

Semaglutide Reduces Opioid Overdose Risk. It Is Not an OUD Treatment.

Clinical Scenario

A patient with opioid use disorder and obesity, stable on buprenorphine, asks about starting semaglutide. Their PCP suggested it for weight management and they have heard it reduces cravings.

The Pearl

GLP-1 receptor agonists modulate mesolimbic dopamine signaling, the same reward pathway that drives compulsive substance use. **A 2024 analysis of 33,006 patients with type 2 diabetes and opioid use disorder found semaglutide was associated with a 42 to 68% lower risk of opioid overdose compared with other antidiabetic medications.** A March 2026 Washington University study found craving reduction across all major addictive substance categories, including opioids, alcohol, nicotine, and cannabis.

GLP-1 receptor agonists are not FDA-approved for any substance use disorder. Current evidence is primarily observational. Randomized controlled trials in SUD populations are underway.

Why It Matters

- Many OTP patients have metabolic comorbidities and may already be prescribed semaglutide or tirzepatide by their PCP without the OTP being informed.
- A veterans database study found GLP-1 users had a 25% lower risk of new opioid use disorder and 50% lower substance-related mortality compared with patients on other antidiabetic medications.

Bottom Line: Acknowledge the emerging evidence without endorsing off-label use for addiction treatment. For patients who qualify on metabolic grounds, coordinate with the prescribing provider, monitor for changes in craving patterns or MOUD requirements, and document the conversation.

References

1. Taplin DL, et al. Semaglutide and Opioid Overdose Risk in Patients With Type 2 Diabetes and Opioid Use Disorder. *PMC*. 2024. PMID: PMC11425147.
2. Washington University School of Medicine. GLP-1 medications get at the heart of addiction: study. *WashU Medicine News*. March 2026.

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