



Weight Loss and Cardiovascular Disease Risk Outcomes of Semaglutide: A One-year Multicentered Cohort Study

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Disclosures

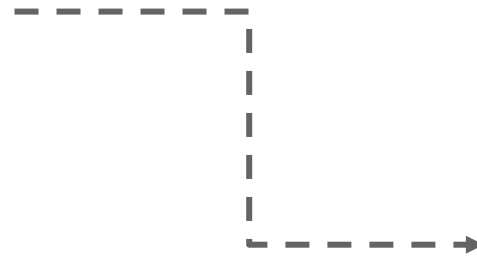
Gila Therapeutics and Phenomix Sciences have licensed Dr. Acosta's research technologies from University of Florida and Mayo Clinic.

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OBESITY- The #1 Chronic Disease

40%
of US adults
are affected by obesity



Obesity leads to
heart disease, stroke,
type 2 diabetes
mellitus (T2DM),
cancer, and
premature death

Obesity drives
\$480B
of direct annual
healthcare costs¹

¹ Milken Institute: America's Obesity Crisis. 2018.

Weight Management Interventions

- **Lifestyle interventions and diets**
- **Anti-obesity medications (AOMs)**
 - Orlistat
 - Phentermine-topiramate
 - Naltrexone-bupropion
 - Liraglutide
 - **Semaglutide**
- **Bariatric procedures**
 - Surgeries
 - Endoscopic interventions

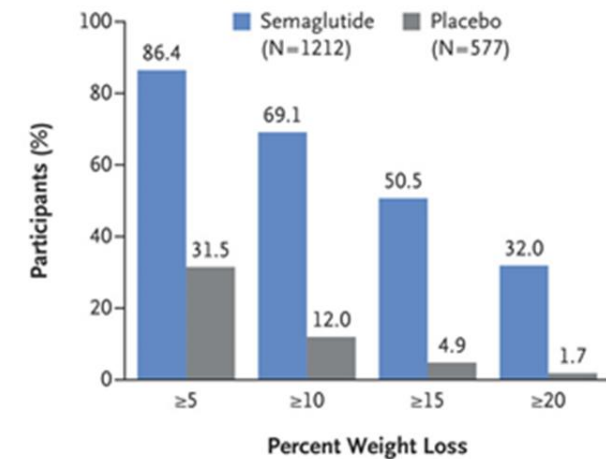
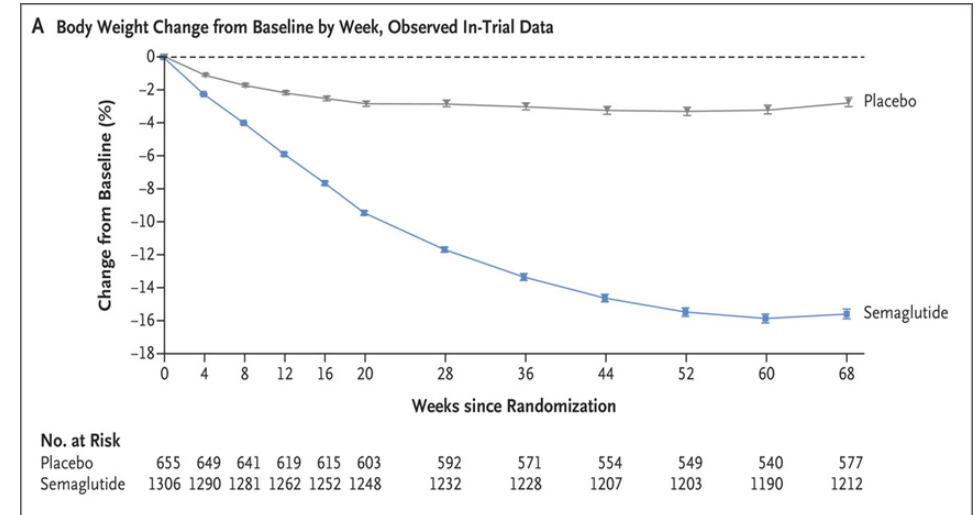
Glucagon-like Peptide-1 Receptor Agonists

- Semaglutide is approved for obesity and T2DM.
- **Mechanism of action:**
 - Induces fullness and slows gastric emptying.¹
 - Stimulates secretion of insulin.²
- **Dosing:**
 - Subcutaneous weekly injections.
 - Dose-escalation protocol (start 0.25 mg, increase monthly).
 - T2DM: 1 and 2 mg.
 - Obesity: 2.4 mg.

