Articles

- Viral loads becoming undetectable in more people across the United States
- HIV patients 65 years or older face higher rates of serious non-HIV illnesses
- New cancer rates climbing with age in HIV patients, but age impact differs by cancer type
- Grip strength—a health indicator—falls faster in older men with HIV than without HIV
- Smoking may shorten life more than 6 years in US men and women with HIV
- Emphysema tied to cough and slower walking with HIV but not without HIV
- Pneumococcal disease 13 times more frequent in people with HIV
- Heavy and binge alcohol drinking tied to missing HIV care appointments
- Main barriers to antiretroviral pill taking in adults, adolescents, and children
- Fat gains continue and lean mass falls in group on long-term HIV therapy
- Weight gain poses higher diabetes risk with HIV in US veterans study
- Injuries more frequent and cause death more often in people with HIV

Definitions

Board and Staff
MISSION
The Center for AIDS Information & Advocacy empowers people living with HIV to make informed decisions about their health care by providing the latest research and treatment information and by advocating for accessible, affordable, and effective treatment options until there’s a cure.

About HIV Treatment Alerts!

*HIV Treatment Alerts!* is a publication of The Center for AIDS Information & Advocacy (The CFA). This newsletter is intended for those affected by HIV and their caregivers. The statements and opinions expressed in this newsletter do not impy recommendations or endorsement. Always consult your doctor before altering a prescribed drug regimen or taking any drug or supplement.

*HIV Treatment Alerts!* is published twice a year. The print version of the newsletter is available for free at the L. Joel Martinez Information Center at Legacy Montrose Clinic, 1415 California Street, Houston, TX 77006. Access to the newsletter is available online from The CFA website ([www.centerforaids.org](http://www.centerforaids.org)).

The CFA also publishes Research Initiative/Treatment Action! (RITA!), a literature-review journal that covers issues in HIV research and policy. This and other publications are available on The CFA website ([www.centerforaids.org](http://www.centerforaids.org)).

*HIV Treatment ALERTS!* thanks Heather Bradley, Eleanor Friedman, Amy Justice, Phillip Grant, Anne Monroe, Krishna Reddy, Hasina Samji, Jennifer Schrack, Leah Shepherd, Michael Silverberg, Janet Tate, and Matthew Triplette for reviewing the reports on their research.
Among HIV-positive people in care in the United States, proportions (1) prescribed antiretroviral therapy* by their provider and (2) reaching an undetectable viral load rose steadily from 2009 through 2013. Young adults had the biggest gains in proportion with an undetectable viral load, but at the end of the study period, the youngest group still lagged older groups in percent with an undetectable viral load.

Antiretroviral therapy improves the health of people with HIV by making the viral load undetectable in blood and by raising the CD4 count, a measure of immune system health. In 2012 US experts recommended that everyone with HIV infection start antiretroviral therapy, whatever their CD4 count. If people with HIV and their providers follow that advice, proportions of people taking antiretroviral therapy and proportions with an undetectable viral load should go up. To find out if that’s happening, researchers from the US Centers for Disease Control and Prevention (CDC) conducted this study.

How the study worked. CDC researchers used findings from the Medical Monitoring Project, a sample of HIV-positive adults (18 or older) representing all adults in care for HIV across the United States. This analysis focused on people who made at least one HIV office visit in 2009, 2010, 2011, 2012, and 2013. Researchers interviewed each HIV-positive participant and collected additional findings from their medical records.

The CDC team aimed to learn three things about each person studied: (1) whether they were prescribed antiretroviral therapy, (2) whether they had a viral load below 200 copies/mL on their last viral load test, and (3) whether they had a viral load below 200 copies/mL on all viral load tests over the past 12 months. The researchers also figured these rates by sex (male or female), age group (18-29, 30-39, 40-49, 50 or older), race/ethnicity (black, Hispanic, white, other), and sexual orientation (men who have sex with men, men who have sex with women, women who have sex with men). The researchers used standard statistical methods to estimate trends for each of these three outcomes.

What the study found. The study involved more than 4000 people with HIV infection in each study year. The percentage of people prescribed antiretroviral therapy rose steadily over the study period, from 88.7% in 2009 to 94.1% in 2013 (Figure 1). The proportion of people with an undetectable viral load on their last test climbed from 71.6% in 2009 to 80.1% in 2013 (Figure 1). And the percentage of people with a viral load below 200 copies/mL on all tests over the past 12 months rose from 57.6% in 2009 to 68.0% in 2013 (Figure 1).

*Words in bold are defined in the Technical Word List at the end of this issue of HIV Treatment Alerts.
The percentage of people prescribed antiretroviral therapy rose more among women than men over the study period (10% versus 5%). As a result, women nearly caught up with men in proportion prescribed antiretrovirals in 2013 (93.7% and 94.3%). From 2009 through 2013, the antiretroviral therapy rate rose most (24%) in the youngest age group (18-29 years old). But in 2013 the youngest age group still lagged older age groups in percentage being prescribed antiretroviral therapy (by 3 percentage points or more). Over the study period, the antiretroviral therapy rate rose more among blacks (8%) and Hispanics (7%) than among whites (3%). But in 2013 blacks still lagged Hispanics and whites in proportion prescribed antiretrovirals (92.9% versus 95.2%).

The percentage of people with an undetectable viral load over the past 12 months rose more in women than men from 2009 through 2013 (21% versus 16%). But by 2013 a lower percentage of women than men met this 12-month viral load goal (63.5% versus 69.6%). Over the study period, the youngest age group (18-29 years old) made the biggest gains in proportions with an undetectable viral load through 12 months (Figure 2). But in the final year of study, 2013, the youngest age group had not caught up with older age groups by this viral load measure (50.5% versus 73.9% in people 50 or older). Over the 2009-2013 study period, blacks made bigger gains toward this viral load goal than Hispanics or whites. But by 2013 the proportion with an undetectable viral load for the past 12 months was still lower in blacks (61.0%) than in Hispanics (69.9%) or whites (76.0%).

The CDC researchers also calculated that increased prescription of antiretroviral therapy explained 30% of the 2009-2013 rise in the rate of undetectable viral loads on the last test. Increased antiretroviral prescription explained 19% of the 2009-2013 rise in the rate of undetectable viral loads over the past 12 months.

What the results mean for you. This large 5-year study of an HIV-positive group representing everyone in care for HIV across the United States made several encouraging findings about growing prescription of antiretroviral therapy and improving rates of undetectable viral loads. All three of the main study outcomes analyzed improved significantly from 2009 through 2013: percentage of HIV-positive people in care prescribed antiretroviral therapy, percentage with an undetectable viral load on their last test, and percentage with an undetectable viral load over the past 12 months. And all of the subgroups studied had improvement in all three measures: women and men, all age groups, all racial/ethnic groups, and all sexual orientation groups.

Figure 2. Among US adults in care for HIV infection from 2009 through 2013, the youngest age group made the greatest gain in proportion with an undetectable viral load on all measures in the last 12 months. But at the end of the study period, the youngest group still lagged all older groups in proportion with an undetectable viral load for 12 months.
But in 2013, the final year analyzed in this study, certain subgroups had not caught up with others in reaching the antiretroviral use goal or viral load goals:

- Lower proportions of women than men had an undetectable viral load on their last test or over the past 12 months.
- Lower proportions in the youngest age group (18-29) were prescribed antiretroviral therapy or had an undetectable viral load on their last test or over the past 12 months.
- Lower proportions of blacks than Hispanics or whites were prescribed antiretroviral therapy or had an undetectable viral load on their last test or over the past 12 months.

These between-group differences indicate that HIV clinicians have to work harder to get all their patients onto antiretroviral therapy and to take their antiretrovirals steadily so they reach and maintain an undetectable viral load. At the same time, everyone with HIV should work with their providers to select and start a suitable antiretroviral combination. And once treatment begins, people must take their antiretroviral pills regularly, exactly as their prescriber instructs. If you have difficulty taking your pills on time, talk to your provider about ways to improve your pill taking. If you think your antiretrovirals are causing side effects, your prescriber may help you resolve those problems or may want to prescribe a different antiretroviral combination. People with HIV should keep all scheduled medical visits so their provider can stay up to date on their progress or problems.

The study also produced evidence that increasing antiretroviral prescription over the 2009-2013 study period accounts for some of the improvement in undetectable viral load rates. HIV experts in the United States and around the world now recommend antiretroviral therapy for HIV-positive people at any CD4 count because of its many benefits in preventing AIDS diseases and non-AIDS diseases. Findings of this CDC study support that advice. The CDC team also suggested that improving viral load results over the years can be partly explained by better pill taking by people with HIV. And better pill taking probably resulted from development of easy-to-take once-daily antiretroviral combinations with fewer side effects.

References


HIV-positive people 65 years old or older have higher rates of common non-AIDS diseases like heart disease and diabetes than HIV-negative people that age. The findings come from analysis of almost 30 million US residents who use Medicare, the government health insurance plan for people 65 or older.

Much research shows that people with HIV have higher rates of age-related non-AIDS diseases than people without HIV. These diseases include cardiovascular disease, bone disease, diabetes, and kidney disease. Some of this research on non-AIDS disease frequency involves HIV-positive people 50 or older, but there has been little research on HIV-positive people 65 or older—the age when most people in the United States start using Medicare. Research suggests that the average age of people treated for HIV in the United States will jump from 49 in 2015 to 58 in 2035, so the US HIV population will include a growing proportion of people 65 and older.

To get a better understanding of how age-related non-AIDS conditions are affecting elderly US HIV patients today, researchers from the Association of Schools and Programs of Public Health (ASPPH) and the Centers for Disease Control and Prevention (CDC) conducted this study.

■ How the study worked. Researchers identified Medicare users (all of whom must be 65 or older) by reviewing Medicare parts A and B claims for at least 11 continuous months in the years 2006 through 2009. (Part A is hospital insurance; part B is medical insurance.) The analysis did not include people using Medicare within a Health Maintenance Organization. The investigators identified Medicare patients with HIV by using medical codes indicating HIV infection in one hospital or nursing facility Medicare claim or two outpatient (nonhospital) claims.

The researchers also used medical codes to determine which Medicare patients with or without HIV had one or more of the five most common chronic health conditions: hypertension (high blood pressure), high lipids (cholesterol and triglycerides), ischemic heart disease, diabetes, and rheumatoid arthritis or osteoarthritis. Then the research team used standard statistical methods to compare chances of having one of these conditions in people with versus without HIV. This type of analysis accounts for the impact of other factors that raise the risk of these conditions—older age, male versus female sex, race or ethnicity, end-stage kidney disease, and use of both Medicare and Medicaid (which indicates lower income). Thus the analysis figures the impact of HIV on chances of these conditions regardless of whatever other risk factors a person has.

■ What the study found. The analysis included 29,060,418 Medicare users age 65 or older. There were 24,735 people with HIV, about one-tenth of 1% of the whole group. As a group, HIV-positive Medicare users were about 4 years younger than the HIV-negative group. Compared with the HIV-negative group, Medicare users with HIV were almost twice as likely to be men and 5 times as likely to be African American or Hispanic. The HIV group was about 3 times more likely than the non-HIV group to use Medicaid as well as Medicare—indicating lower income in the HIV group.

Compared with HIV-negative Medicare users, HIV-positive Medicare patients were twice as likely to have hypertension or arthritis, 80% more likely to have high lipids or heart disease, and 50% more likely to have diabetes (Figure 1). These higher chances of the five conditions with HIV held true regardless of other major risk factors for these conditions.

Compared with HIV-negative people 65 or older, HIV-positive people that age were twice as likely to have hypertension or arthritis.

*Words in **bold** are defined in the Technical Word List at the end of this issue of *HIV Treatment Alerts*. 
In a separate analysis that also considered the impact of several illness risk factors, Medicare users with HIV were more than twice as likely to have 1 or 2 of the five conditions studied than people without HIV (Figure 2). The HIV group was 3 as likely as the HIV-negative group to have 3 of the conditions studied, 4 times as likely to have 4 of those conditions, and 7 times as likely to have all 5 of those conditions (Figure 2). This analysis considered the potential impact of factors that raise the risk of chronic conditions—older age, male versus female sex, race or ethnicity, end-stage kidney disease, and use of both Medicare and Medicaid (which indicate lower income and long-term disabled status).

