HHS Public Access

Author manuscript

AIDS. Author manuscript; available in PMC 2016 September 08.

Published in final edited form as:

AIDS. 2014 March 27; 28(6): 881–890. doi:10.1097/QAD.0000000000000163.

Epidemiologic contributions to recent cancer trends among HIV-infected people in the United States

Hilary A. Robbins, **Meredith S. Shiels**, **Ruth M. Pfeiffer**, and **Eric A. Engels**

Division of Cancer Epidemiology and Genetics, National Cancer Institute, NIH, Bethesda, MD

Abstract

Objective—HIV-infected people have elevated risk for some cancers. Changing incidence of these cancers over time may reflect changes in three factors: HIV population demographic structure (e.g. age distribution), general population (background) cancer rates, and HIV-associated relative risks. We assessed the contributions of these factors to time trends for 10 cancers during 1996–2010.

Design—Population-based registry linkage study.

Methods—We applied Poisson models to data from the U.S. HIV/AIDS Cancer Match Study to estimate annual percent changes (APCs) in incidence rates of AIDS-defining cancers (ADCs: Kaposi sarcoma (KS), non-Hodgkin lymphoma (NHL), and cervical cancer) and 7 non-AIDS-defining cancers (NADCs). We evaluated HIV-infected cancer trends with and without adjustment for demographics, trends in background rates, and trends in standardized incidence ratios (SIRs, to capture relative risk).

Results—Cancer rates among HIV-infected people rose over time for anal (APC 3.8%), liver (8.5%), and prostate (9.8%) cancers, but declined for KS (1996–2000: −29.3%; 2000–2010: −7.8%), NHL (1996–2003: −15.7%; 2003–2010: −5.5%), cervical cancer (−11.1%), Hodgkin lymphoma (HL, −4.0%), and lung cancer (−2.8%). Breast and colorectal cancer incidence did not change over time. Based on comparison to adjusted models, changing demographics contributed to trends for KS and breast, colorectal, liver, lung, and prostate cancers (all $p<0.01$). Trends in background rates were notable for liver (APC 5.6%) and lung (−3.2%) cancers. SIRs declined for ADCs, HL (APC −3.2%), and lung cancer (−4.4%).

Conclusions—Demographic shifts influenced several cancer trends among HIV-infected individuals. Falling relative risks largely explained ADC declines, while background incidence contributed to some NADC trends.

Keywords

HIV/AIDS; cancer; statistical modeling; trends; United States

Corresponding author and requests for reprints: Hilary A. Robbins, 9609 Medical Center Drive, 6-E228, Bethesda, MD 20892, (240) 276-7187, hilary.robbins@nih.gov.

Conflicts of Interest: All authors declare no conflict of interest.

Author Contributions: Conception of study and study design: HAR, MSS, RMP, EAE. Statistical analyses: HAR, RMP. Interpretation of the results: HAR, MSS, RMP, EAE. Drafting of manuscript: HAR. Revision and final approval of manuscript: HAR, MSS, RMP, EAE.

Introduction

People infected with human immunodeficiency virus (HIV) are at elevated risk for developing several cancers (1–3). Some of these malignancies are related to advanced immunodeficiency (i.e., acquired immunodeficiency syndrome or AIDS), and three are considered AIDS-defining cancers (ADCs, i.e., Kaposi sarcoma (KS), non-Hodgkin lymphoma (NHL), and cervical cancer) (4). Risk is also elevated for several non-AIDS-defining cancers (NADCs), including lung cancer, Hodgkin lymphoma (HL), anal cancer, and liver cancer (1–3). The introduction of highly active antiretroviral therapy (HAART) in 1996 was associated with dramatic declines in rates of KS and NHL (5;6). However, rates among people with HIV have increased for other cancers, such as anal and liver cancers (1;2;7–9).

It is useful to consider three broadly defined influences in assessing trends over time in cancer incidence rates within a subset of the general population (i.e., a subpopulation such as HIV-infected people). The first is changes in the demographic structure of the subpopulation. Since the widespread introduction of HAART and subsequent decline of AIDS-related mortality, the U.S. HIV population has aged substantially, and a growing number of people have survived more than 10 years since an AIDS diagnosis (10). Because risk for many cancers varies by age, other demographic characteristics, and degree or duration of immune suppression, these shifts may have led to changing cancer incidence over time.

Second, cancer incidence in a subpopulation is expected to change over time if there are changes in incidence in the underlying general population (i.e., changes in background rates). For example, population-wide changes in exposure to a cancer risk factor would be expected to affect cancer incidence both overall and in HIV-infected people.

Third, cancer incidence in a subpopulation would be expected to change with the relative risk of cancer for that subpopulation compared to the general population. Among HIV-infected people, factors responsible for elevated cancer risk are complex and vary by cancer. They include elevated prevalence and poor immune control of oncogenic viruses (11), high prevalence of tobacco use (12), and differences in screening patterns between the HIV and general populations (13). Relative risks for cancer associated with HIV infection may change if, for example, antiretroviral treatment improves immune function or smoking prevalence among HIV-infected people declines faster than in the general population.

