

Every 5 pounds of weight gained in the first year of **antiretroviral therapy\*** raised diabetes risk 14% in HIV-positive veterans.<sup>1</sup> In contrast, 5 pounds of weight gained in a year raised diabetes risk only 8% in HIV-negative veterans.

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

The study described on pages 37-40 of this issue of *HIV Treatment Reports* found that HIV-positive people continue gaining fat for 7 or more years after starting antiretroviral therapy.<sup>2</sup> But little is known about the health consequences of weight gain after starting antiretrovirals. Researchers working with a US veterans group conducted this study to see how weight gain affects diabetes risk in veterans with and without HIV infection.

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

This analysis included veterans who entered the VACS group between January 1999 and September 2011. Everyone had at least two body mass index measures in the first 18 months they were in the study. For HIV-positive veterans, the study period began when they

first started **antiretroviral therapy**. For HIV-negative veterans, the study period began the first time they first had their body mass index measured. For people with HIV, researchers recorded the body mass index closest to the day they started antiretroviral therapy and closest to a date 1 year later. The main analysis did not include veterans who already had diabetes on their first study date and did not include pregnant women.

The researchers used veterans' medical records to calculate weight gains or losses more than 5 pounds over a 1-year period. They determined how many veterans with or without HIV had newly identified diabetes during the study period.<sup>4</sup> The research team checked veterans' records for up to 5 years, through September 2012. The main study result was new diabetes in HIV-positive and HIV-negative veterans according to weight change category (summarized in reference 5).

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

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

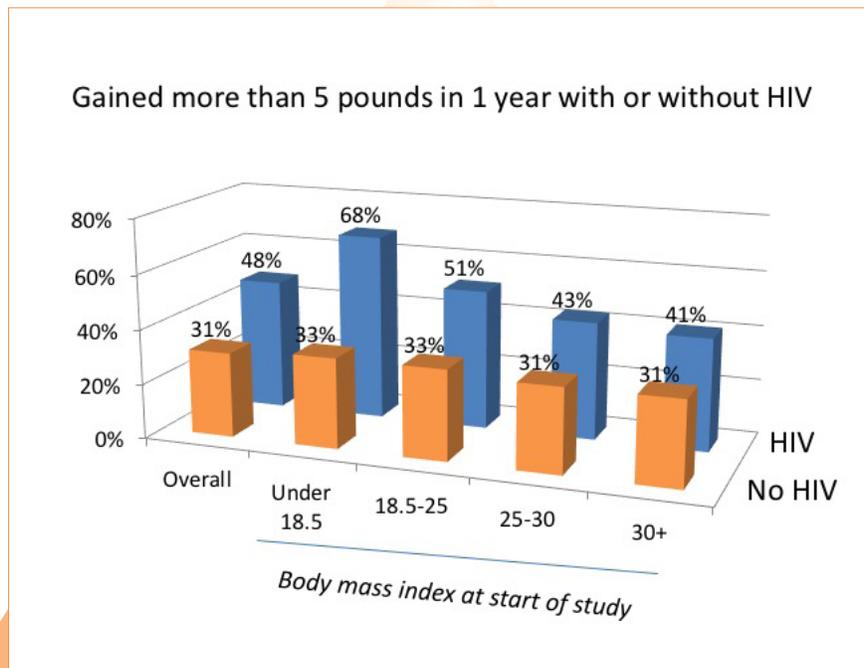
\*Words in **bold** are defined in the Technical Word List at the end of this issue of *HIV Treatment Alerts*.

the study, the HIV group included a higher proportion of normal-weight people (50% versus 22%) and a lower proportion of obese people (14% versus 39%).

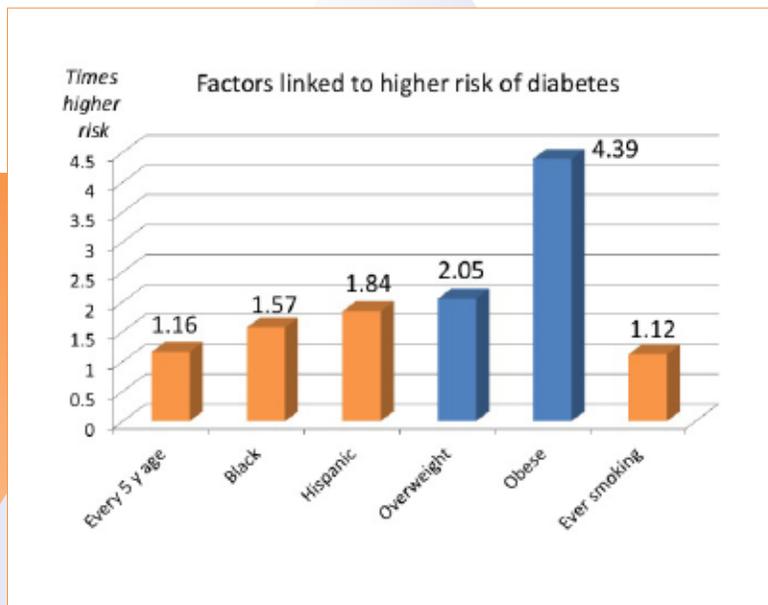
Almost half of veterans with HIV (48%) gained more than 5 pounds during their first year of antiretroviral therapy, compared with 31% of HIV-negative veterans who gained more than 5 pounds in 1 year (**Figure 1**). In the HIV group, two thirds who started the study underweight gained weight in the 12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