If an HIV-positive person had additional risk factors, it was even more likely that this person would have 1 or more chronic conditions. For instance (1) men were more likely than women, (2) African Americans and Hispanics were more likely than whites, (3) people with both Medicare and Medicaid (indicating lower income) were more likely than people only with Medicare, and (4) people with end-stage kidney disease were more likely than those without end-stage kidney disease. Two groups were less likely to have 1 or more of the studied conditions: (1) younger people were less likely than older people, and (2) HIV-positive Asian/Pacific Islanders and Native Americans were less likely than whites.

**Figure 2.** Compared with HIV-negative people 65 or older, HIV-positive people that age ran a higher risk of having 1, 2, 3, 4, or 5 conditions studied: hypertension, arthritis, high lipids, heart disease, and diabetes.
What the results mean for you. This very large study of Medicare users (all 65 or older) across the United States found that older people with HIV were more likely than those without HIV to have all five age-related conditions studied: hypertension (high blood pressure), high cholesterol or triglycerides, ischemic heart disease, diabetes, and arthritis. Compared with HIV-negative Medicare users, HIV-positive Medicare users were more likely to have 1, 2, 3, 4, or all 5 of these conditions.

This study adds to the convincing evidence that people with HIV face greater threats to their health as they age than people without HIV. Most previous studies of aging and HIV were much smaller and used age 50 as the cutoff between middle age and old age. This new study is valuable because it is much larger than previous studies, includes people across the United States, and uses 65 as the middle-to-old-age cutoff.

Because so many HIV-positive people in the United States are taking effective antiretroviral therapy (see the article starting on page 3 of this issue3), they are living well into their 60s and 70s. Even without HIV, they would face an increasing risk of age-related disease as they grew older. This study addresses the question whether HIV-positive people 65 or older face a greater risk of these diseases than people the same age without HIV. The answer is yes.

Many age-related conditions can be prevented or effectively treated if they do develop. Maintaining an active lifestyle and eating a balanced diet can prevent or slow development of many age-related conditions. And preventing or treating one condition can often prevent others. For example, among the conditions in this analysis, preventing or treating hypertension (high blood pressure), high cholesterol, or diabetes can prevent heart disease. High blood pressure, high cholesterol, and diabetes can all be detected with simple tests. It is important to work with your HIV provider to get regular testing for conditions like these, to develop prevention plans, and to get treated for conditions that do arise.

References

1. Friedman EE, Duffus WA. Chronic health conditions in Medicare beneficiaries 65 years and older with HIV infection. *AIDS*. 2016;30:2529-2536.


New cancer rates climbing with age in HIV patients, but age impact differs by cancer type

Development of new cancers rose with older age in a 15,000-person analysis of HIV-positive people across Europe.\(^1\) Overall incidence* (the new cancer detection rate) of infection-related cancers is forecast to drop as rates of untreated HIV infection continue to fall. But overall incidence of cancers not related to infection is forecast to rise, partly because of high rates of smoking and lung cancer in people with HIV.

Compared with the general population, people with HIV run a higher risk of many cancers. The reasons for this higher cancer risk with HIV are not fully understood. Reasons probably include high rates of cancer risk factors like smoking in people with HIV, more frequent infection with viruses that lead to cancers, and a weakened immune system because of HIV infection. Also, when people began living longer with HIV infection thanks to antiretroviral therapy, they began facing a higher risk of cancers that become more common in older age.

To learn more about cancer rates and risk in people with HIV, researchers conducted this large European study. They aimed to assess the impact of aging on two main types of cancer in people with HIV: infection-related cancer and infection-unrelated cancer.

**How the study worked.** The cancer analysis involved members of the EuroSIDA group, an ongoing study of HIV-positive people in 35 European countries, Israel, and Argentina. Twice a year, researchers collect information on EuroSIDA members and send it to a central database, where it can be analyzed later. Such information includes age, sex, CD4 count, viral load, antiretroviral therapy, and newly detected diseases including cancers.

The new cancer study focused on EuroSIDA members who had data recorded after January 1, 2001. Researchers analyzed their data until their last EuroSIDA study visit or death. The main goal was to see what new cancers developed in that time. The research team sorted cancers into two groups: Infection-related cancers include Kaposi sarcoma, Hodgkin lymphoma, non-Hodgkin lymphoma, cervical cancer, cancers of the anus, penis, vulva, vagina, liver, or stomach, and certain head and neck cancers. Infection-unrelated cancers include all other cancers, such as lung cancer and prostate cancer.

The researchers used standard statistical methods to estimate the impact of age on new development of infection-related cancers and infection-unrelated cancers. The method used also accounts for the potential impact of many other factors that can affect cancer risk, such as gender, smoking, CD4 count, viral load, and previous diagnoses of AIDS, cancers, and serious diseases like heart disease, kidney disease, and liver disease. Thus this method can estimate the impact of age alone on new cancers, regardless of whatever other risk factors a person has.

**What the study found.** The study included 15,648 HIV-positive people with data available over a median of 6 years. When people entered the study, 16% were 50 or older and about one third smoked. Most study participants (88%) were white and most (73%) were men. At study entry, 15% of participants had a CD4 count at or below 200, and 55% had a viral load at or below 400 copies.

During the study period, 643 cancers developed in 610 people, including 388 infection-related cancers (60%) and 255 infection-unrelated cancers (40%). The most frequent infection-related cancers were non-Hodgkin lymphoma (116 cases), anal cancer (83 cases), and Kaposi sarcoma (62 cases). The most frequent infection-unrelated cancers were lung cancer (55 cases), prostate cancer (28 cases), and colorectal cancer (23 cases). People with infection-related cancer were older than those with infection-unrelated cancer when the cancer was detected (median 54 versus 46 years). And at cancer detection, people with infection-related cancer had a higher CD4 count (median 466 versus 342).

*Words in **bold** are defined in the Technical Word List at the end of this issue of *HIV Treatment Alerts.*
The analysis that accounts for many cancer risk factors at the same time figured that people 50 or older had a 62% higher incidence (new detection rate) of infection-related cancer than people 36 to 40 years old (Figure 1). Infection-related cancer incidence was 17% higher for every additional 10 years of age. Three HIV-related factors were strongly linked to infection-related cancer incidence: a current viral load above 400 copies meant an almost doubled cancer incidence, a current CD4 count below 200 (versus 500 or higher) was linked to almost a 4-fold higher incidence, and a current CD4 count between 200 and 349 (versus 500 or higher) was linked to almost a doubled incidence (Figure 1).

For infection-unrelated cancers, being 50 or older (versus 36 to 40) was linked to a 7.3-fold higher cancer incidence and being 41 to 50 (versus 36 to 40) was linked to a 2.4-fold higher incidence (Figure 2). Incidence of infection-unrelated cancers doubled with every additional 10 years of age. Current CD4 count below 200 (versus 500 or higher) was linked to a 1.5-fold higher incidence of infection-unrelated cancer (Figure 2). Current smoking was linked to a doubled incidence of infection-unrelated cancer (Figure 2). The link between sub-200 CD4 count and higher infection-unrelated cancer incidence held true in people younger than 50 but not in those 50 or older. In contrast, the link between current smoking and higher infection-unrelated cancer incidence held true in people 50 or older but not in those younger than 50.

Finally, the EuroSIDA researchers focused on 6111 people who entered the study before January 2001. During the study period, 243 infection-related cancers and 161 infection-unrelated cancers developed in this group. Assuming that current new-cancer trends continue, the researchers predicted how cancer incidence would change over the course of 5 years.
They figured that incidence of infection-related cancers will fall from 3.1 cases per 1000 people in 2011 to 2.2 per 1000 after 5 years (Figure 3). In contrast, they projected that incidence of infection-unrelated cancer would rise from 4.1 cases per 1000 in 2011 to 5.9 per 1000 after 5 years. There was one exception to this second forecast: Among people who never smoked, the researchers figured that incidence of infection-unrelated cancers would drop from 1.7 cases per 1000 in 2011 to 0.8 per 1000 after 5 years.

What the results mean for you. This large many-year study made several important findings about cancer risk in people with HIV, including these key results:

- Age 50 or older was linked to a higher incidence (new cancer detection rate) of both infection-related cancers and infection-unrelated cancers.
- The impact of being 50 or older was greater for infection-unrelated cancers (7.3-folder higher incidence) than for infection-related cancers (1.6-fold higher incidence).
- Incidence of infection-related cancer was 1.17-fold higher for every additional 10 years of age, while incidence of infection-unrelated cancer was 2.07-fold higher for every 10 years of age.
- Incidence of infection-related cancer is expected to fall from 3.1 cases per 1000 people to 2.1 per 1000 over 5 years.
- Incidence of infection-unrelated cancer is expected to rise from 4.1 cases per 1000 people to 5.9 per 1000 over 5 years.
- Incidence of infection-unrelated cancer is expected to fall from 1.7 cases per 1000 people to 0.8 per 1000 people over 5 years in people who never smoked.
Infection-unrelated cancers include lung cancer, prostate cancer, cancer of the colon and rectum, and breast cancer. The researchers believe the rate of infection-unrelated cancer will rise for several reasons: (1) The HIV population is aging and these cancers become more frequent with older age. (2) Smoking causes two major infection-unrelated cancers—lung cancer and cancer of the colon and rectum—and a high proportion of people with HIV continue to smoke. (3) Low CD4 count and high viral load add to the risk of infection-related cancers. Because fewer people with HIV have untreated and advanced HIV infection, the rate of infection-related cancers is going down, so infection-unrelated cancers become more prominent.

Because of the projected surge in infection-unrelated cancers in people with HIV, the EuroSIDA researchers believe more attention should be paid to preventing these cancers and to studying the potential benefits of testing for these cancers. Regular testing for three infection-unrelated cancers—prostate cancer, colorectal cancer, and breast cancer—has become routine for many people, especially as they age. High rates of these cancers in people with HIV should encourage anyone with HIV to talk to their provider about current guidelines on testing for these cancers.

The leading infection-unrelated cancer in this EuroSIDA group, and in many HIV populations, is

**Figure 3.** Cancer trends in 6111 people with HIV allowed researchers to project 5-year changes in incidence (new detection) of infection-related cancer (down from 3.1 to 2.2 per 1000 person-years), infection-unrelated cancer (up from 4.1 to 5.9 per 1000 person-years), and infection-unrelated cancer in people who never smoked (down from 1.7 to 0.8 per 1000 person-years).
lung cancer. Avoiding smoking—or quitting if you already smoke—can help prevent not only lung cancer but mouth and throat cancer, colorectal cancer, liver cancer, other cancers, and other major diseases like heart disease and stroke. Quitting smoking isn’t easy, but the United States has more people who quit smoking than who continue to smoke. Your HIV provider can help you quit by prescribing certain drugs or nicotine replacement therapy and by guiding you to effective smoke-ending strategies like the internet-based Positively Smoke Free, created especially for people with HIV (see link at reference 3).

Drinking too much alcohol can lead to cancer of the head and neck, esophagus, liver, breast, colon, and rectum. If you drink too much, talk to your HIV provider or case worker about finding ways to limit or stop drinking.

Some infection-related cancers can be prevented by using condoms to prevent transmission of cancer-causing viruses (HBV, HCV, HPV) and by getting vaccinated against HBV and HPV. Everyone with HIV who does not already carry hepatitis B virus (HBV) should get the HBV vaccine. The CDC recommends the HPV vaccine for women up to age 26, for gay or bisexual men with or without HIV up to age 26, and for other men up to age 21.

References


   http://www.cdc.gov/tobacco/data_statistics/sgr/50th-anniversary/index.htm#report


Grip strength—a health indicator—falls faster in older men with HIV than without HIV

Grip strength fell faster after age 50 in men with HIV than in a similar group of HIV-negative men, according to a 7-year analysis in the United States. A simple measure of physical function, grip strength predicted declining function and death in previous studies. The new study is the first to compare grip strength over several years in older HIV-positive men and in a group of similar men without HIV infection.

