Most Patients with Type 2 Diabetes Maintain HbA1c Improvements a Year After Stopping GLP-1 Medications

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Key Findings:

- Three months after stopping a GLP-1, 40% of patients had further improved their HbA1c compared to when they discontinued the GLP-1, 48% kept some of their improvement, and just 12% had a worse HbA1c compared to their pre-GLP-1 level.
- Twelve months after stopping a GLP-1, 33% of patients had further improved their HbA1c compared to when they discontinued the GLP-1, 46% kept some of their improvement, and 21% had a worse HbA1c compared to their pre-GLP-1 level.
- Early HbA1c trajectory predicted long-term outcomes: among patients with further HbA1c reduction at three months, 55% still had further reduction at twelve months, while patients whose HbA1c exceeded baseline at three months were most likely to remain elevated at twelve months (50%).

Glucagon-like peptide-1 receptor agonists (GLP-1s) have become one of the most widely prescribed medication classes for type 2 diabetes, with more than one in four U.S. adults with diagnosed diabetes using a GLP-1 injectable in 2024.[1] However, many patients stop taking GLP-1s within the first year of treatment due to side effects, cost, insurance barriers, or clinical decisions.[2,3] Prior research has shown mixed results for patients' metabolic rebound, with some showing weight gain after stopping GLP-1s and others showing weight maintenance.[4,5] A rise in HbA1c values after stopping GLP-1s has also been found in prior research, with a 0.65 percentage point increase,[6] though long-term glycemic trajectories after discontinuation remain less understood.

We studied 54,178 adults with type 2 diabetes who had been on a GLP-1 medication for at least 90 days, experienced improvement in their HbA1c results while on the treatment, and subsequently stopped the GLP-1. We measured the absolute change in HbA1c between the value closest to the GLP-1 end date and the value closest to three, six, nine, and twelve months after stopping. HbA1c change was categorized as improved further, kept at least some of the improvement, or worsened to higher levels than the pre-GLP-1 baseline.

Three months after stopping a GLP-1, most patients had sustained or even improved upon their on-treatment HbA1c reduction, as seen in Figure 1. Of the patients with an HbA1c result at three months, 40% had an HbA1c lower than when they discontinued treatment, and another 48% kept at least some of their improvement. Just 12% had an HbA1c that was worse than their pre-GLP-1 baseline.

