



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

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# Disclosures

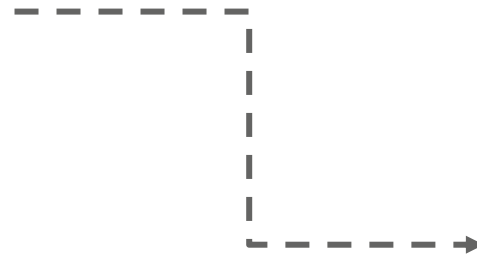
Gila Therapeutics and Phenomix Sciences have licensed Dr. Acosta's research technologies from University of Florida and Mayo Clinic.

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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 costs<sup>1</sup>

<sup>1</sup> 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

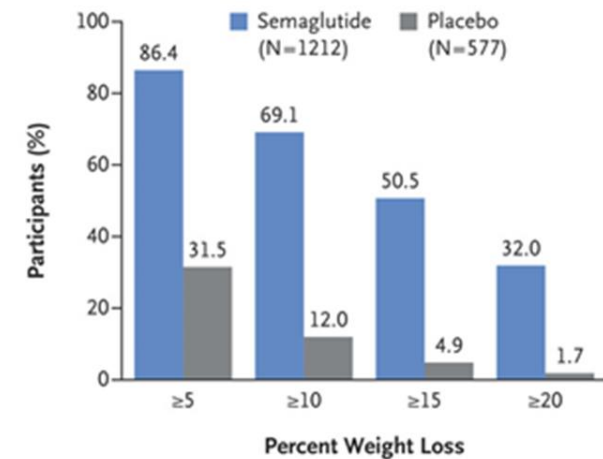
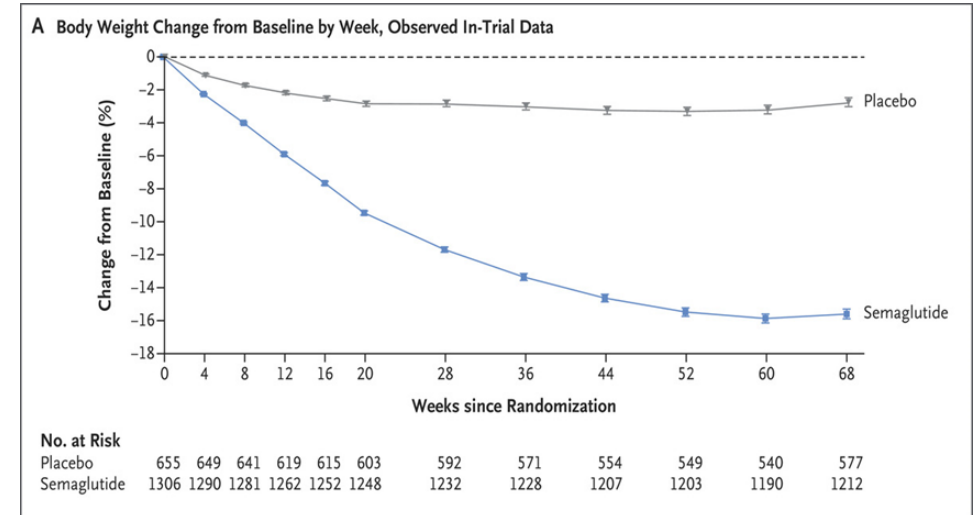
# Glucagon-like Peptide-1 Receptor Agonists

- Semaglutide is approved for obesity and T2DM.
- **Mechanism of action:**
  - Induces fullness and slows gastric emptying.<sup>1</sup>
  - Stimulates secretion of insulin.<sup>2</sup>
- **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%