Thanks to antiretroviral therapy,* people with HIV infection are living much longer. In 2014 about half of all people living with HIV in the United States were 50 or older. But many studies show that older people with HIV face a higher risk of serious disease and disability than people the same age without HIV. Muscle strength is an essential part of healthy living at any age. Research shows that grip strength—easily measured with a simple device—represents strength in the whole body. Studies indicate that grip strength predicts disability, sickness, and death in middle-aged and older people.

To compare changes in grip strength over the course of several years, US researchers conducted this study in middle-aged and older men with HIV and a similar group of HIV-negative men about the same age.

How the study worked. The study involved HIV-positive and negative gay/bisexual men in the Multicenter AIDS Cohort Study (MACS). The MACS is an ongoing US study in which men make study visits twice a year to get examined and have health-related tests.

Since October 2007 men had a grip strength test twice a year using a simple hand-held squeeze device that measures strength on a meter. Men took the grip strength test from October 2007 or from the date they entered MACS until a final measurement in 2014. The investigators defined weakness as a grip strength less than 26 kilograms.

The researchers used a standard statistical method to determine change in grip strength over time. This kind of analysis accounts for the impact of several factors that may affect grip strength. So individual factors that may influence grip strength—like HIV infection—can be said to have that effect regardless of whatever other factors are involved. The research team conducted a separate statistical analysis only in men with HIV to assess the impact of several HIV-related factors on grip strength.

What the study found. The study focused on 716 HIV-positive men and 836 men without HIV. All were at least 50 years old at their first study visit, and all had two or more study visits between October 2007 and September 2014. Age averaged 53.4 years in men with HIV and 56 years in HIV-negative men. The HIV group included a higher proportion of nonwhites (34.5% versus 20.7%) and a higher proportion who used drugs at some time (50.6% versus 39.8%). Men with HIV had taken an HIV-drug combination for an average 9.1 years, and 78.5% had a viral load below 200 copies.

Average grip strength at age 50 was similar in men with HIV (37.9 kilograms) and men without HIV (38.2 kilograms) (Figure 1). But after age 50 grip strength fell faster in HIV-positive men (0.42 kilogram per year) than in HIV-negative men (0.33 kilogram per year) (Figure 1). This difference is statistically significant—meaning that a statistical test indicates that chance does not explain the difference. Compared with HIV-negative men, men with HIV had a 70% greater risk of weakness as measured by grip strength. Other factors linked to a significantly faster drop in grip strength were lower body mass index (weight), nonwhite race, less education, kidney disease, and peripheral neuropathy (persistent weakness, numbness, or pain in the feet or hands).

*Words in bold are defined in the Technical Word List at the end of this issue of HIV Treatment Alerts.
Figure 1. At age 50 men with HIV had an average grip strength (measured in kilograms, kg) similar to men without HIV. But after age 50, men with HIV lost more grip strength yearly than men without HIV.

The new study is the first to compare grip strength over several years in older HIV-positive men and in a group of similar men without HIV infection.

The researchers divided men with HIV into three groups according to how often they had an undetectable viral load at a study visit: undetectable at every study visit, detectable at 1 to 6 visits, and detectable at 7 or more visits (Figure 2). In this analysis HIV-negative men lost grip strength at a rate of 0.39 kilogram per year. In contrast, HIV-positive men with an undetectable viral load at every study visit lost grip strength at a rate of 0.48 kilogram per year; HIV-positive men with a detectable viral load at 1 to 6 visits lost grip strength at a rate of 0.79 kilogram per year; and men with a detectable viral load at 7 or more visits lost grip strength at a rate of 2.39 kilograms per year.

To get an idea of factors that contribute to falling grip strength in men with HIV, the researchers divided those men into two groups—106 men who became weak (grip strength below 26 kilograms) and 610 men who did not become weak (grip strength always 26 kilograms or higher). The weak group differed significantly from the nonweak group in four ways:

- Average 2.2 years older
- Lower body mass index (a measure of weight)
- More likely to have diabetes, kidney disease, or peripheral neuropathy
- Higher total viral load over time
Years infected with HIV or total time taking antiretroviral therapy did not differ significantly between weak men and nonweak men.

**What the results mean for you.** This study focused on grip strength—an easily measured indicator of overall strength and survival. At age 50 gay/bisexual men with HIV had an average grip strength similar to gay/bisexual men without HIV. But as men grew older than 50, the HIV group lost grip strength faster than the HIV-negative group. And men with HIV ran a higher risk of weakness (as defined by grip strength). Decreased strength could contribute to lower quality of life and shorter survival in people with HIV.

HIV-positive men in this study who kept their viral load undetectable all or most of the time lost grip strength more slowly than men whose viral load was detectable more often. The only way to make your viral load undetectable—and to keep it undetectable—is to start antiretroviral therapy and then to take all your HIV medications on time, exactly as your provider instructs. This study adds to the reasons people with HIV should begin antiretroviral therapy as soon as they know they have HIV and then make steady pill-taking a priority of their health care.

The researchers who conducted this study note that further research is needed to develop specific strategies to help preserve strength in aging people with HIV. But it is already clear that a healthy diet and regular physical activity and exercise help people maintain strength as they age. If you do not already exercise, you should get advice from your health care team and other knowledgeable people about planning an exercise program. The types of physical activity or exercise you

---

**Figure 2.** Compared with HIV-negative men, HIV-positive men 50 or older lost more grip strength yearly—and the drops were greater in men with viral load (VL) detectable at more study visits.
Physical activity is important in maintaining strength when aging. The types of physical activity or exercise you do should be the types you like and can do regularly. You should talk to your provider before starting any strenuous exercise program.

Table 1. Exercises to strengthen muscles and promote heart health in older adults

<table>
<thead>
<tr>
<th>Muscle-strengthening exercises</th>
<th>Heart health exercises</th>
</tr>
</thead>
<tbody>
<tr>
<td>➤ Exercises using exercise bands, weight machines, hand-held weights</td>
<td>➤ Walking</td>
</tr>
<tr>
<td>➤ Calisthenics (exercises in which body weight provides resistance to movement)</td>
<td>➤ Jogging</td>
</tr>
<tr>
<td>➤ Digging, lifting, and carrying as part of gardening</td>
<td>➤ Dancing</td>
</tr>
<tr>
<td>➤ Carrying groceries</td>
<td>➤ Swimming</td>
</tr>
<tr>
<td>➤ Some yoga exercises</td>
<td>➤ Water aerobics</td>
</tr>
<tr>
<td>➤ Some tai chi exercises</td>
<td>➤ Bicycle riding (stationary or outdoors)</td>
</tr>
<tr>
<td></td>
<td>➤ Raking or pushing a lawn mower</td>
</tr>
<tr>
<td></td>
<td>➤ Tennis</td>
</tr>
<tr>
<td></td>
<td>➤ Golf (without a cart)</td>
</tr>
</tbody>
</table>


The US Office of Disease Prevention and Health Promotion suggests several types of exercise or physical activity to strengthen muscles or promote heart health in older adults (Table 1).

References

Smoking may shorten life more than 6 years in US men and women with HIV

Compared with HIV-positive 40-year-olds who never smoked, those who do smoke could lose more than 6 years of life as a result. The statistical analysis that provided that estimate also figured that HIV-positive 40-year-olds who quit smoking when they start HIV care could save 5 or 6 years of life. HIV-positive smokers 50 or 60 years old also gain life years if they quit.

Smoking remains the leading preventable cause of death in the United States, according to the Centers for Disease Control and Prevention (CDC). Although smoking shortens life by up to 10 years in the general US population, some of those lost years can be “regained” if people quit smoking. The CDC determined that 42% of HIV-positive adults in the United States smoke, compared with 20% of US adults without HIV. Another 20% of adults with HIV are former smokers, a finding indicating that a sizeable proportion of people with HIV do quit.

US researchers performed this analysis to estimate how many years of life HIV-positive people lose if they smoke—and how many years of life they regain if they quit.

How the study worked. The study relied on a mathematical model that has been used successfully in people with HIV. A mathematical model plugs data into mathematical formulas to predict real-life outcomes. For example, models have a good record in making accurate weather forecasts. Health researchers are refining the ability of models to predict health outcomes—like life expectancy.

The models assume that everyone starts antiretroviral therapy as soon as they begin care for HIV, as US treatment guidelines now recommend. For each individual created by the model, the analysis forecasts the course of their health and eventual death by considering the impact of several real-world factors. Those factors include CD4 count, viral load, AIDS-related diseases, adherence to antiretroviral therapy (taking all pills on time), and keeping medical appointments. For all health-related factors in smokers and nonsmokers—and in people with and without HIV—the researchers used actual findings they collected from previous studies.

The mathematical models aimed to estimate how long HIV-positive people entering care would survive if they never smoked, if they smoked and continued smoking, or if they smoked then quit smoking when they started HIV care. The analysis figured these survival rates for men and women, and for people who stopped smoking 5 or 10 years after they entered HIV care.

The researchers also used models to compare life years lost from smoking in HIV-negative people versus HIV-positive people. And in the HIV-positive group, they compared life years lost from smoking with life years lost from HIV infection. The research team performed this last analysis in (1) HIV-positive people with less than perfect adherence (antiretroviral pill taking) and less than perfect medical appointment keeping, and (2) in HIV-positive people with perfect antiretroviral adherence and appointment keeping.

Finally, mathematical models figured how many life years would be gained if HIV-positive smokers quit smoking when they started HIV care according to (1) sex, (2) age when HIV care began, and (3) CD4 count when HIV care began.

What the study found. The researchers estimated that almost 250,000 HIV-positive 30- to 64-year-olds in care in the United States smoke. The model projected that a 40-year-old man starting HIV care and continuing to smoke could expect to live to age 65.2 (Figure 1). A man who quit smoking when starting HIV care at age 40 could expect to live to age 70.9 (5.7 years longer than the man who did not quit smoking). And a man who never smoked and started HIV care at age 40 could expect to live to 71.9 (6.7 years longer than the man who did not quit smoking).

A woman who started HIV care at age 40 and did not quit smoking could expect to live to age 68.1 (Figure 1).

*Words in bold are defined in the Technical Word List at the end of this issue of HIV Treatment Alerts.
But if that woman quit smoking when she started HIV care she could expect to live to 72.7 (4.6 years longer than if she did not quit smoking). And if she never smoked she could expect to live to 74.4 (6.3 years longer than a smoker who did not quit).

The model makes different predictions for 40-year-old men and women with perfect pill-taking adherence and appointment keeping (Figure 2): Men in this group could expect to lose 8.6 years from smoking but only 3.5 years from HIV. And women could expect to lose 8.2 years from smoking but only 4.3 years from HIV. In other words, HIV-positive people who take their antiretrovirals on time and keep all their medical appointments are less likely to die from HIV, and smoking has a much greater impact on their life expectancy than HIV itself.

The model also figured that smokers who start HIV care but do not quit smoking for another 5 or 10 years still add to their life expectancy when they do quit. For example, a man who smokes and starts HIV care at

---

*Figure 1.* A mathematical projection study estimated that HIV-positive people who start antiretroviral therapy at age 40 and who smoke can expect to live to age 65.2 (men) or age 68.1 (women) if they do not stop smoking. In contrast, 40-year-olds who quit when they enter HIV care at age 40 can expect to live to age 70.9 (men) or 72.7 (women). And 40-year-olds who never smoked can expect to live to age 71.9 (men) or 74.4 (women).
HIV-negative 40-year-old men and women can expect to lose more than 10 years of life from smoking, according to mathematical analysis projections. Among HIV-positive 40-year-olds who take all their antiretrovirals on time and keep all medical appointments, the model projects that smoking subtracts 8.6 years of life in men and 8.2 years in women. In contrast, HIV subtracts only 3.5 years in men and 4.3 years in women who take all their HIV pills and keep appointments.

