Age at Cancer Diagnosis Among Persons With AIDS in the United States

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Background: Studies have reported young ages at cancer diagnosis in HIV-infected persons and have suggested that HIV accelerates carcinogenesis. However, these comparisons did not account for differences in population age structures.

Objective: To compare ages at diagnosis for non–AIDS-defining types of cancer that occur in both the AIDS and general populations, after adjustment for differences in age and other demographic characteristics between these populations.

Design: Registry linkage study.

Setting: 15 HIV/AIDS and cancer registry databases in the United States.

Participants: 212 055 persons with AIDS enrolled in the U.S. HIV/AIDS Cancer Match Study from 1996 to 2007.

Measurements: Comparison of age-at-diagnosis distributions for various types of cancer in both the AIDS and general populations, after adjustment for age and other demographic characteristics.

Results: The proportion of person-time contributed by older persons (age ≥65 years) was far smaller in the AIDS population (1.5%) than in the general population (12.5%). Reflecting this difference, the ages at diagnosis for most types of cancer were approximately 20 years younger among persons with AIDS. However, after adjustment for differences in the populations at risk, the median ages at diagnosis in the AIDS and general populations did not differ for most types of cancer (for example, colon, prostate, or breast cancer; all $P > 0.100$). In contrast, ages at diagnosis of lung (median, 50 vs. 54 years) and anal cancer (median, 42 vs. 45 years) were significantly younger in persons with AIDS than expected in the general population ($P < 0.001$), and the age at diagnosis of Hodgkin lymphoma was significantly older (median, 42 vs. 40 years; $P < 0.001$).

Limitations: Information on other cancer risk factors, including cigarette smoking, was not available. Analysis was restricted to non-Hispanic white and black persons who had AIDS, which could limit the generalizability of the findings to other racial and ethnic groups or to persons with HIV but not AIDS.

Conclusion: For most types of cancer, the age at diagnosis is similar in the AIDS and general populations, after adjustment for the ages of the populations at risk. Modest age differences remained for a few types of cancer, which may indicate either acceleration of carcinogenesis by HIV or earlier exposure to cancer risk factors.

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Infection with HIV increases the risk for certain types of cancer. The risk for Kaposi sarcoma, non-Hodgkin lymphoma, and cervical cancer is so high among HIV-infected persons that these types of cancer are included in the Centers for Disease Control and Prevention's definition of AIDS (advanced HIV infection) (1). In addition, HIV-infected persons have an elevated risk for certain non–AIDS-defining types of cancer (2–6), which is largely attributable to loss of control of oncogenic infections due to HIV-related immune suppression (7, 8) and a high prevalence of exposure to other carcinogens (such as tobacco or alcohol) (2, 9). Use of highly active antiretroviral therapy (HAART) has dramatically improved survival among HIV-infected persons and decreased the incidence of AIDS (10–12). However, the burden of cancer, particularly non–AIDS-defining cancers, is likely to increase as HIV-infected persons live longer.

This elevated cancer incidence and the increased risk for other conditions that typically occur at older ages (such as cardiovascular and bone disease, cognitive impairment, or general frailty) suggest that HIV-infected persons are vulnerable to a syndrome of premature aging (13, 14). For cancer, premature aging would manifest not only as an overall elevated cancer risk but also as a downward shift in the distribution of ages at cancer diagnosis. In support of this possibility, studies of lung (15–17), liver (18, 19), anal (20), and colorectal cancer (21) have noted ages at diagnosis that are 10 to 20 years younger among persons with HIV compared with the general population.

Before concluding that HIV-infected persons generally develop cancer at younger ages, it is important to consider the differences in age distribution between the underlying HIV and general populations. Of note, because of the young age at HIV acquisition in the United States and other western countries and the shorter life expectancy of persons with HIV, the proportion of persons with HIV who are older is far smaller than in the general population. For example, in the United States in 2007,

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only 3% of HIV-infected persons were aged 65 years or older, compared with 13% of the general population (22, 23). Because overall cancer incidence is 10 times higher in persons aged 65 years or older than in persons younger than 65 years (24), the truncated age distribution among persons with HIV precludes observation of most instances of cancer that would occur at older ages, which could explain the dramatic age differences reported in previous studies.

Using data from the U.S. HIV/AIDS Cancer Match Study, we evaluated the ages at diagnosis of 26 non–AIDS-defining types of cancer in both the AIDS and general populations, after adjustment for differences in population age structure. These analyses help clarify the potential effects of HIV infection on cancer development.

