GLP-1 RAs: A New Era?

Presentation Subtitle

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MPCA: A Primary Care Approach to Substance Use Disorders

No Disclosures

Agenda

- Physiology basics
- History of GLP-1s
- Primary outcome measures
- Secondary outcome measures
- The relationship between GLP-1s and addiction
- New horizons
- How should your practice change?

History

1990 – Dr. John Eng, endocrinologist, VA, Bronx, NY was identifying

Earlier NIH research → snake/lizard venom → enlarged pancreas

Were these compounds overstimulating the pancreas?

National Institute of Aging. (2012, July 11). Exendin-4: From lizard to laboratory…and beyond. NIH. https://www.nia.nih.gov/news/exendin-4-lizard-laboratory-and-beyond

History

1990 – Dr. John Eng, endocrinologist, VA, Bronx, NY was identifying

Earlier NIH research → snake/lizard venom → enlarged pancreas

- Gila monster (*Heloderma suspectum*)
  - Slow down metabolism
  - Maintain perfect blood sugar
  - Without ill effects
- Assays of gila monster venom → exendin-4
  - Synthesis and release of insulin

National Institute of Aging. (2012, July 11). Exendin-4: From lizard to laboratory…and beyond. NIH. https://www.nia.nih.gov/news/exendin-4-lizard-laboratory-and-beyond

History

1990 – Dr. John Eng, endocrinologist, VA, Bronx, NY

- Exendin-4 was similar in structure and fxn to GLP-1
- GLP-1, pancreatic hormone → insulin production
  - Only when glucose levels are high
  - Remains active for ~2 minutes

Could this be a long-acting, effective treatment for T2DM?

National Institute of Aging. (2012, July 11). Exendin-4: From lizard to laboratory…and beyond. NIH. https://www.nia.nih.gov/news/exendin-4-lizard-laboratory-and-beyond

History

1990s – NIA researcher, Dr. Josephine Egan, began preclinical trials of exendin-4 in cooperation with Amlyn Pharmceuticals

1999 – efficacy of managing blood sugar demonstration in animal studies and protection of insulin producing cells

2005 – FDA approval Exenatide for T2DM

National Institute of Aging. (2012, July 11). Exendin-4: From lizard to laboratory…and beyond. NIH. https://www.nia.nih.gov/news/exendin-4-lizard-laboratory-and-beyond

ELSEVIER

The Lancet

Volume 372, Issue 9645, 4–10 October 2008, Pages 1240-1250

Articles

Exenatide once weekly versus twice daily for the treatment of type 2 diabetes: a randomised, open-label, non-inferiority study

Dr Daniel J Drucker MD [a], John B Buse MD [b], Kristin Taylor PhD [c], David M Kendall MD [c], Michael Trautmann MD [d], Dongliang Zhuang PhD [c], Lisa Porter MD [c], for the DURATION-1 Study Group

Drucker DJ, Buse JB, Taylor K, Kendall DM, Trautmann M, Zhuang D, Porter L; DURATION-1 Study Group. Exenatide once weekly versus twice daily for the treatment of type 2 diabetes: a randomised, open-label, non-inferiority study. Lancet. 2008 Oct 4;372(9645):1240-50. doi: 10.1016/S0140-6736(08)61206-4. Epub 2008 Sep 7. PMID: 18782641.

Primary Outcomes

JAMA | Special Communication | CURRENT TOPICS IN OBESITY

World Health Organization Guideline on the Use and Indications of Glucagon-Like Peptide-1 Therapies for the Treatment of Obesity in Adults

Francesca Celletti, MD, PhD; Jeremy Farrar, MD, PhD; Luz De Regil, PhD

Celletti F, Farrar J, De Regil L. World Health Organization Guideline on the Use and Indications of Glucagon-Like Peptide-1 Therapies for the Treatment of Obesity in Adults. JAMA. 2025 Dec 1. doi: 10.1001/jama.2025.24288. Epub ahead of print. PMID: 41324410.

Primary Outcomes

JAMA Pediatrics

Home | JAMA Pediatrics | Vol. 179, No. 12

Original Investigation

Efficacy and Safety of GLP-1 RAs in Children and Adolescents With Obesity or Type 2 Diabetes

A Systematic Review and Meta-Analysis

Pareeta Kotecha, PharmD, MS[1,2]; Wenxi Huang, MS[1,2]; Ya-Yun Yeh, MS[1,2] ; et al

» Author Affiliations | Article Information

JAMA Pediatr
Published Online: September 15, 2025
2025;179;(12):1308-1317. doi:10.1001/jamapediatrics.2025.3243

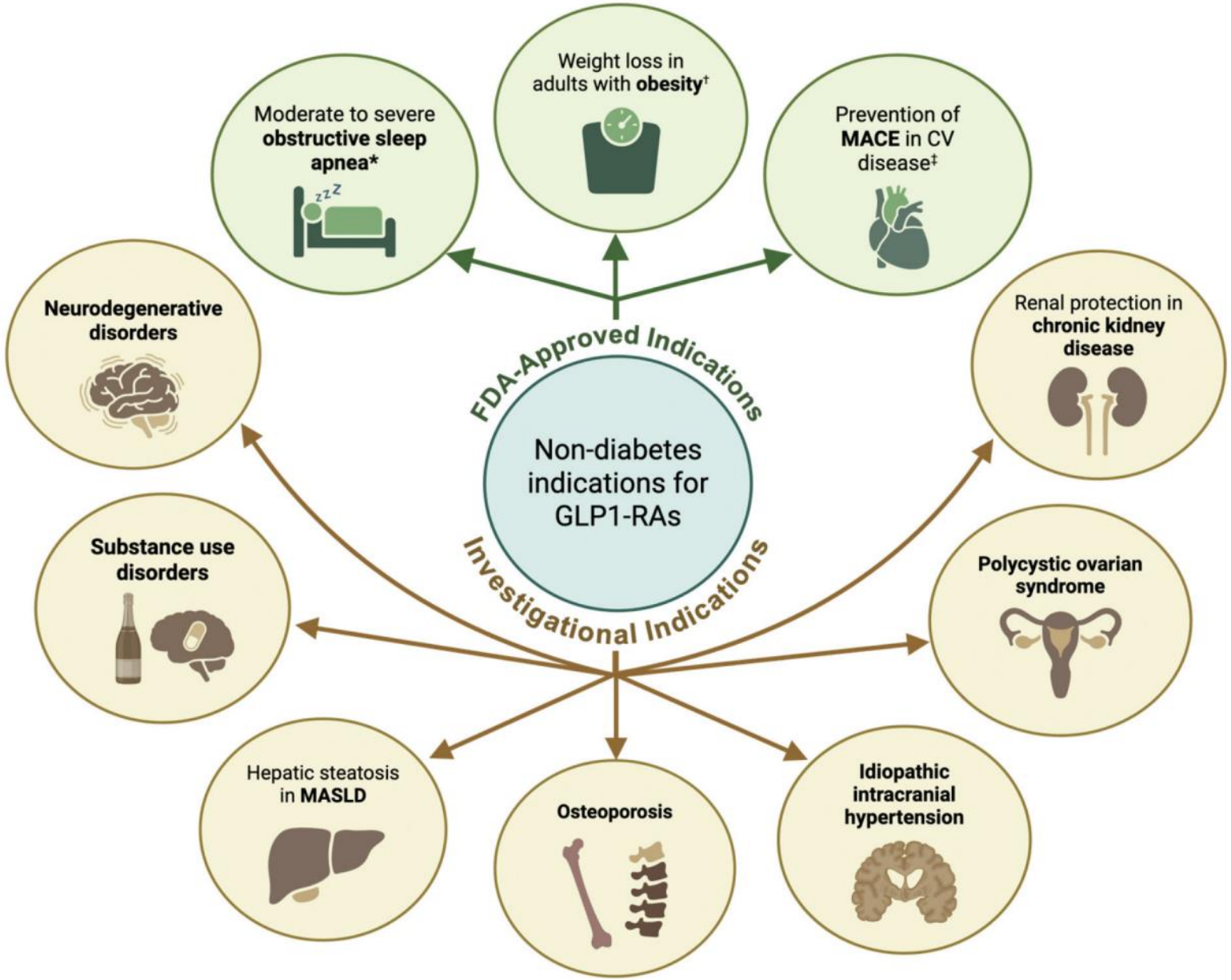
Khor W, Chi K, Lin H, Chang Y. Glucagon-Like Peptide 1 Receptor Agonist Use and Vertebral Fracture Risk in Type 2 Diabetes. JAMA Surg. Published online December 10, 2025. doi:10.1001/jamasurg.2025.5372

Medscape Medical News

Mounjaro Cleared for Type 2 Diabetes in EU Children

The European Medicines Agency has approved Mounjaro for children aged 10 and older with uncontrolled type 2 diabetes, alongside diet and exercise. This extends its use beyond adults, offering a new treatment option for younger patients.

December 12, 2025



Sheth K, Kim S, Porterfield L, Virani SS, Wadhwani S, Vaughan EM. The Expanding Scope of GLP-1 Receptor Agonists: Six Uses Beyond Diabetes. Curr Atheroscler Rep. 2025 Jul 30;27(1):76. doi: 10.1007/s11883-025-01319-6. PMID: 40736924; PMCID: PMC12590185.