Age 40 gains 5.7 years of life if he stops smoking at the same time he starts HIV care, 3.3 years of life if he quits smoking 5 years after starting HIV care, and 2.9 years if he quits smoking 10 years after starting HIV care. Women smokers who start HIV care at age 40 gain 4.6 years if they quit smoking immediately upon starting care, 3.1 years if they quit 5 years after starting care, and 2.8 years if they quit 10 years after starting care. Quitting smoking adds life years not only for people 40 years old when starting HIV care, but also for people 50 or 60 when starting care. For example, the model projected that among men who start HIV care with a CD4 count of 300, those 50 years old can expect to gain 3.6 years of life by quitting smoking and those 60 years old can expect to gain 2.6 years of life. For women who start care with a CD4 count of 300, those 50 years old can expect to gain 3.3 years of life from quitting and those 60 years old can expect to gain 2.4 years.

What the results mean for you. Before this study we knew that 4 in 10 HIV-positive adults in the United States smoke and that smoking has a tremendous (but reversible) impact on the heart and lungs and on cancer risk. By plugging recorded health findings into mathematical formulas, this study expands the understanding of how smoking affects length of life in people with HIV.

HIV-positive people are living much longer because antiretroviral therapy prevents AIDS diseases and other diseases. The new study estimated that a 40-year-old smoker starting HIV care can expect to live to age 65.2 (men) or 68.1 (women) (Figure 1). But if those smokers...
Quitting smoking is not easy, but it can be done and there are ways to improve chances of success. Smokers should realize three things about quitting:

1. Among all HIV-positive people in the United States today, 1 in 5 are people who quit smoking.4
2. Among all people in the United States today, there are more people who quit smoking than still smoke.6
3. Most people who quit smoking fail to quit several times before they succeed. So if you tried to quit and didn’t succeed, keep trying.

Your HIV provider can prescribe nicotine replacement therapy or two drugs—Chantix or Zyban—to help you stop smoking. Some smokers who want to quit get good results from a limited number of counseling sessions. You may want to try a free 8-segment online smoke-ending program created for people with HIV at https://www.positivelysmokefree.com/. The important thing is to make a plan with your HIV provider or with a smoking counselor your provider recommends and then keep trying until you quit.* If you succeed, you will live longer.

*An online publication from the Center for AIDS has a great deal of practical information on quitting. See pages 9-23 at http://centerforaids.org/pdfs/rita0116.pdf

References

HIV-positive people with emphysema (em-fuh-ZEE-ma), a serious lung disease, had more chronic cough and a lower maximum distance walked in 6 minutes than HIV-positive people without emphysema in a US study.\(^1\) The link to cough and slower walking held true even in HIV-positive people with milder emphysema. But emphysema did not affect breathing symptoms and walk distance in a comparison group of people without HIV.

Emphysema is a type of chronic obstructive pulmonary disease (COPD); it is an incurable lung disease marked by shortness of breath and increasingly difficult breathing.\(^2\) This serious but manageable illness involves destruction of air sacs in the lung (Figure 1). It can cause shortness of breath as well as daily or almost daily coughing and phlegm (mucus) production.

Smoking is the major cause of emphysema, and smoking is twice as frequent in US people with HIV as in those without HIV.\(^3\) More than 40% of HIV-positive people in the United States smoke. Researchers who conducted the new emphysema study\(^1\) noted that emphysema is more common and occurs at an earlier age in people with than without HIV, even in analyses that account for the higher smoking rate in HIV-positive people.

But little is known about how emphysema affects health in people with HIV. To learn more about the health impact of emphysema in people with versus without HIV, researchers conducted this comparative study.

**How the study worked.** The analysis focused on a group of US veterans in the Examinations of HIV-Associated Emphysema (EXHALE) study, a substudy of the larger Veterans Aging Cohort Study (VACS). The EXHALE study enrolled HIV-positive and negative veterans. Each HIV-positive veteran was matched to an HIV-negative veteran according to whether they smoked. Over a study period from 2009 through 2012, researchers collected detailed lung-related data. No one who entered the substudy had chronic obstructive lung diseases other than asthma or COPD, and no one had acute lung symptoms within the last month.

![Figure 1. In a person with emphysema, walls of air sacs in the lung (also called alveoli) begin to collapse. As a result, breathing becomes harder. (Illustrations from Servier PowerPoint Image Bank, http://servier.com/Powerpoint-image-bank.)*](image)

*Words in **bold** are defined in the Technical Word List at the end of this issue of *HIV Treatment Alerts.*
All study participants had a chest CT (a scan similar to an x-ray) read by a single CT expert to determine whether each person had emphysema. The CT expert rated each scan on a scale from 0 (no emphysema) to 5 (more than 75% emphysema). Researchers split participants into two groups: (1) no emphysema or trace emphysema (10% or less emphysema on the CT), and (2) mild or worse emphysema (more than 10% emphysema on the CT).

The researchers used medical records and a questionnaire to collect other health data on study participants, including a detailed smoking history. Participants reported whether they had chronic cough and/or phlegm and whether they had shortness of breath upon exertion. They also had a spirometry test, a simple way to measure inhaling and exhaling ability. Finally, researchers measured how far each participant could walk in 6 minutes. (This is a standard test used to see whether lung disease limits walking.) Participants completed all these tests within about 2 weeks of entering the study.

The researchers used an accepted statistical method to determine whether HIV could be linked to emphysema independent of other risk factors including smoking. They used a similar test to explore links between CT-confirmed emphysema and shortness of breath on exertion, chronic cough and/or phlegm, and 6-minute walk distance.

■ What the study found. The study involved 170 veterans with HIV and 153 without HIV. Large majorities of both groups were men, and most participants were in their early to mid-50s. Most veterans were black (72% with HIV, 63% without HIV). According to the study plan, similar high proportions of participants currently smoked (68% with HIV, 58% without HIV). The HIV group had significantly higher proportions with a history of lung diseases like tuberculosis (7.1% versus 1.3%), pneumocystis pneumonia (1.8% versus 0), and bacterial pneumonia (17% versus 3.9%). (In this review “significant” means a statistical test determined that the difference cannot be explained by chance.)

Compared with the HIV-negative group, veterans with HIV had significantly worse lung function measured as ability to transfer gas from inhaled air to red blood cells in the lung. And a significantly higher proportion of HIV-positive veterans reported chronic cough and/or phlegm (66% versus 55% without HIV). Overall, the groups were similar in proportions reporting shortness of breath on exertion (about 40%) and in their 6-minute walk distance (about 425 meters, or 465 yards). Three quarters of veterans with HIV were taking antiretroviral therapy,* and two thirds had an undetectable viral load.

About half of veterans with or without HIV had no evidence of emphysema on their CT scan. But the HIV group had a significantly higher proportion with greater than 10% emphysema on their CT scan (31% versus 16%). Statistical analysis determined that HIV-positive veterans had a 2 times higher chance of worse than 10% emphysema than HIV-negative veterans, regardless of whatever other emphysema risk factors these veterans had (Figure 2). In other words, HIV alone—separately from smoking and other risk factors—doubled the odds of emphysema. Other factors that, by themselves, raised chances of emphysema were older age, more smoking, using inhaled drugs, and injecting illegal drugs.
The researchers compared HIV-positive people with worse than 10% emphysema to HIV-positive people without emphysema. Those with emphysema had 2.6 times higher chances of cough and/or phlegm (Figure 2), and those with emphysema walked 35 meters (38 yards) less on the 6-minute walk test. These outcomes were independent of other risk factors like amount of smoking, age, race, sex, drug use, and certain major illnesses. In the same analysis, HIV-negative people with emphysema did not differ from HIV-negative people without emphysema in chronic cough and/or phlegm or in 6-minute walk distance.

Next the researchers limited these analyses to people without evidence of COPD or obstructive lung disease detected by the spirometry test. HIV-positive people with worse than 10% emphysema had 4.2 times higher chances of chronic cough and/or phlegm than HIV-positive people without emphysema (Figure 2). And HIV-positive people with emphysema walked 60 meters (66 yards) less on the 6-minute walk test. In the same analysis, HIV-negative people with emphysema (but without COPD) did not differ from HIV-negative people without emphysema in chronic cough and/or phlegm or in 6-minute walk distance.

Finally the researchers performed a statistical analysis to determine the impact of worsening emphysema on the 0 to 5 scale (with 0 meaning no emphysema and 5 meaning the worst emphysema). In veterans with HIV, every 1-point higher (worse) emphysema score meant a 40% higher chance of cough and/or phlegm, a 40% higher chance of shortness of breath on exertion, and 9.5 fewer meters (10 yards) walked on the 6-minute walk test. In veterans without HIV, worse emphysema scores did not affect 6-minute walk distance or chances of cough or shortness of breath.
What the results mean for you. This careful comparison of veterans with HIV and a similar group of veterans without HIV made several important findings. First, HIV-positive veterans had a twice higher chance of having emphysema than HIV-negative veterans—regardless of whatever other emphysema risk factors a person had (like smoking). Second, HIV-positive veterans with emphysema had a higher chance of cough or phlegm and could not walk as far in 6 minutes as HIV-positive veterans without emphysema. Third, those findings held true for HIV-positive veterans with milder emphysema and without evidence of COPD measured by the spirometry test. And fourth, in people with HIV worse emphysema measured by CT scan meant worse coughing, worse shortness of breath, and a shorter distance on the 6-minute walk test.

These findings in HIV-positive veterans did not apply to veterans without HIV. That result adds to the evidence that something about HIV makes certain non-HIV diseases more frequent or worse. Since most of these veterans had good control of their HIV with antiretroviral therapy, it is possible that ongoing inflammation despite good HIV control plays a role in making non-HIV diseases more frequent or worse. In people with emphysema, that inflammation probably involves the airways.

These findings are important because emphysema can usually be prevented by avoiding smoking or quitting smoking. And someone who already has emphysema should try hard to quit because smoking will make emphysema worse. This study confirmed earlier research linking more smoking to a higher risk of emphysema. If you smoke, your HIV provider can help you make a plan to quit. That plan may involve nicotine-replacement therapy, a smoke-ending medicine, or an online individual smoke-ending program designed for people with HIV (see the link at reference 4). About 20% of HIV-positive people in the United States are people who successfully quit smoking.

Uncontrolled emphysema can lead to large holes in the lungs, collapsed lung, respiratory failure, and ultimately death. The Centers for Disease Control and Prevention (CDC) estimates that 3.4 million new cases of emphysema developed in the United States in the past year and almost 7500 people died of emphysema. COPD, which includes emphysema, is the third leading cause of death in the United States. Don’t add yourself to those numbers. Stop smoking to avoid emphysema and COPD.

References


4. Positively Smoke Free. Created by experts, refined by real users like you. https://wwwPOSITIVELYSMOKEFREE.com/


Compared with HIV-negative people, people with HIV had a 13 times higher rate of invasive pneumococcal disease, a possibly serious infection with the bacterium *Streptococcus pneumoniae* (Strep) (Figure 1). The rate of new pneumococcal (new-mo-KOK-al) infection in HIV-positive people dropped over the 1996-2011 study period. But in the most recent years analyzed, people with HIV still had more than a 6 times higher rate of invasive pneumococcal disease than a similar group of people without HIV.

Invasive pneumococcal disease can appear as pneumonia, blood infection (bacteremia or sepsis), meningitis, or middle-ear infection. These possibly life-threatening infections can be prevented by vaccination. In 2012 US experts recommended that people with HIV receive the PCV13 vaccine, followed by the PPSV23 vaccine.

Studies suggest that invasive pneumococcal disease rates are falling in people with HIV, but these studies lack an HIV-negative comparison group similar to the HIV group analyzed. Researchers in the Kaiser Permanente Northern California group conducted a new study to provide this kind analysis within this single healthcare system.

**How the study worked.** The research team identified everyone at least 18 years old and in care for HIV at Kaiser Permanente Northern California on or after January 1, 1996. For each HIV-positive person, the researchers selected 10 HIV-negative people the same sex and age (within 5 years) who started care in the same year as the HIV-positive person at the same medical center. The investigators checked medical records of each person until invasive pneumococcal disease developed, or until December 31, 2011, or until the person left the Kaiser system or died. Pneumococcal vaccines are given in the Kaiser system at no extra charge.

