Phase 2 Randomized Trials of GLP-1 Receptor Agonists for Substance Use Disorder

Christian Hendershot
Keck School of Medicine of the University of Southern California
USC Institute for Addiction Science

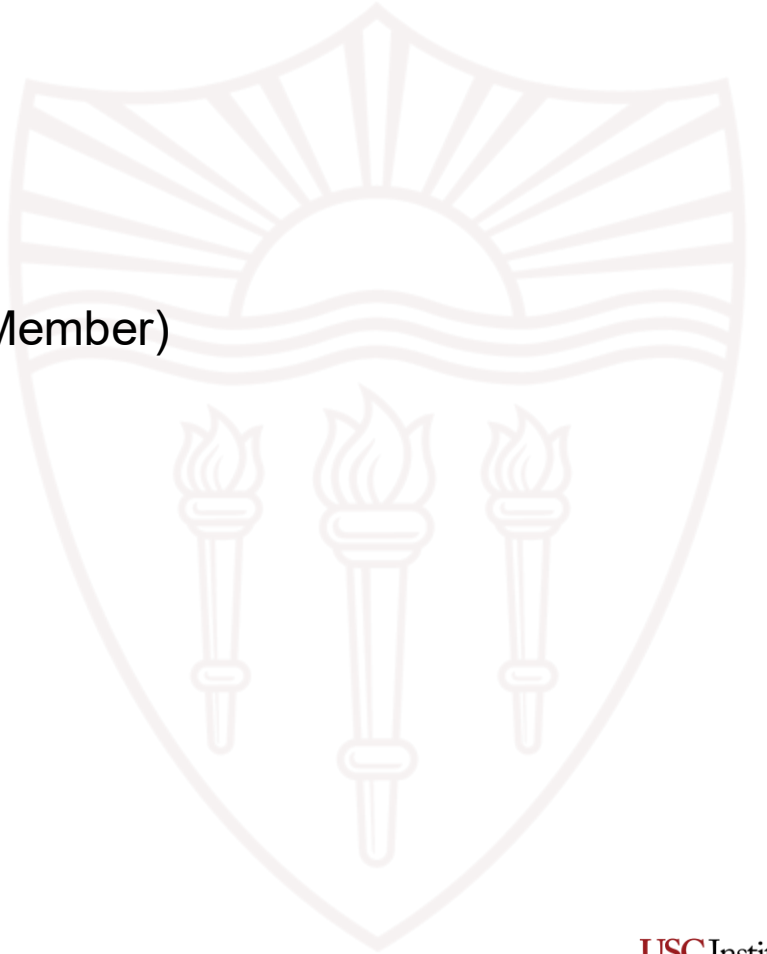
USC

USC Institute for Addiction Science

Disclosures

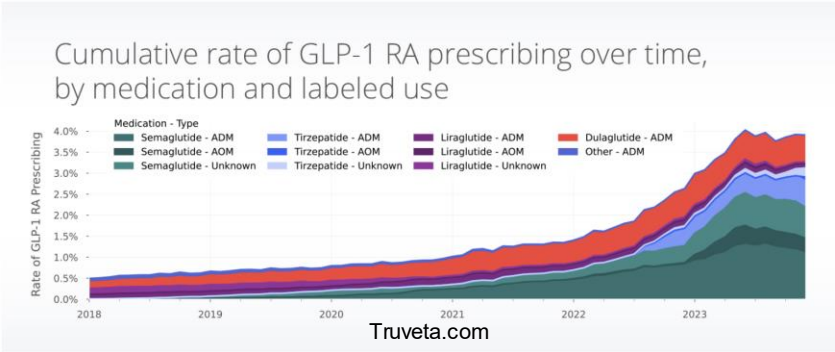
Eli Lilly (Steering Committee Member)

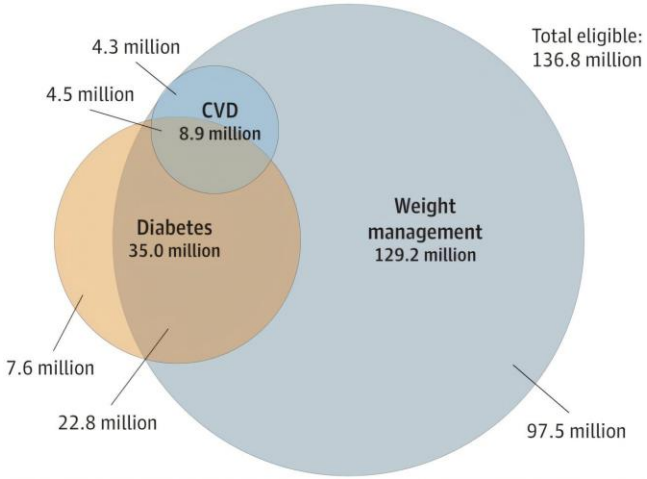
Apollo Therapeutics (Steering Committee Member)



Rapid Increase in GLP-1RA Prescribing Since 2021

- GLP-1RA therapies: $37 billion market in 2023; $125 billion market by 2033
- Semaglutide is now the top medication in terms of U.S. healthcare expenditures
- Estimated that >50% of U.S. adults are eligible for semaglutide
- Broad clinical uptake and public awareness of GLP-1RA presents an ideal scenario for drug repurposing in substance use disorders (SUD)



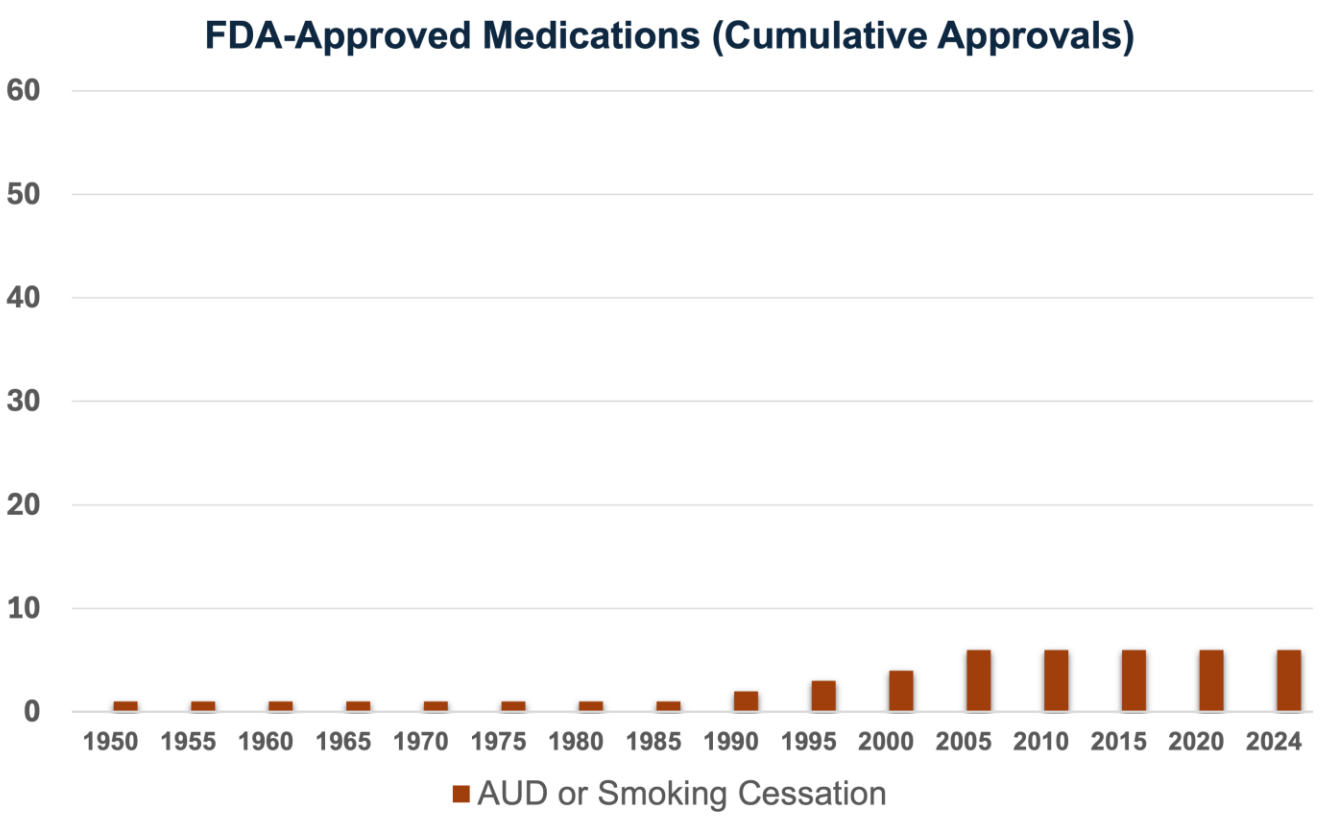


USC

GlobalData; Shi et al., 2024; Tichy et al., 2024

USC Institute for Addiction Science

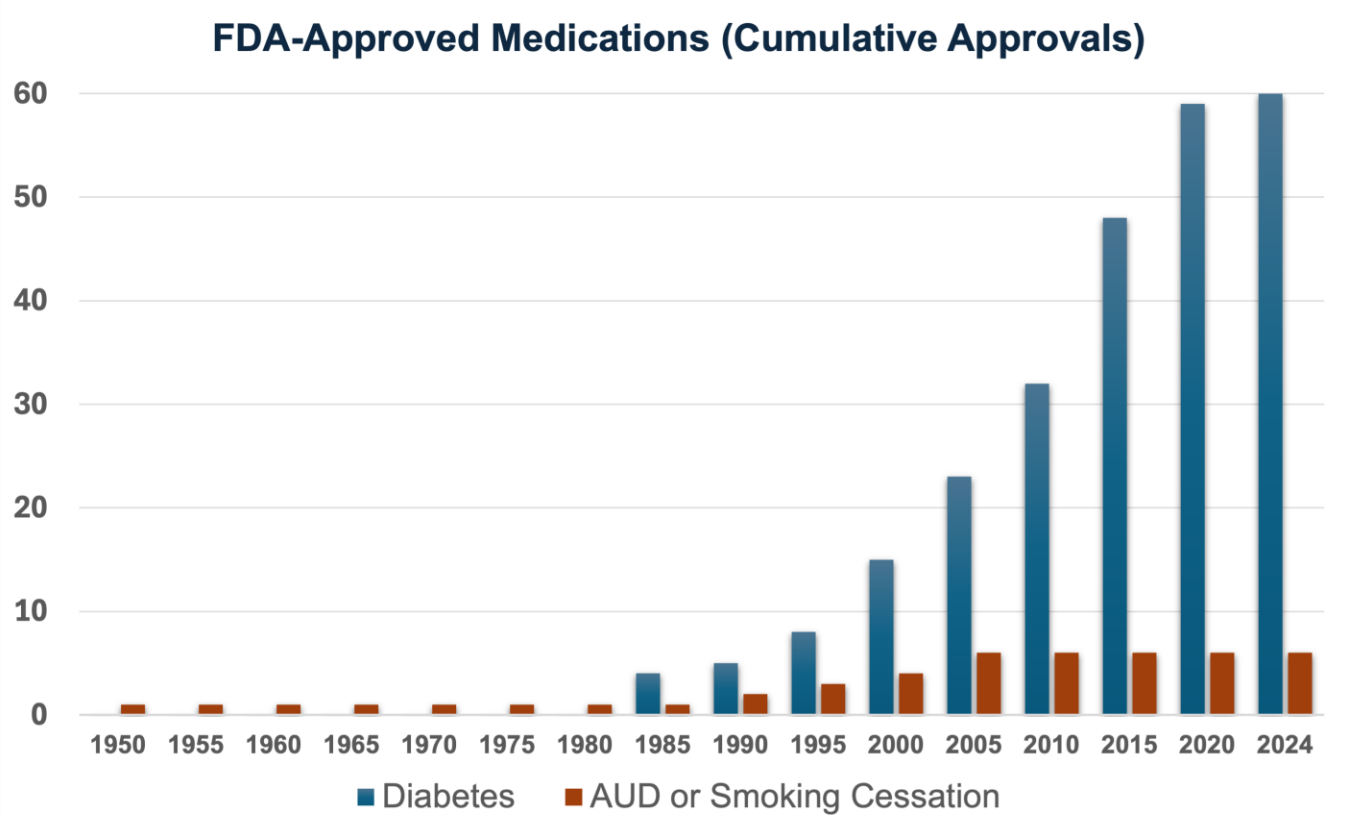
Combined FDA Approvals for Alcohol Use Disorder (AUD) and Smoking Cessation Therapies



