



ASAM
ANNUAL CONFERENCE
Innovations in Addiction Medicine and Science
April 24-27, 2025 | Denver, CO

GLP-1 Receptor Agonists and Nicotine: State of the Science and Future Directions



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A decorative background on the left side of the slide. It features a dark blue vertical bar. To its right, a lighter blue area contains various white line-art icons: a heart, a brain, a microscope, and a caduceus. The words 'HEALTHCARE' and 'SCIENCE' are also visible in a stylized font.

Disclosure Information

Luba Yammine, PhD, APRN, FNP-C

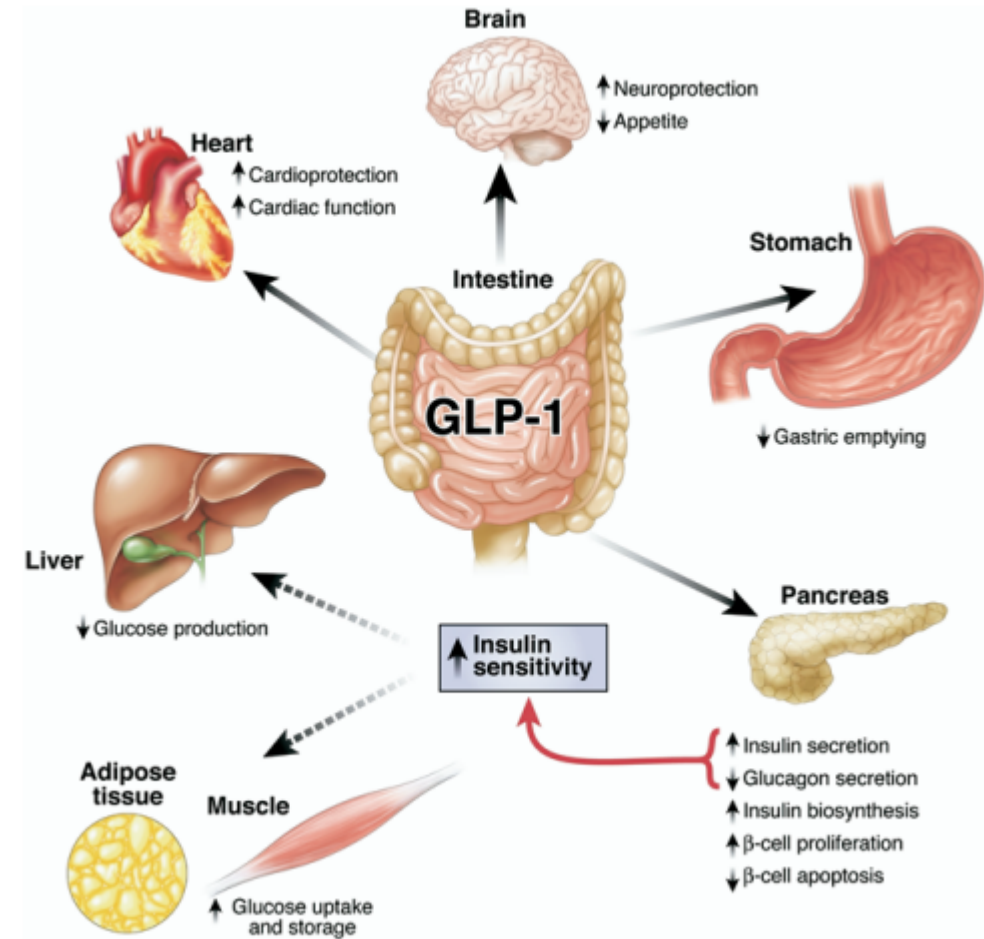
- *Novo Nordisk Inc. – research funding, relationship has not ended.*
- *Eli Lilly – consulting, relationship has not ended.*

Session Outline

- 01 | GLP-1RAs and Nicotine: State of the Science
 - Preclinical research
 - Clinical trials
 - Epidemiological studies
- 02 | GLP-1RAs as a novel approach for smoking cessation and post-cessation weight management.
- 03 | Clinical implications and future directions.