The main study outcome was lab-confirmed development of invasive pneumococcal disease in blood, brain and spinal fluid, bone, or joints. The researchers also collected other health data from the file of each study participant. Then they calculated the rate of invasive pneumococcal disease per 100,000 person-years,* that is, how many cases of invasive pneumococcal disease developed

*Words in **bold** are defined in the Technical Word List at the end of this issue of *HIV Treatment Alerts.*
in 100,000 people each year. They used a standard statistical method to compare pneumococcal disease rates in people with versus without HIV. This kind of analysis considers many invasive pneumococcal disease risk factors at the same time so the comparison between people with and without HIV is more accurate. They used a similar statistical method to identify individual factors that affect risk of invasive pneumococcal disease regardless of whatever other risk factors a person has.

**What the study found.** The study involved 13,079 people with HIV and 137,643 without HIV. Each group averaged about 40 years in age, and about 90% of each group were men. The HIV group included a higher proportion of whites (61% versus 51%) and blacks (18% versus 9%), and lower proportions of Hispanics and others. A significantly higher proportion of people with than without HIV smoked (47% versus 31%). HIV-positive people had HIV infection for an average 4.7 years, and only 48% of them had taken antiretroviral therapy for their HIV.

During the 1996-2011 study period the invasive pneumococcal disease rate was much higher in people with HIV (160 cases per 100,000 person-years) than in people without HIV (8 cases per 100,000 person-years). For the whole study period, people with HIV had a 19-fold higher risk of invasive pneumococcal disease than people without HIV. An analysis that accounted for the impact of age, sex, race, smoking, diabetes, and other risk factors determined that HIV-positive people had a 13-fold higher risk of invasive pneumococcal disease than HIV-negative people.

Over the 5 study periods listed in **Figure 2**, invasive pneumococcal disease incidence (the new-detection rate) dropped by 71% among people with HIV, from 305 cases per 100,000 person-years in 1996-1999 to 88 per 100,000 in 2010-2011. An analysis figuring the impact of other pneumococcal disease risk factors found that risk fell from 18.5 times higher in people with HIV in 1996-1999 to 6.6 times higher with HIV in 2010-2011 (**Figure 2**). But even in 2010-2011, risk of invasive pneumococcal disease was significantly higher in the HIV group. In other words, a statistical test determined that chance did not explain the higher pneumococcal disease rate in the HIV group.

In people with HIV three factors raised the risk of invasive pneumococcal disease regardless of whatever other risk factors a person had: being black (versus white), ever smoking, and having cancer in the past each

**Figure 2.** From 1996-1999 through 2010-2011, HIV-positive people in California always had a higher rate of invasive pneumococcal disease than HIV-negative people. But the higher rate with HIV infection grew smaller over the years.
more than doubled the risk of invasive pneumococcal disease (Figure 3). Two factors lowered the risk of invasive pneumococcal disease in people with HIV: being in higher wealth brackets and having a lower recent HIV viral load. PPSV23 vaccination had no impact on risk of invasive pneumococcal disease in this analysis. Neither did age, sex, or year entering the study.

■ What the results mean for you. Invasive pneumococcal disease is a serious and possibly deadly infection that affects adults and children. Every year about 900,000 people in the United States get pneumococcal pneumonia (one form of invasive pneumococcal disease), and 5% to 7% die from it. About 3700 people in the United States die every year from two other forms of this disease, pneumococcal meningitis (brain and spinal fluid infection) and bacteremia (blood infection).

This study found that adults with HIV had much higher rates of invasive pneumococcal disease than adults of similar age without HIV. Overall, the HIV group had a 13 times higher rate of invasive pneumococcal disease than people without HIV. The good news is that invasive pneumococcal disease rates have dropped over recent years in people with HIV. But even in the most recent study period, 2010-2011, people with HIV had more than a 6 times higher rate of invasive pneumococcal disease.

You can greatly lower your risk of invasive pneumococcal disease by getting the correct vaccinations. For people with HIV, this study found that the PPSV23 vaccine alone did not protect HIV-positive people from invasive pneumococcal disease. US health authorities recommend PCV13 vaccination followed by PPSV23

![Factors that raised or lowered pneumococcal disease risk in people with HIV](image)

**Figure 3.** In people with HIV three factors independently raised the risk of invasive pneumococcal disease 2.3 times: black versus white race, ever smoking, and cancer in the past. Three factors lowered pneumococcal disease risk in people with HIV: being in the highest two of five wealth brackets (versus the lowest) and having a latest HIV viral load (VL) under 500 copies or from 500 to 9999 copies (versus 10,000 copies or higher).
vaccination for HIV-positive adults who have never received a pneumococcal vaccine.\(^3\) HIV-positive adults who have already received a dose of the PPSV23 vaccine should get a dose of the PCV13 vaccine 1 year or more after the last PPSV23 dose.

The study pinpointed individual risk factors for invasive pneumococcal disease in people with HIV. Blacks, smokers, and people who had cancer all had higher rates of invasive pneumococcal disease. People with a recent viral load below 10,000 copies and people in higher wealth brackets had lower rates of invasive pneumococcal disease. These findings underline the importance of avoiding or quitting smoking. Quitting smoking is not easy, but 20% of all HIV-positive people in the United States are people who have quit smoking. See page 21 of this issue for advice on quitting smoking.

Reaching and maintaining an undetectable viral load is the main goal of antiretroviral therapy. This study provides another reason for starting anti-HIV therapy and continuing treatment to keep an undetectable viral load: preventing invasive pneumococcal disease. The researchers believe falling viral loads over the years in HIV-positive people explain the falling invasive pneumococcal disease rate they found over time.

References


Heavy alcohol drinking lowered chances of keeping HIV care appointments more than 20%, according to results of a 9694-person US study. The analysis also linked binge drinking to worse appointment keeping.

Once a person begins care for HIV infection and starts taking antiretroviral therapy, keeping all HIV clinic appointments is crucial to successful treatment and overall health. In the United States more than half of people who test positive for HIV fail to enter care or remain in care. It is important for people with HIV and for their providers to understand specific problems that lead to missed office visits because those problems can often be solved.

About half of HIV-positive people in the United States drink alcohol and almost 10% are heavy drinkers. The National Institute on Alcohol Abuse and Alcoholism defines heavy drinking as more than 4 drinks daily or more than 14 drinks weekly for men, and more than 3 drinks daily or more than 7 drinks weekly for women.

Studies show that both moderate and heavy drinking raise the risk of death in people with HIV. Reasons for this link could include poor antiretroviral pill-taking by HIV-positive alcohol users (see the article on pages 34-36 of this issue) and missing HIV care visits. Because the impact of heavy drinking on HIV care visits is poorly understood, US researchers conducted this study.

How the study worked. The study focused on HIV-positive adults seen at 7 clinics across the United States. Participants reported alcohol and drug use at least every 6 months and had health assessments as directed by their provider. This analysis considered study visits between January 2011 and June 2014. Everyone in this study had HIV primary care visits covering at least 1 year.

Researchers used a standard 3-question test to rate each person for drinking frequency (never, moderate, or heavy) and binge drinking frequency (never, monthly or less than monthly, or weekly or daily). Binge drinking meant 5 or more drinks at a time for men and 4 or more drinks at a time for women. The research team also collected standard personal data (like age, sex, and race) and other health data (like CD4 count, viral load, illegal drug use, and depressive symptoms).

The researchers measured HIV clinic attendance (keeping appointments) in two ways: (1) 2 visits in 12 months: attending at least two HIV care visits within 12 months with each visit separated by at least 90 days, and (2) proportion of HIV care visits kept: visits kept divided by (scheduled visits plus kept visits). The investigators used standard statistical methods to determine the impact of alcohol use on these two measures of appointment keeping. This kind of analysis considers several risk factors at the same time; in this way the analysis can identify alcohol use as an independent risk factor, regardless of whatever other risk factors a person has.

What the study found. The study involved 9694 people, 65% gay or bisexual men, 17% heterosexual men, and 17% women. The group averaged 44 years in age, 46% were white, 35% black, and 14% Hispanic. Almost half of study participants had a CD4 count above 500, and three quarters had an undetectable viral load. Only 15% of participants currently used illegal drugs or party drugs.

Among all people studied, 37% reported never drinking, 38% moderate drinking, and 25% heavy drinking. While 69% reported never binge drinking, 25% reported binge drinking monthly or less, and 6% reported binge drinking daily or weekly. Gay/bisexual
men were more likely to report moderate or heavy drinking than never drinking. White participants were also more likely to report moderate or heavy drinking than never drinking. In the first year of observation, 89% of the study group made at least 2 visits in 12 months, and the proportion of visits kept was 84%.

First the researchers looked for factors that independently affected chances of making at least 2 visits in 12 months. They identified three factors that lowered chances of making at least 2 visits in 12 months (Figure 1): heavy drinking lowered chances by 22%, monthly or less binge drinking lowered chances 11%, and current illegal or party drug use lowered chances by 13%. Having depression symptoms raised chances of making at least 2 visits in 12 months by 15%. These factors affected appointment-keeping by themselves, regardless of whatever other risk factors a person had.

Next the researchers looked for factors that independently affected proportion of HIV care visits kept (Figure 2). Daily or weekly binge drinking lowered chances of keeping a scheduled visit by 10%. Current illegal or party drug use lowered chances of keeping an appointment by 26%, panic symptoms lowered chances by 15%, and depression symptoms lowered chances by 8%. Again these factors lowered chances of appointment keeping regardless of whatever other risk factors a person had.

**What the results mean for you.** This large US study found that heavy alcohol drinking and binge drinking lowered chances of good HIV care appointment keeping. Heavy alcohol drinkers had lower chances of keeping even 2 appointments per year. The links between alcohol overuse and poor appointment keeping held true regardless of whatever risk factors a person had for poor appointment keeping, like drug use or depression.

---

*continued...*
These findings are important for two reasons: (1) keeping all care appointments is critical to HIV control and to the overall health of people with HIV, and (2) alcohol use can be controlled with reliable programs and medicines that have helped millions of people.

Do you have an alcohol problem? It can be hard for a person to judge whether they drink too much alcohol because alcohol overuse often develops slowly over time. The US National Institute on Alcohol and Alcohol Abuse (NIAAA) has a simple online form people can complete in private to learn if their drinking behavior indicates an alcohol use disorder. Click on the link at reference 6 below.

If you believe you may have an alcohol use problem—or if you know you do—the NIAAA advises talking to your primary health provider. Another option is to talk to a counselor in an HIV/AIDS service organization. These professionals can further evaluate your alcohol use pattern and determine whether you need treatment. Successful treatment may involve three strategies, either alone or combined: (1) professional counseling, (2) one of three medicines, and (3) support groups including other people with alcohol problems. For more details, see the online NIAAA page “Treatment for alcohol problems” at the link following reference 7 below. The NIAAA offers many other online brochures and fact sheets listed at the link after reference 8 below.

---

**Figure 2.** Four factors independently lowered chances of keeping an HIV appointment: Daily or weekly binge drinking cut chances by 10%. Use of illegal or party drugs cut chances by 26%. Panic symptoms cut chances by 15%. And depression symptoms cut chances by 8%.
Besides contributing to poor HIV care appointment keeping, drinking too much alcohol can impair health in many ways and can directly lead to death. The NIAAA estimates that almost 88,000 people die every year from alcohol-related problems in the United States. Almost 10,000 automobile accident deaths can be traced to drunk driving every year. Alcohol overuse is the fourth leading preventable cause of death in the United States. Don’t add yourself to these statistics. One third of people treated for alcohol problems have no alcohol abuse symptoms 1 year later, and many others greatly reduce their drinking.

References


Main barriers to antiretroviral pill taking in adults, adolescents, and children

Simply forgetting to take antiretroviral pills, being away from home, and a change in the daily routine headed the list of reasons for inconsistent antiretroviral pill taking in a 125-study analysis. Research shows that certain strategies help HIV-positive people remember to take their pills on time. But by showing that different groups forget to take their antiretrovirals for different reasons, the new study indicates that no single pill-taking strategy will work for everyone.

Antiretroviral combinations available today help most people achieve the main goal of antiretroviral therapy—reaching and maintaining an undetectable viral load. Probably the key barrier to achieving this goal is imperfect antiretroviral adherence—failing to take antiretroviral pills on time every day.