USC

USC Institute for Addiction Science

Combined FDA Approvals for Alcohol Use Disorder (AUD) and Smoking Cessation Therapies



USC

USC Institute for Addiction Science

Early 2023 – Present

The New York Times

Some People on Ozempic Lose the Desire to Drink. Scientists Are Asking Why.

As the diabetes drug gains more attention, a surprising side effect has emerged.

The Atlantic

HEALTH

Did Scientists Accidentally Invent an Anti-addiction Drug?

People taking Ozempic for weight loss say they have also stopped drinking, smoking, shopping, and even nail biting.

By Sarah Zhang

Can diabetes and weight-loss drug Ozempic break addictions too?

Doctors are hearing anecdotal reports of reductions in drinking and smoking, but experts caution that more research is needed

LIVING BETTER

Ozempic seems to curb cravings for alcohol. Here's what scientists think is going on

August 28, 2023 · 5:00 AM ET

Michaeleen Doucleff

npr

THE WALL STREET JOURNAL.

Ozempic Might Help You Drink and Smoke Less

Animal studies suggest GLP-1 drugs alter behaviors associated with reward and pleasure

Weight-loss meds like Ozempic may help curb addictive behaviors, but drugmakers aren't running trials to find out

By Meg Tirrell, CNN

CNN health

NEWS | BRAIN & BEHAVIOR

Hot weight loss drugs tested as addiction treatments

Clinical trials will gauge whether GLP-1 analogs curb drug, alcohol cravings

28 AUG 2023 · 5:05 PM ET · BY MITCH LESLIE

Science

April 19, 2024

Could GLP-1 Receptor Agonists like Semaglutide Treat Addiction, Alzheimer Disease, and Other Conditions?

Rita Rubin, MA[1]

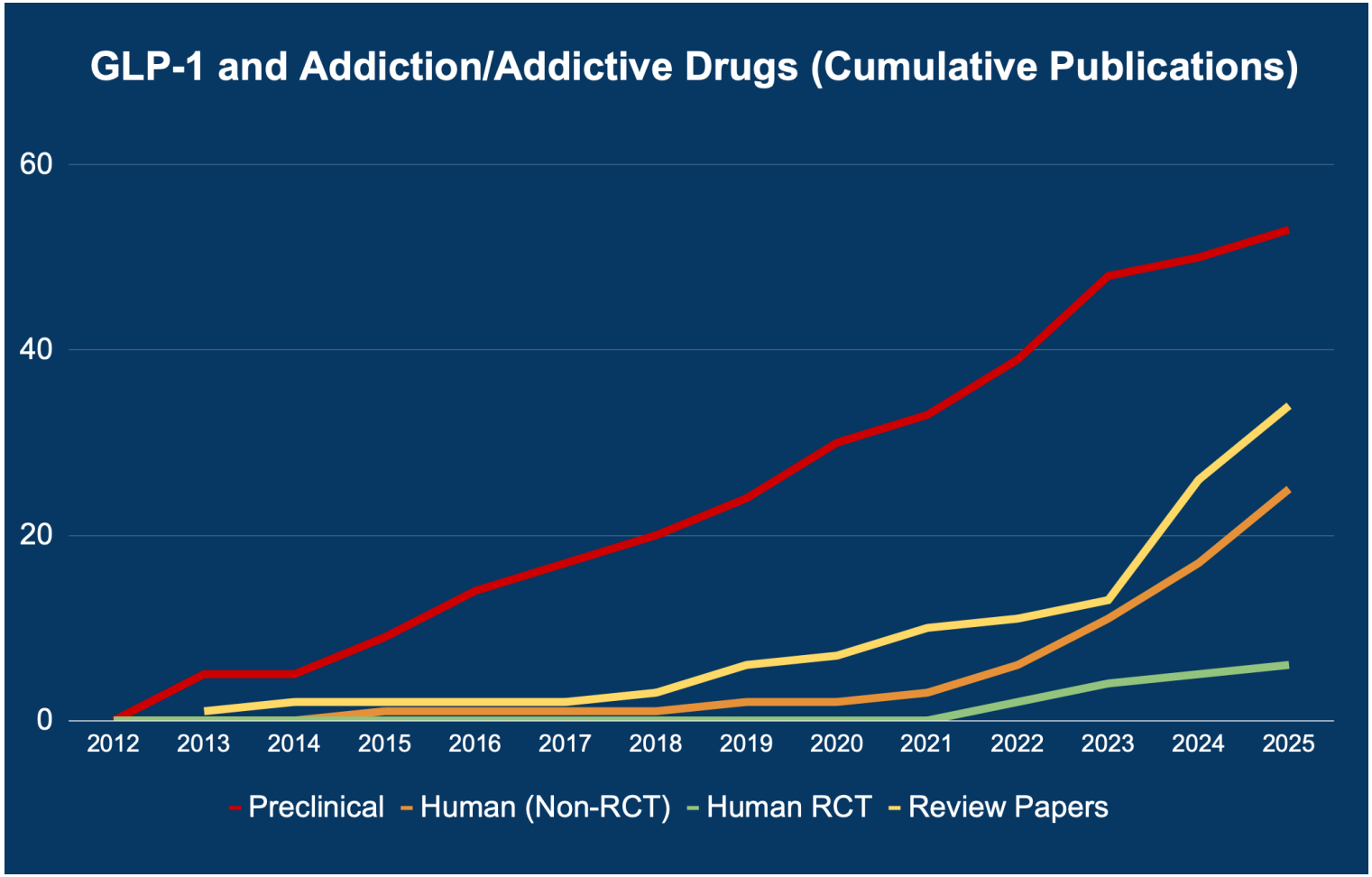
Author Affiliations | Article Information

JAMA. Published online April 19, 2024. doi:10.1001/jama.2024.1017

JAMA Medical News

USC

USC Institute for Addiction Science



USC

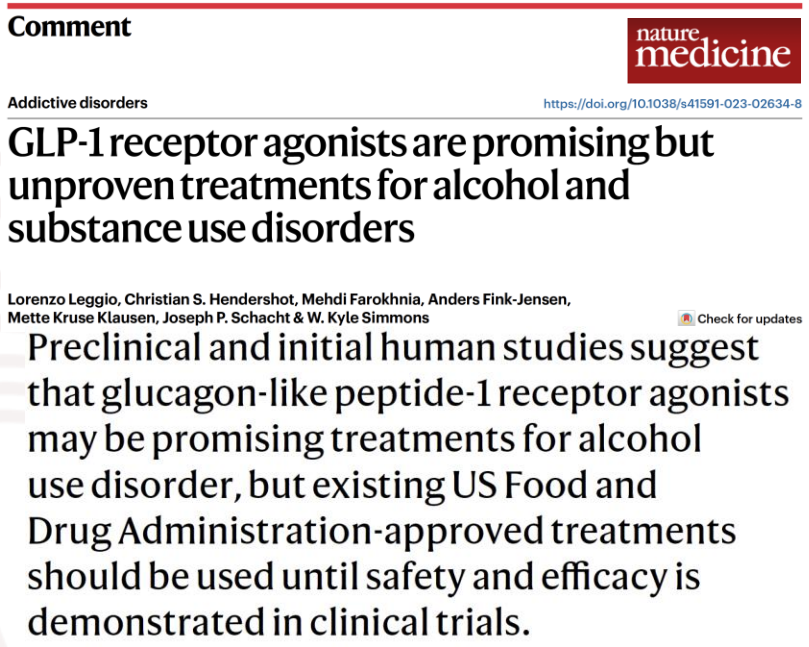
USC Institute for Addiction Science

The Case for GLP-1RA for Alcohol Use Disorder (AUD)

1. Preclinical studies indicate that GLP-1RA attenuate alcohol intake and alcohol reward (for review see Brunchmann et al., 2019; Jerlhag, 2023; 2025)
2. Extensive observational data (anecdotal, media and case series reports)
3. Convergent evidence from pharmacoepidemiology studies
   - Health records data indicate that GLP-1RA exposure is associated with lower incidence of AUD/SUD-related medical codes
     - Wium-Andersen et al., 2022; Wang, Volkow, et al., 2024; Qeadan et al., 2025; Lahteenvuo et al., 2025; Xie et al., 2025; Farokhnia et al., 2025

The Need for Randomized Trials

- Observational reports have significantly outpaced evidence from RCTs
- Off-label prescribing of GLP-1RA for AUD/SUD is occurring
- Randomized trials are needed to establish safety and efficacy of GLP-1RA for AUD



Comment

nature medicine

Addictive disorders

https://doi.org/10.1038/s41591-023-02634-8

GLP-1 receptor agonists are promising but unproven treatments for alcohol and substance use disorders

Lorenzo Leggio, Christian S. Hendershot, Mehdi Farokhnia, Anders Fink-Jensen, Mette Kruse Klausen, Joseph P. Schacht & W. Kyle Simmons

Check for updates

Preclinical and initial human studies suggest that glucagon-like peptide-1 receptor agonists may be promising treatments for alcohol use disorder, but existing US Food and Drug Administration-approved treatments should be used until safety and efficacy is demonstrated in clinical trials.

