

Real-World Glycemic Control With High-Dose Once-Weekly Semaglutide 2 mg in Adults With Type 2 Diabetes

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Plain Language Summary

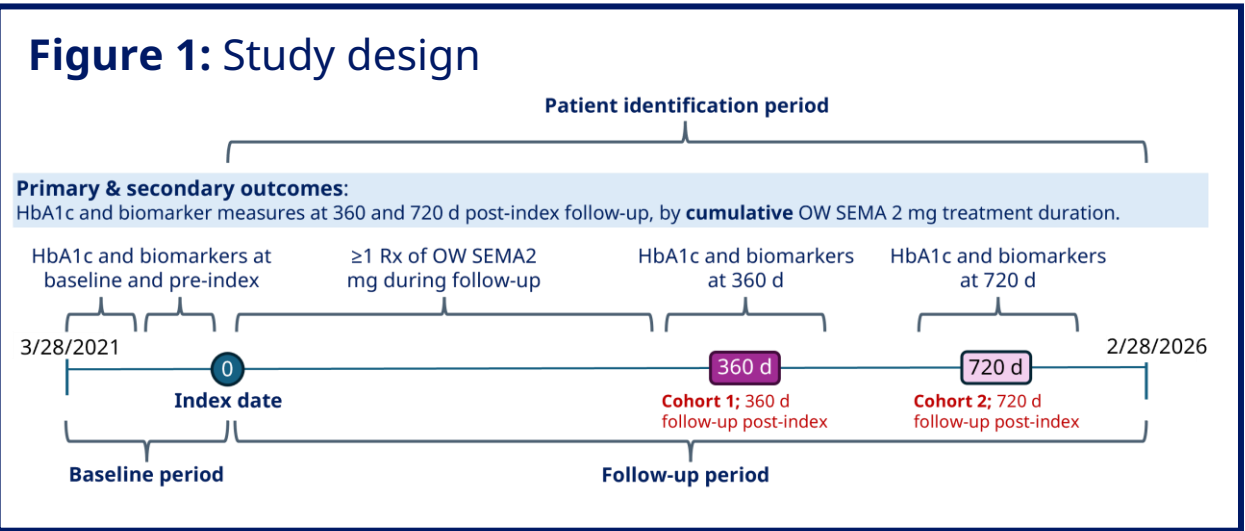
- Why does it matter?** Type 2 diabetes (T2D) is a long-term condition that requires glycemic control to help reduce the risk of health complications. Semaglutide is a treatment that can lower glucose levels, but there is limited real-world evidence of outcomes with the highest approved once-weekly (OW) dose (2 mg) for T2D. This study evaluated whether spending more time on semaglutide 2 mg was associated with improved glycemic control and cardiometabolic biomarkers.
- What did we do?** Using US real-world administrative claims data from the Komodo Healthcare Map, we evaluated changes in blood glucose, blood pressure, and cholesterol levels for 1 to 2 years in adults with T2D who started OW semaglutide 1 mg and escalated to the 2 mg dose. Outcomes were compared according to how long individuals remained on the 2 mg dose.
- What did we find?** People who spent more time receiving semaglutide 2 mg experienced greater reductions in hemoglobin A1c (HbA1c) and were more likely to achieve an HbA1c level below 7.0%. Improvements in blood pressure and cholesterol levels also were observed. These findings suggest that longer time on semaglutide 2 mg may help adults with T2D achieve better glycemic control and improve other cardiometabolic health measures.

Introduction

- Semaglutide (SEMA) is a glucagon-like peptide-1 receptor agonist (GLP-1RA) approved for the treatment of type 2 diabetes (T2D)¹
- SEMA often is initiated early in T2D treatment because of its strong glycemic control, weight loss effects, and demonstrated cardiovascular and renal benefits¹
- Real-world evidence indicates that SEMA at doses up to 1 mg is associated with greater reductions in hemoglobin A1c (HbA1c) and body weight compared with other diabetes therapies^{2,3}
- However, there is limited real-world evidence regarding outcomes at the higher once-weekly (OW) SEMA 2 mg dose
- This study evaluated changes in HbA1c in 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 360 days before index (date of the first prescription for OW SEMA any dose; **Figure 1**)
- Primary objective** was to evaluate changes in HbA1c at approximately 360 and 720 days according to cumulative SEMA 2 mg treatment duration
- 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 HbA1c 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 HbA1c 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 HbA1c and biomarkers were analyzed descriptively across cumulative SEMA 2 mg exposure categories (<6, 6-12, 12-18, and ≥18 months)



