Incidence of Types of Cancer among HIV-Infected Persons Compared with the General Population in the United States, 1992–2003

Pragna Patel, MD, MPH; Debra L. Hanson, MS; Patrick S. Sullivan, DVM, PhD; Richard M. Novak, MD; Anne C. Moorman, BSN, MPH; Tony C. Tong, MS; Scott D. Holmberg, MD, MPH; and John T. Brooks, MD, for the Adult and Adolescent Spectrum of Disease Project and HIV Outpatient Study Investigators*

Background: Persons who are HIV-infected may be at higher risk for certain types of cancer than the general population.

Objective: To compare cancer incidence among HIV-infected persons with incidence in the general population from 1992 to 2003.

Design: Prospective observational cohort studies.

Setting: United States.

Patients: 54 780 HIV-infected persons in the Adult and Adolescent Spectrum of HIV Disease Project (47 832 patients) and the HIV Outpatient Study (6948 patients), who contributed 157 819 person-years of follow-up from 1992 to 2003, and 334 802 121 records from the Surveillance, Epidemiology, and End Results program of 13 geographically defined, population-based, central cancer registries.

Measurements: Standardized rate ratios (SRRs) to compare cancer incidence in the HIV-infected population with standardized cancer incidence in the general population.

Results: The incidence of the following types of non–AIDS-defining cancer was significantly higher in the HIV-infected population than in the general population: anal (SRR, 42.9 [95% CI, 34.1 to 53.3]), vaginal (21.0 [CI, 11.2 to 35.9]), Hodgkin lymphoma (14.7 [CI, 11.6 to 18.2]), liver (7.7 [CI, 5.7 to 10.1]), lung (3.3 [CI, 2.8 to 3.9]), melanoma (2.6 [CI, 1.9 to 3.6]), oropharyngeal (2.6 [CI, 1.9 to 3.4]), leukemia (2.5 [CI, 1.6 to 3.8]), colorectal (2.3 [CI, 1.8 to 2.9]), and renal (1.8 [CI, 1.1 to 2.7]). The incidence of prostate cancer was significantly lower among HIV-infected persons than the general population (SRR, 0.6 [CI, 0.4 to 0.8]). Only the relative incidence of anal cancer increased over time.

Limitations: Lower ascertainment of cancer in the HIV cohorts may result in a potential bias to underestimate rate disparities. Tobacco use as a risk factor and the effect of changes in cancer screening practices could not be evaluated.

Conclusion: The incidence of many types of non–AIDS-defining cancer was higher among HIV-infected persons than among the general population from 1992 to 2003.

Ann Intern Med. 2008;148:728-736. www.annals.org

For author affiliations, see end of text.

* For a list of the Adult and Adolescent Spectrum of Disease Project and HIV Outpatient Study Investigators, see the **Appendix** (available at www.annals.org).

The advent of highly active antiretroviral therapy (HAART) has significantly improved the survival rate of persons with HIV in the United States (1–4) and led to a shift in the natural spectrum of HIV disease. Incidence of AIDS-defining infections and cancer has decreased (4–8), whereas the incidence of many chronic conditions, such as lipodystrophy, the metabolic syndrome, osteopenia, and cardiovascular disease, has increased (9–13). The incidence of several types of non–AIDS-defining cancer has also increased (14–43). However, data from U.S. studies are frequently limited to persons with AIDS or small, demographically limited cohorts. In addition, few reports of cancer incidence have included persons at all stages of HIV infection or trends in cancer incidence after the introduction of HAART (30–34, 38).

To describe cancer diagnoses in persons at all stages of HIV infection, we analyzed data from 2 large prospective cohort studies in the United States: the Adult and Adolescent Spectrum of HIV Disease (ASD) Project and the HIV Outpatient Study (HOPS). We compared incidence rates of cancer among these persons with incidence rates in the general population, derived from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute (44, 45) for 1992 to 2003. In addition, we determined incidence trends for selected types of cancer among persons at all stages of HIV infection and in the general population for 3 periods defined on the basis of HAART availability: 1992 to 1995 (pre-HAART), 1996 to 1999 (early HAART), and 2000 to 2003 (recent HAART). Finally, we examined the risk factors that could lead to increased rates of selected cancer types among HIV-infected persons.

See also:

Print
Editors' Notes 729
Summary for Patients I-46

Web-Only
Appendix
Appendix Tables
Appendix Figures
Conversion of graphics into slides

METHODS

Adult and Adolescent Spectrum of HIV Disease Project

The ASD Project was a multicenter, prospective, observational surveillance project established by the Centers for Disease Control and Prevention (CDC) in 1990 in collaboration with local health departments, including af-

filiated health care centers in 11 geographical areas (Atlanta, Georgia; Los Angeles, California; Dallas, Houston, and San Antonio, Texas; Denver, Colorado; Detroit, Michigan; New Orleans, Louisiana; New York City, New York; Seattle, Washington; and Bayamón, Puerto Rico). Detailed methods for the ASD Project are described elsewhere (46). Participating medical facilities identified HIV-infected patients age 13 years or older. The investigators conducted an initial medical record review for the 12 months preceding enrollment to document sociodemographic characteristics; HIV risk factors; occurrence of AIDS-defining opportunistic illnesses according to the 1993 revised AIDS surveillance definition from the CDC (47); other illnesses, including cancer; medication use; CD4 lymphocyte counts and other relevant laboratory test results; and hospitalizations or other uses of the medical care system. Thereafter, investigators conducted follow-up medical record reviews every 6 months to collect matching interval data. The ASD Project collected detailed information about cancer diagnoses, including anatomical site; morphology; and International Classification of Diseases, Ninth Revision, codes. The investigators enrolled more than 60 000 HIV-infected persons and collected more than 180 000 person-years of observation.

HIV Outpatient Study

The HOPS is an ongoing, multicenter, prospective, observational cohort study that has continuously recruited and followed HIV-infected patients age 18 years or older since 1992 at 9 HIV specialty clinics in 8 U.S. cities (Oakland and San Leandro, California; Denver, Colorado; Tampa, Florida; Chicago, Illinois; Stonybrook, New York; Philadelphia, Pennsylvania; and Washington, DC). Detailed methods for HOPS are described elsewhere (1, 48). Data from physician–patient interactions are electronically collected at the time of clinical encounter and then submitted for central processing and analysis. Data collected include sociodemographic characteristics, HIV risk factors, symptoms, all diagnoses (both definitive and presumptive), medications prescribed, CD4 lymphocyte counts, and all other laboratory test results. Cases of cancer are defined by using clinical information about new cancer diagnoses. The HOPS investigators have enrolled over 8500 HIV-infected persons and collected more than 32 000 person-years of observation with more than 280 000 visits.

Surveillance, Epidemiology, and End Results Program

The SEER program is an ongoing active and passive cancer surveillance system that collects incidence and survival data from 13 geographically defined, population-based central cancer registries in the United States (Oakland, San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; Detroit, Michigan; Atlanta, Georgia; rural Georgia; Connecticut; Iowa; New Mexico; Utah; Alaska; and Hawaii) (45). Geographical areas are selected for inclusion in the SEER program on the basis of ability to operate and maintain a high-quality, population-based cancer reporting system and presence of epidemiologically significant population subgroups. The SEER program includes HIV-infected persons who probably represent fewer than 1% of the total population. We excluded SEER data from Alaska, Hawaii, and rural Georgia from this analysis to best match SEER registries to the ASD Project and HOPS areas. The SEER program defines cancer cases by using anatomical site and histology codes.

Context

Antiretroviral therapy has improved survival of HIV-infected individuals and dramatically decreased cases of AIDS-defining cancer. However, some evidence from small or selected populations with AIDS suggests that non–AIDS-defining cancer cases have increased.

Contribution

This study found that the incidence of several types of non–AIDS-defining cancer (Hodgkin lymphoma; melanoma; leukemia; and cancer of the liver, lung, anus, vagina, oropharynx, colon or rectum, and kidney) were significantly higher among a large, diverse, HIV-infected population than in the general population reported in the SEER database.

Implication

Patients infected with HIV—and their clinicians—should be alert for signs of non–AIDS-related cancer.

—The Editors

Cancer Definition

For this study, we analyzed data on cases of cancer diagnosed from 1992 to 2003. To accurately calculate incidence, we excluded persons in whom cancer was diagnosed within the year before enrollment (prevalent cases), as well as participant observation time after cancer diagnosis. However, we included cases of cancer occurring after cancer of a different type and corresponding participant observation times. Definitions of cancer categories for all cancer types observed in this analysis were established on the basis of the anatomical site of primary significance and International Classification of Diseases, Ninth Revision, codes (**Appendix Table 1**, available at www.annals.org). We calculated incidence rates for types of cancer that occurred at least 5 times in the combined ASD Project and HOPS population during the study period (**Appendix Table 2**, available at www.annals.org). Preliminary examination of the combined ASD Project and HOPS data indicated that the 3 AIDS-defining cancer types and 9 non–AIDS-defining cancer types occurred most frequently (>25 incident cases); we included these types in the trend and multivariable risk factor analyses. We had sufficient power (≥80%) to detect 1.5-fold differences in incidence over time for 6 of the cancer types examined: colorectal, Hodgkin lymphoma, lung, cervical, Kaposi sarcoma, and

non-Hodgkin lymphoma. We excluded recurrences, metastases, and cases of in situ cancer from the analysis.

Statistical Analysis

We calculated incidence rates for persons 15 to 84 years of age as the collective number of newly diagnosed cancer cases annually for the overall analysis period (1992 to 2003) and the pre-HAART (1992 to 1995), early HAART (1996 to 1999), and recent HAART (2000 to 2003) subperiods to account for the transition to and stabilization of HAART use. Incidence rates were expressed per 100 000 prospective person-years of observation during these same periods. Person-years varied slightly for each cancer type due to the exclusion of prevalent cases. We computed person-years at risk for cancer after HIV diagnosis from date of enrollment. Termination was the date of cancer diagnosis, last follow-up visit, or death. We examined incidence rates in the ASD Project and HOPS separately and found them to be similar (**Appendix Table 2**, available at www.annals.org). Because cancer incidence estimated from the ASD Project and HOPS databases were not statistically different, we combined their data to measure cancer incidence among the HIV-infected population captured by both of these studies. In addition, because the ASD Project and HOPS samples are demographically different, the combined ASD Project and HOPS database is more representative of the HIV-infected population than either study alone. We determined cancer incidence rates for the general population by using data from SEER; the SEER rates were directly standardized according to the distribution of 14 age groups, 3 race groups, and sex of the ASD Project and HOPS population. We derived 95% CIs by assuming that the number of cancer cases in each standardization group followed a Poisson distribution (49). To compare the incidence of cancer in the HIV-infected population with that in the general population, we calculated standardized rate ratios for the entire observation period (1992 to 2003) because annual data were too sparse (50, 51).

To evaluate trends over time in incidence of specific types of cancer in the HIV-infected population, we used multivariable Poisson regression in a model controlling for age (15 to 34 years, 35 to 59 years, ≥60 years), race (white, black, other), sex, HIV risk group (men who have sex with men vs. other), nadir CD4 count ($<0.200 \times 10^9$ cells/L, 0.200 to 0.499×10^9 cells/L, ≥0.500 cells/L), and antiretroviral therapy (any vs. none). The linear trend denotes the estimated average change in incidence rate from pre-HAART to early HAART and from early to recent HAART. To evaluate trends over time in the incidence of a specific type of cancer in the SEER population, we used a weighted multivariable Poisson regression to assess linear trends in a model weighted according to the age, race, and sex distribution of the combined ASD Project and HOPS population. To determine whether cancer incidence in the HIV-infected population changed over time relative to the general population, we included a 2-way interaction term between trend and study sample in the multivariable model. To describe factors associated with each type of cancer among HIV-infected persons, we used multivariable Poisson regression, including the covariates as already defined for linear trend, age, race, sex, HIV risk group, nadir CD4 count, antiretroviral use, and hepatitis B or C infection (liver cancer only). We chose these covariates because they had a known association with cancer or were markers of immune function, and we adjusted for them simultaneously.

