HIV infection increases the risk of developing lung cancer by about 70 percent, according to a study conducted by U.S. Department of Veterans Affairs researchers and published online ahead of print by the journal AIDS. However, the researchers note, it is smoking among people living with HIV that poses the greatest risk of developing lung cancer.

The published data, from a large evaluation of both HIV-positive and HIV-negative study subjects, build upon preliminary results reported in 2010 at the 17th Conference on Retroviruses and Opportunistic Infections (CROI) in San Francisco. They stand in contrast with another, arguably much smaller study, indicating that smoking alone is the only significant risk factor for lung cancer in people living with HIV.

Researchers have long known that people with HIV are more likely to get certain cancers, such as Kaposi's sarcoma, especially when their CD4 cell counts drop. They are called AIDS-related cancers (ARC), and the rates of these opportunistic illnesses have fallen dramatically since the introduction of combination antiretroviral (ARV) therapy in the late 1990s.

Other cancers, such as lung cancer, have not traditionally been associated with HIV, but studies conducted in recent years have indicated that people with HIV might be at increased risk of developing such cancers, especially as they live longer and contend with other disease risk factors.

To determine whether HIV adds to the risk of developing lung cancer, Keith Sigel, MD, MPH, from Mount Sinai School of Medicine in New York City and his colleagues examined the medical records of people receiving care through Veterans Administration (VA) clinics and hospitals. So that accurate rates of smoking history could be factored into the study—previous studies on lung cancer in HIV have not controlled for this aspect very well—Sigel’s team focused on veterans who had also filled out a 1999 survey on tobacco use.

In all, Sigel and his colleagues compared lung cancer diagnosis rates and a multitude of risk factors among 37,294 people living with HIV and 75,750 HIV-negative individuals. HIV-positive subjects had an average of 5.8 years of follow-up data available, compared with an average of 7.3 years among the HIV-negative subjects.
“This is the largest cohort study with both HIV-infected and -uninfected subjects and individual-level smoking data to evaluate lung cancer incidence,” the researchers note.

Basic characteristics between the two groups were similar. The median age of both groups was 46, many were nonwhite, and 98 percent were male.

The groups differed somewhat in certain respects. HIV-positive participants were less likely to have never smoked (20 versus 24 percent), but they were more likely to be current smokers (48 versus 46 percent). They were also more likely to have a history of illicit drug use (19 versus 13 percent), to have hepatitis C (35 versus 15 percent) and to have had a history of bacterial pneumonia (5 versus 1 percent). Study subjects living with HIV were no more likely to have been diagnosed with chronic obstructive pulmonary disease (COPD), notably emphysema or chronic bronchitis. HIV-positive study subjects were also more likely to die, of any cause, during follow-up: 29 versus 13 percent of the HIV-negative subjects.

There were more than 1,000 cases of lung cancer in both groups combined during the follow-up period. Four hundred fifty-seven cases of lung cancer were documented in the HIV-positive study subjects, compared with 614 cases among the HIV-negative study subjects.

Nineteen of the lung cancer cases were among people living with HIV who reported never smoking, compared with 30 of the lung cancer cases among HIV-negative study subjects who reported never smoking.

After calculating the absolute numbers of lung cancer cases into incidence rates—remember there were nearly twice as many HIV-negative subjects in the study—Sigel and his colleagues concluded that the overall rate of lung cancer was 70 percent higher among those living with HIV, compared with those uninfected with the virus.

Sigel’s team found that HIV itself, after factoring out other characteristics such as smoking and age, was associated with an increased risk for developing lung cancer—a 70 percent increase in the relative risk compared with HIV-negative participants.

Yet the increased risk associated solely with HIV infection was modest compared with smoking history. People living with HIV who were current smokers were six times more likely to develop lung cancer, compared with those who never smoked. The risk of lung cancer was also three times higher among HIV-positive former smokers, compared with nonsmokers.

A COPD diagnosis also increased the risk of a lung cancer among people living with HIV by 90 percent.

Compared with HIV-negative current and former smokers in the study, the risk of lung cancer among HIV-positive current smokers was 50 to 70 percent higher. Among those who never smoked, the risk of lung cancer was 60 percent higher among those living with HIV compared with
those who were HIV negative. However, this relative risk difference between the two groups was not statistically significant, meaning it could have been due to chance.

Interestingly, Hispanic participants were roughly 40 percent less likely to develop lung cancer than white or black participants, and the author commented that this has been found in several other studies.

“As HIV-infected patients are aging on effective [antiretroviral therapy], lung cancer may become an increasingly common and often fatal diagnosis,” Sigel and his colleagues conclude. “The significantly higher overall mortality rate among HIV-infected patients compared to uninfected patients in our cohort denotes a large competing risk for mortality among HIV-infected patients. This suggests that as AIDS-related mortality decreases with improved treatment, an even greater incidence rate of lung cancer may be noted, and our study may under-represent both the incidence and enhanced risk of lung cancer. Additional investigations are required to understand the mechanisms by which HIV infection may increase the risk for lung cancer.”