Phase 2 Clinical Trials (AUD or Alcohol-Related)

Registration	Timeline	N	Medication (Max Dose)	Duration	Status
NCT03232112	2017-2020	127	Exenatide (2mg)	26 weeks	Completed
NCT05520775	2022-2024	48	Semaglutide (1mg)	8 weeks	Completed
NCT05895643	2023-2026	108	Semaglutide (2.4mg)	26 weeks	Recruitment complete
NCT05891587	2023-2025	80	Semaglutide (1mg)	12 weeks	Recruitment complete
NCT06015893	2023-2025	52	Semaglutide (2.4mg)	20 weeks	Recruiting
NCT05892432	2024-2025	50	Semaglutide (7mg, oral)	8 weeks	Recruiting
NCT06409130	2024-2026	240	Semaglutide, Cagrilintide, NNC0194-0499	28 weeks	Recruiting
NCT06817356	2025-2026	300	Mazdutide	28 weeks	Recruiting
NCT06727331	2025-2026	20	Tirzepatide (2.5mg)	4 weeks	Not yet recruiting
NCT06994338	2025-2027	42	Tirzepatide (5mg)	8 weeks	Not yet recruiting
NCT06939088	2025-2028	108	Tirzepatide	26 weeks	Recruiting
NCT06546384	2025-2027	64	Semaglutide (2.4mg)	16 weeks	Not yet recruiting

Phase 2 Clinical Trials (AUD or Alcohol-Related)

Registration	Timeline	N	Medication (Max Dose)	Duration	Status
NCT03232112	2017-2020	127	Exenatide (2mg)	26 weeks	Completed
NCT05520775	2022-2024	48	Semaglutide (1mg)	8 weeks	Completed
NCT05895643	2023-2026	108	Semaglutide (2.4mg)	26 weeks	Recruitment complete
NCT05891587	2023-2025	80	Semaglutide (1mg)	12 weeks	Recruitment complete
NCT06015893	2023-2025	52	Semaglutide (2.4mg)	20 weeks	Recruiting
NCT05892432	2024-2025	50	Semaglutide (7mg, oral)	8 weeks	Recruiting
NCT06409130	2024-2026	240	Semaglutide, Cagrilintide, NNC0194-0499	28 weeks	Recruiting
NCT06817356	2025-2026	300	Mazdutide	28 weeks	Recruiting
NCT06727331	2025-2026	20	Tirzepatide (2.5mg)	4 weeks	Not yet recruiting
NCT06994338	2025-2027	42	Tirzepatide (5mg)	8 weeks	Not yet recruiting
NCT06939088	2025-2028	108	Tirzepatide	26 weeks	Recruiting
NCT06546384	2025-2027	64	Semaglutide (2.4mg)	16 weeks	Not yet recruiting

Phase 2a Clinical Trial
NCT05520775

JAMA Psychiatry | Original Investigation

Once-Weekly Semaglutide in Adults With Alcohol Use Disorder
A Randomized Clinical Trial

Christian S. Hendershot, PhD; Michael P. Bremmer, MA; Michael B. Paladino, BS; Georgios Kostantinis, BA; Thomas A. Gilmore, BA; Neil R. Sullivan, BA; Amanda C. Tow, MD, PhD; Sarah S. Dermody, PhD, CPsych; Mark A. Prince, PhD; Robyn Jordan, MD, PhD; Sherry A. McKee, PhD; Paul J. Fletcher, PhD; Eric D. Claus, PhD; Klara R. Klein, MD, PhD

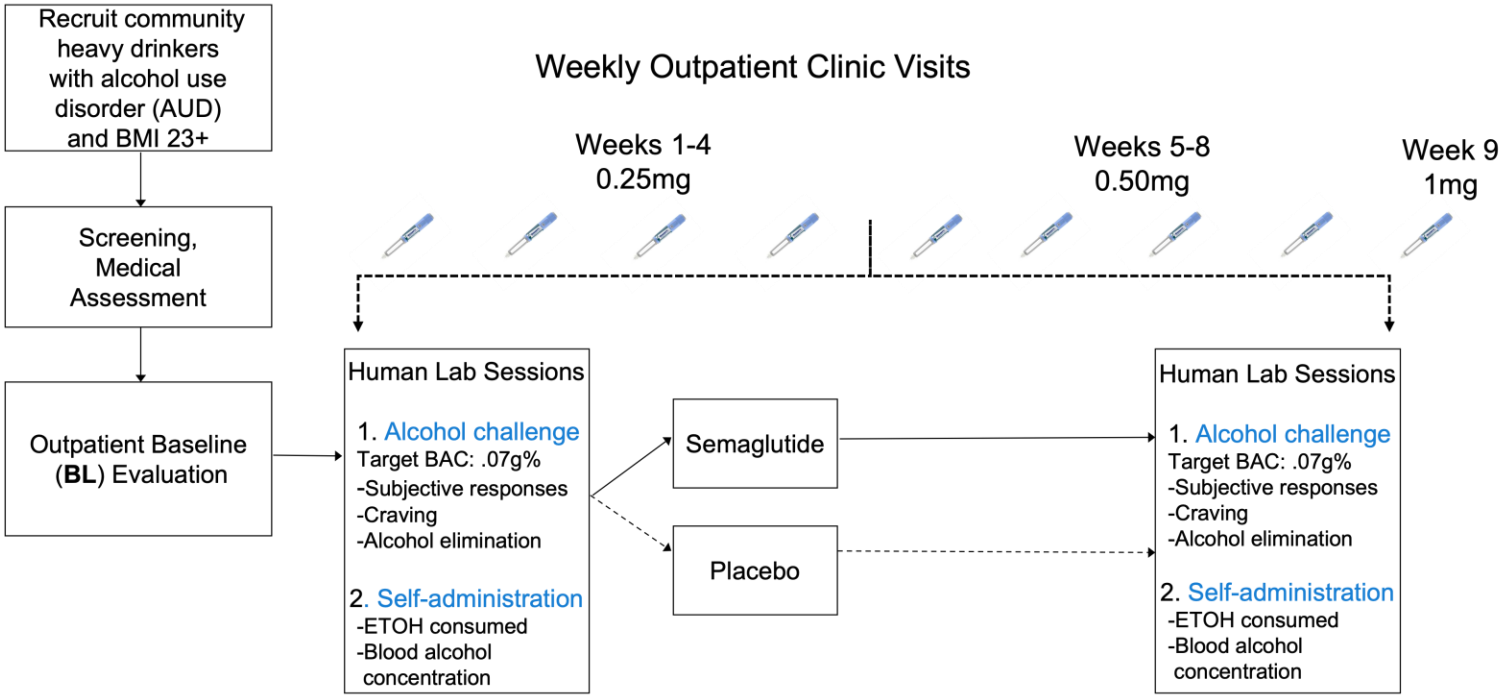
- Investigator-initiated, NIAAA-funded Phase 2a trial
- Aim: Examine safety and efficacy of semaglutide in non-treatment-seeking adults with AUD
- Low-dose treatment: 0.25mg (Weeks 1-4); 0.5mg (Weeks 5-8); final dose of 1.0mg (Week 9)
  - Hybrid clinical trial/human laboratory design
    - Laboratory alcohol self-administration endpoints
    - Naturalistic outcomes during treatment
      - Drinking quantity, frequency; weekly craving

Phase 2a Clinical Trial
NCT05520775

JAMA Psychiatry | Original Investigation

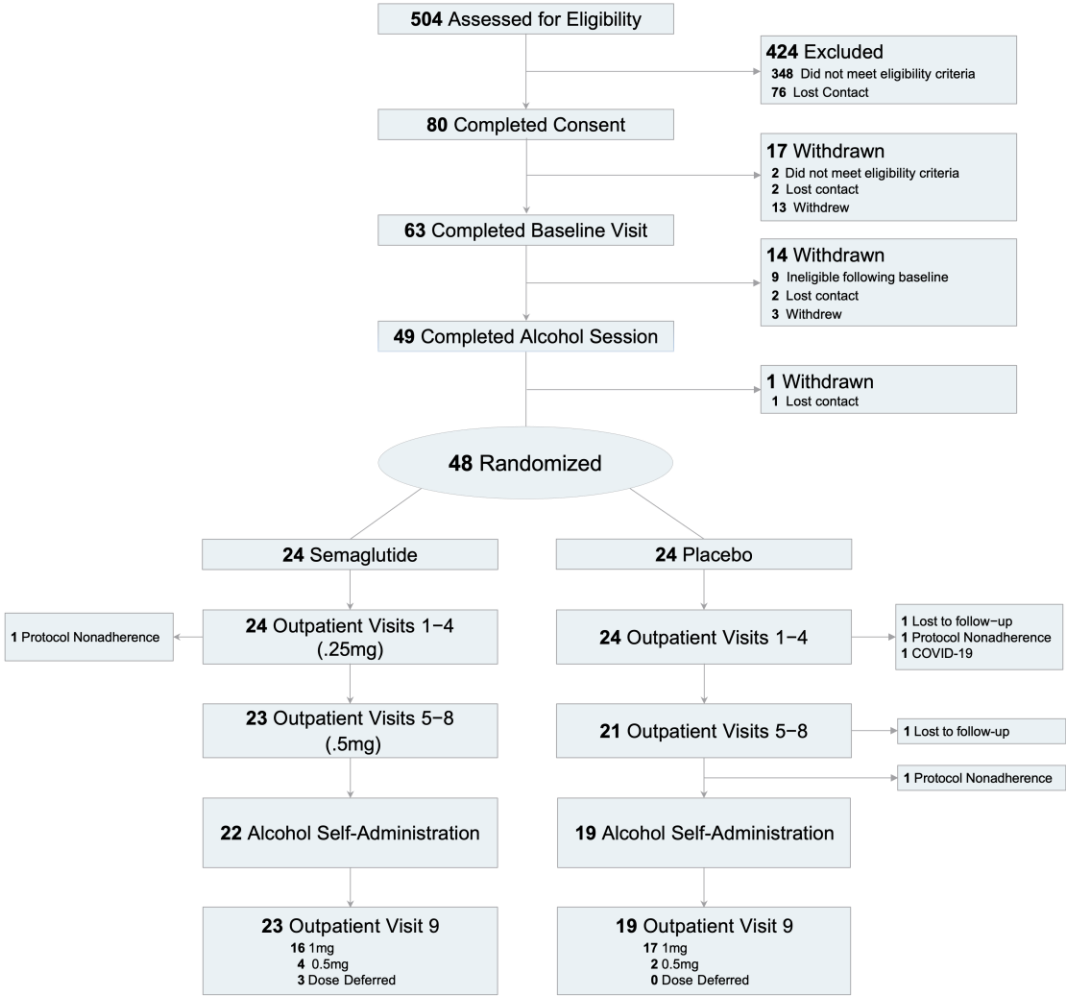
Once-Weekly Semaglutide in Adults With Alcohol Use Disorder
A Randomized Clinical Trial

Christian S. Hendershot, PhD; Michael P. Bremmer, MA; Michael B. Paladino, BS; Georgios Kostantinis, BA; Thomas A. Gilmore, BA; Neil R. Sullivan, BA; Amanda C. Tow, MD, PhD; Sarah S. Dermody, PhD, CPsych; Mark A. Prince, PhD; Robyn Jordan, MD, PhD; Sherry A. McKee, PhD; Paul J. Fletcher, PhD; Eric D. Claus, PhD; Klara R. Klein, MD, PhD