Ethical Review

Both the ASD Project and HOPS have been reviewed annually since their inception by the CDC and each participating site's institutional review board. The ASD Project was granted a waiver of informed consent by the relevant institutional review boards; informed consent was obtained and renewed annually for HOPS. The institutional review board of the National Cancer Institute reviewed SEER and granted the program a waiver of informed consent.

Role of the Funding Source

The CDC supported data collection through cooperative agreements with local health departments (ASD Project) and a contract with the Cerner Corporation (HOPS). The funding source had no role in the design, analysis, or interpretation of the data or in the approval of the manuscript.

RESULTS

From 1992 to 2003, 54 780 HIV-infected persons (47 832 persons from the ASD Project and 6948 from HOPS) contributed 157 819 person-years of observation. The median follow-up time was 2.0 years in the ASD Project and 2.6 years in HOPS. Of the 3550 incidents of cancer identified in the combined ASD Project and HOPS data for this analysis, 2842 (80%) were categorized as AIDS-defining and 708 (20%) as non–AIDS-defining. Of the 27 types of cancer observed, 5 non–AIDS-defining types of cancer occurred seldom or never: penile (4 cases), uterine (2 cases), ovarian (2 cases), gallbladder (0 cases), and biliary (0 cases).

Table 1 shows the age, sex, and race distributions of the combined ASD Project and HOPS and SEER populations. The populations differed in age, race, and sex distributions; HIV-infected persons were more likely to be male (76%) and nonwhite (61%). The age distribution of the combined ASD Project and HOPS population was clustered among young adults (range, 25 to 50 years), whereas the age distribution of the SEER population was more evenly distributed. Distribution of observation time was evenly divided among the 3 periods for both populations (**Table 1**).

Cancer Incidence in the HIV-Infected Population Compared with the General Population

The incidence of several non–AIDS-defining types of cancer was significantly higher in the HIV-infected popu-

lation than in the general population: anal (standardized rate ratio [SRR], 42.9 [95% CI, 34.1 to 53.3]), vaginal (21.0 [CI, 11.2 to 35.9]), Hodgkin lymphoma (14.7 [CI, 11.6 to 18.2]), liver (7.7 [CI, 5.7 to 10.1]), lung (3.3 [CI, 2.8 to 3.9]), melanoma (2.6 [CI, 1.9 to 3.6]), oropharyngeal (2.6 [CI, 1.9 to 3.4]), leukemia (2.5 [CI, 1.6 to 3.8]), colorectal (2.3 [CI, 1.8 to 2.9]), and renal (1.8 [CI, 1.1 to 2.7]). Incidence was significantly lower for prostate cancer (standardized rate ratio, 0.6 [CI, 0.4 to 0.8]) (**Appendix Table 2** and **Appendix Figures 1** and **2**, available at www.annals.org). We found no significant difference between the 2 populations in the rates of other types of cancer we examined.

Incidence Rates among HIV-Infected Persons

The analysis of trends over time in cancer rates for the HIV-infected population indicated that incidence rates decreased significantly for Kaposi sarcoma and non-Hodgkin lymphoma and increased significantly across the 3 periods for anal, prostate, and colorectal cancer; melanoma; and Hodgkin lymphoma (**Table 2; Appendix Tables 3** and **4** and **Appendix Figure 3**, available at www.annals.org). We observed no change in the rates of cervical cancer and several non–AIDS-defining types of cancer (liver, lung, oropharyngeal, and breast cancer).

Incidence Rates among the General Population

Among the general population, standardized incidence rates for Kaposi sarcoma, non-Hodgkin lymphoma, cervical cancer, lung cancer, and oropharyngeal cancer decreased significantly across the 3 periods (**Table 2**). Incidence rates for anal, colorectal, liver, and prostate cancer increased significantly across the 3 periods, and incidence rates for Hodgkin lymphoma, melanoma, and breast cancer remained unchanged.

Relative Incidence Rates in the HIV-Infected and General Populations

The relative incidence of Kaposi sarcoma and non-Hodgkin lymphoma among our HIV-infected study population decreased over time compared with the general population (**Table 3**; **Appendix Table 5** and **Appendix Figure 4**, available at www.annals.org). Conversely, the higher overall relative incidence of anal cancer in the HIV-infected population increased over time, with the adjusted rate ratio almost doubling during the analytic period.

Risk Factors for Cancer

Acquisition of HIV through male–male sex was associated with increased risk for Kaposi sarcoma (relative risk, 2.88; $P < 0.001$) and non-Hodgkin lymphoma (1.53; $P < 0.001$). Antiretroviral therapy was independently associated with decreased risk for Kaposi sarcoma (relative risk, 0.61; $P < 0.001$), non-Hodgkin lymphoma (0.68; $P < 0.001$), cervical cancer (0.48; $P = 0.019$), breast cancer (0.35; $P = 0.013$), colorectal cancer (0.50; $P = 0.027$), and lung cancer (0.52; $P < 0.003$). A low nadir CD4 count was associated with increased risk for Kaposi sarcoma (relative risk, 8.34; $P < 0.001$), non-Hodgkin lymphoma (6.03; $P < 0.001$), cervical cancer (3.70; $P = 0.010$), anal cancer (5.82; $P = 0.017$), colorectal cancer (6.27; $P = 0.013$), and lung cancer (2.42; $P = 0.017$). Co-infection with hepatitis B or C was associated with increased risk for liver cancer (relative risk, 3.63; $P < 0.001$).

Table 1. **Study Population Characteristics, by Contribution to Total Person-Years of Observation***

Characteristic	Person-Years of Observation, %	
	ASD and HOPS† (157 819 Person-Years)	SEER‡ (334 802 121 Person-Years)
Age		
15–19 y	0.5	9.0
20–24 y	3.2	9.1
25–29 y	9.9	10.0
30–34 y	19.0	11.0
35–39 y	23.0	11.0
40–44 y	19.0	10.0
45–49 y	13.0	9.0
50–54 y	6.9	7.4
55–59 y	3.2	5.7
60–64 y	1.5	4.6
65–69 y	0.6	4.1
70–74 y	0.2	3.6
75–79 y	0.0	3.0
80–84 y	0.0	2.0
Race		
White, non-Hispanic	39.0	63.0
Black, non-Hispanic	42.0	10.0
Other	19.0	27.0
Sex		
Male	76.0	49.0
Female	24.0	51.0
CD4 cell count		
$<0.200 \times 10^9$ cells/L	54.7	–
$0.200–0.499 \times 10^9$ cells/L	35.8	–
$\geq 0.500 \times 10^9$ cells/L	9.5	–
HIV database		
ASD	87.0	–
HOPS	13.0	–
Observation period		
1992–1995	30.59	31.86
1996–1999	34.01	33.29
2000–2003	35.40	34.85

* ASD = Adult and Adolescent Spectrum of Disease Project; HOPS = HIV Outpatient Study; SEER = Surveillance, Epidemiology, and End Results, 1992–2003.
† Included Oakland, San Leandro, and Los Angeles, California; Denver, Colorado; Tampa, Florida; Atlanta, Georgia; Chicago, Illinois; New York City and Stonybrook, New York; Philadelphia, Pennsylvania; Washington, DC; Dallas, Houston, and San Antonio, Texas; Detroit, Michigan; New Orleans, Louisiana; Seattle, Washington; and Bayamón, Puerto Rico.
‡ Included Oakland, San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; Detroit, Michigan; Atlanta, Georgia; Connecticut; Iowa; New Mexico; and Utah and excluded rural Georgia, Alaska, and Hawaii for this analysis to best match ASD and HOPS areas.

DISCUSSION

In the largest analyses of cancer incidence trends among HIV-infected persons in the United States, we observed significantly higher rates of several types of cancer from 1992 to 2003 among HIV-infected persons than in the general population. Non–AIDS-defining types of cancer with higher incidence rates were anal, colorectal, liver, lung, oropharyngeal, renal, and vaginal cancer; Hodgkin lymphoma; leukemia; and melanoma. These findings are consistent with previous reports of cancer incidence among persons with HIV or AIDS (**Table 4**). We extend these previous findings by examining cancer incidence trends over time among persons with all stages of HIV infection, showing that incidence rates increased significantly for melanoma; Hodgkin lymphoma; and colorectal, anal, and prostate cancer—despite the advent of HAART. Immune dysfunction (52); concomitant infection with oncogenic viruses (53–55); and lifestyle factors, such as smoking, may account for the higher cancer incidence among HIV-infected persons.

Immunosuppression may accelerate the progression of melanoma and other types of cancer in individuals who are already predisposed to them, as described in studies of transplant recipients (56–62). In our study, a low nadir CD4 cell count was associated with significantly increased risk for colorectal cancer, whereas use of antiretroviral therapy significantly decreased risk, suggesting that pathogenesis of colorectal cancer may be immune-mediated; this finding is consistent with previous reports (63). However, incidence rates for melanoma and colorectal cancer increased significantly across the 3 periods, suggesting a role of other contributing factors (such as behavioral or lifestyle factors).

Although survival in Hodgkin lymphoma has improved, rates of Hodgkin lymphoma have increased in the HAART era (64). The strong association of Hodgkin lymphoma with Epstein–Barr virus infection in HIV-infected individuals and the influence of immunosuppression may explain this finding (35); Righetti and colleagues (65) suggested that immune reconstitution while receiving HAART increases B-cell stimulation and the number of Epstein–Barr virus–infected cells, which may in turn increase risk for Epstein–Barr virus–associated cancer.

Anal cancer is the only type that increased in both incidence among HIV-infected persons and relative incidence compared with the general population over time. Although this finding is concerning, it is not surprising. The predominance of men who have sex with men among the HIV-infected population and the resultant higher prevalence of anal human papillomavirus (HPV) infection are associated with anal intraepithelial neoplasia (66, 67). The interaction between HIV and HPV allows for persistence of HPV infection in HIV-infected persons, who are more commonly infected with the oncogenic HPV subtypes 16 and 18, leading to development of dysplasia (14, 68, 69). Because HAART does not alter the incidence or progression of anal intraepithelial neoplasia (20, 70), persons who are successfully treated with HAART but are co-infected

Table 2. **Trends in Standardized Incidence Rates of AIDS-Defining and Non–AIDS-Defining Types of Cancer among Persons with HIV***

Cancer	ASD and HOPS† (HIV-Infected Population)				SEER‡ (General Population)			
	Standardized Incidence Rate§ per 100 000 Person-Years			Linear Trend‖ *P* Value	Standardized Incidence Rate§ per 100 000 Person-Years			Linear Trend¶ *P* Value
	1992–1995	1996–1999	2000–2003		1992–1995	1996–1999	2000–2003	
Kaposi sarcoma**	2628.5	848.8	356.3	<0.001	14.7	5.4	3.3	<0.001
Non-Hodgkin lymphoma**	1011.8	494.1	212.2	<0.001	17.0	14.3	12.8	<0.001
Cervical**	149.9	194.6	134.5	0.63	15.5	14.2	11.4	<0.001
Anal	19.0	48.3	78.2	<0.001	1.0	1.2	1.3	0.02
Hodgkin lymphoma	34.3	54.7	64.4	0.03	3.4	3.5	3.6	0.12
Liver	19.9	35.9	35.4	0.35	3.3	4.1	4.7	0.01
Lung	91.9	93.8	84.9	0.29	31.6	27.2	23.4	<0.001
Melanoma	15.6	24.8	37.5	<0.05	9.0	9.8	9.9	0.12
Oropharyngeal	29.0	31.0	36.9	0.22	14.4	13.0	11.7	0.01
Colorectal	39.9	39.7	66.2	0.03	20.4	20.5	21.1	<0.01
Breast	56.0	69.9	96.0	0.09	85.6	85.7	82.7	0.08
Prostate	14.7	38.0	37.5	0.01	47.4	54.6	60.9	<0.001

* Refer to **Appendix Table 4** (available at www.annals.org) for independent results from ASD and HOPS. ASD = Adult and Adolescent Spectrum of Disease Project; HOPS = HIV Outpatient Study; SEER = Surveillance, Epidemiology, and End Results, 1992–2003.
† Included Oakland, San Leandro, and Los Angeles, California; Denver, Colorado; Tampa, Florida; Atlanta, Georgia; Chicago, Illinois; New York City and Stonybrook, New York; Philadelphia, Pennsylvania; Washington, DC; Dallas, Houston, and San Antonio, Texas; Detroit, Michigan; New Orleans, Louisiana; Seattle, Washington; and Bayamón, Puerto Rico.
‡ Included Oakland, San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; Detroit, Michigan; Atlanta, Georgia; Connecticut; Iowa; New Mexico; and Utah and excluded rural Georgia, Alaska, and Hawaii for this analysis to best match ASD and HOPS areas.
§ Rates standardized to 14 age groups, 3 race categories, and sex distribution of combined ASD and HOPS HIV data, 1992–2003.
‖ Average change in incidence rate from 1992–1995 to 1996–1999 and from 1996–1999 to 2000–2003.
¶ Average change in standardized incidence rate from 1992–1995 to 1996–1999 and from 1996–1999 to 2000–2003.
** AIDS-defining cancer.