Context

It has been suggested that persons with HIV infection develop non–AIDS-related types of cancer at earlier ages than the general population, and that this may be due to HIV-induced accelerated aging. However, the proportion of persons with HIV who are older is far smaller than that of the general population.

Contribution

Using data from the U.S. HIV/AIDS Cancer Match Study, the investigators evaluated the ages at diagnosis of several types of non–AIDS-defining cancer in the HIV and general populations. After adjustment for differences in the age composition of the populations at risk, the age at cancer diagnosis did not differ between HIV-infected persons and those in the general population for most types of cancer, including prostate, colon, and breast cancer.

Implication

These results do not support an acceleration of carcinogenesis by HIV. On the basis of this study, current cancer screening guidelines for the general population can be applied to HIV-infected persons for most types of cancer.

—The Editors

METHODS

Study Design

The HIV/AIDS Cancer Match Study links 15 U.S. population–based HIV/AIDS and cancer registries in Colorado; Connecticut; Florida; Illinois; Georgia; Massachusetts; Michigan; New Jersey; Texas; Los Angeles, San Diego, and San Francisco, California; New York, New York; Seattle, Washington; and Washington, DC (25). Registry areas were selected to include a large HIV-infected population. This analysis focused on persons who contributed follow-up information during the HAART era (1996 to 2007) for the period from 4 to 60 months after AIDS diagnosis. We restricted our study to non-Hispanic white and black persons because data on Hispanic ethnicity were not consistently available for all years from all of the cancer registries.

Reporting of cases of invasive cancer to each cancer registry is mandated by law. Cases of cancer were categorized according to a modified version of the Surveillance, Epidemiology, and End Results (SEER) program "Site recode with KS and mesothelioma" (26). The cancer registries used SEER summary stage algorithms to code cancer stage. We restricted our analysis to non–AIDS-defining types of cancer that occurred in 10 or more persons with AIDS.

The institutional review boards at each participating registry approved the study.