USC

USC Institute for Addiction Science



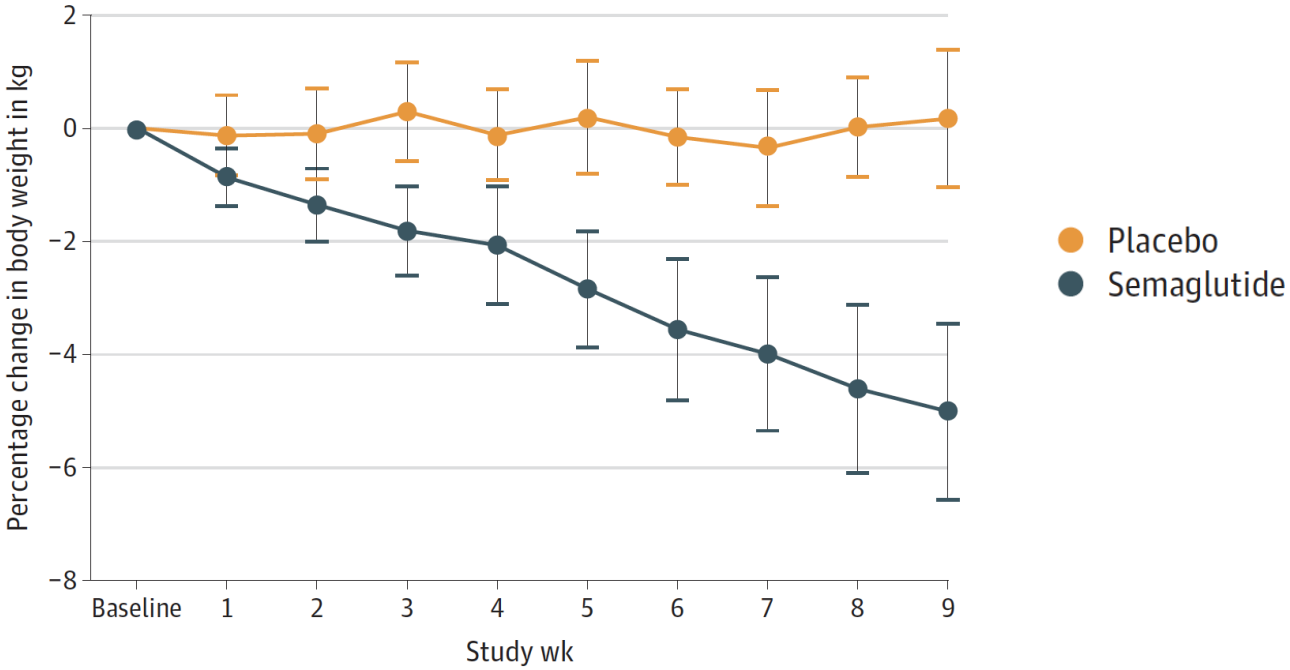
USC

USC Institute for Addiction Science

Baseline Participant Characteristics by Group			
	Mean ± SD or count		
	Placebo	Semaglutide	Total
N (male/female)	24 (7/17)	24 (7/17)	48 (14/34)
Age (years)	39 ± 11	41 ± 10	40 ± 11
Weight (kg)	93.1 ± 15.1	95.4 ± 20.9	94.3 ± 18.1
Body Mass Index (BMI kg/m²)	31.7 ± 4.5	32.4 ± 6.7	32.1 ± 5.6
BMI ≥ 30 (%)	62.5%	50%	56.25%
HbA1C	5.16 ± 0.35	5.09 ± 0.38	5.13 ± 0.36
Depression (CES-D)	11.7 ± 10.0	12.7 ± 7.4	12.2 ± 8.7
Race			
White	18	21	39
Black/ African American	4	3	7
Asian	2	0	2
Hawaiian/ Pacific Islander	0	0	0
Other/ Multiracial	0	0	0
Ethnicity: Hispanic	2	2	4
Baseline Alcohol consumption			
Drinks per day	3.0 ± 1.7	2.57 ± 1.7	2.9 ± 1.7
Drinks per drinking day	4.5 ± 2.5	3.8 ± 1.8	4.2 ± 2.2
Drinking days	19.6 ± 5.5	20.8 ± 6.8	20.2 ± 6.1
Heavy drinking days	9.8 ± 5.5	8.4 ± 7.9	9.1 ± 6.8
AUD symptoms (DSM-5)	4.3 ± 2.0	4.1 ± 1.5	4.2 ± 1.7
AUDIT score	14.2 ± 6.5	12.7 ± 5.6	13.4 ± 6.0

Participant characteristics separated by treatment group for all randomized participants. Values represent the mean and SD or count unless otherwise noted.

Body Weight (kg, % change from baseline)



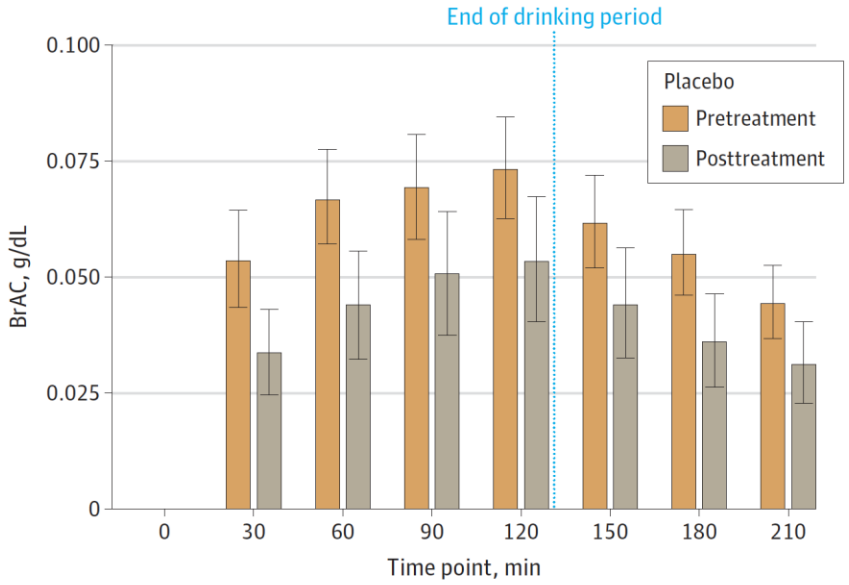
Time x Medication: β = -.07; 95% CI [-.08, .-05]; p < .001

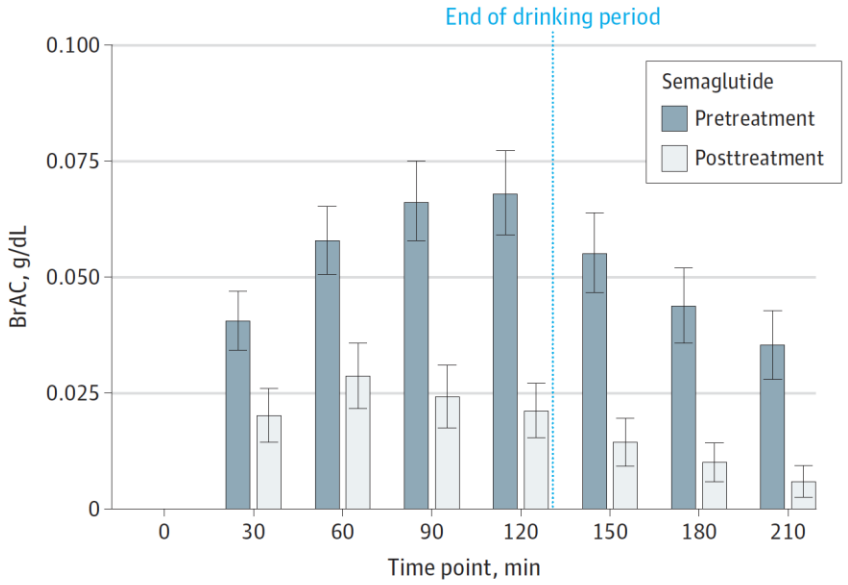
USC

Hendershot et al. (2025) *JAMA Psychiatry* 82(4) 395-405

USC Institute for Addiction Science

Pre-Treatment and Post-Treatment Laboratory Alcohol Consumption



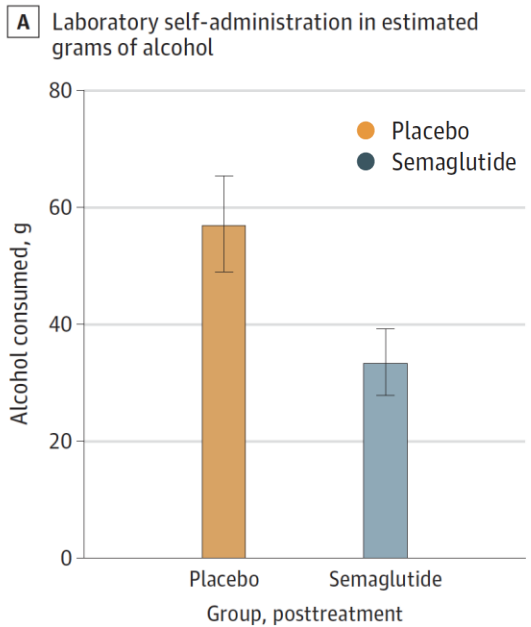


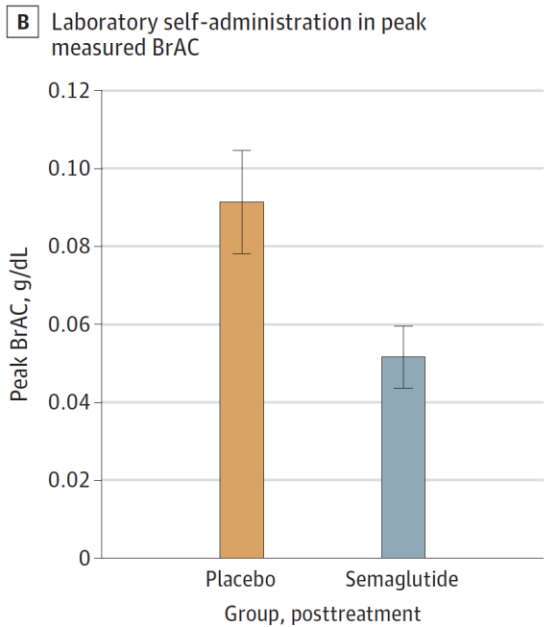
USC

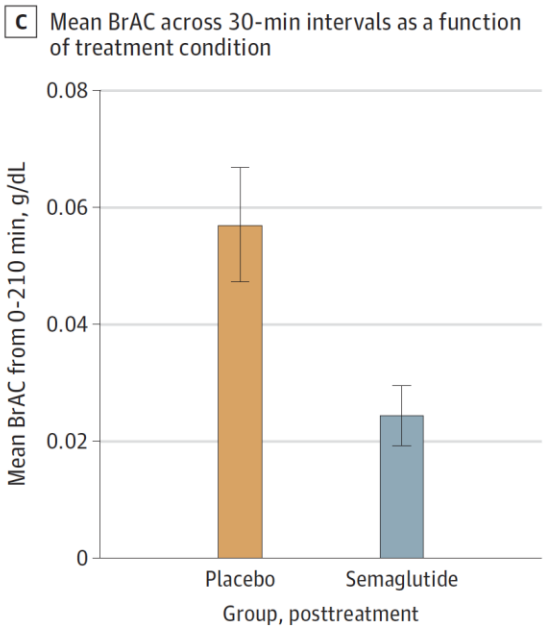
Hendershot et al. (2025) *JAMA Psychiatry* 82(4) 395-405

