

Real-World Body Weight Reduction With High-Dose Once-Weekly Semaglutide 2 mg in Adults With Type 2 Diabetes

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Plain Language Summary

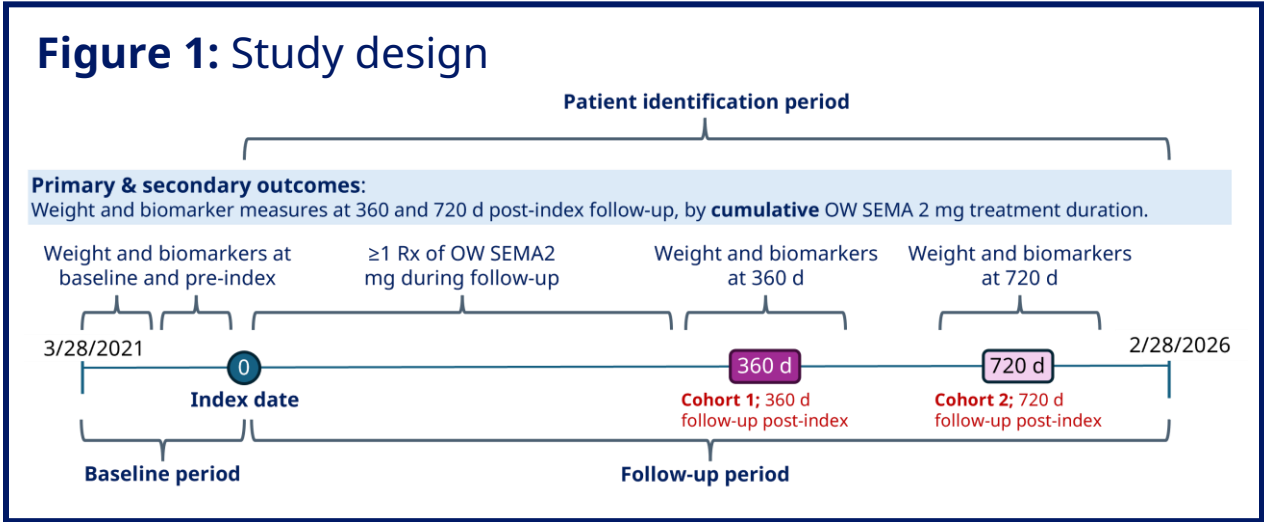
- Why does it matter?** Many adults with type 2 diabetes (T2D) struggle to achieve and maintain meaningful weight loss, which is an important part of managing overall health and reducing cardiometabolic risk. Semaglutide can support weight reduction, but limited real-world information is available on outcomes with the highest approved once-weekly (OW) dose (2 mg) for T2D. This study evaluated whether spending more time on semaglutide 2 mg was associated with greater weight loss and improved cardiometabolic biomarkers.
- What did we do?** Using large US real-world administrative claims data from the Komodo Healthcare Map, we evaluated changes in body weight, blood pressure, and cholesterol levels for 1 to 2 years in adults with T2D who started OW semaglutide and escalated to the 2 mg dose. Outcomes were compared according to the amount of time patients accumulated on the 2 mg dose.
- What did we find?** Clinically meaningful weight loss was observed across all groups. Patients with longer cumulative exposure to semaglutide 2 mg generally experienced greater weight reduction and were more likely to achieve larger weight-loss thresholds. Favorable changes in blood pressure and cholesterol levels also were observed. These findings suggest that sustained treatment with semaglutide 2 mg may support long-term weight management and cardiometabolic health in adults with T2D.