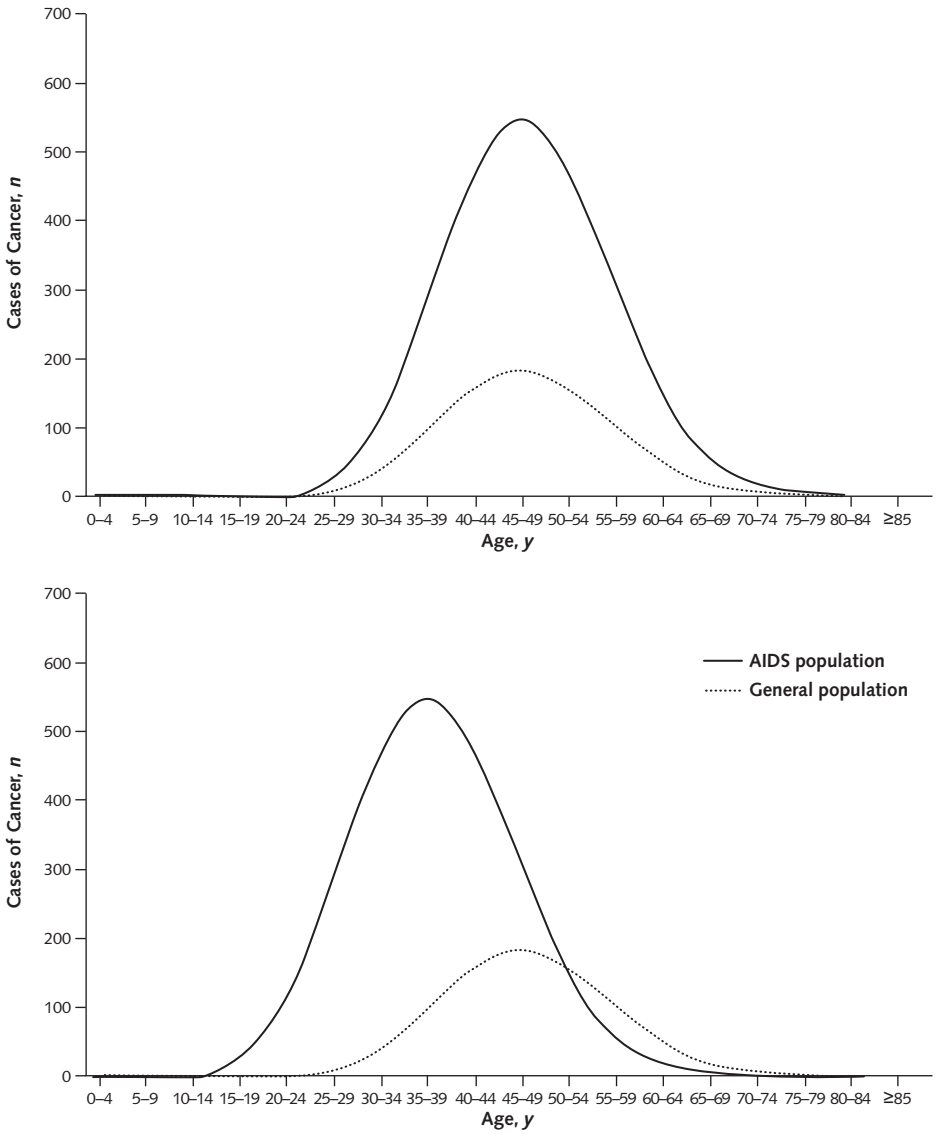
Statistical Analysis

For each type of cancer, we determined the age-at-diagnosis distributions for persons with AIDS and those in the general population on the basis of cancer registry data. However, these age distributions are strongly dependent on the age structure of the underlying populations, and differences in these structures can lead to bias. Therefore, we also considered the ages at cancer diagnosis for cases that would be expected to occur in the general population if it had the same demographic structure as the AIDS population. Specifically, we estimated the expected cases of cancer in the general population by applying the observed cancer incidence rates in the general population to the accumulated person-time among persons with AIDS, stratified by single years of attained age, sex, race, calendar year, and registry (that is, indirect standardization). Thus, the expected cases are cases in the general population after adjustment for population characteristics; these results address the question of what the age-at-diagnosis distribution of cancer would be in the general population if the general population were demographically similar to the AIDS population.

If risk for cancer is increased among persons with AIDS relative to the general population, we envision 2 scenarios (**Figure 1**). First, if HIV merely increases the risk for that cancer, the age-at-diagnosis curve for the AIDS population would be expected to have the same shape as that for the expected cases in the general population (including the same median age), except that the curve for the AIDS cases would enclose a larger area (**Figure 1**, *top*). In contrast, if HIV accelerates the development of that cancer, then the age-at-diagnosis curve for the AIDS population would be shifted to the left, and the median age would be lower than for the expected cases in the general population (**Figure 1**, *bottom*).

To test whether the ages at cancer diagnosis observed in persons with AIDS differed from those expected in the general population, we assumed that the rates applied to estimate expected cases of cancer in the general population were known without error. We therefore multiplied expected case counts by 10 000 and then created a data set with 1 record per observed case in persons with AIDS and

Figure 1. **Hypothetical age-at-diagnosis distributions of cancer in the AIDS and general populations.**



In addition to illustrating differences in age at onset, these curves provide information on relative risk for cancer in persons with AIDS, because the ratio of the areas that they enclose is the standardized incidence ratio (observed cases of cancer to expected cases of cancer). **Top.** Distribution if the risk for cancer is increased in the AIDS population, but the age distribution is the same. **Bottom.** Distribution if the risk for cancer is increased in the AIDS population and the age distribution is younger.

expected case in the general population. We tested for differences in median age by using the Brown–Mood test (27) for each type of cancer. A Bonferroni correction was applied to account for multiple comparisons. A *P* value less than 0.0019 (0.05 divided by 26 cases of cancer) was considered statistically significant.

To further evaluate the age-at-diagnosis distributions of non–AIDS-defining cancers in the AIDS and general populations, we estimated standardized incidence ratios (SIRs), which measure risk in persons with AIDS relative to the general population. The SIRs were calculated as the number of observed cases in the AIDS population divided by the number of expected cases in the general population, if the general population were demographically similar to the AIDS population. For selected types of cancer, we estimated the SIRs overall and in age groups 0 to 29 years, 30 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, and 70 years or older. Exact 2-sided CIs of the SIRs were calculated, and SIR trends were evaluated by using Poisson regression. If age acceleration is present, relatively more cases of cancer would occur at young ages, which would manifest as higher SIRs at younger than older ages (**Figure 1**). Finally, for selected cases of carcinoma, we calculated SIRs by cancer stage.

Role of the Funding Source

Our study was funded by the Intramural Research Program of the National Cancer Institute. The funding source reviewed and approved final submission but did not have a role in design and conduct of the study; collection, management, analysis, and interpretation of the data; or preparation of the manuscript.