Though incidence of some cancers has changed over time among the U.S. HIV population, it is not known how these epidemiologic factors have contributed to trends. Systematic evaluation of these influences may aid understanding of past trends, as well as inform expectations of future trends in cancer incidence. In this study, we characterize trends in incidence of 10 cancers in the U.S. HIV population during 1996–2010. We then separately assess contributions to these trends of demographic shifts in the HIV population, changes in general population cancer incidence, and changes in the HIV-associated relative risk of cancer.

Methods

Data Sources

The HIV/AIDS Cancer Match (HACM) Study links state HIV and cancer registries to identify cancers occurring in HIV-infected people (www.hivmatch.cancer.gov) (2). The present study utilizes HACM data from states and years where both name-based HIV reporting and cancer registry coverage are considered complete, including Colorado (1996–2007), Connecticut (200292013;2010), Florida (1998–2002), Georgia (2004–2008), Michigan (1996–2010), New Jersey (1996–2007), and Texas (1997–2009) (person-time contributed by individual registries in each year is presented in Supplemental Digital Content 1). Individuals began follow-up at report of HIV infection or the beginning of data coverage, whichever came later, and exited follow-up at death or the end of data coverage, whichever came earlier. Multiple cancer diagnoses were allowed for a given individual, but for a given cancer site only the first diagnosis was included. Analyses were restricted to non-Hispanic whites, non-Hispanic blacks, and Hispanics. The HACM Study was approved by institutional review boards, as required, at participating registries.

We used International Classification of Diseases for Oncology, 3rd Edition (ICD-O3) codes to identify cases of 10 cancers of interest in HIV-infected people. These cancers are associated with HIV infection or are otherwise common, and include KS, NHL, Hodgkin lymphoma, and cancers of the cervix, anus, female breast, colorectum, liver, lung, and prostate. Though only certain subtypes of NHL are considered ADCs, most NHL cases among HIV-infected people are the AIDS-defining subtypes (14); thus, we considered all NHLs together.

Statistical Analysis

For each cancer site, we used Joinpoint software (15) to identify change points in HIV-infected cancer incidence rates among all registries combined during 1996–2010. Change points are years in which statistically significant changes occurred in the slope across yearly incidence rates (i.e., the annual percent change or APC). Then, we conducted separate analyses for time segments defined by any change points. To estimate time trends in HIV-infected cancer incidence in each time segment, we used Poisson regression adjusted only for registry (referred to as “crude trends”). We tested for heterogeneity in trends between registries by adding an interaction term between calendar year and each registry, and additionally tested for heterogeneity in the adjusted trends described below. However, because we sought to describe overall trends, we did not include interaction terms in our main analyses.

To evaluate the contribution of changing HIV demographics, we further adjusted the crude Poisson models for age, sex, HIV risk group, race/ethnicity, and HIV/AIDS-relative time (“adjusted trends,” see Table 2 footnote for details). We assumed that changing demographic structure influenced HIV-infected trends for cancers where these adjusted trends differed from the crude trends, based upon a test of statistical significance that relied on a parametric bootstrap procedure. Specifically, for each bootstrap dataset (N=500), the counts in each cell were generated based on a Poisson distribution applied to the observed person-years, where

the Poisson mean was estimated from the adjusted model generated by the original dataset. We then separately fit the crude and adjusted models to the bootstrap data and computed the difference of the coefficients for calendar year. The empirical variance of this difference was used in a chi-square test of the null hypothesis that the difference between the crude and adjusted parameters is equal to zero. In a supplementary analysis, we aimed to attribute demographic contributions to individual demographic factors. We thus adjusted crude models separately for age, HIV risk group and sex, race/ethnicity, and HIV/AIDS-relative time, and used the resulting APCs to assess which factor(s) accounted for the difference in APCs between the crude and adjusted models.

To evaluate the contribution of changing background incidence, we assessed time trends in general population cancer incidence rates. We standardized these incidence rates from HACM cancer registries to the 2002 HIV population separately for each registry. Then, we estimated time trends in standardized general population incidence using linear regression models that accounted for the variability in the incidence rates and were additionally adjusted for registry. We did not perform this analysis for KS, because almost all KS cases in the general population occur among HIV-infected people (16).

The HIV-associated relative risk of cancer was captured using the standardized incidence ratio (SIR), which is the ratio of observed to expected cancer cases. We calculated expected counts using general population cancer rates in strata defined by year, registry, age, sex, and race/ethnicity. Expected counts for KS were based on 1973–1979 rates (16). We used Poisson regression to assess time trends in the SIRs, adjusted for demographic factors (see Table 2 footnote). Changing relative risk was assumed to influence HIV-infected trends if a significant trend was observed.