RCT: STEP 1 Trial

- Patients without T2DM on 2.4 mg
- TBWL at 68 weeks: 16%

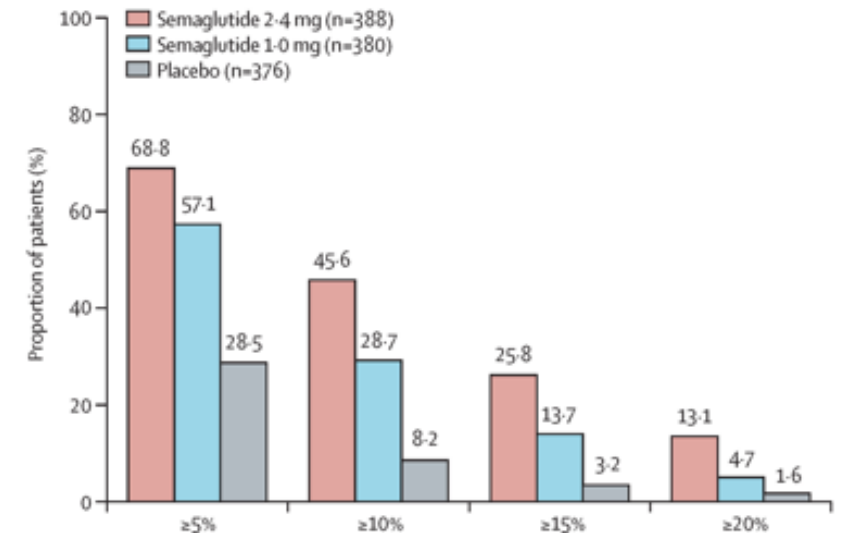
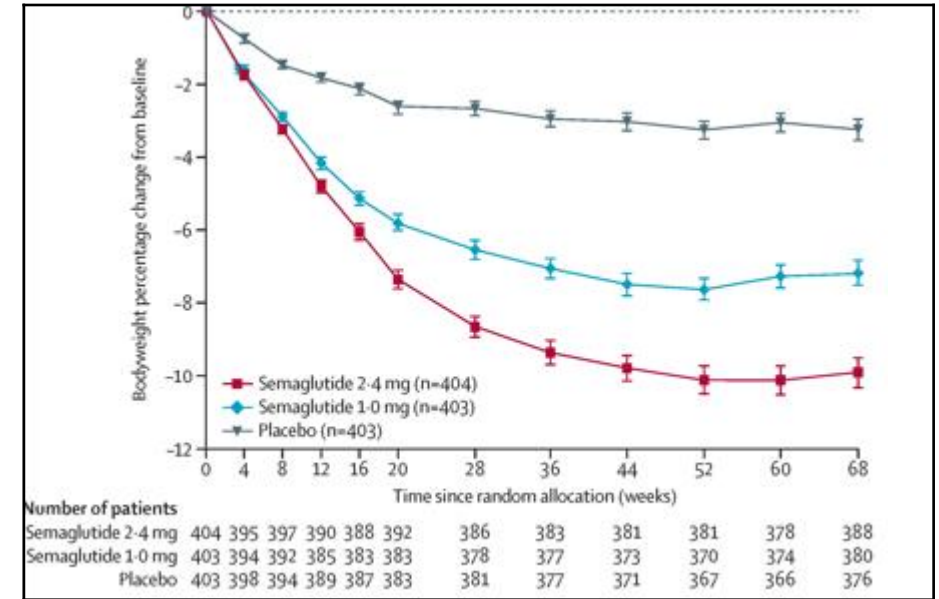
- TBWL $\geq 5\%$: 86.4% of patients
- TBWL $\geq 10\%$: 69.1% of patients
- TBWL $\geq 15\%$: 50.5% of patients
- TBWL $\geq 20\%$: 32.0% of patients



