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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.

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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).

HIV Treatment ALERTS! thanks Todd Brown, Laurence Brunet, Ronald Dallas, Ellen Eaton, Kristine Erlandson, Alonso Hernandez-Romieu, Marina Klein, Andrew Phillips, Peter Rebeiro, Caroline Sabin, and Adam Trickey for reviewing the reports on their research.
Survival with HIV continued to improve from 2000 to 2010 among people taking antiretroviral therapy* (ART), according to analysis of 88,504 people in Europe and North America. From 1996 to 2010, life expectancy in 20-year-olds starting ART rose about 9 years in women and 10 years in men.

Individual antiretrovirals (anti-HIV drugs) and antiretroviral combinations have improved greatly over the past 20 years. Compared with earlier antiretrovirals, those used today are stronger, safer, and easier to take—often as one pill daily. Other improvements in care of people with HIV include detection and treatment of AIDS diseases and non-AIDS diseases like heart disease and diabetes.

Because of these improvements, some large studies in the United States, Canada, and Europe found much lower death rates and increasing survival in antiretroviral-treated people with HIV over the last 20 years. Researchers working with the Antiretroviral Therapy Cohort Collaboration (ART-CC) conducted a large and detailed study covering people starting ART between 1996 and 2010.

How the study worked. The ART-CC study group includes HIV-positive people at least 16 years old who are taking antiretroviral therapy and live in several European countries or in the United States and Canada. This analysis focused on group members who started combination antiretroviral therapy between 1996 and 2010.

The researchers divided study participants into 3- or 4-year periods according to when they started antiretroviral therapy: 1996-1999, 2000-2003, 2004-2007, and 2008-2010. Then the investigators determined how many people died after starting antiretroviral therapy in each period and whether they died from an AIDS disease or a non-AIDS disease.

The research team used an accepted statistical method to determine the risk of death 1 year and 2 to 3 years after starting antiretroviral therapy in 1996-1999, 2004-2007, and 2008-2010, compared with 2000-2003. This kind of analysis considers the potential impact of factors like age, sex, CD4 count, and viral load on risk of death. In this way the researchers could pinpoint year of starting antiretrovirals as an individual death risk factor—regardless of whatever other risk factors a person had. Finally, the researchers used a standard statistical method to estimate life expectancy of a 20-year-old starting antiretroviral therapy and compared that estimate with figures from the general populations of the United States and France. In this study life expectancy is the age to which a 20-year-old can expect to live.


Next the researchers looked at death risk 2 to 3 years after starting ART. Compared with people who started

*Words in bold are defined in the Technical Word List at the end of this issue of HIV Treatment Alerts.
therapy in 2000-2003, those who started in 2004-2007 had a 21% lower risk of death from any cause, and those who started in 2008-2010 had a 43% lower risk. Further analysis determined that CD4 count and viral load 1 year after ART began did not fully explain these lower all-cause death risks in 2004-2007 and 2008-2010.

Compared with people who started ART in 2000-2003, those who started in 2008-2010 had about a 30% lower risk of dying from AIDS in the first year of treatment and about a 50% lower risk of dying from a non-AIDS disease in the first year (Figure 1). Over the four 3- to 4-year study periods, risk of dying from AIDS in the first year of ART dropped 7% per period and risk of dying from a non-AIDS disease dropped 13% per period (Figure 2).

Compared with people who started ART in 2000-2003, those who started in 2008-2010 had about a 65% lower risk of dying from AIDS in the second and third years of ART and around a 71% lower risk of dying from a non-AIDS disease in the second and third years (Figure 1). Over the four 3- to 4-year study periods, risk of dying from AIDS in the second and third years of ART fell 31% per period and risk of dying from a non-AIDS disease dropped 25% per period (Figure 2).
For people starting ART at age 20, life expectancy rose from about 55 years in men and about 58 in women when ART began in 1996-1999 to about 64 in men and about 66 in women when ART began in 2008-2010. Despite these big improvements in life expectancy, projected survival fell short of life expectancy in the general US population (78 in men and 82 in women) or in the general French population (79 in men and 85 in women). However, people who started ART in 2008-2010 and had a CD4 count above 350 after 1 year of ART had an estimated life expectancy close to that of the general population.

■ What the findings mean for you. Starting around 1996, people with HIV began taking three- or four-drug antiretroviral combinations that protected them from AIDS diseases and added many years to their lives. This very large and careful study shows that death rates from AIDS diseases and non-AIDS diseases continued to fall steadily across four periods in which people started antiretroviral therapy: 1996-1999 to 2000-2003 to 2004-2007 to 2008-2010. As a result, the age to which a person starting antiretrovirals can expect to live (life expectancy) rose over the whole study period.

One reason for the falling death rate and rising life expectancy is the steady improvement in individual antiretroviral drugs and in the antiretroviral combinations they can form. Newer antiretrovirals are stronger (controlling HIV better and faster). Also, newer antiretrovirals cause fewer side effects than older drugs, so people with HIV can take them steadily without problems. And newer antiretrovirals are easier to take (often requiring only one dose daily and often combined in the same pill with two other antiretrovirals).

For these reasons, newer antiretrovirals make viral loads undetectable faster and more consistently, and they boost CD4 counts higher faster. But statistical analysis in this study showed that lower viral loads and higher CD4 counts did not completely explain the impact of newer antiretrovirals on death rates and life expectancy. So other aspects of care probably contribute to lower deaths rates in more recent years. Researchers who conducted this study suggest some other aspects of care that may lengthen survival in people taking antiretrovirals: better care for people who start ART at a lower CD4 count and overall improvements in healthcare for people with HIV, including steps to prevent and treat non-AIDS illnesses like heart disease, hepatitis C virus (HCV) infection, and cancer.

Despite lower death rates and longer life expectancy with antiretroviral therapy in more recent years, life expectancy of most people with HIV has not caught up with life expectancy in the general population. This finding should encourage people with HIV to take other steps to lower their death risk. For example, quitting smoking, heavy alcohol drinking, and injected and noninjected drugs could have a big positive impact on survival. At the same time, the overall improvements in survival found in this study underline the importance of starting antiretroviral therapy as soon as possible, continuing to take antiretrovirals steadily, and keeping all appointments with your HIV provider.

References

People spending a greater proportion of time in care for HIV (by not missing appointments) had a lower death risk than those who spent less time in care, according to results of a 44,432-person analysis in the United Kingdom (Great Britain).\(^1\) Worse CD4 counts\(^*\) in people who spent less time in care largely explained their higher death risk.

After a person with HIV enters care, it is crucial to keep all appointments and work closely with your HIV provider to control your HIV infection. Research shows that people who miss clinic visits do not gain as many CD4 cells as steady appointment-keepers and reach an undetectable viral load less consistently. As a result, poor appointment-keepers run a higher risk of the many diseases related to poorly controlled HIV infection. Researchers conducted this study to see if those factors combined to raise the risk of death in people who miss HIV care appointments.

**How the study worked.** This analysis involves the UK Collaborative HIV Cohort (UK CHIC), an ongoing study of HIV-positive people receiving care in many of the UK’s largest HIV centers. Workers collect routine health data from UK CHIC participants and send that information to a central databank where it can be analyzed in studies like this one. This study included UK CHIC members at least 16 years old who had at least one HIV visit between January 2000 and December 2012.

In previous research, the investigators developed and tested a new method to calculate time spent in HIV care.\(^2\) They used this method in the new study to classify each month as a month that a person was in care or out of care. With these findings they could calculate the total proportion of months a person spent in care, which they called percent time in care.

The researchers used a standard statistical method to assess the impact of percent time in care on death occurring at least 1 year in the future. They used the future death rate to avoid a well-known statistical mistake in which cause and effect get reversed. In this case that would mean sicker people (those most likely to die) would keep more appointments and thus create an artificial link between steadier clinic attendance and death. This statistical method figures the impact of percent time in care on death regardless of other risk factors, such as age, sex (male or female), HIV transmission group (straight sex, gay sex, or injecting drugs), racial or ethnic group, and latest CD4 count. Finally, the researchers conducted a separate analysis to assess the impact of percent time in care on death in people in care for at least 1 year before starting antiretroviral therapy (ART).

**What the study found.** The study included 44,432 people, 28% of them women, 53% white, and 29% black. Median (midpoint) age stood at 36 years. Half of the group became infected with HIV during sex between men, 39% during sex between men and women, 3% while injecting drugs, and the rest for other or unknown reasons. Through a median follow-up period of 5.5 years, 2279 people (5%) died.

Statistical analysis determined that people with a higher percent time in care had a 9% lower risk of death (Figure 1). People with a higher percent time in care and taking antiretroviral therapy had a 10% lower risk of death. These links between percent time in care and lower death risk held true regardless of other factors like age, race, sex, or HIV risk group. When the researchers also considered latest CD4 count in the analysis, people with higher percent time in care had only a 4% lower risk of death (Figure 1). This result, compared with the other listed results, indicates that lower CD4 counts in people who spent less time in care partly explains their higher risk of death.

