mannkind MEDICAL

Addressing Therapeutic Challenges with Inhaled Insulin

- Introduction to Technosphere Insulin
- INHALE-1 (Pediatric)
- INHALE-3 (Adult)
- Meal Challenges
- Afrezza Prescribing Information

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Unmet Needs in Insulin-Treated Diabetes[1-3]

Barriers to Glycemic Management

- Therapeutic inertia (limited visit time, fragmented care, outdated protocols)
- Access issues (insurance restrictions, cost of medications)
- Physician burnout
- Adherence challenges (fear of hypoglycemia, poor insulin absorption, needle aversion, regimen complexity, injecting in public, weight gain)
- Perceptions surrounding insulin efficacy

Limitations of Insulin Pumps

- Unplanned infusion set changes
- Skin irritation and infusion-site reactions
- Maladaptive wound healing
- Lipohypertrophy

Advantages of Technosphere Insulin (TI)

- Rapid absorption and shorter duration of action → mitigates risk of late post-meal hypoglycemia
- Flexible dosing with lower risk of "stacking"
- Weight neutrality or slight weight loss compared to RAAs
- Eliminates needles and injection pain; often improves medication taking
- Proven HbA1c reduction in patients with T1D with significantly lower hypoglycemia risk[3]

HbA1c, hemoglobin A1c; RAA, rapid-acting insulin analog; T1D, Type 1 diabetes.

1. Hirsch IB, Parkin CG. *Diabetes Technol Ther.* 2026;28(1_suppl):14S-18S. 2. Hood KK, Polonsky WH. *Diabetes Technol Ther.* 2026;28(1_suppl):64S-69S. 3. Bode BW, et al. *Diabetes Care.* 2015;38(12):2266-2273.

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Delivery Considerations of Injectable Insulins

- **Pain**[1]
- **Needle phobia**[2]
- **Risk of infection**[3]
- **Changes at the injection site (e.g., lipoatrophy, lipoma)**[2]
- **Higher rates of hypoglycemia at >2-5 hours post meal in comparison to TI in AFFINITY-1 trial***[,4]

*Randomized, open-label, multicenter, 24-week, noninferiority phase 3 trial; primary endpoint: change in HbA1c from baseline to week 24.

HbA1c, hemoglobin A1c.

1. Goldman JD, Angueira-Serrano E, Gonzalez, JS, et al. *Clinical Diabetes* 2023;41(2):244–257. 2. Ludvigsson J. *Pediatr Endocrinol Rev*. 2020;17(Suppl 1):183-190. 3. Patel B, Priefer R. *Diabetes Metab Syndr* 2021;15(2):519-524. 4. Bode BW, McGill JB, Lorber DL, et al. *Diabetes Care*. 2015;38:2266-2273.

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ADA Standards of Care in Diabetes 2026: Approach to Glycemic Treatment[1,2]

Considerations for Insulin Initiation

Evaluate insulin dose and insulin-taking behaviors at every visit to determine the need for modifications to the method of insulin administration (e.g., switching to/from MDI, AID, inhaled insulin)

Reassessment or Titration of Insulin

Frequently reassess blood glucose levels using CGM and/or SMBG. Adjust basal and prandial insulin doses based on individual goals and hypoglycemia or hyperglycemia patterns

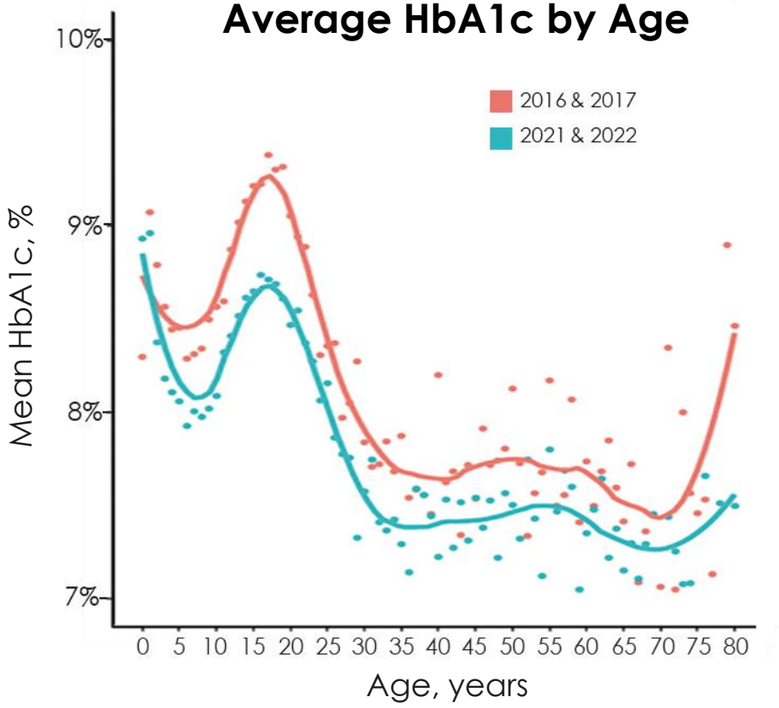
ADA, American Diabetes Association; AID, automated insulin delivery; CGM, continuous glucose monitoring; MDI, multiple daily injections; SMBG; self-monitoring of blood glucose.

