

# Some Diabetic Complications Less Likely Among Type 1 Diabetics on GLP-1s

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## Key Findings:

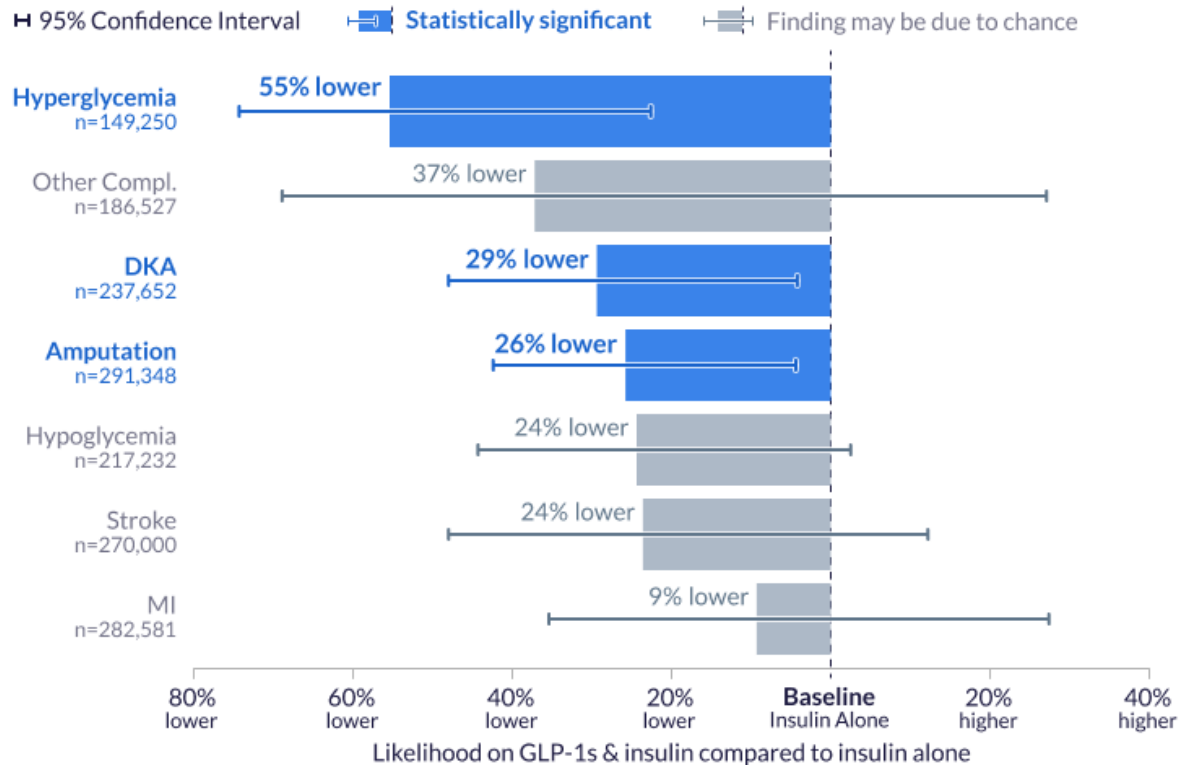
- Patients with type 1 diabetes (T1D) who are prescribed a GLP-1 medication and insulin are 55% less likely to have a hyperglycemia-related ED visit, 26% less likely to have an amputation-related visit, and 29% less likely to have a diabetic ketoacidosis (DKA)-related ED visit in the following year compared to those on insulin alone.

Type 1 diabetes (T1D) requires lifelong insulin therapy, and recent interest has emerged in the use of GLP-1 medications as an adjunct treatment.<sup>1,2</sup> GLP-1s, such as semaglutide and liraglutide, are approved for type 2 diabetes to improve glycemic control and promote weight loss by enhancing insulin secretion, suppressing glucagon release, and slowing gastric emptying.<sup>3</sup> Although they are not approved for T1D, some patients may receive them off-label or for weight control.

To better understand the relationship between GLP-1 use and diabetes-related outcomes in patients with T1D, we compared 7,010 adult patients with T1D who were prescribed GLP-1s and insulin to 304,422 adult patients with T1D who were on insulin alone.

After taking into account patient demographics, BMI, HbA1c, smoking history, and hypertension, we found that patients with T1D who had no history of the given complication who used a GLP-1 medication were 55% less likely to have a hyperglycemia-related ED visit, 29% less likely to have a diabetic ketoacidosis (DKA)-related ED visit, and 26% less likely to have an amputation-related visit compared to those on insulin alone, as seen in Figure 1. While we saw some decrease in the rate of ED care for novel stroke, myocardial infarction (MI), hypoglycemia, or other T1D complications for those on GLP-1s, these findings were not statistically significant and might be due to random chance. It is important to note that the rates of new diabetic complications in one year for both groups were around 1%, indicating that these are uncommon outcomes regardless of medication use.