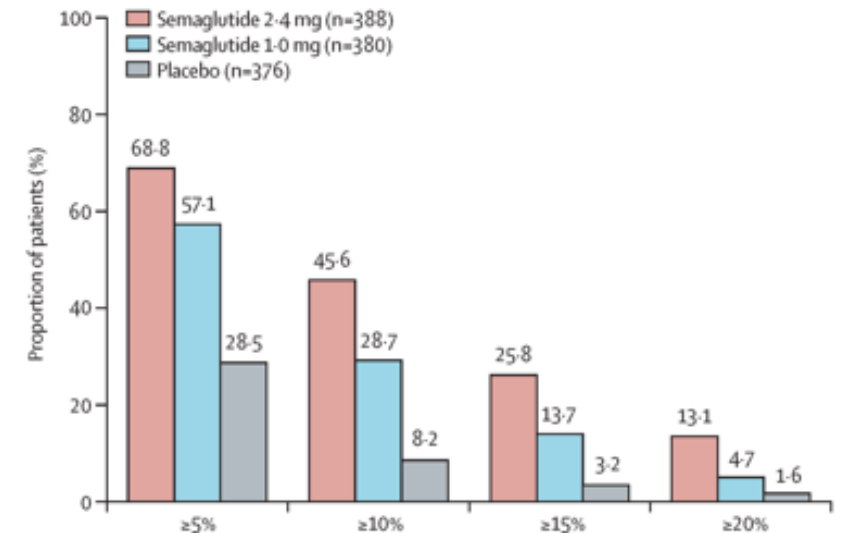
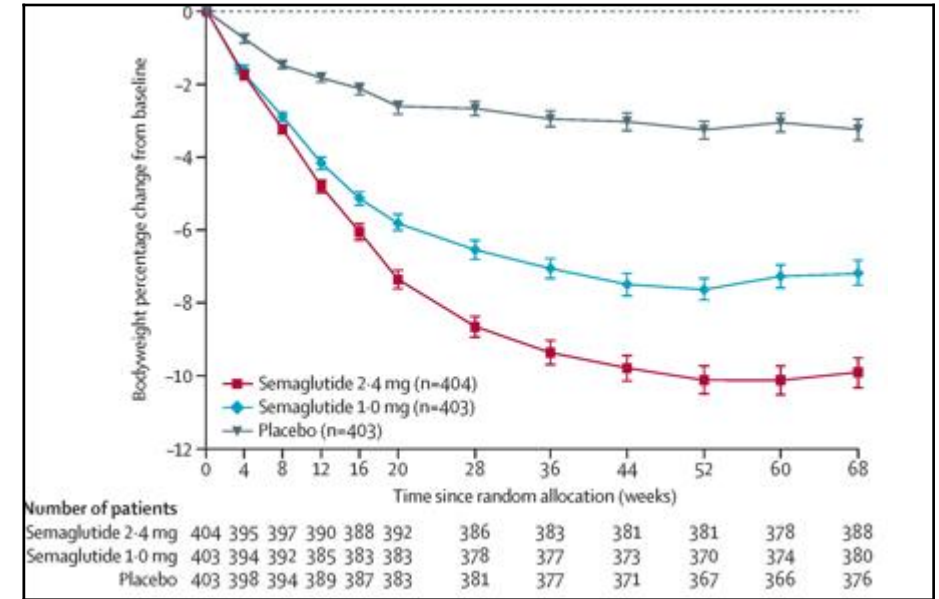
- TBWL  $\geq 5\%$ : 86.4% of patients
- TBWL  $\geq 10\%$ : 69.1% of patients
- TBWL  $\geq 15\%$ : 50.5% of patients
- TBWL  $\geq 20\%$ : 32.0% of patients