Glucagon-like peptide-1 (GLP-1)

- Incretin hormone and satiation factor with pleiotropic effects
- Produced in intestinal L-cells and hindbrain nucleus tractus solitarius
- Centrally, GLP-1R are expressed in areas associated with hedonic and reward-related behaviors



Preclinical Studies on Nicotine

- GLP-1RA (Ex-4, liraglutide)
 - block expression of conditioned place preference
 - attenuate nicotine-induced locomotor activation, nicotine self-administration, and nicotine-evoked dopamine release in NAc
 - reduce nicotine withdrawal induced hyperphagia and weight gain

Completed Clinical Trials, 1/2

- Exenatide 2mg once weekly adjunct to nicotine patch X 6 weeks (n=84)
 - Abstinence: exenatide 46.3%, placebo 26.8%
 - **Post-cessation body weight: exenatide -0.22 kg, placebo +1.3 kg**
- Dulaglutide 1.5 mg once weekly adjunct to varenicline X 12 weeks (n=255)
 - Abstinence: dulaglutide 63%, placebo 65%
 - **Post-cessation body weight: dulaglutide -1kg [SD=2.7]), placebo +1.9kg [SD=2.4]**
- Semaglutide once weekly X 8 weeks (0.25 mg X 4 weeks, 0.5 mg X 4 weeks)
 - Greater declines in cigarettes per day in the semaglutide group vs. placebo
 - **Change in body weight: semaglutide -5.05%, placebo +0.18%**

Completed Clinical Trials, 2/2

- **NCT05530577:** Semaglutide once weekly up to 1 mg/week X 9 weeks (n=48)
- **NCT03712098:** Daily liraglutide 3 mg/day X 32 weeks (n=40)

Epidemiological Studies

- Analyses of EHR data from patients with type 2 diabetes (T2D):
 - Compared to patients who used other medications for T2D, patients who used GLP-1RA were less likely to receive a diagnosis of nicotine misuse
 - In patients with T2D and comorbid tobacco smoking - compared to patients who used other medications for T2D, GLP-1RA use was associated with less healthcare utilization for tobacco use disorder

Other Evidence

- Analysis of social media posts:
 - 23% of nicotine related comments stated complete cessation of nicotine intake

To: Yammine, Luba <Luba.Yammine@uth.tmc.edu>

Subject: Reg- Los Angeles times report

External: Increase caution when handling links and attachments.

Hello,

My name is Utkarshini Kheror and I read about your research today In Los Angeles times about GLP-1 drugs and their effect on curbing smoking.

I just wanted to state my personal experience. I am a 43 year old female, always been overweight/obese. I started smoking when I was about 24 years old. I did stop for extended periods of time while pregnant and breastfeeding but always resumed.

This is the first time in my life that I have not had any desire to smoke since I quit about 6 months ago. I had started taking semaglutide for weight loss, and it had this unexpected benefit.

I recently stopped semaglutide, and I still don't have any desire to smoke. Let's see how long it lasts.

The reason I am sharing this is that I don't see many people talk about this effect of the drug and hence was excited to read that you are researching on this.

Thanks for your time.

In Summary

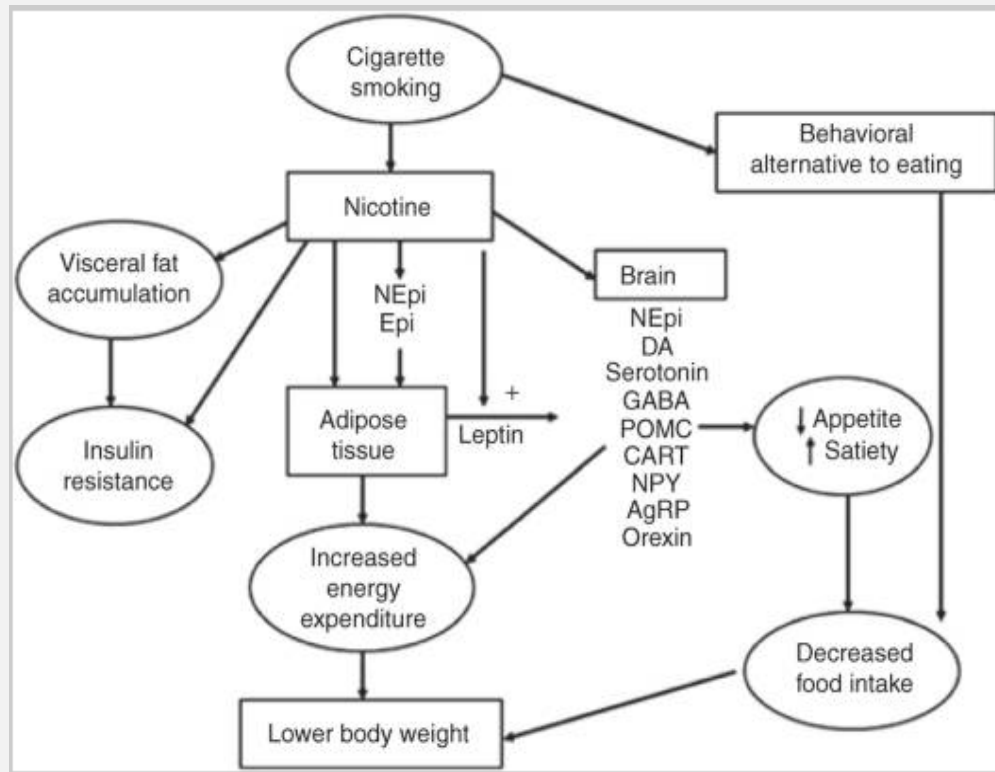
- Promising preclinical and epidemiological data
- Completed RCTs are few: different GLP-1RAs/smoking cessation medications; different study populations
- Consistently positive impact on preventing weight gain in the context of smoking cessation
- Further clinical research is needed