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\(^*\)Words in **bold** are defined in the Technical Word List at the end of this issue of *HIV Treatment Alerts*. 
The second major analysis involved 8730 people who began antiretroviral therapy at a median age of 37 years, 22% of them women. In this group 63% were white and 21% black; 62% picked up HIV during sex between men, 31% during sex between men and women, and 3% while injecting drugs. Through a median follow-up period of 4.3 years, 237 people who started antiretroviral therapy (3%) died.

Statistical analysis determined that people with a higher percent time in care who started antiretroviral therapy had a 69% lower risk of death regardless of other factors like age, race, sex, or HIV risk group (Figure 2). After statistical adjustment for pre-antiretroviral therapy CD4 count and viral load, people with a higher percent time in care still had a 64% lower risk of death regardless of other risk factors. But after additional statistical adjustment for latest CD4 count and viral load, a higher percent time in care was no longer linked to lower death risk independent of other risk factors. This result indicates that lower latest CD4 counts and higher latest viral load largely explained the greater death risk in people with less time in HIV care.

**Figure 1.** In a study of 44,432 people, statistical analysis showed a lower death risk with more time in HIV care independent of (1) fixed risk factors like age, sex, and race and (2) those risk factors plus taking antiretroviral therapy (ART). Further statistical adjustment for (3) latest CD4 count diminished the lowered death risk to -4%, meaning a lower latest CD4 count partly explained the greater death risk in people with less time in HIV care.

**Figure 2.** Statistical analysis of 8730 people who started antiretroviral therapy showed a lower death risk with more time in HIV care independent of (1) fixed risk factors like age, sex, and race and (2) those factors plus CD4 count and viral load (RNA) before antiretroviral therapy (ART). But further statistical adjustment for (3) latest CD4 count and viral load (RNA) did not find a lower death risk with more time in care, meaning a lower latest CD4 count and higher viral load largely explained the greater death risk in people with less time in HIV care.
load in people who spent less time in care largely explains their higher risk of death among people who started ART.

What the findings mean for you. The findings of this large and careful study underline the great importance of keeping all scheduled HIV clinic appointments. Previous research linked missing appointments to lower CD4 counts and higher viral loads. This study shows that missing clinic visits also raises the risk of death. This link between missed appointments and higher death risk held true regardless of age, sex, race, or how a person acquired HIV infection. And the link held true for people who start antiretroviral therapy.

Keeping all scheduled appointments is important for a number of reasons. (1) Regular check-ups are essential for your provider to determine whether your HIV infection is changing in any way that requires action—whether or not you are taking antiretroviral therapy. (2) If you do take antiretrovirals, clinic visits let your provider check to see that the antiretrovirals are working, while giving you the opportunity to report any problems you’re having taking antiretrovirals or any side effects you believe they’re causing. (3) Regular clinic visits let your provider check you for several conditions or complications often seen in people with HIV and to take steps to prevent or treat those conditions. (4) Routine check-ups let your provider reinforce good-health practices and to administer vaccines you may need, like flu and pneumonia vaccines.

People who cannot keep an appointment should reschedule the appointment for the next available time convenient for the person with HIV and the HIV provider.

References

Women and older people had a lower risk of interruptions in steady HIV care in a 17,000-person analysis in the United States and Canada. But blacks had a higher risk of interrupted care than nonblacks, and drug injectors had a higher risk than people who got infected with HIV during sex.

Once people test positive for HIV, they must enter care, stay in care, start antiretroviral therapy, and reach an undetectable viral load to control their HIV and regain health. But some people fail to keep HIV care appointments and fall in and out of care over extended periods. Research in the United States and the United Kingdom links breaks in steady HIV care to a higher risk of death. (See the preceding article in this issue.)

A recent US study found that only 71% of HIV-positive people in this country stay in care steadily. In that analysis, steady HIV care differed by sex (male or female), race, and HIV infection risk (sex between men, sex between men and women, and injecting drugs). To learn more about how these three factors affect steady appointment keeping in a large US-Canadian group taking antiretroviral therapy, researchers analyzed data from the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD).

**How the study worked.** The analysis involved US and Canadian people in NA-ACCORD, an ongoing study of HIV-positive people in care. This analysis focused on people at least 18 years old who began antiretroviral therapy and had at least one HIV care visit between January 2000 and December 2010 and at least one CD4 count after starting antiretrovirals. The researchers set these requirements for their study to ensure that they focused on people who had similar access to HIV care. The NA-ACCORD group is similar in its makeup to the entire US and Canadian HIV populations.

The researchers defined staying in care as having two or more HIV care visits within 12 months, with each visit separated by at least 90 days. They defined falling out of care as the first time a person failed to meet this definition after starting antiretroviral therapy.

The researchers used a standard statistical method to estimate the risk of falling out of care after starting antiretroviral therapy. This method considers several risk factors for dropping out of care, including age and CD4 count when antiretroviral therapy began, sex, black race, getting HIV infection by injecting drugs, and death. Thus this statistical method identifies individual factors that raise the risk of falling out of care, regardless of whatever other risk factors a person has.

**What the study found.** The study included 17,171 people, 84% of them men, 44% black, and 19% drug injectors. Median (midpoint) age was 47 years. During a median follow-up time of 4 years, 9% of the study group died, 42% remained in steady care, and 49% had at least one interruption in their care.

*Words in bold are defined in the Technical Word List at the end of this issue of HIV Treatment Alerts.*
The statistical analysis that considers several risk factors at the same time identified two factors that lowered the risk of an interruption in steady care and two factors that raised the risk of an interruption. These factors affected the risk of interrupted care by themselves— independent of other risk factors considered.

The two factors that lowered chances of interrupted care were older age (39% lower risk for every added 10 years of age) and being a woman rather than a man (16% lower risk) (Figure 1). The two factors that raised chances of interrupted care were being black rather than nonblack (17% higher risk) and being a drug injector rather than having another HIV risk (33% higher risk) (Figure 1). Risk of death was 29% higher for every added 10 years of age but did not differ by sex, race, or HIV infection risk.

Further analysis showed that black men had a higher risk of interrupted care than nonblack men whether they were straight men or gay/bisexual men. And drug injectors had a higher risk of interrupted care than noninjectors whether they were straight men or women. Black race did not affect risk of interrupted care among women.

What the findings mean for you. This large study of adults who started antiretroviral therapy throughout the United States and Canada found that half of them did not keep two appointments per year through 4 years. The study group is similar in makeup to the entire US and Canadian HIV-positive populations, so chances are good that this finding reflects consistency of care throughout the United States and Canada. Failure to keep HIV care appointments steadily has been linked to lower CD4 counts, higher viral loads, and a higher risk of death.2,3

The study found that older people (versus younger people) and women (versus men) were more likely to maintain steady care. Black people (versus nonblacks) and drug injectors (versus people who picked up HIV during sex) ran a higher risk of interrupted care. The better chance of steady care among older people could be explained by a greater concern for health as people age and by a more open daily schedule after retirement that makes appointment keeping easier. People who picked up HIV while injecting drugs would have a lower chance of steady care if they continue to inject drugs because of the frequent lack of daily routine among drug injectors.

It is less clear why women had a better chance of steady care than men, and why blacks had a worse chance than nonblacks. Everyone in this study had started antiretroviral therapy, so everyone had reasonable access to care. The researchers note that their analysis did not include data on income, education, employment, or insurance, and those factors could affect a person’s ability to keep regular healthcare appointments.

Figure 1. A study of 17,171 people in the US and Canada determined that two factors lowered the risk of interruptions in steady HIV care—every additional 10 years of age and being a woman. Two factors raised the risk of interruptions in steady care—black race and drug injection as an HIV risk factor.
Because maintaining steady care is so important to the health of people with HIV, they should make every effort to keep appointments or to address difficulties in keeping appointments. Tell your HIV provider or others on your healthcare team if you have difficulty in maintaining steady care or believe such difficulties may arise. Problems may include loss of insurance, transportation difficulties, child care needs, or job obstacles. Your provider can guide you to a case worker or social worker who can help you solve these problems and maintain steady care for your HIV infection.

References

Based on analysis of more than 16,000 people who reached an undetectable viral load* with antiretroviral therapy (below 50 copies), researchers in the United Kingdom (Great Britain) estimate that the rebound rate (chance of a later detectable viral load) falls close to 1% per year after 7 years of viral control. Viral load rebound risk fell with (1) older age, (2) longer time since starting antiretroviral therapy, (3) later year starting therapy, and other factors.

The goal of antiretroviral therapy is to reach an undetectable viral load, which indicates that HIV is no longer making copies of itself inside the body. People starting antiretroviral therapy usually reach an undetectable viral load in 3 to 6 months. Reaching and keeping an undetectable viral load depend on steady pill taking by a person using antiretroviral therapy. Research shows that the chance of viral rebound falls as time with an undetectable viral load grows. But how long today’s antiretroviral combinations keep viral loads undetectable remains unknown. To address these issues, researchers in the United Kingdom conducted this study.

