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Article

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Excess Cancers Among HIV-Infected People in the United States

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Abstract

Background: Nearly 900 000 people in the United States are living with diagnosed human immunodeficiency virus (HIV) infection and therefore increased cancer risk. The total number of cancers occurring among HIV-infected people and the excess number above expected background cases are unknown.

Methods: We derived cancer incidence rates for the United States HIV-infected and general populations from Poisson models applied to linked HIV and cancer registry data and from Surveillance, Epidemiology, and End Results program data, respectively. We applied these rates to estimates of people living with diagnosed HIV at mid-year 2010 to estimate total and expected cancer counts, respectively. We subtracted expected from total cancers to estimate excess cancers.

Results: An estimated 7760 (95% confidence interval [CI] = 7330 to 8320) cancers occurred in 2010 among HIV-infected people, of which 3920 cancers (95% CI = 3480 to 4470) or 50% (95% CI = 48 to 54%) were in excess of expected. The most common excess cancers were non-Hodgkin's lymphoma (NHL; n = 1440 excess cancers, occurring in 88% excess), Kaposi's sarcoma (KS, n = 910, 100% excess), anal cancer (n = 740, 97% excess), and lung cancer (n = 440, 52% excess). The proportion of excess cancers that were AIDS defining (ie, KS, NHL, cervical cancer) declined with age and time since AIDS diagnosis (both $P < .001$). For anal cancer, 83% of excess cases occurred among men who have sex with men, and 71% among those living five or more years since AIDS onset. Among injection drug users, 22% of excess cancers were lung cancer, and 16% were liver cancer.

Conclusions: The excess cancer burden in the US HIV population is substantial, and patterns across groups highlight opportunities for cancer control initiatives targeted to HIV-infected people.

Nearly 900 000 people were living with diagnosed human immunodeficiency virus (HIV) infection in the United States at the end of 2010 (1). Among HIV-infected people, cancer risk is increased because of immunosuppression, frequent coinfection with oncogenic viruses, and risk behaviors including smoking (2–4). Since the introduction of highly active antiretroviral therapy (HAART) in 1996, mortality related to advanced immunodeficiency (ie, acquired immunodeficiency syndrome [AIDS]) has

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declined (5,6), leading to increasing numbers of people living with HIV and an overall aging of the HIV population (7).

Three virus-related cancers are considered by the Centers for Disease Control and Prevention (CDC) to define the onset of AIDS in an HIV-infected person: Kaposi's sarcoma (KS), non-Hodgkin's lymphoma (NHL), and cervical cancer. The incidence of these AIDS-defining cancers (ADCs) has decreased since the introduction of HAART, but the incidence of some non–AIDS defining cancers (NADCs) has increased (8). Due largely to the increasing size and advancing age of the HIV population, the number of NADCs has risen, leading to growth in the overall cancer burden among HIV-infected people (7).

The burden of cancer in a population can be described in terms of the number of cases, both overall and attributable to specific exposures such as infections, alcohol, and excess body mass index (9–12). Such estimates allow cancer and its risk factors to be understood in a broad context to inform research and public health planning. Until recently, incomplete national HIV surveillance data prevented estimation of the cancer burden in the HIV-infected population for the entire United States (7). Some cancer cases are expected in the HIV population, because of background risk alone, and these can be estimated using cancer incidence rates from the general population. However, given higher risks, larger numbers of cases would be expected in the HIV population for many cancer types. These excess cancers highlight differences in the cancer burden between HIV-infected people and the general population, providing one framework for considering how cancer control strategies can be tailored to HIV-infected people. In principle, the excess cancer burden represents cases that could be eliminated if one could intervene on all aspects of being HIV-infected, thus reducing cancer risks to those in the general population.

Defining optimal strategies for cancer prevention and early detection in this growing, high-risk population with unique public health needs is a rising challenge (13). To provide context for research and public health efforts, we quantified the total and excess cancer burden among HIV-infected people in the United States using population-based data from HIV and cancer registries.

Methods

Overall Approach and Data Sources

In overview, we estimated national counts of cancers in HIV-infected individuals by applying cancer incidence rates for HIV-infected people to the US HIV population. We obtained excess counts by subtracting the expected number of cancers, calculated using general population cancer rates.