A person with very poor antiretroviral adherence—missing pills regularly more than a few days—faces several risks, including development of HIV resistant to antiretrovirals, development of AIDS illnesses, and death. To get a better understanding of barriers to good adherence in HIV-positive people across the world, an international team of researchers conducted this combined analysis of studies addressing adherence.

**How the study worked.** The researchers reviewed online medical databases and major HIV meetings for studies focused on barriers to adherence. The investigators included only studies that had adherence barriers reported for at least 50 adults or 20 children. They analyzed only findings on study participants with nonadherence, according to each study’s definition of nonadherence. All studies were presented between January 1997 and March 2016. The research team also collected information on study design, study location, and patient age.

The researchers created a list of barriers to resistance identified in the studies they analyzed. They recorded proportions of adults, adolescents, and children in each study who reported each barrier to adherence. For

*Words in bold are defined in the Technical Word List at the end of this issue of *HIV Treatment Alerts.*

**Figure 1.** A 125-study analysis of more than 19,000 people with HIV found that the most frequent barriers to resistance were similar in adults, adolescents, and children. But frequency of these barriers was always higher in adolescents than in adults or children. (*Alcohol/substance* means alcohol or substance misuse.)
children, parents or other caregivers often reported adherence. Then the investigators used standard statistical methods to combine data from each study into a single calculation of the proportion of patients facing each barrier to adherence.

- **What the study found.** The researchers found 125 studies that met their needs. The studies included 19,016 people with antiretroviral adherence problems: 17,061 adults, 856 adolescents, and 1099 children. Most studies took place in Africa (55 studies) or Europe (14 studies). Most studies defined adherence as missing no antiretroviral doses or taking more than 95% of doses.

The most frequent barriers to adherence were similar in adults, adolescents, and children (Figure 1). The most frequent barriers were (1) simply forgetting to take pills (41.4% of adults, 63.1% of adolescents, 29.2% of children), (2) being away from home (30.4% of adults, 40.7% of adolescents, 18.5% of children), (3) a change in daily routine (28.0% of adults, 32.4% of adolescents, 26.3% of children), (4) depression (15.5% of adults, 25.7% of adolescents, 15.1% of children), and (5) alcohol or substance misuse (12.9% of adults, 28.8% of adolescents).

Rates of some barriers to adherence differed by age group. Among adults, higher proportions reported feeling sick versus feeling good as a reason for nonadherence (15.9% versus 9.3%) (Figure 2). In contrast, feeling good caused nonadherence more than feeling sick in adolescents (26.5% versus 19.9%) and in children (10.6% versus 7.1%). A need for secrecy was a frequent cause of nonadherence among adolescents (40.1%) and children (22.3%) but was less frequent among adults (13.6%).

A desire to avoid antiretroviral side effects was frequent among adults (19.1%) and adolescents (19.6%). A similar concern, antiretroviral toxicity (harmful effects), was also frequent among adults (18.8%) and less frequent among adolescents (12.6%) and children (6.1%) (Figure 2). Palatability (good versus bad taste) was a frequent concern of adolescents (29.2%) but less frequent in children (18.4%) or adults (11.8%).

Statistical analysis indicated that the frequency of some reported barriers to adherence decreased over time, including antiretroviral toxicity, side effects, too many pills, palatability, and feeling sick.
What the results mean for you. Once you start antiretroviral therapy, the most important thing to do is take all your antiretroviral pills on time, exactly as your HIV provider instructs. Taking all your pills on time should make your viral load undetectable and raise your CD4 count. As a result your chance of getting an AIDS disease will fall sharply and your health will improve in other ways.

The most-used antiretroviral combinations today require only a few pills—often just one—and most combinations are taken just once a day. These combinations are easy to take, and many people quickly get into the habit of taking their antiretrovirals every day. But this study shows that several problems can upset daily pill taking—from simply forgetting to take the pills to worrying about antiretroviral side effects. You have probably faced one or more of these problems from time to time. It is important to know that strategies exist to overcome or control many of these problems. Careful studies in people with HIV show that these strategies work, as noted by the authors of this study1 (Table 1).

If you face any difficulty in taking your antiretroviral pills on time, tell your HIV provider. There is a very good chance that your provider can help you find a solution to the problem. The solution may be one of those listed in Table 1. Or your provider may have a different idea. If your antiretroviral combination requires several pills—or if you think your antiretrovirals are causing side effects—your provider may be able to switch you to a different equally effective combination.

Some adherence problems are harder to fix. If you suffer from depression, let your HIV provider know. There are effective treatments for depression, including medications and short-term counseling. Substance abuse problems—whether alcohol, party drugs, or injected drugs—can upset good adherence and threaten your health in other ways. Team up with your provider to tackle these problems by finding a program that helps you overcome them.

Don’t let adherence problems linger. After you take the first step to solving adherence problems, the later steps may be easier than you imagined.

Table 1. Strategies that eased adherence problems in randomized trials

<table>
<thead>
<tr>
<th>Adherence barrier</th>
<th>Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forgetting to take pills</td>
<td>Text messaging; reminder devices</td>
</tr>
<tr>
<td>Travel</td>
<td>Pillbox organizers</td>
</tr>
<tr>
<td>Antiretroviral toxicity (harmful effects)</td>
<td>Different antiretrovirals with less toxicity</td>
</tr>
<tr>
<td>Depression</td>
<td>Mental health support</td>
</tr>
<tr>
<td>Alcohol or substance misuse</td>
<td>Counseling</td>
</tr>
<tr>
<td>Antiretroviral medicine palatability (taste)</td>
<td>Improved medication types for children</td>
</tr>
<tr>
<td>Too many antiretroviral pills</td>
<td>2-in-1 or 3-in-1 antiretroviral pills</td>
</tr>
</tbody>
</table>

References

Fat gains continue and lean mass falls in group on long-term HIV therapy

People with HIV gained more lean body mass and fat in the first 96 weeks of antiretroviral therapy than did HIV-negative people over the same length of time. But after 96 weeks, through another 5 years of observation, the HIV group lost lean mass compared with the HIV-negative group and continued to gain more fat. US researchers who conducted the study warned that long-term lean mass loss and fat gains could promote obesity-related diseases (like diabetes) and harm physical function in people with HIV.

Body composition, including fat and lean mass, has an important impact on overall health. People with long-term diseases like AIDS often lose both fat and lean mass (which includes muscle). When HIV-positive people first start antiretroviral therapy, they usually gain both fat and lean mass as their health improves. But few studies have explored changes in body composition for several years after people start antiretrovirals. And no studies have compared long-term body composition changes in people with and without HIV. Understanding how fat and lean mass change over time in people with HIV is important because such changes can have direct effects of health.

Researchers working with the US AIDS Clinical Trials Group (ACTG) conducted this study to learn more about multiyear body composition changes in HIV-positive people taking antiretroviral therapy. They compared those changes with an HIV-negative group around the same age.

For the new analysis, ACTG researchers attempted to contact all of these 269 people and invited them to have another DXA scan. This final DXA scan was done about 5 years after the 96-week scan. The ACTG team compared findings in the three scans—the one done when people entered the original trial, the one done after 96 weeks of treatment in the original trial, and the one done about 5 years after that for the new analysis.

The researchers created an HIV-negative comparison group from two long-term studies of men and women who had whole-body DXA scans done over the course of several years. These HIV-negative men and women were in the same age range as HIV-positive people when the HIV group had their first DXA scan: 20 to 64 years for men and 23 to 55 years for women.

The ACTG team used standard statistical methods to compare rates of body composition change (lean mass, total fat, trunk fat, limb fat) in HIV-positive and HIV-negative people during the first 96 weeks of follow-up and in the multiyear period after the first 96 weeks. This type of analysis accounts for the impact of several factors on body composition: age, male versus female sex, physical activity level, cigarette smoking, and alcohol use. As a result, the analysis provides a good estimate of how treated HIV infection alone affects body composition over time. In people with HIV, the researchers conducted further analyses to identify factors that independently affect rates of body composition change.

How the study worked. This analysis involved HIV-positive adults who participated in an ACTG trial that compared diverse first-line antiretroviral combinations. Some people in that trial agreed to have whole-body DXA scans, a simple imaging study that measures body composition, including fat and lean mass. These 269 people had a DXA scan when they entered the study and another scan 96 weeks later.

What the study found. This analysis focused on 97 people with HIV and 614 HIV-negative people. Median (midpoint) age was younger in the HIV group than in the HIV-negative group (40 versus 46 years), and the HIV group had a longer time between their first and final DXA scan (7.6 versus 6.9 years). Most people in both groups, about 87%, were men. At the time of the final DXA scan, 86% of HIV-positive people had a viral load below 200 copies, and their median CD4 count stood at 598.

---

*Words in **bold** are defined in the Technical Word List at the end of this issue of HIV Treatment Alerts.*
Compared with HIV-negative people, those with HIV had a lower body mass index (a measure of weight) at the time for the first DXA scan (24 versus 28 kilograms per height in meters squared) and at the time of the final DXA scan (27 versus 29 kg/m²).

During the first 96 weeks of observation (between the first and second DXA scans), people with HIV gained significantly more lean mass than people without HIV (average 0.53 versus 0.06 kilogram per year) (Figure 1). In this comparison and the following comparisons, “significant” means statistical tests show that the difference between groups does not result from chance. During this 96-week period, the HIV group also gained significantly more total fat than the HIV-negative group (average 0.70 versus 0.15 kilogram per year), more trunk fat (0.69 versus 0.07 kilogram per year), and more limb fat (0.70 versus 0.08 kilogram per year).

About 5 years passed between the second the third DXA scans in the two study groups. During this period, the HIV group lost lean mass while the HIV-negative group continued to gain lean mass (average –0.28 versus +0.06 kilogram per year) (Figure 2). This difference and the following differences in fat changes were significant, meaning statistical analysis shows they did not result from chance.

Compared with the HIV-negative group, people with HIV gained significantly more total fat in the 5 years between the second and third DXA scans (average 0.70 versus 0.15 kilogram per year). In this 5-year period, people with HIV also gained significantly more trunk fat than the HIV-negative group (average 0.58 versus 0.07 kilogram per year) and more limb fat (0.28 versus 0.08 kilogram per year).

Statistical analysis identified a single factor linked to greater gains in lean mass, total fat, trunk fat, and limb fat in the 96 weeks between the first and second DXA scans in people with HIV: A lower pretreatment CD4 count meant a greater gain in lean mass and the three fat measures—regardless of whatever other factors might be affecting lean mass and fat gains. A similar analysis showed that older age and black race favored loss of lean mass in the 5 years between the second and third DXA scans. During that same period, older age and female sex favored smaller gains in total fat, trunk fat, and limb fat.

**Figure 1.** In the first 96 weeks of antiretroviral therapy, people with HIV made significantly greater healthy gains in lean mass and fat (in kilograms per year) than a comparison group of HIV-negative people not taking antiretrovirals.
What the results mean for you. This long study comparing antiretroviral-treated HIV-positive people with HIV-negative people made several important findings: First, it confirmed earlier research showing that HIV-positive people gain both lean mass and fat in the first 2 years of antiretroviral therapy—and they gain more lean mass and fat than HIV-negative people. For people low in fat and lean mass because of HIV infection, those gains are a sign of returning health with antiretroviral therapy.

But the second major finding of this study raises concerns: Compared with HIV-negative people, HIV-positive people continued to gain fat over the next 5 years of follow-up, while they lost lean mass. High fat and low lean mass can threaten good health. For example, the researchers suggest that those fat and lean mass changes could explain higher rates of frailty in people with HIV versus without HIV.4,5 High weight is a well-known risk factor for diabetes, as shown in the next study reviewed in this issue of HIV Treatment Alerts (see page 41).6

This study does not explain why HIV-positive people taking antiretrovirals for many years lose lean mass and gain fat. The analysis showed that these changes could not be explained by the type of antiretrovirals people were taking or by smoking, alcohol use, or lack of physical activity. The statistical analysis did link older age and black race to lean mass loss. This does not mean older age and black race cause lean mass to decrease, but it does suggest older people and blacks run a higher risk of this drop.