**How the study worked.** The analysis involved people in an ongoing study of HIV-positive adults seen at one of 21 HIV clinics across the United Kingdom. Researchers regularly collect personal and medical data on study participants and relay findings to a central database. For the new analysis researchers focused on people (1) who began their first antiretroviral combination between January 1998 and May 2013, (2) who reached an undetectable viral load within 9 months of starting therapy, and (3) who were taking antiretrovirals 9 months after starting.

The researchers determined how many people in this group had a viral load rebound, defined as at least one viral load above 200 copies or a treatment interruption of at least 1 month. The research team then used accepted statistical methods to learn three things: (1) individual factors linked to having a viral load rebound, (2) viral rebound rate according to several key factors including age, year starting antiretroviral therapy, and time since starting antiretroviral therapy, and (3) probability of viral rebound from year to year in a 35-year-old man who started antiretroviral therapy after 2008. The analysis of individual factors linked to rebound considered several possible factors at the same time, so identified individual factors can be said to affect rebound risk by themselves, regardless of whatever other risk factors a person has.

**What the study found.** The analysis included 16,101 adults who started a first antiretroviral combination and reached an undetectable viral load (below 50 copies) within 9 months. Women made up 25% of the study group, and blacks made up 26%. While 54% of the group became infected with HIV during sex between men, 39% became infected during sex between men and women, 2% while injecting drugs, and 5% for unknown reasons.

Through up to 15 years of viral load testing, the researchers counted 4519 viral load rebounds. That number translated into a rebound rate of 7.8 per 100 person-years (meaning about 8 of every 100 people had a rebound each year). In the group of 4519 people with a rebound, 69% had a measured viral load above 200 copies and 31% had a treatment interruption of at least 1 month.

The viral load rebound rate fell steadily from year to year after a person had reached 9 months on treatment. The rebound rate stood at 12.6 per 100 person-years in the first year after this 9-month point, fell below 10 per 100 person-years in the second year, and then continued to fall in the following years. Ten to 15 years after viral load testing began, the rebound rate stayed at 2.5 per 100 person-years. This means that among people who reached an undetectable viral load on their first antiretroviral combination and continued taking the combination for 10 years, fewer than 3 in every 100 people had a rebound each year after 10 years.

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*Words in **bold** are defined in the Technical Word List at the end of this issue of *HIV Treatment Alerts*.**
Statistical analysis that included the impact of pretreatment viral load and **CD4 count** identified several factors that independently lowered or raised risk of a viral load rebound:

- **Older age when starting antiretroviral therapy lowered rebound risk:** For example, compared with people younger than 20 when starting therapy, those 25 to 30 or 30 to 35 had a 59% lower rebound risk, and those 45 or older had a 66% lower risk.

- **Later year starting antiretroviral therapy lowered rebound risk:** For example, compared with people starting in 2008 or later, those starting in 2002-2003 had a 38% higher rebound risk and those starting in 1998-1999 had a 120% higher rebound risk.

- **Higher CD4 count when starting antiretroviral therapy raised rebound risk:** Every 100-cell higher pretreatment CD4 count raised the rebound risk 4%.

- **Higher viral load when starting antiretroviral therapy raised rebound risk:** Every 10-fold higher pretreatment viral load raised the rebound risk 8%.

- **Sex between men and women among blacks raised rebound risk:** Compared with men who got HIV during sex with other men, black men who got HIV during sex with women had an 88% higher rebound risk, and black women who got HIV during sex with men had a 65% higher rebound risk.

Finally, the researchers found that the viral load rebound rate per year fell lower with each year a person kept an undetectable viral load. For example, a man who (1) got infected with HIV while having sex with another man, (2) started antiretroviral therapy after 2008, (3) was 35 years old when starting antiretroviral therapy, and (4) had an undetectable viral load within 9 months of starting therapy had a rebound rate of 8.1% per year 1 year after starting therapy, 4.6% per year after 3 years, 3.2% per year after 5 years, 1.5% per year after 10 years, and 1.4% per year after 31 years (Figure 1). When the researchers did not count temporary viral load blips followed by an undetectable load without a change in antiretrovirals, rebound rates were 5.8% per year 1 year after starting therapy, 3.3% per year after 3 years, 2.3% per year after 5 years, 1.1% per year after 10 years, and 1.0% per year after 31 years (Figure 1).

**Figure 1.** In a 35-year-old man who reaches an undetectable viral load (below 50 copies) after starting antiretroviral therapy, the predicted viral load rebound rate per year falls over time, as long as the man maintains an undetectable viral load. The top (blue) graph shows the overall predicted rebound rate per year at five points after starting antiretroviral therapy. The bottom (orange) graph shows predicted rebound rate per year for those same five points when the analysis does include temporary viral load blips above 50 copies.
What the findings mean for you. The main goal of antiretroviral therapy is the same for everyone: reach an undetectable viral load and keep the viral load undetectable. This very large and well-planned study shows for the first time that the viral load rebound rate falls steeply with each year without a rebound. After 10 years the rebound rate per year is under 2% per year for most people and as low as 1% per year in some groups.

In other words, the longer you keep your viral load undetectable with antiretroviral therapy, the lower your chance that the viral load will become detectable again.

All antiretroviral combinations recommended today can make a person’s viral load undetectable and keep it undetectable. That success depends mainly on one thing: taking antiretroviral medicines regularly, day after day, exactly as your provider directs. That task has become easier in recent years because most antiretroviral combinations have to be taken only once a day, and many combinations include all the anti-HIV medicines you need in a single pill. If you have trouble taking your antiretroviral medicines daily, talk to your provider right away. Together you can pinpoint the reasons for missing doses and probably figure out how to solve these problems.

The study identified two groups with a higher chance of viral load rebound during antiretroviral therapy: (1) younger people compared with older people, and (2) black men and women infected during sex between men and women compared with men infected during sex between men. These results probably reflect the frequent finding that younger people2-4 and blacks3,5 face greater challenges in taking their antiretroviral pills regularly. Again, those challenges can usually be identified and often solved.

The overall low rebound rates found in people who reach an undetectable viral load suggest to the researchers “that many people on antiretroviral therapy will not have viral rebound over their lifetime.”

References

Slightly more than 10% of HIV-positive adults in the United States have diabetes, according to analysis of an HIV group representing the HIV population receiving medical care in the US. The diabetes rate was almost 4% higher in people with HIV relative to the general US population. Diabetes was more common in younger adults and in nonobese adults with HIV than in those groups in the general population.

The United States has 29 million people with diabetes, a lifelong disease marked by high sugar levels in blood. Diet or medications can control high blood sugar. If high blood sugar is not controlled, diabetes can lead to blindness, heart disease, stroke, and kidney disease.

Research shows that diabetes poses a growing threat to HIV-positive people living longer because of antiretroviral therapy. But no studies have assessed diabetes rates in an HIV population similar to the entire HIV population in the United States. Researchers from Emory University and the Centers for Disease Control and Prevention (CDC) aimed to calculate diabetes rates in such an HIV population and to compare those findings to rates in the general US population.

How the study worked. The researchers focused on two study groups, the Medical Monitoring Project of adults with HIV, and the National Health and Nutrition Examination Survey (NHANES) of adults in the general US population. The Medical Monitoring Project is an ongoing study of people selected to represent the HIV population receiving medical care in the US, while NHANES represents the entire US population not in institutions like nursing homes. Everyone in both groups was at least 20 years old and made study visits in 2009 and 2010.

To determine how many people in the Medical Monitoring Project and NHANES had diabetes, researchers checked study records to see who had a physician diagnosis of diabetes or was taking drugs to control diabetes. They also collected other information like age, sex at birth, race, body weight, and education. They calculated weight as body mass index, which can be used to classify a person as underweight, normal weight, overweight, or obese (click on link at reference 4).

Then the research team compared the diabetes rate (prevalence) in people with versus without HIV. They also compared diabetes rates in subgroups of both groups, defining different subgroups by age, sex, race or ethnicity, obesity, and other factors. Focusing only on the HIV group, the researchers used a standard statistical method to identify risk factors for diabetes. This type of analysis figures whether individual factors affect risk, regardless of whatever other risk factors a person has.

What the study found. The study included 8610 adults with HIV and 5604 adults in the general US population. Higher proportions of people with than without HIV were men (74% versus 49%) and blacks (41% versus 12%), and a lower proportion of the HIV group was white (35% versus 67%). A higher proportion of people with than without HIV was 45 years old or older (60% versus 51%), and a higher proportion with HIV lived below the poverty level (43.5% versus 8.5%).

The researchers found that 10.3% of people with HIV had diabetes, compared with 8.3% of people without HIV. Statistical analysis adjusting for major differences between the HIV group and the general population (like age and race) determined that the diabetes rate was 3.8% higher in people with HIV.

The biggest diabetes rate differences between the HIV group and the general population (Figures 1 and 2) occurred in people with hepatitis C virus (HCV) infection (6.3% higher with HIV), people with a high school education (5.1% higher with HIV), women (5.0% higher with HIV), whites (4.9% higher with HIV), people living at or below the poverty level (4.6% higher with HIV), obese people (4.4% higher with HIV), and people 20 to 44 years old (4.1% higher with HIV). Nonobese
people with HIV had a 3.5% higher diabetes rate than nonobese people without HIV.