As described in the Supplementary Methods (available online), we derived cancer rates for the US HIV population from the HIV/AIDS Cancer Match (HACM) Study, a linkage of population-based state HIV and cancer registries (http://www.hivmatch.cancer.gov) (14). Only anonymized data were retained by investigators. The HACM Study was approved by institutional review boards and, as required, at participating registries.

We identified cancers in HIV-infected people from six states in the HACM Study using linked cancer registry data, and counted the first instance of each cancer type. We evaluated 11 cancer outcomes: the three ADCs, five NADCs that occur at elevated rates in HIV-infected people (Hodgkin's lymphoma [HL] and cancers of the lung, anus, liver, and oral cavity/pharynx), and three cancers common in the general population (prostate, colorectum, and female breast). We grouped the remaining cancers into a "miscellaneous" category. KS, NHL, and cervical cancer occurring as AIDS-defining events were classified as occurring among people with HIV-only (ie, people who had not developed AIDS).

We corrected for two known errors in the HACM data (see Supplementary Methods, available online). First, we corrected for outmigration that prevents cancer ascertainment by decreasing person-time by 10% for HIV-infected people assessed 10 or more years since being documented to live in their registry area (15). Second, we increased cancer rates for HIV-infected people by 23.3% to adjust for imperfect sensitivity of the HIV cancer registry match (16).

We obtained 2010 US general population cancer rates from 18 Surveillance, Epidemiology, and End Results (SEER) cancer registries. For KS, we instead used 1973 to 1979 SEER rates, because subsequent rates were strongly influenced by HIV-infected cases (17).

We applied cancer rates to CDC surveillance estimates of the number of individuals living with diagnosed HIV at mid-year (ie, July 1) 2010 (1). Data reported through June 2012 to the CDC's National HIV Surveillance System were used to generate estimates stratified by calendar year, age at year-end, transmission category (ie, sex and HIV risk group), race/ethnicity, and time since AIDS. These estimates adjusted for reporting delays and missing transmission category but not incomplete reporting. To obtain 2010 mid-year estimates, we averaged 2009 and 2010 end-of-year counts.

Statistical Analysis

To estimate 2010 cancer incidence rates for HIV-infected people, we fit Poisson regression models to 2003–2010 HACM data separately for each cancer type. Models included calendar year (as a continuous variable) and adjustment for age, sex, race/ethnicity, HIV risk group, time since AIDS, and registry area (see categories in Table 1 and additional details in the Supplementary Methods, available online). Using these models, we predicted 2010 cancer rates specific to age, sex, race/ethnicity, HIV risk group, time since AIDS, and registry area. We collapsed the six registry-specific incidence rates by weighting estimates based on registry size (see Supplementary Methods, available online).

To estimate total cancers among HIV-infected people, we applied these rates to the 2010 mid-year HIV population stratified by age, sex, race/ethnicity, HIV risk group, and time since AIDS. Separately, we estimated expected cancers by applying SEER rates, stratified by age, sex, and race/ethnicity, to the same population.

We estimated excess cancers by subtracting expected cancers from total cancers. For individual cancer types or demographic groups, we calculated the percentage of total cancers that were excess ("percentage excess") as (total – expected total)/total. The percentage excess can be approximated as (SIR – 1)/SIR, where the SIR is the standardized incidence ratio, which is often used to quantify the relative risk of cancer in HIV-infected people. Where deficits occurred, we calculated the percentage of expected cases that were in deficit ("percentage deficit") as (total – expected total)/expected total.

We performed a parametric bootstrap procedure to obtain 95% confidence intervals and *P* values for equality of and trends in proportions. Equality *P* values were based on the empirical distribution of squared differences in proportions generated under the null hypothesis of no difference, while trend *P* values were derived from linear regression models fit to log-transformed estimates of the proportions (see Supplementary

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Table 1. Demographic and HIV-related characteristics of people living with diagnosed HIV infection based on CDC surveillance estimates (mid-year 2010) and person-time in the HACM study (2003–2010)*