# RCT: STEP 2 Trial

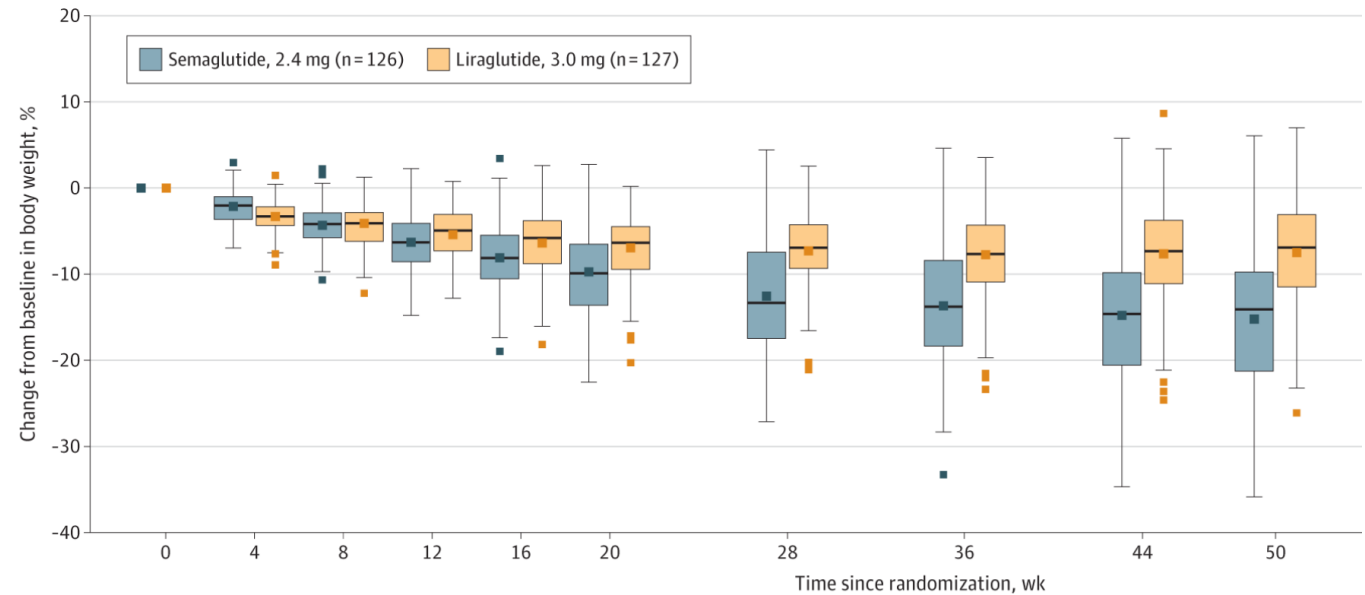
- Patients with T2DM
- 2.4 mg vs 1.0 mg vs Placebo
- TBWL: 9.6% vs 7.0% vs 3.4%

- 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 | 0   | 4   | 8   | 12  | 16  | 20  | 28 | 36  | 44  | 50  |
|---------------------|-----|-----|-----|-----|-----|-----|----|-----|-----|-----|
| Semaglutide, 2.4 mg | 126 | 125 | 122 | 124 | 117 | 102 | 76 | 105 | 114 | 107 |
| Liraglutide, 3.0 mg | 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/m<sup>2</sup>
- 2. Taking semaglutide