Among people with HIV the lowest diabetes rate occurred in people 20 to 44 years old (6.7%), while the highest rate occurred in people 60 or older (19.6%). Statistical analysis of the HIV group linked three factors to a higher diabetes risk independently of other risk factors—obesity, older age, and more time since testing HIV positive.

What the findings mean for you. This large and careful comparison of diabetes rates in US adults with versus without HIV found that 1 in 10 HIV-positive people have diabetes. Compared with the general US population, people with HIV have a 3.8% higher diabetes rate. The 10% diabetes rate in US people with HIV is much higher than rates reported from HIV groups in other countries, which are usually around 3%.

The study confirmed previous research linking older age and obesity to diabetes in people with HIV. But HIV-positive people in the study’s youngest age group (20 to 44) had a 4.1% higher diabetes rate than people that age in the general population. And nonobese people with HIV had a 3.5% higher diabetes rate than nonobese people without HIV. Those findings suggest that HIV infection may be a risk factor for diabetes in the absence of traditional risk factors like old age and obesity.
Table 1. Changeable and unchangeable diabetes risk factors

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<td>➤ Overweight or obesity</td>
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<td>➤ Low “good cholesterol” or high triglycerides</td>
<td>➤ African American, Hispanic, Native American, Asian</td>
</tr>
<tr>
<td>➤ Not physically active</td>
<td>➤ Had gestational diabetes (diabetes during pregnancy)</td>
</tr>
<tr>
<td>➤ Depression</td>
<td>➤ Have or had heart disease or stroke</td>
</tr>
<tr>
<td></td>
<td>➤ Have polycystic ovary syndrome</td>
</tr>
<tr>
<td></td>
<td>➤ Have acanthosis nigricans*</td>
</tr>
</tbody>
</table>

*Dark, thick, velvety skin around the neck and armpits.

Diabetes is a lifelong disease caused by high sugar levels in the blood. If someone with diabetes does not get proper treatment, that person runs a higher risk of other serious diseases, like heart disease, stroke, and kidney failure.

Because people with HIV may have a higher risk of diabetes, they should take any steps they can to lower this risk. The National Institute of Diabetes and Digestive and Kidney Diseases lists a dozen diabetes risk factors (Table 1). Some of these risk factors—like older age and black race—cannot be changed. But it is important to know these unchangeable risk factors to get an overall understanding of your diabetes risk. Five listed risk factors can be changed (Table 1). People with HIV should work with their providers to address these five risk factors.

The Website of the National Institute of Diabetes and Digestive and Kidney Diseases includes an interactive or printable diabetes risk test (click on link at reference 6 below). The site also features an easy-to-understand section on preventing diabetes. This section answers important questions like (1) How can I lower my chances of developing type 2 diabetes?* (2) What should I do if my health care professional told me I have prediabetes?* (3) If I had gestational diabetes when I was pregnant, how can I lower my chances of developing type 2 diabetes?7

Summing up their findings, the researchers advise HIV providers to follow current guidelines in checking HIV patients for diabetes† before and after they start antiretroviral therapy.8

*Type 2 diabetes is the kind that develops in adulthood. Prediabetes is high blood sugar approaching the level that indicates diabetes.
†By measuring fasting blood glucose and HbA1c.

...continued
Fractures (broken bones) occurred twice as often in HIV-positive men 50 to 59 years old as in HIV-negative men that age, according to results of a large US comparison. Hypertension* (high blood pressure) raised the fracture risk in men with or without HIV infection.

Low bone density affects people with HIV more than HIV-negative people and leads to higher fracture rates in HIV-positive men and women. Fracture risk increases with age, so fractures may become even more common in HIV-positive people as they live longer thanks to antiretroviral therapy. Other risk factors for weak bones also affect high proportions of people with HIV, including smoking and drinking too much alcohol.

US researchers conducted this study to compare fracture rates in 10-year age groups of men with versus without HIV infection.

How the study worked. This analysis involved gay or bisexual men in the Multicenter AIDS Cohort Study (MACS), which includes HIV-positive men and HIV-negative men at risk of HIV infection. Men in MACS make two study visits every year to get a checkup and answer questions related to their behavior and health. Since 2001 MACS men reported whether they had broken a bone since their last visit.

This study focused on two groups of fractures: (1) all fractures except those of the facial bones, skull, fingers, or toes, and (2) fragility fractures, defined as those of the spine, wrist, femur (long bone in the upper leg), and humerus (long bone in the upper arm) (Figure 1). Fragility fractures are those thought likely to result from low bone density.

Figure 1. Fragility fractures in these four areas—thought to be due to low bone density—occurred twice as often in HIV-positive men in their 50s as in HIV-negative men that age. (Image from Servier PowerPoint Image Bank http://servier.com/Powerpoint-image-bank.)

*Words in **bold** are defined in the Technical Word List at the end of this issue of HIV Treatment Alerts.
The researchers divided men into three age groups: 40 to 49, 50 to 59, and 60 or older. They used a statistical method that determined whether HIV status by itself (being HIV-positive or negative) raised the fracture risk in each of these three age groups, independently of risk factors like white race, smoking, drinking too much alcohol, low weight, and other illnesses.

**What the study found.** The study included 1221 gay or bisexual men with HIV and 1408 without HIV. The HIV group had a lower proportion of whites (59% versus 73%) and a higher proportion of blacks or Hispanics (41% versus 27%). About 30% of both groups called themselves moderate to heavy alcohol drinkers, and a somewhat higher proportion of men with HIV smoked (38% versus 31%).

Among men with HIV, 182 of 1221 had a new fracture during the study, compared with 197 of 1408 men without HIV. Those numbers gave a new-fracture rate of 12.8 per 1000 person-years in men with HIV and 10.0 per 1000 person-years in men without HIV (Figure 2). A rate of 12.8 per 1000 person-years means about 13 of every 1000 men broke a bone each year.

In men in their 40s, the new-fracture rate for all fractures was about 10 per 1000 person-years in both HIV-positive and HIV-negative men. Among men in their 50s, the new-fracture rate for all fractures stayed around 10 per 1000 person-years in HIV-negative men but jumped to almost 20 per 1000 person-years in men with HIV. Among men in their 60s, the new-fracture rate was similar in men with and without HIV, both about 15 per 1000 person-years.

The rate of new fragility fractures was also higher in men with than without HIV: 4.6 versus 3.4 per 1000 person-years (Figure 2). Again, the new-fracture rate for fragility fractures was similar with and without HIV among men in their 40s. But HIV-positive men in their 50s had a much higher new-fracture rate for fragility fractures, while the rate stayed the same in HIV-negative men in their 50s. New-fracture rates for fragility fractures were similar in HIV-positive and negative men in their 60s.

The statistical analysis that measures the impact of several fracture risk factors at the same time figured that HIV-positive men in their 50s had a doubled rate of all fractures compared with HIV-negative men the same age. HIV-positive men in their 50s also had a doubled rate of fragility fractures compared with HIV-negative men. These findings mean that among men in their 50s, HIV infection by itself doubles the risk of all fractures and of fragility fractures.

Total use of anti-HIV protease inhibitors (like Prezista or Reyataz) or the antiretroviral tenofovir (a part of combination drugs like Stribild and Atripla) was not linked to rates of all fractures or fragility fractures.
One other fracture risk factor, by itself, raised the risk of all fractures: High blood pressure raised the all-fracture risk by 32%.

**What the findings mean for you.** As we get older, our bone density decreases and we run a higher risk of breaking a bone. This is true for people with and without HIV. This new study shows that, for men with HIV, the fracture risk starts to climb when they are in their 50s. In contrast, among men without HIV, the fracture risk does not start climbing until they are in their 60s. In other words, the study shows that HIV infection status by itself is a fracture risk factor for men in their 50s.

Because of this finding, the researchers who conducted this study recommend that HIV clinicians start checking bone density in HIV-positive men when they reach their 50s. Current HIV guidelines already make that recommendation, but the extent to which these guidelines are followed is not clear. Those guidelines also recommend bone density testing for HIV-positive women who have reached the menopause and for people who have already had a fragility fracture.

This study also pinpointed hypertension (high blood pressure) as a fracture risk factor in men with or without HIV. Hypertension is common among people with HIV and can lead to serious heart disease. High blood pressure has no symptoms you can feel, but it’s easy to detect with a quick blood pressure cuff test. Hypertension usually responds to drug therapy and to lifestyle changes including diet, limiting alcohol drinking, and quitting smoking.

Other research in people with and without HIV identifies several other risk factors for low bone density. See Table 1 on page 24. Some of these risk factors can be avoided or changed, including (1) lack of weight-bearing exercise, (2) smoking, (3) drinking too much alcohol, (4) consuming too little calcium or vitamin D, and (5) weighing less than normal. Because HIV itself is a fracture risk factor, people with HIV should work with their provider to address these changeable risk factors. Low bone density (osteopenia or osteoporosis) can be treated. People who already have low bone density should take precautions to avoid falling. See the link at Reference 6 below for tips on preventing falls.