	CDC, mid-year 2010		HACM Study, 2003–2010	
Characteristic	No. people	Percentage	No. person-years	Percentage
Total	859 522	100	825 415	100
Age, y				
0–14	4307	0.5	7072	0.9
15–29	86 287	10.0	77 569	9.4
30–39	163 945	19.1	209 851	25.4
40–49	312 526	36.4	324 952	39.4
50–59	216 430	25.2	161 154	19.5
60–69	62 728	7.3	37 087	4.5
≥70	13 300	1.5	7730	0.9
Sex				
Male	643 627	74.9	613 835	74.4
Female	215 896	25.1	211 581	25.6
HIV risk group				
MSM	478 956	55.7	370 179	44.8
Male heterosexual	69 342	8.1	48 054	5.8
Female heterosexual	153 950	17.9	94 432	11.4
Male IDU	87 037	10.1	95 989	11.6
Female IDU	54 412	6.3	53 271	6.5
Other/unknown†	15 826	1.8	163 490	19.8
Time since an AIDS diagnosis, mo				
HIV-only	385 221	44.8	333 386	40.4
1–3	6371	0.7	9897	1.2
4–24	48 232	5.6	65 825	8.0
25–60	83 774	9.7	106 941	13.0
>60	335 925	39.1	309 367	37.5
Race/ethnicity				
Non-Hispanic white	291 921	34.0	274 913	33.3
Non-Hispanic black	377 094	43.9	380 372	46.1
Hispanic/Latino	161 969	18.8	158 129	19.2
Other/unknown	28 540	3.3	12 001	1.5

* CDC mid-year 2010 counts were obtained by averaging 2009 and 2010 end-of-year counts. Sums within a category may not exactly equal the overall total because of rounding. Individuals who are both men who have sex with men (MSM) and injection drug users are classified as MSM. CDC = Centers for Disease Control and Prevention; HACM = HIV/AIDS Cancer Match; IDU = injection drug users; MSM = men who have sex with men.
† CDC imputes HIV risk groups for people with unknown risk group status, thereby assigning them to other groups.

Methods, available online). A *P* value of less than .05 was considered statistically significant, and all statistical tests were two-sided.

We summed across stratified estimates of cancer counts to present total and excess cancers by cancer type and demographic subgroup. We also cross-classifed excess cancers by demographic category and cancer type.

Results

An estimated 859 522 people were living with diagnosed HIV infection in the United States at mid-year 2010 (Table 1). The majority were age 40 to 59 years, and 74.9% were male, predominantly men who have sex with men (MSM). While 44.8% had no prior AIDS diagnosis (ie, HIV-only), another 39.1% had been living five or more years since AIDS. As shown in Table 1, the distribution of person-time in the HACM Study (2003–2010), from which cancer rates for HIV-infected people were derived, was similar, except that a larger proportion of individuals in the HACM Study had other/unknown HIV risk group. This difference arises because the CDC imputes HIV risk groups for people of unknown risk group (1), thereby assigning them to other groups.

An estimated 7760 (95% confidence interval [CI] = 7330 to 8320) total cancers occurred among HIV-infected people in 2010 (Table 2). Approximately one-third (34%) were ADCs, and two-thirds (66%) were NADCs. The most common cancers were NHL (n = 1650), KS (n = 910), lung cancer (n = 840), and anal cancer (n = 760).

After subtracting expected background cancers, a statistically significant excess occurred for NHL, KS, HL, and cervical, lung, anal, liver, and oral cavity/pharyngeal cancers (Table 2). Among the 4460 excess cancers, roughly half were ADCs (54%) and half NADCs (46%). The largest percentage excess was for KS (essentially all cases were excess), followed by anal cancer (97%), HL (91%), and NHL (88%). Seventy-nine percent of excess cases (n = 3530) were NHL, KS, anal cancer, or lung cancer. Fewer than expected cases occurred for prostate cancer (deficit of 41% of expected cases) and breast cancer (42%). Accounting for deficit cancers, the net excess was approximately half of total cancers (50%, n = 3920, 95% CI = 3480 to 4470) (Table 2).

The magnitude of the cancer burden varied across demographic groups (Table 3). Total cancer burden was highest among people age 50 to 59 years (n = 2540), MSM (n = 4540), those living five or more years with AIDS (n = 3410), and non-Hispanic blacks (n = 3290). The largest excess burden was among people age 40 to 49 years (n = 1610), though the largest percentage excess was among people age 15 to 29 years (93%). There was no excess among people age 70 years and older, among whom a small deficit (6%) was observed.