RCT: STEP 2 Trial

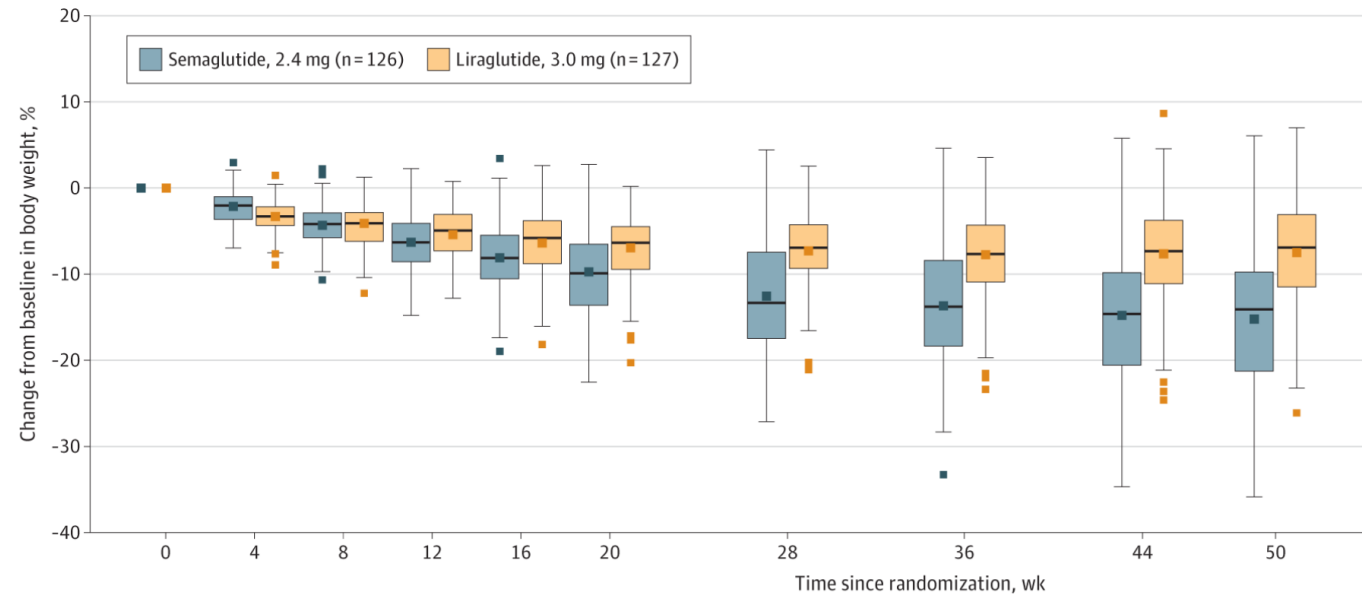
- Patients with T2DM
- 2.4 mg vs 1.0 mg vs Placebo
- TBWL: 9.6% vs 7.0% vs 3.4%

- TBWL $\geq 5\%$: 69% vs 57% vs 29%
- TBWL $\geq 10\%$: 46% vs 29% vs 8%
- TBWL $\geq 15\%$: 26% vs 14% vs 3%
- TBWL $\geq 20\%$: 13% vs 5% vs 2%



RCT: STEP 8 Trial

- **Semaglutide 2.4 mg vs Liraglutide 3.0 mg**
- **TBWL: 15.8% vs 6.4%**



No. of participants
Semaglutide, 2.4 mg
Liraglutide, 3.0 mg

126	125	122	124	117	102	76	105	114	107
127	124	124	125	118	101	66	102	99	98

Background

- **Superior weight loss outcomes compared to other AOMs.**
- **Improvement in metabolic and anthropometric characteristics.**
- **Limited data on real-world outcomes of semaglutide.**

Hypothesis

- **Question:**

- What are the weight loss and metabolic outcomes of semaglutide in real-world setting?

- **Hypothesis:**

- Similar outcomes between RCTs and real-world studies.



Aims

- **Primary End point:**

- Weight loss outcomes at 12 months.

- **Secondary Outcomes:**

- Weight loss outcomes at 3, 6, and 9 months.
- Metabolic and comorbidities changes.
- Compare weight loss outcomes by T2DM status and semaglutide dose.
- Cardiovascular disease risk improvement.
- Side effect profile.

Methods

- **Multicentered retrospective cohort study**
 - Mayo Clinic Hospitals in Minnesota, Florida, Arizona and other affiliated hospitals in the Mayo Clinic Health System.
 - January 1, 2021, and January 15, 2023.
- **Intervention**
 - Subcutaneous weekly semaglutide injections.
 - Purpose: weight loss.
 - Doses: 0.25, 0.5, 1, 1.7, 2, and 2.4 mg.