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### References


Lower bone density in people with HIV but not faster decline over time

Compared with HIV-negative people in a large study in Ireland, HIV-positive people had lower bone mineral density, putting them at a higher risk of breaking a bone.1 But over a period of 3 years bone density fell at a similar rate in people with HIV and without HIV. HIV-positive people who did not take antiretroviral therapy* lost bone density faster than people taking continuous antiretroviral therapy.

Several studies of women and men with HIV infection record high rates of low bone density. Other studies show that bone mineral density drops by 2% to 6% over the first 2 years of antiretroviral therapy, but after that bone density stays stable. Understanding how bone density changes over time and risk factors for falling bone density is important because maintaining healthy bones is necessary to prevent fractures (broken bones).

To learn more about these issues, researchers in Ireland compared bone density over time in people with HIV and a similar group of people without HIV.

How the study worked. The study included HIV-positive adults in care at an infectious disease clinic in Dublin, Ireland, and a similar group of HIV-negative people living in the same community. Over a period of 3 years, all study participants had two or three DXA scans of bone at the femoral neck, the total hip, and the lumbar spine (Figure 1). DXA scans make images of bone that show their density.

The main goal of the study was to compare changes in bone density at these three bone sites between people with and without HIV over 3 years. The researchers determined whether common risk factors or HIV-related factors affected changes in bone density among people with HIV. Common factors include older age, female sex, being white instead of nonwhite, low weight, smoking, and drinking too much alcohol. The type of analysis used to pinpoint risk factors identifies individual factors that affect bone density, regardless of whatever other risk factors a person has.

Figure 1. In a study of 176 adults with HIV and 208 without HIV, the HIV group had significantly lower bone density at three bone sites when researchers first measured bone density in a 3-year study. (Density is measured in grams per centimeter squared, g/cm². Images from Servier PowerPoint Image Bank. http://servier.com/Powerpoint-image-bank.)

*Words in bold are defined in the Technical Word List at the end of this issue of HIV Treatment Alerts.
What the study found. The study included 176 adults with HIV and 208 without HIV. The HIV group was younger than the non-HIV group (median age 39 versus 43 years) and included a higher proportion of men (61% versus 46%) and a higher proportion of blacks (39% versus 18%). Most people with HIV (88%) were taking antiretroviral therapy, and 78% had an undetectable viral load.

On the first DXA scan, people with HIV had significantly lower bone density than people without HIV at all three bone areas measured—the femoral neck, total hip, and lumbar spine (Figure 1). “Significantly” here means that a statistical test shows that chance does not explain these differences between the HIV group and the non-HIV group.

Most study participants had two more DXA scans during the 3-year study. Among people with HIV, bone density fell significantly from year to year at the femoral neck and total hip but not at the lumbar spine (Figure 2). In people without HIV, bone density also fell significantly from year to year at the femoral neck and total hip but not at the lumbar spine. Year-to-year drops in bone density were not significantly greater in the HIV group than in the HIV-negative group.

Focusing only on people with HIV, statistical analysis linked three factors to a greater decline in bone density per year at the femoral neck, regardless of whatever other risk factors a person had:

- Age over 30 versus younger
- White versus nonwhite race
- Not taking antiretroviral therapy versus taking continuous antiretroviral therapy

Taking certain types of antiretrovirals did not affect changes in bone density over time, including taking protease inhibitors (like Prezista or Reyataz) or tenofovir (a part of combination drugs like Stribild and Atripla).

What the findings mean for you. People with low bone density run a higher risk of broken bones. This study of 176 adults with HIV and a similar group of 208 people without HIV made several important findings about bone density. When researchers first measured...
bone density in these two groups, they found that people with HIV had significantly lower bone density at three bone sites (Figure 1). This finding confirms previous reports of lower bone density in people with HIV.

But when researchers compared bone density measurements made over 3 years, they found that bone density did not drop yearly more in people with HIV than in the HIV-negative group (Figure 2). Bone density dropped at a similar rate in both groups.

Third, in people with HIV the researchers found that those not taking antiretroviral therapy had faster drops in bone density per year than people taking continuous antiretroviral therapy. In other words, steady antiretroviral therapy protected against bone loss in this study group. Also, certain types of antiretrovirals studied did not affect the rate of bone density loss in people with HIV.

The study also confirmed two other risk factors for faster bone density loss: older age and white race.

Because people with HIV infection tend to have lower bone density than people without HIV, they should be aware of risk factors for bone loss. Some of these risk factors—like older age and white race—cannot be changed (Table 1). But people who have these risk factors in addition to HIV infection should try especially hard to avoid or correct risk factors that can be changed, including lack of exercise, smoking, and drinking too much alcohol (Table 1). Importantly, this study found that antiretroviral therapy is not a bone loss risk factor. In fact, continuous antiretroviral therapy protected against faster bone loss. Your HIV provider will know which non-HIV diseases boost the risk of low bone density.

### Table 1. Changeable and unchangeable risk factors for bone density loss

<table>
<thead>
<tr>
<th>Changeable factors</th>
<th>Unchangeable factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>➤ Lack of weight-bearing exercise</td>
<td>➤ Being a woman</td>
</tr>
<tr>
<td>➤ Smoking</td>
<td>➤ Older age</td>
</tr>
<tr>
<td>➤ Drinking too much alcohol</td>
<td>➤ Menopause before age 45</td>
</tr>
<tr>
<td>➤ Consuming too little calcium or vitamin D</td>
<td>➤ Being white or Asian</td>
</tr>
<tr>
<td>➤ Weighing less than normal</td>
<td>➤ Having a parent or sibling with low bone density</td>
</tr>
<tr>
<td>➤ Drinking too much alcohol</td>
<td>➤ Having a small body frame</td>
</tr>
<tr>
<td>➤ Consuming too little calcium or vitamin D</td>
<td>➤ Breaking a bone in the past</td>
</tr>
</tbody>
</table>


Reference:

Article 8

Depression rate drops during first year of antiretroviral therapy

In a group of HIV-positive people starting antiretroviral therapy,* chances of depression fell sharply in the first year of treatment.1 A score indicating level of depression dropped by half—from 6 to 3—during the first year of antiretroviral therapy.

Depression—feeling very sad or hopeless much of the time—is not just a mood or a feeling: It’s a serious illness that can be assessed with standard tests and often responds to treatment. Analysis of a group representing everyone in care for HIV in the United States determined that more than 1 in 3 HIV-positive people have depression.2 Almost half of these people with depression did not have a diagnosis of depression in their medical file, meaning many of them never discussed depression with their HIV care provider. A study of 2596 people with or without HIV calculated that the HIV group had almost a doubled risk of major depression.3

Research has linked depression to poor antiretroviral pill taking and to worsening HIV infection and death.4 Depression can make it harder to work, harder to sleep, and harder to enjoy the good things in life.

A team at the University of Alabama at Birmingham conducted this study to measure changes in depression rate and severity during the first 12 months of antiretroviral therapy and to identify factors linked to depression after 12 months of therapy.

How the study worked. The study focused on adults starting their first antiretroviral combination between January 2007 and December 2012. Everyone received care at the University of Alabama at Birmingham HIV clinic. The researchers checked clinic records to gather information on these people (like age and race) and to note their scores on a standard depression test.

This test, the Patient Health Questionnaire depression scale (PHQ-9), can be used to determine whether a person has mild, moderate, moderately severe, or severe depression.5 For this study the researchers divided people into those with major depression (score 10 or higher) or mild or no depression (score 9 or lower). You can see the PHQ-9 by clicking on the link following reference 6.

For each person, the researchers recorded PHQ-9 scores at two points: (1) in the year before they started antiretroviral therapy and (2) at the point closest to 12 months after they started antiretroviral therapy. Then the investigators used a standard statistical test to identify personal and health-related factors linked to depression after 12 months of antiretroviral therapy. This statistical test pinpoints individual factors related to depression, no matter what other risk factors a person may have.

What the study found. The study included 281 people, 48 (17%) of them women, 170 (60%) black, and 111 (40%) white. While 38% of the study group were younger than 30 years old, 41% were 30 to 45 and 21% were older than 45. Records showed that 8% of the group had public health insurance (like Medicaid or Medicare), 44% had private insurance, and 48% had no insurance.

Among the 281 study participants, 196 (70%) had mild or no depression and 85 (30%) had major depression. Eighty-seven people (31%) had depression before ever starting antiretroviral therapy. That number dropped to 59 (21%) with depression after 12 months of therapy. Among the 87 people with depression before therapy, only 37 (43%) still had depression while taking antiretroviral therapy.

The median (midpoint) depression score fell from 6 before antiretroviral therapy began to 3 after 12 months of therapy. This drop is highly statistically significant, meaning that chance cannot explain the difference. Risk of depression was more than 2 times higher before antiretroviral therapy than during therapy.