Table 2. Estimated total and excess cancer cases among people living with HIV in the United States in 2010, by cancer type

Cancer type	Estimated cases*			Percentage excess or deficit† (95% CI)	Percentage of total excess‡ (95% CI)
	Total No. (95% CI)	Expected No.	Excess or deficit No. (95% CI)		
AIDS-defining cancers	2640 (2400 to 2890)	230	2410 (2170 to 2660)	91 (90 to 92)	54 (49 to 58)
Non-Hodgkin's lymphoma§	1650 (1470 to 1840)	200	1440 (1270 to 1630)	88 (86 to 89)	32 (28 to 36)
Kaposi's sarcoma	910 (780 to 1060)	2	910 (780 to 1060)	100 (100 to 100)	20 (18 to 23)
Cervix	80 (50 to 120)	30	50 (20 to 90)	66 (46 to 78)	1 (0 to 2)
Non–AIDS defining cancers	5130 (4780 to 5580)	3620	1510 (1170 to 1960)	29 (24 to 35)	46 (42 to 51)
Lung	840 (710 to 1000)	400	440 (300 to 600)	52 (43 to 60)	10 (7 to 13)
Anus	760 (630 to 930)	20	740 (610 to 910)	97 (97 to 98)	17 (14 to 19)
Prostate	570 (450 to 720)	970	-390 (-520 to -250)	-41 (-53 to -26)	0 (0 to 0)
Liver	390 (300 to 500)	110	280 (200 to 390)	73 (65 to 79)	6 (4 to 9)
Colorectum	360 (270 to 470)	380	-20 (-110 to 90)	-6 (-28 to 20)	0 (0 to 2)
Hodgkin's lymphoma	320 (240 to 420)	30	290 (210 to 390)	91 (88 to 93)	6 (5 to 9)
Oral cavity and pharynx	280 (210 to 380)	140	140 (70 to 240)	51 (34 to 64)	3 (2 to 5)
Female breast	180 (120 to 260)	300	-130 (-190 to -40)	-42 (-61 to -14)	0 (0 to 0)
Miscellaneous	1430 (1270 to 1620)	1270	160 (-9 to 350)	11 (-1 to 22)	4 (0 to 8)
All cancers (total)	7760 (7330 to 8320)	3850	3920 (3480 to 4470) ‖	50 (48 to 54)	100

* Cancer cases are rounded to the nearest ten and may not always sum exactly.

† The percentage excess is calculated as excess/total; the percentage deficit is calculated as deficit/expected (see Methods).

‡ This calculation is restricted to the cancers that were present in excess. Deficit cancers were therefore set equal to zero, giving a denominator of 4460 cancer cases for the point estimates. For the groups of AIDS-defining and non–AIDS defining cancers, percentages are calculated as the sum of the percentages for individual cancer sites.

§ Only certain subtypes of non-Hodgkin's lymphoma (NHL) are AIDS defining, but we grouped all NHLs together, as most cases among HIV-infected people are the AIDS-defining subtypes (40).

‖ The excess displayed for all cancers is the net excess. Disregarding cancers occurring in deficit, the total excess is 4460 cancers.

MSM represent 55.7% of the total HIV population (Table 1), and 65% of all excess cancers occurred in this group (n = 2540) (Table 3). Only 18% of excess cancers occurred among women (n = 700). Individuals living five or more years since AIDS experienced the largest absolute excess (n = 1500), followed by those with HIV-only (n = 1380), reflecting large population sizes in those groups (Table 1). However, the percentage excess was largest one to three months after AIDS (91%), declining to 44% for five or more years post-AIDS. Though most excess cancers occurred among non-Hispanic blacks (n = 1470) and whites (n = 1380), a larger percentage of cancers was excess among Hispanics/Latinos (64%) and the small group with other/unknown race/ethnicity (74%).

Cross-classifications of excess cancers by demographic category and cancer type are displayed graphically in Figures 1 and 2 (see also Supplementary Tables 1–4, available online). Most excess cases of NHL, KS, anal cancer, and lung cancer were in people age 30 to 59 years (Figure 1A). On a percentage scale (Figure 1B), among people age 15 to 29 years, 77% of excess cancers were ADCs. This percentage declined with age ($P_{trend} < .001$), reaching 22% for people age 70 years and older, as the percentage represented by anal, lung, and liver cancers increased (5% in people age 15 to 29 years vs 55% in people age 70 years and older).