RESULTS

Study Participants

Our analysis included 212 055 persons with AIDS who were followed for cancer during the HAART era in the United States. The study sample was predominately male (76.1%) and included a larger proportion of black (57.7%) than white persons (42.3%). The median age at AIDS diagnosis was 38 years. From 1996 to 2007, 2540 cases of non–AIDS-defining cancer occurred during 591 378 person-years of follow-up after the onset of AIDS. The most common types of cancer were lung cancer (605 cases [24%]), anal cancer (282 cases [11%]), and Hodgkin lymphoma (226 cases [9%]).

Figure 2 presents the age distributions in the AIDS and general populations of the included registry areas. Although the median age of persons at risk for cancer was slightly higher in the AIDS population (40 years vs. 35 years in the general population), the age distribution was much wider in the general population. In particular, the proportion of total person-years contributed by persons aged 65 or older, who are at the greatest risk for cancer, was much smaller among persons with AIDS than in the general population (1.5% vs. 12.5%).

Age at Cancer Diagnosis

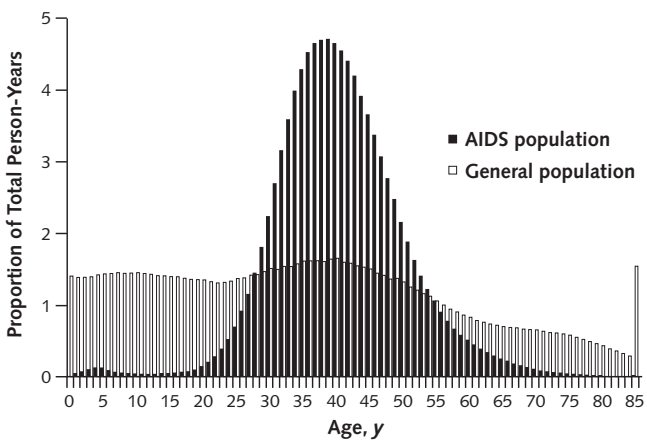
For most types of cancer, the median observed ages at diagnosis were approximately 20 years younger among persons with AIDS than in the general population (**Table 1**), which reflects the difference in age structure between the AIDS and general populations. However, after we adjusted for the underlying population structures, we found either no difference or very small differences between the observed ages at cancer diagnosis in the AIDS population and the expected ages at diagnosis in the general population. For example, the median observed age at diagnosis of colon cancer in persons with AIDS was 52 years, compared with 72 years in the general population. However, the median observed age in the AIDS population and the median expected age in the general population were identical (52 years; $P = 0.53$).

Ages at diagnosis among persons with AIDS were younger than expected in the general population for anal cancer (median, 42 vs. 45 years; $P < 0.001$) and lung cancer (median, 50 vs. 54 years; $P < 0.001$) (**Table 1**). In contrast, the ages at diagnosis of observed Hodgkin lymphoma cases were significantly higher in persons with AIDS than expected cases in the general population (median, 42 vs. 40 years; $P < 0.001$).

Figure 3 illustrates age-at-diagnosis distributions for anal cancer, lung cancer, Hodgkin lymphoma, and liver cancer, which are common among persons with AIDS, and prostate, breast, and colon cancer, which are common in the general population. For prostate, colon, and breast cancer, the age-at-diagnosis curves for observed cases in the general population are shifted toward much older ages than for the AIDS population, which indicates greater frequency at older ages; however, after adjustment, the age-at-diagnosis distributions for expected cases in the general population are similar to those for observed cases in the AIDS population. Of note, the areas under the curve for these types of cancer are smaller for persons with AIDS than for expected cases in the general population, which reflects a reduced risk for prostate, breast, and colon cancer in the AIDS population. Although the reason for this reduced risk is unclear, it has been seen previously and may reflect a protective effect of HIV infection or differences in cancer screening (5, 6, 28). For liver cancer, the age-at-diagnosis curve is similar for observed cases in persons with AIDS and expected cases in the general population, but the larger area under the curve for persons with AIDS reflects their elevated overall risk for liver cancer.

For anal cancer, lung cancer, and Hodgkin lymphoma (**Figure**), persons with AIDS have a higher risk than the general population, which corresponds to the greater areas under the age-at-diagnosis curves for the AIDS population than for expected cases in the general population. After adjustment, the expected age-at-diagnosis curves for anal and lung cancer in the general population are shifted downward from the observed curves in the general population but remain shifted toward slightly older ages than those for the AIDS population. In contrast, for Hodgkin lymphoma, the age-at-diagnosis curves show that observed

Figure 2. **Age distribution in the AIDS and general populations.**



Follow-up time at risk for cancer in both the AIDS and general populations, by age, for regions covered by the HIV/AIDS Cancer Match Study (1996 to 2007).

cases in the AIDS population occur at older ages than expected in the general population. Of note, Hodgkin lymphoma has a bimodal age-at-diagnosis distribution in the general population; however, the age-at-diagnosis distributions for observed cases in the AIDS population and expected cases in the general population are unimodal.