d, day(s); HbA1c, hemoglobin A1c; 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 10,139 and 3,985 individuals were included in the 360- and 720-day cohorts
- Mean follow-up time was approximately 20.1 months in Cohort 1 and 30.2 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 = 10,139	N = 3,985
Age, years, mean (SD)	58.33 (11.19)	58.93 (10.65)
Sex, female, n (%)	5,424 (53.50)	2,187 (54.88)
Race/Ethnicity, n (%)		
White	5,694 (56.16)	2,346 (58.87)
Black or African American	1,243 (12.26)	486 (12.20)
Hispanic or Latino	1,454 (14.34)	485 (12.17)
Asian or Pacific Islander	355 (3.50)	136 (3.41)
Other/Unknown	1,393 (13.74)	532 (13.35)
Follow-up time, months, mean (SD)	20.07 (6.58)	30.16 (4.66)
CCI, mean (SD)	2.34 (1.73)	2.30 (1.72)
Number of DM, mean (SD)	2.46 (1.07)	2.56 (1.05)
Time from index to 1st Rx of OW SEMA 2 mg, months, mean (SD)	6.67 (2.95)	11.53 (6.12)
Cumulative time (months) on OW SEMA 2 mg, n (%)		
<6	6,517 (64.3)	-
≥6	3,622 (35.7)	-
<6	-	1,002 (25.14)
6-12	-	1,118 (28.06)
12-18	-	1,198 (30.06)
≥18	-	667 (16.74)

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

Results (cont'd)

- At 360 and 720 days, mean HbA1c reductions were consistent across cumulative SEMA 2 mg exposure groups, ranging from -1.3% to -1.4% (360-day: $P=.12$; 720-day: $P=.23$; **Table 2**)
- Pre-index HbA1c values were higher among patients with shorter cumulative SEMA 2 mg exposure and decreased with greater exposure duration at both follow-up time points ($P\leq.01$)
- Greater cumulative 2 mg exposure was associated with improved glycemic goal attainment at 360 and 720 days ($P\leq.01$)
- Among patients with available body weight measurements, clinically meaningful weight reductions were observed across all exposure groups. Mean weight change ranged from -8.6 to -10.1 kg at 360 days ($P=.50$) and from -8.0 to -12.3 kg at 720 days ($P=.02$), with greater reductions observed among patients with longer cumulative SEMA 2 mg exposure

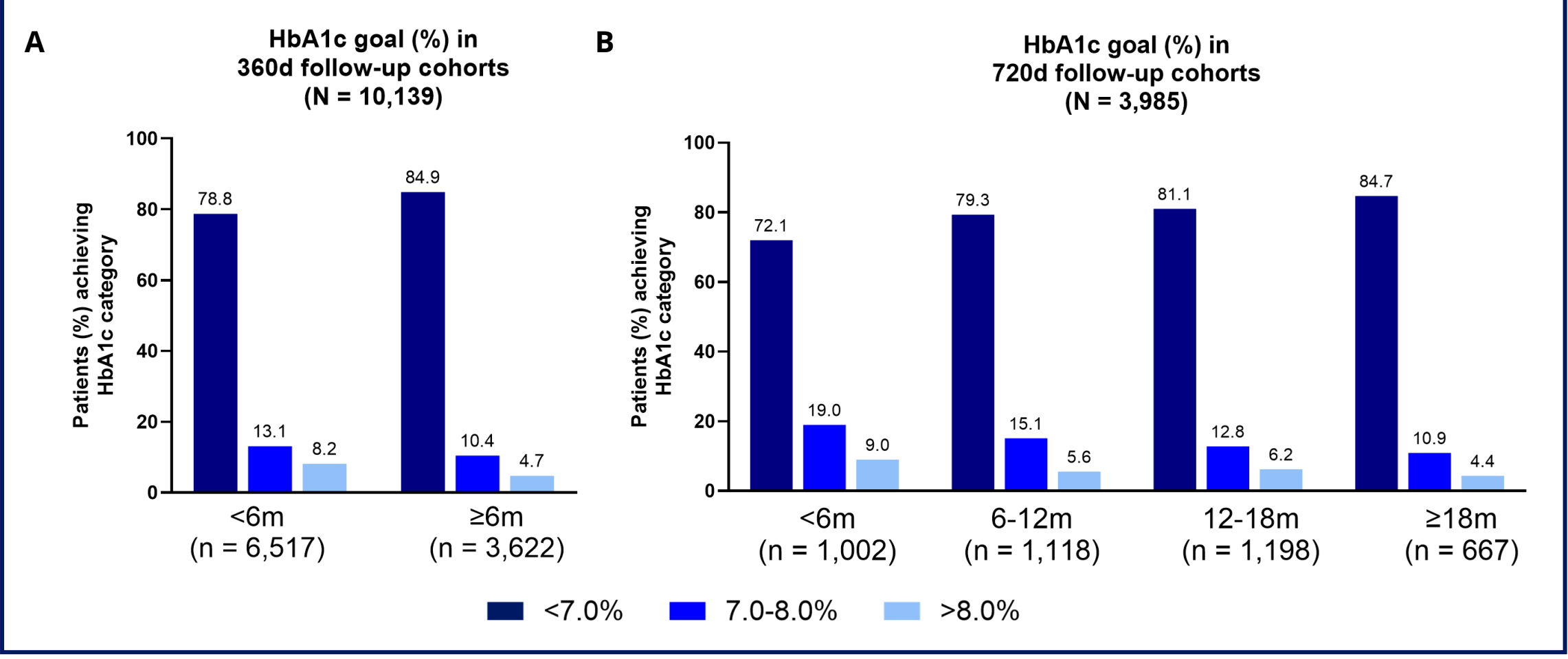
Table 2: Glycemic outcomes (change and percent reduction in HbA1c) and weight change by cumulative duration of OW SEMA 2 mg use