Secondary Outcomes

JAMA Surgery

Research Letter

Glucagon-Like Peptide 1 Receptor Agonist Use and Vertebral Fracture Risk in Type 2 Diabetes

Wei-Thing Khor, MD[1]; Kuan-Yu Chi, MD[2]; Hong-Min Lin, MD[3] ; et al

» Author Affiliations | Article Information

JAMA Surg
Published Online: December 10, 2025
doi: 10.1001/jamasurg.2025.5372

Khor W, Chi K, Lin H, Chang Y. Glucagon-Like Peptide 1 Receptor Agonist Use and Vertebral Fracture Risk in Type 2 Diabetes. JAMA Surg. Published online December 10, 2025. doi:10.1001/jamasurg.2025.5372

Secondary Outcomes

JAMA Ophthalmology

Home | JAMA Ophthalmology | Vol. 143, No. 12

Original Investigation

Glucagon-Like Peptide-1 Receptor Agonists and Age-Related Macular Degeneration

Abhimanyu S. Ahuja, MD[1]; Alfredo A. Paredes III, BS[2]; Benjamin K. Young, MD, MS[1]

JAMA Ophthalmol
Published Online: October 23, 2025
2025;143;(12):999-1003. doi:10.1001/jamaophthalmol.2025.3821

Ahuja AS, Paredes AA, Young BK. Glucagon-Like Peptide-1 Receptor Agonists and Age-Related Macular Degeneration. JAMA Ophthalmol. 2025;143(12):999–1003. doi:10.1001/jamaophthalmol.2025.3821

Neuropeptides 94 (2022) 102250

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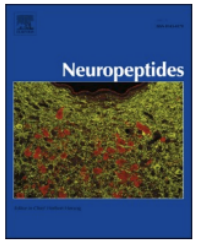
journal homepage: www.elsevier.com/locate/npep



News and Reviews

Neuroprotective effects of glucagon-like peptide-1 (GLP-1) analogues in epilepsy and associated comorbidities

Mohammad Amin Manavi

Department of Pharmacology and Toxicology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Keywords:
GLP-1
Liraglutide
Epilepsy
Seizure
Diabetes
Anti-seizure medication

ABSTRACT

Epilepsy is a common neurological condition induced by losing equilibrium of different pathway as well as neurotransmitters that affects over 50 million people globally. Furthermore, long-term administration of anti-seizure medications has been associated with psychological adverse effects. Also, epilepsy has been related to an increased prevalence of obesity and called type 2 diabetes mellitus. On the other hand, GLP-1 receptors are located throughout the brain, including the hippocampus, which have been associated to majority of neurological conditions, such as epilepsy and psychiatric disorders. Moreover, the impact of different GLP-1 analogues on diverse neurotransmitter systems and associated cellular and molecular pathways as a potential therapeutic target for epilepsy and associated comorbidities has piqued curiosity. In this regard, the anticonvulsant effects of GLP-1 analogues have been investigated in various animal models and promising results such as anticonvulsants as well as cognitive improvements have been observed. For instance, GLP-1 analogues like liraglutide in addition to their possible anticonvulsant benefits, could be utilized to alleviate mental cognitive problems caused by both epilepsy and anti-seizure medication side effects. In this review and growing protective function of GLP-1 in epilepsy induced by disturbed neurotransmitter pathways and the probable mechanisms of action of GLP-1 analogues as well as the GLP-1 receptor in these effects have been discussed.

Mohammad Amin Manavi, Neuroprotective effects of glucagon-like peptide-1 (GLP-1) analogues in epilepsy and associated comorbidities, Neuropeptides, Volume 94, 2022, 102250, ISSN 0143-4179, https://doi.org/10.1016/j.npep.2022.102250.

JAMA Cardiology

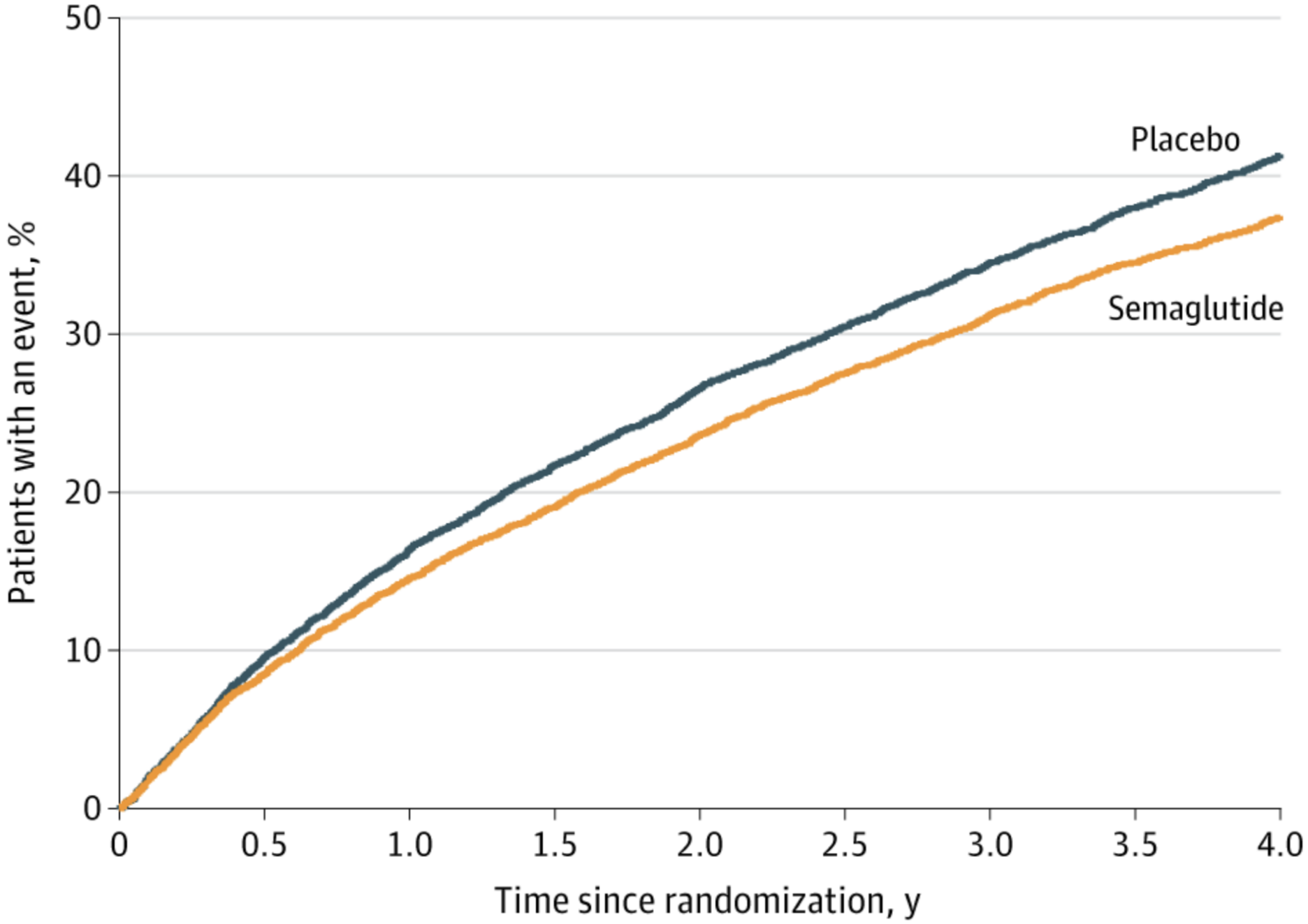
Original Investigation

Semaglutide and Hospitalizations in Patients With Obesity and Established Cardiovascular Disease

An Exploratory Analysis of the SELECT Randomized Clinical Trial

Stephen J. Nicholls, MD[1]; Donna H. Ryan, MD[2]; John Deanfield, MD[3] ; et al

Nicholls SJ, Ryan DH, Deanfield J, Ferreira D, Lang CC, Lincoff AM, Lingvay I, Lübker C, Terns PP, Rasmussen S, Stensen S, Weeke PE, Kahn SE; SELECT Trial Investigators. Semaglutide and Hospitalizations in Patients With Obesity and Established Cardiovascular Disease: An Exploratory Analysis of the SELECT Randomized Clinical Trial. JAMA Cardiol. 2025 Dec 23:e254824. doi: 10.1001/jamacardio.2025.4824. Epub ahead of print. PMID: 41433034; PMCID: PMC12728728.



Nicholls SJ, Ryan DH, Deanfield J, Ferreira D, Lang CC, Lincoff AM, Lingvay I, Lübker C, Terns PP, Rasmussen S, Stensen S, Weeke PE, Kahn SE; SELECT Trial Investigators. Semaglutide and Hospitalizations in Patients With Obesity and Established Cardiovascular Disease: An Exploratory Analysis of the SELECT Randomized Clinical Trial. JAMA Cardiol. 2025 Dec 23:e254824. doi: 10.1001/jamacardio.2025.4824. Epub ahead of print. PMID: 41433034; PMCID: PMC12728728.

