



# Switching From New to Old Tenofovir May Reverse Weight Gain

Switching from TAF to TDF may help people lose weight, but this must be balanced against the risk of kidney problems and bone loss.

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Prior studies have shown that people living with HIV who start or switch to an antiretroviral regimen containing tenofovir alafenamide (TAF), especially in combination with an integrase inhibitor, are likely to gain weight. Now, new research shows that switching—or switching back—to the older tenofovir disoproxil fumarate (TDF) may help people lose weight.

In recent years, there has been growing concern about [weight gain](#) after starting antiretroviral treatment or switching to a new regimen. Women—Black women in particular—are more prone to putting on pounds.

Weight gain in the context of HIV treatment is not fully understood. Some of the largest increases have been seen in people who start potent integrase inhibitors, such as dolutegravir (sold alone as Tivicay and a component of the Triumeq, Dovato and Juluca single-tablet regimens). TAF, the newer form of tenofovir in Descovy and in single-tablet regimens such as Biktarvy and Symtuza, has been linked to more weight gain than TDF, the older form in Truvada and in combination pills including Atripla, Complera and Delstrigo. (Click here to learn more about [the differences between TAF and TDF](#).)

For example, [in the ADVANCE trial in South Africa](#), which compared three first-line antiretroviral regimens, participants randomly assigned to start on dolutegravir, TAF and emtricitabine gained more weight than those who used dolutegravir, TDF and emtricitabine, who in turn gained more than those who used efavirenz, TDF and emtricitabine. Final results at 192 weeks, presented at last summer's International AIDS Conference, showed that after nearly four years, people in the three treatment groups gained about 19 pounds, 13 pounds and 7 pounds, respectively, with women gaining more than men. All three regimens worked equally well for suppressing HIV.

Among people already on treatment with an undetectable viral load, a study of [nearly 7,000 participants in the U.S. OPERA cohort](#) found that those who switched from TDF to TAF experienced “pronounced weight gain,” especially if they also switched to an integrase inhibitor at the same time. Likewise, an analysis of [more than 700 people who changed regimens in the U.S. HIV Outpatient Study](#) found that those who switched to an integrase inhibitor or TAF saw increases in

their body mass index. As reported at the 2022 Conference on Retroviruses and Opportunistic Infections and in the [Journal of Acquired Immune Deficiency Syndrome](#), weight gain was greatest during the first eight months, mostly associated with integrase inhibitor use, after which there was a more gradual increase, largely attributed to TAF use.

But integrase inhibitors and TAF may not be entirely to blame for added pounds. TDF can lead to reduced cholesterol and triglyceride levels and either a small amount of weight loss or absence of expected weight gain over time. This has been seen in HIV-negative people taking Truvada for pre-exposure prophylaxis (PrEP) as well as HIV-positive people using TDF-containing treatment regimens.

TAF lacks this weight-suppressing effect, so people who switch from TDF to TAF—as is often recommended to avoid the kidney and bone side effects of TDF—may experience rising blood fat levels and weight gain. But weight gain has also been seen in people who switch to a TDF-sparing regimen that does not contain TAF. And some research suggests that other antiretrovirals, including efavirenz, may also inhibit weight gain.

### Switching to TDF

Whatever its cause, unwanted weight gain is not just a cosmetic or self-esteem issue. Excess weight—especially the accumulation of visceral abdominal fat deep within the belly—raises the risk of cardiovascular disease, diabetes, fatty liver disease, several types of cancer and other health problems.

To manage unwanted weight gain, experts recommend lifestyle changes such as eating a healthy plant-based diet, increasing physical activity and getting enough sleep. But many people are unable to lose weight through diet and exercise alone, raising the question of whether switching antiretrovirals might help.

As reported in [Clinical Infectious Diseases](#), Francois Venter, MD, PhD, of the University of the Witwatersrand in Johannesburg, and colleagues analyzed weight and metabolic changes among people in the ADVANCE trial who switched to a new regimen.

As described above, more than 1,000 ADVANCE participants were randomized to start treatment with either dolutegravir, TAF and emtricitabine; dolutegravir, TDF and emtricitabine; or efavirenz, TDF and emtricitabine. After nearly four years on their assigned initial regimen, they switched to dolutegravir, TDF and lamivudine when national treatment guidelines changed.

Venter's team focused on 172 people in Johannesburg who joined a follow-up sub-study dubbed CHARACTERISE. After one year, those who switched from dolutegravir, TAF and emtricitabine or from efavirenz, TDF and emtricitabine to the new regimen saw notable reductions in weight, blood lipids and blood sugar.

Women who switched from dolutegravir, TAF and emtricitabine to dolutegravir, TDF and lamivudine lost a median 3.5 pounds, but the men lost only 0.4 pounds. Among participants who

switched from efavirenz, TDF and emtricitabine to the new regimen, the women lost a median 6.4 pounds, while the men lost a median 5.1 pounds. Among those who switched from dolutegravir, TDF and emtricitabine to dolutegravir, TDF and lamivudine—a very similar regimen—neither the women nor the men saw a significant change in weight.

Participants who switched from dolutegravir, TAF and emtricitabine to dolutegravir, TDF and lamivudine showed significant declines in total cholesterol, low-density lipoprotein (LDL, or bad cholesterol), triglycerides, blood glucose and HbA1C, another measure of blood sugar. Those who switched from efavirenz, TDF and emtricitabine to the new regimen saw significant drops in total cholesterol, LDL, high-density lipoprotein (HDL, or good cholesterol), triglycerides and HbA1C. Finally, people who switched from dolutegravir, TDF and emtricitabine to dolutegravir, TDF and lamivudine saw an increase in total cholesterol but no significant changes in the other measures.

In a related study [reported in the journal AIDS](#), Jussi Sutinen, MD, PhD, of the University of Helsinki, and colleagues looked at the effects of switching from TAF to TDF, while keeping other antiretrovirals and lipid-lowering medications unchanged, in a retrospective chart review that included nearly 300 people with HIV in Finland, most of whom were white men.

Among the 146 people who switched from TAF to TDF, body weight remained stable after two years, while it rose by about 3 pounds on average in a matched group of people who stayed on TAF. Total cholesterol and LDL each declined by about 12% in the switch group after one year. But HDL also decreased, so the total cholesterol-to-HDL ratio—an indicator of cardiovascular risk—did not change. No significant changes were observed in the control group that did not switch. What's more, the atherosclerotic cardiovascular disease risk score decreased slightly in the switch group (from 6.3% to 6.0%) but rose in the control group (from 8.4% to 9.1%).

Taken together, these studies suggest that some people might benefit from switching, or switching back, from TAF to TDF. But the advantages of doing so must be weighed against the risk of impaired kidney function and bone loss due to TDF, side effects that TAF does not share. The findings underscore the importance of individualized treatment that takes into account comorbidities and other factors that could raise the risk of negative outcomes.

Click here for more news about [HIV and weight gain](#).