USC Institute for Addiction Science

Post-Treatment Laboratory Alcohol Consumption
Residualized Change Models (Controlling for Pre-Treatment)







β = −0.48; 95%CI [−0.85 to −0.11], p = .01

β, = −0.46; 95%CI [−0.87 to −0.06], p = .03

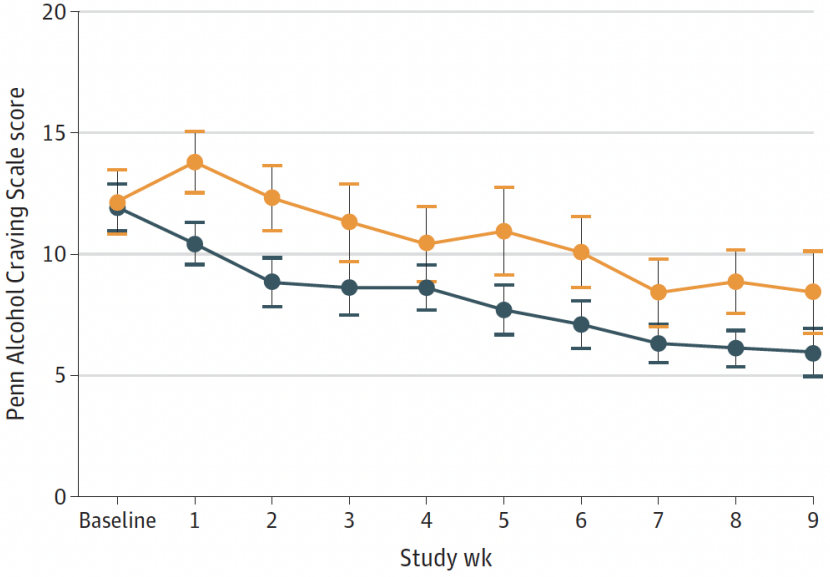
β = −0.48, 95% CI [−0.87 to −0.09], p = .02

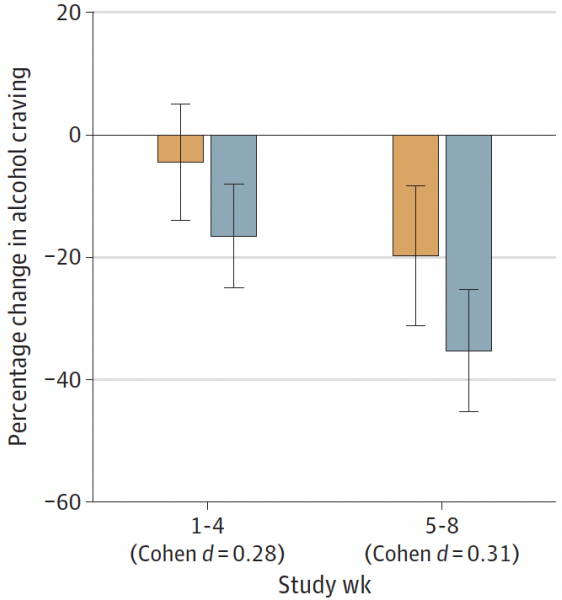
USC

Hendershot et al. (2025) *JAMA Psychiatry* 82(4) 395-405

USC Institute for Addiction Science

Alcohol Craving (Penn Alcohol Craving Scale)





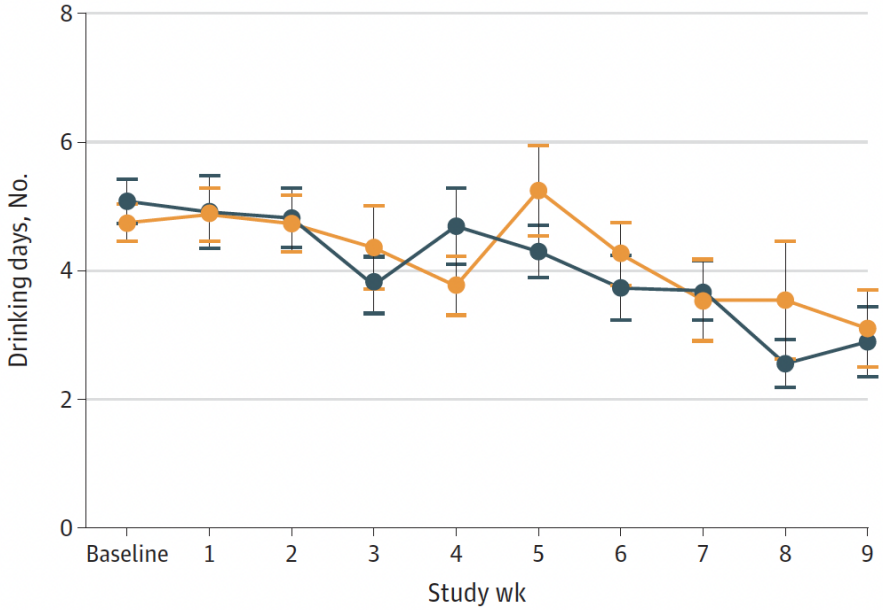
Medication: β, −0.39; 95% CI: −0.73 to −0.06; p = .01