SIRs for Cancer

Table 2 shows the SIRs for the same types of cancer shown in **Figure 3**. The overall SIRs for anal cancer, lung cancer, Hodgkin lymphoma, and liver cancer were elevated. The SIRs for anal and lung cancer were highest in the youngest ages and declined significantly across age groups ($P < 0.001$ for all trends). In contrast, the SIRs for Hodgkin lymphoma increased significantly across age groups ($P < 0.001$ for trend), with the highest SIRs at the oldest ages. No significant SIR trends were observed across age groups for liver, prostate, breast, or colon cancer.

The **Appendix Table** (available at www.annals.org) presents SIRs by stage of anal or lung cancer (for which the observed age in persons with AIDS was younger than expected in the general population). The SIR for local-stage anal cancer was higher than that for distant-stage cancer, whereas the SIRs for local- and distant-stage lung cancer were similar.

DISCUSSION

When we did not account for the underlying population age structures, we found that many types of cancer occurred at much younger ages in persons with AIDS than in the general population, as suggested in previous studies (15–21). However, these differences were almost completely driven by differences in the underlying age structures of the populations at risk for cancer. The previous studies that reported younger ages at cancer diagnosis in persons with HIV/AIDS did not take into account that very few HIV-infected persons who are at risk for cancer have attained older age, when most cases of cancer develop. For example, only 1.5% of person-time among the persons with AIDS in our study was contributed by persons aged 65 years or older. This underlying age difference creates a bias when the ages at cancer diagnosis are compared between these populations.

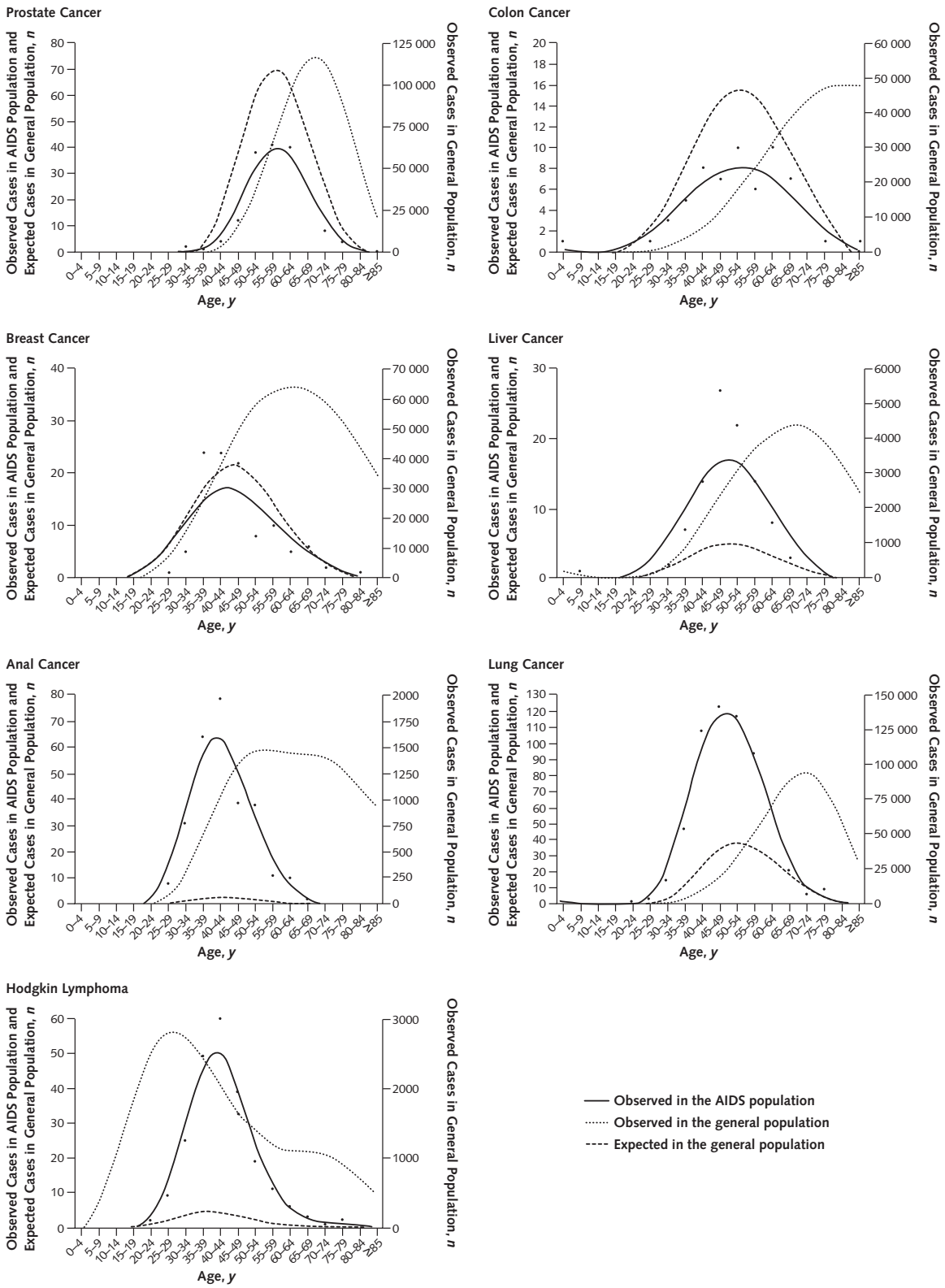
Cancer has recently been considered as a component of a potential syndrome of premature aging caused by HIV