The multifactor statistical analysis determined that three factors made depression more likely after 12 months

*Words in bold are defined in the Technical Word List at the end of this issue of HIV Treatment Alerts.
People with no health insurance had a 2.6 times higher chance of depression during antiretroviral therapy.

The same statistical analysis found no evidence linking the antiretroviral efavirenz to depression. Efavirenz is also called Sustiva and is part of the 3-in-1 pill Atripla. Some earlier research linked efavirenz to depression, but other research did not. Results of the new study support the argument that efavirenz does not lead to depression.

What the findings mean for you. Depression—a “persistent sad, anxious, or ‘empty’ mood”—is a serious illness. The National Institute of Mental Health says depression can cause “severe symptoms that affect how you feel, think, and handle daily activities, such as sleeping, eating, or working.” Yet people are sometimes reluctant to discuss depression with their providers. People with HIV and their providers should work together to determine if a person has depression, because depression can be treated successfully with counseling, medication, or both.

A study of a large US HIV group figured that one third had major depression. Results of the new study agree with that estimate, finding that almost 1 in 3 HIV-positive people had major depression before they started their first antiretroviral therapy. But after about 12 months of therapy, the proportion of people with depression had dropped to 1 in 5. At the same time, depression severity fell by half in this HIV group.

These findings do not mean antiretroviral therapy itself relieves depression. Rather, the lower depression rate after antiretroviral therapy began may indicate that being in care for HIV infection and having contact with health professionals helps people overcome depression. The study also found that people without health insurance had more than a doubled risk of depression.

If you think you may have depression, you can look at the National Institute of Mental Health list of depression signs and symptoms (Table 1). If you have some of these feelings most of the day for at least 2 weeks, you may have depression and you should talk about it with your HIV provider.
Table 1. Signs and symptoms of depression

If you have been experiencing some of the following signs and symptoms most of the day, nearly every day, for at least two weeks, you may be suffering from depression:

- Persistent sad, anxious, or “empty” mood
- Feelings of hopelessness, or pessimism
- Irritability
- Feelings of guilt, worthlessness, or helplessness
- Loss of interest or pleasure in hobbies and activities
- Decreased energy or fatigue
- Moving or talking more slowly
- Feeling restless or having trouble sitting still
- Difficulty concentrating, remembering, or making decisions
- Difficulty sleeping, early-morning awakening, or oversleeping
- Changes in appetite or weight
- Thoughts of death or suicide, or suicide attempts
- Aches or pains, headaches, cramps, or digestive problems without a clear physical cause and/or that do not ease even with treatment


References

Prescription of opioid painkillers falls with longer time in HIV care

More than one quarter of a large HIV group in North Carolina had a prescription for opioid painkillers at least 2 years in a row, and many of those people had opioid prescriptions more than half of the time they spent in care for HIV. But opioid prescriptions dropped substantially with longer time in HIV care.

Opioids are strong pain medications that a provider can prescribe or that can be obtained illegally (see “What you should know about opioid painkillers,”2,3). An opioid use crisis has spread through many parts of the United States.2 Health authorities estimate that in 2015 about 2 million people in the United States misused prescription opioid pain relievers.3 Some research indicates that people with HIV get opioid prescriptions twice as often as people without HIV.4 The Centers for Disease Control and Prevention (CDC) has guidelines on proper opioid prescribing,5 but some work indicates that these guidelines are not always followed in people with HIV.6

Because little is known about trends in opioid prescriptions over time in people with HIV, researchers at the University of North Carolina conducted this study of people in care for HIV at their HIV clinic.

How the study worked. The researchers focused on adults in North Carolina who had at least one HIV care visit per year in at least 5 years between 2000 and 2014. For each person, the study start date was the first year of their HIV care in 2000 or later.

The research team checked medical records of these people to see how often they received a prescription for an opioid. They divided study participants into three opioid prescription groups:

- Never/sporadic use: no opioid prescription or rare prescription
- Episodic use: at least 1 opioid prescription in at least 2 consecutive years
- Chronic use: an opioid prescription during at least half of the years in care

The researchers used a standard statistical method to identify factors that raised chances of belonging to the episodic opioid use group or the chronic opioid use group. This kind of analysis identifies individual risk factors that have an impact regardless of whatever other risk factors a person has.

What you should know about opioid painkillers

- Opioids are strong pain medications that a provider can prescribe or that can be obtained illegally.
- Opioids include (1) prescription medicines like oxycodone (OxyContin), hydrocodone (Vicodin), fentanyl, codeine, and morphine, and (2) illegal drugs like heroin.
- Besides relieving pain, opioids can cause euphoria—a strong sensation of excitement and well-being.
- Opioids are usually safe when taken as a provider directs. But if opioids are misused (taken too often or without a prescription), they can cause addiction, overdose, and death.
- There are medications that successfully treat opioid misuse—methadone, buprenorphine, and naloxone. Naloxone can reverse opioid overdose.
- In 2015 opioid overdoses killed 33,000 people in the United States.
- In 2015 an estimated 2 million people in the United States had substance use disorders related to prescription opioid pain relievers.
- About 80% of people who use heroin first misused prescription opioids.

National Institute of Drug Addiction. Opioids.3

*Words in bold are defined in the Technical Word List at the end of this issue of HIV Treatment Alerts.*
What the study found. The study group included 1239 people in care for HIV infection between 2000 and 2014. Group members received care for a median (midpoint) of 9 years. Most study participants were men (70%), and most were black (60%). The midpoint age when these people began care was 39. Only 25 study participants (2%) had a medical record noting chronic pain, a common reason for having an opioid prescription.

The researchers determined that 898 study group members (72%) fell into the never/sporadic use group, 141 (11%) were episodic users, and 200 (16%) were chronic users. After 1, 5, 10, and 15 years of care, opioid prescription probabilities were 16%, 8%, 8%, and 6% in never/sporadic users, 7%, 22%, 51%, and 14% in episodic users, and 64%, 69%, 60%, and 35% in chronic users (Figure 1). Thus opioid prescriptions fell sharply over time in episodic users and chronic users.

Statistical analysis pinpointed several independent predictors of belonging to the episodic use group or the chronic use group. Compared with never/sporadic users, episodic users were more likely to be women, to have depression, to have a drug-related diagnosis, to use antiretroviral therapy, and to have an undetectable viral load. Compared with never/sporadic users, chronic users were more likely to be women, to be older, and to have a mental illness.

What the findings mean for you. This 15-year study of more than 1200 people with HIV in North Carolina found that 27% of them—more than one quarter—used prescription opioids episodically (at least 1 opioid prescription in at least 2 consecutive years) or chronically (an opioid prescription during at least half of the years in care). Episodic or chronic opioid users were more likely to be women, older people, and people with depression or other mental illness.

Opioids include prescription drugs like oxycodone (OxyContin), hydrocodone (Vicodin), fentanyl, codeine, and morphine—as well as illegal drugs like heroin. These drugs are powerful painkillers that providers can prescribe to help people cope with pain, for example, after surgery. But opioids can also give users a sense of intense happiness or well-being. As a result, using them over a prolonged period can be addictive. Some people who start with prescription opioids go on to acquire them illegally, and some end up using heroin.

The National Institute of Drug Addiction warns that the United States faces an opioid crisis. Researchers estimate that about one quarter of people who take prescription opioids misuse them. Misuse can result in overdose and death. In 2015 more than 33,000 people in the United States died of opioid overdose, including overdose of prescription opioids, heroin, and...
Although US providers began prescribing fewer opioids starting in 2010, in 2015 the amount of opioids prescribed in the United States was still 3 times higher than in 1999 and almost 4 times higher than the prescribing rate in Europe. The Centers for Disease Control and Prevention (CDC) has guidelines for providers on proper opioid prescribing.3

If your provider prescribes an opioid like OxyContin or Vicodin, it is critical to take the drug exactly as your provider directs and not to continue using it longer than directed. If you are misusing prescription opioids or started using illegal opioids, get help to stop from your provider or from a drug treatment center. Several drugs—methadone, buprenorphine, and naltrexone—can help people recover from opioid addiction.9

A hopeful finding emerged from the study of opioid use in people with HIV:1 Episodic and chronic opioid users proved less likely to get an opioid prescription with longer time in HIV care. That encouraging trend could reflect the overall benefits of maintaining steady HIV care, such as prevention or treatment of serious non-HIV diseases that may call for an opioid prescription.

References

Another HCV infection after HCV cure most frequent in high risk takers

New drug therapies cure hepatitis C virus (HCV) infection in most treated people. But after a cure a person can get another HCV infection. A large study of people with HCV and HIV in Canada found that two groups had the highest risk of new HCV infection after cure—people who inject drugs often, and gay or bisexual men who have risky sex.¹

HCV and HIV (the AIDS virus) often occur in the same person because the viruses use the same routes to pass from an infected person to an uninfected person. HCV and HIV can be passed along when people share drug-injecting equipment, and they can be passed along during sex (often sex without a condom).