To illustrate trends, we graphically depict yearly incidence rates for each cancer in the HIV-infected and general populations. These estimates are aggregated over registries, so they do not correspond directly to the statistical analyses which adjust for registry. Therefore, some significant trends in our main analyses may not be apparent in the figures. For HIV-infected people, we show crude incidence along with incidence standardized to the 2002 HIV population. Differences between the trends for these two rates in the HIV population support contributions of changing HIV demographics. For the general population, we present cancer incidence standardized to the 2002 HIV population, and changes in these rates over time imply contributions from changing background rates. The gap between the standardized HIV-infected rates and general population rates approximates the SIR, as we use a logarithmic scale.

We express time trends using APCs, calculated using the formula $APC = \exp(\beta_{year}) - 1$ where β_{year} is the coefficient for calendar year. We used a two-sided significance level of $\alpha=0.05$ for statistical tests.

Results

We evaluated 275,975 HIV-infected people who contributed 1,471,866 person-years of follow-up during 1996–2010 (Table 1). Over this period, the proportion of follow-up time

contributed by individuals aged 50 or older increased from 13.0% (1996–2000) to 27.3% (2006–2010), illustrating a shift in age distribution that may have affected rates of some cancers. The population increasingly comprised individuals who had never been diagnosed with AIDS (an increase from 33.5% to 41.3% of person-time) and those surviving more than 5 years after an AIDS diagnosis (from 17.5% to 38.4%). The distribution of person-time by HIV risk group, sex, and race/ethnicity did not change appreciably.

The number of HIV-infected cancer cases over follow-up ranged from 261 for female breast cancer to 2,437 for KS and 4,136 for NHL (Table 2). As indicated by SIRs (see Table, Supplemental Digital Content 2, which lists incidence rates and SIRs), risks were strongly elevated for KS, anal cancer, and NHL. Risk was not elevated for colorectal cancer and was lower among HIV-infected people than the general population for breast and prostate cancers. For some cancers, SIRs differed noticeably by time period; trends in SIRs (as a measure of risk relative to the general population) are analyzed formally below.

We show cancer incidence time trends from statistical analyses in Table 2, and graphical depictions in Figures 1 (ADCs) and 2 (NADCs). Change points for HIV-infected incidence rates were identified for KS in 2000 and for NHL in 2003, but not for other cancers; thus analyses for KS and NHL were separated into two time segments. In crude models, incidence in HIV-infected people increased over time for anal cancer (APC 3.8%, 95% CI 1.4%, 6.2%), liver cancer (8.5%, 95% CI 4.6%, 12.5%), and prostate cancer (9.8%, 95% CI 6.4%, 13.3%), and decreased for KS (1996–2000: APC −29.3%, 95% CI −32.9%, −25.5%; 2000–2010: −7.8%, 95% CI −9.6%, −5.8%), NHL (1996–2003: −15.7%, 95% CI −17.3%, −14.0%; 2003–2010: −5.5%, 95% CI −7.8%, −3.0%), cervical cancer (−11.1%, 95% CI −14.3%, −7.7%), HL (−4.0%, 95% CI −6.5%, −1.4%), and lung cancer (−2.8%, 95% CI −4.5%, −1.1%) (Table 2). With the exception of HL, these changes over time are visible graphically as trends in crude incidence for the combined registries (trends in solid lines, Figures 1A–C, 2A, 2E–G). Breast and colorectal cancers showed no time trend. For anal cancer, crude trends were significantly heterogeneous ($p<0.001$) and appeared to differ qualitatively across registries (Figure, Supplemental Digital Content 3). This pattern was not apparent for other cancer sites. Results were similar for adjusted trends, although the heterogeneity in the anal cancer trend was somewhat attenuated ($p=0.017$, Figure, Supplemental Digital Content 3).

In comparison to these crude trends, time trends after adjustment for demographics were significantly weaker for KS (1996–2000: adjusted APC −25.6%, 95% CI −29.5%, −21.6%, $p<0.001$ for comparison with crude trend; 2000–2010: −5.7%, 95% CI −7.7%, −3.7%, $p<0.001$), liver cancer (6.6%, 95% CI 2.7%, 10.7%, $p=0.006$), and prostate cancer (2.9%, 95% CI −0.3%, 6.3%, $p<0.001$) (Table 2). For lung cancer, the decreasing trend became stronger after adjustment (APC −6.8%, 95% CI −8.5%, −5.0%, $p<0.001$). For breast and colorectal cancers, adjusted trends differed significantly from crude trends ($p<0.001$ for both), but neither differed significantly from zero. For liver, lung, and prostate cancers, these differences in trends are visible graphically by comparison of crude and standardized HIV-infected cancer incidence rates (comparison of solid and dashed lines, Figures 2E–G). In our supplementary analysis, adjustment only for age accounted for the difference in crude and adjusted APCs for breast, colorectal, liver, lung, and prostate cancers (see Table,

Supplemental Digital Content 4, which lists APCs adjusted for individual demographic factors). This implies that among various demographic shifts over time, aging specifically had the greatest influence on incidence rates of these cancers. For KS, on the other hand, adjustment for HIV/AIDS-relative time had the greatest impact.