Table 3. **Standardized Rate Ratios of AIDS-Defining and Non–AIDS-Defining Types of Cancer among Persons with HIV***

Cancer	Standardized Rate Ratio† (95% CI), ASD and HOPS‡ to SEER§		
	1992–1995	1996–1999	2000–2003
Kaposi sarcoma‖¶	197.0 (185.0–209.7)	174.7 (156.3–195.4)	112.1 (94.7–132.8)
Non-Hodgkin lymphoma‖¶	79.4 (72.4–87.1)	40.3 (35.6–45.6)	17.0 (14.3–20.3)
Cervical‖	11.8 (7.2–19.2)	13.3 (9.1–19.4)	10.1 (6.5–15.7)
Anal**	31.4 (16.2–60.8)	48.2 (32.4–71.6)	59.4 (44.0–80.3)
Hodgkin lymphoma	11.7 (7.5–18.2)	16.6 (11.5–24.0)	17.9 (12.6–25.5)
Liver	9.3 (4.8–18.0)	10.2 (6.5–16.1)	7.0 (4.6–10.7)
Lung	3.5 (2.5–4.9)	3.8 (2.8–5.0)	3.6 (2.8–4.6)
Melanoma	1.3 (0.6–2.8)	2.2 (1.3–3.9)	3.0 (2.0–4.7)
Oropharyngeal	2.5 (1.4–4.4)	2.5 (1.6–4.1)	3.0 (2.0–4.5)
Colorectal	2.5 (1.6–4.0)	2.0 (1.3–3.1)	2.4 (1.7–3.3)
Breast	0.7 (0.3–1.9)	0.8 (0.4–1.6)	1.1 (0.7–1.8)
Prostate	0.3 (0.1–0.9)	0.7 (0.4–1.3)	0.7 (0.4–1.0)

* Refer to **Appendix Table 5** (available at www.annals.org) for independent results from ASD and HOPS. ASD = Adult and Adolescent Spectrum of Disease Project; HOPS = HIV Outpatient Study; SEER = Surveillance, Epidemiology, and End Results, 1992–2003.
† Calculated from incidence rates standardized to 14 age groups, 3 race categories, and sex distribution of combined ASD and HOPS HIV data, 1992–2003.
‡ Included Oakland, San Leandro, Los Angeles, California; Denver, Colorado; Tampa, Florida; Atlanta, Georgia; Chicago, Illinois; New York City and Stonybrook, New York; Philadelphia, Pennsylvania; Washington, DC; Dallas, Houston, and San Antonio, Texas; Detroit, Michigan; New Orleans, Louisiana; Seattle, Washington; and Bayamón, Puerto Rico.
§ Included Oakland, San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; Detroit, Michigan; Atlanta, Georgia; Connecticut; Iowa; New Mexico; and Utah and excluded rural Georgia, Alaska, and Hawaii for this analysis to best match ASD and HOPS areas.
‖ AIDS-defining cancer.
¶ Significant ($P < 0.001$) decreasing trend.
** Significant ($P = 0.02$) increasing trend.

with HIV and HPV are expected to remain at greater risk for anal cancer over time and incidence rates are expected to increase as HIV-infected persons live longer.

We found a lower rate of prostate cancer among HIV-infected persons than in the general population, in contrast to smaller published reports (19, 40). However, our results were consistent with those from an AIDS–cancer registry match (32) in which the investigators attributed the lower

Table 4. **Summary of Studies Reporting Incidence of Multiple Cases of Non–AIDS-Defining Cancer in Persons with HIV or AIDS***

Study, Year (Reference)	Location	Study Type	Persons with HIV or AIDS, *n*	Cases of Cancer, *n*	Period	Trend in HAART Era
Grulich et al., 2002 (22)	Australia	Registry match	13 067 with HIV or AIDS	35 275	1978–1996	No
Grulich et al., 1999 (23)	Australia	Registry match	3616 with HIV or AIDS	778	1980–1993	No
Newnham et al., 2005 (24)	England	Registry match	33 190 with HIV or AIDS	2022	1985–2001	No
Del Maso et al., 2003 (25)	Italy	Registry match	12 104 with AIDS	1162	1985–1998	No
Allardice et al., 2003 (26)	Scotland	Registry match	2574 with HIV	162	1981–1996	No
Galceran et al., 2007 (27)	Spain	Registry match	1659 with AIDS	192	1981–1999	No
Clifford et al., 2005 (28)	Switzerland	Registry match	7304 with HIV or AIDS	624	1985–2003	Yes
Mbulaiteye et al., 2006 (29)	Uganda	Registry match	12 607 with HIV or AIDS	378	1988–2002	No
Bedimo et al., 2004 (30)	United States: Alabama	Cohort	2882 with HIV or AIDS	227	1989–2002	Yes
Biggar et al., 2007 (31)	United States: 12 regions	Registry match	325 516 with AIDS	22 180	1990–2002	Yes
Biggar et al., 2004 (32)	United States: 11 regions	Registry match	8828 elderly with AIDS	1148	1981–1996	No
Burgi et al., 2005 (33)	United States, military HIV clinics	Cohort	4144 with HIV or AIDS	133	1988–2003	Yes
Engels et al., 2006 (34)	United States: 11 regions	Registry match	375 933 with AIDS	20 569	1980–2002	Yes
Frisch et al., 2001 (35)	United States: 11 regions	Registry match	302 834 with AIDS	35 275	1978–1996	No
Frisch et al., 2000 (36)	United States: 11 regions	Registry match	309 365 with AIDS	1586	1995–1998	No
Gallagher et al., 2001 (37)	United States: New York	Registry match	122 993 with AIDS	12 698	1981–1994	No
Goedert et al., 2006 (38)	United States: 12 regions	Registry match	85 268 women with AIDS	368	1980–2002	Yes
Hessol et al., 2004 (39)	United States: 6 regions	Cohort	1559 women with HIV or AIDS	41	1994–2001	No
Hessol et al., 2007 (40)	United States: San Francisco	Registry match	14 210 with AIDS	482	1990–2000	No
Mubulaiteye et al., 2003 (41)	United States: 11 regions	Registry match	82 217 with AIDS	3557	1990–1996	No
Phelps et al., 2001 (42)	United States: 4 regions	Cohort	871 women with HIV or AIDS	26	1993–1995	No
International Collaboration on HIV and Cancer, 2000 (43)	North America, Europe, Australia	Cohort	47 936 with HIV or AIDS	–	1992–1999	Yes

* HAART = highly active antiretroviral therapy.

observed risk in the general population to less prostate cancer screening. In our analyses, rates of prostate cancer among HIV-infected persons increased over time but remained consistently lower than in the general population. We know of no reason why HIV-related immunosuppression would decrease prostate cancer risk (71). Differential screening among men with and without HIV may explain these results, although many men with HIV are under closer medical supervision. In addition, persons with HIV are known to have lower androgen levels, which may in turn decrease their risk for prostate cancer. Because androgens have long been known to contribute to the risk for prostate cancer (19), patients receiving replacement therapy with exogenous testosterone or anabolic steroids may need to be monitored carefully.

Our study has limitations. First, the case ascertainment standard for SEER is 98% (44), whereas case ascertainment in the ASD Project and HOPS is undoubtedly lower (75% to 85%, as determined by an ASD Project–local cancer registry match in select project areas). In addition, the completeness of cancer ascertainment has not been formally evaluated in the ASD Project or HOPS. Because the HIV incidence rate is in the numerator, the potential bias would be to underestimate the standardized rate ratio—suggesting that standardized rate ratios showing increased incidence are minimum estimates of the rate disparity. Standardized rate ratios may be further underestimated by double-counting of cases in areas where SEER registries overlap with the ASD Project or HOPS sites, because SEER does not collect data on HIV status. Second, although the ASD Project and HOPS have large cohorts, they are not representative of all persons with HIV infection in the United States, and SEER is not representative of the general U.S. population; our findings may therefore have limited generalizability. The SEER program covers 14% of the U.S. population, has a higher proportion of foreign-born persons, and tends to be more urban than the general population (44). In a comparison of SEER data with data from the National Program of Cancer Registries, the incidence rates of head or neck cancer, anal cancer, and Hodgkin disease were similar; however, the rate of lung cancer was slightly underestimated and the rates of melanoma and liver cancer were slightly overestimated (72). The ASD Project and HOPS also represent different geographical areas from SEER. Third, we had inadequate information on smoking behavior; because the prevalence of smoking varies among specific groups in the United States (for example, by sex, race, or HIV risk), some characteristics associated with cancer in our analyses may have been surrogates for smoking status. Finally, we could not account for changes in screening practices over time.

In conclusion, our findings indicate that HIV-infected persons are at higher risk than the general population for many non–AIDS-defining types of cancer. In addition to encouraging tobacco cessation, HIV care providers should be aware of these elevated risks and screen for preventable diseases, such as cervical and colorectal cancer (73–75). Screening programs for early detection and treatment of precancerous anal lesions should be evaluated and will probably become more important as the HIV-infected population ages and lives longer. Furthermore, primary prevention strategies to reduce HPV infection and HPV-associated diseases, such as vaccination and circumcision, warrant further evaluation.

From the Centers for Disease Control and Prevention, Emory University, and Northrop Grumman Information Technology, Atlanta, Georgia, and the University of Illinois at Chicago, Chicago, Illinois.

Acknowledgment: The authors thank Harold Jaffe and Robert Newton, Department of Public Health, University of Oxford, and Valerie Beral and Andrew Roddam, Nuffield Department of Clinical Medicine, Cancer Research UK Epidemiology Unit, University of Oxford, for their helpful comments and suggestions on this analysis. They also thank Milton Eisner of the SEER program for support with data management and analysis.

Grant Support: The ASD Project was funded through a program announcement and cooperative agreement with Program Announcement 00005 and HIV/AIDS Surveillance Seroprevalence. The HOPS was funded through a contract with the Cerner Corporation and the CDC (200-2006-18797).

Potential Financial Conflicts of Interest: None disclosed.

