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Brief Communication

Cumulative incidence of anal cancer since HIV or AIDS diagnosis in the United States

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Abstract

Treatment of screen-detected anal high-grade squamous intraepithelial lesions has been shown to effectively reduce the incidence of invasive anal cancer in people with HIV. We provide population-based estimates of cumulative incidence of anal cancer by risk group and age at HIV or AIDS diagnosis. The 0- to 10-year cumulative incidence of anal cancer for men who have sex with men and are younger than 30 years of age at HIV diagnosis was 0.17% (95% confidence interval [CI] = 0.13% to 0.20%) compared with 0.04% (95% CI = 0.02% to 0.06%) in other men and 0.03% (95% CI = 0.01% to 0.04%) in women. For men who have sex with men and have a diagnosis of AIDS and are younger than 30 years of age, the 0- to 10-year cumulative incidence was 0.35% (95% CI = 0.28% to 0.41%). Among people with HIV, men who have sex with men are at the greatest risk of anal cancer, and those with a diagnosis of AIDS had higher risk than those without AIDS. These estimates may inform recommendations for priority populations that could benefit most from anal cancer screening and treatment.

Anal cancer is one of the most common cancers in people with HIV (1). HIV-related immunosuppression increases the risk of human papillomavirus–associated cancers, including anal cancer (2). Among people with HIV, cancer risk is highest among men who have sex with men (MSM) compared with other men and women, increases with age, and is highest among people with HIV who had a prior AIDS diagnosis (2,3). Between 2000 and 2012, approximately 1% of MSM 45 years of age or older developed anal cancer within 10 years following AIDS diagnosis (2). Anal cancer rates have declined among people with HIV (4), however; thus, updates to absolute risk estimates are warranted.

Although precancerous anal high-grade squamous intraepithelial lesions can be detected through anal cytology or by performing high-resolution anoscopy–guided biopsies, national screening guidelines for clinical practice have yet to be established (5). In 2022, a randomized controlled trial among people with HIV showed that treatment of screen-detected anal high-grade squamous intraepithelial lesions effectively reduced the incidence of invasive anal cancer (6). As the number of trained clinicians able to perform high-resolution anoscopy is limited, it is important to identify groups with the highest absolute risks who should be prioritized for screening. We provide recent estimates for anal cancer risk according to risk group, AIDS diagnosis, and age from a population of people with HIV in the United States.

We conducted this study using data from the HIV/AIDS Cancer Match Study, a linkage between US HIV surveillance and cancer registries for 14 regions in the United States from 2019 to 2000. We started follow-up at the latest HIV diagnosis date (or AIDS diagnosis for those in the AIDS-specific analyses) or beginning of systematic name-based state HIV and cancer registration, which has a high degree of completeness. Follow-up ended at the earliest of anal cancer diagnosis, death, or end of cancer registry coverage.

We estimated the cumulative incidence of anal cancer within risk group (MSM, men not classified as MSM, and women). We used the Fine and Gray method (7) to estimate nonparametric cumulative incidence curves for anal cancer to allow for death as a competing event; we report estimates for 0 to 10 and 10 to 20 years with an HIV or AIDS diagnosis within age groups as the time of origin. The longer time period of 10 to 20 years since diagnosis extends previous estimates and further provides comparisons for effects of duration of infection. We used weighting to account for delayed entry for individuals with an HIV or AIDS diagnosis before the beginning of follow up. We interpreted overlapping 95% confidence intervals (CIs) as not statistically different point estimates. We conducted additional sensitivity analyses to investigate effects of calendar year of HIV or AIDS diagnosis on cumulative incidence.

Analyses were conducted using R, version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria). The study was approved by institutional review boards at participating registries.