Table 1. **Age at Cancer Diagnosis Among Persons With AIDS and the General Population in the United States, 1996–2007**

Type of Cancer	Age at Cancer Diagnosis				*P* Value*
	Observed in the General Population, *y*†	Observed in the AIDS Population		Expected in the General Population	
		Cases, *n*	Median Age (25th, 75th Percentile), *y*	Median Age (25th, 75th Percentile), *y*	
Oral cavity and pharynx	63	137	49 (44, 57)	50 (44, 56)	0.40
Esophageal	69	36	50.5 (45, 58.5)	54 (48, 60)	0.50
Stomach	72	36	49.5 (44, 58)	51 (44, 59)	0.50
Colon	73	61	52 (44, 62)	52 (46, 61)	0.53
Rectal	69	52	46 (39, 52.5)	51 (45, 58)	0.007
Anal	62	282	42 (37, 48)	45 (40, 51)	<0.001‡
Liver	66	98	49 (45, 55)	50 (45, 55)	0.53
Pancreatic	71	21	51 (49, 57)	53 (46, 60)	0.59
Larynx	65	72	48 (44, 55.5)	52 (47, 59)	0.003
Lung	70	605	50 (44, 56)	54 (47, 61)	<0.001‡
Soft tissue, including heart	58	26	40.5 (34, 52)	43 (37, 50)	0.42
Melanoma	60	74	46 (39, 54)	45 (39, 53)	0.45
Breast	62	110	44.5 (38, 53)	46 (41, 52)	0.177
Ovarian	63	13	42 (37, 44)	46 (40, 53)	0.025
Vulvar	70	12	41.5 (38, 56)	44 (39, 50)	0.39
Prostate	68	176	58.5 (53.5, 63.5)	58 (52, 64)	0.40
Testicular	34	33	35 (33, 39)	38 (34, 42)	0.018
Penis	68	16	49.5 (38.5, 54.5)	48 (43, 56)	0.58
Urinary bladder	73	23	48 (41, 58)	54 (47, 62)	0.069
Kidney and renal pelvis	66	47	49 (43, 54)	50 (44, 57)	0.171
Brain	56	16	43 (38, 52)	45 (38, 52)	0.61
Thyroid	47	22	43.5 (36, 52)	43 (37, 49)	0.72
Hodgkin lymphoma	37	226	42 (36, 47)	40 (34, 46)	<0.001‡
Myeloma	70	45	47 (40, 52)	52 (46, 59)	0.004
Lymphocytic leukemia	25	11	43 (26, 52)	43 (37, 51)	0.88
Myeloid or monocytic leukemia	68	46	48 (39, 55)	45 (38, 53)	0.178

* Compares median ages among observed cancer cases in persons with AIDS and expected cancer cases in the general population. Expected cases are adjusted for age, sex, race, calendar year, and registry.
† Median.
‡ Comparison was statistically significant after Bonferroni correction for multiple comparisons ($P < 0.0019$).

Figure 3. **Age at cancer diagnosis among persons with AIDS and the general population in the United States, 1996–2007.**



Points represent cases of cancer observed among persons with AIDS.