Methods

- **Inclusion Criteria:**

- 1. BMI \geq 27 kg/m²
- 2. Taking semaglutide

- **Exclusion Criteria:**

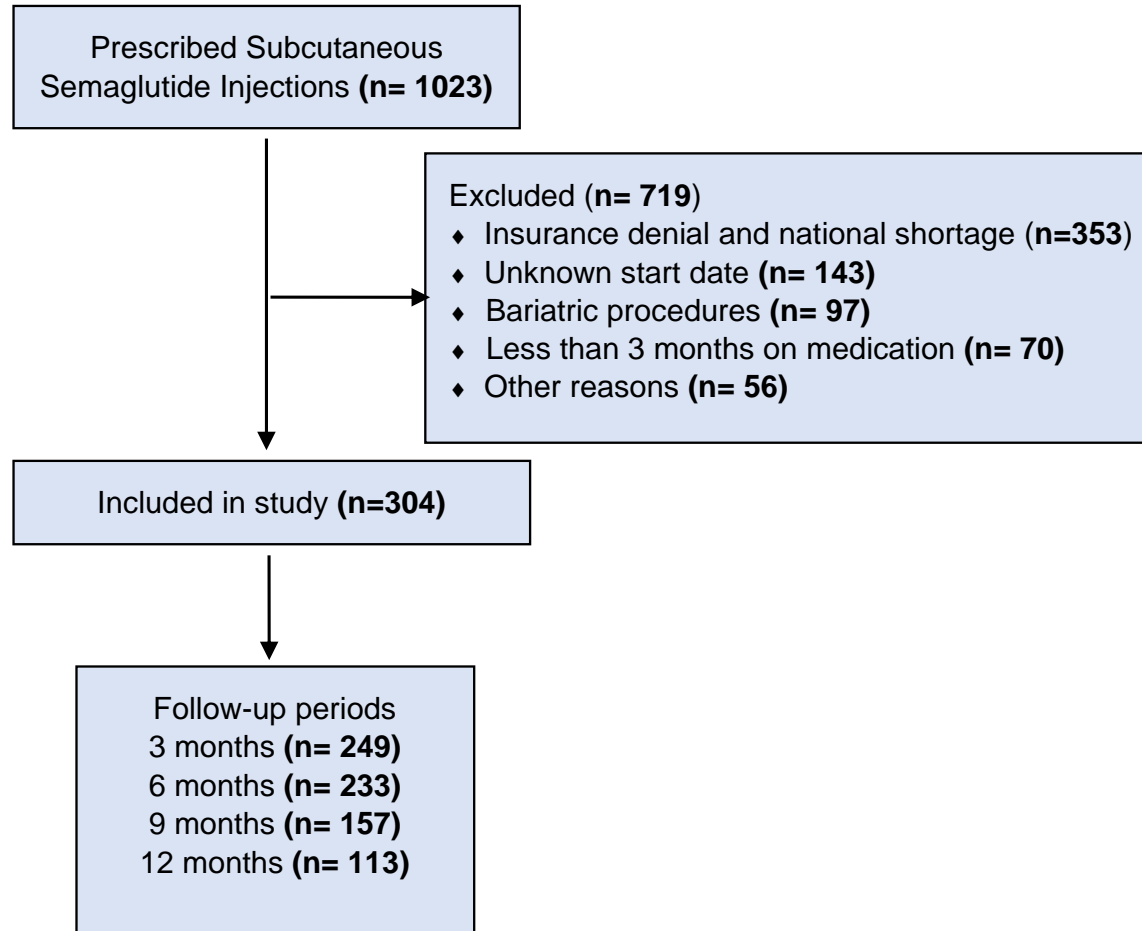
- 1. History of bariatric surgery
- 2. Taking another AOM
- 3. Active malignancy or pregnancy

Statistical Analysis

- **Primary end point:**
 - Matched paired t-test.

- **Secondary end points:**
 - Categorical data with a Fisher exact test.
 - Continuous data using 2-sample independent t-test.