Incidence in the general population increased over time for anal (APC 3.3%, 95% CI 1.4%, 5.2%) and liver cancers (5.6%, 95% CI 4.6%, 6.6%), and decreased for NHL (2003–2010: −2.2%, 95% CI −3.3%, −1.0%) and cervical (−2.4%, 95% CI −3.4%, −1.3%), breast (−0.8%, 95% CI −1.2%, −0.5%), colorectal (−0.7%, 95% CI −1.1%, −0.3%), and lung (−3.2%, 95% CI −3.5%, −2.8%) cancers (Table 2). The directions of these trends were consistent with those in the HIV population, with the exception of breast and colorectal cancers which showed no significant trend in the HIV population. General population trends are visually evident for cervical, anal, liver, and lung cancers (solid lines with markers, Figures 1C, 2A, 2E, and 2F).

Decreasing SIRs contributed to trends over time for KS (1996–2000: APC −26.3%, 95% CI −30.2%, −22.3% and 2000–2010: −2.7%, 95% CI −4.8%, −0.7%), NHL (1996–2003: −14.5%, 95% CI −16.2%, −12.7% and 2003–2010: −4.0%, 95% CI −6.5%, −1.5%), cervical cancer (−9.4%, 95% CI −12.9%, −5.8%), HL (−3.2%, 95% CI −5.9%, −0.5%), and lung cancer (−4.4%, 95% CI −6.2%, −2.6%) (Table 2). Graphically, the declining magnitude of SIRs is visible as a decreasing gap over time between standardized incidence rates in the HIV-infected and general populations for NHL, cervical cancer, and lung cancer (decreasing gap between dashed lines and solid lines with markers, Figures 1B, 1C, and 2F).

Discussion

The incidence of many cancers changed over time in the U.S. HIV population during 1996–2010, and these trends were variably influenced by demographic shifts in the HIV population, changing cancer rates in the general population, and changes in the HIV-associated relative risk of cancer. In Table 3, we summarize these trends and the epidemiologic factors contributing to them. As we elaborate below, our results suggest that changes in demographics and in general population incidence rates were influential for most NADCs. In contrast, declines in ADCs were largely driven by decreasing relative risks.

Each ADC has a viral cause: human herpesvirus 8 for KS, Epstein-Barr virus (EBV) for a large fraction of NHLs, and human papillomavirus (HPV) for cervical cancer. Dramatic declines in KS and NHL have been attributed to improved immune control of oncogenic viruses with HIV treatment (5;6;17). Since 1996, clinical guidelines have recommended earlier HIV treatment, raising and finally eliminating the minimum CD4+ cell count threshold for treatment initiation (18–20). Further, during 2000–2008, HAART use increased in the U.S. HIV population (21). The falling SIRs that we observed for KS and NHL likely reflect this expanding uptake and increasing effectiveness of HAART. For cervical cancer, declining relative risk may reflect the effects of HAART on HPV infection (22;23) or perhaps improvements in cervical cancer screening among HIV-infected women.

It has been suggested that aging and other demographic shifts in the HIV population are producing a rise in incidence of NADCs (8;10;11). Our results indicate this is true for some, though not all, of the cancers we studied. We found that demographic shifts contributed to increases in liver cancer, and they were the only factor contributing to the rise in prostate cancer. These demographic shifts also masked a more rapid decline in lung cancer that would have been observed if the population characteristics had not changed over time. For these NADCs, aging was the main factor influencing trends (see Table, Supplemental Digital Content 4). Adjustment for HIV/AIDS-relative time produced the largest change for KS (see Table, Supplemental Digital Content 4), due to lower KS risk among the increasing number of individuals surviving more than 5 years after an AIDS diagnosis (data not shown).

Time trends in general population incidence rates contributed to HIV-infected trends for several NADCs, specifically, for anal, breast, colorectal, liver, and lung cancers. Increasing liver cancer incidence in the U.S. general population has been attributed to long-term exposure to hepatitis B and C viruses (24), which have high prevalence in the HIV population (25). For lung cancer, declines in the general population are due to falling smoking prevalence (26), which may also be occurring in the HIV population. For breast and colorectal cancers, gradual decreases in the general population were countered by aging in the HIV population (Table 2, Supplemental Digital Content 4) leading to non-significant upward HIV-infected trends. Among ADCs, declines in the general population contributed to favorable NHL and cervical cancer trends, although changes in SIRs were likely more important.

Among NADCs, we observed decreasing trends in SIRs for lung cancer and HL. For lung cancer, this could reflect a faster decline in smoking prevalence in the HIV population than in the general population. Alternatively, the declining SIR may reflect benefits of HAART, since immune suppression and inflammation have been linked to development of lung cancer (12;27). For HL, previous studies (including some using data from the HACM Study) reported an increase or no change over time in incidence among HIV-infected people (1;2;10;28), but we observed a decline. This difference may be due to the addition of more recent data (through 2010) or the inclusion of large numbers of HIV-infected people who have not developed AIDS. HAART facilitates immune control of EBV, which contributes to the majority of HL cases among HIV-infected people (29).

