalence, cancer incidence, and mortality.

This study is the first of its kind in DC, where HIV/AIDS and cancer burdens rank among the highest in the USA. Going forward, documentation of behavioral and viral risk factors in addition to use of HAART and receipt of cancer-screening services will enhance our understanding and interpretation of these trends. In the interim, this study's findings support emphasizing early,

aggressive cancer screening, including: pap smears for cervical cancer; routine anal cancer screening, including oral examinations; behavioral modifications; vaccination against preventable infections; and early HAART initiation to prevent cancer among HIV cases.

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Disclosure statement

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