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GLP-1 Receptor Agonists and Substance Use Disorders: A Public Health Opportunity with Emerging Safety Concerns

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According to the Global Burden of Disease Study (GBD), mental and substance use disorders accounted for approximately 183.9 million disability-adjusted life years (DALYs) worldwide in 2010, representing 7.4% of all global DALYs. Within this group, illicit drug use disorders alone were responsible for an estimated 20 million DALYs [1]. SUDs are also strongly associated with years lived with disability (YLDs): together with mental disorders, they account for approximately 22.9% of all global YLDs [2]. This highlights the chronic and debilitating nature of these conditions, and the considerable strain they place on healthcare systems and social structures. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have significantly improved metabolic outcomes in patients with obesity and type 2 diabetes [3]. Beyond their established role, emerging evidence suggests potential efficacy in addressing substance use disorders (SUDs) and behavioral addictions [4,5]. This intersects critically with public health priorities, given the high global burden of both obesity and SUDs, often co-occurring in vulnerable populations.

Preclinical studies indicate that GLP-1RAs modulate dopaminergic reward pathways, attenuating craving, compulsive use, and withdrawal-related behaviors [6,7]. Observational data further suggest reduced rates of alcohol intoxication and opioid overdose in patients treated with GLP-1RAs [8,9]. These findings offer promising avenues for integrated care strategies targeting metabolic and addictive comorbidities. However, recent population-based studies raise concerns regarding psychiatric safety. GLP-1RA use has been associated with increased risks of depression, anxiety, and suicidal behavior, particularly in patients with rapid weight loss or pre-existing psychological vulnerabilities [10]. While causality remains to be confirmed, such findings necessitate caution in off-label or experimental use. From a public health perspective, the potential expansion of GLP-1RAs to populations with SUDs underscores the need for: (i) targeted pharmacovigilance, (ii) risk-benefit assessments in diverse demographic groups, and (iii) [11] integration of mental health screening into treatment protocols. Furthermore, anecdotal reports and pharmacosurveillance data have noted rising instances of misuse and non-medical use, particularly of semaglutide [12].

In conclusion, while GLP-1RAs represent a novel and potentially transformative tool in managing SUDs and associated comorbidities, robust epidemiological evidence and continuous safety monitoring must guide their implementation. Public health systems should prioritize real-world data collection and long-term outcome evaluation before widespread adoption in this context.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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