Results



Baseline Demographic Data

Demographic information	All patients
<i>N</i>	304
Age, years (SD)	49 (12)
Sex (%)	
Female	222 (73)
Male	82 (27)
Race (%)	
White	284 (93)
Asian	11 (4)
Black or African American	9 (3)
Anthropometric characteristics	
Weight, mean (SD), kg	118 (30)
Body-mass index, kg/m²	
Mean	40.8 (9.6)
Distribution, (%)	
27-30	13 (4)
≥30 to <35	75 (25)
≥35 to <40	89 (26)
≥40	136 (45)

Obesity Comorbidities

Medical Comorbidities, n (%)	
Dyslipidemia	155 (51)
Prediabetes	47 (16)
Diabetes mellitus	81 (27)
Hypertension	148 (49)
GERD	112 (37)
Obstructive sleep apnea	115 (38)
NAFLD	42 (13)
Major depressive disorder	117 (38)
Anxiety	113 (37)

Blood Pressure and Baseline Labs

Blood Pressure, mean, (SD), mmHg	
Systolic Blood pressure	129 (15)
Diastolic blood pressure	80 (10)
Laboratory tests (SD)	
Fasting blood glucose, n=244	117 (44)
Glycated hemoglobin, n=190	6.2 (1.3)
Total cholesterol, n=256	180 (41)
HDL cholesterol, n=256	49 (13)
LDL cholesterol, n=250	102 (36)
Triglycerides, n=256	148 (77)
ALT, n=42	64 (58)
AST, n=42	46 (34)
Total Bilirubin, n=42	0.5 (0.3)

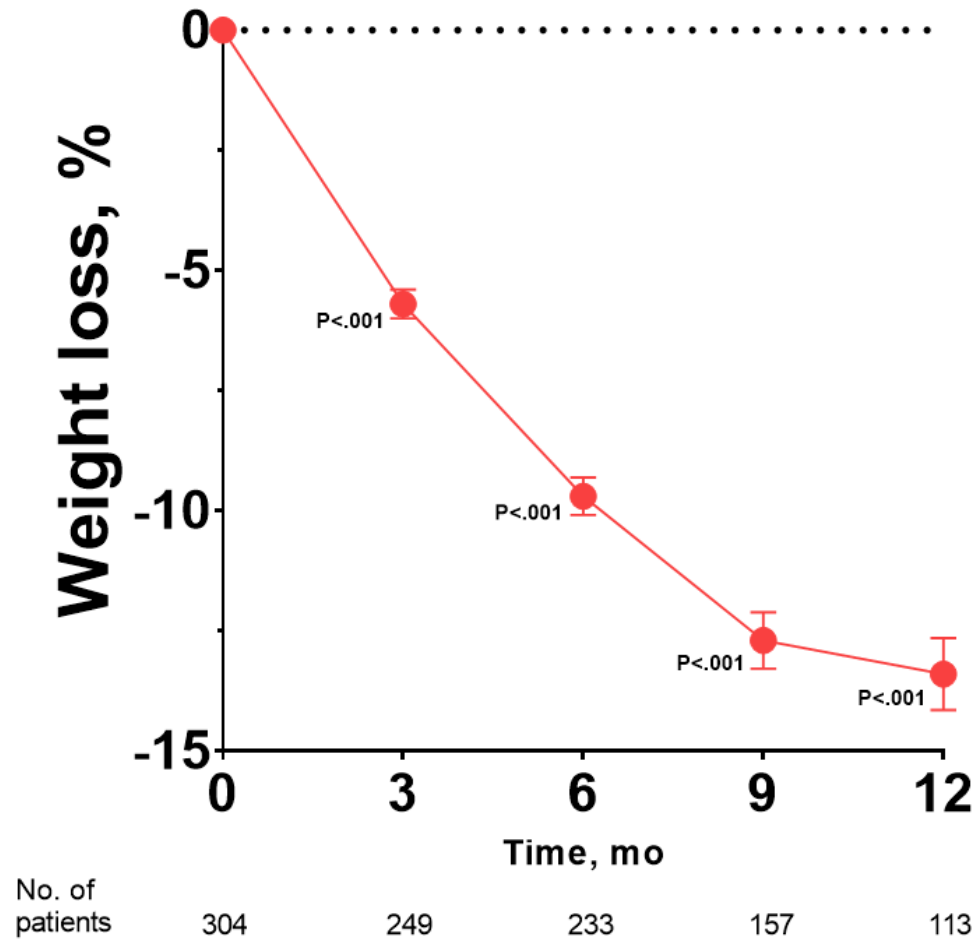
Dietitian and Psychology Visits

Visits Information, n (%)	
Patients with dietitian visits	73 (24)
Patients with psychologist visit	32 (11)