We observed 3444 anal cancers during approximately 11 million person-years among people with HIV, of which 2678 cases of anal cancer occurred among people with a prior diagnosis of

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Table 1. Cumulative incidence of anal cancer among people with HIV and among those with AIDS at 10 years from HIV or AIDS diagnosis and between 10 and 20 years from diagnosis[a]

Sex/risk group stratified by age at HIV/AIDS diagnosis	Cumulative incidence, % (95% confidence interval)			
	HIV, 0-10 y	AIDS, 0-10 y	HIV, 10-20 y	AIDS, 10-20 y
MSM				
<30 y	0.17 (0.13 to 0.20)	0.35 (0.28 to 0.41)	0.88 (0.75 to 1.01)	1.23 (1.05 to 1.40)
30-34 y	0.22 (0.18 to 0.26)	0.42 (0.35 to 0.48)	0.86 (0.75 to 0.98)	1.26 (1.10 to 1.42)
35-39 y	0.27 (0.23 to 0.31)	0.51 (0.43 to 0.58)	0.76 (0.66 to 0.86)	1.17 (1.00 to 1.33)
40-44 y	0.27 (0.22 to 0.31)	0.55 (0.46 to 0.64)	0.68 (0.58 to 0.78)	1.12 (0.93 to 1.32)
45-59 y	0.24 (0.21 to 0.28)	0.60 (0.51 to 0.68)	0.63 (0.55 to 0.71)	0.96 (0.78 to 1.14)
≥60 y	0.32 (0.20 to 0.43)	0.63 (0.37 to 0.90)	0.38 (0.22 to 0.54)	0.44 (0.05 to 0.84)
Other men				
<30 y	0.04 (0.02 to 0.06)	0.09 (0.04 to 0.13)	0.22 (0.14 to 0.29)	0.35 (0.22 to 0.48)
30-34 y	0.12 (0.07 to 0.16)	0.20 (0.13 to 0.27)	0.36 (0.25 to 0.47)	0.51 (0.36 to 0.67)
35-39 y	0.11 (0.08 to 0.15)	0.18 (0.12 to 0.23)	0.35 (0.26 to 0.44)	0.37 (0.26 to 0.49)
40-44 y	0.09 (0.06 to 0.12)	0.20 (0.15 to 0.26)	0.30 (0.22 to 0.37)	0.38 (0.26 to 0.49)
45-59 y	0.09 (0.07 to 0.11)	0.17 (0.13 to 0.22)	0.21 (0.16 to 0.26)	0.35 (0.24 to 0.47)
≥60 y	0.08 (0.03 to 0.13)	0.10 (0.02 to 0.18)	0.19 (0.07 to 0.31)	0.33 (0.03 to 0.63)
Women				
<30 y	0.03 (0.01 to 0.04)	0.09 (0.05 to 0.13)	0.25 (0.19 to 0.31)	0.47 (0.33 to 0.60)
30-34 y	0.06 (0.03 to 0.09)	0.11 (0.06 to 0.16)	0.20 (0.13 to 0.26)	0.41 (0.27 to 0.54)
35-39 y	0.07 (0.04 to 0.10)	0.17 (0.11 to 0.22)	0.24 (0.17 to 0.31)	0.40 (0.27 to 0.53)
40-44 y	0.06 (0.03 to 0.09)	0.13 (0.08 to 0.19)	0.31 (0.22 to 0.39)	0.36 (0.21 to 0.51)
45-59 y	0.09 (0.06 to 0.12)	0.20 (0.14 to 0.26)	0.22 (0.15 to 0.28)	0.34 (0.21 to 0.48)
≥60 y	0.04 (0.00 to 0.09)	0.08 (0.00 to 0.17)	0.14 (0.00 to 0.29)	0.07 (0.00 to 0.21)

[a] Age is in years and was measured at AIDS diagnosis (for people with AIDS) or HIV report (for people with HIV only). Cumulative incidence estimates for people with HIV do not censor at the onset of AIDS. MSM, men who have sex with men.

AIDS. MSM had the greatest absolute risk compared with non-MSM men and women with HIV in all age groups and among those with and without AIDS (Table 1). During the 0- to 10-year period following HIV diagnosis, MSM younger than 30 years of age at HIV diagnosis had a cumulative incidence of anal cancer of 0.17% (95% CI = 0.13% to 0.20%) compared with 0.04% (95% CI = 0.02% to 0.06%) in other men and 0.03% (95% CI = 0.01% to 0.04%) in women. The 10- to 20-year cumulative incidence of anal cancer for MSM with HIV who were younger than 30 years of age at the time of HIV diagnosis was 0.88% (95% CI = 0.75% to 1.01%), an approximately 5-fold increase in risk compared with the first 10 years since HIV diagnosis.