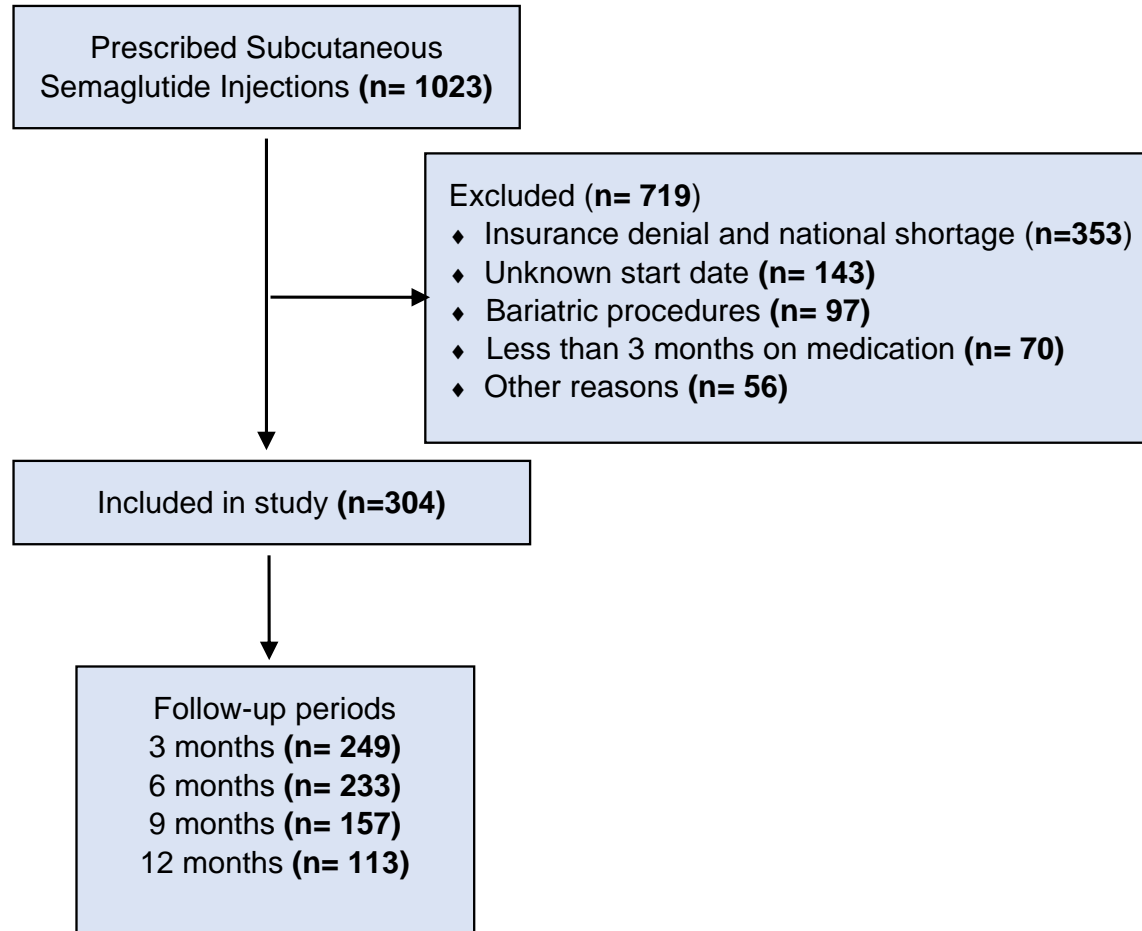
- **Exclusion Criteria:**

- 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)      |
| <b>Sex (%)</b>                           |              |
| Female                                   | 222 (73)     |
| Male                                     | 82 (27)      |
| <b>Race (%)</b>                          |              |
| White                                    | 284 (93)     |
| Asian                                    | 11 (4)       |
| Black or African American                | 9 (3)        |
| <b>Anthropometric characteristics</b>    |              |
| Weight, mean (SD), kg                    | 118 (30)     |
| <b>Body-mass index, kg/m<sup>2</sup></b> |              |
| Mean                                     | 40.8 (9.6)   |
| <b>Distribution, (%)</b>                 |              |
| 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

| <b>Blood Pressure, mean, (SD), mmHg</b> |           |
|---|-----------|
| Systolic Blood pressure                 | 129 (15)  |
| Diastolic blood pressure                | 80 (10)   |
| <b>Laboratory tests (SD)</b>            |           |
| 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) |

