Finding the A1c Sweet Spot Lowers Cardiovascular Risk Among Patients with Diabetes

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Key Findings:

- Diabetic patients with an HbA1c between 7.0 and 7.4% are 13% more likely to experience a novel myocardial infarction (MI) and 8% more likely to experience a novel stroke compared to those with an HbA1c between 6.75 and 6.99%.
- The likelihood of cardiovascular complications increases with higher average HbA1c levels, up to 153% for MI and 140% for stroke for those with an HbA1c of 10.0% or higher.
- The likelihood of an MI is reduced by about 10% among patients with an HbA1c between 5.4 and 6.0% compared to those with an HbA1c between 6.75 and 6.99%.

HbA1c is a widely used measure of long-term glucose control in diabetes management. Clinical guidelines typically recommend maintaining HbA1c below 7% for adults with type 2 diabetes to reduce the risk of complications, including cardiovascular events.[1]

To better understand the relationship between specific HbA1c values and cardiovascular event risk in diabetics, we studied 852,243 patients with type 2 diabetes and no prior history of stroke or MI. Time-weighted average HbA1c levels were tracked for three years starting at least one year post-diagnosis and monitored for evidence of new stroke or MI. We accounted for patient demographics, smoking status, BMI classifications, social vulnerability, and comorbidities in our analysis.

We found that the likelihood of MI rose progressively at higher average HbA1c levels, particularly above 7.0%, as seen in Figure 1. Patients with an average HbA1c between 7.0 and 7.4% were 13% more likely to experience an MI, and those with an average HbA1c of 10.0% or higher were 153% more likely, compared to patients with an average HbA1c between 6.75 and 6.99%. Notably, average HbA1c levels below 5.4% did not confer any additional benefit, with MI risk similar to or higher than for those with an average HbA1c between 6.75 and 6.99%.

Likelihood of MI by Average HbA1c

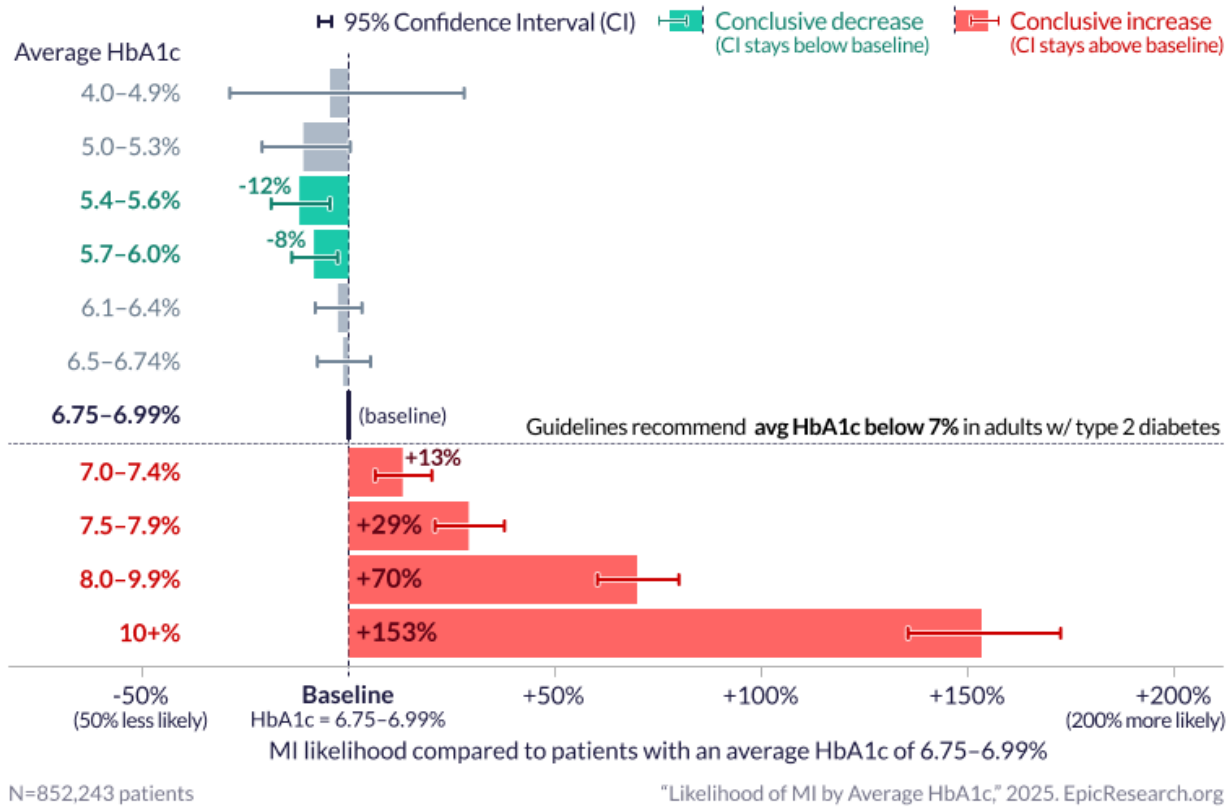

Figure 1. The likelihood of a diabetic patient experiencing an MI by their average HbA1c level.