Table 2. **Standardized Incidence Ratios for Selected Cancer Types, by Age Group, for Persons With AIDS Compared With the General Population**

Cancer Type	Standardized Incidence Ratio (95% CI)							*P* Value for Trend*
	Overall	0–29 y	30–39 y	40–49 y	50–59 y	60–69 y	≥70 y	
Anal	25.1 (22.3–28.3)	97.4 (42.0–191.9)	39.0 (31.6–47.7)	22.1 (18.3–26.5)	19.7 (14.6–26.1)	17.4 (9.0–30.3)	0 (0–19.6)	<0.001
Lung	3.0 (2.8–3.2)	21.6 (7.0–50.4)	7.1 (5.4–9.0)	3.9 (3.4–4.4)	2.8 (2.5–3.2)	1.8 (1.4–2.2)	1.2 (0.66–1.9)	<0.001
Hodgkin lymphoma	10.8 (9.4–12.3)	5.9 (3.0–10.6)	8.7 (6.9–11.0)	13.1 (10.6–15.9)	12.6 (8.5–17.9)	14.9 (6.8–28.2)	24.2 (5.0–70.8)	<0.001
Liver	3.4 (2.7–4.1)	6.1 (0.16–34.2)	5.0 (2.3–9.5)	3.4 (2.5–4.6)	3.3 (2.3–4.6)	3.3 (1.6–5.9)	0 (0–4.2)	0.117
Prostate	0.54 (0.47–0.63)	0 (0–231)	3.3 (0.69–9.8)	0.36 (0.21–0.59)	0.57 (0.45–0.70)	0.58 (0.45–0.74)	0.46 (0.25–0.79)	0.80
Breast	0.83 (0.68–1.0)	0.70 (0.02–3.9)	1.1 (0.76–1.6)	0.75 (0.55–1.0)	0.62 (0.37–0.97)	1.1 (0.55–2.0)	0.94 (0.19–2.8)	0.48
Colon	0.59 (0.45–0.75)	4.0 (0.49–14.5)	0.87 (0.38–1.7)	0.49 (0.27–0.81)	0.46 (0.26–0.75)	0.80 (0.47–1.29)	0.39 (0.08–1.13)	0.49

* Calculated across age categories.

infection, motivated by clinical observations that average age of onset of age-related cancer is younger in HIV-infected persons than in the general population (15–21). However, as we show, these dramatic age differences are influenced by age differences in the populations at risk. Although we are not aware of previous mention of this type of confounding in the literature on HIV/AIDS and cancer, a similar mechanism has been discussed in studies of inherited diseases, such as Crohn disease. Studies of parent–child pairs of patients with Crohn disease have observed that children are diagnosed at younger ages than their parents were (29, 30). However, these generational age differences occurred because the children were younger than their parents when they were assessed for disease status and were thus not followed across the same age range as their parents (31, 32). After the differences in the periods at risk for Crohn disease were properly accounted for, these age differences were eliminated (32). This analysis highlights how statistical adjustment for differences in time at risk is essential when comparing ages at diagnosis (32). In our study, indirect standardization allowed us to compare the ages at cancer diagnosis in the AIDS and general populations after controlling for differences in the distributions of age and other demographic characteristics.

We observed small but statistically significant differences in the ages at diagnosis for anal cancer, lung cancer, and Hodgkin lymphoma after adjusting for differences in population structure. These types of cancer are among the selected group for which cancer risk is elevated among HIV-infected persons (2–5, 8). We propose 2 potential explanations for the younger age at diagnosis of anal and lung cancer among persons with AIDS. First, it may represent an effect of HIV on the development of these types of cancer. For example, HIV increases risk for cancer by inducing loss of immune control of oncogenic infections (such as human papillomavirus for anal cancer) (7, 8). By increasing the transition rate through the intermediate stages of infection on the pathway to cancer, this biological mechanism dramatically increases the number of persons with cancer and may also lead to slightly earlier ages at cancer diagnosis. Second, an early onset of cancer in persons with AIDS could reflect differences in the timing or intensity of exposure to other key risk factors for these types of cancer, such as earlier age at initiation of tobacco smoking or sexual debut (leading to human papillomavirus infection) or a greater number of cigarettes smoked per day. These explanations are not mutually exclusive, and both could explain the younger age at diagnosis for types of cancer known to be linked to HIV infection. Regardless, if AIDS directly accelerates the development of anal and lung cancer, we would expect to observe more cases of rapidly growing, distant-stage cancer. However, we did not observe higher SIRs for distant-stage anal or lung cancer compared with local- or regional-stage cancer.