Reproducible Research Statement: *Study protocol:* Not available. *Statistical code:* Available from the authors. *Data set:* The ASD Project, HOPS, and SEER program are all public-use data sets and are available to readers. However, confidentiality protections that govern the ASD Project and HOPS data require authors to strip record identifiers; it will therefore take some time to make these data available. In addition, CDC's heightened security procedures require persons who want to analyze ASD Project and HOPS data to 1) prepare a written proposal for CDC review and approval, 2) sign confidentiality and data use agreements, 3) conduct analyses in Atlanta, and 4) go through CDC security clearance for access to facilities. The authors would be happy to facilitate these procedures for persons interested in conducting analyses using ASD Project and HOPS data and welcome these requests.

Requests for Single Reprints: Pragna Patel, MD, MPH, Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, 1600 Clifton Road, Mailstop E-46, Atlanta, GA 30333; e-mail, plp3@cdc.gov.

Current author addresses and author contributions are available at www.annals.org.

References

1. **Palella FJ Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, et al.** Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. N Engl J Med. 1998;338:853-60. [PMID: 9516219]

2. **Moore RD, Chaisson RE.** Natural history of HIV infection in the era of combination antiretroviral therapy. AIDS. 1999;13:1933-42. [PMID: 10513653]

3. **Lohse N, Hansen AB, Pedersen G, Kronborg G, Gerstoft J, Sørensen HT, et al.** Survival of persons with and without HIV infection in Denmark, 1995-

2005. Ann Intern Med. 2007;146:87-95. [PMID: 17227932]
4. **Brodt HR, Kamps BS, Gute P, Knupp B, Staszewski S, Helm EB.** Changing incidence of AIDS-defining illnesses in the era of antiretroviral combination therapy. AIDS. 1997;11:1731-8. [PMID: 9386808]
5. **Eltom MA, Jemal A, Mbulaiteye SM, Devesa SS, Biggar RJ.** Trends in Kaposi's sarcoma and non-Hodgkin's lymphoma incidence in the United States from 1973 through 1998. J Natl Cancer Inst. 2002;94:1204-10. [PMID: 12189223]
6. **Rabkin CS, Biggar RJ, Baptiste MS, Abe T, Kohler BA, Nasca PC.** Cancer incidence trends in women at high risk of human immunodeficiency virus (HIV) infection. Int J Cancer. 1993;55:208-12. [PMID: 8370617]
7. **Grulich AE, Li Y, McDonald AM, Correll PK, Law MG, Kaldor JM.** Decreasing rates of Kaposi's sarcoma and non-Hodgkin's lymphoma in the era of potent combination anti-retroviral therapy. AIDS. 2001;15:629-33. [PMID: 11317001]
8. **Gates AE, Kaplan LD.** AIDS malignancies in the era of highly active antiretroviral therapy. Oncology (Williston Park). 2002;16:441-51, 456, 459. [PMID: 12017534]
9. **Lichtenstein KA, Ward DJ, Moorman AC, Delaney KM, Young B, Palella FJ Jr, et al. HIV Outpatient Study Investigators.** Clinical assessment of HIV-associated lipodystrophy in an ambulatory population. AIDS. 2001;15:1389-98. [PMID: 11504960]
10. **Sackoff JE, Hanna DB, Pfeiffer MR, Torian LV.** Causes of death among persons with AIDS in the era of highly active antiretroviral therapy: New York City. Ann Intern Med. 2006;145:397-406. [PMID: 16983127]
11. **Holmberg SD, Moorman AC, Williamson JM, Tong TC, Ward DJ, Wood KC, et al. HIV Outpatient Study (HOPS) investigators.** Protease inhibitors and cardiovascular outcomes in patients with HIV-1. Lancet. 2002;360:1747-8. [PMID: 12480430]
12. **Mondy K, Yarasheski K, Powderly WG, Whyte M, Claxton S, DeMarco D, et al.** Longitudinal evolution of bone mineral density and bone markers in human immunodeficiency virus-infected individuals. Clin Infect Dis. 2003;36:482-90. [PMID: 12567307]
13. **Grinspoon S.** Mechanisms and strategies for insulin resistance in acquired immune deficiency syndrome. Clin Infect Dis. 2003;37 Suppl 2:S85-90. [PMID: 12942379]
14. **Gates AE, Kaplan LD.** AIDS malignancies in the era of highly active antiretroviral therapy. Oncology (Williston Park). 2002;16:657-65; discussion 665, 668-70. [PMID: 12108891]
15. **Hessol NA, Katz MH, Liu JY, Buchbinder SP, Rubino CJ, Holmberg SD.** Increased incidence of Hodgkin disease in homosexual men with HIV infection. Ann Intern Med. 1992;117:309-11. [PMID: 1637026]
16. **Bower M, Powles T, Nelson M, Shah P, Cox S, Mandelia S, et al.** HIV-related lung cancer in the era of highly active antiretroviral therapy. AIDS. 2003;17:371-5. [PMID: 12556691]
17. **Dal Maso L, Polesel J, Serraino D, Franceschi S.** Lung cancer in persons with AIDS in Italy, 1985-1998 [Letter]. AIDS. 2003;17:2117-9. [PMID: 14502015]
18. **Chaturvedi AK, Pfeiffer RM, Chang L, Goedert JJ, Biggar RJ, Engels EA.** Elevated risk of lung cancer among people with AIDS. AIDS. 2007;21:207-13. [PMID: 17197812]
19. **Crum NF, Spencer CR, Amling CL.** Prostate carcinoma among men with human immunodeficiency virus infection. Cancer. 2004;101:294-9. [PMID: 15241826]
20. **Bower M, Powles T, Newsom-Davis T, Thirlwell C, Stebbing J, Mandalia S, et al.** HIV-associated anal cancer: has highly active antiretroviral therapy reduced the incidence or improved the outcome? J Acquir Immune Defic Syndr. 2004;37:1563-5. [PMID: 15577408]
21. **Cooley TP.** Non-AIDS-defining cancer in HIV-infected people. Hematol Oncol Clin North Am. 2003;17:889-99. [PMID: 12852661]
22. **Grulich AE, Li Y, McDonald A, Correll PK, Law MG, Kaldor JM.** Rates of non-AIDS-defining cancers in people with HIV infection before and after AIDS diagnosis. AIDS. 2002;16:1155-61. [PMID: 12004274]
23. **Grulich AE, Wan X, Law MG, Coates M, Kaldor JM.** Risk of cancer in people with AIDS. AIDS. 1999;13:839-43. [PMID: 10357384]
24. **Newnham A, Harris J, Evans HS, Evans BG, Møller H.** The risk of cancer in HIV-infected people in southeast England: a cohort study. Br J Cancer. 2005;92:194-200. [PMID: 15583689]
25. **Dal Maso L, Franceschi S, Polesel J, Braga C, Piselli P, Crocetti E, et al.** Cancer and AIDS Registy Linkage Study. Risk of cancer in persons with AIDS in Italy, 1985-1998. Br J Cancer. 2003;89:94-100. [PMID: 12838307]
26. **Allardice GM, Hole DJ, Brewster DH, Boyd J, Goldberg DJ.** Incidence of malignant neoplasms among HIV-infected persons in Scotland. Br J Cancer. 2003;89:505-7. [PMID: 12888821]
27. **Galceran J, Marcos-Gragera R, Soler M, Romaguera A, Ameijide A, Izquierdo A, et al.** Cancer incidence in AIDS patients in Catalonia, Spain. Eur J Cancer. 2007;43:1085-91. [PMID: 17349785]
28. **Clifford GM, Polesel J, Rickenbach M, Dal Maso L, Keiser O, Kofler A, et al. Swiss HIV Cohort.** Cancer risk in the Swiss HIV Cohort Study: associations with immunodeficiency, smoking, and highly active antiretroviral therapy. J Natl Cancer Inst. 2005;97:425-32. [PMID: 15770006]
29. **Mbulaiteye SM, Katabira ET, Wabinga H, Parkin DM, Virgo P, Ochai R, et al.** Spectrum of cancers among HIV-infected persons in Africa: the Uganda AIDS-Cancer Registry Match Study. Int J Cancer. 2006;118:985-90. [PMID: 16106415]
30. **Bedimo R, Chen RY, Accortt NA, Raper JL, Linn C, Allison JJ, et al.** Trends in AIDS-defining and non-AIDS-defining malignancies among HIV-infected patients: 1989-2002. Clin Infect Dis. 2004;39:1380-4. [PMID: 15494916]
31. **Biggar RJ, Chaturvedi AK, Goedert JJ, Engels EA. HIV/AIDS Cancer Match Study.** AIDS-related cancer and severity of immunosuppression in persons with AIDS. J Natl Cancer Inst. 2007;99:962-72. [PMID: 17565153]
32. **Biggar RJ, Kirby KA, Atkinson J, McNeel TS, Engels E. For the AIDS Cancer Match Study Group.** Cancer risk in elderly persons with HIV/AIDS. J Acquir Immune Defic Syndr. 2004;36:861-8. [PMID: 15213571]
33. **Burgi A, Brodine S, Wegner S, Milazzo M, Wallace MR, Spooner K, et al.** Incidence and risk factors for the occurrence of non-AIDS-defining cancers among human immunodeficiency virus-infected individuals. Cancer. 2005;104:1505-11. [PMID: 16104038]
34. **Engels EA, Pfeiffer RM, Goedert JJ, Virgo P, McNeel TS, Scoppa SM, et al. For the HIV/AIDS Cancer Match Study.** Trends in cancer risk among people with AIDS in the United States 1980-2002. AIDS. 2006;20:1645-54. [PMID: 16868446]
35. **Frisch M, Biggar RJ, Engels EA, Goedert JJ. AIDS-Cancer Match Registry Study Group.** Association of cancer with AIDS-related immunosuppression in adults. JAMA. 2001;285:1736-45. [PMID: 11277828]
36. **Frisch M, Biggar RJ, Goedert JJ.** Human papillomavirus-associated cancers in patients with human immunodeficiency virus infection and acquired immunodeficiency syndrome. J Natl Cancer Inst. 2000;92:1500-10. [PMID: 10995805]
37. **Gallagher B, Wang Z, Schymura MJ, Kahn A, Fordyce EJ.** Cancer incidence in New York State acquired immunodeficiency syndrome patients. Am J Epidemiol. 2001;154:544-56. [PMID: 11549560]
38. **Goedert JJ, Schairer C, McNeel TS, Hessol NA, Rabkin CS, Engels EA. HIV/AIDS Cancer Match Study.** Risk of breast, ovary, and uterine corpus cancers among 85, 268 women with AIDS. Br J Cancer. 2006;95:642-8. [PMID: 16868538]
39. **Hessol NA, Seaberg EC, Preston-Martin S, Massad LS, Sacks HS, Silver S, et al. For the WIHS Collaborative Study Group.** Cancer risk among participants in the women's interagency HIV study. J Acquir Immune Defic Syndr. 2004;36:978-85. [PMID: 15220706]
40. **Hessol NA, Pipkin S, Schwarcz S, Cress RD, Bacchetti P, Scheer S.** The impact of highly active antiretroviral therapy on non-AIDS-defining cancers among adults with AIDS. Am J Epidemiol. 2007;165:1143-53. [PMID: 17344204]
41. **Mbulaiteye SM, Biggar RJ, Goedert JJ, Engels EA.** Immune deficiency and risk for malignancy among persons with AIDS. J Acquir Immune Defic Syndr. 2003;32:527-33. [PMID: 12679705]
42. **Phelps RM, Smith DK, Heilig CM, Gardner LI, Carpenter CC, Klein RS, et al. HER Study Group.** Cancer incidence in women with or at risk for HIV. Int J Cancer. 2001;94:753-7. [PMID: 11745473]
43. **International Collaboration on HIV and Cancer.** Highly active antiretroviral therapy and incidence of cancer in human immunodeficiency virus-infected adults. J Natl Cancer Inst. 2000;92:1823-30. [PMID: 11078759]
44. **Hankey BF, Ries LA, Edwards BK.** The surveillance, epidemiology, and end results program: a national resource. Cancer Epidemiol Biomarkers Prev. 1999;8:1117-21. [PMID: 10613347]
45. **National Cancer Institute.** Surveillance, epidemiology, and end results. Accessed at www.seer.cancer.gov on 4 April 2008.
46. **Farizo KM, Buehler JW, Chamberland ME, Whyte BM, Froelicher ES,**