HbA1c Change Category Three Months After Stopping GLP-1s

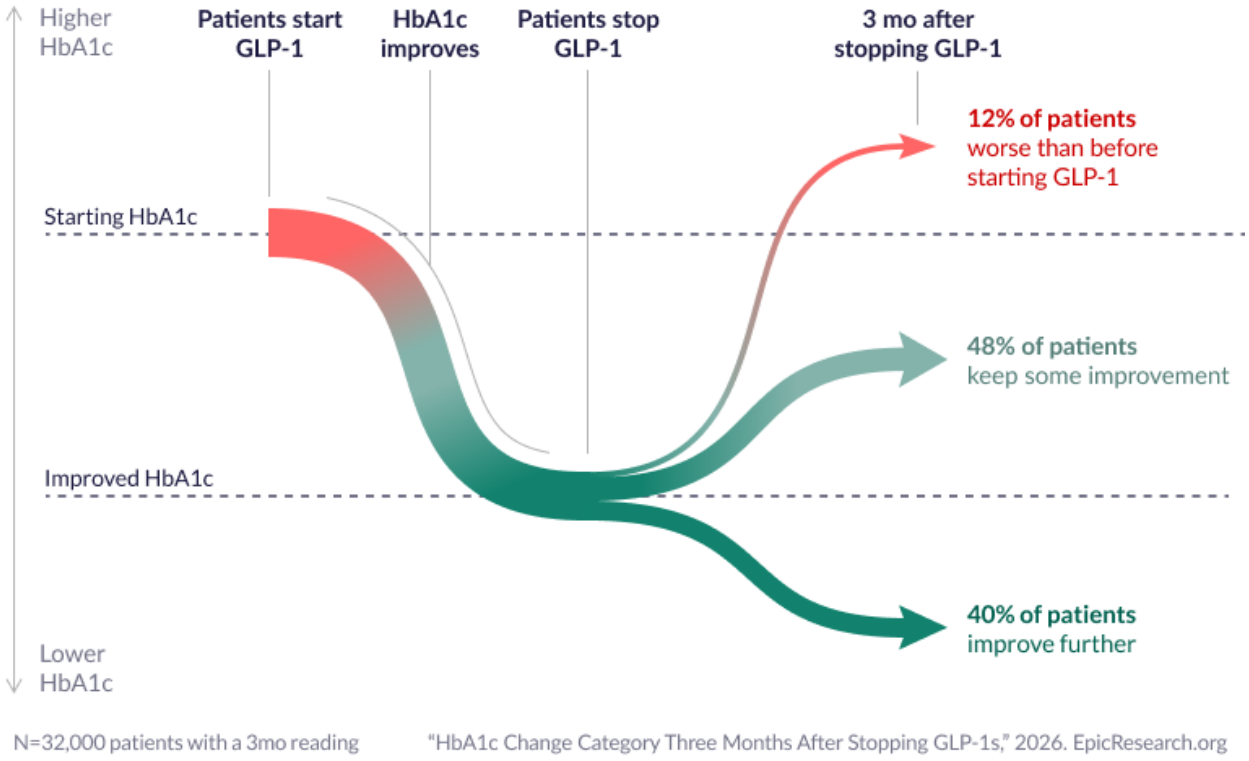

Figure 1. The distribution of HbA1c change categories three months after stopping a GLP-1 medication.

The pattern of durable glycemic improvement persisted over the full year of follow-up, though with a gradual shift over time. By six months, the proportion of patients with further HbA1c improvement had decreased to 34%, while those whose HbA1c was worse than their pre-GLP-1 level grew to 16%. At nine and twelve months the distribution continued to shift modestly, with 33% still showing further improvement, and 20% and 21% worse than their pre-GLP-1 level, respectively. Even at one year, roughly four in five patients had not returned to their pre-treatment HbA1c level.

HbA1c Change Category at Three, Six, Nine, and Twelve Months After Stopping GLP-1s

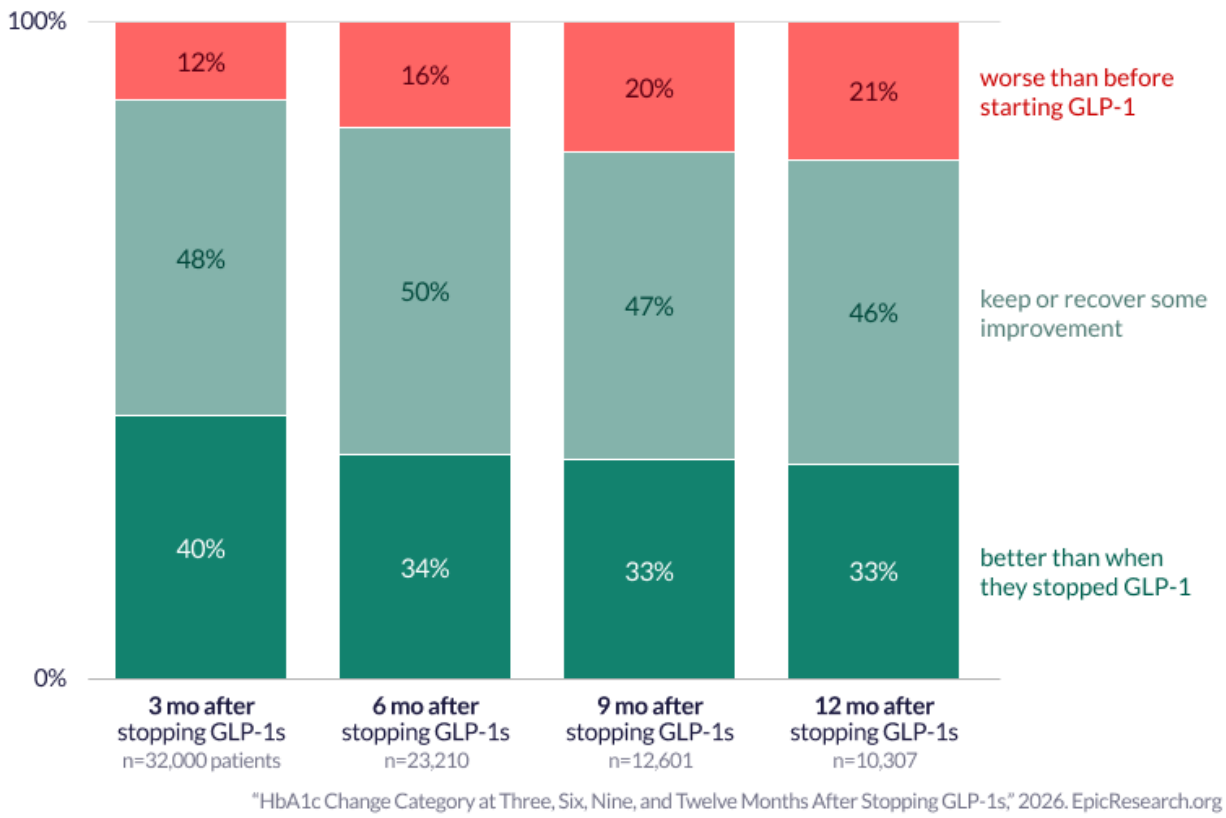

Figure 2. The distribution of HbA1c change categories at three, six, nine, and twelve months after stopping a GLP-1 medication.