A person is shown from the chest up, holding a lit cigarette in their right hand. The image is heavily stylized with a dark blue overlay and a white vertical bar on the left side. The text is white and positioned to the right of the bar.

GLP-1RAs as a novel approach for
smoking cessation and post-cessation
weight management.

Cigarette Smoking

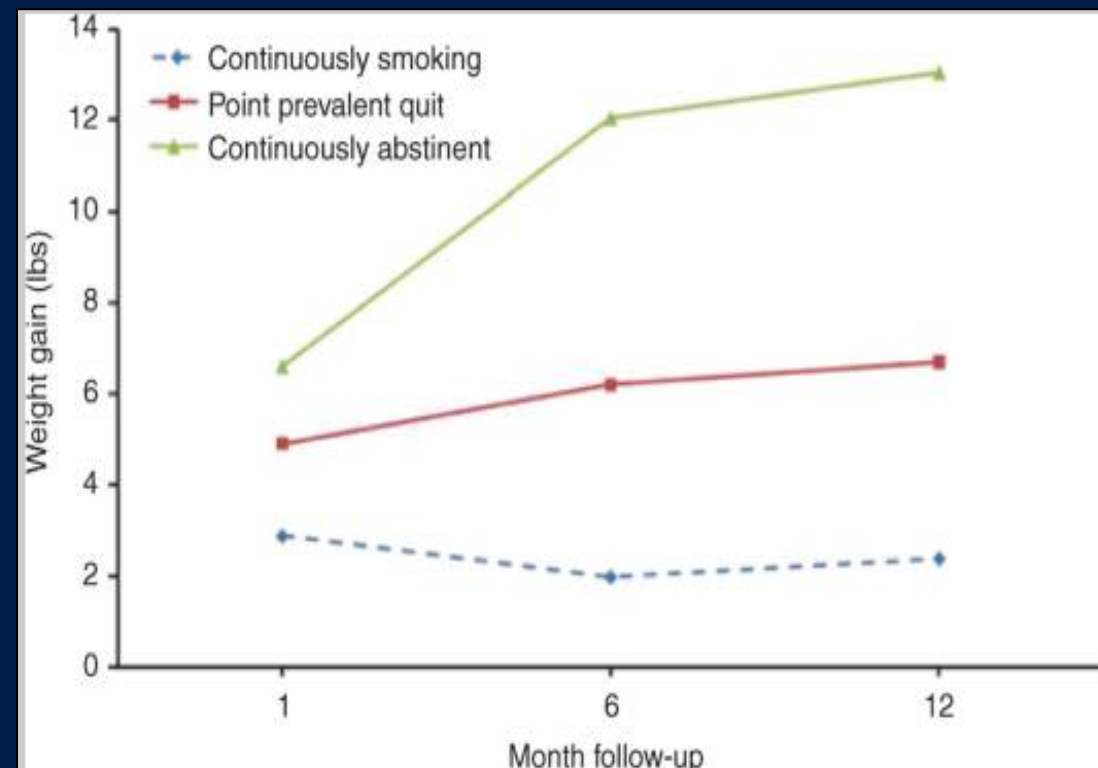


Smoking Cessation

- Removal of nicotine's anorexigenic effects
- Replacement of smoking reward with food reward; increased rewarding value of food
- Decreased energy expenditure

Changes in Weight After Smoking Cessation

- 80-90% of people who quit smoking gain weight
- On average, former smokers gain 5-15 lbs at 12 months
- 13-14% gain over 20 lbs



