SCORE

Semaglutide effects on Cardiovascular Outcomes in people with Overweight or Obesity in the Real World

Results from the SCORE study

NCT0687475

Real-world evidence

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Conclusion

Semaglutide 2.4 mg was associated with a significantly lower risk of MACE-3 in this real-world study.

Real-world evidence cannot be directly compared to randomized control trial data

Objective

To evaluate semaglutide 2.4 mg effectiveness in reducing the risk of CV events in US adults with ASCVD and overweight or obesity without T2D in clinical practice.

Study population

- Adults aged ≥45 years
- Overweight/ obesity (diagnosis or BMI ≥27 kg/m^2)
- Established ASCVD (MI, ischemic stroke, or PAD)
- Two cohorts: semaglutide 2.4 mg users and non-users
- Komodo Research Database
- Nationally representative US population

Study design and outcomes

Propensity score matching (1:2) ***N=27,963***

- **Semaglutide 2.4 mg OW s.c. users (N=9,321)**
- **Matched non-users (N=18,642)**

Baseline period* — ***Follow-up period***

Index date[†]

Mean follow-up after semaglutide 2.4 mg initiation: ~7 months[‡]

Follow-up period

Until earliest of:

- End of continuous enrollment
- End of data availability
- Initiation of a (non-semaglutide) GLP-1 or GLP-1/GIP receptor agonist
- Bariatric surgery
- Death

Endpoint evaluated: MACE-3 (composite of time to first MI, stroke[§], or CV-related mortality[¶])

Study period: Jan 1, 2016 – Dec 31, 2023. *Baseline period: 12-month continuous insurance enrollment prior to index date. Patients had to have re-confirmation of overweight/obesity during the baseline period; [†]Index date: identification of cohorts on or after June 4, 2021; (semaglutide 2.4 mg users: semaglutide 2.4 mg initiation; non-users: randomly selected pharmacy claim); [‡]Mean ± SD [median] follow-up duration in months: 7.1 ± 5.5 [6.4] for semaglutide users, 6.4 ± 5.7 [5.0] for non-users; [§]MI or stroke was defined by a primary diagnosis during an inpatient encounter; [¶]CV-related mortality was defined as death within 30 days of a CV event.
Exclusion criteria: Baseline non-semaglutide 2.4 mg GLP-1 or GLP-1/GIP receptor agonist use; bariatric surgery; diabetes; pancreatitis; ESKD; multiple endocrine neoplasia type 2; medullary thyroid carcinoma; or pregnancy.

Key baseline demographics and characteristics*

	Semaglutide 2.4 mg users, N=9,321	Non-users, N=18,642
Age (years, mean)	56.8	57.1
Female	68.3%	67.5%
Living with obesity	93.3%	93.7%
BMI (kg/m^2, mean)[†]	37.3	37.1
White	49.4%	48.6%
Black / African American	12.8%	12.7%
Hispanic / Latino	10.5%	10.6%
Other ethnicities[‡]	27.3%	28.0%
Prevalence of ASCVD		
Myocardial infarction	34.1%	34.2%
Ischemic stroke	30.9%	30.1%
PAD	44.6%	44.2%

Standardized mean difference ≤0.10 for all demographics and characteristics. *Baseline is data at index date.
[†]Among those with available BMI data (n=6,032 for semaglutide 2.4 mg users; n=12,103 for non-users);
[‡]Includes Asian or Pacific Islander and patients without ethnicity data reported (i.e. 'unknown').