1. American Diabetes Association Professional Practice Committee for Diabetes. *Diabetes Care*. 2026;49(Supplement_1):S150-S165. 2. American Diabetes Association Professional Practice Committee for Diabetes. *Diabetes Care*. 2026;49(Supplement_1):S183-S215. :10.2337/dc26-S009

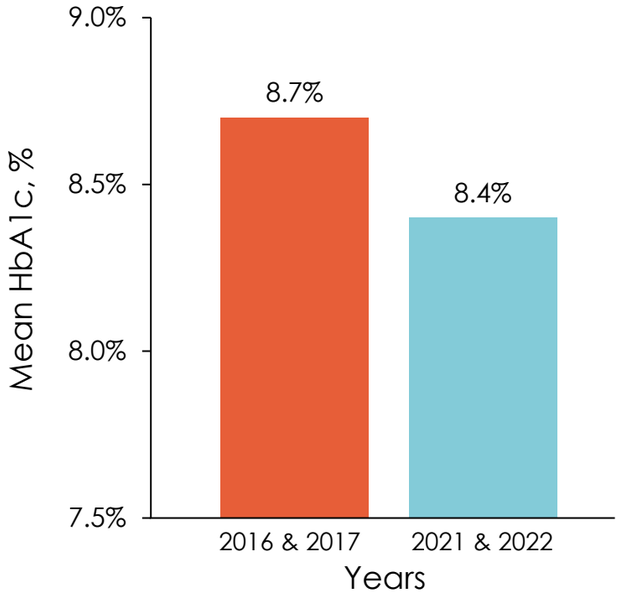
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State of Diabetes Control: T1D

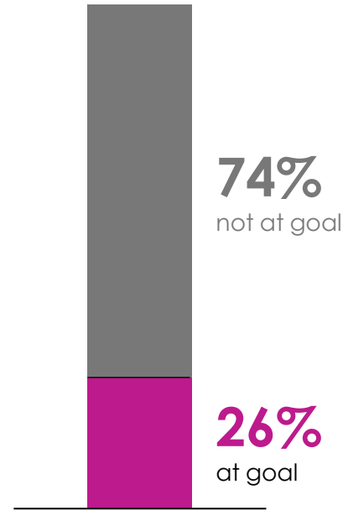
Average HbA1c by Age



Average HbA1c



Glycemic Control in 2021 and 2022



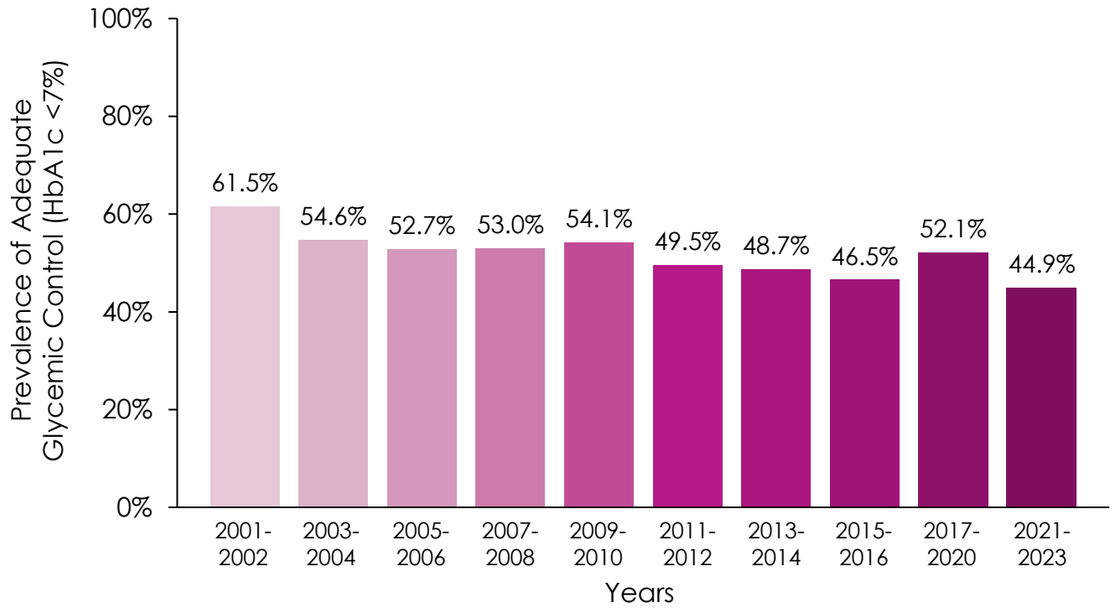
HbA1c goal of 7%

HbA1c, hemoglobin A1c; T1D, type 1 diabetes.
Adapted from Ebekozien O et al. *Diabetes Technol Ther.* 2023;25(11):765-773.

