

# Inhaled and Injectable Insulin Produce Comparable A1c Reductions Among Diabetics

Team A: Christopher Alban, MD; Grant Keane

Team B: Kersten Bartelt, RN; Joe Deckert, PhD

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## Key Findings:

- Among patients with type 1 diabetes, inhaled insulin use was associated with a 0.68 percentage point reduction in average HbA1c, while injectable insulin was associated with a 0.82 percentage point reduction.
- Among patients with type 2 diabetes, inhaled insulin was associated with a 0.50 percentage point reduction in average HbA1c, while injectable insulin was associated with a 0.46 percentage point reduction.

Inhaled insulin offers an alternative to injectable fast-acting insulin, potentially improving adherence and patient satisfaction. Approved for adults with diabetes, inhaled formulations have seen limited adoption due to concerns about pulmonary safety, variability in absorption, and cost.<sup>1,2</sup> While clinical trials suggest similar glycemic efficacy between inhaled and injectable insulins, real-world comparative effectiveness data remain limited.<sup>1</sup>

We studied 118,940 patients with type 1 or 2 diabetes who were newly prescribed injectable fast-acting insulin or inhaled insulin between January 2017 and May 2025. Patients were excluded if they had a history of smoking, asthma, COPD, or pregnancy during the study period to ensure all patients were eligible for either kind of insulin. All patients had a baseline HbA1c lab within the 12 months prior to the prescription, with the closest lab to the prescription being used if there were multiple. All included patients also had a follow-up HbA1c lab in the 3 to 12 months after the prescription was given.

We found that patients with type 1 diabetes who were prescribed inhaled insulin had an average HbA1c reduction of 0.68 percentage points, compared to 0.82 points for those on injectable insulin, as seen in Figure 1. For patients with type 2 diabetes, inhaled insulin users had an average reduction of 0.50 percentage points, while those on injectable insulin had a 0.46 percentage point reduction. Prior literature suggests a 0.5 percent point change in HbA1c between readings is considered significant.<sup>3</sup>

