GLP-1 Meds May Improve Heart, Liver and Gut Health for People With HIV

Weight-loss medications agonists could be a global game changer, but they need to be accessible and affordable.

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Popular GLP-1 weight-loss medications generally work well for people living with HIV, and they may improve heart, liver and gut health and reduce smoking, along with their well-known benefits for obesity and diabetes, according to studies presented at the Conference on Retroviruses and Opportunistic Infections (CROI 2026). However, much remains to be learned about their long-term use in this population.

“With the exception of antiretroviral therapy, I can’t think of another class of medications where there has been so much buzz,” Todd Brown, MD, PhD, of Johns Hopkins Medicine said during his plenary talk entitled GLP-1 Agonists: Are They a Cure for Everything? He concluded that the enthusiasm is warranted, but there are unanswered questions for people with HIV, and “global access will be a major challenge.”

Weight gain and metabolic abnormalities are a growing concern for people with HIV as they age. Glucagon-like peptide-1 (GLP-1) receptor agonists, including semaglutide (Ozempic or Wegovy), mimic a natural hormone that suppresses appetite, regulates insulin and blood sugar and slows emptying of the stomach. Tirzepatide (Mounjaro or Zepbound) targets both GLP-1 and another gut hormone called GIP. Originally developed to treat type 2 diabetes, these drugs are now widely used to manage obesity. They have been shown to reduce the risk of heart and kidney disease and some types of cancer and improve sleep apnea and arthritis pain, and they are currently being studied for fatty liver disease, addiction and other conditions.

Real-World Use

Three studies at CROI looked at real-world use of GLP-1 agonists among people living with HIV.

Lauren O’Connor, PhD, MPH, of George Washington University Milken Institute School of Public Health, and colleagues assessed outcomes among 362 HIV-positive people in the DC Cohort Longitudinal Status Neutral Study who took GLP-1 medications for at least six months. Most had diabetes (82%) or obesity (78%). The most commonly used GLP-1 was semaglutide (50%). The

average time on the drugs was 3.2 years, but 71% had more than a three-month gap in their prescription.

Nearly one in five participants (19%) lost 5% to 10% of their baseline body weight, and 11% lost 10% or more, but that left more than two thirds below the 5% weight-loss threshold. Black people appeared to lose less weight than white people, but the difference was not statistically significant after adjusting for other factors. People with diabetes were less likely to experience at least 10% weight loss than those with obesity alone, which is also the case for HIV-negative people. Age and CD4 T-cell count did not differ across weight-loss categories.

Daniel Lee, MD, of the University of California San Diego, and colleagues looked specifically at use of tirzepatide, which leads to greater weight loss than semaglutide in the general population. In this analysis of 61 people with HIV, the overall mean weight loss was about 14% of baseline body weight at 12 months—slightly less than the 17% loss seen in the population at large. Here, too, people with diabetes lost less weight than those with obesity/overweight alone (22 versus 37 pounds, respectively). Participants also saw significant reductions in hemoglobin A1C (a measure of blood sugar) and blood pressure, improved HDL cholesterol levels and lower 10-year cardiovascular disease risk scores. However, more than a quarter (26%) stopped taking tirzepatide before completing one year, mostly due to either side effects or insurance issues.

Heidi Crane, MD, MPH, of the University of Washington in Seattle, and colleagues compared use of semaglutide versus tirzepatide among people in the Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) cohort, which follows HIV-positive adults receiving care at academic clinics across the United States. Three quarters were men, and the median age was approximately 52 years. About 80% had obesity and half had diabetes. A total of 2,187 people started semaglutide between April 2018 and July 2025, but only 497 started tirzepatide, which was not approved until 2022. Although percentage weight loss was less in this study compared with the previous two, people who used tirzepatide lost more weight and saw more improvement in A1C levels compared with semaglutide recipients.

Specific Conditions

Crane’s team also looked at changes in cigarette smoking among people who received semaglutide in the CNICS cohort. In this analysis, 204 people with HIV reported smoking at the time they initiated semaglutide for diabetes or weight management, with an average of 10.5 cigarettes a day. After starting the drug, smoking fell by 2.7 cigarettes a day—a 26% decrease. “Semaglutide may result in additional benefit to overall health in people with HIV,” the researchers concluded.

In another CNICS analysis, Lara Haidar, PharmD, of the University of Manitoba in Canada, and colleagues assessed the impact of semaglutide on depression in people with HIV. Although some early reports suggested GLP-1 agonists might be associated with an increased risk of suicide, extensive investigations by the Food and Drug Administration found no such link—and in fact, some studies saw a reduced risk. Reassuringly, Haidar’s study, which included 354 HIV-positive

people starting semaglutide, found that the drug was not associated with overall worsening of depressive symptoms among those with absent, mild, moderate or severe depression at baseline.

Looking again at the CNICS cohort, Jimmy Ma, MD, of the University of Washington, and colleagues assessed the association between semaglutide use and liver fibrosis. Metabolic dysfunction-associated steatotic liver disease (MASLD) and its more severe form, metabolic dysfunction-associated steatohepatitis (MASH), are a growing concern for people with HIV. Over time, the buildup of fat in the liver can lead to inflammation, fibrosis (liver scarring), cirrhosis and liver cancer. Based on a study of HIV-negative people, the Food and Drug Administration last year approved Wegovy for the treatment of MASH in people with moderate to advanced fibrosis.