An additional explanation for these age differences is increased medical surveillance of persons with AIDS, resulting in lead-time bias. This explanation is partly supported by our data for anal cancer. The SIR for anal cancer was highest for local-stage disease, which would be consistent with a stage shift due to screening with anal Papanicolaou tests (targeted toward HIV-infected men who have sex with men). However, because many HIV-infected persons do not receive regular medical care or cancer screening (33, 34), the overall magnitude and direction of this effect on age at cancer diagnosis are uncertain.

Among persons with AIDS, Hodgkin lymphoma was diagnosed at an older age than in the general population; however, the complexities of Hodgkin lymphoma epidemiology hinder the interpretation of this observation. In the general population, Hodgkin lymphoma exhibits a bimodal pattern in its age at onset. Nodular sclerosis often affects teenagers and young adults and is less strongly associated with Epstein–Barr virus (EBV) than other subtypes, whereas mixed cellularity (often EBV-positive) is the most common subtype among older adults (35). Among persons with HIV, Hodgkin lymphoma mainly resembles this second peak, in which the mixed cellularity subtype predominates (36, 37) and EBV is detectable in 80% to 100% of cases (38). Of note, the age distribution of persons with AIDS who have Hodgkin lymphoma did not

show the bimodal pattern seen in the general population (**Figure 3**), which reflects the relative lack of young and old persons with AIDS (**Figure 2**). Thus, the single peak in persons with AIDS represents a mixture of both EBV-negative and EBV-positive cases of Hodgkin lymphoma. We speculate that the apparent shift to older ages in the observed cases among persons with AIDS represents a strong increase in the risk for the EBV-positive cases that occur at older ages, rather than a shift of EBV-negative cases to older ages. The development of EBV-positive Hodgkin lymphoma could be accelerated by HIV, possibly by a loss of immune control of EBV infection.

Our study has several strengths. Most important, our comparisons of age at cancer diagnosis were corrected for bias due to the differing underlying age structures of the AIDS and general populations. In addition, the HIV/AIDS Cancer Match Study includes data from a large and representative sample of persons with AIDS in the United States (for example, these analyses included approximately 20% of the 1.05 million cumulative AIDS cases in the United States).

The main limitation of our study was the lack of risk factor information, including information on cigarette smoking, which prevented us from directly assessing how exposure to known cancer risk factors influenced the age at cancer diagnosis. In addition, our study was restricted to non-Hispanic white and black persons with AIDS, which may limit the generalizability of our findings. However, any biological effect of HIV that accelerates the development of cancer should be similar across racial and ethnic groups, and the lack of acceleration in cancer development among persons with AIDS, who are most immunocompromised, argues against an important effect in persons with earlier HIV disease. Finally, we assumed that cancer rates were known without error, because the cancer registries included in our study cover a very large population with more than 875 million person-years of follow-up. If this assumption is incorrect, then the variance of our estimates would be underestimated, which would increase the probability of observing a statistically significant age difference when one does not exist. However, we do not believe that making this assumption biased our results because we observed no age differences for most types of cancer.

In conclusion, our results do not support including cancer as part of a general syndrome of premature aging in HIV-infected persons. Ages at cancer diagnosis are observed to be younger in HIV-infected persons largely because very few persons with AIDS have been followed during older age, when most cases of cancer occur. As the AIDS population continues to age, we would expect more cases of non–AIDS-defining cancer to occur at older ages, which would attenuate or eliminate the apparent age differences at cancer diagnosis. Our results do not support an accelerated screening schedule in HIV-infected persons for most types of cancer (such as prostate, colon, or breast cancer). However, HIV-infected persons should still receive regular cancer screening, on the basis of recommendations made for the general population and established guidelines made specifically for HIV-infected persons, for those types of cancer for which the risk is particularly high, such as cervical or anal cancer (39).

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Reproducible Research Statement: *Study protocol and data set:* Not available. *Statistical code:* Available from Dr. Shiels (e-mail, shielsms@mail.nih.gov).

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Appendix Table. **Standardized Incidence Ratios for Selected Cancer Types, by Stage at Diagnosis, for Persons With AIDS Compared With the General Population**

Cancer Type and Stage	Observed Cases of Cancer, *n*	Standardized Incidence Ratio (95% CI)
Anal		
Local	151	28.6 (24.2–33.6)
Regional	67	20.9 (16.2–26.5)
Distant	12	15.2 (7.9–26.6)
Unstaged	50	27.7 (20.6–36.6)
Lung		
Local	76	2.9 (2.3–3.6)
Regional	137	2.7 (2.3–3.2)
Distant	295	2.9 (2.5–3.2)
Unstaged	90	4.7 (3.7–5.7)