Untreated HCV infection can lead to serious liver disease, and liver problems develop faster in HCV-infected people who also have HIV.² Strong anti-HCV drugs that became available in the past few years are curing high proportions of people with HCV infection, including people who also have HIV. But people whose HCV gets cured through drug therapy may become infected again with another HCV virus. Getting cured does not protect a person from picking up HCV infection again.

The researchers divided their study group into three subgroups, which also reflect how people got HCV and HIV infection:

- **Recent high-frequency drug injector:** Any self-reported use of injected cocaine or methamphetamine in the last 6 months
- **Low-frequency drug injector:** Any self-reported use of injected drugs other than cocaine or methamphetamine
- **Recent high-risk sex by gay or bisexual men:** More than 1 sex partner and less than 100% condom use in the last 6 months or a sexually transmitted infection in the last 6 months

The researchers created a comparison group of men who were not Aboriginal* and who did not have male sex partners or inject drugs in the past 6 months.

Using statistical methods appropriate for relatively small study groups, the researchers estimated the HCV repeat-infection rate in these three subgroups. This kind of analysis considers several HCV risk factors at the same time, including the type of HCV risk (one of the three subgroups), sex (male or female), age, CD4 count,† and ethnic background (Aboriginal or not). Such an analysis allows researchers to identify individual HCV risk factors, regardless of whatever other risk factors a person may have.

The research team estimated HCV repeat-infection rates within 1 year of the HCV cure, between 1 and 3 years after the cure, and more than 3 years after the cure.

*Aboriginal (or indigenous) people are the original inhabitants of the land that is now Canada. Their ancestors came from Asia thousands of years before Europeans.

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

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³ Abbreviation for cluster of different immune system cells.
What the study found. The study focused on 257 people infected with both HIV and HCV. Anti-HCV drugs cured HCV infection in all these people, and all had at least one HCV test after their cure. Most study participants (82%) were men, 74% had injected drugs, 11% were recent high-frequency drug injectors, and 25% were recent high-risk gay or bisexual men. Median (midpoint) age of the study group stood at 49 years. This study population reflected the overall Canadian population of people with HCV and HIV.

Through a median follow-up of 2.5 years after their cure, 18 people (7%) became infected again with HCV, including 12 drug injectors and 6 gay or bisexual men. In these 18 people with repeat infection, 5 people had spontaneous clearance of HCV, meaning their immune system controlled the HCV without the help of drugs. But the other 13 of these 18 need more anti-HCV drugs to try once again to cure the infection.

The overall repeat-infection rate was 31 per 1000 person-years, which means that in a study of 1000 people, 31 would get repeat HCV infection during each year of follow-up. The repeat-infection rate was 12 per 1000 person-years in the first year after cure, 18 per 1000 between 1 and 3 years after the cure, and 16 per 1000 more than 3 years after the cure. These results indicate that the repeat-infection rate rose with longer time after the HCV cure (Figure 1).

In the comparison group of low-risk people, the repeat infection rate in the first year after cure was 10 per 1000 person-years, meaning 10 of every 1000 people would get a new HCV infection in each year of follow-up. The repeat-infection rate was only somewhat higher in gay or bisexual men who did not fit into the high-risk gay group—16 per 1000 person-years (Figure 2). The repeat-infection rate was higher in low-frequency drug injectors (22 per 1000), higher still in recent high-risk gay or bisexual men (26 per 1000) and highest in recent high-frequency drug injectors (58 per 1000). Further statistical analysis determined that recent high-frequency drug injectors had a 6 times higher risk of repeat HCV infection than the low-risk comparison group.

What the findings mean for you. This study shows that HIV-positive people cured of HCV infection can get a new HCV infection in the first few years after their cure. More than 1 in 20 people cured of HCV with anti-HCV drugs got infected with HCV again during the study period. A previous study of gay and bisexual men in Amsterdam found an even higher repeat-infection rate. And other research described a large international network of HCV transmission among gay and bisexual men.

The new study in Canada demonstrates that HIV-positive active drug injectors have an even higher rate of repeat HCV infection than HIV-positive gay and bisexual men.
After HCV cure, the repeat HCV infection rate rose higher more than 1 year after the cure—a finding indicating a need for regular HCV testing in high-risk people.

Figure 2. The rate of repeat HCV infection after HCV cure was 10 per 1000 person-years in a group with HCV and HIV and low sexual or drug-injecting risk of HCV. Rates were higher (left to right) in gay or bisexual men with a low risk, drug injectors with a low risk, gay or bisexual men with a high risk, and drug injectors with a high risk.

bisexual men. These were people who recently injected cocaine or methamphetamine, not heroin or other drugs. They had a 6 times higher risk of repeat HCV infection than people with a low sexual or drug-related risk of HCV infection.

Another important finding of the Canadian study is that the rate of repeat HCV did not fall over time after the HCV cure. In fact, the repeat infection rate was higher more than 1 year after the HCV cure than in the first year after the cure. This finding underlines the need for regular HCV testing in people who continue to inject drugs or continue to have sex without condoms.

If you inject any drugs, you should talk to your HIV provider about how you can reduce the harms of drug use (for example, by getting into a drug treatment program, accessing safe injection equipment, and avoiding sharing equipment). A counselor at a local AIDS service organization may also be able to help.

As this study shows, injecting drugs raises the risk of picking up serious infections that can be carried in blood, like HCV. Cocaine is an addictive drug that harms brain function and can lead to heart attack, stroke, seizure, and coma. Methamphetamine is highly addictive and can lead to hallucinations, changed brain structure and function, poor thinking, and aggressive or violent behavior. Finally, people who inject drugs before sex are more likely to have sex without condoms.

This study emphasizes the importance of using condoms during sex. HIV-positive people should remember that condoms do more than protect their sex partners from picking up their HIV; condoms also protect the HIV-positive partner from picking up other sexually transmitted infections—like HCV, hepatitis B virus, syphilis, chlamydia, genital herpes, and HPV infection, which can lead to anal cancer or cervical cancer. The Centers for Disease Control and Prevention (CDC) has a useful online guide to condom use at the link provided in reference 8 below.

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High disability and frailty rates in middle-aged to older HIV group

Almost 1 in 5 middle-aged and older adults with HIV had self-reported difficulty in daily activities like housekeeping, shopping, or managing medications in a US study. This rate is much higher than in the general US population. The study identified two risk factors for this type of disability that a person can change—smoking and low physical activity.

Thanks to antiretroviral therapy, people with HIV are living to an older age. Like all older people, they face age-related diseases like heart disease, kidney disease, and osteoporosis. These conditions can contribute to disability and frailty, which standard tests can measure. Already-completed studies show that people with HIV run a higher risk of both frailty and disability than HIV-negative people.

US researchers conducted this new study to determine rates of disability and frailty in people with HIV and to examine the overlap between disability and frailty.

How the study worked. The researchers focused on an ongoing study group, the AIDS Clinical Trials Group (ACTG) HAILO group. HAILO includes HIV-positive people at least 40 years old who began antiretroviral therapy in an ACTG trial and remained under observation afterwards. They entered HAILO in 2013 and 2014.

Study participants were tested for disability with the Instrumental Activities of Daily Living (IADL) Questionnaire. The questionnaire asks if people feel limitations in any of 8 activities: housekeeping, money management, cooking, transportation, telephone use, shopping, laundry, and medication management. The researchers determined how many people had 0, 1, or 2 or more IADL limitations.

Participants also completed a standard frailty test, which measures five tasks: 4-meter walk speed, grip strength, unintentional weight loss in the past 12 months, exhaustion, and low activity. A deficit in 3 to 5 of these tasks indicates frailty; a deficit in 1 or 2 tasks indicates prefrailty. The researchers classified participants as nonfrail, prefrail, or frail.

The research team collected personal information (like age and sex), HIV factors (like CD4 count), and occurrence of other diseases and conditions. They used a standard statistical method to identify factors that predicted IADL impairment. This method identifies individual factors linked to IADL impairment, regardless of whatever other factors a person has.

What the study found. The study involved 1015 HIV-positive people with a median (midpoint) age of 51 years, including 15% who were 60 or older. Almost half of the group (48%) was white, while 29% were black and 20% Hispanic. Women made up 19% of the study group, and 80% of the group had health insurance. Two thirds of the study group had a CD4 count above 500, and 94% had a viral load below 200 copies.

While 837 people in the study group (82%) had no IADL impairments, 115 (11%) had 1 impairment and 63 (6%) had 2 or more impairments. The most frequent IADL impairments involved housekeeping (in 48% with any impairment), transportation (in 36%), and shopping (in 28%). Only 5% had impaired medication management, which includes taking medications on time every day.

Statistical analysis identified 5 factors linked to having an IADL impairment (Figure 1)—less education, Medicare or Medicaid versus private insurance, current smoking, lower physical activity, and cognitive impairment (problems with memory, language, thinking, or judgment) at the first study visit. Sex (male or female), older age, and HIV factors like CD4 count did not affect chances of IADL impairment.