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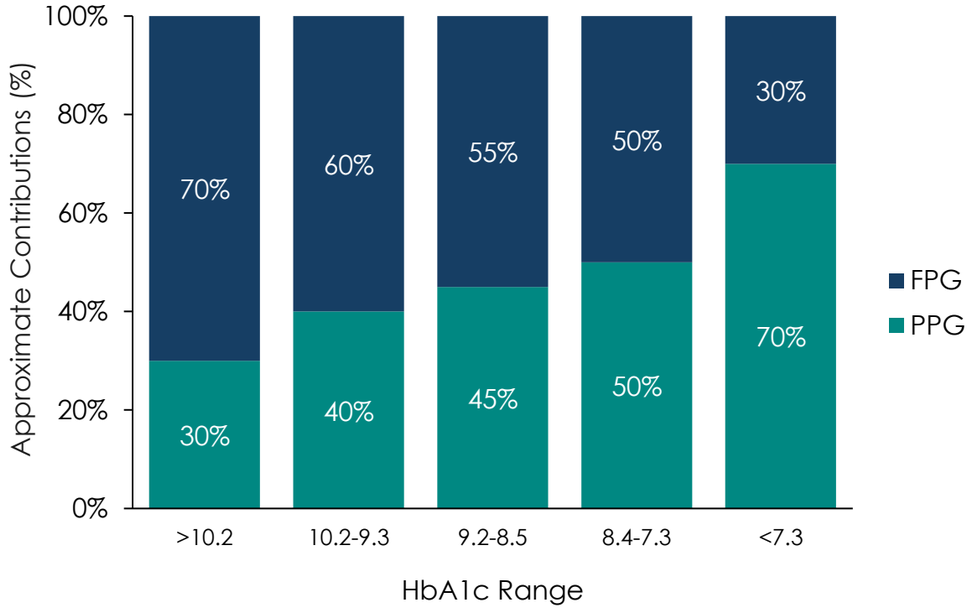
State of Diabetes Control: T2D

Minor Improvement of HbA1c in Patients With Diabetes[1]



>90% of the participants were expected to have T2D

Relative Contributions of Fasting and Postprandial Hyperglycemia Across HbA1c Quintiles[2]



FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; PPG, prandial plasma glucose; T2D, type 2 diabetes.

1. Adapted from Hu M, et al. *Acta Diabetol*. 2025;62(12):2159-2170. 2. Monnier L, et al. *Diabetes Care*. 2003;26(3):881-885.

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Technosphere® Insulin Inhalation Powder & Inhaler

Indications and Usage

- AFREZZA is a rapid acting inhaled human insulin indicated to improve glycemic control in adult and pediatric patients 6 years of age and older with diabetes mellitus

Limitations of Use

- Not recommended for the treatment of DKA
- Not recommended in patients who smoke or who have recently stopped smoking

Boxed Warning

WARNING: RISK OF ACUTE BRONCHOSPASM IN PATIENTS WITH CHRONIC LUNG DISEASE

- Acute bronchospasm has been observed in AFREZZA-treated patients with asthma and COPD (5.1)
- AFREZZA is contraindicated in patients with chronic lung disease such as asthma or COPD (4)
- Before initiating AFREZZA, perform a detailed medical history, physical examination, and spirometry (FEV_1) to identify potential lung disease in all patients (2.1), (5.1)

Contraindications

- During episodes of hypoglycemia *[see Warnings and Precautions (5.3)]*.
- Chronic lung disease, such as asthma or COPD, because of the risk of acute bronchospasm *[see Warnings and Precautions (5.1)]*
- Hypersensitivity to regular human insulin or any of the excipients in AFREZZA *[see Warnings and Precautions (5.7)]*

Adverse Reactions

- The most common adverse reactions associated with AFREZZA (2% or greater incidence) are hypoglycemia, cough, and throat pain or irritation (6)

Drug/Device Combination Product

- Compact inhaler
- Pre-filled single-use cartridges (4-, 8-, 12-unit cartridges)
- Breath-powered delivery

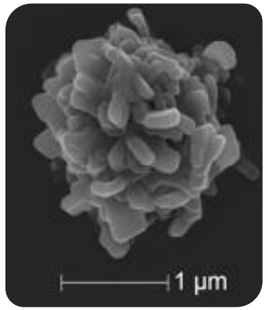


Cartridges not to scale

COPD, chronic obstructive pulmonary disease; DKA, diabetic ketoacidosis; FEV_1, forced expiratory volume in 1 second.
Afrezza® (insulin human) Inhalation Powder Prescribing Information. MannKind Corporation.