Hopkins SG, et al. Spectrum of disease in persons with human immunodeficiency virus infection in the United States. JAMA. 1992;267:1798-805. [PMID: 1347573]
47. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR Recomm Rep. 1992;41:1-19. [PMID: 1361652]
48. **Moorman AC, Holmberg SD, Marlowe SI, Von Bargen JC, Yangco BG, Palella FJ, et al.** Changing conditions and treatments in a dynamic cohort of ambulatory HIV patients: the HIV outpatient study (HOPS). Ann Epidemiol. 1999;9:349-57. [PMID: 10475534]
49. **Dobson AJ, Kuulasmaa K, Eberle E, Scherer J.** Confidence intervals for weighted sums of Poisson parameters. Stat Med. 1991;10:457-62. [PMID: 2028128]
50. **Breslow NE, Day NE.** Statistical Methods in Cancer Research. Vol II, The Design and Analysis of Cohort Studies (IARC Scientific Publication No. 82). Lyon, France: International Agency for Research on Cancer; 1987.
51. **Sahai H, Khurshid A.** Statistics in Epidemiology: Methods, Techniques, and Applications. Boca Raton, Florida: CRC Press; 1996.
52. **Smith C, Lilly S, Mann KP, Livingston E, Myers S, Lyerly HK, et al.** AIDS-related malignancies. Ann Med. 1998;30:323-44. [PMID: 9783831]
53. **Wistuba II, Behrens C, Gazdar AF.** Pathogenesis of non-AIDS-defining cancers: a review. AIDS Patient Care STDS. 1999;13:415-26. [PMID: 10870595]
54. **Moradpour D, Blum HE.** Pathogenesis of hepatocellular carcinoma. Eur J Gastroenterol Hepatol. 2005;17:477-83. [PMID: 15827436]
55. **Forastiere A, Koch W, Trotti A, Sidransky D.** Head and neck cancer. N Engl J Med. 2001;345:1890-900. [PMID: 11756581]
56. **Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM.** Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet. 2007;370:59-67. [PMID: 17617273]
57. **Hollenbeak CS, Todd MM, Billingsley EM, Harper G, Dyer AM, Lengerich EJ.** Increased incidence of melanoma in renal transplantation recipients. Cancer. 2005;104:1962-7. [PMID: 16187269]
58. **Euvrard S, Kanitakis J, Claudy A.** Skin cancers after organ transplantation. N Engl J Med. 2003;348:1681-91. [PMID: 12711744]
59. **Adani GL, Baccarani U, Lorenzin D, Bresadola V, Currò G, Sainz M, et al.** Role of cytomegalovirus and Epstein-Barr virus in patients with de novo colon cancer after renal transplantation. Tumori. 2006;92:219-21. [PMID: 16869239]
60. **Villeneuve PJ, Schaubel DE, Fenton SS, Shepherd FA, Jiang Y, Mao Y.** Cancer incidence among Canadian kidney transplant recipients. Am J Transplant. 2007;7:941-8. [PMID: 17331115]
61. **Vajdic CM, McDonald SP, McCredie MR, van Leeuwen MT, Stewart JH, Law M, et al.** Cancer incidence before and after kidney transplantation. JAMA. 2006;296:2823-31. [PMID: 17179459]
62. **Adami J, Gäbel H, Lindelöf B, Ekström K, Rydh B, Glimelius B, et al.** Cancer risk following organ transplantation: a nationwide cohort study in Sweden. Br J Cancer. 2003;89:1221-7. [PMID: 14520450]
63. **Beni EJ, Park J, Francois F.** Use of flexible sigmoidoscopy to screen for colorectal cancer in HIV-infected patients 50 years of age and older. Arch Intern Med. 2006;166:1626-31. [PMID: 16908796]
64. **Gérard L, Galicier L, Boulanger E, Quint L, Lebrette MG, Mortier E, et al.** Improved survival in HIV-related Hodgkin's lymphoma since the introduction of highly active antiretroviral therapy. AIDS. 2003;17:81-7. [PMID: 12478072]
65. **Righetti E, Ballon G, Ometto L, Cattelan AM, Menin C, Zanchetta M, et al.** Dynamics of Epstein-Barr virus in HIV-1-infected subjects on highly active antiretroviral therapy. AIDS. 2002;16:63-73. [PMID: 11741164]
66. **Chin-Hong PV, Palefsky JM.** Natural history and clinical management of anal human papillomavirus disease in men and women infected with human immunodeficiency virus. Clin Infect Dis. 2002;35:1127-34. [PMID: 12384848]
67. **Dunne EF, Burstein GR, Stone KM.** Anogenital human papillomavirus infection in males. Adolesc Med. 2003;14:613-32, vi-vii. [PMID: 15122164]
68. **Mitsuyasu R.** Oncological complications of human immunodeficiency virus disease and hematologic consequences of their treatment. Clin Infect Dis. 1999; 29:35-43. [PMID: 10433562]
69. **Daling JR, Madeleine MM, Johnson LG, Schwartz SM, Shera KA, Wurscher MA, et al.** Human papillomavirus, smoking, and sexual practices in the etiology of anal cancer. Cancer. 2004;101:270-80. [PMID: 15241823]
70. **Palefsky JM, Holly EA, Ralston ML, Da Costa M, Bonner H, Jay N, et al.** Effect of highly active antiretroviral therapy on the natural history of anal squamous intraepithelial lesions and anal human papillomavirus infection. J Acquir Immune Defic Syndr. 2001;28:422-8. [PMID: 11744829]
71. **Nelson WG, De Marzo AM, Isaacs WB.** Prostate cancer. N Engl J Med. 2003;349:366-81. [PMID: 12878745]
72. **Wingo PA, Jamison PM, Hiatt RA, Weir HK, Gargiullo PM, Hutton M, et al.** Building the infrastructure for nationwide cancer surveillance and control—a comparison between the National Program of Cancer Registries (NPCR) and the Surveillance, Epidemiology, and End Results (SEER) Program (United States). Cancer Causes Control. 2003;14:175-93. [PMID: 12749723]
73. **Centers for Disease Control and Prevention.** Sexually transmitted diseases treatment guidelines, 2006. MMWR Recomm Rep. 2006;55:1-94. [PMID: 16888612]
74. **Smith RA, Saslow D, Sawyer KA, Burke W, Costanza ME, Evans WP 3rd, et al. American Cancer Society High-Risk Work Group.** American Cancer Society guidelines for breast cancer screening: update 2003. CA Cancer J Clin. 2003;53:141-69. [PMID: 12809408]
75. **Franceschi S, Jaffe H.** Cervical cancer screening of women living with HIV infection: a must in the era of antiretroviral therapy. Clin Infect Dis. 2007;45: 510-3. [PMID: 17638204]

Current Author Addresses: Dr. Patel: Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, 1600 Clifton Road, Mailstop E-46, Atlanta, GA 30333.
Ms. Hanson: Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, 1600 Clifton Road, Mailstop E-48, Atlanta, GA 30333.
Dr. Sullivan: Rollins School of Public Health, Emory University, 1518 Clifton Road NE, 4th Floor, Atlanta GA 30322.
Dr. Novak: University of Illinois at Chicago, 808 South Wood Street, Room 888 M/C735, Chicago, IL 60612.
Ms. Moorman and Dr. Holmberg: Division of Viral Hepatitis, Centers for Disease Control and Prevention, 1600 Clifton Road, Mailstop G-37, Atlanta, GA 30333.
Mr. Tong and Dr. Brooks: Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, 1600 Clifton Road, Mailstop E-45, Atlanta, GA 30333.

Author Contributions: Conception and design: P. Patel, D.L. Hanson, P.S. Sullivan, R.M. Novak, S.D. Holmberg, J.T. Brooks.
Analysis and interpretation of the data: P. Patel, D.L. Hanson, P.S. Sullivan, R.M. Novak, T.C. Tong, J.T. Brooks.
Drafting of the article: P. Patel, D.L. Hanson, R.M. Novak, J.T. Brooks.
Critical revision of the article for important intellectual content: P. Patel, D.L. Hanson, P.S. Sullivan, R.M. Novak, S.D. Holmberg, J.T. Brooks.
Final approval of the article: P. Patel, P.S. Sullivan, R.M. Novak, A.C. Moorman, S.D. Holmberg, J.T. Brooks.
Statistical expertise: D.L. Hanson, T.C. Tong.
Obtaining of funding: A.C. Moorman, S.D. Holmberg.
Administrative, technical, or logistic support: P.S. Sullivan, S.D. Holmberg.
Collection and assembly of data: P.S. Sullivan, T.C. Tong.

Appendix

ASD Project Investigators

AIDS Research Consortium of Atlanta, Atlanta, Georgia: Melanie Thompson, MD, and Erica Sinclair, MS.

Denver Department of Health and Hospitals, Denver, Colorado: David Cohen, MD; Arthur Davidson, MD; and Cornelius Rietmeijer, MD.

Los Angeles County Department of Health Services, Los Angeles, California: Wendy Garland and Amy Wohl, PhD.

Louisiana Department of Health, New Orleans, Louisiana: Anne Morse, BS.

Michigan Department of Health, Detroit, Michigan: Linda Wotring, PhD, and Eve Mokotoff, MPH.

New York City Department of Health, New York City, New York: Chris Murrill, PhD, and Marie Antoinette Bernard, MD.

Universidad Central de Caribe, Bayamón, Puerto Rico: Alejandro Amill; Robert Hunter, MD; and Maria de los Angeles Gomez, PhD.

Puerto Rico Department of Health, San Juan, Puerto Rico: Sandra Miranda.

Seattle-King County Department of Health, Seattle, Washington: Susan Buskin, PhD, and Elizabeth Barash.

Texas Department of Health, Austin, Texas: Sylvia Odem, MPH.

Parkland Hospital, Dallas, Texas: Philip Keiser, MD.

Department of Health and Human Services, Houston, Texas: Adebowale Awosika-Olumo, MD.

HOPS Investigators

Cerner, Vienna, Virginia: Kathleen C. Wood and Rose K. Baker.

Northwestern University Medical School, Chicago, Illinois: Frank J. Palella, Joan S. Chmiel, and Janet Cheley.

Rose Medical Center, Denver, Colorado: Kenneth A. Lichtenstein, Kenneth S. Greenberg, Benjamin Young, Barbara Widick, Cheryl Stewart, and Peggy Zellner.

Infectious Disease Research Institute, Tampa, Florida: Bienvenido G. Yangco and Kalliope Halkias.

Dupont Circle Physicians Group, Washington, DC: Douglas J. Ward and Charles A. Fiorentino.

State University of New York, Stonybrook, New York: Jack Fuhrer, Linda Ording-Bauer, Rita Kelly, and Jane Esteves.