A similar trend in cancer types occurred across time living with AIDS. While most excess cancers among those with HIV-only were ADCs (73%), the excess burden increasingly comprised NADCs with advancing time since AIDS ($P_{trend} < .001$) (Figure 1D). Accordingly, while approximately half of excess KS and NHL cases occurred in people with HIV-only as AIDS-defining events (46% and 50%, respectively), most excess anal cancers (71%) and oral cavity/pharyngeal cancers (69%) occurred among those living five or more years with AIDS (Figure 1C).

Excess cancer types also varied across HIV risk and racial/ethnic groups. The majority of excess cancers were in MSM (Figure 2A): 88% of all excess KS cases, 83% of excess anal cancers, and 62% of excess NHLs occurred in MSM. Though injection drug users (IDUs) represented only 16.5% of the HIV population (Table 1), 46% of excess liver cancers and 42% of excess lung cancers occurred in IDUs (Figure 2A). Accordingly, for male and female IDUs combined, compared with MSM and heterosexuals combined, higher percentages of the excess burden were liver cancer (16% vs 4%, $P < .001$) and lung cancer (22% vs 7%, $P < .001$) (Figure 2B). While non-Hispanic whites and blacks experienced similar total numbers of excess cancers, (Figure 2C), a higher percentage was anal cancer in whites compared with blacks (24% vs 13%, $P < .001$) (Figure 2D) and a lower percentage was lung cancer (7% vs 13%, $P < .001$).

Discussion

In the US HIV population in 2010, there were an estimated 7760 total cancers, of which roughly half (n = 3920) were net excess cases, ie, cases above what would be expected based on general population rates. Among the excess cancers, approximately half were ADCs and half NADCs, and excess cases generally occurred in groups with large representation in the HIV population such as MSM. The excess cancer burden reflects elevated risks of certain cancers among HIV-infected people, and many cases could theoretically be prevented through targeted efforts directed at known risk factors.

Most cancers showing a high excess in Table 2 are caused by viruses (18). HIV-infected individuals have a high prevalence

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Table 3. Estimated total and excess cancer cases among people living with HIV in the United States in 2010, by demographic and HIV-related characteristics

Characteristic	Estimated cases*			Percentage excess or deficit† (95% CI)	Percentage of total excess‡ (95% CI)
	Total No. (95% CI)	Expected No.	Excess or deficit No. (95% CI)		
Age, y					
0–14	4 (2 to 8)	1	4 (1 to 8)	87 (70 to 93)	0 (0 to 0)
15–29	350 (300 to 400)	30	320 (280 to 370)	93 (92 to 94)	8 (7 to 9)
30–39	970 (890 to 1080)	140	830 (750 to 930)	85 (84 to 87)	21 (19 to 23)
40–49	2370 (2200 to 2560)	760	1610 (1450 to 1810)	68 (66 to 70)	41 (38 to 44)
50–59	2540 (2370 to 2740)	1590	950 (780 to 1150)	37 (33 to 42)	24 (21 to 27)
60–69	1240 (1120 to 1380)	1020	220 (100 to 360)	18 (9 to 26)	6 (3 to 8)
≥70	290 (250 to 350)	310	-20 (-60 to 40)	-6 (-21 to 11)	0 (0 to 1)
Sex					
Male	6240 (5880 to 6710)	3020	3210 (2850 to 3690)	52 (49 to 55)	82 (78 to 86)
Female	1530 (1370 to 1710)	830	700 (540 to 890)	46 (40 to 52)	18 (14 to 22)
HIV risk group					
MSM§	4540 (4260 to 4920)	2000	2540 (2260 to 2920)	56 (53 to 59)	65 (61 to 69)
Male heterosexual	730 (640 to 830)	410	320 (230 to 420)	44 (36 to 51)	8 (6 to 10)
Female heterosexual	980 (860 to 1120)	570	410 (290 to 550)	42 (34 to 49)	10 (8 to 13)
Male IDU	920 (840 to 1030)	590	320 (240 to 430)	35 (29 to 42)	8 (7 to 10)
Female IDU	520 (450 to 590)	240	270 (210 to 350)	53 (46 to 59)	7 (5 to 9)
Other/unknown	80 (70 to 90)	30	50 (40 to 60)	59 (55 to 64)	1 (1 to 1)
Time since an AIDS diagnosis					
HIV-only	2810 (2620 to 3060)	1430	1380 (1190 to 1630)	49 (45 to 53)	35 (32 to 38)
1–3 months	240 (210 to 280)	20	220 (190 to 260)	91 (90 to 92)	6 (5 to 6)
4–24 months	540 (480 to 600)	160	370 (320 to 440)	70 (66 to 73)	10 (8 to 11)
25–60 months	760 (690 to 840)	320	440 (370 to 520)	58 (53 to 62)	11 (10 to 13)
>60 months	3410 (3170 to 3720)	1910	1500 (1260 to 1800)	44 (40 to 48)	38 (35 to 42)
Race/ethnicity					
Non-Hispanic white	2870 (2670 to 3130)	1490	1380 (1180 to 1640)	48 (44 to 52)	35 (32 to 38)
Non-Hispanic black	3290 (3080 to 3560)	1820	1470 (1260 to 1740)	45 (41 to 49)	38 (34 to 41)
Hispanic/Latino	1270 (1170 to 1390)	450	820 (720 to 940)	64 (61 to 67)	21 (19 to 23)
Other/unknown	330 (270 to 410)	90	240 (180 to 320)	74 (67 to 79)	6 (5 to 8)