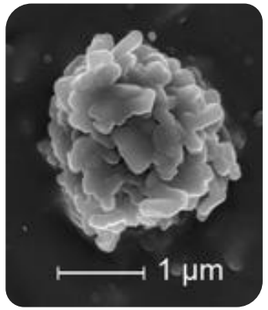
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Oral Inhalation Insulin Delivery



Technosphere
Microparticles (FDKP)

Water + Human Regular Insulin =



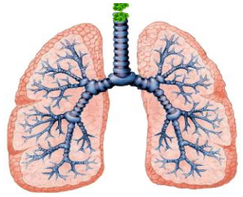
Technosphere
Insulin

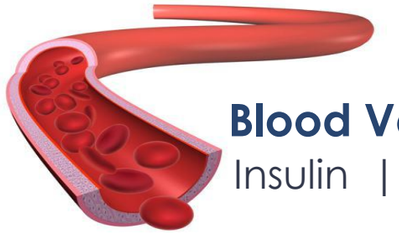
pH <6 Technosphere Insulin: Insulin adsorption onto FDKP particle



pH >6 (physiologic pH)

- Inhaled particles dissolve rapidly and separate
- FDKP and insulin are then quickly absorbed across the lung membrane





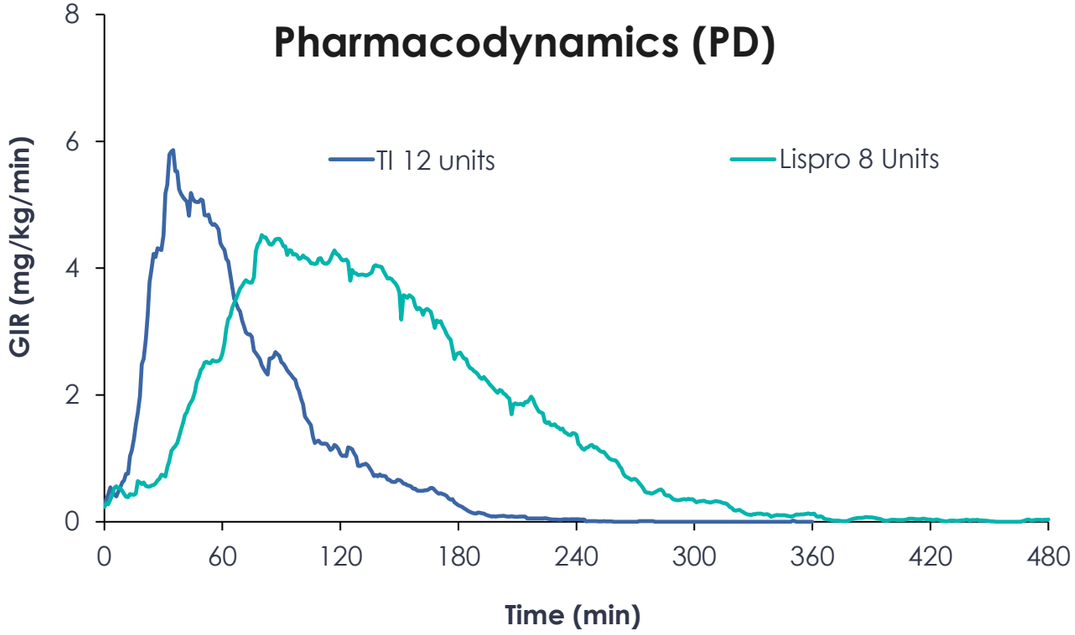
Blood Vessel
Insulin | FDKP

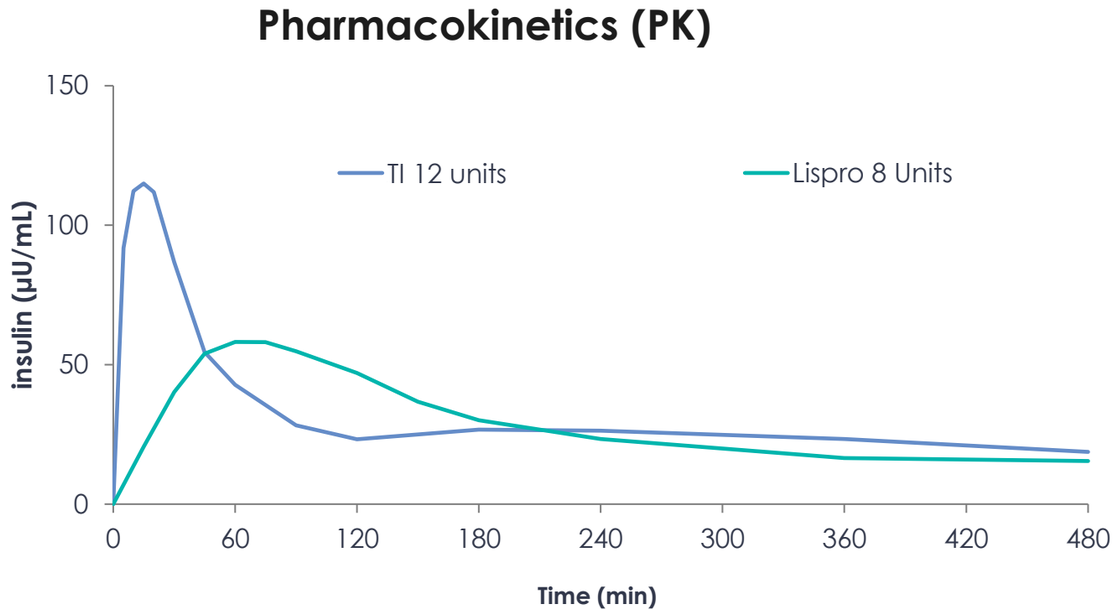
FDKP, fumaryl diketopiperazine.