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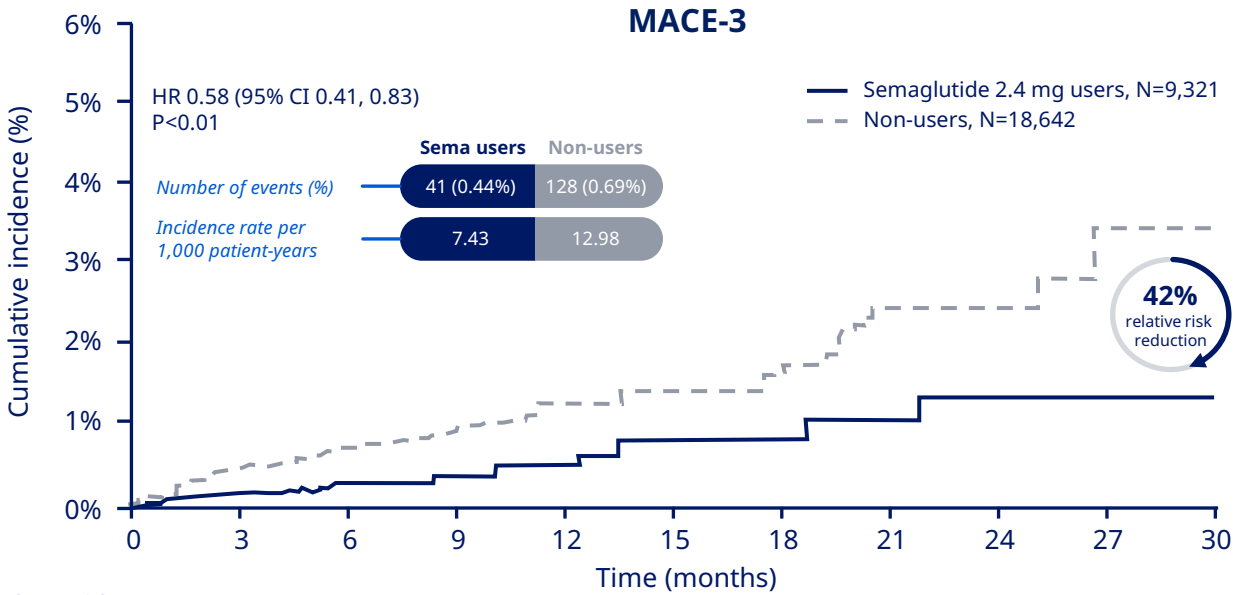
Lower risk of MACE-3 with semaglutide 2.4 mg



Number at risk

Non-users	18,642	12,546	7,798	4,256	2,020	1,522	1,096	729	414	190	37
Sema 2.4 mg	9,321	7,256	4,962	2,364	894	719	584	425	227	91	3

Cox proportional hazards models were used to describe and compare outcomes between the two cohorts. Sema, semaglutide.

Conclusions

In this real-world study of patients in the US with overweight or obesity and ASCVD without T2D, semaglutide 2.4 mg was associated with significantly lower relative risk of MACE-3 (nonfatal MI, nonfatal stroke, or CV death)

Limitations

- Administrative data such as ICD-10 or procedure codes may be subject to coding inaccuracies or lack clinical detail, and laboratory and clinical assessments reflected routine clinical practice, which may result in variability in data.
- Caution should be exercised when interpreting the results of observational studies due to the potential of bias from unmeasured or residual confounding.
- The approval of semaglutide 2.4 mg in 2021 resulted in a relatively short duration of follow-up, limiting the assessment of long-term outcomes, and COVID-19 pandemic may have impacted data.
- Patients were required to have ≥12 months of continuous enrollment, which excluded patients who were treated with semaglutide 2.4 mg but experienced a change in insurance coverage during this period.

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CI, confidence interval; CV, cardiovascular; ESKD, end-stage kidney disease; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; HR, hazard ratio; ICD, International Classification of Diseases; MACE, major adverse cardiovascular events; MACE-3, 3-point MACE; MI, myocardial infarction; OW, once weekly; PAD, peripheral artery disease; s.c., subcutaneous; SD, standard deviation; sema, semaglutide; T2D, type 2 diabetes; US, United States.

Reference: Zhao Z et al. Poster presented at the American College of Cardiology Scientific Session, March 29–31, 2025, Chicago, IL, USA.

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