Over 80% of anal cancers are caused by prolonged HPV infection (30), and HIV-infected people have nearly 30-fold increased anal cancer risk (31). According to our results, increasing anal cancer incidence among people with HIV was attributable to increasing background rates. However, because HIV-infected anal cancers have strongly influenced general population trends among men (32), the background trend we observed was likely affected by HIV-infected cases. If one were able to remove the HIV-infected cases, the general population trend would be flatter (32). Thus, we cannot exclude that the trend in the HIV population is actually due to a masked trend in relative risk. Further, we observed heterogeneity among registries for anal cancer. In additional analyses, the HIV-infected anal cancer trend was no longer significant upon removal of the New Jersey registry, which showed a robust upward trend (Figure, Supplemental Digital Content 3). We do not have an explanation for this heterogeneity, but its presence complicates understanding of the average

trends across registries. For these reasons, our results for anal cancer should be interpreted with caution.

Changes in cancer screening programs over time, including screening methods, recommendations, and public awareness, can influence cancer trends in complex ways that vary by cancer site. In our analysis, the observed impact of screening trends largely depends on how changes in screening compare between the HIV and general populations. Specifically, if screening among HIV-infected people increases over time for a cancer where screening reduces incidence (e.g., cervical cancer), then the HIV-infected incidence will show a downward trend. A general population contribution to this trend will be observed if the rate of screening uptake in the HIV population reflects the same uptake in the general population. If uptake is more rapid in the HIV population, then the relative difference will manifest as a decreasing SIR.

Strengths of our study include use of population-based data from seven U.S. states that cover most of the HAART era. We used a unique approach to evaluate complementary influences on cancer trends among HIV-infected people. One limitation is that our methodology may have failed to detect small contributions to these trends. For example, the lack of a significant p-value for a weak trend in the general population does not rule out that a trend in background incidence has affected the HIV population. While it would be ideal to explicitly decompose the crude trends into three components, our method does not allow us to quantify the relative contributions of the three factors to the crude trend. For instance, one should not expect the APCs for the general population and SIR to sum to either the adjusted or crude APC. As noted above, our data are derived from 7 different registries whose period of coverage is not homogeneous, though our analyses adjust for this limitation. Finally, we lack individual-level data describing HIV treatment, diagnosis or treatment of carcinogenic infections such as hepatitis B and C viruses, and cancer screening. Thus, we were unable to address these factors in our analyses.

In conclusion, our results indicate that the causes of recent trends in cancer incidence among HIV-infected people were multifaceted and differed by cancer site. HAART has reduced the incidence of many virus-related cancers by lowering the relative risk, and this result highlights the importance of continued improvement in accessible, early, and effective HIV treatment. However, for anal and liver cancers, the SIRs have not changed and incidence has increased. These adverse trends support efforts to make screening and prevention of these cancers a priority. For other cancers, especially prostate cancer, increasing incidence largely reflects the consequences of aging, and incidence should be expected to rise further as the HIV population continues to age.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Source of Funding: This research was supported, in part, by the Intramural Research Program of the National Cancer Institute, National Institutes of Health.

The authors gratefully acknowledge the support and assistance provided by individuals at the following state HIV/AIDS and cancer registries: Colorado, Connecticut, Florida, Georgia, Michigan, New Jersey, and Texas. We also thank Timothy McNeel at Information Management Services for programming support.

The following cancer registries were supported by the SEER Program of the National Cancer Institute: Connecticut (HHSN261201000024C) and New Jersey (HHSN261201000027C, N01-PC-2010-0027). The following cancer registries were supported by the National Program of Cancer Registries of the Centers for Disease Control and Prevention: Colorado (U58 DP000848-04), Georgia (5U58DP003875-01), Michigan (5U58DP000812-03), New Jersey (1US58/DP0039311-01), and Texas (5U58DP000824-04). The New Jersey Cancer Registry was also supported by the state of New Jersey.

The views expressed in this paper are those of the authors and should not be interpreted to reflect the views or policies of the National Cancer Institute, HIV/AIDS or cancer registries, or their contractors.