Pfützner A, Forst T. *Expert Opin Drug Deliv*. 2005;2(6):1097-1106.

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PK/PD: Inhaled Insulin Compared to Injected Lispro[1,2]





The clinical significance of these PK/PD differences has not been established

GIR, glucose infusion rate.

1. Adapted from Heinemann L, et al. *J Diabetes Res*. 2018;2018:4568903. 2. Adapted from Grant M, et al. *Clin Pharmacokinet*. 2022;61(3):413-422.

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Technosphere Insulin (TI) Considerations

Patient Selection[1]

- T1D patients requiring prandial insulin
  - Those struggling with delayed absorption or hypoglycemia due to insulin stacking
- T2D patients who are not achieving their HbA1c goal on oral agents
- Unpredictable meal schedules
- Patients with "sticky highs" who are resistant to correction with subcutaneous insulin
- Pump users may benefit from TI, particularly those desiring rapid onset and clearance

Rapid on/ Rapid off PK/PD

- Allows for supplemental dosing 1-2 hours post prandial without increasing the time in hypoglycemia[2]
- Reduced late post prandial hypoglycemia vs comparators[3]
- Suppresses endogenous glucose production more rapidly than lispro to lower BG levels[4]
- Higher TDD needed when converting to TI from injectable RAA[2,3,5]

TI has a different bioavailability than injectable insulins resulting in a higher total daily dose, and with less weight gain[5-7]

BG, blood glucose; PK, pharmacokinetics; PD, pharmacodynamics; RAA, rapid-acting insulin analog; T1D, type 1 diabetes; T2D, type 2 diabetes; TDD, total daily dose.

1. Edelman SV, et al. *Diabetes Technol Ther.* 2026;28(1_suppl):8S-13S. 2. Akturk HK, et al. *Diabetes Technol Ther.* 2018;20(10):639-647. 3. Bode BW, et al. *Diabetes Care*. 2015;38(12):2266-2273. 4. Potocka E, et al. Poster 1561-P Presented at: American Diabetes Association Conference; June 2010; Orlando, Florida. 5. Hirsch IB, et al. *Diabetes Care*. 2025;48(1):1-8. 6. Beck RW, et al. *Diabetes Technol Ther.* 2025;27(3):161-169. 7 . Grant M, et al. *Clin Pharmacokinet*. 2022;61(3):413-422.

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Clinical Considerations: Dosing

Patient education is critical for successful initiation

- Explain TI's rapid action, dosing guidelines and titration strategies
- Explain due to differences in bioavailability, a higher dose of TI is required to achieve the same glycemic effect as subcutaneous insulin
- Emphasize importance of individualized dosing based on meal size, pre-meal glucose levels, and insulin sensitivity
- Educate about safety
  - Low risk of hypoglycemia and lack of long-term adverse lung effects

Examples of TI Use in Clinical Practice

Edelman

- For patients who are using CGM, Initiate TI as correction dose
  - 4U if >220 mg/dL, if it doesn't correct hyperglycemia, correct with an 8U cartridge
  - 8U if insulin-resistant
- Repeat or adjust doses based on individual response

Hirsch

- Starting dose is ~2x required RAA units, rounded down to the nearest available TI cartridge
  - Closer to 3x dose may be necessary for effectiveness
- Start insulin-naive patients on 4 units of TI, then titrate to effect based on PPG
- Ensure patient is on correct basal dose before starting TI

Blevins

- Patients are advised to titrate TI dose based on size of meal and their premeal glucose levels
  - Large meals may require higher doses
- Take correction dose 1-2 h after a meal if >180 mg/dL
- Correct glucose levels >140 mg/dL at bedtime to optimize morning readings.

