The Veterans Administration cares for more people with human immunodeficiency virus (HIV) than any other organization in the country. All of these patients are included in the Veterans Aging Cohort Study (VACS), the nation’s largest longitudinal study of people with HIV. Now 20 years old, VACS monitors more than 50,000 patients with HIV and, as a control, more than 100,000 patients uninfected with the virus. The extensive long-term data collected by VACS has allowed research and treatment in many areas of medicine, including cancer.

The Principal Investigator on VACS is Amy Justice, MD, PhD, Professor of Medicine and Public Health and a member of Yale Cancer Center’s Virus and Other Infection-associated Cancers Research Program. Dr. Justice has been researching HIV and its associations with other diseases, including cancer, for more than 25 years. Much has changed. “When I started working on HIV the median survival after an AIDS diagnosis was six months. Now, because of antiretroviral therapy, it’s 30 years,” she says.

This astonishing success has created new complications. Patients with HIV began living long enough to develop other medical problems. Dr. Justice wanted to know if HIV contributed to them, and also how the disease intersected with the process of aging.

“Even if we can suppress the virus with treatment, the virus does substantial damage to the immune system at the beginning of the infection and it often remains active in viral reservoirs, which sets them up for all kinds of conditions associated with aging, cancer common among them,” she says.

In fact, older HIV patients rarely die from AIDS-defining conditions; the main cause of death is non-HIV-related cancer. Studying the relationship between HIV and cancer may open a window into the etiology of cancer that could benefit all cancer patients. In April, Dr. Justice and a colleague received a $3 million grant from the National Cancer Institute to study liver cancer in veterans both with and without HIV to determine whether the cancer functions differently in these two groups.

For this project and others, VACS data will be mined for insights. Because of VACS, notes Dr. Justice, we know that people with HIV have more virally-related or infectious-related cancers than do people without HIV. This is true even when VACS controls for risk factors associated with HIV such as drugs, alcohol, tobacco, race, and socioeconomic status.

“Folks with HIV just have more of these cancers, across the age spectrum,” she says, “and because we have the big sample, we can prepare what is really driving outcomes for people aging with HIV.” For instance, the standard measure of an HIV patient’s health is the number of CD4 T-lymphocytes in a blood sample—the higher, the better. “But through VACS, “ says Dr. Justice, “we’ve shown that CD4 count alone doesn’t really tell you much. Also considering kidney function, liver function, bone marrow function—all tell you a lot more.”

That’s why Dr. Justice and colleagues developed the VACS Index, a diagnostic tool that combines measures from major organ systems to predict various clinical events. The Index has been validated to work not only for the average patient with HIV but also for all the main subgroups broken down by race, gender, age, and other factors. Given the patients’ age, the index’s advanced biostatistical values the program calculates a risk score which can be translated into an overall risk of mortality.

“HIV causes subtle injury to organ systems over time,” explains Dr. Justice, “and it also increases your risk of many comorbid conditions. To understand how sick a patient really is, you need a measure of their overall burden of disease.”

Dr. Justice is extending what she has learned from VACS. She is developing an even larger cohort—all veterans under VA care born between 1945 and 1965, roughly six million people. She also has a grant from the VA Million Veteran Program, which so far has enrolled more than 500,000 veterans, who have provided DNA samples and full access to their electronic records. By combining the phenotypes developed and validated in VACS with this trove of genomic information, she says, “We’ll be able to characterize a tumor and then link it to the patient’s longitudinal record and full genome. That will create an invaluable resource for discovery.”