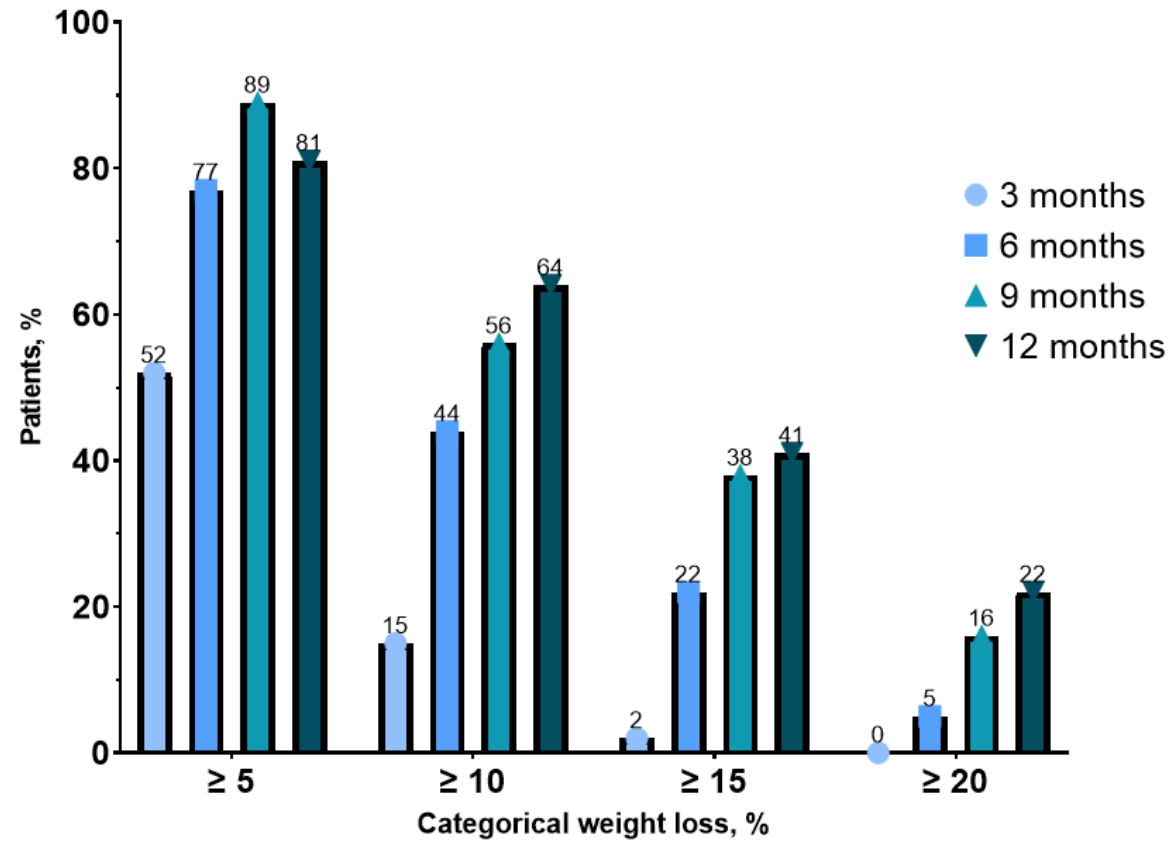
Visits Type

Visit Type (%)	In-person	Virtual
Baseline	289 (95)	15 (5)
3 months	220 (88)	29 (12)
6 months	215 (92)	18 (8)
9 months	147 (94)	10 (6)
12 months	105 (93)	8 (7)
Total	976 (92)	80 (8)