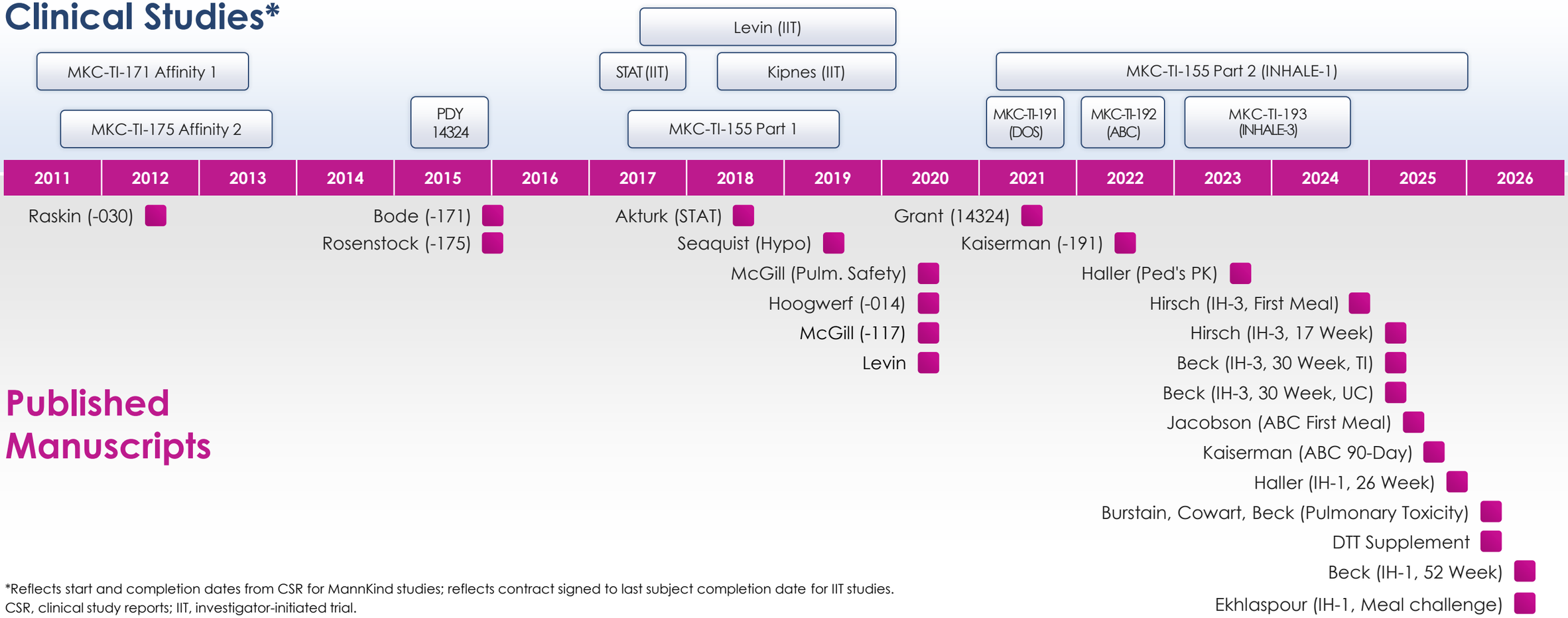
CGM, continuous glucose monitor; PPG, post-prandial glucose; RAA, rapid-acting insulin analog.

Edelman SV, et al. *Diabetes Technol Ther.* 2026;28(1_suppl):8S-13S.

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Clinical Studies and Manuscripts

Clinical Studies*



Published Manuscripts

*Reflects start and completion dates from CSR for MannKind studies; reflects contract signed to last subject completion date for IIT studies.
CSR, clinical study reports; IIT, investigator-initiated trial.

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INHALE-1 (Pediatric)

Randomized trial of youth ≥4 to <18 years old with T1D or T2D at 38 U.S. sites[1,2]

- 1:1 randomization (26 weeks)
  - **TI group:** TI + basal insulin
  - **RAA injection group:** Insulin aspart, insulin lispro or insulin glulisine + basal insulin
- Primary outcome: HbA1c (non-inferiority) at 26 weeks
- Secondary outcomes: CGM metrics, insulin dose, weight, DTSQ
- Safety outcomes: severe hypoglycemia/DKA, pulmonary and other AEs, FEV_1



INHALE-1 26-week extension phase followed 26-week randomized phase[3]

- 2 groups: **Continued TI** and **RAA crossover**
- Key outcomes: HbA1c and FEV_1 at week 52

INHALE-1 RCT > | INHALE-1 extension phase >

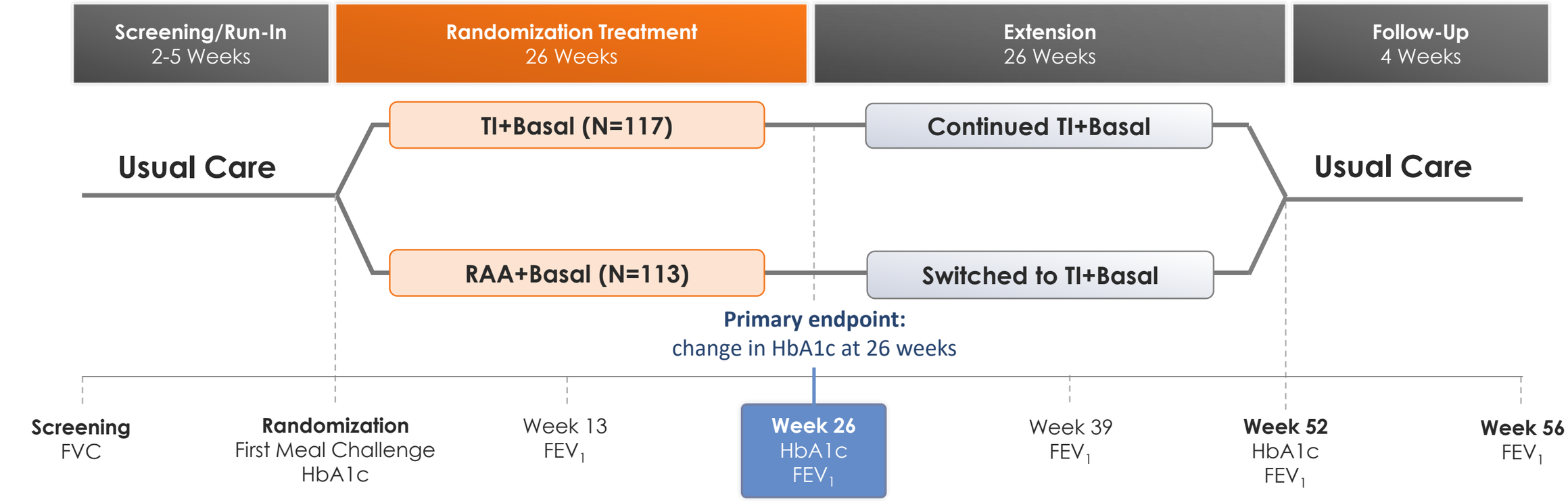
AE adverse event; CGM, continuous glucose monitor; DKA, diabetic ketoacidosis; DTSQ, Diabetes Treatment Satisfaction Questionnaire; FEV_1, forced expiratory volume in 1 second; HbA1c, hemoglobin A1c; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; T1D, type 1 diabetes; T2D, type 2 diabetes; TI, Technosphere Insulin.

