GLP-1 RAs for Substance Use Disorder: The Potential and the Challenges

Hari Nugroho[1,3,4]; Retty Dwi Handayani[2,5]; Savitri Yuanita[3,6]; Rina K. Kusumaratna[4]; Dace S. Svikis[1]
1. Humphrey Fellowship Program VCU; 2. Humphrey Fellowship Program Emory University; 3. The National Narcotics Board of Indonesia (BNN)
4. Department of Public Health University of Trisakti; 5. Indonesia Food and Drug Agency (BPOM); 6. Psychiatry Residency Program of Department of Psychiatry-The University of Udayana

Introduction

- Substance Use Disorders (SUDs) represent a significant global health burden. Recently, Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 RAs), initially developed for type 2 diabetes and obesity, have emerged as a potential novel treatment for SUDs.
- Preclinical studies and anecdotal reports suggest they may reduce cravings and consumption of alcohol, nicotine, and other psychoactive substances.

Objective

- This review examines the current evidence, underlying mechanisms, and the considerable challenges facing the repurposing of GLP-1 RAs for SUD treatment, particularly in the context of rising off-label use and illicit online markets.

Methods

- A narrative review was conducted by searching PubMed, Scopus, and Google Scholar for articles published between 2015 and 2025.
- Keywords such as "GLP-1," "semaglutide,“ “exenatide”, "liraglutide, "substance use disorder," "addiction," "alcohol," and "nicotine." Over 25 relevant preclinical and clinical studies were analyzed.
- Additionally, this review incorporates a regulatory analysis of a report from Indonesia's National Agency of Food and Drug Control (BPOM) on the abuse potential of GLP-1 RAs and an observational analysis of their illicit online sale patterns on Indonesian social media and e-commerce platforms.

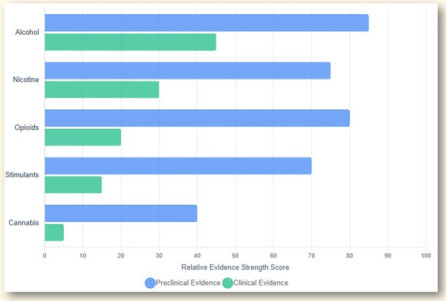
Discussion

- GLP-1 RAs present a mechanistically plausible and promising new avenue for SUD pharmacotherapy.
- However, the current evidence is largely preclinical, and the hype surrounding their weight-loss effects has dangerously outpaced clinical validation for SUDs.
- The analysis of the Indonesian landscape, as highlighted by the BPOM report, reveals a critical public health threat: a burgeoning black market driven by social media.
- This illicit trade not only exposes users to counterfeit products but also circumvents the necessary medical supervision required to manage significant side effects and complex comorbidities, such as diabetes.
- A standardized therapeutic framework for SUDs is completely absent, making unsupervised use particularly hazardous.

Acknowledgements This study was conducted as part of a professional affiliation during the Hubert H. Humphrey Fellowship program, which is funded by the U.S. Department of State and administered by the Institute of International Education (IIE).

References
Guerrero et al. Pharmacoepidemiology 2024, *3*(4), 365-372; doi: 10.3390/pharma3040025
Jerlhag E. Front. Pharmacol. 2023;14:1063033. doi: 10.3389/fphar.2023.1063033
Meneses et al. Int J Mol Sci. 2025 Jun 1;26(11):5338. doi: 10.3390/ijms26115338

Results: The Dual Narrative of Potential and Challenges



Preclinical & Early Clinical Evidence

- Promising reductions in substance intake across various models.
- Data is still limited, but the trend is consistent.

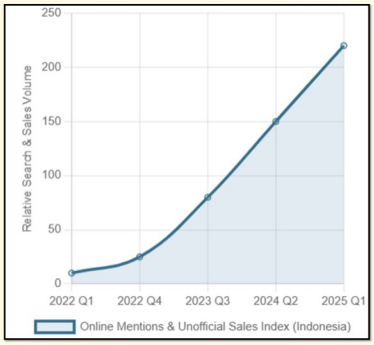
CHALLENGE 1: The Regulatory & Abuse Landscape

BPOM Indonesia: Key Findings

- Sharp increase in non-prescribed use for weight loss, fueled by social media.
- Identified illegal online promotion and sales channels.
- Significant risk of counterfeit or substandard products circulating online.
- Emphasizes that GLP-1 RAs are prescription-only drugs requiring medical supervision.

The Illicit Online Sales Pathway

Social Media Hype & Unverified Claims
↓
Illicit Sales on E-Commerce & Social Platforms
↓
Purchase Without Prescription or Medical Oversight
↓
High Risk of Counterfeit Drugs, Improper Dosing & Unmanaged Side Effects



Platform Type	Number of Accounts/Listings Found
Marketplace (Tokopedia, Shopee, etc.)	19
Social Media (TikTok, Instagram)	3
Website	1

Regarding GLP-1 Receptor Agonists (GLP-1 RA) and their potential for SUD treatment, the discussion on Indonesian social media is not as prevalent or specific compared to its main uses for diabetes and obesity.

CHALLENGE 2: Clinical & Safety Barriers

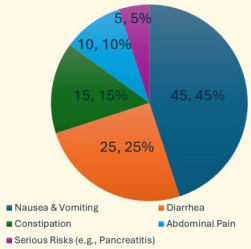
No Standardized Protocols: Optimal dosing, duration, and patient selection for SUDs are unknown.

Comorbidity Risks: Potential for severe hypoglycemia in patients with comorbid diabetes using other glucose-lowering agents.

Psychiatric Effects: Reports of depression and suicidal ideation are under investigation and require careful monitoring.

Long-Term Efficacy: Durability of effect after treatment cessation is not established.

Side Effects (Proportion of Reports [%])



Conclusions

- GLP-1 RAs hold significant potential for treating SUDs, but they are not a "magic bullet" and are far from ready for widespread clinical use for this indication.
- Conduct large-scale, randomized controlled trials (RCTs) to establish efficacy and safety for various SUDs.
- Develop evidence-based clinical guidelines for dosing, monitoring, and patient selection.
- Increase regulatory surveillance and public awareness campaigns to combat illicit online sales and the dangers of self-medication.