	Cohort 1 ≥360 d follow-up			Cohort 2 ≥720 d follow-up				
	<6 m (n = 6,517)	≥6 m (n = 3,622)	P value	<6 m (n = 1,002)	6-12 m (n = 1,118)	12-18 m (n = 1,198)	≥18 m (n = 667)	P value
Difference between pre- and post-index HbA1c								
Mean (SD)	-1.33 (1.42)	-1.38 (1.41)	.12	-1.27 (1.42)	-1.28 (1.26)	-1.30 (1.40)	-1.40 (1.47)	.23
Pre-index HbA1c								
Mean (SD)	7.67 (1.63)	7.52 (1.54)	<.01	7.78 (1.62)	7.58 (1.44)	7.56 (1.56)	7.53 (1.51)	<.01
Post-index HbA1c Goal, n (%)								
<7%	5,133 (78.76)	3,074 (84.87)	<.01	722 (72.06)	887 (79.34)	971 (81.05)	565 (84.71)	<.01
≥7%	1,384 (21.24)	548 (15.13)		280 (27.94)	231 (20.66)	227 (18.95)	102 (15.29)	
Difference between pre- and post-index weight								
n	3,506	2,045	<.01	537	612	652	400	<.01
Mean (SD)	-8.55 (8.30)	-10.05 (8.94)		-8.02 (7.71)	-9.77 (10.49)	-10.77 (9.32)	-12.25 (9.76)	
Pre-index weight, kg								
Mean (SD)	111.07 (23.09)	111.51 (23.40)	.50	106.99 (21.89)	109.98 (23.37)	111.18 (22.81)	109.67 (22.78)	.02

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

- At 360 days, the proportion of patients achieving HbA1c <7.0% increased from 78.8% among those with <6 months of cumulative exposure to 84.9% among those with ≥6 months of exposure, while the proportion with HbA1c ≥7.0% decreased correspondingly (21.2% vs 15.1%; **Figure 2A**)
- Similarly, at 720 days, the proportion achieving HbA1c <7.0% increased from 72.1% among those with <6 months of cumulative exposure to 84.7% among those with ≥18 months of exposure, while the proportion with HbA1c >8.0% decreased correspondingly (**Figure 2B**)

Figure 2: HbA1c goal at 360-day (Cohort 1) and 720-day (Cohort 2) follow-up by duration of OW SEMA 2 mg use



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

- Improvements in cardiometabolic parameters were also observed across both 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 from 0.8 mg/dL at 360 days to 2.5 mg/dL at 720 days
- Mean LDL-C decreased consistently across cohorts with reductions of approximately 10 mg/dL at both assessment periods
- Mean TC decreased 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 = 10,139	N = 3,573
Change in SBP, mm Hg		
n	5,251	2,043
Mean (SD)	-4.99 (16.19)	-4.72 (16.65)
Change in DBP, mm Hg		
n	5,248	2,042
Mean (SD)	-1.91 (10.55)	-2.19 (10.60)
Change in HDL-C, mg/dL		
n	2,968	1,147
Mean (SD)	0.77 (7.94)	2.51 (8.48)
Change in LDL-C, mg/dL		
n	2,577	986
Mean (SD)	-9.58 (31.32)	-10.71 (31.77)
Change in TC, mg/dL		
n	2,331	883
Mean (SD)	-16.07 (37.41)	-16.31 (39.01)

d, days; DBP, diastolic blood pressure; HbA1c, hemoglobin A1c; 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 HbA1c reductions were maintained through 360- and 720-day follow-up
- Greater cumulative semaglutide 2 mg exposure was associated with higher rates of HbA1c goal attainment and greater weight reduction
- HbA1c improvements were observed across all exposure-duration groups, with the highest rates of HbA1c <7.0% among patients with the longest cumulative 2 mg exposure
- Favorable improvements in blood pressure and lipid parameters also were observed with semaglutide 2 mg treatment
- Consistent findings across the 360- and 720-day cohorts suggest durable benefits with continued semaglutide 2 mg treatment
- These real-world findings support semaglutide 2 mg as an effective treatment intensification option for improving glycemic control and cardiometabolic risk factors in adults with T2D

References:
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