Secondary Outcomes

Cardiovascular Protection

- ↓ MACE in pt w ↑ BMI, no DMII[1]
- ↓ CV events and mortality in pts with DMII[2.]
- Benefits to CV, renal and mortality outcomes with DMII[3]
- ↑ outcomes in atherosclerotic CV in person w DMII[4]

Secondary Outcomes

Renal Protection

- ↑ in clinically important kidney outcomes and death in persons with CKD and DMII[5]

Heart Failure

- HFpEF and ↑BMI → ↑physical limitations, exercise fxn, ↓wt[6]
- HFpEF, ↓ HF-related hospitalization and all-cause mortality[7]

Secondary Outcomes

Obstructive Sleep Apnea

- Mod to severe OSA/↑BMI → ↓ AHI, BMI, hypoxic burden, [hsCRP], SBP[8]

Liver Disease

- Improvement in NASH resolution[9]
- Resolution of MASH w/o worsening fibrosis[10]

Secondary Outcomes

Musculoskeletal pain and dysfunction

- ↓ BMI and OA-related knee pain[11]

Neurological conditions

- ↓ dementia and CVA risk[12]
- ↓ progression of motor disability symptoms in Parkinson's[13]

Secondary Outcomes

Malignancies

- ↓ risks of specific types of obesity-associated cancers for pts on GLP-1s versus metformin or insulins in pts with T2DM[14]

Secondary Outcomes

JAMA Psychiatry | Original Investigation

Semaglutide and Early-Stage Metabolic Abnormalities in Individuals With Schizophrenia Spectrum Disorders

A Randomized Clinical Trial

Marie R. Sass, PhD; Mette Kruse Klausen, PhD; Christine R. Schwarz, PhD; Line Rasmussen, MB; Malte E. B. Giver; Malthe Hviid, MD; Christoffer Schilling, MD; Alexandra Zamorski, MD; Andreas Jensen, PhD; Maria Gefke, MD; Heidi Storgaard, PhD; Peter S. Oturai, MD; Andreas Kjaer, DMSci; Bolette Hartmann, PhD; Jens J. Holst, DMSci; Claus T. Ekstrøm, PhD; Maj Vinberg, DMSci; Christoph U. Correll, MD; Tina Vilsbøll, DMSci; Anders Fink-Jensen, DMSci

Sass MR, Klausen MK, Schwarz CR, Rasmussen L, Giver MEB, Hviid M, Schilling C, Zamorski A, Jensen A, Gefke M, Storgaard H, Oturai PS, Kjaer A, Hartmann B, Holst JJ, Ekstrøm CT, Vinberg M, Correll CU, Vilsbøll T, Fink-Jensen A. Semaglutide and Early-Stage Metabolic Abnormalities in Individuals With Schizophrenia Spectrum Disorders: A Randomized Clinical Trial. JAMA Psychiatry. 2025 Dec 3:e253639. doi: 10.1001/jamapsychiatry.2025.3639. Epub ahead of print. PMID: 41335431; PMCID: PMC12676471.

JAMA Psychiatry

RCT: Semaglutide and Early-Stage Metabolic Abnormalities in Individuals With Schizophrenia Spectrum Disorders

POPULATION

25 Men, 48 Women

Adults with schizophrenia spectrum disorders taking clozapine/olanzapine ≤5 y; HbA_{1C} 5.4%-7.4%; no antidiabetic drugs

Mean (range) age, 35 (18-65) y

INTERVENTION

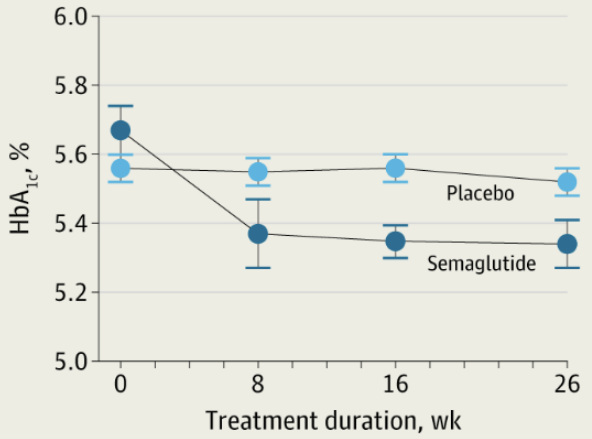
73 Participants randomized

36 Semaglutide, 1 mg, weekly
Adjunct once-weekly subcutaneous semaglutide; dose escalated from 0.25 mg to 1.0 mg by wk 8; maintained 26 wk; 0.5 mg if not tolerated

37 Placebo once weekly
Matching adjunct subcutaneous injection with clozapine/olanzapine for 26 wk

FINDINGS

Semaglutide significantly reduced HbA_{1C} compared to placebo injection



HbA_{1C} change at 26 wk:
Semaglutide group: -0.31%
Placebo group: +0.02%
Between-group change in HbA_{1C}:
-0.25%; 95% CI, -0.33% to -0.16%; *P*<.001

SETTINGS / LOCATIONS

3 Clinical sites in Denmark

PRIMARY OUTCOME

Percentage change in HbA_{1C} from baseline to wk 26

Sass MR, Klausen MK, Schwarz CR, et al. Semaglutide and early-stage metabolic abnormalities in individuals with schizophrenia spectrum disorders: a randomized clinical trial. *JAMA Psychiatry*. Published online December 3, 2025. doi:10.1001/jamapsychiatry.2025.3639

Current FDA Approved Uses

- T2DM
- Weight management
- Cardiovascular risk reduction
- Obstructive sleep apnea

Sheth K, Kim S, Porterfield L, Virani SS, Wadhwani S, Vaughan EM. The Expanding Scope of GLP-1 Receptor Agonists: Six Uses Beyond Diabetes. Curr Atheroscler Rep. 2025 Jul 30;27(1):76. doi: 10.1007/s11883-025-01319-6. PMID: 40736924; PMCID: PMC12590185.

EDITORIAL NEWS TOP HEADLINES SPORTS WEATHER CLASSIFIEDS

TWO CENTS 2¢ EACH

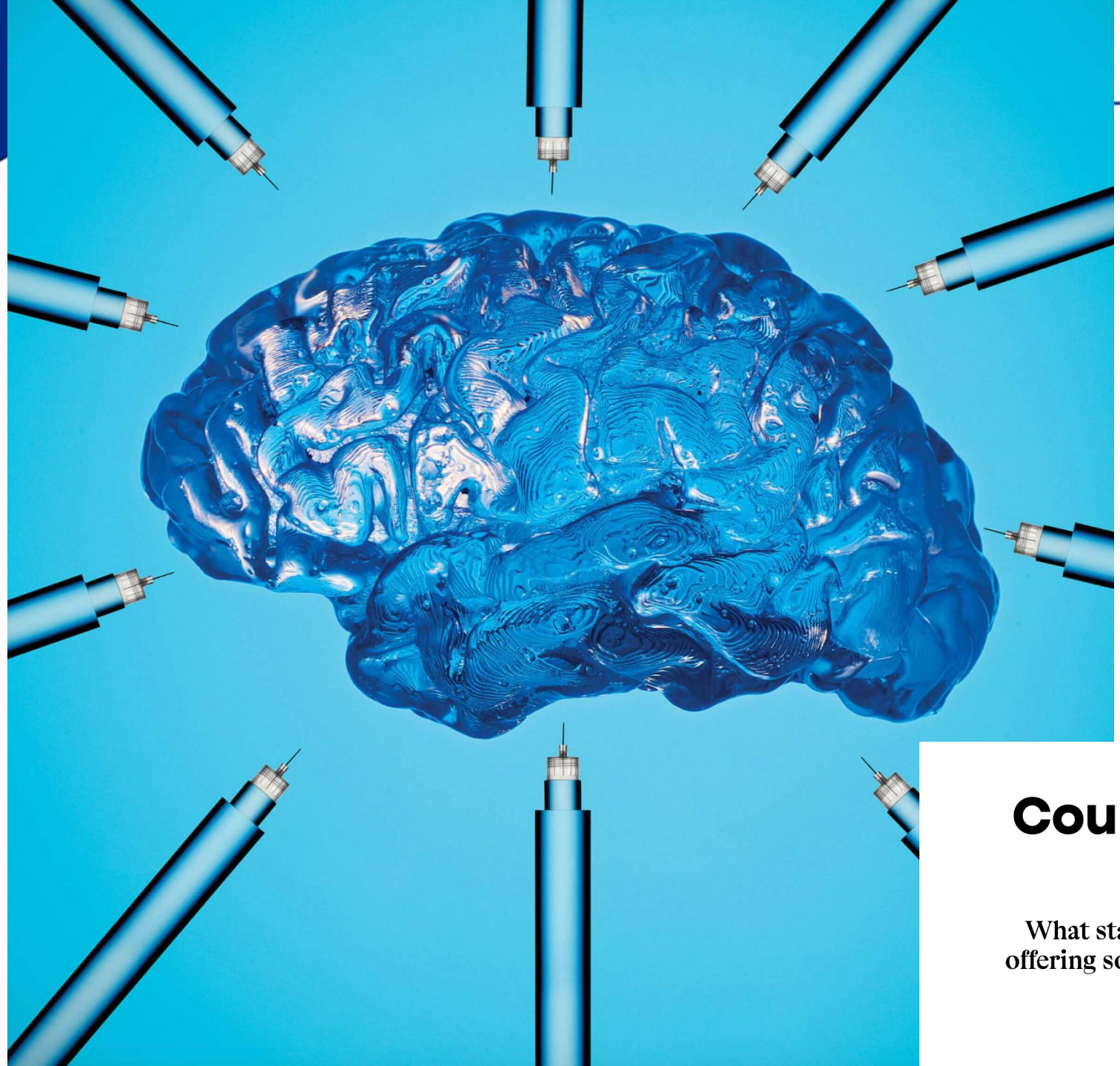
DAILY

THE VINTAGE NEWSPAPER

NO. 11 SATURDAY, OCTOBER 5TH, 1925 TWO CENT EDITION

EXTRA! EXTRA!