1. Haller MJ, et al. *Diabetes Care*. 2026;49(1):179-187. 2. Data on File (MKC-TI-155 Part 2, Clinical Study Report, 2025). MannKind Corporation. 3. Beck RW, et al. *Diabetes Technol Ther*. Published online February 4, 2026. doi:10.1177/15209156261420176

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INHALE-1 Study[1,2]

38 US Sites
≥4 and <18 years old T1D or T2D



FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; HbA1c; hemoglobin A1c; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; T1D, type 1 diabetes; T2D, type 2 diabetes.

1. Haller MJ, et al. *Diabetes Care.* 2026;49(1):179-187. 2. Data on File (MKC-TI-155, Clinical Study Report, 2025). MannKind Corporation.

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Eligibility Criteria

Key Inclusion Criteria

- Age ≥4 to <18 years
- Clinical diagnosis of T1D or T2D and on insulin for 6 months (T1D) or 3 months (T2D)
- MDI for at least 2 weeks
- HbA1c ≥7.0% and ≤11.0%
- At least 2 units of prandial insulin per meal
- CGM use ≥70% over 2 weeks

Key Exclusion Criteria

- Asthma treatment in prior 12 months
- Smoking in prior 6 months
- Positive cotinine test
- History of lung cancer
- Pregnant or breastfeeding
- DKA or severe hypoglycemia in prior 3 months
- FEV_1 or FEV_1/FVC ≤80% of predicted GLI value

CGM, continuous glucose monitor; DKA, diabetic ketoacidosis; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GLI, global lung function initiative; HbA1c, hemoglobin A1c; MDI, multiple daily injections; RCT, randomized controlled trial; T1D, type 1 diabetes; T2D, type 2 diabetes.

Haller MJ, et al. *Diabetes Care*. 2026;49(1):179-187.

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INHALE-1 Dosing Protocol

TI Titration Protocol

- Titrate to target 60- to 90-minute post-prandial glucose level within 70 to 160 mg/dL
- For meals, subjects were advised to add 4 units if the pre-meal glucose was >160 mg/dL or for a larger-than-usual carbohydrate meal, and to decrease by 4 units for a smaller-than-usual meal

Glucose Value 60-90 Minutes Post-prandial (mg/dL)	Recommended Mealtime Dose Titration
<70	- 4 units
70-160	No Change
>160	+ 4 units

TI Correction Dosing

- Correction dosing with TI is particularly important at bedtime
- Subjects may take correction doses larger than 4 units at the discretion of the investigator

Glucose Range (mg/dL)	Time from Last TI Dose	Units Given
>160	1 – 1.5 hours (day/bedtime)	4 units

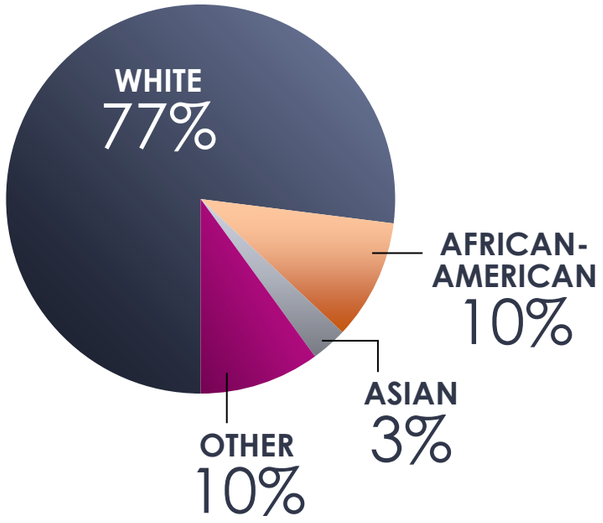
Subjects were instructed to inject basal insulin each evening as 1 dose or per investigator's discretion. If fasting morning glucose <70 mg/dL or >120mg/dL, investigator should consider titrating.

RCT, randomized controlled trial.
Data on File (MKC-TI-155 Part 2 Protocol, 2023). MannKind Corporation.

