

Good CD4 Cell Recovery Linked to Lower Cancer Risk for People With HIV

People with a higher recent CD4 count and those who experienced larger CD4 cell gains after starting antiretroviral treatment were less likely to develop cancer overall, especially infection-related malignancies.

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HIV-positive people who maintain or regain an adequate CD4 T-cell count on antiretroviral therapy are less likely to develop cancer, according to study results reported in [Clinical Infectious Diseases](#). Those who do not experience good immune recovery, however, have a higher risk for cancer, underscoring the importance of prompt HIV treatment.

Cancer is a growing concern as the HIV population ages. Thanks to effective antiretroviral treatment, cancer and heart disease are now among the leading causes of death for people with HIV, as they are for the population at large. On the whole, HIV-positive people have [more cancer risk factors](#)—including higher rates of smoking and a greater likelihood of coinfections like [human papillomavirus](#) (which causes anal, cervical and oral cancers) and hepatitis B or C (which cause liver cancer)—but the role of HIV itself is not fully understood.

Prior studies of the links between HIV, viral suppression, CD4 count, CD4/CD8 ratio and cancer risk have yielded mixed results. It is well known that people with advanced immune suppression have an elevated risk for AIDS-defining malignancies, such as [Kaposi sarcoma](#) and non-Hodgkin lymphoma. But even less severe impairment can reduce the immune system's ability to fight cancer. HIV-positive people are [at greater risk for anal cancer](#) even when their CD4 count is adequate. Several studies have seen [higher rates of lung cancer](#) and liver cancer among people with HIV; conversely, some have found a [lower incidence of prostate cancer](#). Rates of many other cancer types appear to be similar for HIV-positive and HIV-negative people, but those living with HIV may be diagnosed at an earlier age or with [more advanced disease](#).

Win Min Han, MD PhD, of the Kirby Institute at the University of New South Wales, and colleagues looked at the impact of long-term viral suppression and CD4 cell recovery on cancer incidence among people living with HIV

The study included more than 48,000 adults in the D:A:D (Data Collection on Adverse Events of Anti-HIV Drugs) and RESPOND cohort collaborations in Europe and Australia who had maintained viral suppression on antiretroviral therapy for at least two years between December 1999 and

December 2022. About three quarters were men, the median age was 43 years and they had been diagnosed with HIV for a median of seven years. The researchers noted that this relatively young age is a limitation of the study, as a majority of cancer is diagnosed at older ages. The median current CD4 count was relatively high, at 540, but the median nadir (lowest-ever) count was 245, reflecting substantial immune suppression.

Over more than 300,000 person years of follow-up, a total of 1,933 participants (3.9%) were newly diagnosed with cancer after at least two years with viral suppression. Non-melanoma skin cancer and precancerous dysplasia were excluded, and the researchers didn't count cases of cancer recurrence. By limiting the analysis to people with sustained viral suppression, the researchers could more clearly isolate the effect of CD4 count.

These included 258 AIDS-defining cancers (incidence 0.5%) and 1,675 non-AIDS cancers (incidence 3.5%). About a third (645 cases) were infection-related malignancies, while 1,288 were considered infection-unrelated. The most common specific cancer types were lung cancer, anal cancer, prostate cancer, non-Hodgkin lymphoma and breast cancer. Lung, prostate and breast cancer are also among the [most common cancer types in the U.S. general population](#), along with melanoma and colorectal cancer, but anal cancer is rare.

Having a higher recent CD4 count was significantly associated with a reduced risk for cancer overall, as were larger CD4 cell gains after starting antiretroviral treatment. People with a count of 750 or higher had the lowest cancer incidence, but those with 500 to 749 or 350 to 499 CD4 cells had lower rates than those who fell below 350. This was the case for both AIDS-defining and non-AIDS cancers—though the association was weaker for the latter—for smoking-related and obesity-related cancers, and for all specific malignancies except prostate cancer. The link between higher CD4 count and lower cancer risk held for both men and women and for people older and younger than 50.

The degree of risk reduction was greater for infection-related cancers. People with a CD4 count of 750 or more were nearly 90% less likely to develop infection-related cancers and about 60% less likely to develop infection-unrelated cancers compared to those with a count below 350. The association between a higher recent CD4 count and reduced cancer incidence held regardless of whether the lowest-ever count was above 350, 200 to 350 or below 200 (the threshold for an AIDS diagnosis). However, the pre-treatment nadir CD4 count itself was only associated with reduced risk for AIDS-defining and some infection-related cancers, not for cancer overall.

“Despite virological suppression on antiretroviral therapy for more than two years, people with poorer immune recovery experience a significantly higher incidence of cancer,” the study authors concluded.

These findings add to the evidence that starting antiretroviral therapy promptly, before immune function declines, and staying on treatment consistently are [leads to better outcomes](#). The large START trial, for example, showed that people who started HIV treatment immediately rather than waiting until their CD4 count fell below 350 [reduced their cancer risk by 64%](#). Effective treatment

not only limits damage to cancer-fighting immune cells, but it also helps reduce cancer-causing inflammation.

Yet according to the National Comprehensive Cancer Network (NCCN), people living with HIV are two to three times less likely to receive appropriate cancer care. A [recent study](#) found that structural barriers, such as lower income and education level, were associated with not receiving potentially lifesaving treatment.

“These findings reinforce the importance of optimal immune recovery on the incidence of cancers in people with HIV,” Han and colleagues wrote. “This highlights the critical importance of diagnosing HIV at the earliest opportunity, promptly initiating antiretroviral therapy to ensure optimal immune recovery and sustained cancer risk reduction and ensuring people with poor immune recovery despite effective antiretroviral therapy undergo appropriate cancer screening strategies.”

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