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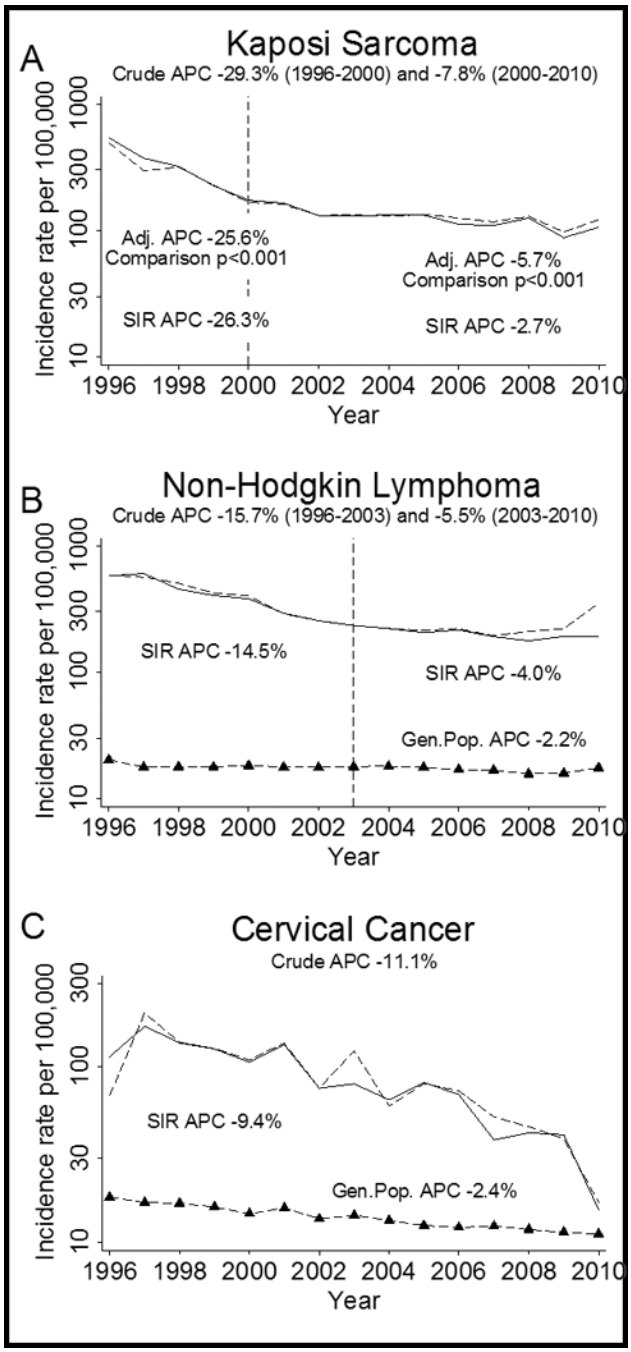

Figure 1. Incidence rates of AIDS-defining cancers in the U.S. HIV/AIDS Cancer Match Study, 1996–2010

Solid and dashed lines depict crude and standardized incidence in the HIV population, respectively, and lines with triangle markers depict standardized incidence in the general population. Vertical dashed lines are displayed for years in which a Joinpoint was identified. In panel A, we do not show standardized incidence in the general population, because the majority of Kaposi sarcoma cases are in HIV-infected people (16). Rates are displayed on a logarithmic scale; note differing y-axis scales for individual panels. Panels are annotated with the relevant data substantiating the epidemiologic contributions to cancer trends listed

in Table 3. Abbreviations in annotations: APC, annual percent change; adj., adjusted; SIR, standardized incidence ratio; Gen.Pop., general population; comparison p, p-value for comparison between crude and adjusted HIV-infected trends.