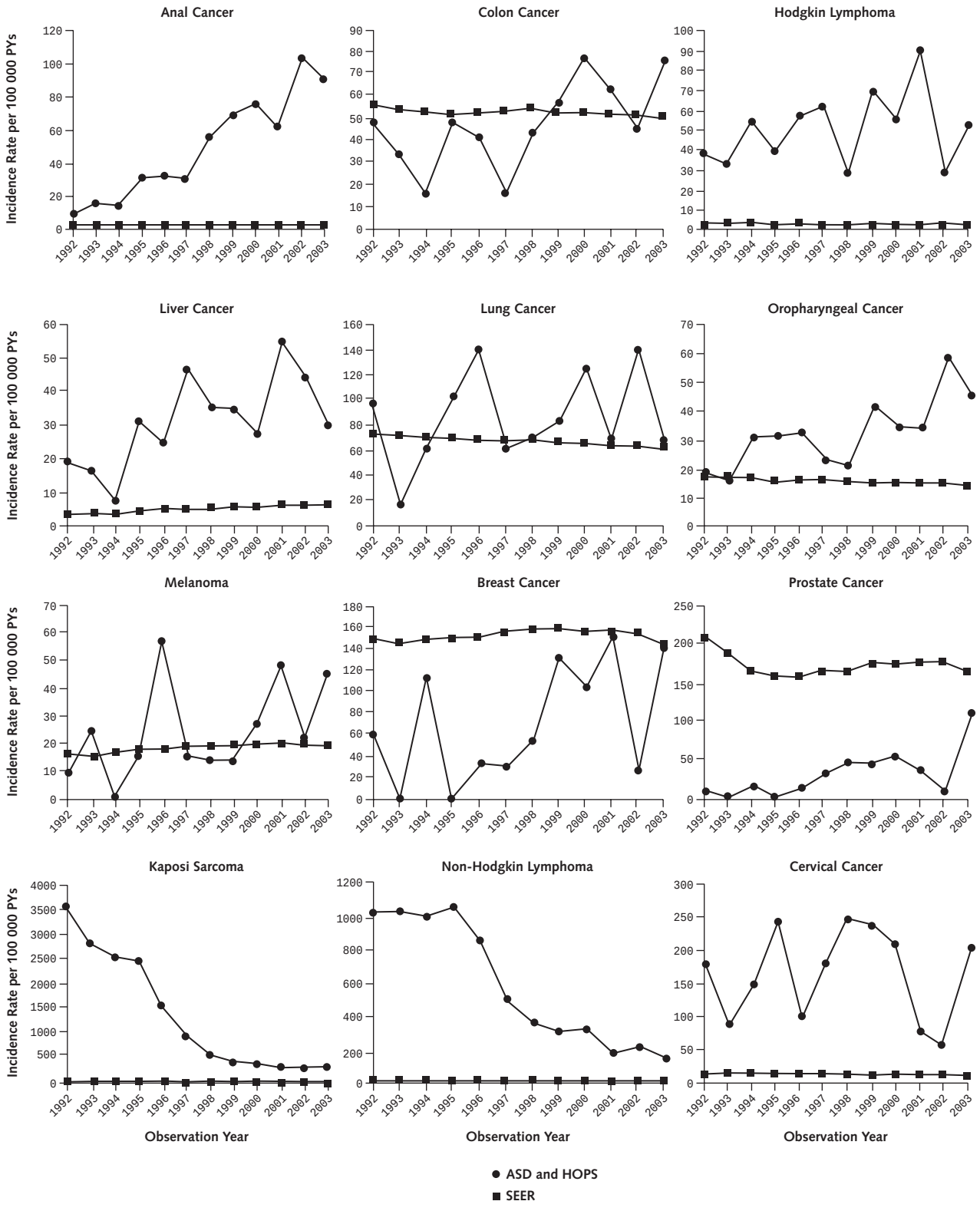
Temple University Hospital, Philadelphia, Pennsylvania: Ellen M. Tedaldi, Ramona Christian, and Faye Ruley.

Adult Immunology Clinic, Oakland, California: Joseph B. Marzouk, Roger T. Phelps, and Mark Rachel.

Fairmont Hospital, San Leandro, California: Robert E. McCabe and Mark Rachel.

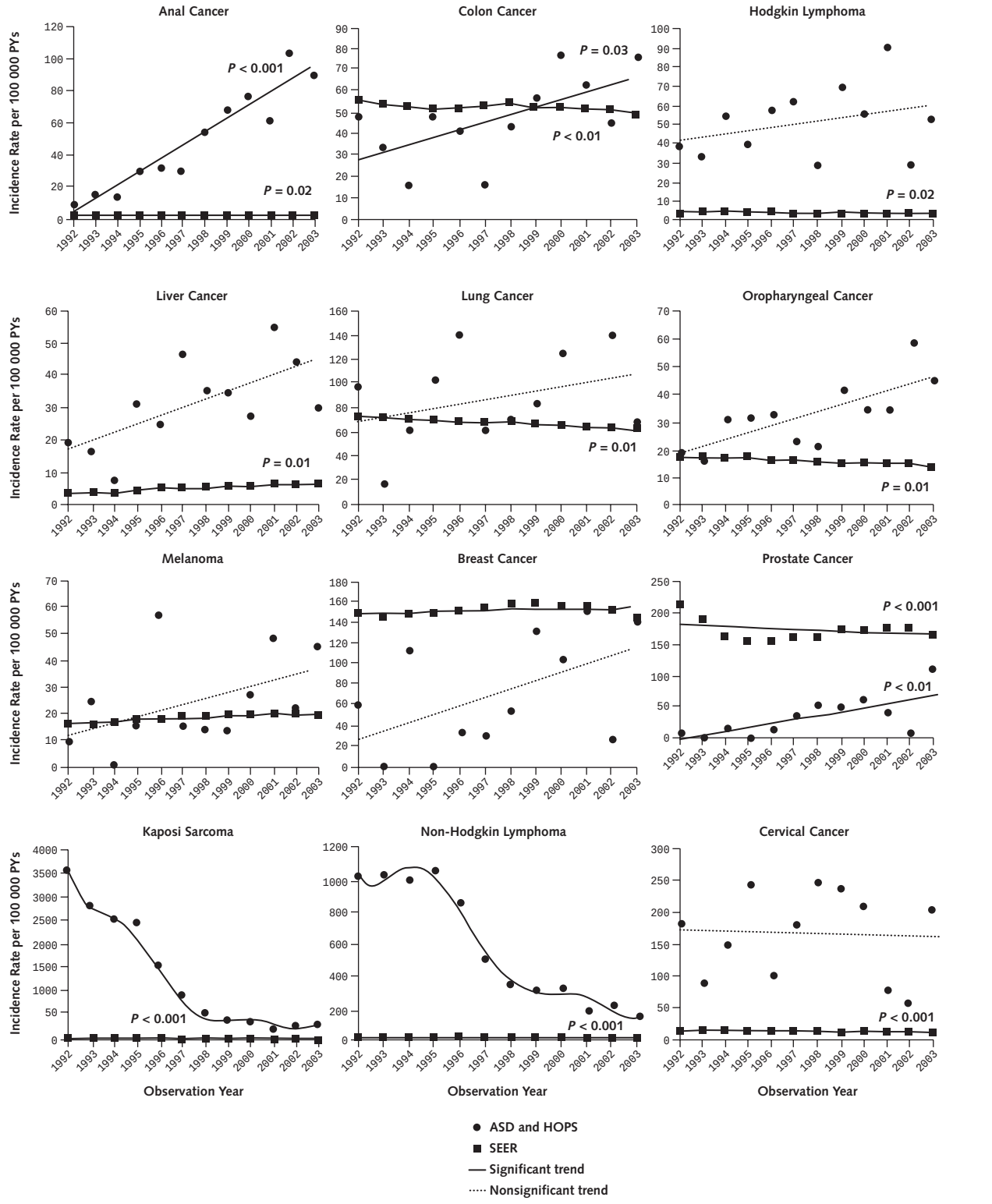
University of Illinois at Chicago, Chicago, Illinois: Richard M. Novak, Jonathan P. Uy, and Andrea Wendrow.

Appendix Figure 1. **Annual incidence rates of 3 AIDS-defining (*top row*) and 9 non–AIDS-defining types of cancer among HIV-infected persons and the general population.**



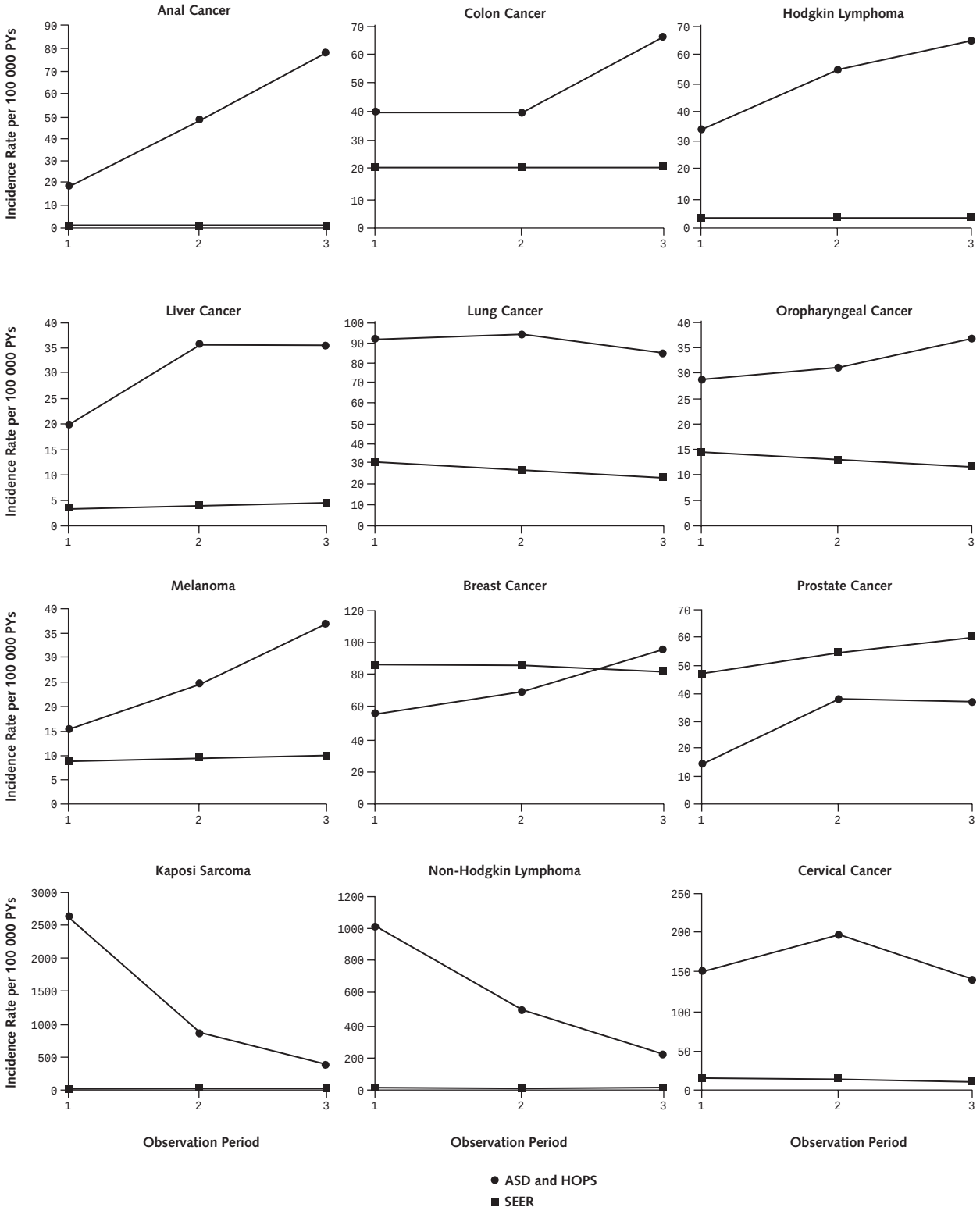
Rates are unadjusted incidence rates per 100 000 person-years (*PYs*). Data for HIV-infected persons are drawn from the Adult and Adolescent Spectrum of Disease Project (*ASD*) and the HIV Outpatient Study (*HOPS*); general population data are estimated from Surveillance, Epidemiology, and End Results (*SEER*) program data, 1992–2003.