This analysis included 1,850 people with HIV who started semaglutide for diabetes or weight loss and had available data to calculate a FIB-4 liver fibrosis score (age, platelet count and ALT and AST liver enzyme levels). About three quarters were men, the median age was 52 years, most had an undetectable HIV viral load and the mean CD4 count was approximately 800. Based on FIB-4 scores, 74% had absent to mild fibrosis, 23% had moderate fibrosis and 3% had advanced fibrosis.

Semaglutide was associated with reduced FIB-4 fibrosis scores in participants with moderate to advanced liver stiffness, with the greatest improvement seen in those with the worst fibrosis. “Our findings, together with earlier studies, suggest semaglutide could play a role in managing MASLD and liver fibrosis in people with HIV, especially as they age and experience the longer-term impacts of cardiometabolic disease,” the researchers concluded.

While the studies above were observational, Allison Ross Eckard, MD, of the Medical University of South Carolina, and colleagues reported new findings from a randomized controlled trial of semaglutide versus placebo in people with HIV, focusing on subclinical cardiovascular health. This trial enrolled 108 nondiabetic people on stable antiretroviral therapy with viral suppression who had lipohypertrophy, or central fat accumulation. About 60% were men, and the median age was 53 years.

The researchers previously reported that participants assigned to semaglutide showed improvements in weight, total body fat, visceral fat, blood pressure, glucose metabolism and lipid levels compared with placebo recipients at 32 weeks. In the current analysis, they saw “no discernible effects” on markers of subclinical vascular disease (including endothelial function and arterial stiffness) or calcified atherosclerotic plaque. However, they did observe “improvements in overall cardiometabolic health and cardiovascular disease risk,” including a significant decline in C-reactive protein (an inflammation biomarker), a significant decrease in 10-year cardiovascular disease risk scores and a trend toward improved oxygen consumption.

Finally, Miguel Marin, PhD, of the Africa Health Research Institute, and colleagues looked at changes in gut health in a subset of participants in the LIROH (Liraglutide for Obesity in HIV) trial in South Africa. HIV is known to disrupt gut homeostasis and the integrity of the intestinal epithelial lining, contributing to chronic immune activation and inflammation despite viral suppression on antiretroviral therapy. Liraglutide (Victoza or Saxenda) is an older GLP-1 agonist injected once

daily, while semaglutide and tirzepatide are once-weekly injections.

The researchers collected blood samples and intestinal biopsies of colon and duodenal tissue from five trial participants at four time points. As expected, liraglutide led to weight loss and reduced A1C levels. Biopsy samples showed favorable changes in gut T cells and epithelial cells after starting liraglutide, while blood samples showed decreases in various inflammation biomarkers. Based on these findings, the researchers suggested that GLP-1 receptor agonists might be "a potential strategy to mitigate gut pathology in people with HIV."

Hopes and Obstacles

These studies represent just the tip of the iceberg when it comes to research on GLP-1 medications for people living with HIV. At last year's CROI, researchers reported data showing that semaglutide may slow biological aging, improve cognitive function and gut health and reduce alcohol use in people living with HIV.

Reviewing the body of evidence to date, Brown noted that these drugs appear to significantly improve inflammation even before people lose much weight, possibly due to a direct effect on T cells. Their well-known ability to reduce "food noise" could carry over to other cravings and addictions. They are even being explored as longevity drugs.

But outstanding questions remain. People on GLP-1 agonists typically lose lean body mass in addition to fat, but it is not yet clear whether this leads to functional decline due to muscle loss or fractures due to bone loss. Weight loss tends to reverse when the drugs are stopped, and little is known about maintenance strategies, such as lower doses or less frequent dosing. Pivotal clinical trials included few participants over 75, so more research is needed on outcomes as people age. Are the risks and benefits of these meds any different in people with HIV compared to those without HIV? Can the drugs reduce the chronic inflammation and immune activation seen in people with HIV, and if so, how will they impact common comorbid conditions?

Brown noted that it's been estimated that 27% of the global population is eligible for GLP-1 medications and that with universal access, we could reduce global obesity by 20% and save 28 million lives over a five-year period. The World Health Organization recently issued guidelines saying that GLP-1 therapies may be used as treatment for obesity.

"Of course, the challenge is getting these drugs to the people who need them the most," Brown said. "Here we get to the real Achilles' heel of these therapies. I hope that the changing landscape will decrease cost, increase production and improve access to these medications."

Patents for semaglutide are now expiring in several countries, including India and China, paving the way for cheaper generics (though people in the United States will have to wait until 2030). Andrew Hill, PhD, of the University of Liverpool—known for his analyses of how much the cost of HIV and hepatitis C drugs could be brought down—has estimated that injectable semaglutide could be produced for just $3 per month. Brown predicted that the recently approved Wegovy pill and

other forthcoming oral medications, which are easier to produce and distribute, will be a game changer. More than 60 experimental GLP-1 agonists and related drugs are in development for various indications, he noted, which has the potential to increase competition and lower prices.

“So back to our first question. Is our exuberance regarding GLP-1 receptor agonists rational or irrational?” Brown asked. “I’d say it’s rational. This class of medications has really transformed the way that we treat multiple diseases, and we really are just at the beginning of this transformation.”

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