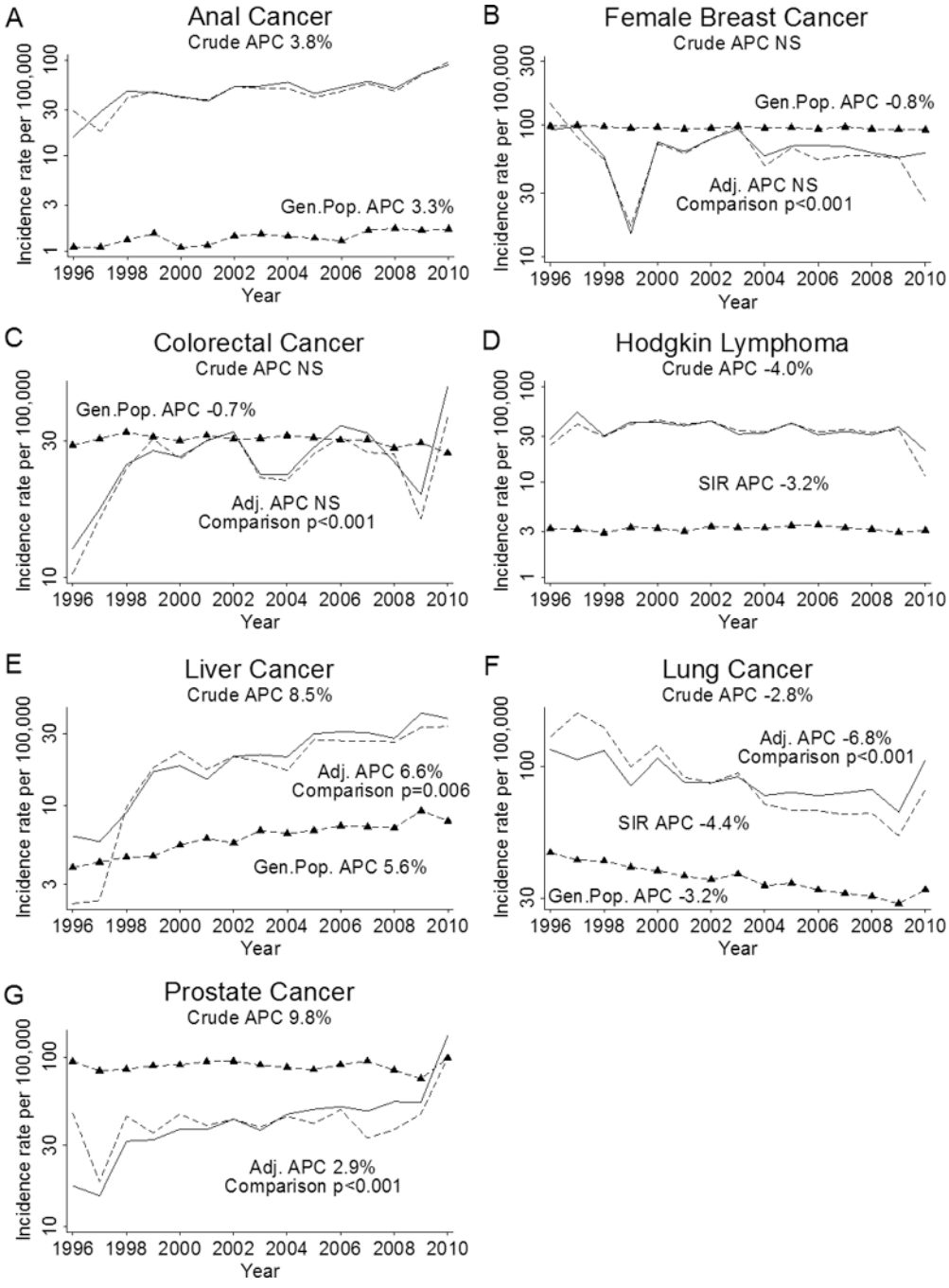

Figure 2. Incidence rates of non-AIDS-defining cancers in the U.S. HIV/AIDS Cancer Match Study, 1996–2010

Solid and dashed lines depict crude and standardized incidence in the HIV population, respectively, and lines with triangle markers depict standardized incidence in the general population. Rates are displayed on a logarithmic scale; note differing y-axis scales for individual panels. Panels are annotated with the relevant data substantiating the epidemiologic contributions to cancer trends listed in Table 3. Abbreviations in annotations: APC, annual percent change; adj., adjusted; SIR, standardized incidence ratio; Gen.Pop.,

general population; comparison p, p-value for comparison between crude and adjusted HIV-infected trends.

Table 1

Demographic characteristics of person-time among HIV-infected people in the U.S. HIV/AIDS Cancer Match Study, 1996–2010

	1996–2000 N (%)	2001–2005 N (%)	2006–2010 N (%)
Total person-years with HIV	386,568 (100)	600,230 (100)	485,068 (100)
Age category			
0–14	6,527 (1.7)	7,268 (1.2)	3,402 (0.7)
15–29	41,936 (10.8)	54,908 (9.1)	48,014 (9.9)
30–39	156,209 (40.4)	187,179 (31.2)	112,404 (23.2)
40–49	131,674 (34.1)	232,536 (38.7)	188,974 (39.0)
50–59	38,770 (10.0)	93,123 (15.5)	102,588 (21.1)
60–69	9,360 (2.4)	20,746 (3.5)	24,583 (5.1)
70+	2,092 (0.5)	4,471 (0.7)	5,103 (1.1)
Weighted mean age	39.0	41.3	43.1
Sex			
Male	284,691 (73.6)	439,063 (73.1)	361,716 (74.6)
Female	101,876 (26.4)	161,167 (26.9)	123,352 (25.4)
HIV risk group			
MSM	167,172 (43.2)	258,282 (43.0)	220,898 (45.5)
Non-MSM male IDU	56,146 (14.5)	75,005 (12.5)	51,925 (10.7)
Male heterosexual	25,464 (6.6)	40,867 (6.8)	27,992 (5.8)
Male other/unknown	35,910 (9.3)	64,909 (10.8)	60,901 (12.6)
Female IDU	32,759 (8.5)	43,293 (7.2)	28,596 (5.9)
Female heterosexual	47,346 (12.2)	77,348 (12.9)	55,232 (11.4)
Female other/unknown	21,771 (5.6)	40,526 (6.8)	39,524 (8.1)
Race/ethnicity			
Non-Hispanic White	138,955 (35.9)	205,708 (34.3)	161,735 (33.3)
Non-Hispanic Black	181,939 (47.1)	281,907 (47.0)	228,746 (47.2)
Hispanic	65,674 (17.0)	112,616 (18.8)	94,587 (19.5)
HIV/AIDS-relative time			
HIV only	129,309 (33.5)	230,357 (38.4)	200,507 (41.3)
1–24 months post AIDS	79,726 (20.6)	70,111 (11.7)	39,225 (8.1)
25–60 months post AIDS	109,756 (28.4)	97,741 (16.3)	58,939 (12.2)
61+ months post AIDS	67,776 (17.5)	202,022 (33.7)	186,398 (38.4)

Abbreviations: MSM, men who have sex with men; IDU, injection drug users MSM includes individuals who are both MSM and IDU. Estimates are based on 275,975 HIV-infected individuals from individual registries as follows: Colorado, 11,466; Connecticut, 12,645; Florida, 74,472; Georgia, 32,377; Michigan, 19,208; New Jersey, 46,786; Texas, 79,021.