Prior AIDS was strongly associated with increased risk of anal cancer. For MSM with a diagnosis of AIDS who were younger than 30 years of age, the 0- to 10-year cumulative incidence was 0.35% (95% CI = 0.28% to 0.41%), an approximately 2-fold increase in risk compared with the estimate following people starting at 0 to 10 years after HIV diagnosis. The risk during 10 to 20 years following AIDS diagnosis among MSM younger than 30 years of age was approximately triple that of the first 10 years, with a cumulative incidence of 1.23% (95% CI = 1.05% to 1.40%). When comparing cumulative incidence within each risk group, there was considerable overlap in estimates across age groups (Figure 1). In sensitivity analyses that compared 0- to 10-year cumulative incidence for people with HIV diagnosed before 1996, 1996 to 2004, 2004 to 2008, and after 2008, we did not observe any notable differences between time periods (not shown).

MSM with AIDS continue to be at the greatest risk of anal cancer. For context, as of 2019 among MSM in New York with HIV, 64% had been living for more than 10 years since their HIV diagnosis; among those with a prior AIDS diagnosis, 70% had been living for more than 10 years since their AIDS diagnosis. These recent estimates allow for inference into screening recommendations and extend cumulative incidence to 20 years since diagnosis, reflecting the infection duration among the current population of people with HIV. Many of the relative comparisons between risk groups and with respect to prior AIDS diagnosis are consistent with prior estimates (2).

Within each HIV risk group, the cumulative incidence of anal cancer was similar across age groups. In contrast, there were much larger differences across strata defined by AIDS status and time since HIV or AIDS diagnosis. For instance, even a 10-year cumulative incidence of 0.5% (seen in MSM aged 35-39 years with AIDS) is concerning and represents a risk of anal cancer equal to 1 in 200 individuals over 10 years. There was a dramatic increase in the subsequent 10 years after AIDS diagnosis (1.17%, equal to 1 in 85), however. Similarly, the effect of duration of immunosuppression can be seen by comparing the cumulative incidence among MSM 40 to 50 years of age in 2 scenarios: the 0- to 10-year cumulative incidence for an individual diagnosed with AIDS at 40 years of age (0.57%) vs the 10- to 20-year cumulative incidence of an individual diagnosed with AIDS at 30 years of age (1.32%). These comparisons suggest that the effects of duration of HIV infection may supersede any age-related effects and may be more informative for risk-stratifying individuals.

Because of the limited number of outcomes within the risk and age group and the dependency of times since HIV diagnosis and calendar year, we were unable to further explore changes in cumulative incidence that may have resulted from any changes in regional or institutional screening policies. In addition, we had limited covariates, such as measures of immunosuppression or smoking history. We note, however, that previous studies have been mostly null or weak after incorporating basic demographic information (8,9).

Our population-based linkage study provides the largest cohort for estimating anal cancer among people with HIV in the United States. As committees convene to consider anal cancer screening recommendations, these estimates provide insight for prioritizing individuals and populations for screening. Although MSM with HIV constitute a well-established high-risk group, our results suggest that clinicians should prioritize those with a