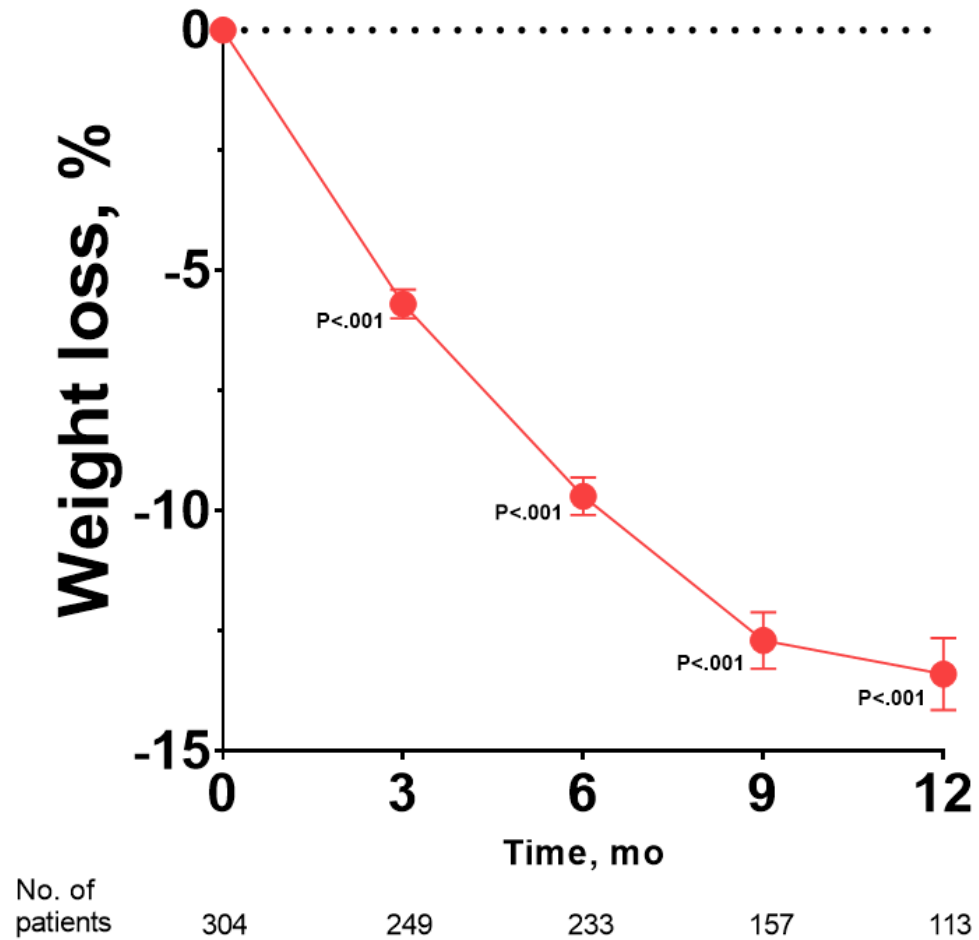
# Dietitian and Psychology Visits

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

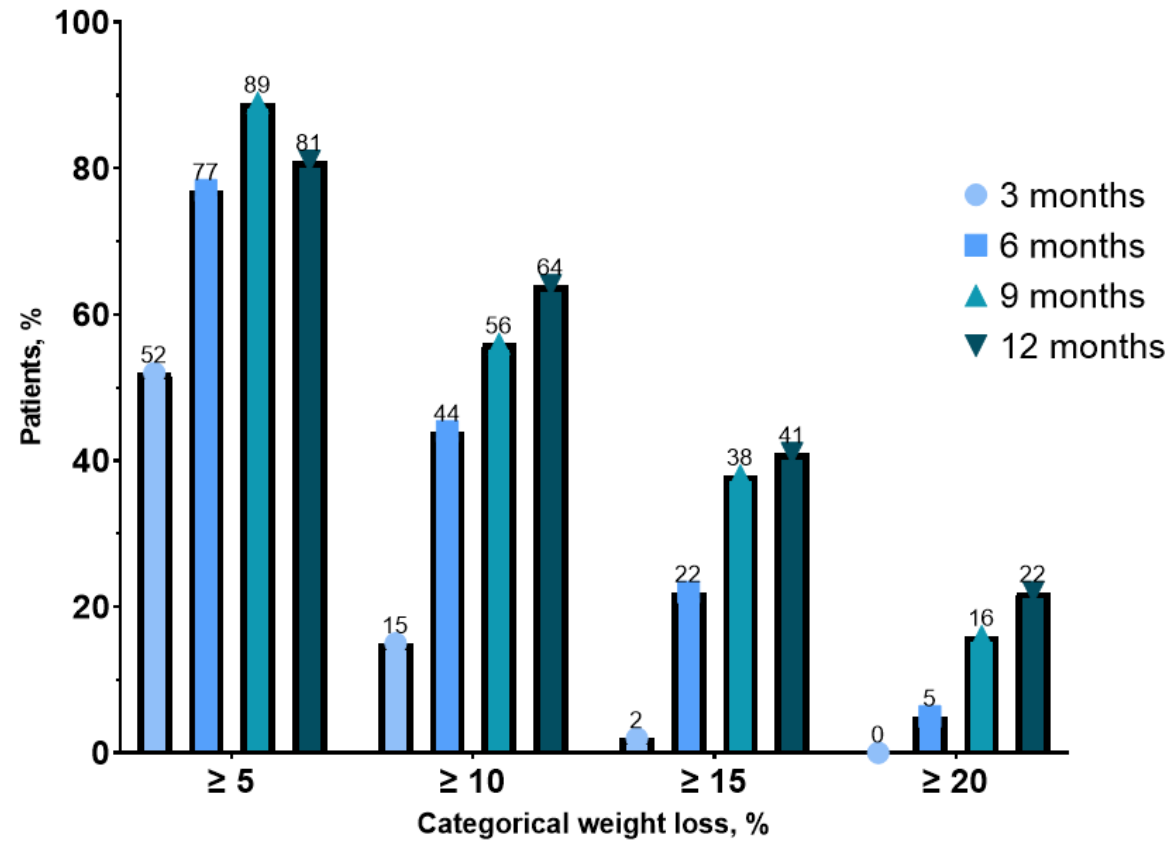
# Visits Type

| 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)  |

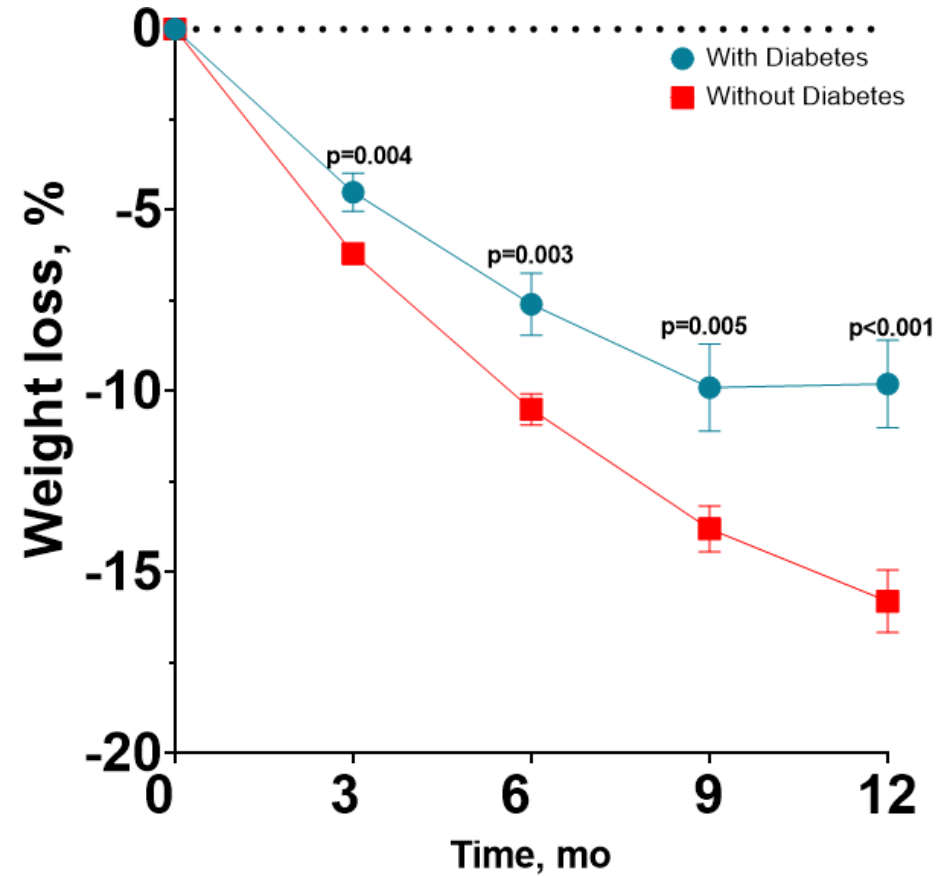
# Weight loss Outcomes



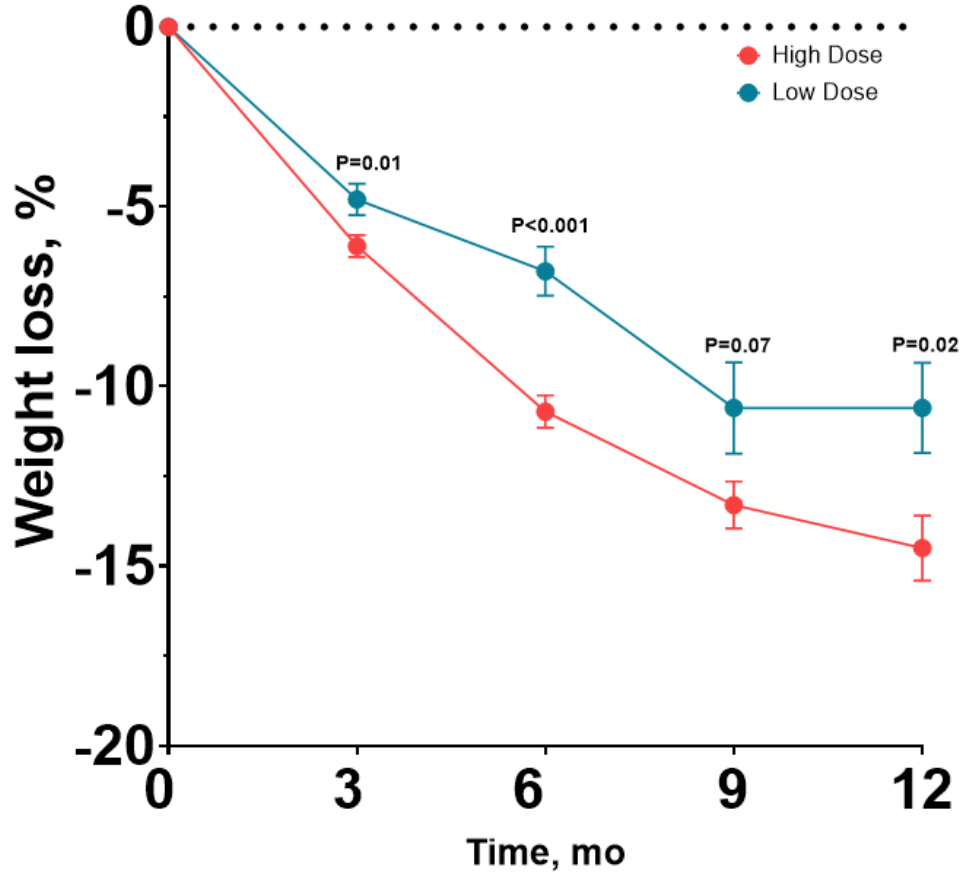
# Categorical weight loss outcomes



# 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 |
|-------------------------------------|-----------|-----------|------------|----------------|---------|
| <b>Blood pressure</b>               |           |           |            |                |         |
| 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  |
| <b>Glucose Homeostasis</b>          |           |           |            |                |         |
| 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  |
| <b>Lipid Panel</b>                  |           |           |            |                |         |
| 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    |
| <b>Liver Function Tests</b>         |           |           |            |                |         |
| 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

| <b>Side effects, N (%)</b>                 | <b>304 (100)</b> |
|--|------------------|
| 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)            |
| <b>Side Effects Severity, N (%)</b>        |                  |
| 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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