READ ALL ABOUT IT



Could GLP-1s Be the Next Big Mental Health Drug?

What started out as a medication for diabetes and weight loss is offering something unexpected—and completely life-changing—for many women.

By **Talia Barrington**
Photographs by **Jarren Vink**

biogirl85 • 15d ago

I still drink but frequently find myself done after 1/2 a drink. Just not as interested.

2 Reply Award Share ...

Future_Researcher_11 • 15d ago

I was on a GLP-1 for 6 months (stopped to get pregnant) and honestly it did kill my desire to drink. I also loved to get drinks and go out but I've essentially been sober since I started my GLP-1.

meljan1977 • 13d ago

I was never a big drinker, but MJ has completely turned me off to alcohol. It's not a bad thing.

1 Reply Award Share ...

https://www.reddit.com/r/PCOS/comments/1pt5w1o/glp1s_and_alcohol/

ShipElectronic2141 • 15d ago

I'm not a drinker, but my GLP-1 has made me a THC lightweight. I have half a gummy and I am as happy and as joyful as can be. Maybe depending on where you are you could do a switch? I switched to THC from alcohol over a year ago and I love it.

5 Reply Award Share ...

wortziks OP • 15d ago

Ugh I wish 😭 Sadly THC gives me bad anxiety

2 Reply Award Share ...

hot4jew • 15d ago

I no longer get tipsy, drunk, or crunk even while drinking ample amounts of alcohol.

Only negative so far on glp lmao. I literally can't get drunk, no matter how much I drink.

1 Reply Award Share ...

https://www.reddit.com/r/PCOS/comments/1pt5w1o/glp1s_and_alcohol/

reddit

Nicotine & Tobacco Research, 2021, 1682–1690
doi:10.1093/ntr/ntab066
Original Investigation
Received August 3, 2020; Editorial Decision April 2, 2021; Accepted April 5, 2021

Original Investigation

Exenatide Adjunct to Nicotine Patch Facilitates Smoking Cessation and May Reduce Post-Cessation Weight Gain: A Pilot Randomized Controlled Trial

Yammine L, Green CE, Kosten TR, de Dios C, Suchting R, Lane SD, Verrico CD, Schmitz JM. Exenatide Adjunct to Nicotine Patch Facilitates Smoking Cessation and May Reduce Post-Cessation Weight Gain: A Pilot Randomized Controlled Trial. Nicotine Tob Res. 2021 Aug 29;23(10):1682-1690. doi: 10.1093/ntr/ntab066. PMID: 33831213; PMCID: PMC8517504.

Exenatide adjunct for smoking cessation

- RCT of 84 pre-diabetic or overweight smokers
- 1:1 once weekly placebo or exenatide, 2 mg SC
- All participants received NRT (21 mg patch) plus smoking cessation counseling
- Primary outcome measures: smoking cessation, craving, nicotine withdrawal symptoms
- Secondary outcome measures: post-cessation wt body weight

Yammine L, Green CE, Kosten TR, de Dios C, Suchting R, Lane SD, Verrico CD, Schmitz JM. Exenatide Adjunct to Nicotine Patch Facilitates Smoking Cessation and May Reduce Post-Cessation Weight Gain: A Pilot Randomized Controlled Trial. Nicotine Tob Res. 2021 Aug 29;23(10):1682-1690. doi: 10.1093/ntr/ntab066. PMID: 33831213; PMCID: PMC8517504.

Exenatide adjunct for smoking cessation

Following 6 weeks of treatment…

Yammine L, Green CE, Kosten TR, de Dios C, Suchting R, Lane SD, Verrico CD, Schmitz JM. Exenatide Adjunct to Nicotine Patch Facilitates Smoking Cessation and May Reduce Post-Cessation Weight Gain: A Pilot Randomized Controlled Trial. Nicotine Tob Res. 2021 Aug 29;23(10):1682-1690. doi: 10.1093/ntr/ntab066. PMID: 33831213; PMCID: PMC8517504.

Exenatide adjunct for smoking cessation

Following 6 weeks of treatment…

Exenatide

↑ risk for smoking abstinence v placebo (46.3% and 26.8%, respectively), (risk ratio [RR] = 1.70; 95% credible interval = [0.96, 3.27]; PP = 96.5%)

↓ cravings in the overall sample and end-of-tx abstainers (as measured by QSU)

Yammine L, Green CE, Kosten TR, de Dios C, Suchting R, Lane SD, Verrico CD, Schmitz JM. Exenatide Adjunct to Nicotine Patch Facilitates Smoking Cessation and May Reduce Post-Cessation Weight Gain: A Pilot Randomized Controlled Trial. Nicotine Tob Res. 2021 Aug 29;23(10):1682-1690. doi: 10.1093/ntr/ntab066. PMID: 33831213; PMCID: PMC8517504.

Exenatide adjunct for smoking cessation

Following 6 weeks of treatment…

Exenatide

↓ withdrawal in abstainers

Post cessation body weight was 5.6 pounds lower (PP = 97.4%)

9.5% of participants reported side-effects v only 2.3% in the placebo group

Yammine L, Green CE, Kosten TR, de Dios C, Suchting R, Lane SD, Verrico CD, Schmitz JM. Exenatide Adjunct to Nicotine Patch Facilitates Smoking Cessation and May Reduce Post-Cessation Weight Gain: A Pilot Randomized Controlled Trial. Nicotine Tob Res. 2021 Aug 29;23(10):1682-1690. doi: 10.1093/ntr/ntab066. PMID: 33831213; PMCID: PMC8517504.

Exenatide adjunct for smoking cessation

Following 6 weeks of treatment…

Exenatide plus NRT confers a greater than 9 in 10 chance of producing abstinence and lower post-cessation weight gain compared to NRT alone.

Yammine L, Green CE, Kosten TR, de Dios C, Suchting R, Lane SD, Verrico CD, Schmitz JM. Exenatide Adjunct to Nicotine Patch Facilitates Smoking Cessation and May Reduce Post-Cessation Weight Gain: A Pilot Randomized Controlled Trial. Nicotine Tob Res. 2021 Aug 29;23(10):1682-1690. doi: 10.1093/ntr/ntab066. PMID: 33831213; PMCID: PMC8517504.

JAMA Psychiatry

Home | JAMA Psychiatry | Vol. 82, No. 4

Original Investigation

Once-Weekly Semaglutide in Adults With Alcohol Use Disorder

A Randomized Clinical Trial

Christian S. Hendershot, PhD[1,2,3]; Michael P. Bremmer, MA[3,4]; Michael B. Paladino, BS[3,4] ; et al

» Author Affiliations | Article Information

Hendershot CS, Bremmer MP, Paladino MB, et al. Once-Weekly Semaglutide in Adults With Alcohol Use Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2025;82(4):395–405. doi:10.1001/jamapsychiatry.2024.4789

