

Screening and Early Treatment Reduce Anal Cancer in People With HIV

Prompt detection and treatment of precancerous lesions cut the likelihood of developing anal cancer by more than half.

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Screening people with HIV for precancerous anal cell changes and treating them promptly lowered the risk of progression to anal cancer by more than half, according to results from the ANCHOR study [published this week](#) in the New England Journal of Medicine.

“We believe that screening for anal cancer precursors and treating them should become the standard of care for people with HIV over the age of 35 years,” lead investigator Joel Palefsky, MD, of the University of California at San Francisco (UCSF) told POZ. “We are working on detailed guidelines for anal screening in people with HIV now, and we hope these will be out in the very near future.”

[Anal cancer](#), like [cervical cancer](#), is caused by human papillomavirus (HPV), one of the most common sexually transmitted infections. The virus triggers abnormal cell growth that can progress to precancerous dysplasia (known as high-grade squamous intraepithelial lesions, or HSIL) and invasive cancer. The [Gardasil 9 vaccine](#), which protects against nine high-risk HPV types, can prevent anal, cervical and [oral cancer](#). The vaccine is recommended for girls and boys at ages 11 or 12, with catch-up vaccination through age 26.

While anal cancer is uncommon in the general population, rates have been rising for both men and women since the 1970s, Robert Yarchoan, MD, director of the National Cancer Institute’s [Office of HIV and AIDS Malignancy](#), said during a June 15 media briefing. HIV-positive people—especially men who have sex with men—are at greater risk for developing anal cancer even if they are on effective antiretroviral treatment and have a high CD4 count. In fact, anal cancer is the fourth most common cancer among people living with HIV. But unlike cervical cancer, anal cancer is not considered an AIDS-defining illness.

Widespread Pap smear screening and early treatment of precancerous lesions has dramatically reduced the prevalence and mortality of cervical cancer since the 1950s. But this is not yet the standard of care for people at risk for anal cancer because—until now—there was no direct evidence that it would work. What’s more, Palefsky [previously told POZ](#), “If a woman has [cervical]

HSIL, you can remove a large portion of the cervix. But you can't do that in the anal canal, obviously."

The [ANCHOR study](#) (Anal Cancer HSIL Outcomes Research; [NCT02135419](#)) was designed to evaluate whether treating anal HSIL early is safe and whether it can reduce the incidence of anal cancer in people living with HIV. The study also created a data and specimen bank to aid further research on factors that contribute to disease progression.

The study, funded by the [AIDS Malignancy Consortium](#), enrolled 10,732 HIV-positive participants ages 35 and older at 25 sites across the United States. Most (78%) were men—mainly gay or bisexual—19% were women and 3% were transgender. The median age was 51, and they had been living with HIV for a median of 17 years. About one third were white, 42% were Black and 16% were Latino. More than 80% were on antiretroviral treatment with an undetectable viral load. The median current CD4 count was high (approximately 600), but half had a nadir (lowest-ever) count below 200, qualifying them for an AIDS diagnosis.

At study entry, the participants were screened for HSIL using anal Pap smears (cytology) and a technique called high-resolution anoscopy, which uses a magnifying scope to examine the anal canal. If HSIL was suspected, a biopsy sample was collected for further analysis.

More than half of the participants (53% of men, 46% of women and 67% of transgender people) were found to have HSIL, and 17 were diagnosed with pre-existing anal cancer. The prevalence of HSIL was about what was expected for men, but was higher than expected for women, Palefsky said when he [presented the study findings](#) at this year's Conference on Retroviruses and Opportunistic Infections (CROI) in February.

The 4,459 participants found to have HSIL were then evenly randomized to receive either immediate treatment or active monitoring (the current standard of care) at least every six months. The most common treatment was office-based electrocautery, a method that uses electricity to burn off abnormal lesions. A small number were treated with topical imiquimod or 5-fluorouracil cream or underwent surgery for more advanced disease.

[As previously reported](#), the trial was halted ahead of schedule in October 2021 after an interim analysis showed that screening and early treatment confers a clear benefit: Detecting and removing precancerous lesions significantly reduced the likelihood of progression to anal cancer.

Nine people in the immediate treatment arm and 21 in the active monitoring arm were diagnosed with invasive anal cancer, meaning screening and treatment reduced the risk by 57%. The incidence of anal cancer was 173 cases per 100,000 person-years of follow-up in the immediate treatment group compared with 402 cases in the monitoring group. Most people diagnosed with anal cancer in both groups were at an early stage.

Treatment was generally safe and well tolerated, although there were "more treatment failures than we would have liked," Palefsky said during the media briefing. Seven people in the immediate treatment group and one in the active monitoring group experienced serious adverse events

related to biopsy or treatment procedures.

These findings support the inclusion of routine anal screening and early treatment as part of the standard of care for people living with HIV, the researchers concluded. What's more, having results from a randomized clinical trial should encourage insurers to cover these procedures.

"Until now, you had to be lucky or privileged enough to live someplace with progressive and knowledgeable HIV providers willing to perform these procedures and have insurance that would pay for it," Jeff Taylor, a long-time HIV advocate who has had anal cancer himself, [previously told POZ](#).

However, the lack of clinicians trained to perform high-resolution anoscopy remains a barrier, according to Palefsky, who established the world's first clinic devoted to anal cancer prevention at UCSF in 1991.

"Anal cancer will increase as the HIV population ages," he said at CROI. "This is a great time to train the workforce and get them ready for when that inevitable increase happens."

A digital rectal exam, which can detect abnormal growths, is a good first step for people experiencing symptoms such as anal bleeding, pain or lumps, Palefsky said. When the availability of high-resolution anoscopy is limited, first priority should go to people who have symptoms of anal HSIL or cancer, followed by older individuals and those with a low current or nadir CD4 count.

While this study enrolled only people living with HIV, the results suggest that screening and early treatment could be similarly beneficial for other groups known to be at increased risk for anal cancer, including immunocompromised people, HIV-negative gay and bisexual men, and women with a history of cervical cancer, according to Palefsky.

"This trial provides the groundwork to change practice for the treatment of HSIL and the screening of it in persons living with HIV and possibly other high-risk groups," Yarchoan said in a [UCSF press release](#). "It will certainly have an impact on reducing the pain and suffering from anal cancer."

Click here to read the [study abstract](#).

Click here to learn more about [anal cancer](#).

Click here for a POZ feature about [cancer in people living with HIV](#).