The findings underline the importance of maintaining lean mass (including muscle) and avoiding too much weight gain during the many years people can expect to take antiretroviral therapy. The HIV group in this study started antiretroviral therapy with a normal

Figure 2. From week 96 of antiretroviral therapy through the following 5 or more years, people with HIV lost lean mass and gained more fat (in kilograms per year) than HIV-negative people not taking antiretrovirals.
median body mass index of 24. Seven years later, the group had a median body mass index of 27, which is in the overweight range. (Normal body mass index runs from 18.5 to 24.9, overweight from 25 to 29.9, and obesity from 30 on up. You can find a body mass index calculator at reference 7 below.)

If you are losing muscle or gaining too much weight, talk to your HIV provider. Your provider can refer you to a nutritionist for dietary advice or to an exercise planner to help you gain or maintain lean mass.

References


Every 5 pounds of weight gained in the first year of antiretroviral therapy* raised diabetes risk 14% in HIV-positive veterans. In contrast, 5 pounds of weight gained in a year raised diabetes risk only 8% in HIV-negative veterans.

People with HIV often gain weight when they start antiretroviral therapy. That’s a good thing for underweight people starting antiretrovirals because being underweight has health risks. But when normal-weight or overweight people with HIV gain more weight after starting antiretrovirals, the overall health impact may be negative. For example, overweight people run a higher risk of diabetes, a serious lifelong illness.

The study described on pages 37-40 of this issue of HIV Treatment Reports found that HIV-positive people continue gaining fat for 7 or more years after starting antiretroviral therapy. But little is known about the health consequences of weight gain after starting antiretrovirals. Researchers working with a US veterans group conducted this study to see how weight gain affects diabetes risk in veterans with and without HIV infection.

■ How the study worked. This analysis involved veterans in the Veterans Aging Cohort Study (VACS), an ongoing health study in the United States. VACS matches every HIV-positive veteran to 2 HIV-negative veterans by age, sex, race, and site of care. VACS began measuring height and weight in the year 2000. With height and weight, you can calculate body mass index, as explained at the link in reference 3 below. A body mass index below 18.5 is underweight, 18.5 to 24.9 is normal weight, 25 to 29.9 is overweight, and 30 or more is obese.

This analysis included veterans who entered the VACS group between January 1999 and September 2011. Everyone had at least two body mass index measures in the first 18 months they were in the study. For HIV-positive veterans, the study period began when they first started antiretroviral therapy. For HIV-negative veterans, the study period began the first time they first had their body mass index measured. For people with HIV, researchers recorded the body mass index closest to the day they started antiretroviral therapy and closest to a date 1 year later. The main analysis did not include veterans who already had diabetes on their first study date and did not include pregnant women.

The researchers used veterans’ medical records to calculate weight gains or losses more than 5 pounds over a 1-year period. They determined how many veterans with or without HIV had newly identified diabetes during the study period. The research team checked veterans’ records for up to 5 years, through September 2012. The main study result was new diabetes in HIV-positive and HIV-negative veterans according to weight change category (summarized in reference 5).

The investigators used a standard statistical method to compare new diabetes risk in veterans with versus without HIV. This kind of analysis considers several weight risk factors at the same time so that researchers can identify individual factors that affect diabetes regardless of whatever other risk factors a person may have. The new diabetes analysis did not include people who entered the study with a body mass index below 18.5 (underweight people) because the new diabetes rate was very low in that group and gaining weight is beneficial for underweight people.

■ What the study found. The researchers focused on 7177 veterans with HIV and 24,621 HIV-negative veterans. Almost all study participants (97%) were men. The HIV group was slightly older (median 50 years versus 48 years in the HIV-negative group) and had a lower proportion of whites (36% versus 44%) and a higher proportion of blacks (52% versus 43%). Veterans with HIV included a higher proportion of current smokers (58% versus 48% without HIV). At the start of

*Words in bold are defined in the Technical Word List at the end of this issue of HIV Treatment Alerts.
the study, the HIV group included a higher proportion of normal-weight people (50% versus 22%) and a lower proportion of obese people (14% versus 39%).

Almost half of veterans with HIV (48%) gained more than 5 pounds during their first year of antiretroviral therapy, compared with 31% of HIV-negative veterans who gained more than 5 pounds in 1 year (Figure 1). In the HIV group, two thirds who started the study underweight gained weight in the 12 months after starting antiretroviral therapy, a good sign reflecting a return to health with therapy. But half of normal-weight HIV-positive veterans gained weight in the first year of therapy, and 40% of already overweight or obese HIV-positive veterans gained weight in the first year of treatment (Figure 1). In every start-of-study weight group—underweight, normal weight, overweight, and obese—a larger proportion of veterans with than without HIV gained weight (Figure 1), and weight gains were greater in the HIV group.

Over the 5-year study period, new diabetes developed in a lower proportion of HIV-positive veterans than HIV-negative veterans (5% versus 11%). New diabetes rates were 13 per 1000 person-years with HIV versus 27 per 1000 person-years without HIV. (A rate of 13 per 1000 person-years means 13 of every 1000 HIV-positive veterans got diagnosed with diabetes every year.) In veterans both with and without HIV, the researchers saw a link between more weight gain during the study and the new diabetes rate.

Statistical analysis in the combined group of veterans with or without HIV identified several factors that independently increased the risk of diabetes (that is, these factors increased diabetes risk regardless of whatever other risk factors a person had) (Figure 2): (1) older age, (2) being black or Hispanic versus white, (3) being overweight or obese versus normal weight when entering the study, (4) every 5 pounds of weight gained (Figure 3), and (5) ever smoking versus never smoking.

Figure 1. In a study of almost 32,000 US veterans, higher proportions of those with HIV than without HIV gained more than 5 pounds in 1 year. This was true in every group according to body mass index at the start of the study: under 18.5 (underweight), 18.5 to 25 (normal weight), 25 to 30 (overweight), and 30 or more (obese).
Several individual factors raised the risk of diabetes regardless of whatever other risk factors a person had, including the six factors listed above in this figure plus every 5 pounds of weight gained (Figure 3). Among both HIV-positive and HIV-negative veterans, being overweight doubled the risk of diabetes and being obese raised the risk more than 4 times.

Every 5 pounds of weight gained in 1 year raised diabetes risk 1.14 times (14%) in veterans with HIV, compared with 1.08 times (8%) in veterans without HIV.
In this analysis, having HIV infection nearly cut in half the risk of new diabetes. However, gaining weight during the study had a bigger impact on diabetes risk in HIV-positive veterans than HIV-negative veterans. In veterans with HIV, every 5 pounds of weight gained in 1 year raised diabetes risk 14%. In veterans without HIV, every 5 pounds of weight gained raised the diabetes risk 8% (Figure 3). This difference in the impact of weight is statistically significant, meaning a statistical test shows that the difference does not result from chance.

What the results mean for you. Three main findings emerged from this large and careful comparison of US veterans with and without HIV infection. First, a higher proportion of veterans with HIV than without HIV gained more than 5 pounds in their first year of antiretroviral therapy (48% versus 31%). Gaining weight is healthy for veterans who started the study underweight, but high proportions of normal-weight veterans with HIV (51%), overweight veterans with HIV (43%), and obese veterans with HIV (41%) gained more than 5 pounds in the first year of therapy (Figure 1). That weight gain is not healthy for normal-weight veterans if it made them overweight. And gaining weight is not healthy for anyone who is already overweight or obese. The researchers who conducted the veterans study advise that normal-weight people with HIV should avoid gaining more than 10 pounds.1 Although the study did not address the impact of losing weight, health experts agree that overweight and obese people should try to lose weight.

The second key finding of this study is that gaining weight raised the risk of diabetes more in veterans with HIV than in veterans without HIV. The researchers calculated that every 5 pounds of weight gain boosted diabetes risk 14% in veterans with HIV versus 8% in veterans without HIV. Diabetes (very high blood sugar) is a serious lifelong disease. Diet and medication can control diabetes but must continue for life. Uncontrolled diabetes can lead to heart disease and other serious complications.

Third, the study also had some good news for people with HIV. When the study began, a lower proportion of veterans with HIV than without HIV already had diabetes. And over the course of the study period, new diabetes developed in fewer veterans with HIV than without HIV. These findings could reflect the overall lower proportion of obese veterans with HIV at the start of the study (14% versus 39% without HIV) and the overall higher proportion of normal-weight veterans with HIV at the start of the study (51% versus 33%). HIV-positive veterans may also benefit from more regular care than veterans without HIV. In the veterans healthcare system, people with HIV are scheduled to make 3 or 4 clinic visits every year. Veterans without HIV are expected to see their provider at least once a year. More regular care would allow HIV-positive veterans and their providers to work together to control high blood sugar that can lead to diabetes.

Besides overweight and obesity, the study confirmed some other diabetes risk factors. Older people, blacks, Hispanics, and smokers all had higher risks of new diabetes in veterans with and without HIV. Among veterans with HIV, hepatitis C virus (HCV) infection made diabetes more likely.

A simple blood test can detect high blood sugar (sometimes called prediabetes) and diabetes itself. HIV experts recommend that HIV-positive people get tested for diabetes before starting antiretroviral therapy and within 3 months of starting therapy.6 Diet and exercise by themselves can sometimes control high blood sugar. If they cannot, your HIV provider can prescribe medications to help control high blood sugar. The authors of the veterans study point out that it is easier to avoid gaining weight than it is to lose weight. If you are already overweight or obese, you and your provider should work hard to lower your weight.


4. The researchers defined new diabetes as hemoglobin A1c at or above 6.5%.

5. Weight change categories in the veterans study were (1) lost more than 5 pounds, (2) lost or gained up to 5 pounds, (3) gained more than 5 pound to 10 pounds, (4) gained more than 10 pounds to 15 pounds, (5) gained more than 15 pounds to 20 pounds, (6) gained more than 20 pounds to 30 pounds, and (7) gained more than 30 pounds.

HIV-positive people had higher rates of intentional and accidental injury than HIV-negative people, according to results of a large comparison in Canada. Injuries accounted for a much higher proportion of deaths in people with HIV than in the HIV-negative comparison group.

Because antiretroviral therapy* protects many HIV-positive people from HIV-related disease, more research now focuses on non-HIV causes of sickness and death in HIV populations. Across the world injuries are responsible for 10% of all sickness and death. But relatively little is known about the frequency and impact of injury in HIV-positive people. And experts have not compared injury rates, causes, and consequences in people with versus without HIV. To learn more about these issues, researchers in Canada’s province of British Columbia conducted this large comparison of injury in people with or without HIV.

How the study worked. Researchers drew on two large data banks to create study populations with and without HIV. HIV data came from the British Columbia Centre for Excellence in HIV/AIDS, which oversees free antiretroviral therapy and maintains records for all HIV-positive people who have ever received treatment in the province of British Columbia. The Centre also records health data that helped identify people who tested positive for HIV but never started treatment. Population Data BC tracks individual health data for all 4.6 million people living in the province.

This study included two HIV groups: The first group included all people known to be HIV positive between April 1996 and March 2013—all of them at least 20 years old. The second HIV group was limited to people who had ever begun treatment and had at least one detectable viral load and/or began combination antiretroviral therapy. The general-population comparison group consisted of a 10% random sample of the entire British Columbia population at least 20 years old between April 1996 and March 2013. This comparison group included no one with HIV. Records were available for a median of 85 months (7.1 years) for the HIV group and 149 months (12.4 years) for the general population.

The researchers used medical records to determine how many people in the HIV group and the general population had an injury during the study period. They grouped injuries as intentional or unintentional (accidental). There were 2 kinds of intentional injuries—self-harm and assault. There were 9 kinds of accidental injuries—including falls, motor vehicle accidents, and poisoning. The research team used medical records to see who had other illnesses and conditions like kidney disease, liver disease, and depression.

The investigators used standard statistical methods to determine whether HIV itself affected intentional and accidental injury rates. This kind of analysis considers several injury risk factors at the same time to identify individual factors that affect injury rates regardless of whatever other risk factors a person has.