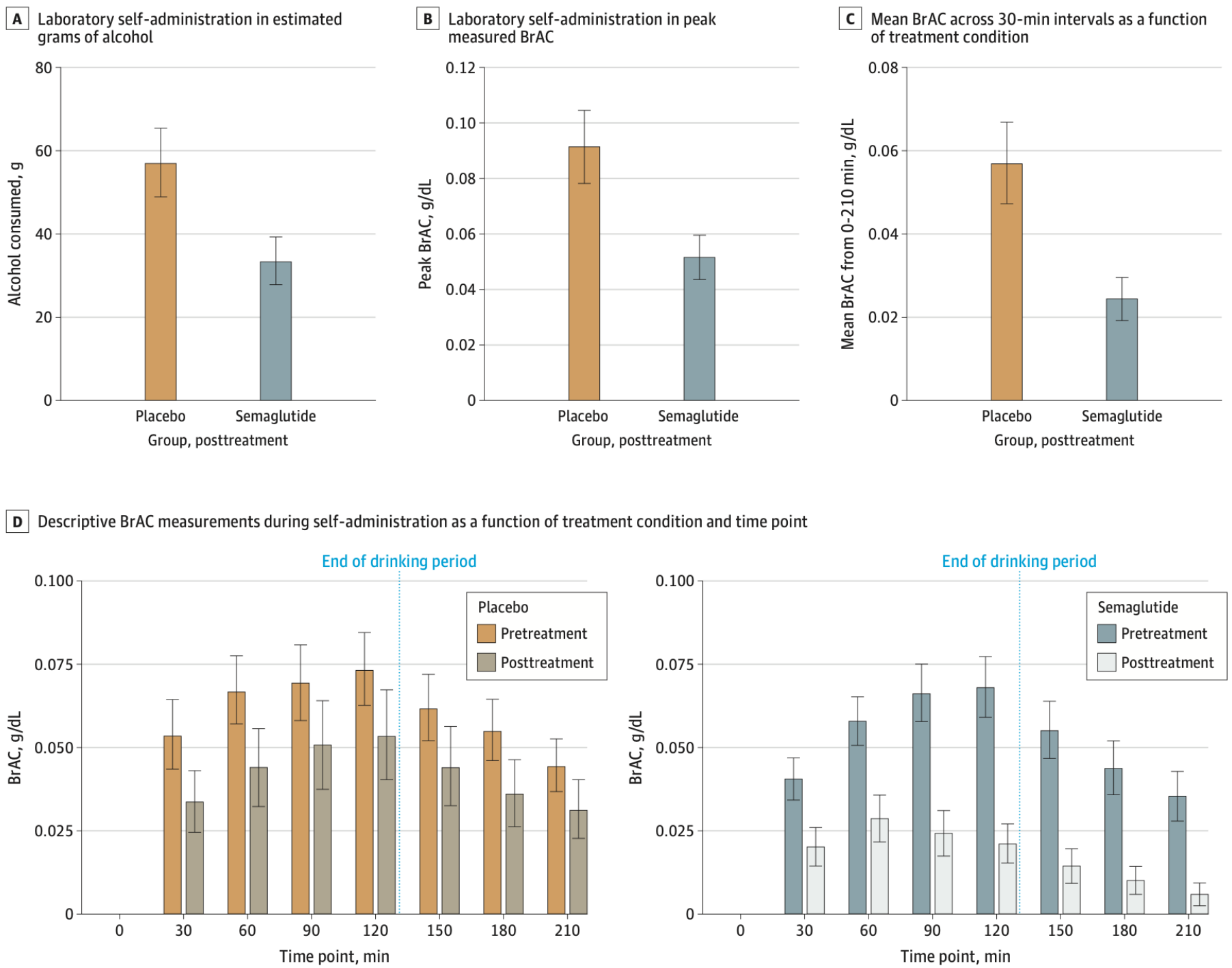
Once-Weekly Semaglutide in Adults With Alcohol Use Disorder

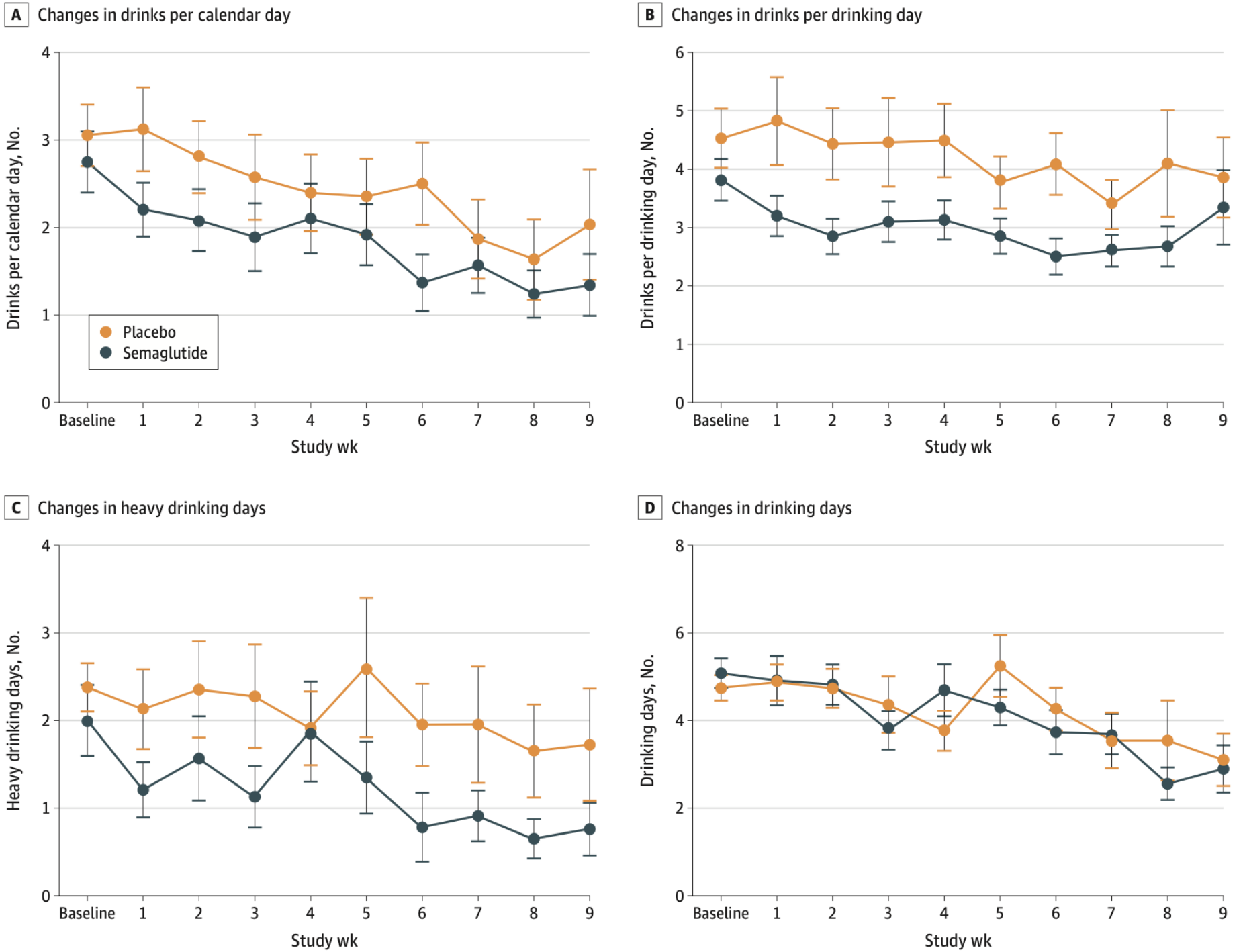
A Randomized Clinical Trial

- Phase 2, double blind, RCT, 9 weeks
- 48 non-tx seeking participants with AUD were randomized
- 0.25 mg/wk of semaglutide x4wks → 0.5 x4 wks → 1.0 mg x1 wk
- Primary: laboratory EtOH self-administration
- Secondary: changes in EtOH consumption and craving

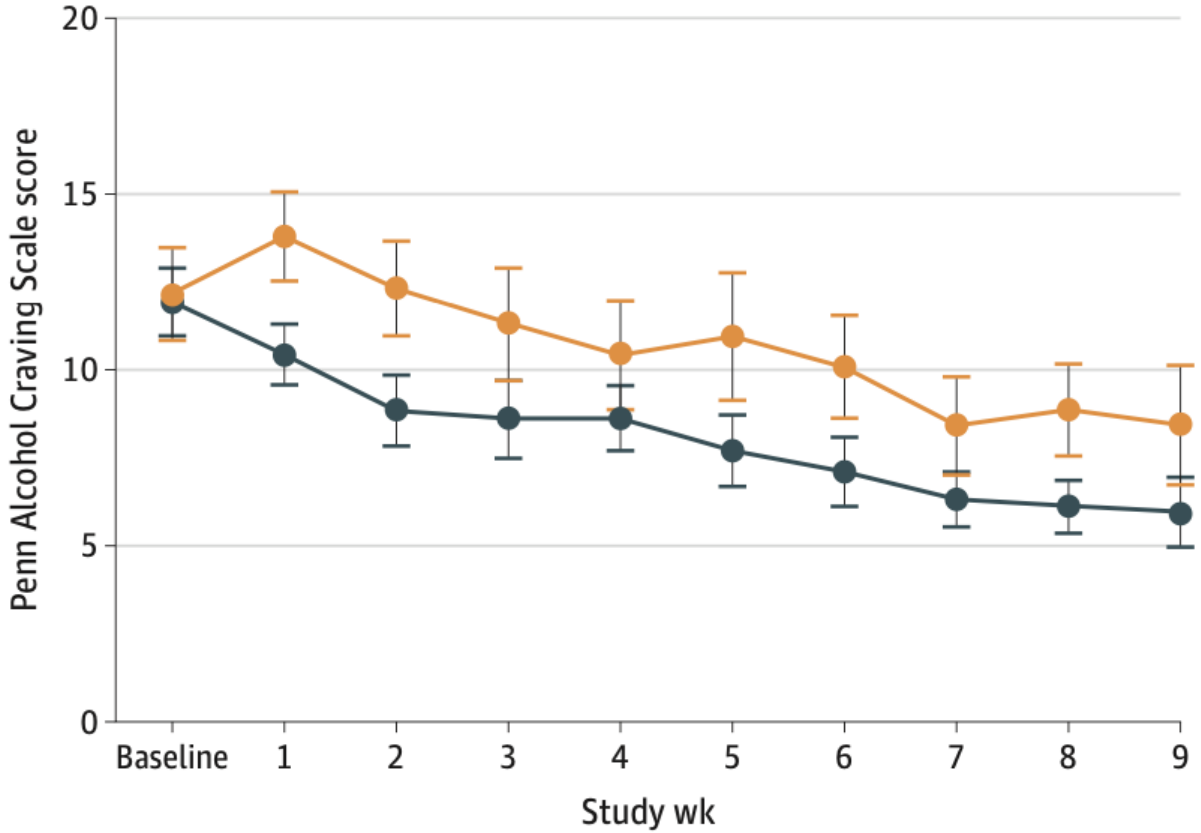
- Lab procedures. . .