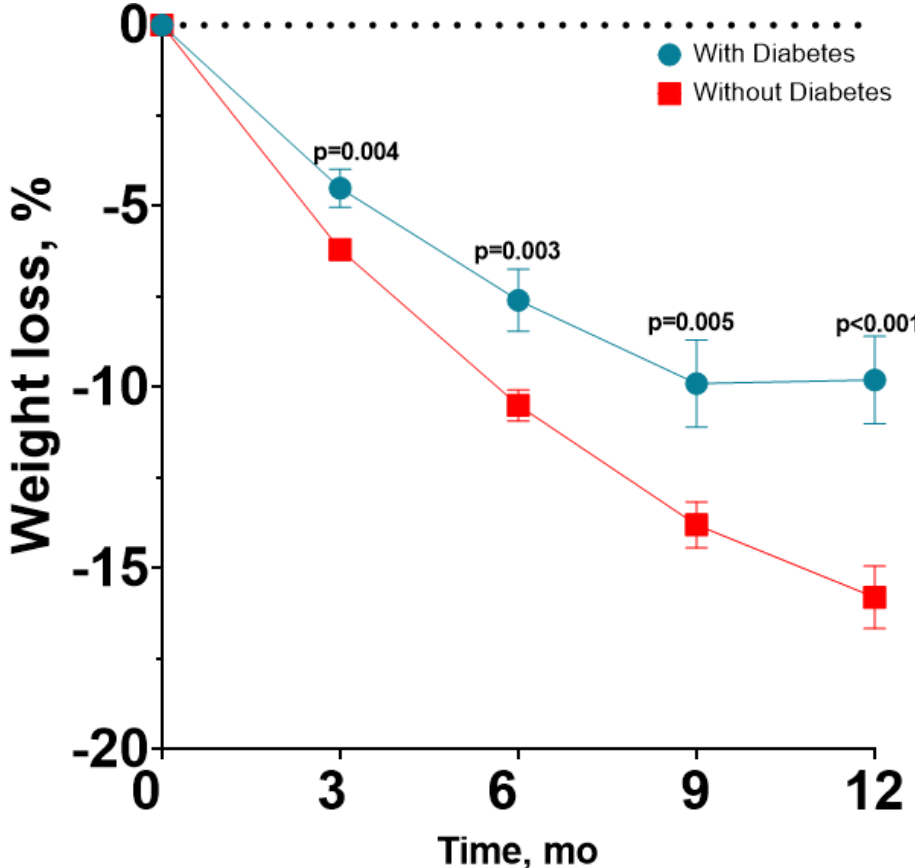
Weight loss Outcomes



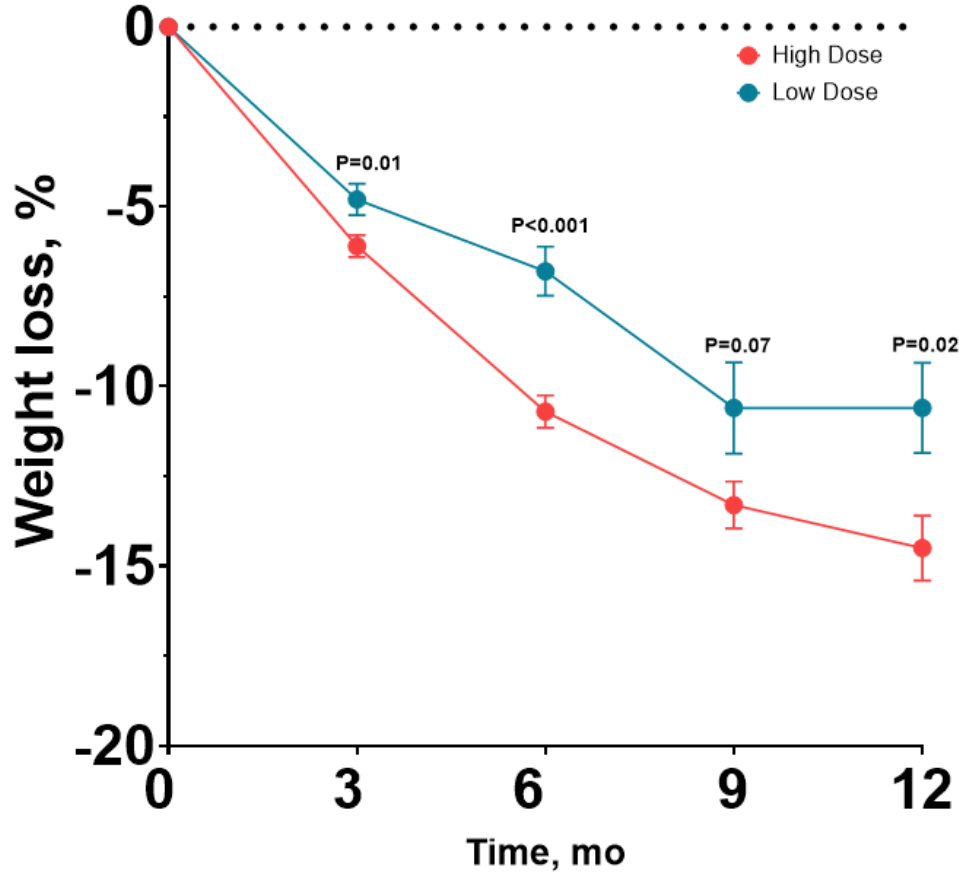
Categorical weight loss outcomes



Weight Loss Outcome with T2DM



Weight Loss Outcome with Semaglutide Doses



Metabolic Changes

Clinical and Laboratory Information	Baseline	Follow-up	Difference	95% CI	p-value
Blood pressure					
SBP, mmHg, n=263	129 (15)	122 (13)	-6.8	-8.5 to -5.1	<0.001
DBP, mmHg, n=263	80 (10)	77 (9)	-2.6	-3.9 to -1.2	<0.001
Glucose Homeostasis					
Fasting Glucose, mg/dL, n= 128	125 (60)	106 (38)	-19	-28.3 to -10.1	<0.001
HbA1c, %, n=107	6.6 (1.7)	5.9 (1.2)	-0.72	-0.9 to -0.5	<0.001
Lipid Panel					
Total Cholesterol, mg/dL, n= 132	179 (42)	169 (39)	-10.3	-16.0 to -4.7	<0.001
Total Triglycerides, mg/dL, n= 131	155 (88)	134 (73)	-20.4	-33.6 to -7.2	0.003
LDL, mg/dl, n= 129	101 (36)	96 (35)	-5.2	-10.0 to -0.4	0.04
HDL, mg/dl, n= 131	48 (14)	48 (13)	-0.1	-1.5 to 1.4	0.95
Liver Function Tests					
AST, U/L, n= 34	50 (34)	37 (24)	-13.1	-23.5 to -2.7	0.02
ALT, U/L, n= 34	70 (58)	45 (39)	-24.9	-42.0 to -7.7	0.006

Cardiovascular disease risk

Cardiovascular risk	Baseline	Follow-up	Difference	95% CI	p-value
10-year ASCVD risk, n= 103	8.0 (8.3)	6.7 (6.4)	-1.3	-2.1 to -0.6	<0.001

Comorbidity Medication Change

Comorbidities Medications/treatments number	Baseline	Follow-up	Difference	95% CI	p-value
Hypertension, n=148	1.75 (0.98)	1.66 (1.03)	-0.08	-0.17 to 0.01	0.08
Dyslipidemia, n=154	0.99 (0.86)	0.97 (0.87)	-0.03	-0.09 to 0.04	0.4
Diabetes Mellitus, n=81	2.07 (1.23)	2.01 (1.22)	-0.06	-0.19 to 0.07	0.8