* Cancer cases are rounded to the nearest ten and may not always sum exactly. IDU = injection drug users; MSM = men who have sex with men.
† The percentage excess is calculated as excess/total; the percentage deficit is calculated as deficit/expected (see Methods).
‡ Deficit cancers are set equal to zero to calculate percent of total excess.
§ Individuals who are both MSM and IDU are classified as MSM.

of many of these viruses and are likely to lose immune control of infections (3,19). Almost all cases of KS (caused by human herpesvirus 8) and anal cancer (human papillomavirus [HPV]) occurred in excess (18). Most NHL and HL cases among HIV-infected people are caused by Epstein-Barr virus (EBV) (18), and about 90% of both cancers were excess cases. Excesses in the range of 51% to 73% were observed for cervical cancer (for which HPV is a necessary cause), oral cavity/pharyngeal cancers (for which a subset is HPV-related), and liver cancer (which is often caused by hepatitis B or C viruses [HBV, HCV]) (18). Finally, much of the 52% excess of lung cancer is because of frequent tobacco use (20), although immunosuppression and/or inflammation may also be important (20,21).

With advancing age and time since AIDS, the excess cancer burden shifted from ADCs to NADCs (Figure 1). This pattern likely has several explanations. First, many ADCs occurred as AIDS-defining events, either in people with HIV-only or in the subsequent three-month period (where excess cases may represent delayed diagnoses of AIDS-defining events). Second, rates of successful HIV treatment, related to engagement in care and compliance with medication regimens, increase with age and time living with AIDS (22,23). These treatment trends contribute to a decline in the excess burden of ADCs, because HAART use reduces ADC risk (24,25). Finally, the shift to NADCs reflects prolonged exposure to risk factors such as smoking, HPV, and HCV. For example, anal cancer develops over a prolonged period of HPV infection and HIV-associated immunosuppression (26). Consistent with this model, we observed that over 70% of excess anal cancers occurred five or more years after AIDS diagnosis.

The concentration of cancer risk behaviors in certain groups explains some of our findings. Eighty-three percent of excess anal cancers occurred among MSM, who are at high risk for anal HPV infection. In contrast, IDUs experienced a disproportionate excess burden of liver and lung cancers. IDUs acquire HBV/HCV because of needle sharing, and nearly all IDUs are current or former smokers (20,27). By racial/ethnic group, there were more excess anal cancers in whites and more excess lung cancers in blacks. This likely reflects that most HIV-infected whites are MSM, while more blacks are IDUs or acquired HIV via heterosexual intercourse (1).

Our results quantify how the cancer burden in the HIV population differs from the general population and provide a framework for considering cancer control initiatives tailored to HIV-infected people. While the incidence of ADCs has declined, we highlight that 14 years after the introduction of HAART, over half of excess cancers were still ADCs.