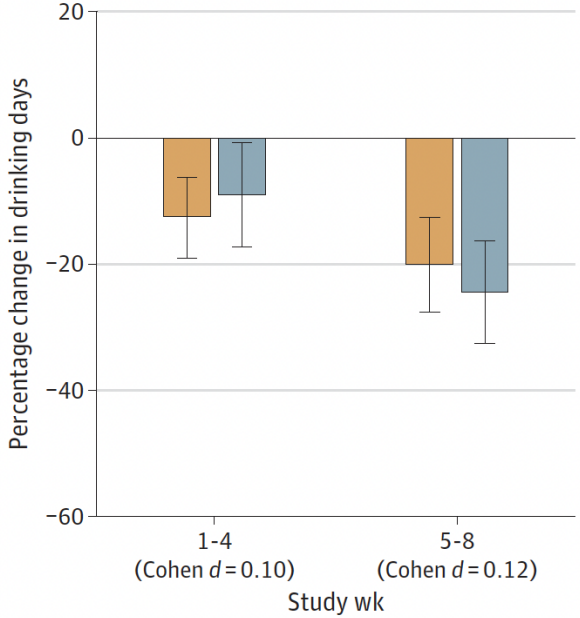
USC

Hendershot et al. (2025) *JAMA Psychiatry* 82(4) 395-405

USC Institute for Addiction Science

% Drinking Days



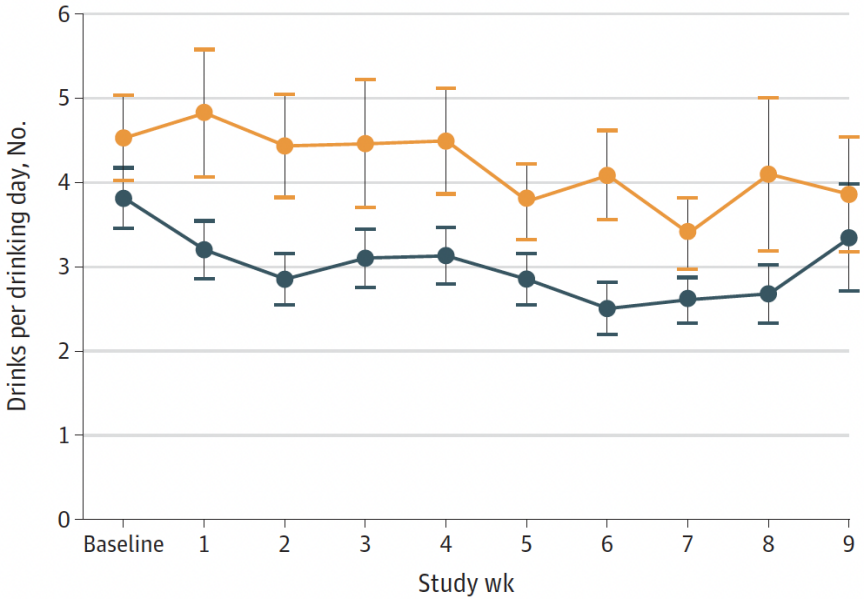


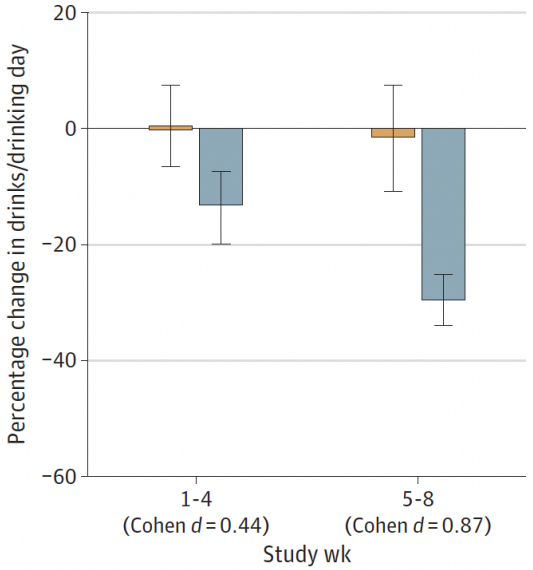
USC

Hendershot et al. (2025) *JAMA Psychiatry* 82(4) 395-405

USC Institute for Addiction Science

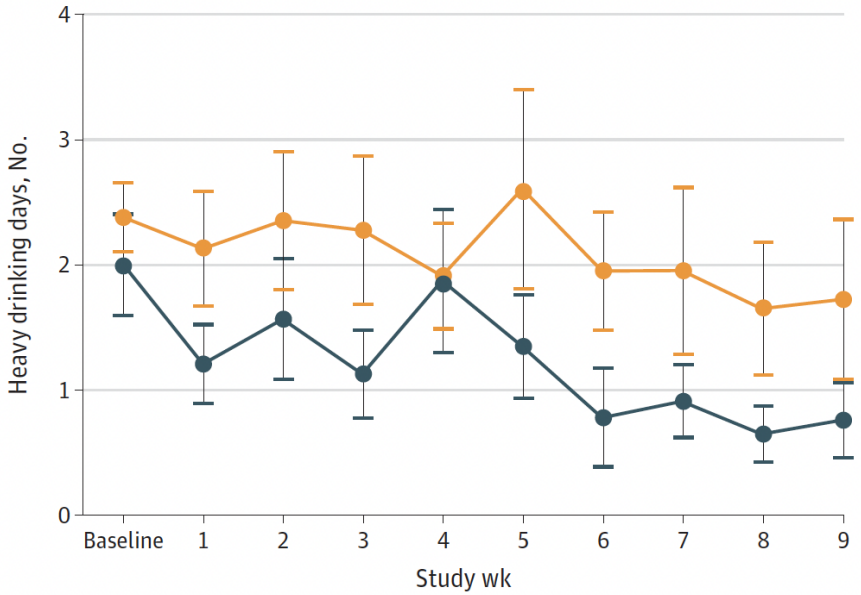
Drinks Per Drinking Day

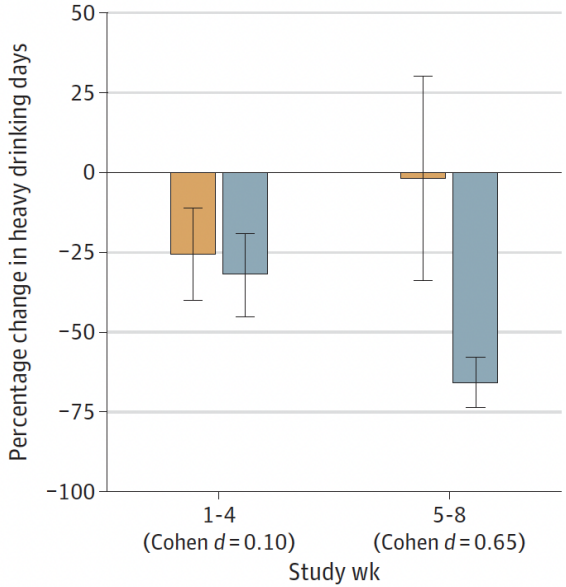




Medication: β, −0.41; 95% CI: −0.73 to −0.09; p = .04

Number of Heavy Drinking Days





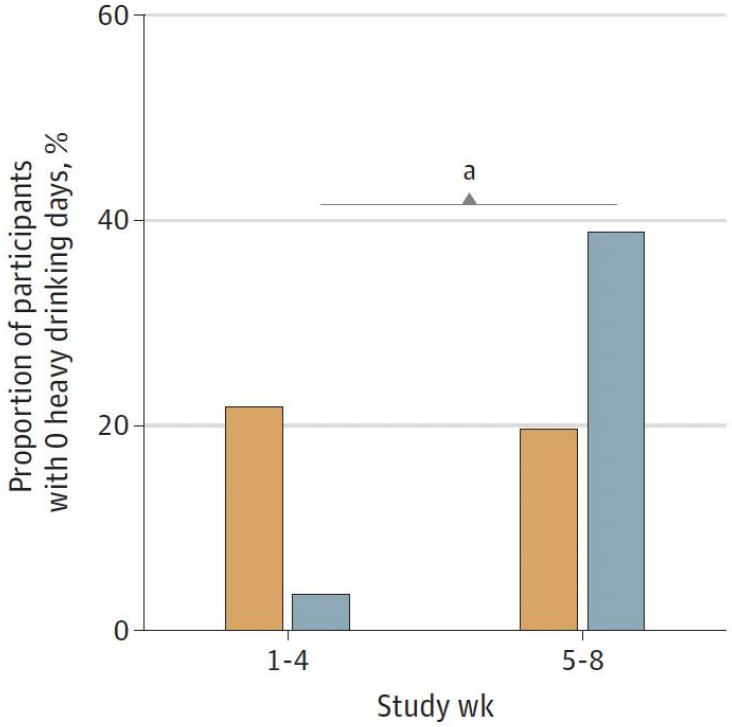
Time x Medication: β, 0.84; 95% CI: 0.71 to 0.99; p = .04

USC

Hendershot et al. (2025) *JAMA Psychiatry* 82(4) 395-405

USC Institute for Addiction Science

% of Participants with No Heavy Drinking Days



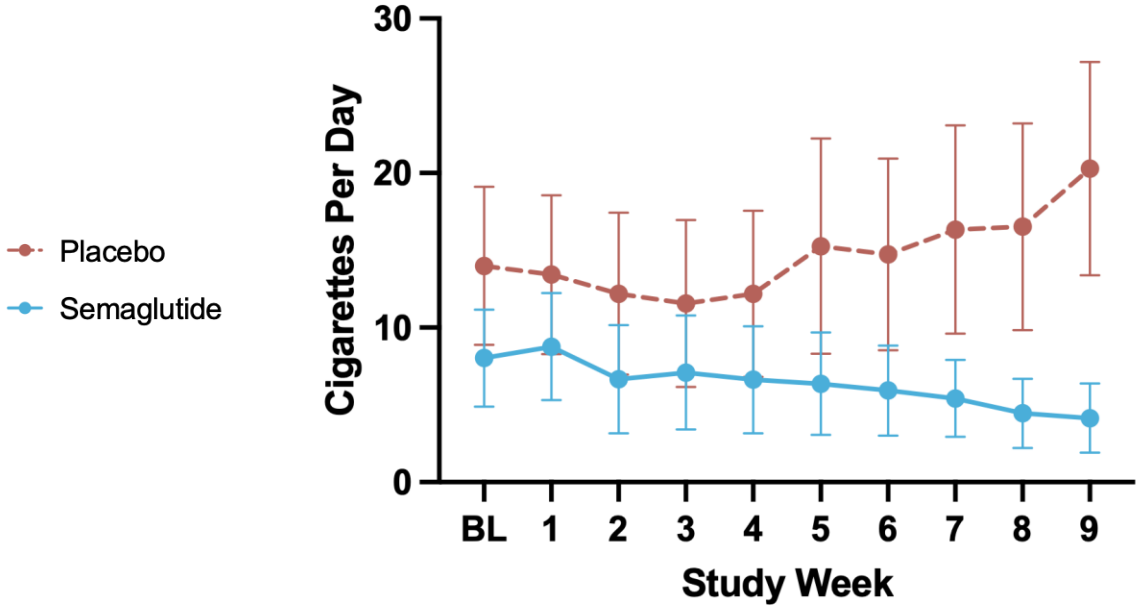
Change in semaglutide group: $z = -2.93$; $p = .003$

Hendershot et al. (2025) *JAMA Psychiatry* 82(4) 395-405

USC

USC Institute for Addiction Science

Cigarettes Per Day in Subgroup with Regular Cigarette Use at Baseline (n = 13)



Time x Medication: β, −0.10; 95%CI, −0.16 to −0.03; p = .005

Phase 2 Nicotine Clinical Trials (Tobacco Use, Smoking Cessation, Post-Cessation Weight Gain)

Registration	Timeline	N	Medication (Max Dose)	Duration	Status
NCT02975297	2016-2020	84	Exenatide (2mg)	6 weeks	Completed
NCT03712098	2018-2022	40	Liraglutide (3mg)	32 weeks	Completed
NCT03204396	2017-2021	255	Dulaglutide (1.5mg)	12 weeks	Completed
NCT05530577	2022-2024	48	Semaglutide (1mg)	9 weeks	Completed
NCT05610800	2022-2026	216	Exenatide (2mg)	14 weeks	Recruiting
NCT06173778	2024-2027	177	Semaglutide (2.4mg)	28 weeks	Recruiting
NCT06986993	2024-2028	40	Semaglutide (1mg)	12 weeks	Recruiting
NCT06924697	2024-2025	46	Semaglutide (1mg)	28 weeks	Recruiting

Summary

- The number of GLP-1RA/AUD trials has grown rapidly in last 24 months
  - Other RCTs underway (tobacco use disorder, opioid use disorder)
- First Phase 2 AUD semaglutide trial:
  - Low-dose treatment reduces laboratory consumption, weekly craving, drinks per drinking day, and heavy drinking days in adults with AUD
  - No effect on drinking frequency (% of drinking vs. abstinent days)
  - Monthly estimates suggested medium to large effect sizes at the lowest clinically effective dose (0.5mg/week)
  - Apparent dose effects (greater effect sizes at 0.5mg vs. 0.25mg)
  - Evidence for safety of semaglutide during short-term treatment

Summary

- Additional clinical trials are needed to establish safety and efficacy:
  - At higher doses and longer treatment duration
  - In larger samples of treatment-seeking participants
  - In co-occurring SUD (e.g., AUD + tobacco use disorder)
  - Across a broader range of body weight/BMI levels
- Challenges for investigator-initiated trials:
  - Long titration schedules (e.g., several months to reach maximum dose)
  - High medication cost
  - Rapid pace of progress in the incretin treatment field

Drug	MOA	Indication	Company	Phase	Formulation
semaglutide (Ozembic, Wegovy, Reybelsus)	**GLP1**	**D, O**	**Novo Nordisk**	**FDA (2017)**	**O, I**
exenatide (Byetta, Bydureon)	**GLP1**		**AstraZeneca**	**FDA (2005, 2012)**	**O, I**
dulaglutide (Trulicity)	**GLP1**		**Lilly**	**FDA (2014)**	**I**
liraglutide (Victoza, Saxenda)	**GLP1**	**D, O**	**Novo Nordisk**	**FDA (2010)**	**O**
lixisenatide (Adlyxin, Lyxumia)	**GLP1**		**Sanofi**	**FDA (2016)**	**O**
albiglutide (Tanzeum)	GLP1		GSK	D/C (economic)	
orforglipron	GLP1	O	Lilly	3	O
danuglipron (PF-06882961)	GLP1	D, O	Pfizer	3 (1 optimized)	O
VCT-220	GLP1	D, O	Vincentage Pharm	3	
RGT001-075	GLP1	O	Regor Ther.	2	O
aleniglipron (GSBR-1290)	GLP1	O	Structure Ther.	2	O
AZD5004	GLP1	D, O	AstraZeneca	2	O
NLY01-PD (NLY01-AD)	GLP1	Alz,Pkin	Neuraly	2	
XW003, XW004, XW014	GLP1	D, O	Siwind Bio	2	O,I
bremelanotidide (Vylessi)	GLP1	O, hyposex	Palatin Tech	2 (3)	
HDM1002	GLP1	O	Hangzhou Zhongmei Huadong	2	
MDR-001	GLP1	D, O	MindRank	2	
PEG-loxenatide	GLP1	D, O	Hansoh Pharm	2	I
HRS-7535	GLP1	O	Shangdong Suncadia Medicine	2	
RG6652 (CT-996)	GLP1	D,O	Roche	1	I
TERN-601	GLP1	O	Terns	1	O
liraglutide	GLP1	D	Dongguan HEC Bio	1	
semaglutide + NNC0165-1875	GLP1 / PPY	O	Novo Nordisk	3	I
semaglutide + NNC0165-1562	GLP1 / PPY	O	Novo Nordisk	1	I
semaglutide + cagrilintide ("CagriSema")	GLP1 / amylin	D, O	Novo Nordisk	3	I
amycretin (NNC0487-0111)	GLP1 / amylin	D, O	Novo Nordisk	2	O
semaglutide + bimagrumab	GLP1 / activin-2	O	Lilly (Versanis)	2	
tirzepatide (Monjaro, Zepbound)	**GLP1 / GIP**	**D, O**	**Lilly**	**FDA (2022)**	**I**
HRS-9531	GLP1 / GIP	D, O, overy cyst	Fujian Shengi Pharm	3	
AMG-133 (maridebart cafraglutide "maritide")	GLP1 / GIP antag	O	Amgen	2	I
RG6641 (CT-868)	GLP1 / GIP	D	Roche	2	I (once daily)
RG6640 (CT-388)	GLP1 / GIP	O	Roche	2	I
NNC0519-0130	GLP1 / GIP	O, D	Novo Nordisk	2	I
VK-2735	GLP1 / GIP	O	Viking Ther.	2	
HDM1005	GLP1 / GIP	D, O	Hangzhou Zhongmei Huadong	2	
GIP/GLP-1 Coagonist III	GLP1 / GIP	CVM	Lilly	1	O,I
SCO-094	GLP1 / GIP	D, O, NASH	Scohia Pharma	1	O
DR10628	GLP1 / GIP	O	Zhejiang Doer Bio	1	
MWN-115	GLP1 / GIP	O	Shanghai Minwei Bio	preclinical	
tirzepetide + midbavademab (REGN-4461)	GLP1 / GIP / leptin		Lilly	2	I
tirzpetide + eloralintide (LY3841136)	GLP1 / GIP / amylin		Lilly	2	I