## Likelihood of New Diabetes Complications by GLP-1 Usage



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Figure 1. The likelihood of T1D patients experiencing diabetes complication by GLP-1 usage. Confidence intervals that cross the baseline likelihood indicate that the observed change in likelihood might be due to random chance. Patients with a history of the condition evaluated were excluded from analysis for that condition.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 296 million patient records from 1,600 hospitals and more than 39,000 clinics from all 50 states, Lebanon, and Saudi Arabia. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

## References

1. Delrue C, Speeckaert MM. Mechanistic pathways and clinical implications of GLP-1 receptor agonists in type 1 diabetes management. *Int J Mol Sci.* 2024;25(17):9351. doi:10.3390/ijms25179351
2. Li P, Li Z, Staton E, et al. GLP-1 Receptor Agonist and SGLT2 Inhibitor Prescribing in People With Type 1 Diabetes. *JAMA Network.* 2024;332(19):1667-1669. <https://jamanetwork.com/journals/jama/article-abstract/2825312>. Accessed February 4, 2025.
3. Cornell S. A review of GLP-1 receptor agonists in type 2 diabetes: A focus on the mechanism of action of once-weekly agents. *J Clin Pharm Ther.* 2020;45 Suppl 1(Suppl 1):17-27. doi:10.1111/jcpt.13230

## Data Definitions

Term	Definition
Study period	1/1/2021 to 1/14/2024, with follow up through 1/14/2025
Study population	<p>Adult patients:</p> <ul style="list-style-type: none"> <li>Diagnosed with type 1 diabetes (<b>T1D</b>)</li> <li>At least one year of follow-up time after their <b>index event</b></li> <li>With <b>insulin</b> prescribed prior to or on the <b>index event</b> date</li> </ul> <p>Patients with documentation of an <b>outcome</b> prior to their index event or within the first 30 days of the index event were excluded from that outcome analysis.</p>
Index event	<p>For the GLP-1 cohort, the start of their first <b>GLP-1 medication</b> prescription with concurrent <b>insulin</b>. They must continually receive the GLP-1 medication for a year.</p> <p>For controls, the date of a random <b>insulin</b> prescription order that occurs after their T1D diagnosis and at least a year prior to the start of any GLP-1 medication (if ever given).</p>
Outcomes	<p>An ED encounter with one of the following diagnoses within a year of the index event:</p> <ul style="list-style-type: none"> <li>DKA: ICD-10-CM code E10.1* or SNOMED code 420422005</li> <li>Hypoglycemia: ICD-10-CM code E16.1, E16.2, or E10.64*</li> <li>Hyperglycemia: ICD-10-CM code E10.65* or SNOMED code 310505005</li> <li>Stroke: ICD-10-CM code I60*, I63*, I69.3*, Z86.73, or G45.9</li> <li>MI: ICD-10-CM code I21*-I23*</li> <li>Other T1D complications: ICD-10-CM E10.2*-E10.5*, or E10.61*-E10.63*</li> </ul> <p>A clinical encounter with the following diagnosis within a year of the index event:</p> <ul style="list-style-type: none"> <li>Lower body amputation: ICD-10-CM code Z89.41*-Z89.44*, Z89.51*, or Z89.61*. Procedure ICD-9-CM Volume 3 code 84.10 or 84.12-84.19 or ICD-10-PCS code 0Y6*</li> </ul>
Confounders	<p>Legal sex</p> <p>History of smoking</p> <p>Hypertension before the <b>index event</b>: ICD-10-CM code I10</p> <p>Age</p> <ul style="list-style-type: none"> <li>18-34</li> <li>35-64</li> <li>65-79</li> <li>80+</li> </ul> <p>BMI (highest in the year prior to index date through one year after <b>index event</b>)</p> <ul style="list-style-type: none"> <li>&lt;18.5</li> <li>18.5-&lt;25</li> <li>25-&lt;30</li> <li>30-&lt;40</li> <li>40+</li> </ul> <p><b>HbA1c</b> (on the <b>index event date</b> or the most recent from the preceding year)</p>

	<ul style="list-style-type: none"> <li>• &lt; 5.7</li> <li>• 5.7-6.4</li> <li>• 6.5-7.9</li> <li>• 8.0-8.9</li> <li>• 9.0-9.9</li> <li>• 10+</li> </ul>
	<b>Race and ethnicity</b> <b>Social Vulnerability Index quintile</b>
<b>T1D</b>	A diagnosis with ICD-10-CM code E10*
<b>GLP-1 medication</b>	An order for a medication with a pharmaceutical class of "ANTIHYPERTENSIVE - INCRETIN MIMETICS COMBINATION," "ANTIHYPERTENSIVE,INSULIN,LONG ACT-GLP-1 RECEPTOR AGONIST," "ANTI-OBESITY GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONIST," or "ANTIHYPERTENSIVE,INCRETIN MIMETIC(GLP-1 RECEPTOR AGONIST)" and a simple generic name that further categorizes it as dulaglutide, semaglutide, liraglutide, tirzepatide, or exenatide
<b>Insulin</b>	A prescription with a pharmaceutical class of "INSULIN" and route of "injection," "intravenous," or "subcutaneous" or pharmaceutical class of "ANTIHYPERTENSIVE,INSULIN,LONG ACT-GLP-1 RECEPTOR AGONIST"
<b>HbA1c</b>	A lab with LOINC code 17855-8, 17856-6, 4548-4, or 4549-2
<b>Race and ethnicity</b>	Non-exclusive flags for Black and Hispanic
<b>Social Vulnerability Index</b>	The social vulnerability quintile for the ZIP Code of the patient's most recent address

**Table 1: Likelihood of New Diabetes Complications by GLP-1 Usage**

Condition	Odds Ratio	95% CI Low	95% CI High
Hyperglycemia	0.45	0.26	0.77
Other Complication	0.63	0.31	1.27
DKA	0.71	0.52	0.96
Amputation	0.74	0.58	0.96
Hypoglycemia	0.76	0.56	1.03
Stroke	0.76	0.52	1.12
MI	0.91	0.65	1.27