Ongoing Studies

- **NCT05610800:** A Randomized Controlled Trial of Exenatide as an Adjunct to Nicotine Patch for Smoking Cessation and Prevention of Post-Cessation Weight Gain (R01 DA053241; PI: Yammine, Co-PI: Verrico)
- **NCT06173778:** A Randomized Controlled Trial of Once-Weekly Semaglutide for Limiting Post-Smoking Cessation Weight Gain in Adult Smokers with Overweight/Obesity (Novo Nordisk Investigator Initiated Trial; PI: Yammine, Co-PI: Leidy)



Clinical Implications and Future Directions

- Dosing, treatment duration, sustainability of effects, safety considerations
- Monotherapy vs. adjunct to smoking cessation treatments
- Suitable patient candidates
- Mechanisms



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2. Funding for pilot study of exenatide: UTHealth Center for Clinical and Translational Sciences (CCTS), UTHealth PARTNERS.
3. Funding for exenatide trial: NIH/NIDA R01 DA053241
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5. These sources of support had no role in the study design, collection, management, analysis, and interpretation of the data, the preparation of the materials and/or the ideas presented herein
6. Presenter: Luba.Yammine@uth.tmc.edu

Thank You!

References

1. Baggio LL, Drucker DJ. Biology of Incretins: GLP-1 and GIP. *Gastroenterology* 2007;132:2131-57
2. Audrain-McGovern J, Benowitz NL. Cigarette smoking, nicotine, and body weight. *Clin Pharmacol Ther* 2011;90:164-8.\
3. Egecioglu E, Engel JA, Jerlhag E. The glucagon-like peptide 1 analogue Exendin-4 attenuates the nicotine-induced locomotor stimulation, accumbal dopamine release, conditioned place preference as well as the expression of locomotor sensitization in mice. *PloS one* 2013;8:e77284.
4. Tuesta LM, Chen Z, Duncan A, et al. GLP-1 acts on habenular avoidance circuits to control nicotine intake. *Nature neuroscience* 2017;20:708-16.
5. Herman RJ, Hayes MR, Audrain-McGovern J, Ashare RL, Schmidt HD. Liraglutide attenuates nicotine self-administration as well as nicotine seeking and hyperphagia during withdrawal in male and female rats. *Psychopharmacology* 2023;240:1373-86.
6. Falk S, Petersen J, Svendsen C, et al. GLP-1 and nicotine combination therapy engages hypothalamic and mesolimbic pathways to reverse obesity. *Cell Rep* 2023;42:112466.
7. Yammine L., Green C.E., Kosten T.R., et al. (2021). Exenatide Adjunct to Nicotine Patch Facilitates Smoking Cessation and May Reduce Post-Cessation Weight Gain: a Pilot Randomized Controlled Trial. *Nicotine Tob Res*

References

8. Lengsfeld S, Burkard T, Meienberg A, et al. Effect of dulaglutide in promoting abstinence during smoking cessation: a single-centre, randomized, double-blind, placebo-controlled, parallel group trial. *EClinicalMedicine* 2023;57:101865.
9. Hendershot CS, Bremmer MP, Paladino MB, et al. Once-Weekly Semaglutide in Adults With Alcohol Use Disorder: A Randomized Clinical Trial. *JAMA psychiatry* 2025
10. De Giorgi R, Koychev I, Adler AI, et al. 12-month neurological and psychiatric outcomes of semaglutide use for type 2 diabetes: a propensity-score matched cohort study. *eClinicalMedicine* 2024;74
11. Wang W, Volkow ND, Berger NA, Davis PB, Kaelber DC, Xu R. Association of Semaglutide With Tobacco Use Disorder in Patients With Type 2 Diabetes : Target Trial Emulation Using Real-World Data. *Annals of internal medicine* 2024;177:1016-27.
12. Arillotta D, Floresta G, Papanti Pelletier GD, et al. Exploring the Potential Impact of GLP-1 Receptor Agonists on Substance Use, Compulsive Behavior, and Libido: Insights from Social Media Using a Mixed-Methods Approach. *Brain Sci* 2024;14.
13. Volkow ND, Wang GJ, Fowler JS, Telang F. Overlapping neuronal circuits in addiction and obesity: evidence of systems pathology. *Philosophical transactions of the Royal Society of London Series B, Biological sciences* 2008;363:3191-200.
14. Aubin H-J, Farley A, Lycett D, Lahmek P, Aveyard P. Weight gain in smokers after quitting cigarettes: meta-analysis. *BMJ* 2012;345:e4439-e