Drug	MOA	Indication	Company	Phase	Formulation
retatrutide (LY3437943)	GLP1 / GIP / GCG	D, O, CV	Lilly	3	I
efocipegtrutide (HM15211)	**GLP1 / GIP / GCG**	**O, MASLD, NASH**	**Hanmi Pharma**	**FDA FastTrack (Ph2a & 2b)**	
MWN-101	GLP1 / GIP / GCG	O	Shanghai Minwei Bio	2	
HM15275	GLP1 / GIP / GCG	D, O, CVM	Hanmi Pharma	1	I
DR10627	GLP1 / GIP / GCG	O	Zhejiang Doer Bio	1	
MWN-109	GLP1 / GIP / GCG	O	Shanghai Minwei Bio	1	
HRS-4729	GLP1 / GIP / GCG	O	Hengrui Pharm	1	
pemvidutide (ALT-801)	GLP1 / GCG	O, MASH/NASH	Altimmune	3	I
survodutide	GLP1 / GCG	O, MASH	BI (w/ Zealand Pharma)	3	I
mazdutide (LY3305677)	GLP1 / GCG	O	Lilly	2	I
efinopegdutide	GLP1 / GCG	O, MASH	Hanmi Pharma	2	I
DA-1726	GLP1 / GCG	O	NeuroBo Pharm	1	
AZD9550	GLP1 / GCG	NASH	AstraZeneca	1	
DR10624	GLP1 / GCG / FGF21	O (with HT)	Hangzhou Zhongmei Huadong	2	
DR10624	GLP1 / GCG / FGF21	D, O, NASH	Zhejiang Doer Bio	2	
MWN-105	GLP1 / GCG / FGF21	NASH	Shanghai Minwei Bio	1	
MWN-103	GLP1 / GIP / GCG / FGF21	NASH, others?	Shanghai Minwei Bio	1	
dapiglutide	GLP1 / GLP2	O, inflam	Zealand Pharma	1	I
CIN-209	GLP1 / GD15	O	CinRx Pharm	preclinical	
CIN-210	GLP1 / PPY	O	CinRx Pharm	preclinical	
NNC0165-1875	PPY	O	Novo Nordisk	2	
NNC0165-1562	PPY	O	Novo Nordisk	1	
Y-14	PPY	O	Zihipp	1	
nisotirostide (+tirzepetide?)	PYY	D	Lilly	1	I
CIN-110	PPY	O	CinRx Pharma		
eloralintide (LY3841136)	amylin	O	Lilly	2	I
cagrilintide	amylin	O	Novo Nordisk	2	
AZD6234	amylin	O	AstraZeneca	2	
petrelintide (ZP8396)	amylin	O	Zealand Pharma	2	
XW015, XW016	amylin	D, O	Siwind Bio	2	O,I
amlyin agonist (long acting)	amylin	O	Lilly	1	
amylin 355	amylin	O	Novo Nordisk	1	I
GIPR Agonist Long Acting	GIP	CVM	Lilly	1	
macupatide	GIP	CVM	Lilly	1	I
XW017	GIP	D, O	Sciwind	1	
ZP6590	GIP	O	Zealand Pharma	preclinical	
setmelanotide (IMCIVREE)	MC4	O	Rhythm Pharm	3	FDA (2020)
bivamelagon (LB-54640)	MC4	O	Rhythm Pharm	2	
CIN-109 (JNJ-9090)	GD15	O	CinRx Pharm	2	
NNC247-0829	GD15	O	Novo Nordisk	1	
Glucose sensing insulin receptor agonist	GSI	D	Lilly	1	
Glucose sensitive insulin analouge	GSI	D	Novo Nordisk	1	O

USC

Source: Daniel Falk, NIH/NIAAA

Information publicly available (e.g., Melson et al., *Int J Obes*, *49*, 433-451, 2025)

USC Institute for Addiction Science

Team Science Approach

Pharmacotherapies for Alcohol And Substance Use Disorders Alliance (PASA) AUD Trial

Christian Hendershot, PhD
Principal Investigator

Lorenzo Leggio, MD, PhD
Principal Investigator

Anders Fink-Jensen, MD, DMSci
Collaborating Investigator

Joseph Schacht, PhD
Collaborating Investigator

Kyle Simmons, PhD
Collaborating Investigator

Klara Klein, MD
Collaborating Investigator

Mehdi Farokhnia, MD, MPH
Collaborating Investigator

Mette Kruse Klausen, MD, PhD
Collaborating Investigator

Elliott Pauli, MPH, BS, PMP
Collaborating Investigator

Andrew Saxon, MD
Collaborating Investigator

USC

USC Institute for Addiction Science

Acknowledgements

Project Co-Investigators & Consultants

Klara Klein, M.D., Ph.D.

Amanda Tow, M.D., Ph.D.

Robyn Jordan, M.D., Ph.D.

Sarah Dermody, Ph.D.

Sherry McKee, Ph.D.

Eric Claus, Ph.D.

Paul Fletcher, Ph.D.

Students and Staff

Michael Bremmer

Michael Paladino

Georgios Kostantinis

Tom Gilmore

Neil Sullivan

Andrew Jenkins

Mengshan Zhang

EndoCRU Staff

Funding and Support

NIAAA R21AA026931, NIDA R21DA047663,

Pharmacotherapies for Alcohol and Substance Use Disorders Alliance (PASA)

Department of Psychiatry and Bowles Center for Alcohol Studies, UNC-Chapel Hill

NC Translational and Clinical Sciences Institute (NIH UM1TR004406)