GERD, n= 112	0.79 (0.49)	0.72 (0.52)	-0.06	-0.13 to 0.01	0.09
Depression/anxiety, n=168	1.33 (0.84)	1.30 (0.88)	-0.04	-0.1 to 0.05	0.4

Side Effect Profile

Side effects, N (%)	304 (100)
Total number of patients with side effects	154 (51)
Nausea/vomiting	116 (38)
Diarrhea	27 (9)
Abdominal pain	25 (8)
Constipation	23 (8)
Fatigue	21 (7)
Acid Reflux	11 (4)
Headache	8 (3)
Dizziness	7 (2)
Bloating	7 (2)
Others	5 (2)
Side Effects Severity, N (%)	
None	150 (49)
Mild	106 (35)
Moderate	32 (11)
Severe	16 (5)

Strengths

- Adequate sample size from multiple health centers.
- Follow-up of 1-year.
- Objective measurement of metabolic and cardiovascular disease risk outcomes.
- Lack of similar real-world data in the literature.

Limitation

- Lacking a control group (e.g., lifestyle intervention alone).
- Majority of White female.
- Increased susceptibility to coding errors and inaccurate documentation in the extraction phase.
- Some weight measurements collected from virtual visits .
 - Uncalibrated scales.

Conclusion

- In this study, patients with overweight or obesity achieved significant weight loss, metabolic, and cardiovascular disease risk outcomes after taking semaglutide for weight loss.
- These results demonstrate the effectiveness and tolerability of this medication in enhancing weight loss outcomes.
- More studies with longer follow-up periods are needed to evaluate changes in body weight after stopping this medication.



Thank you for your attention!
Questions or Comments?



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