Hendershot CS, Bremmer MP, Paladino MB, et al. Once-Weekly Semaglutide in Adults With Alcohol Use Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2025;82(4):395–405. doi:10.1001/jamapsychiatry.2024.4789

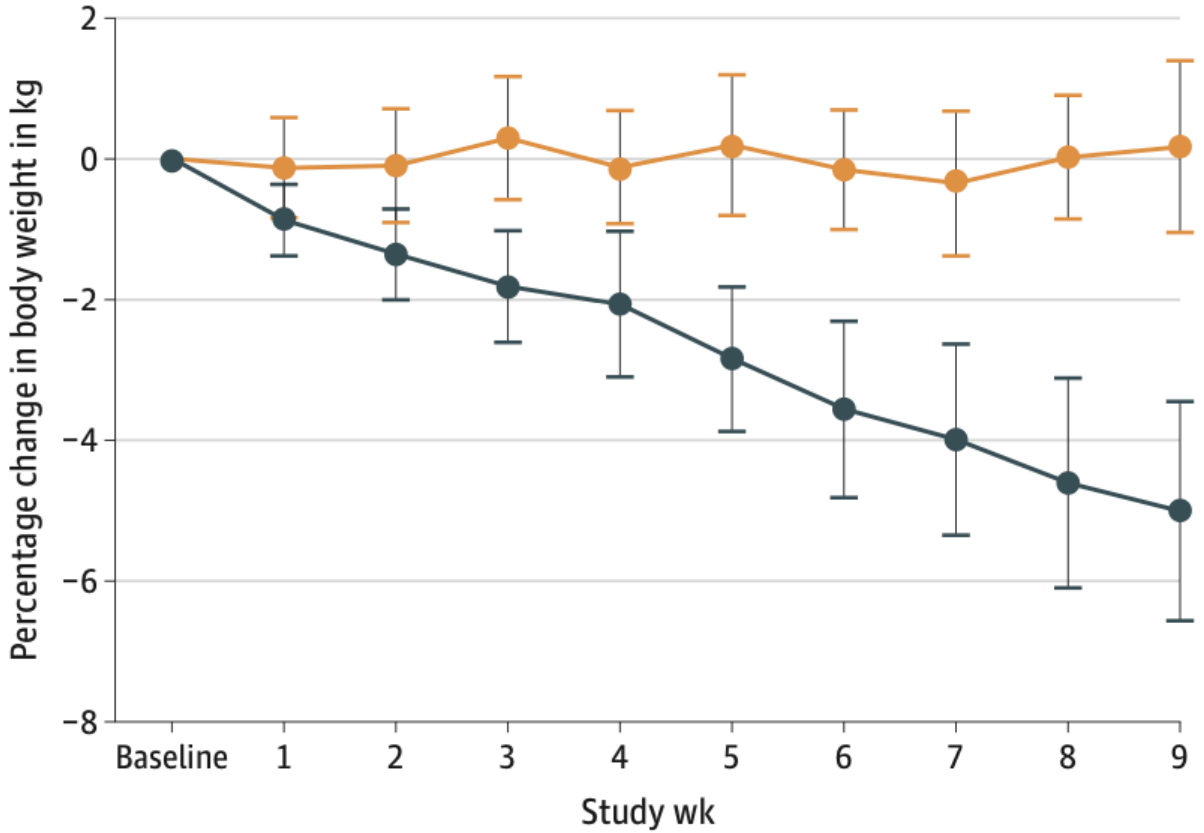

A
Laboratory self-administration in estimated grams of alcohol
Alcohol consumed, g
80
60
40
20
0
Placebo
Semaglutide
Group, posttreatment
B
Laboratory self-administration in peak measured BrAC
Peak BrAC, g/dL
0.12
0.10
0.08
0.06
0.04
0.02
0
Placebo
Semaglutide
Group, posttreatment
C
Mean BrAC across 30-min intervals as a function of treatment condition
Mean BrAC from 0-210 min, g/dL
0.08
0.06
0.04
0.02
0
Placebo
Semaglutide
Group, posttreatment
D
Descriptive BrAC measurements during self-administration as a function of treatment condition and time point
End of drinking period
BrAC, g/dL
0.100
0.075
0.050
0.025
0
Placebo
Pretreatment
Posttreatment
0
30
60
90
120
150
180
210
Time point, min
End of drinking period
BrAC, g/dL
0.100
0.075
0.050
0.025
0
Semaglutide
Pretreatment
Posttreatment
0
30
60
90
120
150
180
210
Time point, min


A
Changes in drinks per calendar day
Drinks per calendar day, No.
Placebo
Semaglutide
Baseline
Study wk
B
Changes in drinks per drinking day
Drinks per drinking day, No.
C
Changes in heavy drinking days
Heavy drinking days, No.
D
Changes in drinking days
Drinking days, No.

E Changes in alcohol craving assessed by the Penn Alcohol Craving Scale



F Change in body weight



Limitations

- Sample size
- Short duration
- Low dose of semaglutide
- AUD, moderate
- >29.4 BMI

Hendershot CS, Bremmer MP, Paladino MB, et al. Once-Weekly Semaglutide in Adults With Alcohol Use Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2025;82(4):395–405. doi:10.1001/jamapsychiatry.2024.4789

JAMA Psychiatry

RCT: Once-Weekly Semaglutide in Adults with Alcohol Use Disorder

POPULATION

14 Men, 34 Women

Non–treatment-seeking adults meeting criteria for alcohol use disorder

Mean (SD) age, 39.9 (10.6) y

SETTINGS / LOCATIONS

1 US academic medical center

INTERVENTION

48 Participants randomized and analyzed

24 Semaglutide
Once-weekly semaglutide

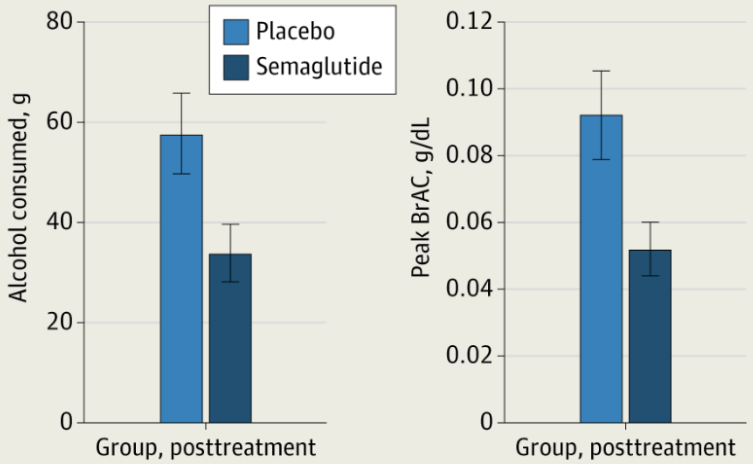
24 Placebo
Placebo injections

PRIMARY OUTCOME

Estimated alcohol consumed over 120 min during laboratory self-administration (estimated alcohol consumed in grams and peak breath alcohol concentration [BrAC] in g/dL)

FINDINGS

Among participants consuming alcohol in a laboratory session following 8 wk of treatment, those in the semaglutide group drank significantly less alcohol than those in the placebo group



Mean (SD) alcohol consumed: Semaglutide: 33.62 (20.72) g; placebo: 57.19 (28.15) g
Mean (SD) peak BrAC: Semaglutide: 0.052 (0.029) g/dL; placebo: 0.092 (0.046) g/dL
Effect sizes: Alcohol consumed: β, −0.48; 95% CI, −0.85 to −0.11; *P* = .01; peak BrAC: β, −0.46; 95% CI, −0.87 to −0.06; *P* = .03

Hendershot CS, Bremmer MP, Paladino MB, et al. Once-weekly semaglutide in adults with alcohol use disorder: a randomized clinical trial. *JAMA Psychiatry*. Published online February 12, 2025. doi:10.1001/jamapsychiatry.2024.4789

Molecular Psychiatry

356

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IMMEDIATE COMMUNICATION OPEN

Check for updates

Association of semaglutide with reduced incidence and relapse of cannabis use disorder in real-world populations: a retrospective cohort study

William Wang[1], Nora D. Volkow[2]✉, Nathan A. Berger[1], Pamela B. Davis[3], David C. Kaelber[4] and Rong Xu[5]✉

JAMA Network | Open

Research Letter | Psychiatry

Semaglutide and Opioid Overdose Risk in Patients With Type 2 Diabetes and Opioid Use Disorder