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*Words in bold are defined in the Technical Word List at the end of this issue of HIV Treatment Alerts.
The frailty tests classified 62 people (6%) as frail and 377 (37%) as prefrail. About half of frail participants (52%) had at least 1 IADL impairment, while 21% of prefrail participants had an IADL impairment. Among nonfrail people, three factors predicted IADL impairment—less education, current smoking, and Medicare or Medicaid versus private insurance. Among prefrail people, three factors predicted IADL impairment—cognitive impairment, Medicare or Medicaid versus private insurance, and lower physical activity.

What the findings mean for you. This study of 1015 middle-aged and older adults with HIV found that almost 1 in 5 (18%) had disability as measured by impairment of Instrumental Activities of Daily Living (IADL) like housekeeping, transportation, and shopping. A standard frailty test classified 1 in 20 people as frail and 1 in 3 as prefrail. Yet everyone in this HIV group had started antiretroviral therapy, and almost everyone had an undetectable viral load and a good CD4 count.

The 18% IADL impairment rate in this middle-aged to older HIV group was much higher than the 6% to 8% rate found in 65- to 74-year-olds in the general population. In the HIV study group, IADL-measured disability did not affect older people significantly more than younger people. Among 203 people 44 or younger, 31 (15%) had 1 or more IADL impairments.

Risk factors for IADL impairment included two factors that people can change—smoking and lower physical activity. About 40% of HIV-positive people smoke, a rate twice higher than in the general population. Smoking can cause lung cancer and other cancers, heart disease, and stroke. If you don’t smoke now, don’t start. If you already smoke, talk to your provider about making a plan to quit. Your provider can prescribe medications that can help you quit. A free online interactive program designed specifically for people with HIV has had success in helping people quit. Go to the link following reference 9 below.

The study also found that people who got fewer than 3 days of moderate or vigorous physical activity per week had a doubled chance of IADL impairment compared with more active people (Figure 1). If you get little exercise, talk to your HIV provider to see which kinds of physical activity may be right for you. Exercise can include simple activities you may enjoy, like walking, gardening, and tennis.

The aidsmap site has a practical online guide to exercise for people with HIV. (http://www.aidsmap.com/Exercise/page/1188930/).


Youth with HIV and poor body image more likely to have condom-free sex

HIV-positive teens and young adults with a less favorable image of their own body were more likely to have sex without condoms in a US study.1 Having six or more sex partners lowered chances of using a condom.

Research shows that concerns about body image often affect adults with HIV.2 Those concerns may affect whether an adult has risky sex (without a condom and/or with many sex partners)3 and how well an adult cares for their health by keeping medical appointments and taking anti-HIV drugs regularly. Much less is known about how body image affects young people with HIV, although it is clear that body image is highly important to young people as they begin having sex.

Researchers at St. Jude Children’s Research Hospital in Tennessee conducted this study to learn more about body image and its impact on young people with HIV. They wanted to see if poor body image and other factors affect whether young people have sex without condoms. Condoms are a reliable way to prevent passing HIV to a sex partner during sex. Condoms also prevent passing along or picking up other sexually transmitted infections like syphilis, gonorrhea, and hepatitis C virus (HCV) infection.

How the study worked. Researchers invited HIV-positive people 16 through 23 years old to complete a private computer-based survey. Everyone knew they had HIV infection, and everyone spoke English. The computer survey collected basic personal information (like age, sex, and race) and information about sexual behavior, drug use, and feelings about body image. From a standard body image test, the researchers created a score that estimated a person’s overall body image. The computer survey also included a well-known test to assess depression* in study participants.4

The researchers used a standard statistical method to identify factors that predicted risky sexual behavior. This type of analysis pinpoints individual risk factors that affect behavior by themselves, regardless of whatever other risk factors a person has.

What the study found. The study included 143 HIV-positive people with an average age of 20.7 years and an age range from 16 to almost 24 years. Ninety-nine study participants (69%) were men, 82 (57%) became infected with HIV during sex between men, and 136 (95%) were black. The group’s $\text{CD}_4$ count averaged 653 cells/mm$^3$.

People who had a better image of their own body (reflected in a higher overall body image score) had doubled chances of using a condom during their last sex (Figure 1). In other words, a better body image by itself—separately from other risk factors—almost doubled chances of condom use. Compared with people who had 1 to 5 sex partners, those with 6 or more sex partners had a 61% lower chance of using a condom the last time they had sex (Figure 1). People who had 6 or more sex partners were about 2.5 times more likely to use drugs or alcohol the last time they had sex.

A separate statistical analysis identified four individual factors that raised chances a young person with HIV would tell a sex partner they had HIV: Believing anti-HIV medicines change the body tripled chances of telling a sex partner about having HIV. Having a high-school degree raised chances more than 8 times. Having an undetectable viral load because of taking anti-HIV medicines raised chance 4.5 times. And having an HIV-related disease in the past raised chances 6 times.

Another analysis pinpointed four individual factors that raised or lowered chances of having 6 or more sex partners. Being overweight lowered chances of having six or more sex partners about 80%. Being obese lowered chances 60%. (See Note 5 in the References below for definitions of overweight and obesity.) People who told their sex partner they had HIV had more than a 3 times higher chance of having six or more sex partners. And using alcohol or drugs during sex more than doubled chances of having six or more sex partners.

What the findings mean for you. This careful study produced the first good evidence showing how a young HIV-positive person’s feelings about their own body

*Words in **bold** are defined in the Technical Word List at the end of this issue of HIV Treatment Alerts.
In a study of young people with HIV, those with a better body self-image had almost a doubled chance of using a condom the last time they had sex.

**Figure 1.** HIV-positive teens and young adults with a better body self-image had a 1.93 times higher chance (almost a doubled chance) of using a condom the last time they had sex. In contrast, young people with six or more sex partners had a 61% lower chance of using a condom the last time they had sex. People with six or more sex partners had a 2.49 times higher chance of using drugs or alcohol the last time they had sex.

Affect their sexual behavior. People with a better image of their own body were almost twice as likely to use a condom the last time they had sex. On the other hand, young people who were actually overweight or obese were less likely to have six or more sex partners.

The finding linking better body self-image to condom use reflects results of a multistudy analysis of adults with HIV. This analysis found that people who feel bad about their own body tend to see little value in using condoms. Thus the new study of young people and the recent analysis of several studies see links between good body image and likely condom use.

The researchers suggested that young people satisfied with their own body are more likely to protect their body, for example, by using a condom. Limiting your number of sex partners and always using a condom—even with steady sex partners—are good ways to protect yourself and your sex partners from exchanging sexually transmitted diseases, including HIV infection.

A person forms an image of their own body through a complex process that involves many factors, including (1) actual body shape (like being heavy or thin), (2) a person’s mental health and overall feelings about themselves, and (3) opinions held by the social group to which a person belongs.

Young people unhappy about how their body looks can do things to change that feeling. First, they can take steps to change how their body actually looks through exercise and diet. Both resistance training and aerobic exercise improve muscle tone and promote weight loss. Resistance training involves lifting weights or using weight machines. Aerobic exercise includes running, playing basketball, or doing any exercise that raises the heart rate for a sustained period. Your HIV provider can help you find an exercise that suits you and will help change your body. Don’t begin any strenuous exercise program without getting your provider’s advice.

The aidsmap site has good online guides to exercise and diet for people with HIV.
Second, exercise is especially helpful in changing body shape if accompanied by a good diet. Again, your HIV provider is a good place to start in planning a healthy diet. A good diet includes protein from fish, meat, nuts, and dairy products and carbohydrates from vegetables and fruits. A large US study identified seven diet factors often linked to poor heart health:

**Too much**
- Salt
- Processed meats
- Sugary drinks

**Too little**
- Nuts and seeds
- Fish oil
- Vegetables
- Fruits

Finally, a person’s image of their own body is part of their overall mood. People with depression—feeling sad or hopeless much of the time—may be more likely than others to have a poor body self-image. Depression is a disease that responds to treatment with antidepressant drugs, to counseling, or to both. If you struggle with sad and hopeless feelings, talk to your HIV provider, who can determine if you have depression and what treatment will help.

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**References**

5. Normal weight, overweight, and obesity are determined by body mass index, which figures weight as kilograms per meters in height squared (kg/m²). Overweight means having a body mass index between 25 and 29.9 kg/m². Obesity means having a body mass index of 30 kg/m² or more. Normal weight is a body mass index of 18.5 to 24.9 kg/m². Underweight is a body mass index below 18.5 kg/m². Go to [https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm](https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm) to calculate your body mass index by using pounds for weight and inches for height.
Antiretrovirals are drugs used to treat HIV infection.

Antiretroviral therapy (often abbreviated ART) usually means treatment with three or more antiretrovirals.

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

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.

Cognitive impairment involves problems in memory, language, thinking, or judgment.

Depression is “a persistent sad, anxious, or ‘empty’ mood,” according to the National Institute of Mental Health.

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.

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 can differ 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.

Osteoporosis is “a condition characterized by progressive loss of bone density, thinning of bone tissue and increased vulnerability to fractures,” according to the National Institutes of Health.

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 each year.

A stroke occurs when blood stops flowing to part of the brain.

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