The pattern for stroke was similar but less steep, with a significant rise beginning at average HbA1c levels above 7.0%. Patients are 140% more likely to have a stroke if their average HbA1c was 10.0% or higher compared to patients with an average HbA1c between 6.75 and 6.99%. The likelihood of stroke was 5% lower among patients with an average HbA1c between 6.1 and 6.4%, while the likelihood was 7% lower for those with an average HbA1c between 5.7 and 6.0%. Notably, average HbA1c levels below 5.7% did not confer any additional benefit, with stroke risk similar to or higher than for those with an average HbA1c between 6.75 and 6.99%.

Likelihood of Stroke by Average HbA1c

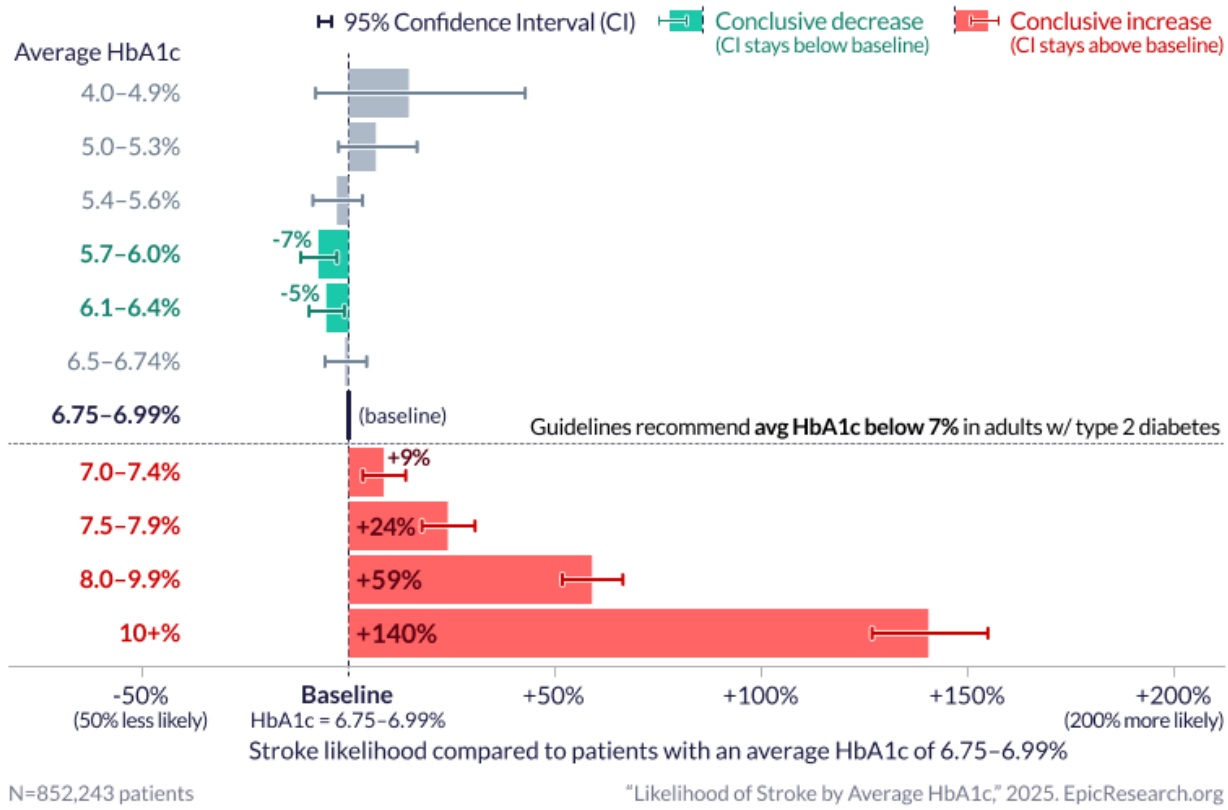

Figure 2. The likelihood of a diabetic patient experiencing a stroke by their average HbA1c level.

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 1,700 hospitals and more than 40,000 clinics from all 50 U.S. 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. American Diabetes Association Professional Practice Committee. 6. Glycemic goals and hypoglycemia: Standards of care in diabetes-2024. Diabetes Care. 2024;47(Suppl 1):S111-S125. doi:10.2337/dc24-S006

Data Definitions

Term	Definition
Study period	1/1/2000 to 4/28/2025
Study population: inclusions	Patients aged 35 or older with: • A **type 2 diabetes** diagnosis • A **face-to-face encounter** at least a year before their first **type 2 diabetes** diagnosis • At least two **HbA1c** result in the three years after the index date Index date: The date of their first **HbA1c** value at least a year after their **type 2 diabetes** onset.