While the overall distribution shifted gradually over time, individual patients' early HbA1c trajectories were a strong predictor of where they would be at one year. Patients whose HbA1c was lower than their pre-GLP-1 level at three months most often had improvement at twelve months as well (55%). Patients whose HbA1c had already become worse than their pre-GLP-1 baseline at three months were most likely to remain in that category at twelve months (50%), though 25% had improved to below their pre-GLP-1 level by twelve months.

HbA1c Trajectories from Three to Twelve Months After Stopping GLP-1s

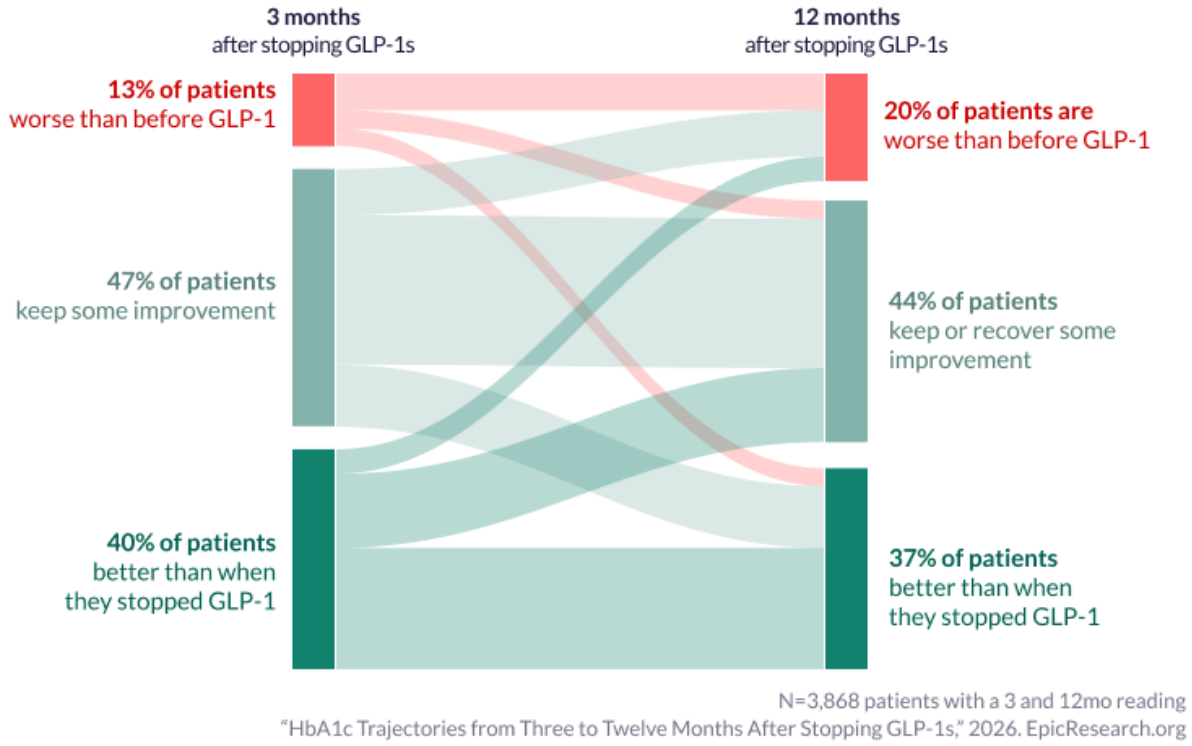

Figure 3. HbA1c change categories at three months versus twelve months after stopping a GLP-1.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 300 million patient records from 2,000 hospitals and more than 47,000 clinics from all 50 U.S. states, Canada, Lebanon, and Saudi Arabia. This study was completed by two teams that worked independently, each composed of a clinician and research scientist. The two teams came to similar conclusions. Graphics by Brian Olson.