## Change in HbA1c by Insulin Route

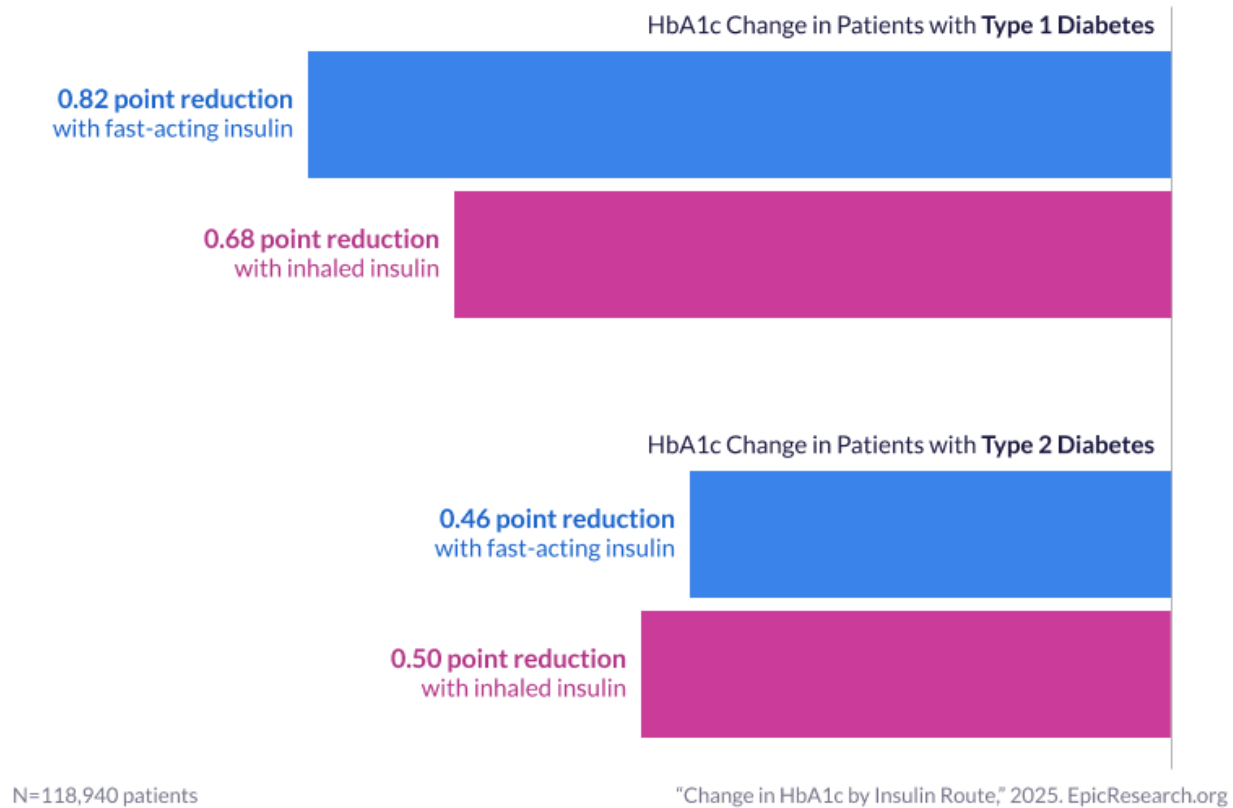


Figure 1. The absolute change in HbA1c by the route of insulin prescribed and the type of diabetes the patient was diagnosed with.

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 1,800 hospitals and more than 41,000 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 scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

## References

1. Fala L. Afrezza (Insulin Human) Inhalation Powder Approved for the Treatment of Patients with Type 1 or Type 2 Diabetes. *Am Health Drug Benefits*. 2015;8(Spec Feature):40-43.
2. American Diabetes Association Professional Practice Committee. 9. Pharmacologic approaches to glycemic treatment: Standards of care in diabetes-2025. *Diabetes Care*. 2025;48(1 Suppl 1):S181-S206. doi:10.2337/dc25-S009
3. Weykamp C. HbA1c: a review of analytical and clinical aspects. *Ann Lab Med*. 2013;33(6):393-400. doi:10.3343/alm.2013.33.6.393

## Data Definitions

Term	Definition
Study period	1/2017 to 5/2025
Study population: inclusion	Patients with: <ul style="list-style-type: none"> <li>• A new prescription for <b>inhaled</b> or <b>injectable fast-acting insulin</b></li> <li>• No history of <b>inhaled</b> or <b>injectable fast-acting insulin</b></li> <li>• A billing, encounter, or problem list diagnosis of type 1 diabetes (ICD-10-CM code E10*) or type 2 diabetes (ICD-10-CM code E11*)</li> <li>• An <b>HbA1c</b> result 3 to 12 months following the <b>exposure</b></li> <li>• An <b>HbA1c</b> result within the 12 months prior to <b>exposure</b>, with the one closest to the exposure used as baseline</li> </ul>
Study population: exclusion	Patients with: <ul style="list-style-type: none"> <li>• A history of smoking</li> <li>• A history of COPD: a billing, encounter, or problem list diagnosis with ICD-10-CM code J41*-J44*</li> <li>• A history of asthma: a billing, encounter, or problem list diagnosis with ICD-10-CM code J45*</li> <li>• A pregnancy during study period</li> </ul>
Outcomes	Average <b>HbA1c</b> in the 3 to 12 months following <b>exposure</b>
Inhaled insulin	An order with ATC code A10AF*
Injectable fast-acting insulin	An order with ATC code A10AB* or A10AD* with a route of injection/subcutaneous
HbA1c	A lab with LOINC code 17856-6, 17855-8, 4548-4, or 4549-2
Model specifications	Linear regression. Additionally, a sensitivity analysis was performed for changes between HbA1c categories.

**Table 1: Change in HbA1c by Insulin Route**

	Type	Mean Absolute HbA1c Change
Type 1 Diabetes	Fast acting Insulin	0.82
	Inhaled Insulin	0.68
Type 2 Diabetes	Fast acting Insulin	0.46
	Inhaled Insulin	0.50