USC

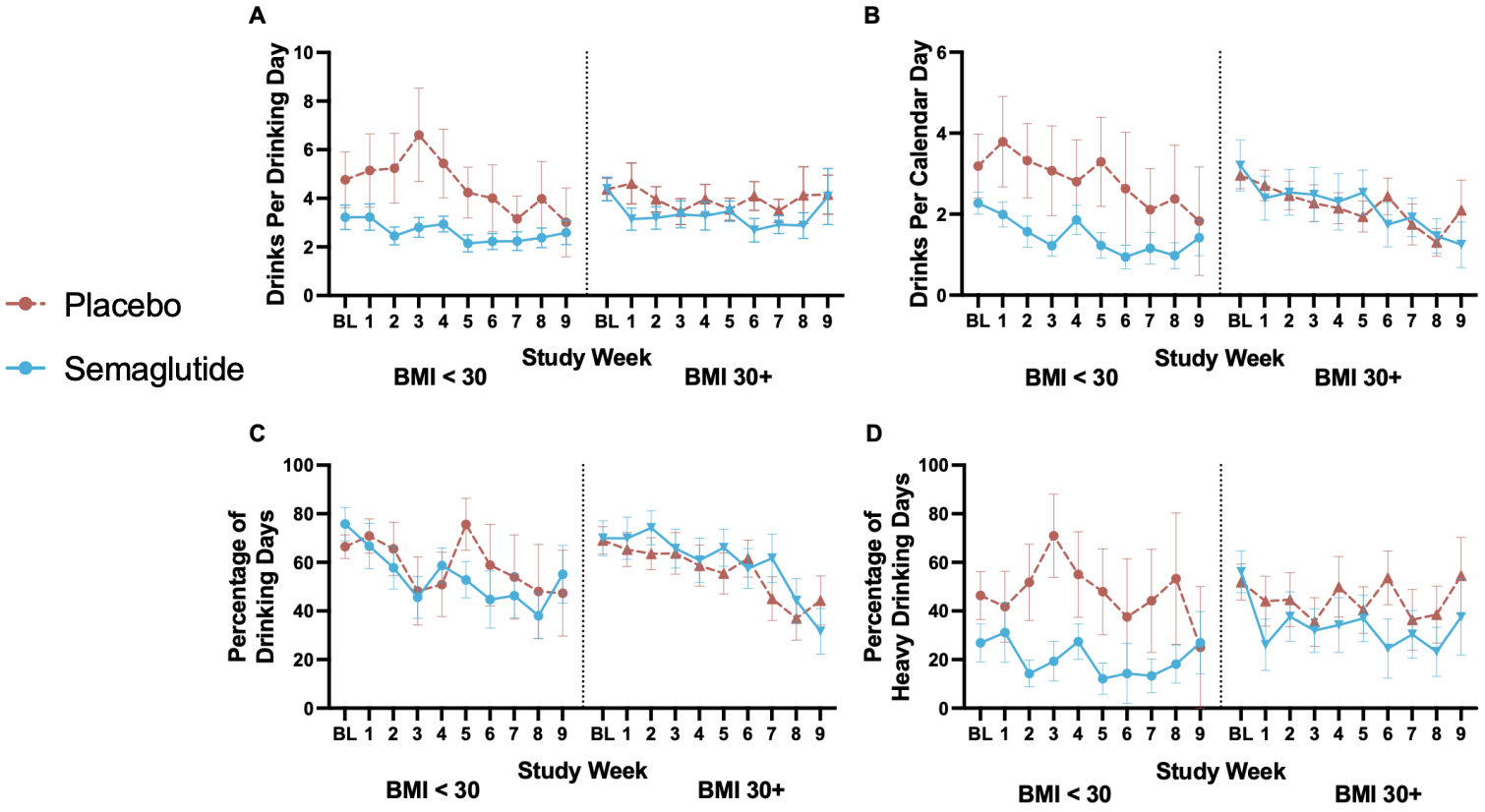
USC Institute for Addiction Science

USC

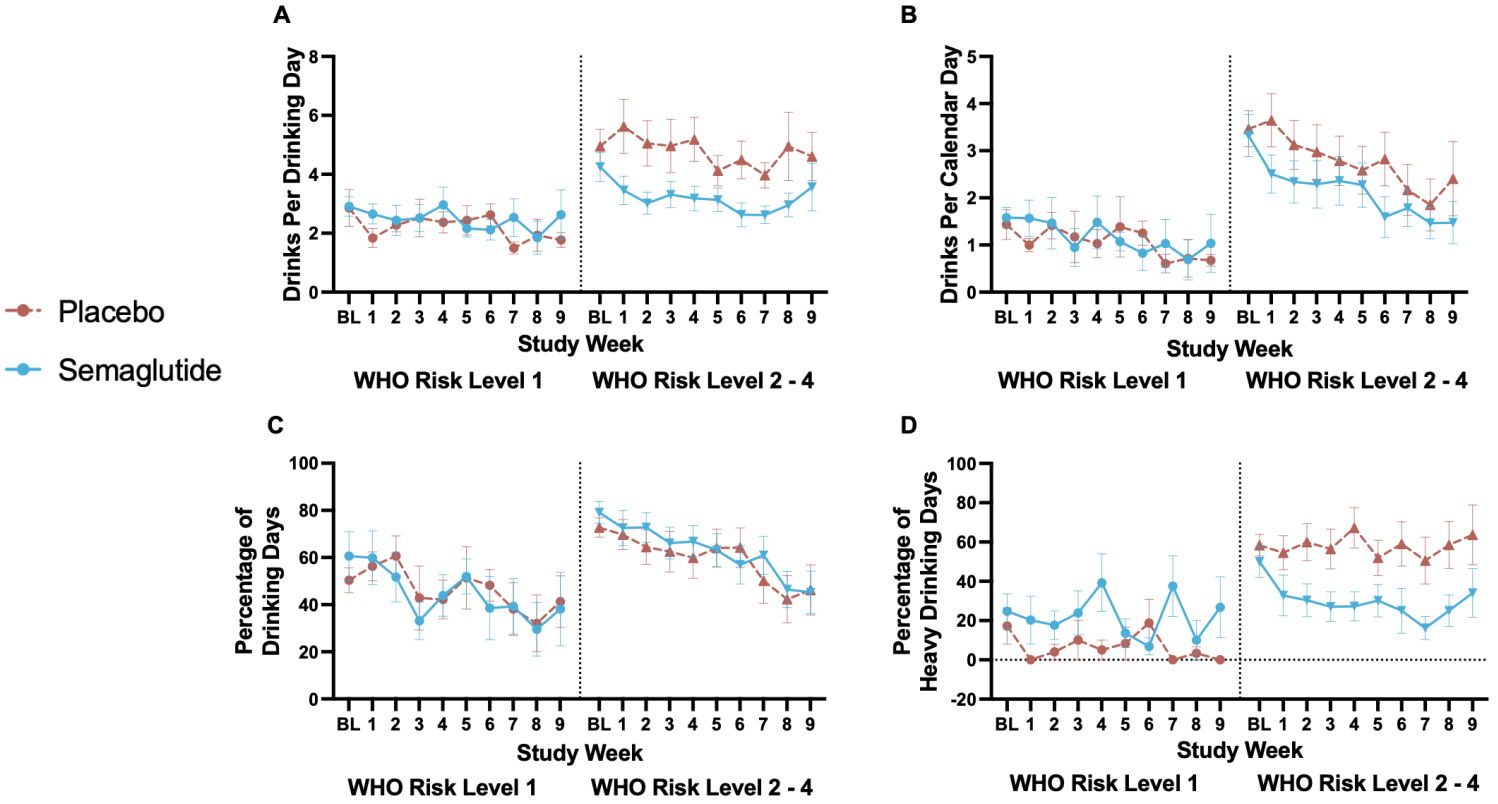
Contact: christian.hendershot@usc.edu

USC Institute for Addiction Science

Stratification by Baseline BMI



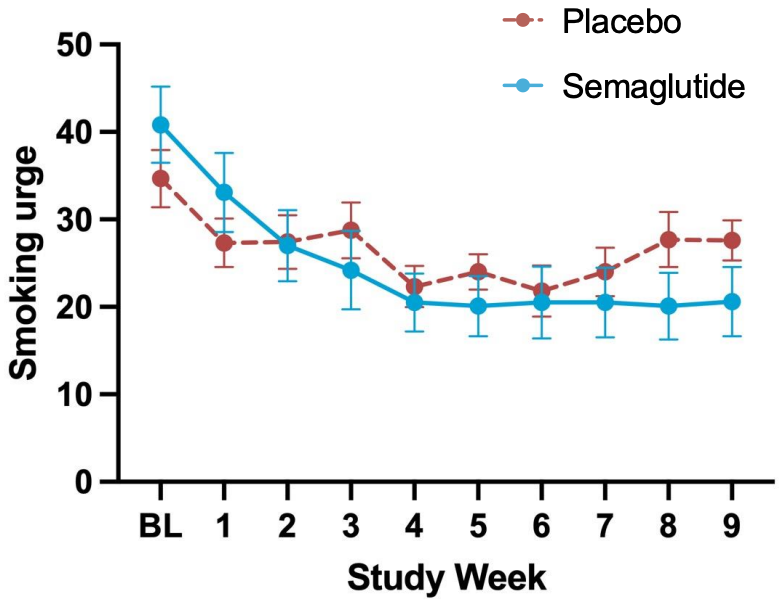
Stratification by Baseline Drinking (WHO Risk Level)

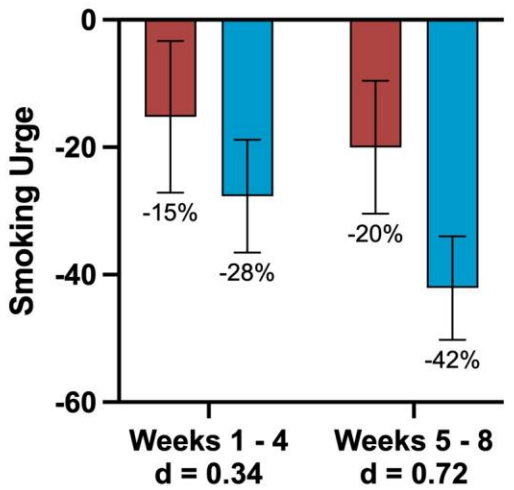


USC

USC Institute for Addiction Science

Preliminary Data from Phase II Trial of Daily Smokers
NIDA R21DA047663 (N=24 randomized)
Weekly Changes in Smoking Urge (TQSU)

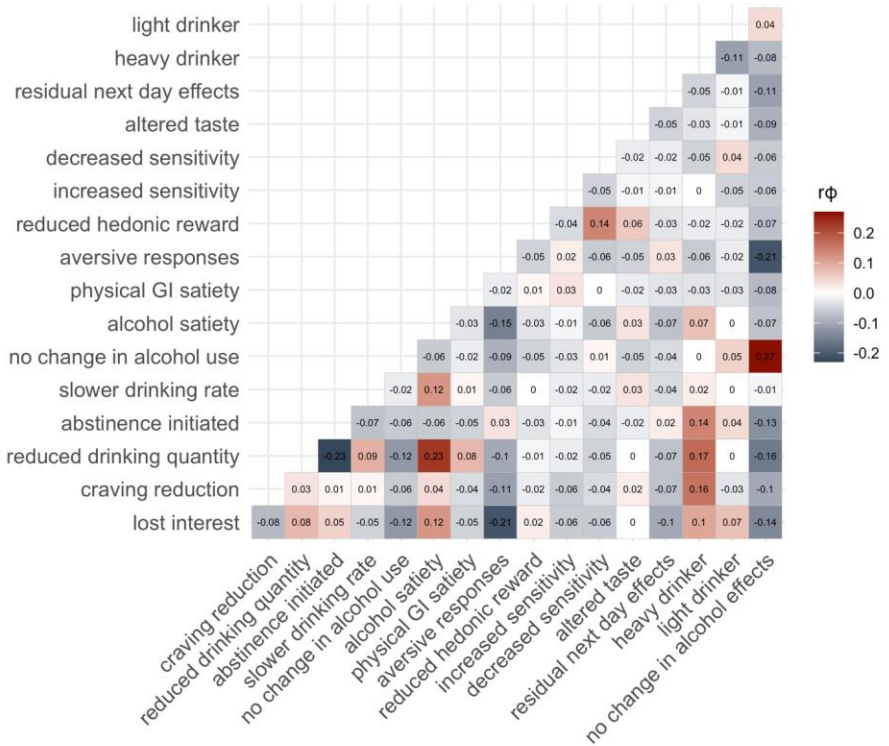




Medication: b = -0.41; 95% CI [-6.90, -7.71]; p = .91
Time: b = -.31; 95% CI [-.82, -.19]; ***p* <.001**
Time x Medication: b = -.96; 95% CI [-1.68, .23]; ***p* = .01**

Social Media as Pharmacovigilance?
Observational Data from Online Reports (Reddit)

	Count (Total=1503)	Frequency
Lost interest in alcohol	428	28.5%
Craving reduction	157	10.4%
Consumption patterns		
reduced drinking quantity	466	31.0%
initiated abstinence	163	10.8%
slower drinking rate	57	3.8%
no change in alcohol use	50	3.3%
drinking more	10	0.7%
Satiety		
alcohol satiety (satisfied without drinking, or drinking less)	154	10.2%
physical/gastrointestinal	64	4.3%
Subjective response		
aversive responses while drinking	396	26.3%
reduction in hedonic/rewarding effects	101	6.7%
altered taste	99	6.6%
increased sensitivity to alcohol effects	91	6.1%
decreased sensitivity to alcohol effects	50	3.3%
improved control over consumption	19	1.3%
Residual/next-day effects		
headache/hangover	86	5.7%
residual nausea	57	3.8%
other	47	3.1%
Participant characteristics		
heavy drinker	211	14.0%
light drinker	102	6.8%
Other		
no change in alcohol effects	176	11.7%
missing drinking	47	3.1%
skipping medication dose to facilitate drinking	10	0.7%
sought medication to decrease drinking	3	0.2%



Bremmer & Hendershot (2024) *J Stud Alcohol Drugs*

Pharmacoepidemiology Findings

- GLP-1RA exposure associated with:
  - Reduced incidence of alcohol-related medical contacts in the early months of treatment (Wium-Andersen et al., 2022; Danish population registry)
  - Lower incidence and recurrence of AUD diagnoses (Wang et al., 2024; TriNetX)
  - Lower alcohol intoxication events in those with AUD (Qeadan et al., 2025; Cerner)
  - Lower risk of AUD-related hospitalizations (Lahteenvuo et al., 2025; Swedish healthcare registry)
  - Greater reductions in self-reported alcohol consumption (Farokhnia et el., 2025; Department of Veterans Affairs data)
  - Reduced risk of AUD and other substance use disorders (Xie et al., 2025; U.S. Department of Veterans Affairs data)