Study population: exclusions	Patients with:
	• A **pregnancy** between the index date and the three years to follow
	• A history of **outcome** for each analysis
	• A history of one of the following:
	  • Type 1 diabetes: ICD-10-CM code E10*
	  • Other diabetes: ICD-10-CM code E08*-E09*, E13*
	  • Hemolytic anemia: ICD-10-CM code D55*-D59*
	  • Aplastic anemia: ICD-10-CM code D60*-D64*
	  • Methemoglobinemia: ICD-10-CM code D74*
	  • Other/Unspecified disease of blood/blood forming organs: ICD-10-CM code D75*
	  • Cancer: ICD-10-CM code C*
	  • HIV: ICD-10-CM code B20*

Exposure	Time-weighted average HbA1c over the three years starting at the index date
Outcomes	A diagnosis of **stroke** or **MI**
Confounders	Age at index: 30-49, 50-64, 65+ BMI classification: • Underweight: <18.5 • Healthy: 18.5-<25 • Overweight: 25-<30 • Obese: 30+ Weighted average HbA1c: • 4.0–4.9% • 5.0–5.3% • 5.4–5.6% • 5.7–6.0% • 6.1–6.4% • 6.5–6.74% • 6.75–6.99% • 7.0–7.4% • 7.5–7.9% • 8.0–9.9% • 10.0%+ **CVD** prior to or within three years of index date **Family history of CVD** **Gestational diabetes** prior to or within three years of index date **Hyperlipidemia** prior to or within three years of index date **Hypertension** prior to or within three years of index date **Race and ethnicity**: Hispanic, Asian Non-Hispanic, Black Non-Hispanic, Other Non-Hispanic, White Non-Hispanic) RUCA**:** Metropolitan, Micropolitan, Small Town, Rural Legal sex Documentation of current or past smoking Social Vulnerability Index quintile (based on most recent ZIP code)
Race and ethnicity	Mutually exclusive categories for Hispanic, Asian Non-Hispanic, Black Non-Hispanic, Other Non-Hispanic, and White Non-Hispanic
Model specifications	Cox PH Regressions
Stroke	A diagnosis with ICD-10-CM code I60*, I63*, I69.3*, Z86.73, or G45.9

MI	A diagnosis with ICD-10-CM code I21*, I22*, or I23*
CVD	Diagnosis with ICD-10-CM code I20*-I26*, I30*-I49*, I51*, I70*-I79*
Family history of CVD	Diagnosis with ICD-10-CM code Z82.4*
Gestational diabetes	Diagnosis of O24.1* or O24.4*
HbA1c	Lab result with LOINC code 17856-6, 17855-8, 4548-4, or 4549-2 with a result value between 4.0% and 29.0%
Hyperlipidemia	Diagnosis of ICD-10-CM E78.2*-E78.5*
Hypertension	Diagnosis of ICD-10-CM I10*-I16*
Face-to-face encounter	An encounter with a type of Emergency, Office Visit, Well Child, Follow-up, Telemedicine, Urgent Care, Walk-In, Routine Prenatal, Postpartum Visit, or Fetal Care Consult
Type 2 diabetes	Diagnosis with ICD-10-CM code E11*

Table 1: Likelihood of MI by Average HbA1c

Average HbA1c	Ratio	95% CI Low	95% CI High
4.0–4.9%	0.95	0.71	1.28
5.0–5.3%	0.89	0.79	1.00
5.4–5.6%	0.88	0.81	0.95
5.7–6.0%	0.92	0.86	0.97
6.1–6.4%	0.97	0.92	1.03
6.5–6.74%	0.99	0.92	1.05
baseline			
7.0–7.4%	1.13	1.06	1.20
7.5–7.9%	1.29	1.21	1.38
8.0–9.9%	1.70	1.60	1.80
10+%	2.53	2.36	2.73

Table 2: Likelihood of Stroke by Average HbA1c

Average HbA1c	Ratio	95% CI Low	95% CI High
4.0–4.9%	1.15	0.92	1.43
5.0–5.3%	1.07	0.98	1.17
5.4–5.6%	0.97	0.91	1.03
5.7–6.0%	0.93	0.88	0.97
6.1–6.4%	0.95	0.90	0.99
6.5–6.74%	0.99	0.94	1.04
baseline			
7.0–7.4%	1.09	1.03	1.14
7.5–7.9%	1.24	1.18	1.31
8.0–9.9%	1.59	1.52	1.66

10+%	2.40	2.27	2.55