For Most, Starting HIV Treatment Is Associated With Weight Gain

Newer drug classes are tied to a higher risk of weight gain, which is more likely to occur among Black women in particular.

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People typically gain weight after starting antiretroviral (ARV) treatment for HIV, and not necessarily because of what is known as the return-to-health effect, in which people put on weight because of the resolution of disease.

A new pooled analysis of eight randomized controlled clinical trials of people starting HIV treatment for the first time found that newer ARV classes were associated with greater weight gain and that certain demographics of individuals, Black women in particular, are more susceptible to such increases in weight.

The analysis was led by Moupali Das, MD, MPH, of Gilead Sciences, the dominant pharmaceutical player in the ARV market, and published in Clinical Infectious Diseases.

The included studies all had data on a baseline study visit and follow-up visits conducted every 12 weeks through week 96, at which data were collected about body weight, CD4 count and viral load. The 5,680 participants started ARV treatment between 2003 and 2015. They were followed for more than 10,000 cumulative years of follow-up.

The median body mass index (BMI) of the participants when they started ARVs was 24.8. At that time, 16.3% had a BMI of at least 30 (meaning they were obese), 31.4% had a BMI of 25 to 29.9 (overweight) and 52.2% had a BMI of 18.5 to 24.9 (normal weight) or less than 18.5 (underweight).

Participants' baseline weight and CD4 count were each higher in more recent trials.

All the arms of the studies saw weight gains among the participants, with greater magnitudes of weight gain in the more recent trials. Investigational ARVs were consistently associated with more weight gain than the approved drugs to which they were being compared.

Across all the studies, participants gained a median of 4.4 pounds after 96 weeks of treatment, with the greatest proportion of that weight gain occurring during the first 48 weeks. Through 96 weeks, the proportion of participants experiencing at least a 3%, 5% and 10% increase in weight

was 48.6%, 36.6% and 17.3%, respectively.

Granted, 30.2% of participants lost weight.

Over time, the proportion of participants who fell into the overweight and obese BMI ranges increased.

After adjusting the data to account for various differences between the study participants, the researchers found that baseline CD4 count was the factor most strongly associated with weight gain. Those who had an initial CD4 count below 200 gained an average of 6.5 pounds more after 96 weeks than those with an initial CD4 count of at least 200. There was a close correlation between increases in CD4 count and weight over time while individuals were on ARVs.

Having a baseline viral load above 100,000 was associated with a 2.1-pound greater average weight gain compared with initially having a viral load below that threshold. Those starting with symptomatic HIV or AIDS gained an average of 1.1 more pounds than those with asymptomatic HIV. Those who did not inject drugs gained an average of 3.1 pounds more than those who did. Black individuals gained 2.2 pounds more on average than non-Blacks.

Being female, younger than 50 years old and starting on ARVs with an obese BMI were all associated with smaller yet significantly greater weight gain.

Stratifying their results by both sex and race, the investigators found that Black women had the greatest average weight gain on ARVs, followed by Black men.

Looking at the third ARV in individuals' HIV regimens, whether integrase inhibitors, non-nucleoside reverse transcriptase inhibitors (NNRTIs) or protease inhibitors, the investigators found average weight gains of 7.1 pounds, 4.2 pounds and 3.8 pounds, respectively.

Numerous recent studies have analyzed the association between integrase inhibitors and weight gain.

As for specific types of integrase inhibitors, those taking bictegravir or dolutegravir experienced a similar average weight gain, of 9.3 pounds or 9.0 pounds, respectively, while those taking cobicistat-boosted elvitegravir gained an average of 6.0 pounds.

Bictegravir is included in Biktarvy (bictegravir/tenofovir alafenamide/emtricitabine). Dolutegravir is sold under the individual brand name Tivicay and is included in Dovato (dolutegravir/lamivudine), Juluca (dolutegravir/rilpivirine) and Triumeq (dolutegravir/abacavir/lamivudine). Boosted elvitegravir is included in Genvoya (elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine) and Stribild (elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine).

Among participants taking NNRTI-containing ARV regimens, those taking rilpivirine gained more weight, at an average of 6.6 pounds, than those taking efavirenz, who put on an average of 3.7 pounds.

Rilpivirine is sold under the brand name Edurant and is included in Complera (rilpivirine/tenofovir disoproxil fumarate/emtricitabine), Juluca (dolutegravir/rilpivirine) and Odefsey (emtricitabine/rilpivirine/tenofovir alafenamide). The drug is also included in a long-acting form in the investigational injectable regimen Cabenuva, which also includes cabotegravir, and is dosed every four weeks. This regimen is poised for a decision from the Food and Drug Administration, likely in the coming weeks.

Efavirenz is sold under the brand name Sustiva and is included in Atripla (efavirenz/tenofovir disoproxil fumarate/emtricitabine), Symfi (efavirenz 600 mg/lamivudine/tenofovir disoproxil fumarate) and Symfi Lo (efavirenz 400 mg/lamivudine/tenofovir disoproxil fumarate).

As for those taking specific nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), the average weight gain after 96 weeks was 9.35 pounds for tenofovir alafenamide, 6.8 pounds for abacavir, 6.8 pounds for tenofovir disoproxil fumarate and effectively no gain for zidovudine, or AZT.

Tenofovir alafenamide is sold as a treatment for hepatitis B virus (HBV) under the name Vemlidy and is included in the HIV combination tablets Biktarvy, Genvoya, Odefsey, Symtuza (darunavir/cobicistat/tenofovir alafenamide/emtricitabine) and Descovy (tenofovir alafenamide/emtricitabine). Abacavir's brand name as an individual tablet is Ziagen, and it is included in Triumeq, Epzicom (abacavir/lamivudine) and Trizivir (abacavir/zidovudine/lamivudine). Tenofovir disoproxil fumarate is sold as the brand-name pill Viread and is included in Atripla, Complera, Delstrigo (doravirine/tenofovir disoproxil fumarate/lamivudine), Cimduo (lamivudine/tenofovir disoproxil fumarate) and Truvada (tenofovir disoproxil fumarate/emtricitabine).

Truvada and Descovy are approved for use as pre-exposure prophylaxis (PrEP).

Multiple studies have recently identified tenofovir alafenamide's association with weight gain.

"Our findings raise the possibility that modern [ARV treatment] regimens with improved tolerability and potency may lead to weight gain in some [people with HIV], necessitating increased clinical attention to the maintenance of healthy body weight, lifestyle modification and exercise at [treatment] initiation," the study authors concluded.

To read the study abstract, click here.

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