Table 2

Cancer trends among the U.S. HIV and general populations.

Cancer and calendar period	Cases (N)	Crude HIV-infected trend[a]		Adjusted HIV-infected trend[b]		p-value for comparison[c]	General population trend[d]		SIR trend[b]	
		APC	(95% CI)	APC	(95% CI)		APC	(95% CI)	APC	(95% CI)
KS	2,437									
1996–2000		−29.3	(−32.9, −25.5)	−25.6	(−29.5, −21.6)	< 0.001	NA	NA	−26.3	(−30.2, −22.3)
2000–2010		−7.8	(−9.6, −5.8)	−5.7	(−7.7, −3.7)	< 0.001	NA	NA	−2.7	(−4.8, −0.7)
NHL	4,136									
1996–2003		−15.7	(−17.3, −14.0)	−15.4	(−17.1, −13.6)	0.274	−0.5	(−1.7, 0.7)	−14.5	(−16.2, −12.7)
2003–2010		−5.5	(−7.8, −3.0)	−5.2	(−7.6, −2.7)	0.206	−2.2	(−3.3, −1.0)	−4.0	(−6.5, −1.5)
Cervix	329	−11.1	(−14.3, −7.7)	−11.6	(−15.0, −8.1)	0.354	−2.4	(−3.4, −1.3)	−9.4	(−12.9, −5.8)
Anus	737	3.8	(1.4, 6.2)	3.4	(0.8, 5.9)	0.315	3.3	(1.4, 5.2)	1.0	(−1.5, 3.6)
Female breast	261	1.1	(−2.8, 5.1)	−1.6	(−5.6, 2.6)	< 0.001	−0.8	(−1.2, −0.5)	−1.7	(−5.7, 2.5)
Colorectum	404	2.2	(−1.0, 5.5)	−0.9	(−4.2, 2.5)	< 0.001	−0.7	(−1.1, −0.3)	−1.0	(−4.3, 2.5)
HL	542	−4.0	(−6.5, −1.4)	−3.4	(−6.0, −0.7)	0.156	−0.1	(−1.2, 1.1)	−3.2	(−5.9, −0.5)
Liver	339	8.5	(4.6, 12.5)	6.6	(2.7, 10.7)	0.006	5.6	(4.6, 6.6)	1.3	(−2.6, 5.4)
Lung	1,277	−2.8	(−4.5, −1.1)	−6.8	(−8.5, −5.0)	< 0.001	−3.2	(−3.5, −2.8)	−4.4	(−6.2, −2.6)
Prostate	475	9.8	(6.4, 13.3)	2.9	(−0.3, 6.3)	< 0.001	0.1	(−0.2, 0.3)	2.0	(−1.2, 5.4)

Abbreviations: KS, Kaposi sarcoma; NHL, non-Hodgkin lymphoma; HL, Hodgkin lymphoma; SIR, standardized incidence ratio; CI, confidence interval; NA, not assessed; APC, annual percent change, calculated as ($e^{\beta}-1$) where β is the coefficient for year.

[a] Adjusted for registry

[b] Adjusted for registry, age (0–14, 15–29, 30–39, 40–49, 50–59, 60–69, and >70 years; modeled with 1 degree of freedom), race/ethnicity (non-Hispanic white, non-Hispanic black, and Hispanic), sex, HIV risk group (men who have sex with men (MSM), non-MSM injection drug users (IDU), heterosexual, and other/unknown), and HIV/AIDS-relative time (HIV without AIDS (i.e., HIV only), and 1–24, 25–60, and >61 months since AIDS diagnosis)

[c] Comparison of the crude and adjusted trends; $p<0.05$ indicates that the crude and adjusted APCs are significantly different.

[d] Rates standardized to the 2002 HIV population.

Only females were evaluated for breast and cervical cancers, and only males for prostate cancer.

Table 3

Summary of contributions to cancer trends among HIV-infected people.

Cancer and calendar period	Crude time trend	Contributions to trends among HIV-Infected people		
		Changes in HIV demographics	Changes in general population incidence	Changes in the SIR
KS				
1996–2000	Decreasing	Yes	Not assessed	Yes
2000–2010	Decreasing	Yes	Not assessed	Yes
NHL				
1996–2003	Decreasing	No	No	Yes
2003–2010	Decreasing	No	Yes	Yes
Cervix	Decreasing	No	Yes	Yes
Anus	Increasing	No	Yes	No
Female breast	No change	Yes	Yes	No
Colorectum	No change	Yes	Yes	No
HL	Decreasing	No	No	Yes
Liver	Increasing	Yes	Yes	No
Lung	Decreasing	Yes	Yes	Yes
Prostate	Increasing	Yes	No	No

Abbreviations: KS, Kaposi sarcoma; NHL, non-Hodgkin lymphoma; HL, Hodgkin lymphoma; SIR, standardized incidence ratio