Appendix Figure 2. **Trends in annual incidence rates of 3 AIDS-defining (*top row*) and 9 non-AIDS-defining types of cancer among HIV-infected persons relative to the general population, using Poisson regression and nonlinear spline representations, 1992–2003.**



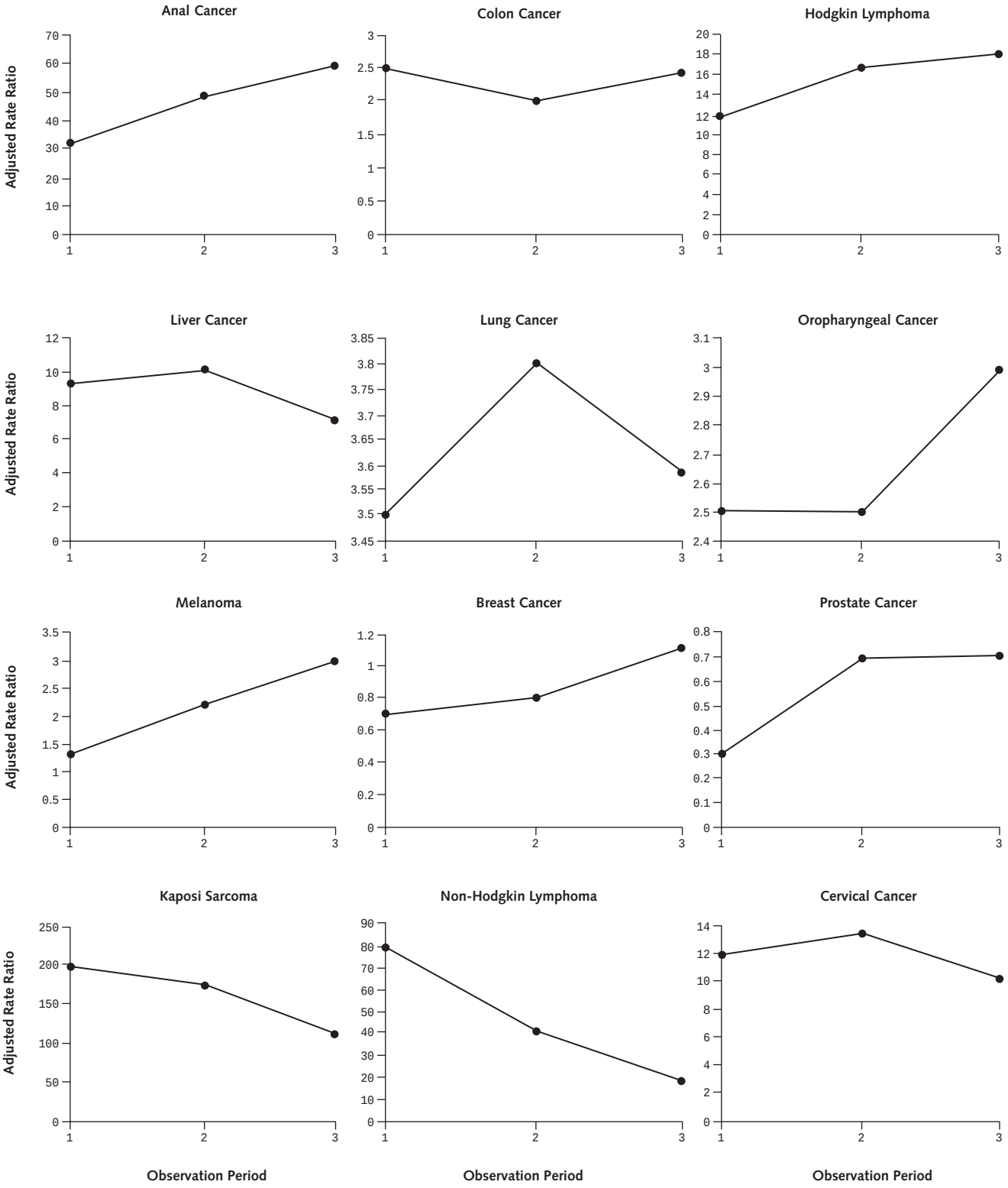
Data for HIV-infected persons are drawn from the Adult and Adolescent Spectrum of Disease Project (*ASD*) and the HIV Outpatient Study (*HOPS*); general population data are estimated from Surveillance, Epidemiology, and End Results (*SEER*) program data. *P* values of significant trends are depicted; dotted lines represent nonsignificant results. PY = person-year.

Appendix Figure 3. **Trends in standardized incidence rates of 3 AIDS-defining (*top row*) and 9 non–AIDS-defining types of cancer among HIV-infected persons and the general population, stratified by 3 periods from 1992 to 2003.**



Data for HIV-infected persons are drawn from the Adult and Adolescent Spectrum of Disease Project (*ASD*) and the HIV Outpatient Study (*HOPS*); general population data are estimated from Surveillance, Epidemiology, and End Results (*SEER*) program data.

Appendix Figure 4. **Standardized rate ratios of 3 AIDS-defining (*top row*) and 9 non–AIDS-defining types of cancer among HIV-infected persons relative to the general population, stratified by 3 periods from 1992 to 2003.**



Data for HIV-infected persons are drawn from the Adult and Adolescent Spectrum of Disease Project (*ASD*) and the HIV Outpatient Study (*HOPS*); general population data are estimated from Surveillance, Epidemiology, and End Results (*SEER*) program data.

Appendix Table 1. Cancer Definition, as Determined from Source Data*

Cancer Categories Used for Analysis	Source Data	
	Diagnosis Code and Anatomical Site	ICD-9 Code
AIDS-defining cancer		
Kaposi sarcoma	Kaposi sarcoma (all sites)	173, 176
Non-Hodgkin lymphoma	Non-Hodgkin lymphoma	200, 202.0–202.2, 202.8–202.9
Cervical (invasive)	Cervix, uterus	180
Non–AIDS-defining cancer		
Anal	Anus, anal canal, anorectum	154.2–154.8
Vaginal	Vagina, vulva	184.0–184.4
Hodgkin lymphoma	Hodgkin lymphoma	201
Liver	Liver	155.0, 155.2
Lung	Lung, bronchus	162.2–162.9
Melanoma	Melanoma of skin	172
Oropharyngeal	Oral cavity, pharynx, larynx	140–149, 161
Leukemia	Leukemia (all sites)	202.4, 203.1, 204, 205, 206, 207, 208
Colorectal	Colon, rectum, rectosigmoid junction	153, 154.0, 154.1, 159.0
Esophageal	Esophagus	150
Renal	Kidney, renal pelvis, ureter, urinary organs	189
Testicular	Testicles	186
Multiple myeloma	Multiple myeloma	203
Stomach	Stomach	151
Breast	Breast	174
Pancreatic	Pancreas	157
Prostate	Prostate	185
Thyroid	Thyroid	193
Bladder	Bladder, urachus, ureteric orifice	188
Penile	Penis	187.1–187.4
Uterine	Uterus	182
Ovarian	Ovary, fallopian tube, uterine adnexa	183
Gallbladder	Gallbladder	156.0
Biliary	Intrahepatic and extrahepatic bile ducts	155.1, 156.1, 156.8, 156.9

* ICD-9 = International Classification of Disease, Ninth Revision.

Appendix Table 4. Trends in Standardized Incidence Rates of AIDS-Defining and Non–AIDS-Defining Types of Cancer among HIV-Infected Persons*

Cancer	ASD†				HOPS‡			
	Standardized Incidence Rate§ per 100 000 Person-Years			Linear Trend‖ *P* Value	Standardized Incidence Rate§ per 100 000 Person-Years			Linear Trend‖ *P* Value
	1992–1995	1996–1999	2000–2003		1992–1995	1996–1999	2000–2003	
Kaposi sarcoma¶	2760.3	921.5	389.4	<0.001	1692.0	529.8	237.3	<0.001
Non-Hodgkin lymphoma¶	1042.5	530.2	204.0	<0.001	1046.4	321.2	227.1	0.005
Cervical¶	161.3	190.7	113.6	0.32	0	276.5	194.5	0.25
Anal	18.2	42.5	63.3	0.001	84.5	91.2	119.8	0.03
Hodgkin lymphoma	33.4	55.8	61.2	0.05	33.2	54.2	70.9	0.35
Liver	21.2	31.1	30.5	0.69	9.7	64.8	69.5	0.48
Lung	91.7	88.4	80.6	0.54	45.9	93.3	76.5	0.52
Melanoma	15.1	24.3	33.5	0.12	13.8	24.5	46.5	0.32
Oropharyngeal	29.0	38.3	38.3	0.28	25.5	21.3	55.3	0.31
Colorectal	44.1	46.1	77.6	0.02	10.6	32.4	24.1	0.80
Breast	57.7	69.5	80.7	0.26	0	73.7	183.6	0.13
Prostate	15.2	34.8	29.3	0.06	0	58.2	76.9	0.17

* ASD = Adult and Adolescent Spectrum of Disease Project; HOPS = HIV Outpatient Study.
† Included Los Angeles, California; Denver, Colorado; Atlanta, Georgia; Chicago, Illinois; New York City, New York; Dallas, Houston, and San Antonio, Texas; Detroit, Michigan; New Orleans, Louisiana; Seattle, Washington; and Bayamón, Puerto Rico.
‡ Included Oakland and San Leandro, California; Denver, Colorado; Tampa, Florida; Chicago, Illinois; Stonybrook, New York; Philadelphia, Pennsylvania; and Washington, DC.
§ Rates standardized to 14 age groups, 3 race categories, and sex distribution of combined ASD and HOPS HIV data, 1992–2003.
‖ Average change in standardized incidence rate from 1992–1995 to 1996–1999 and from 1996–1999 to 2000–2003.
¶ AIDS-defining cancer.

Appendix Table 5. Adjusted Rate Ratios of AIDS-Defining and Non–AIDS-Defining Types of Cancer among HIV-Infected Persons*

Cancer	ASD†/SEER§				HOPS‡/SEER§			
	Adjusted Rate Ratio‖			Linear Trend¶ *P* Value	Adjusted Rate Ratio‖			Linear Trend¶ *P* Value
	1992–1995	1996–1999	2000–2003		1992–1995	1996–1999	2000–2003	
Kaposi sarcoma**	203.8	181.7	116.8	0.01	130.9	125.7	85.1	0.12
Non-Hodgkin lymphoma**	82.4	43.9	16.8	<0.001	54.1	26.3	18.0	<0.001
Cervical**	12.5	13.0	9.0	0.31	NE	15.4	16.2	NE
Anal	27.1	41.7	46.7	0.09	71.7	76.4	100.7	0.33
Hodgkin lymphoma	11.0	16.8	17.7	0.09	19.1	15.7	18.6	0.88

* ASD = Adult and Adolescent Spectrum of Disease Project; HOPS = HIV Outpatient Study; NE = not estimated (due to insufficient data); SEER = Surveillance, Epidemiology, and End Results, 1992–2003.
† Included Los Angeles, California; Denver, Colorado; Atlanta, Georgia; Chicago, Illinois; New York City, New York; Dallas, Houston, and San Antonio, Texas; Detroit, Michigan; New Orleans, Louisiana; Seattle, Washington; and Bayamón, Puerto Rico.
‡ Included Oakland and San Leandro, California; Denver, Colorado; Tampa, Florida; Chicago, Illinois; Stonybrook, New York; Philadelphia, Pennsylvania; and Washington, DC.
§ Included Oakland, San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; Detroit, Michigan; Atlanta, Georgia; Connecticut; Iowa; New Mexico; and Utah and excluded rural Georgia, Alaska, and Hawaii for this analysis to best match ASD and HOPS areas.
‖ Poisson regression model–based estimates, adjusted for age, race, and sex.
¶ By study population 2-way interaction effect.
** AIDS-defining cancer.