Introduction

- Semaglutide (SEMA) is a glucagon-like peptide-1 receptor agonist (GLP-1RA) approved for the treatment of type 2 diabetes (T2D)¹
- Semaglutide commonly is used early in T2D management because of its effects on glycemic control, body weight, and cardiometabolic outcomes¹
- Real-world studies have shown that SEMA doses up to 1 mg are associated with clinically meaningful reductions in body weight among adults with T2D^{2,3}
- However, real-world evidence describing weight outcomes with the higher once-weekly (OW) SEMA 2 mg dose among adults with T2D remains limited
- This study evaluated changes in body weight among adults with T2D who initiated OW SEMA and escalated to the 2 mg dose

Methods

- Retrospective observational study of US adults with T2D who initiated OW SEMA and escalated to 2 mg in the Komodo Healthcare Map database (March 2021-February 2026); baseline was the 360 days before index (date of the first prescription for OW SEMA any dose; **Figure 1**)
- Primary objective** was to evaluate changes in body weight at approximately 360 and 720 days by cumulative SEMA 2 mg exposure
- Secondary objective** was to evaluate changes in cardiometabolic biomarkers, including systolic blood pressure (SBP), diastolic blood pressure (DBP), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and total cholesterol (TC)
- Cohort 1** required ≥360 days of follow-up and **Cohort 2** required ≥720 days of follow-up, with evaluable baseline and follow-up body weight measurements; patients could contribute to both cohorts
- Cumulative SEMA 2 mg exposure included all periods of 2 mg use regardless of treatment interruptions; outcomes were changes in body weight and cardiometabolic biomarkers, measured as the difference between the pre-index value [-90,0 day] and the value closest to day 360 or 720 within a ±90-day window
- Changes in body weight and biomarkers were analyzed descriptively across cumulative SEMA 2 mg exposure categories (<6, 6-12, 12-18, and ≥18 months)



d, days; OW, once-weekly; Rx, prescription; SEMA, semaglutide.

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Results

- Baseline demographic and clinical characteristics were generally similar across the 360-day (Cohort 1) and 720-day (Cohort 2) cumulative exposure cohorts (**Table 1**)
- A total of 9,830 and 3,867 individuals were included in the 360- and 720-day cohorts, respectively
- Mean follow-up time was approximately 20.0 months in Cohort 1 and 29.9 months in Cohort 2, consistent with cohort definitions

Table 1: Select baseline demographic and clinical characteristics

	Cohort 1 ≥360 d follow-up	Cohort 2 ≥720 d follow-up
	N = 9,830	N = 3,867
Age, years, mean (SD)	58.77 (11.23)	59.12 (10.75)
Sex, female, n (%)	5,433 (55.27)	2,207 (57.07)
Race/Ethnicity, n (%)		
White	6,210 (63.17)	2,563 (66.28)
Black or African American	1,342 (13.65)	519 (13.42)
Hispanic or Latino	1,248 (12.70)	429 (11.09)
Asian or Pacific Islander	326 (3.32)	126 (3.26)
Other/Unknown	704 (7.16)	230 (5.95)
Follow-up time, months, mean (SD)	20.04 (6.62)	29.94 (4.61)
CCI, mean (SD)	2.48 (1.82)	2.43 (1.81)
Number of ADM, mean (SD)	2.43 (1.06)	2.54 (1.06)
Time from index to 1st Rx of OW SEMA 2 mg, months, mean (SD)	6.57 (2.94)	11.32 (6.06)
Cumulative time (months) on OW SEMA 2 mg, n (%)		
<6	6,210 (63.17)	-
≥6	3,620 (36.82)	-
<6	-	942 (24.36)
6-12	-	1,048 (27.10)
12-18	-	1,178 (30.46)
≥18	-	699 (18.08)

ADM, antidiabetic medications; BMI, body mass index; CCI, Charlson Comorbidity Index; d, days; HbA1c, hemoglobin A1c; OW, once-weekly; Rx, prescription; SEMA, semaglutide.

Results (cont'd)