William Wang; Nora D. Volkow, MD; QuangQiu Wang, MS; Nathan A. Berger, MD; Pamela B. Davis, MD, PhD; David C. Kaelber, MD, PhD, MPH; Rong Xu, PhD

ORIGINAL RESEARCH

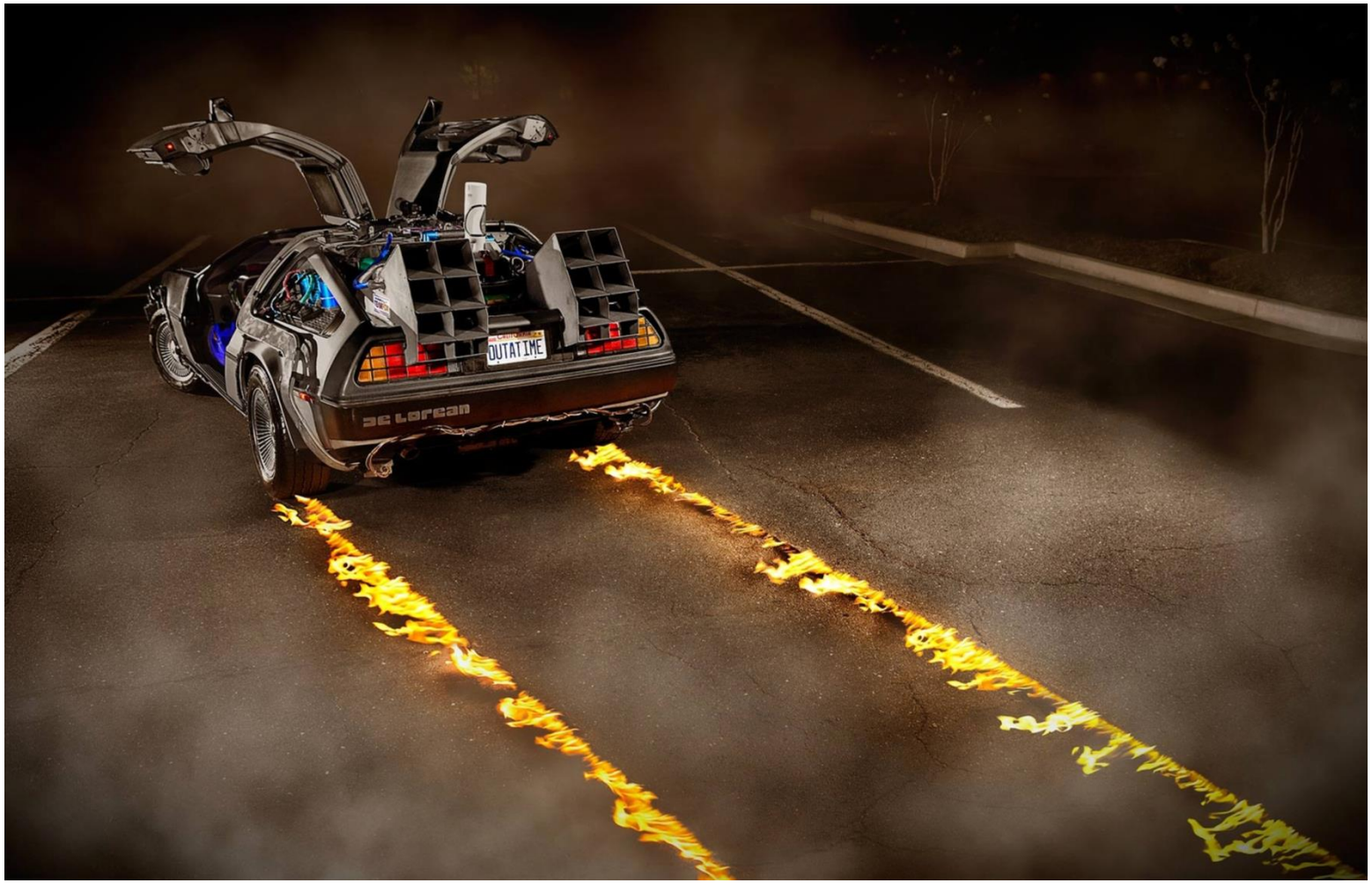
Annals of Internal Medicine

Association of Semaglutide With Tobacco Use Disorder in Patients With Type 2 Diabetes

Target Trial Emulation Using Real-World Data

William Wang; Nora D. Volkow, MD; Nathan A. Berger, MD; Pamela B. Davis, MD, PhD; David C. Kaelber, MD, PhD, MPH; and Rong Xu, PhD

What’s in the future?



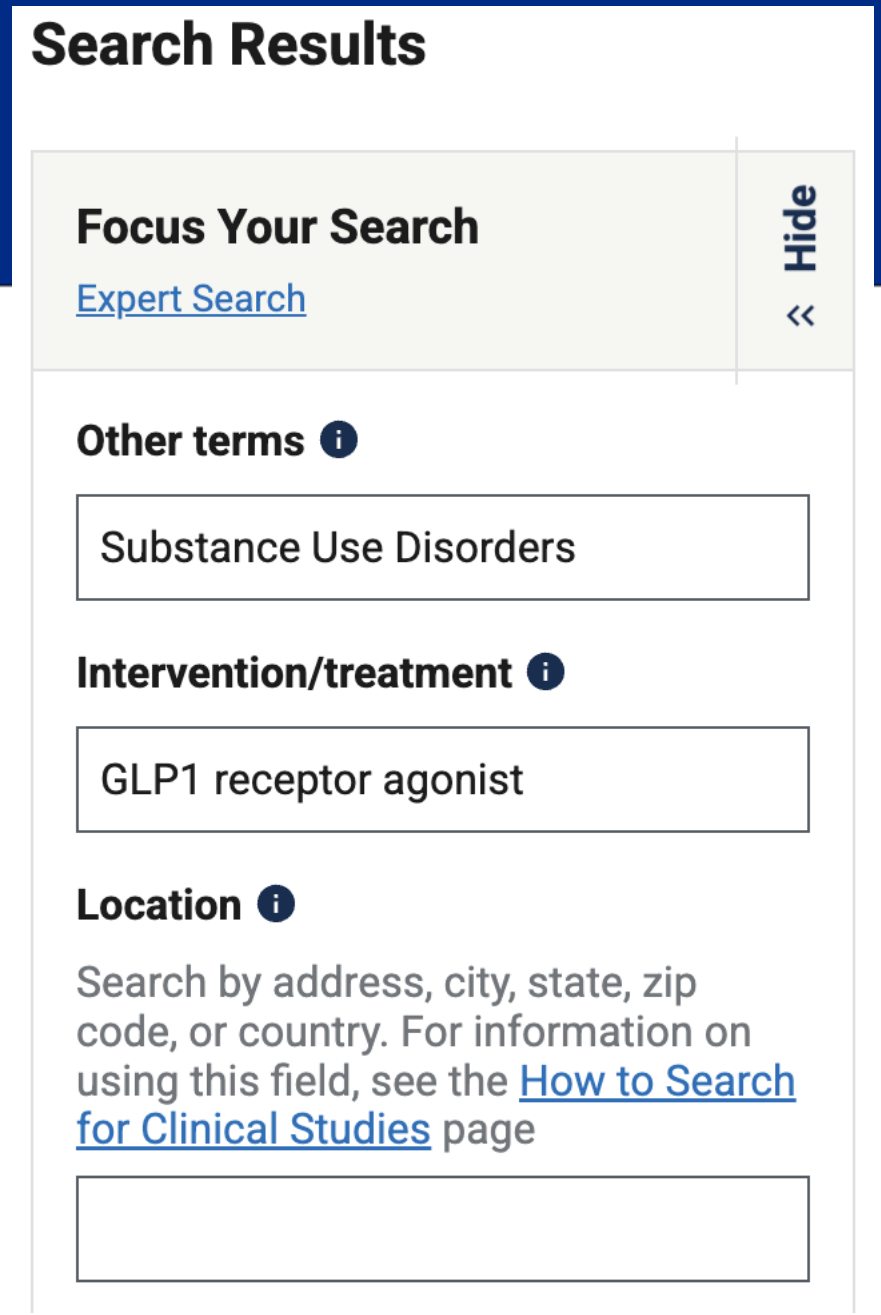
What’s in the future?

ClinicalTrials.gov

What's in the future?

NIH National Library of Medicine
National Center for Biotechnology Information

ClinicalTrials.gov



What’s in the future?

7 trials investigating effects on alcohol use disorder

2 trials on opioid use disorder

1 trial on cocaine use disorder

How should I alter how I practice?