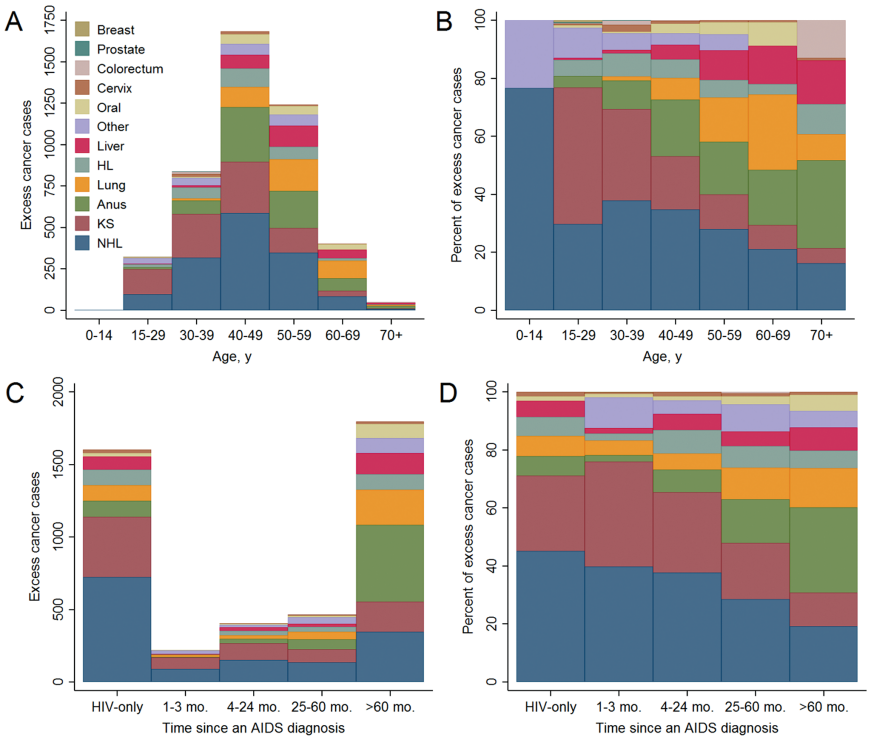

Figure 1. Estimated excess cancer cases among people living with human immunodeficiency virus (HIV) in the United States in 2010, by age and time since an AIDS diagnosis. Excess cancer cases are displayed by age **(A and B)** and time since an AIDS diagnosis **(C and D)** on an absolute scale **(A and C)** and on a percentage scale **(B and D)**. Totals for individual groups do not match Table 3 exactly, as deficits (ie, negative excesses) for individual cancer sites within each group are set equal to zero for graphical presentation. Estimates of excess cancers, including deficits, simultaneously stratified by cancer type and demographic and HIV-related characteristics, are presented in Supplementary Tables 1–4 (available online). HIV = human immunodeficiency virus; HL = Hodgkin's lymphoma; KS = Kaposi's sarcoma; NHL = non-Hodgkin's lymphoma.

This continuing excess illustrates that improvements in HIV treatment at the population level must remain a priority. Implementing measures to promote access and adherence to HAART, especially targeted to young people and people with HIV-only, could prevent many excess ADCs. Indeed, while our results reflect an era when treatment for individuals with HIV-only was based on disease stage (ie, CD4 cell count), guidelines now recommend that all HIV-infected individuals be offered HAART (28,29).

Lung and anal cancers together represented 27% of the total excess, underscoring that the development of strategies for prevention and early detection of these cancers among HIV-infected people is warranted. These strategies might be targeted to subgroups that experience substantial NADC risk and excess burden. For example, anal Pap screening has been advocated for MSM (30,31), and while the utility of this approach is debated (32) our results highlight that targeting anal cancer prevention in older people and those with AIDS should be a priority. Additionally, HPV vaccination for HIV-infected individuals may aid prevention of anal, cervical, and oral cavity/pharyngeal cancers (33). However, vaccination confers less benefit to individuals with prior sexual partners, likely lessening overall effectiveness for the HIV population. IDUs are an appropriate population to prioritize for HCV testing and treatment (34) and screening for liver cancer (35). Heavy smokers (both IDUs and non-IDUs) might benefit from smoking cessation interventions or lung cancer screening (36).

We observed a 40% deficit for breast and prostate cancers, reflecting decreased incidence in HIV-infected people (9) and no excess of colorectal cancer. For prostate cancer, the deficit may partly reflect decreased prostate-specific antigen screening among HIV-infected people (37), while the cause of decreased breast cancer risk is unclear (38). Despite a lack of excess, the total burden of these cancers is substantial (n = 1110 or 14% of all cancers in 2010) and will increase as the HIV population ages and grows in size (7). Screening based on general population guidelines for these cancers is likely appropriate for HIV-infected people.