References

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Data Definitions

Term	Definition
Study period	1/1/2017 to 12/31/2025
Study population: inclusion	Adult patients with: • **Type 2 diabetes** • A **GLP-1** order lasting at least 90 days in the **study period** • On at least one other **non-insulin diabetes medication** at the time of their HbA1c measurement after stopping the GLP-1 • A reduction in HbA1c while on GLP-1
Study population: exclusion	**Pregnancy** during **GLP-1** use or follow-up period Patients on **insulin** Patients with type 1 diabetes: ICD-10-CM code E10*
Censoring	Patient begins a **GLP-1** medication again
Exposures	Time since stopping GLP-1: three months, six months, nine months, twelve months
Outcomes	Change in HbA1c from the closest value to the **GLP-1** end date and the nearest value to three, six, nine, or twelve months (within 30 days of time window) of stopping the GLP-1
Type 2 diabetes	A diagnosis with ICD-10-CM code E11*
GLP-1	Order of a simple generic of "dulaglutide," "exenatide," "exenatide microspheres," "liraglutide," "semaglutide," or "tirzepatide" and a pharmaceutical class of "ANTIHYPERGLYCEMIC – INCRETIN MIMETICS COMBINATION," "ANTIHYPERGLY,INSULIN,LONG ACT-GLP-1 RECEPT.AGONIST," "ANTI-OBESITY GLUCAGON-LIKE PEPTIDE-1 RECEP AGONIST," "ANTIHYPERGLY,INCRETIN MIMETIC(GLP-1 RECEP.AGONIST)," or "ANTI-OBESITY – INCRETIN MIMETICS COMBINATION"
Pregnancy	Pregnancy start date: Between 12 months before the first reading through the follow-up reading Pregnancy end date, delivery, or if it's ambiguous what point in the pregnancy the patient would be at (e.g., an encounter or billing diagnosis with ICD-10-CM O*): Between 12 months before the first reading through 9 months after the follow-up reading
Non-insulin diabetes medications	SGLT2i: ATC code A10BK* Biguanides: ATC code A10BA* Sulfonylureas: ATC code A10BB* DPP-4 inhibitor: ATC code A10BH* Combination
HbA1c	A lab result with LOINC code 17856-6, 17855-8, 4548-4, or 4549-2
Insulin	A medication with ATC code A10A*
Race and ethnicity	Non-exclusive flags for Black race and Hispanic ethnicity
Limitations	Medications prescribed outside participating health systems might be missing on patients' records. Reasons for GLP-1 discontinuation (e.g., cost, side effects, clinical decision) were not available. Changes in lifestyle behaviors after stopping GLP-1s could not be assessed.

Table 1. HbA1c Change Category Three Months After Stopping GLP-1s

Regain Category	Population Size	Percent
further reduction	12,870	40.22%
0 to 25% regain	7,994	24.98%
25 to 50% regain	3,417	10.68%
50 to 75% regain	2,199	6.87%
75% to 100% regain	1,780	5.56%
increase past baseline	3,740	11.69%

Table 2. HbA1c Change Category at Three, Six, Nine, and Twelve Months After Stopping GLP-1s

Follow Up Period	Regain Category	N	Percent
3Mo	further reduction	12,870	40.22%
3Mo	0 to 25% regain	7,994	24.98%
3Mo	25 to 50% regain	3,417	10.68%
3Mo	50 to 75% regain	2,199	6.87%
3Mo	75% to 100% regain	1,780	5.56%
3Mo	increase past baseline	3,740	11.69%
6Mo	further reduction	7,920	34.12%
6Mo	0 to 25% regain	5,191	22.37%
6Mo	25 to 50% regain	2,741	11.81%
6Mo	50 to 75% regain	1,984	8.55%
6Mo	75% to 100% regain	1,677	7.23%
6Mo	increase past baseline	3,697	15.93%
9Mo	further reduction	4,207	33.39%
9Mo	0 to 25% regain	2,369	18.80%
9Mo	25 to 50% regain	1,435	11.39%
9Mo	50 to 75% regain	1,138	9.03%
9Mo	75% to 100% regain	980	7.78%
9Mo	increase past baseline	2,472	19.62%
12Mo	further reduction	3,376	32.75%
12Mo	0 to 25% regain	1,840	17.85%
12Mo	25 to 50% regain	1,171	11.36%
12Mo	50 to 75% regain	963	9.34%
12Mo	75% to 100% regain	804	7.80%
12Mo	increase past baseline	2,153	20.89%

Table 3. HbA1c Trajectories from Three to Twelve Months After Stopping GLP-1s

Change at Three Months	Change at Twelve Months	N
Worse than before GLP-1	Worse than before GLP-1	255
Worse than before GLP-1	Kept some improvement	128
Worse than before GLP-1	Further reduction	124
Kept some improvement	Worse than before GLP-1	324
Kept some improvement	Kept some improvement	1,052
Kept some improvement	Further reduction	438

Further reduction	Worse than before GLP-1	178
Further reduction	Kept some improvement	516
Further reduction	Further reduction	853