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

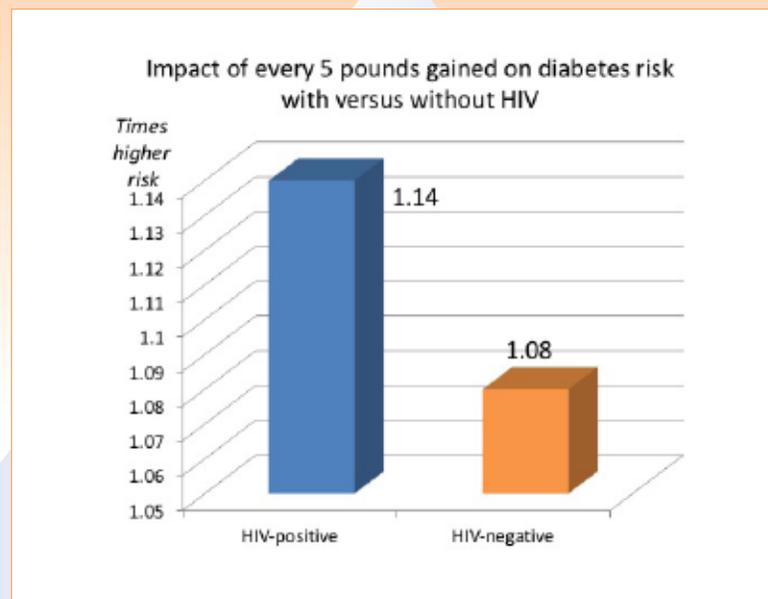
Statistical analysis in the combined group of veterans with or without HIV identified several factors that independently increased the risk of diabetes (that is, these factors increased diabetes risk regardless of whatever other risk factors a person had) (**Figure 2**): (1) older age, (2) being black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



**Figure 1.** In a study of almost 32,000 US veterans, higher proportions of those with HIV than without HIV gained more than 5 pounds in 1 year. This was true in every group according to body mass index at the start of the study: under 18.5 (underweight), 18.5 to 25 (normal weight), 25 to 30 (overweight), and 30 or more (obese).



**Figure 2.** Several individual factors raised the risk of diabetes regardless of whatever other risk factors a person had, including the six factors listed above in this figure plus every 5 pounds of weight gained (**Figure 3**). Among both HIV-positive and HIV-negative veterans, being overweight doubled the risk of diabetes and being obese raised the risk more than 4 times.



**Figure 3.** Every 5 pounds of weight gained in 1 year raised diabetes risk 1.14 times (14%) in veterans with HIV, compared with 1.08 times (8%) in veterans without HIV.

*When normal-weight or overweight people with HIV gain more weight after starting antiretrovirals, the overall health impact may be negative. For example, overweight people run a higher risk of diabetes, a serious lifelong illness.*

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

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

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

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

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

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



## References

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2. Grant PM, Kitch D, McComsey GA, et al. Long-term body composition changes in antiretroviral-treated HIV-infected individuals. *AIDS*. 2016;30:2805-2813.
3. National Heart, Lung, and Blood Institute. Calculate your body mass index. [http://www.nhlbi.nih.gov/health/educational/lose\\_wt/BMI/bmicalc.htm](http://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm)
4. The researchers defined new diabetes as hemoglobin A1c at or above 6.5%.
5. Weight change categories in the veterans study were (1) lost more than 5 pounds, (2) lost or gained up to 5 pounds, (3) gained more than 5 pound to 10 pounds, (4) gained more than 10 pounds to 15 pounds, (5) gained more than 15 pounds to 20 pounds, (6) gained more than 20 pounds to 30 pounds, and (7) gained more than 30 pounds.
6. Aberg JA, Gallant JE, Ghanem KG, Emmanuel P, Zingman BS, Horberg MA; Infectious Diseases Society of America. Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. 2014;58:e1-34.