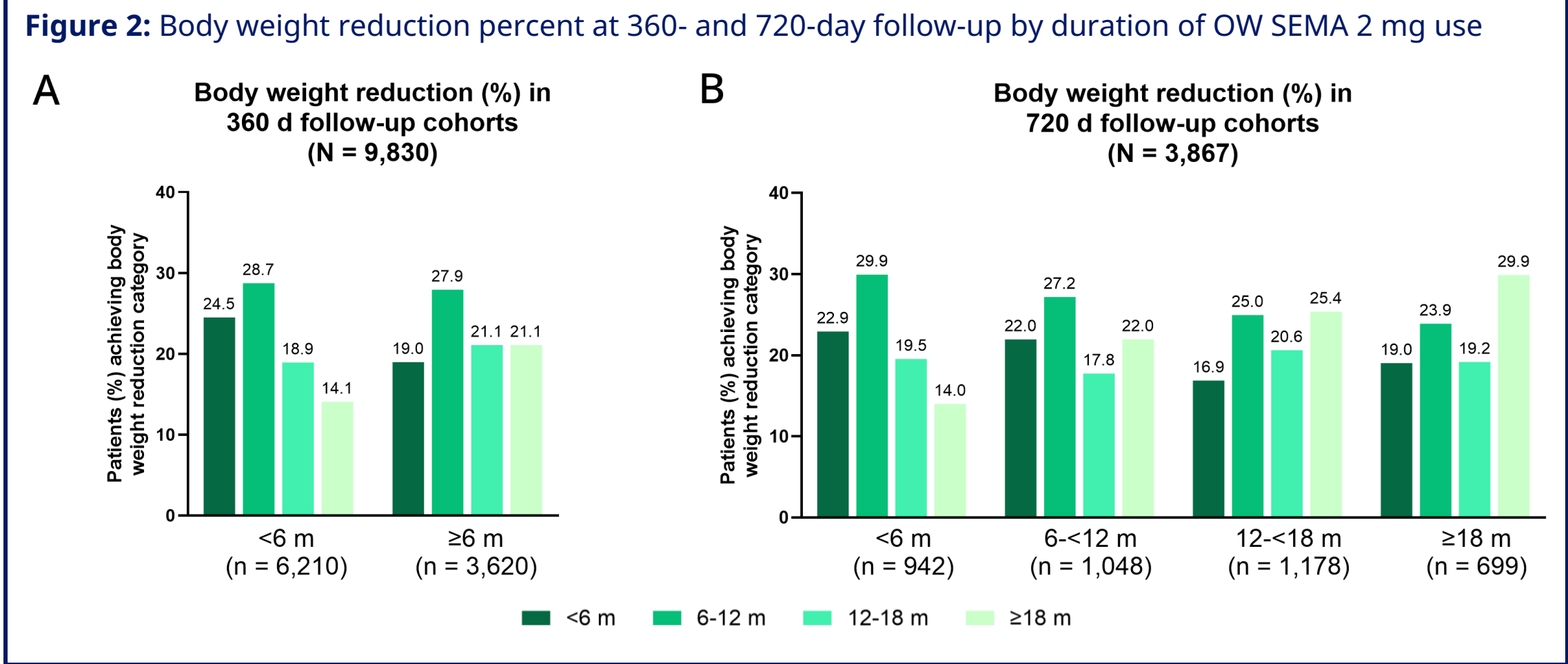
- Pre-index body weight was generally similar across cumulative SEMA 2 mg exposure groups at both follow-up time points (360 days: 110.8 vs 111.4 kg, $P=.20$; 720 days: 107.9-110.5 kg; **Table 2**)
- Mean body weight reductions increased with longer cumulative SEMA 2 mg exposure, ranging from -8.3 to -10.1 kg at 360 days and from -8.4 to -12.3 kg at 720 days ($P<.01$ for both)
- Greater cumulative SEMA 2 mg exposure was associated with larger reductions in body weight at 360- and 720-day follow-up
- Among patients with available hemoglobin A1c (HbA1c) measurements, mean HbA1c reductions were consistent across exposure groups and follow-up periods, decreasing by approximately 1.3%-1.4% (360 days: $P=.02$; 720 days: $P=.90$)

Table 2: Body weight and HbA1c outcomes (change and percent reduction) by cumulative duration of OW SEMA 2 mg use