Our estimates apply to the entire US HIV population, and they are based on robust data sources for cancer rates and enumeration of the HIV population. One limitation is that people who are infected but not diagnosed with HIV (approximately 16% of the total HIV-infected population [39]) are not included, because precise counts of these individuals and their cancer rates are unknown. Therefore, these are underestimates of the true cancer burden in HIV-infected people. Further, our results are based on cancer rates for HIV-infected people derived from six state registries that are demographically similar to the overall 2010 US HIV population. Our analysis requires that stratum-specific rates from these registries represent cancer risk in the corresponding strata for the entire US HIV population, and large violations of this assumption, though unlikely, would invalidate our results. Additionally, our analysis synthesizes multiple data sources and could be limited by inconsistencies across them, and there is uncertainty related to use of modeling to derive rates. Finally, while our estimates provide one framework for tailoring cancer control strategies for HIV-infected people, additional factors should be considered, such as the absolute and relative risks for cancer and the potential risks and benefits of specific interventions.

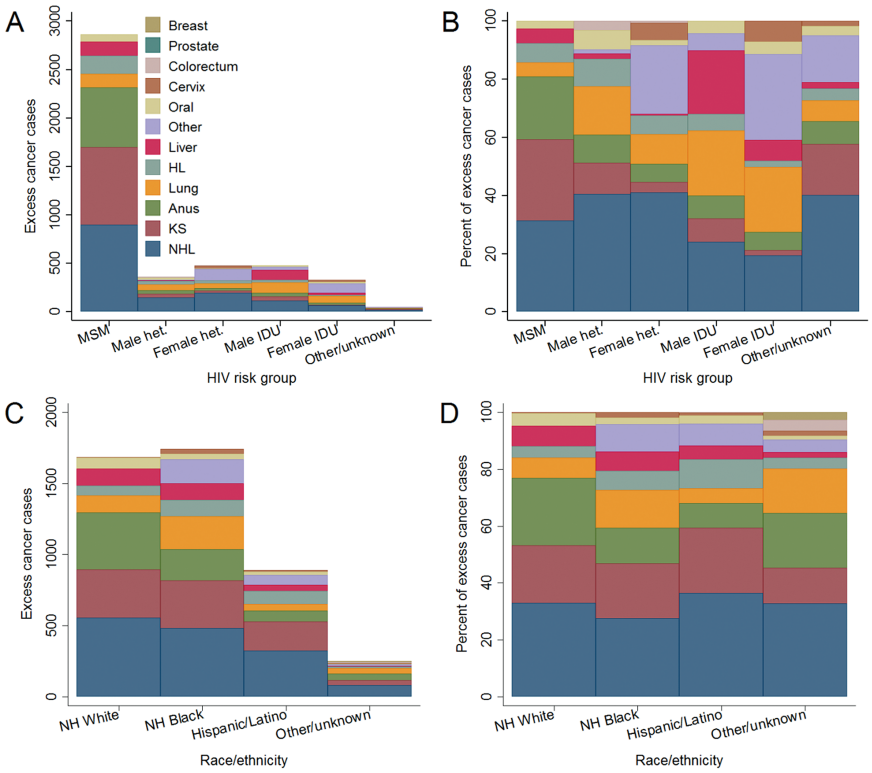

Figure 2. Estimated excess cancer cases among people living HIV in the United States in 2010, by HIV risk group and race/ethnicity. Excess cancer cases are displayed by HIV risk group **(A and B)** and race/ethnicity **(C and D)** on an absolute scale **(A and C)** and on a percentage scale **(B and D)**. Totals for individual groups do not match Table 3 exactly, as deficits (ie, negative excesses) for individual cancer sites within each group are set equal to zero for graphical presentation. Estimates of excess cancers, including deficits, simultaneously stratified by cancer type and demographic and HIV-related characteristics are presented in Supplementary Tables 1–4 (available online). Individuals who are both men who have sex with men (MSM) and injection drug users are classified as MSM. het. = heterosexuals; HIV = human immunodeficiency virus; IDU = injection drug users; KS = Kaposi's sarcoma; MSM = men who have sex with men; NH = non-Hispanic; NHL = non-Hodgkin's lymphoma.

Our study is the first to provide a national snapshot of cancer burden in HIV-infected people. Over time, the number and composition of these cancers will change with cancer incidence rates and the size and demographic makeup of the HIV population (7,8). The variation in the spectrum of excess cancers across groups reveals opportunities for cancer control initiatives targeted to HIV-infected people.

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