What the study found. The study included 13,764 people with HIV and 417,416 people without HIV. Median age was 38 years in the HIV group and 40 in the HIV-negative group. Most people with HIV (81%) were men, while half without HIV were men. About 62% of both groups were employed, and average income was similar. Much higher proportions of the HIV-positive group than the HIV-negative group had a mental health condition (73% versus 37%), depression (50% versus 26%), liver disease (35% versus 3.5%), or kidney disease (42% versus 12%).

The overall injury rate was 3 times higher in people with HIV than in the HIV-negative group: 29.16 injuries per 1000 person-years with HIV versus 9.49 per 1000 person-years without HIV. A rate of 29.16 per 1000 person-years means about 29 of every 1000 HIV-positive people got injured every year. The intentional injury rate was more than twice higher in people with HIV (18.56 versus 8.51 injuries per 1000 person-years),

*Words in bold are defined in the Technical Word List at the end of this issue of HIV Treatment Alerts.
and the accidental injury rate was 10 times higher in people with HIV (10.60 versus 0.99 injuries per 1000 person-years). These differences between HIV-positive and negative people are statistically significant, meaning a statistical test calculated that the difference cannot be explained by chance.

Statistical analysis determined that HIV-positive people were 42% more likely to report accidental injury than HIV-negative people—regardless of whatever other injury risk factors a person had. People with HIV were 93% more likely to report intentional injury than HIV-negative people. During the study period, injury accounted for 13.5% of deaths among people with HIV versus 5.5% of deaths among HIV-negative people.

**Figure 1** shows rates of the major intentional and accidental injuries in people with and without HIV. The leading causes of accidental injury in the HIV group were falls, poisoning, and motor vehicle accidents. Among intentional injuries, more than 6 in 1000 HIV-positive people harmed themselves every year, and more than 4 in 1000 were a victim of assault (including murder) (**Figure 1**).

Among people with HIV, the accidental injury rate fell from more than 30 to less than 20 injuries per 1000 person-years from 1996 through 2012. Among HIV-negative people, the accidental injury rate remained flat across the years (about 10 per 1000 person-years) but always much lower than in HIV-positive people. The intentional injury rate also fell from 1996 through 2012 in people with HIV, from almost 20 to about 10 injuries per 1000 person-years. In HIV-negative people, the intentional injury rate remained about 1 per 1000 person-years across the study period.

Statistical analysis identified several factors independently linked to higher rates of accidental injury in people with HIV: older age, lower income, injecting drugs, living in rural areas, earlier year of injury, and indigenous (native) ancestry.* This analysis also linked several non-HIV illnesses to higher rates of accidental injury in people with HIV: kidney disease, liver disease, hepatitis B virus infection, cardiovascular disease, kidney disease, and mental health conditions (**Table 1**).

*Indigenous people are those who came to North America from Asia thousands of years before Europeans arrived.

**Figure 1.** Overall rates of accidental injuries and intentional injuries were significantly higher in people with HIV than in HIV-negative people in a large Canadian study. Rates of individual accidental and intentional injury were also higher in the HIV group.
Factors independently linked to higher rates of intentional injury in people with HIV were younger age, male sex, unemployment, injecting drugs, living in rural areas, and earlier year of injury. Four non-HIV illnesses were linked to higher rates of intentional injury: liver disease, hepatitis B virus infection, depression, and mental health conditions (Table 1).

What the results mean for you. This large comparison of HIV-positive and HIV-negative adults throughout Canada’s province of British Columbia found that intentional injury (including self-harm and assault) was almost twice as likely in people with HIV. Accidental injury (including falls and car accidents) was more than 40% more likely in people with HIV.

These findings are important for two main reasons: (1) Most injuries can be prevented, and (2) the study also showed which HIV-positive people run the highest risk of injury. People who fall into one or more of these high-risk groups can be especially alert to the possibility of injury and can take steps to avoid injury, as discussed in the following paragraphs.

The most frequent kinds of injury in people with HIV were falls, self-harm (including suicide), assault (including murder), poisoning, and motor vehicle accidents. Risk factors for injury in people with HIV included depression and other mental illnesses, hepatitis B virus (HBV) infection and other liver disease, kidney disease, indigenous (native) ancestry, lower income, and living in rural areas. Most of these risk factors cannot be changed or are hard to change.

Older age is a key risk factor for accidental injury that cannot be changed. But older people should be aware of their higher risk of injury and think about injury risks in their daily life. For example, older people risk

### Table 1. Factors independently linked to higher rate of injury with HIV

<table>
<thead>
<tr>
<th>Accidental injury</th>
<th>Intentional injury</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Social, genetic, and economic factors</strong></td>
<td></td>
</tr>
<tr>
<td>Older age</td>
<td>Younger age</td>
</tr>
<tr>
<td>Lower income</td>
<td>Unemployment</td>
</tr>
<tr>
<td>Injecting drugs</td>
<td>Injecting drugs</td>
</tr>
<tr>
<td>Living in rural area</td>
<td>Living in rural area</td>
</tr>
<tr>
<td>Earlier year of injury</td>
<td>Earlier year of injury</td>
</tr>
<tr>
<td>Indigenous ancestry</td>
<td>Male sex</td>
</tr>
<tr>
<td><strong>Non-HIV diseases and conditions</strong></td>
<td></td>
</tr>
<tr>
<td>Liver disease</td>
<td>Liver disease</td>
</tr>
<tr>
<td>HBV infection</td>
<td>HBV infection*</td>
</tr>
<tr>
<td>Mental health conditions</td>
<td>Mental health conditions</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>Depression</td>
</tr>
<tr>
<td>Cardiovascular (heart) disease</td>
<td></td>
</tr>
</tbody>
</table>

*HBV, hepatitis B virus.
falling more than younger people, and falls were among the most frequent injuries in this study. Fall prevention tips from the US National Institute of Arthritis and Musculoskeletal and Skin Diseases appear in Table 2.3 Other useful fall prevention tips can be found at the Mayo Clinic site.4 The National Council on Aging offers younger adults advice on helping older loved ones avoid falls.5

Depression (feeling sad or helpless much of the time) and other mental illnesses also made injury—including self-harm—more likely. Depression is more frequent in HIV-positive people than in the general population.6 HIV care providers often fail to notice depression in their patients, and depression often goes untreated.6 If you feel depressed, talk to your HIV provider about it. Depression (and other mental conditions like panic) can be treated successfully with medicines, counseling, or both.

Injecting drugs can lead to HBV infection and other liver disease. Statistical analysis linked all three of these factors (injecting, HBV, and liver disease) to a higher injury risk. These findings are not surprising because substance abuse, violence, and HIV infection are often related.7 Lower income and unemployment—two other injury risk factors in this study—may also expose people to violence that may result in injury. Your provider or a case worker recommended by your provider can guide you to programs that help people end substance abuse and cope with money-related problems. All HIV-positive people who have not already been exposed to HBV should get the HBV vaccine to prevent liver injury with HBV.

Table 2. Preventing falls indoors and outdoors

<table>
<thead>
<tr>
<th>INDOORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>➤ Keep rooms free of clutter, especially on floors.</td>
</tr>
<tr>
<td>➤ Use plastic or carpet runners.</td>
</tr>
<tr>
<td>➤ Wear low-heeled shoes.</td>
</tr>
<tr>
<td>➤ Do not walk in socks, stockings, or slippers.</td>
</tr>
<tr>
<td>➤ Be sure rugs have skid-proof backs or are tacked to the floor.</td>
</tr>
<tr>
<td>➤ Be sure stairs are well lit and have rails on both sides.</td>
</tr>
<tr>
<td>➤ Put grab bars on bathroom walls near tub, shower, and toilet.</td>
</tr>
<tr>
<td>➤ Use a nonskid bath mat in the shower or tub.</td>
</tr>
<tr>
<td>➤ Keep a flashlight next to your bed.</td>
</tr>
<tr>
<td>➤ Use a sturdy stepstool with a handrail and wide steps.</td>
</tr>
<tr>
<td>➤ Add more lights in rooms.</td>
</tr>
<tr>
<td>➤ Buy a cordless phone so that you don’t have to rush to the phone when it rings and so that you can call for help if you fall.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OUTDOORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>➤ Use a cane or walker.</td>
</tr>
<tr>
<td>➤ Wear rubber-soled shoes so you don’t slip.</td>
</tr>
<tr>
<td>➤ Walk on grass when sidewalks are slick.</td>
</tr>
<tr>
<td>➤ Put salt or kitty litter on icy sidewalks.</td>
</tr>
</tbody>
</table>

Source: National Institute of Arthritis and Musculoskeletal and Skin Diseases.3
Living in rural areas may heighten injury risk because rural residents may have more contact with guns, dangerous farm machinery, and open areas of water. People living in rural areas may also drink more alcohol and have lower incomes than urban residents. Finally, rural residents often have a harder time locating and using resources—like counselors and support groups—that can help them overcome social and economic problems. State HIV help lines in the United States can guide you to the nearest services. See the link at reference 8.

References

Adherence means taking medications, such as antiretrovirals, according to the schedule set by your healthcare provider.

Antiretrovirals are drugs used to treat HIV infection. Antiretroviral therapy (often abbreviated ART) usually means treatment with three or more antiretrovirals.

Arthritis is inflammation of the joints that causes pain and stiffness.

Body mass index, or BMI, is a measure of weight often used in medical studies. BMI equals weight in kilograms divided by height in meters squared. A BMI below 18.5 is underweight, 18.5 to 24.9 is normal, 25 to 29.9 is overweight, and 30 or higher is obese. You can find a BMI calculator at http://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm

Cardiovascular is the term used to include the heart and blood vessels. Cardiovascular disease can include heart attacks and other heart diseases, stroke, and other blood vessel disease.

CD4 cells are one type of cell necessary to fight infection. HIV attacks CD4 cells, so CD4 counts fall when a person is not taking antiretrovirals to control HIV or when treatment fails.

CD4 count measures the number of CD4 cells in a cubic millimeter of blood. People with CD4 counts below 500 have a harder time controlling infections. The risk of uncontrolled infections gets higher as the CD4 count gets lower.

Depression is feeling sad or hopeless much of the time.

Diabetes is a lifelong disease in which there are high levels of sugar in the blood. Diabetes can be caused by too little insulin, resistance to insulin, or both.

Hypertension is high blood pressure against artery walls as blood circulates through the body. Blood pressure below 120/80 mm Hg (millimeters of mercury) is considered normal; 120-139/80-89 is considered prehypertension; and 140/90 or higher is considered hypertension.

The immune system is the collection of cells and organs that help the body fight infections and cancers.

Incidence is the rate at which an event (such as infection with a virus or a heart attack) occurs over a defined period of time (such as 1 year).

Inflammation, marked by increased blood flow and fluid release, is the body’s natural response to infection or injury. Ongoing inflammation can contribute to heart disease, certain cancers, and other diseases in people with HIV.

Ischemic heart disease is marked by reduced blood supply to the heart. Examples are angina and myocardial infarction (heart attack).

A median is a midpoint—the number above which half of all the numbers in a series lie, and below which half of all the numbers in a series lie. A median age of 45 years means half of the people being studied are under 45 and half are over 45. The median number differs from the average (or mean) number. For example, in the series 1, 3, 8, 9, and 14, the median is 8 because half of the other numbers lie above it and the remaining half lie below. But the average of 1, 3, 8, 9, and 14 is 7.

A person-year is a measure of time used in medical studies. A single person-year is 1 year lived by 1 person. An HIV infection rate of 2 per 100 person-years means 2 of 100 people are infected with HIV within a year.

Viral load is the number of HIV particles in a milliliter of blood or another body fluid, such as semen or cerebrospinal fluid.
Articles

- Viral loads becoming undetectable in more people across the United States.
- HIV patients 65 years or older face higher rates of serious non-HIV illnesses.
- New cancer rates climbing with age in HIV patients, but age impact differs by cancer type.
- Grip strength—a health indicator—falls faster in older men with HIV than without.
- Smoking may shorten life more than 6 years in US men and women with HIV.
- Pneumococcal disease 13 times more frequent in people with HIV.
- Heavy and binge alcohol drinking tied to missing HIV care appointments.
- Weight gain poses higher diabetes risk with HIV in US veterans study.
- Injuries more frequent and cause death more often in people with HIV.