No strong evidence that SGLT2 inhibitors offer effect

Metformin offers only a peripheral benefit may stabilize blood sugar
→ fewer mood swings and fatigue triggers (HALT)

Only GLP-1s are being actively studied as a potential treatment

Diabetes Care. 2025;49(Supplement_1):S183-S215. doi:10.2337/dc26-S009

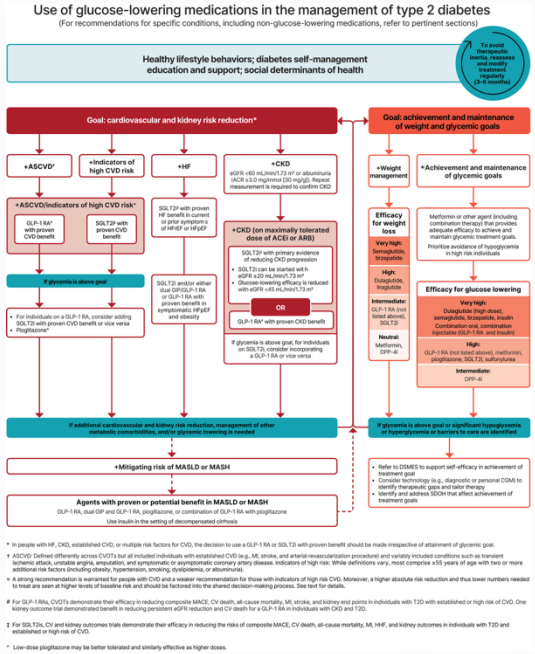
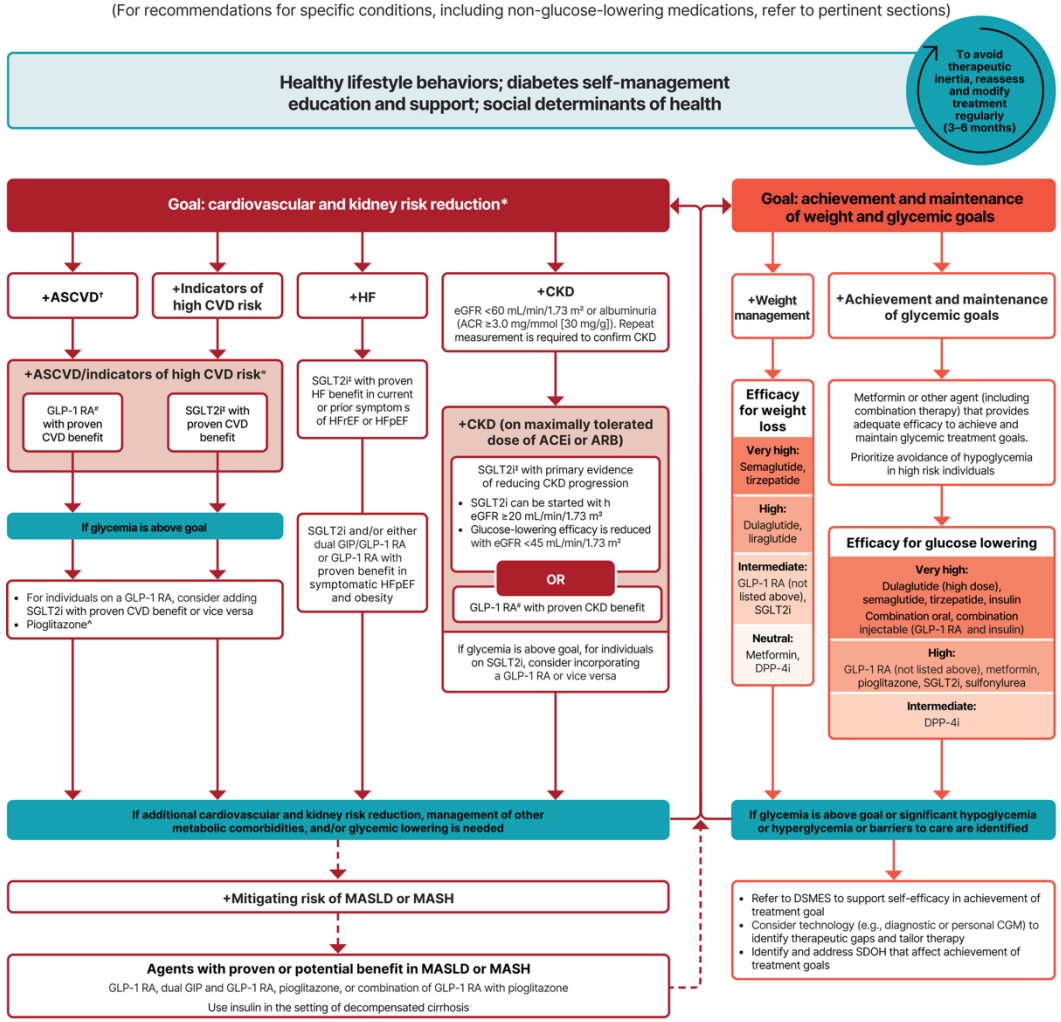


Figure Legend:

Use of glucose-lowering medications in the management of type 2 diabetes. The left side of the algorithm prioritizes mitigation of diabetes-related complications and end-organ effects, while the right side addresses weight and glucose management goals. ACEi, angiotensinconverting enzyme inhibitor; ACR, albumin-to-creatinine ratio; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; CGM, continuous glucose monitoring; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease;

Use of glucose-lowering medications in the management of type 2 diabetes

(For recommendations for specific conditions, including non-glucose-lowering medications, refer to pertinent sections)



* In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be made irrespective of attainment of glycemic goal.

† ASCVD: Defined differently across CVOTs but all included individuals with established CVD (e.g., MI, stroke, and arterial revascularization procedure) and variably included conditions such as transient ischemic attack, unstable angina, amputation, and symptomatic or asymptomatic coronary artery disease. Indicators of high risk: While definitions vary, most comprise ≥55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria).

≈ A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high risk CVD. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details.

For GLP-1 RAs, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and kidney end points in individuals with T2D with established or high risk of CVD. One kidney outcome trial demonstrated benefit in reducing persistent eGFR reduction and CV death for a GLP-1 RA in individuals with CKD and T2D.

‡ For SGLT2is, CV and kidney outcomes trials demonstrate their efficacy in reducing the risks of composite MACE, CV death, all-cause mortality, MI, HHF, and kidney outcomes in individuals with T2D and established or high risk of CVD.

^ Low-dose pioglitazone may be better tolerated and similarly effective as higher doses.

Diabetes Care. 2025;49(Supplement_1):S183-S215. doi:10.2337/dc26-S009

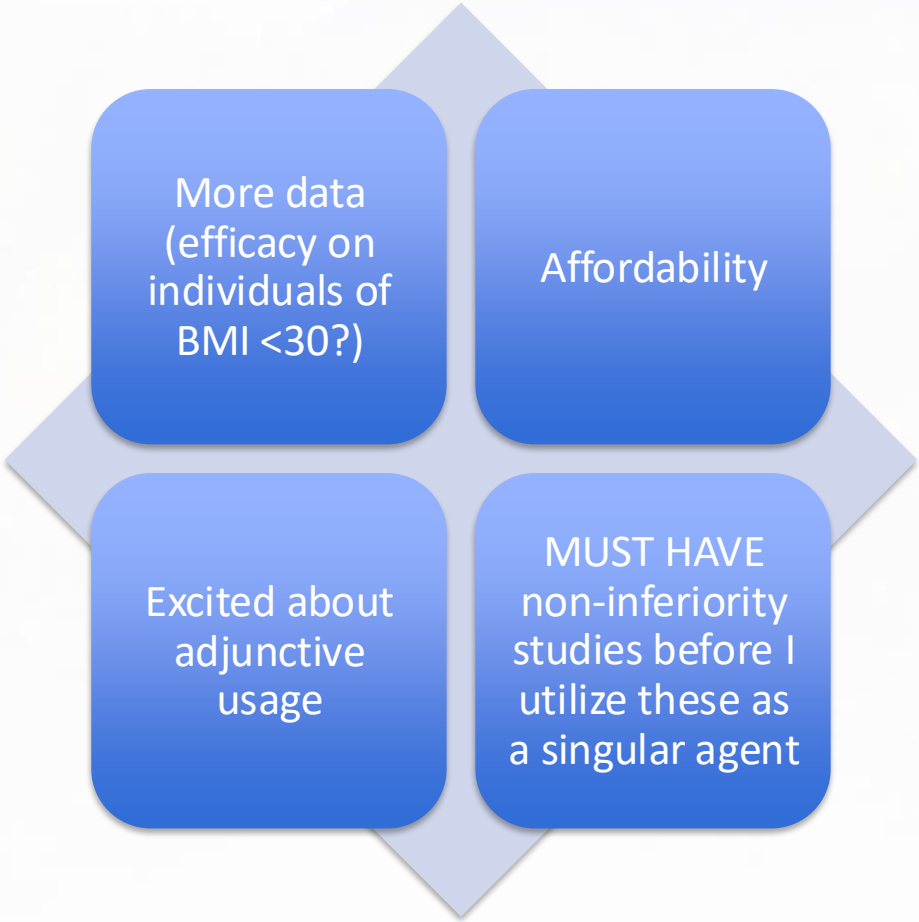
ADA 2026 Standards of Care

Δ in priorities from HgbA1c to heart, kidney, weight, glycemia

1. CV and kidney risk reduction
2. Weight management
3. Achieve glycemic goals
4. Address MASLD/MASH risk factors

Diabetes Care. 2025;49(Supplement_1):S183-S215. doi:10.2337/dc26-S009

What does this addictionologist need to Rx?



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