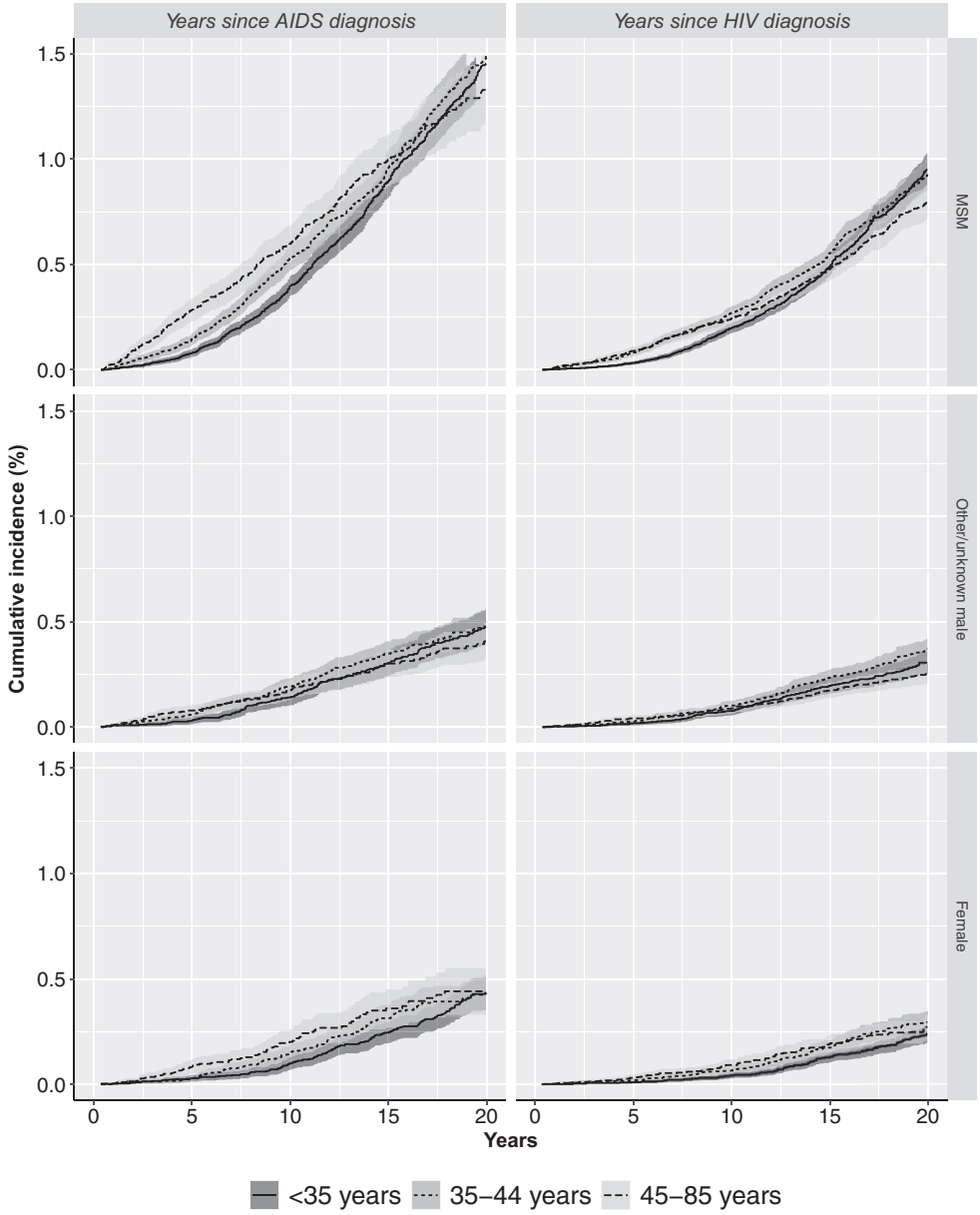

Figure 1. Cumulative incidence of anal cancer since time of HIV (upper panel) and AIDS (lower panel) diagnosis, stratified by risk group and age at HIV or AIDS diagnosis. MSM = men who have sex with men.

diagnosis of AIDS, especially if the time since AIDS diagnosis is more than 10 years.

Data availability

Interested investigators can access data from individual state (or region) linkages by obtaining approval directly from the HIV and cancer registries in those states. In addition, collaboration between outside investigators and the National Cancer Institute (NCI) is possible. Data analyses can be done by NCI staff or, in some circumstances, NCI may be able to release tabulated data.

Author contributions

Cameron Brady Haas, PhD, MPH (Conceptualization; Formal analysis; Investigation; Methodology; Visualization; Writing—original draft), Eric Engels, MD (Data curation; Methodology; Project administration; Resources; Supervision; Writing—review & editing), Marie-Josèphe Horner, PhD (Formal analysis; Methodology; Writing—review & editing), Ruth Pfeiffer, PhD (Methodology; Writing—review & editing), Qianlai Luo, PhD (Investigation; Project administration; Writing—review & editing), Aimée Kreimer, PhD (Writing—review & editing), Joel Palefsky, MD (Supervision; Writing—review & editing), Meredith Shiels, PhD, MPH (Data curation; Funding acquisition; Supervision; Writing—review & editing).

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Conflicts of interest

Authors do not have any disclosures to report.

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