Appendix Table 2. **Standardized Rate Ratios of AIDS-Defining and Non–AIDS-Defining Types of Cancer***

Cancer	ASD†	HOPS‡	ASD and HOPS§ (HIV-Infected Population)			SEER‖ (General Population)				SRR¶ (95% CI)
	Observed Rate per 100 000 PYs (95% CI)	Observed Rate per 100 000 PYs (95% CI)	Cases, *n*	PYs	Observed Rate per 100 000 PY (95% CI)	Cases, *n*	PYs	Observed Rate per 100 000 PYs (95% CI)	Standardized Rate** per 100 000 PYs (95% CI)	
Kaposi sarcoma††	1356.9 (1293.9–1422.2)	685.0 (583.9–798.6)	1904	152 103	1251.8 (1196.2–1309.3)	9452	334 802 121	2.8 (2.8–2.9)	7.7 (6.4–9.0)	163.0 (155.7–170.4)
Non-Hodgkin lymphoma††	585.4 (544.8–628.1)	413.3 (336.6–502.2)	875	156 665	558.5 (552.1–596.8)	70 339	334 802 121	21.0 (20.9–21.2)	14.6 (13.1–16.1)	38.3 (35.8–40.9)
Cervical††	161.4 (121.3–210.6)	192.9 (88.2–366.3)	63	38 118	165.3 (127.0–211.5)	20 449	170 285 195	12.0 (11.8–12.2)	13.6 (11.8–15.4)	12.2 (9.4–15.6)
Anal	39.9 (29.9–52.2)	113.6 (75.5–164.2)	81	157 534	51.4 (40.8–63.9)	4933	334 802 121	1.5 (1.4–1.5)	1.2 (0.8–1.6)	42.9 (34.1–53.3)
Vaginal	32.7 (16.3–58.5)	42.4 (5.1–153.3)	13	38 365	33.9 (18.0–57.9)	5511	170 285 195	3.2 (3.2–3.3)	1.6 (1.0–2.2)	21.0 (11.2–35.9)
Hodgkin lymphoma	49.7 (38.4–63.2)	60.9 (34.1–100.4)	81	157 456	51.4 (40.9–63.9)	11 187	334 802 121	3.3 (3.3–3.4)	3.5 (2.8–4.3)	14.7 (11.6–18.2)
Liver	27.1 (19.0–37.5)	56.7 (31.0–95.1)	50	157 698	31.7 (23.5–41.8)	17 659	334 802 121	5.3 (5.2–5.4)	4.1 (3.5–4.8)	7.7 (5.7–10.1)
Lung	84.3 (69.3–101.3)	113.4 (75.4–163.9)	140	157 625	88.8 (74.7–104.8)	225 816	334 802 121	67.5 (67.2–67.7)	27.0 (25.5–28.5)	3.3 (2.8–3.9)
Melanoma	20.3 (13.4–29.6)	48.6 (25.1–85.0)	39	157 621	24.7 (17.6–33.8)	61 709	334 802 121	18.4 (18.3–18.6)	9.5 (8.2–10.7)	2.6 (1.9–3.6)
Oropharyngeal	30.8 (22.1–41.8)	44.6 (22.3–79.8)	52	157 583	33.0 (24.6–43.3)	53 821	334 802 121	16.1 (16.0–16.2)	12.8 (11.6–14.0)	2.6 (1.9–3.4)
Leukemia	16.5 (10.4–25.1)	8.1 (1.0–29.2)	24	157 688	15.2 (9.8–22.7)	40 773	334 802 121	12.2 (12.1–12.3)	6.0 (5.1–6.9)	2.5 (1.6–3.8)
Colorectal	50.4 (39.1–64.0)	28.4 (11.4–58.4)	74	157 567	47.0 (36.9–59.0)	173 929	334 802 121	52.0 (51.7–52.2)	20.6 (19.1–22.0)	2.3 (1.8–2.9)
Esophageal	4.5 (1.7–9.8)	12.1 (2.5–35.5)	9	157 704	5.7 (2.6–10.8)	16 088	334 802 121	4.8 (4.7–4.9)	3.1 (2.6–3.7)	1.8 (0.8–3.5)
Renal	14.3 (8.6–22.3)	12.1 (2.5–35.5)	22	157 667	14.0 (8.8–21.1)	43 419	334 802 121	13.0 (12.8–13.1)	7.9 (6.9–8.8)	1.8 (1.1–2.7)
Testicular	13.1 (7.0–22.4)	5.0 (0.1–27.9)	14	119 254	11.7 (6.4–19.7)	11 593	164 516 926	7.0 (6.9–7.2)	7.3 (5.9–8.8)	1.6 (0.9–2.7)
Myeloma	5.3 (2.1–10.1)	0.0 (0.0–15.0)	7	157 699	4.4 (1.8–9.2)	20 149	334 802 121	6.0 (5.9–6.1)	3.2 (2.6–3.7)	1.4 (0.6–2.9)
Stomach	7.5 (3.6–13.8)	0.0 (0.0–15.0)	10	157 703	6.3 (3.0–11.7)	29 830	334 802 121	8.9 (8.8–9.0)	4.8 (4.1–5.5)	1.3 (0.6–2.4)
Breast	68.5 (43.4–102.7)	127.5 (46.8–277.6)	29	38 298	75.7 (50.7–108.8)	258 664	170 285 195	151.9 (151.3–152.5)	83.4 (79.3–87.6)	0.9 (0.6–1.3)
Pancreatic	4.5 (1.7–9.8)	0.0 (0.0–15.0)	6	157 695	3.8 (1.4–8.3)	37 622	334 802 121	11.2 (11.1–11.4)	4.5 (3.9–5.2)	0.8 (0.3–1.8)
Prostate	25.2 (16.3–37.2)	70.2 (38.4–117.7)	39	119 210	32.7 (23.3–44.7)	285 442	164 516 926	173.5 (172.9–174.1)	55.0 (53.0–57.1)	0.6 (0.4–0.8)
Thyroid	2.3 (0.5–6.6)	8.1 (1.0–29.3)	5	157 676	3.2 (1.0–7.4)	28 931	334 802 121	8.6 (8.5–8.7)	5.1 (4.3–5.9)	0.6 (0.2–1.5)
Bladder	2.3 (0.5–6.6)	8.1 (1.0–29.2)	5	157 689	3.2 (1.0–7.4)	69 988	334 802 121	20.9 (20.8,21.1)	6.7 (5.9,7.5)	0.5 (0.2–1.1)

* ASD = Adult and Adolescent Spectrum of Disease Project; HOPS = HIV Outpatient Study; PY = person-year; SEER = Surveillance, Epidemiology, and End Results, 1992–2003; SRR = standardized rate ratio.
† Included Los Angeles, California; Denver, Colorado; Atlanta, Georgia; Chicago, Illinois; New York City, New York; Dallas, Houston, and San Antonio, Texas; Detroit, Michigan; New Orleans, Louisiana; Seattle, Washington; and Bayamon, Puerto Rico.
‡ Included Oakland and San Leandro, California; Denver, Colorado; Tampa, Florida; Chicago, Illinois; Stonybrook, New York; Philadelphia, Pennsylvania; and Washington, DC.
§ Included Oakland, San Leandro, and Los Angeles, California; Denver, Colorado; Tampa, Florida; Atlanta, Georgia; Chicago, Illinois; New York City and Stonybrook, New York; Philadelphia, Pennsylvania; Washington, DC; Dallas, Houston, and San Antonio, Texas; Detroit, Michigan; New Orleans, Louisiana; Seattle, Washington; and Bayamón, Puerto Rico.
‖ Included Oakland, San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; Detroit, Michigan; Atlanta, Georgia; Connecticut; Iowa; New Mexico; and Utah and excluded rural Georgia, Alaska, and Hawaii for this analysis to best match ASD and HOPS areas.
¶ Observed HIV rate (ASD and HOPS) to standardized rate (SEER).
** Rates standardized to 14 age groups, 3 race categories, and sex distribution of combined ASD and HOPS HIV data, 1992–2003.
†† AIDS-defining cancer.

Appendix Table 3. **Multivariable Model Results for Cancer Incidence Trends in HIV Study Population***

Cancer	Adjusted Rate Ratio (*P* Value)												
	Model 1†	Model 2‡	Model 3§										
			1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003
Kaposi sarcoma	0.4 (<0.001)	0.8 (<0.001)	0.8 (<0.01)	0.7 (<0.001)	0.7 (<0.001)	0.5 (<0.001)	0.3 (<0.001)	0.2 (<0.001)	0.1 (<0.001)	0.1 (<0.001)	0.1 (<0.001)	0.1 (<0.001)	0.1 (<0.001)
Non-Hodgkin lymphoma	0.5 (<0.001)	0.8 (<0.001)	1.0 (0.85)	1.0 (0.87)	1.0 (0.87)	0.9 (0.25)	0.5 (<0.001)	0.4 (<0.001)	0.3 (<0.001)	0.4 (<0.001)	0.2 (<0.001)	0.2 (<0.001)	0.2 (<0.001)
Cervical	0.9 (0.63)	1.0 (0.99)	0.5 (0.40)	0.8 (0.75)	1.3 (0.72)	0.5 (0.45)	1.0 (0.96)	1.4 (0.61)	1.4 (0.61)	1.2 (0.75)	0.5 (0.34)	0.3 (0.22)	1.2 (0.80)
Anal	2.0 (<0.001)	1.2 (<0.001)	1.8 (0.64)	1.7 (0.68)	3.3 (0.29)	3.5 (0.27)	3.3 (0.28)	6.2 (0.09)	7.4 (0.06)	8.1 (<0.05)	6.6 (0.07)	10.8 (0.02)	9.5 (0.03)
Hodgkin lymphoma	1.4 (0.03)	1.1 (0.04)	0.9 (0.89)	1.5 (0.49)	1.1 (0.85)	1.8 (0.37)	2.0 (0.25)	1.0 (0.98)	2.5 (0.12)	2.1 (0.24)	3.4 (0.03)	1.1 (0.86)	2.1 (0.26)
Liver	1.2 (0.35)	1.0 (0.36)	0.8 (0.86)	0.4 (0.42)	1.4 (0.68)	1.1 (0.94)	2.0 (0.41)	1.4 (0.68)	1.3 (0.73)	1.0 (0.98)	2.0 (0.39)	1.6 (0.59)	1.1 (0.95)
Lung	1.1 (0.29)	1.0 (0.60)	0.2 (0.02)	0.6 (0.28)	0.9 (0.88)	1.3 (0.57)	0.6 (0.22)	0.6 (0.29)	0.7 (0.42)	1.0 (0.97)	0.8 (0.53)	1.1 (0.83)	0.5 (0.15)
Melanoma	1.5 (<0.05)	1.1 (0.13)	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Oropharyngeal	1.3 (0.22)	1.1 (0.14)	0.9 (0.91)	1.7 (0.56)	1.7 (0.56)	1.7 (0.54)	1.2 (0.84)	1.1 (0.92)	2.1 (0.37)	1.7 (0.53)	1.7 (0.55)	2.8 (0.20)	2.1 (0.38)
Colorectal	1.4 (0.03)	1.1 (0.03)	0.7 (0.59)	0.3 (0.17)	0.9 (0.93)	0.8 (0.78)	0.3 (0.19)	0.9 (0.90)	1.2 (0.74)	1.6 (0.36)	1.3 (0.61)	0.9 (0.91)	1.6 (0.41)
Breast	1.6 (0.09)	1.1 (0.07)	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Prostate	1.8 (<0.01)	1.2 (<0.01)	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE

* The HIV study population was derived from the Adult and Adolescent Spectrum of Disease Project and the HIV Outpatient Study. NE = not estimated (because of insufficient data).
† Includes linear trend over three 4-year periods (see text).
‡ Includes linear trend over twelve 1-year periods.
§ Includes 11 dummy-coded variables for comparison with 1992 cancer incidence.