	Cohort 1 ≥360 d follow-up			Cohort 2 ≥720 d follow-up				
	<6 m (n = 6,210)	≥6 m (n = 3,620)	P value	<6 m (n = 942)	6-<12 m (n = 1,048)	12-<18 m (n = 1,178)	≥18 m (n = 699)	P value
Difference between pre-index and post-index weight, kg								
Mean (SD)	-8.33 (8.59)	-10.12 (9.11)	<.01	-8.40 (8.36)	-9.78 (10.44)	-10.80 (9.92)	-12.25 (9.95)	<.01
Pre-index weight, kg								
Mean (SD)	110.78 (23.14)	111.42 (23.53)	.20	107.91 (21.85)	108.51 (22.68)	110.44 (22.98)	110.50 (23.14)	.02
Difference between pre-index and post-index HbA1c, %								
n	3,506	2,045		537	612	652	400	
Mean (SD)	-1.33 (1.40)	-1.42 (1.41)	.02	-1.33 (1.46)	-1.39 (1.31)	-1.36 (1.42)	-1.39 (1.40)	.90
Pre-index HbA1c, %								
Mean (SD)	7.68 (1.59)	7.58 (1.53)	.02	7.78 (1.61)	7.66 (1.51)	7.63 (1.58)	7.49 (1.48)	.04

d, days; HbA1c, hemoglobin A1c; m, months; OW, once-weekly.

- At 360 days, patients with ≥6 months of cumulative SEMA 2 mg exposure were more likely to achieve clinically meaningful weight-loss thresholds, including ≥10% and ≥15% body weight reduction, than those with <6 months of exposure (**Figure 2A**)
- At 720 days, longer cumulative SEMA 2 mg exposure was associated with higher rates of clinically meaningful weight loss and lower rates of minimal weight change, with the greatest weight reductions and highest rates of substantial weight loss observed among patients with ≥18 months of exposure (**Figure 2B**)



d, days; m, months; OW, once weekly.

- Improvements in cardiometabolic parameters were observed in the 360- and 720-day cohorts (**Table 3**)
- Mean SBP decreased by approximately 5.0 mm Hg and DBP by approximately 2.0 mm Hg across 360- and 720-day follow-up
- Mean HDL-C increased modestly at 360 days and showed greater improvement at 720 days, with mean increases of approximately 2.6 mg/dL
- Mean LDL-C decreased by approximately 10 mg/dL at 360 and 720 days
- TC declined across 360- and 720-day follow-up by approximately 16 mg/dL across cohorts

Table 3: Biomarker outcomes (blood pressure and lipid parameters) at 360- and 720-day follow-up

	Cohort 1 ≥360 d follow-up	Cohort 2 ≥720 d follow-up
	N = 8,378	N = 3,235
Change in SBP, mm Hg		
n	8,153	3,132
Mean (SD)	-5.04 (16.53)	-4.65 (17.02)
Change in DBP, mm Hg		
N	8,156	3,134
Mean (SD)	-1.92 (10.62)	-2.01 (10.67)
Change in HDL-C, mg/dL		
n	2,714	1,042
Mean (SD)	0.74 (8.32)	2.56 (8.38)
Change in LDL-C, mg/dL		
n	2,352	893
Mean (SD)	-9.99 (31.73)	-10.69 (32.00)
Change in TC, mg/dL		
n	2,089	781
Mean (SD)	-16.25 (37.85)	-16.34 (39.11)

d, days; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol.

Conclusions

- Among US adults with T2D who initiated OW semaglutide and escalated to 2 mg, clinically meaningful weight reductions were maintained through 360- and 720-day follow-up
- Greater cumulative semaglutide 2 mg exposure was associated with greater weight reduction and higher rates of achieving clinically meaningful weight-loss thresholds
- Weight loss was observed across all exposure-duration groups, with the largest reductions among patients with the longest cumulative semaglutide 2 mg exposure
- Favorable improvements in blood pressure and lipid parameters were also observed with semaglutide 2 mg treatment
- These real-world findings suggest that semaglutide 2 mg is an effective treatment intensification option for body weight management and cardiometabolic risk reduction in adults with T2D

References:

- (1) ElSayed NA et al. *Diabetes Care* 2023;46(Suppl 1):S97-S110.
- (2) Davies M et al. *JAMA* 2017;318(15):1460-1470.
- (3) Buse JB et al. *BMJ Open Diabetes Res Care* 2023;11(3):e003206.

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