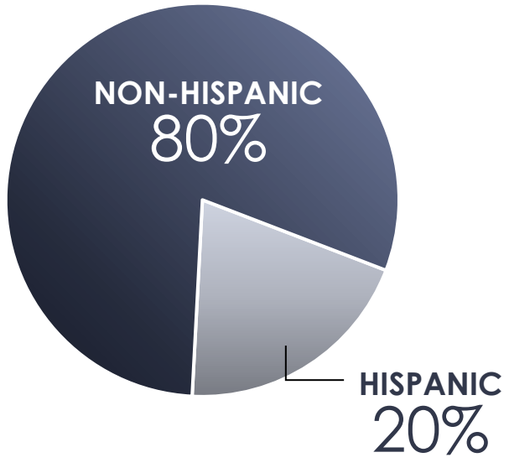
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Baseline Characteristics and Diabetes History[1,2]

Race



Ethnicity



Intent to Treat Population	
	Overall (N=230)
Age, years	
Mean (SD)	12.6 (3.0)
Median (min, max)	13.0 (4,17)
4 to <13	105 (46)
13 to <18	125 (54)
Female	38%
Diabetes type, n (%)	
T1DM	225 (98)
T2DM	5 (2)
Age at diagnosis of diabetes, years	
Mean (SD)	8.17 (3.450)
Median (min, max)	8.00 (1.0,17.0)
Baseline HbA1c, %	
Mean (SD)	8.2 (0.9)
Median (min, max)	8.00 (6.3,11.0)
<7.0 (<53 mmol/mol)	8 (3)
7.0-8.4 (53-68 mmol/mol)	138 (60)
8.5-9.9 (69-85 mmol/mol)	73 (32)
≥10.0 (≥86 mmol/mol)	11 (5)
BMI	
Mean Percentile/ ≥95th %	74.4 / 23%

BMI, body mass index; HbA1c, hemoglobin A1c; RCT, randomized controlled trial; SD, standard deviation; T1DM, Type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

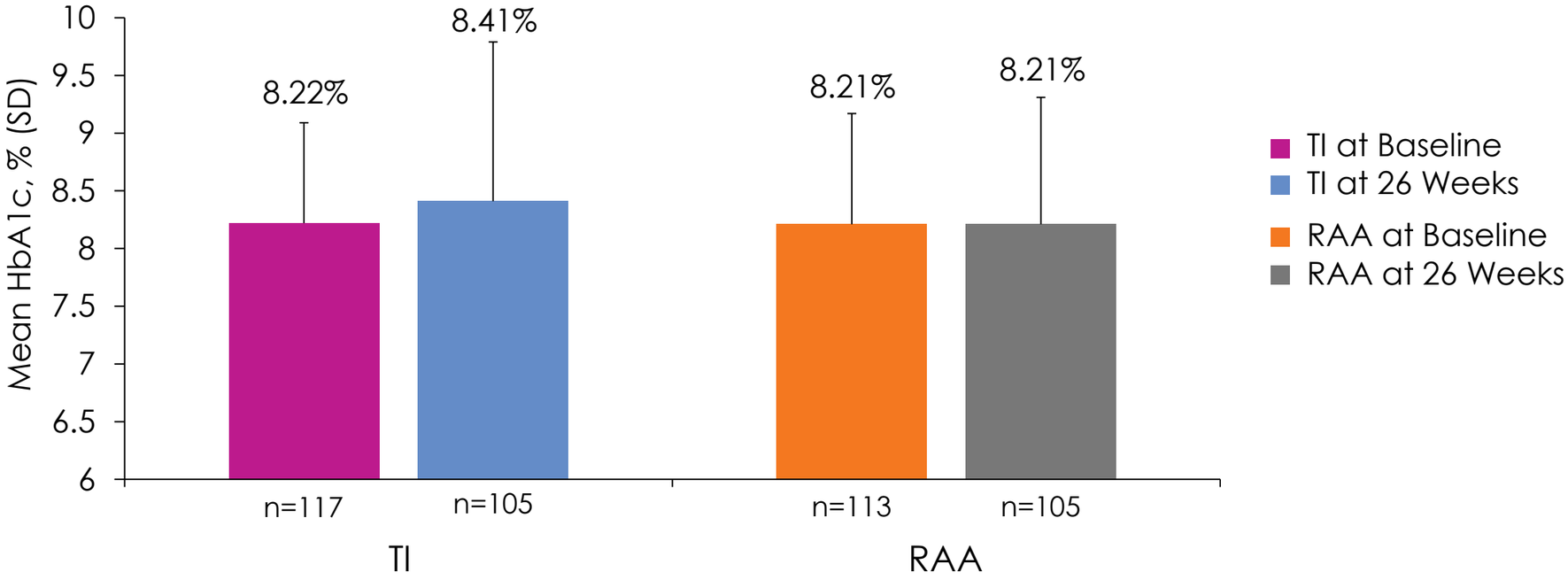
1. Haller MJ, et al. *Diabetes Care.* 2026;49(1):179-187. 2. Data on File (MKC-TI-155 Part 2, Clinical Study Report, 2025). MannKind Corporation.

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HbA1c: Primary Endpoint

Change in Mean HbA1c from Baseline to 26 Weeks

Adjusted Difference 0.18% (95% CI -0.07 to 0.43); *P*=0.091 for noninferiority*



*noninferiority margin 0.4%

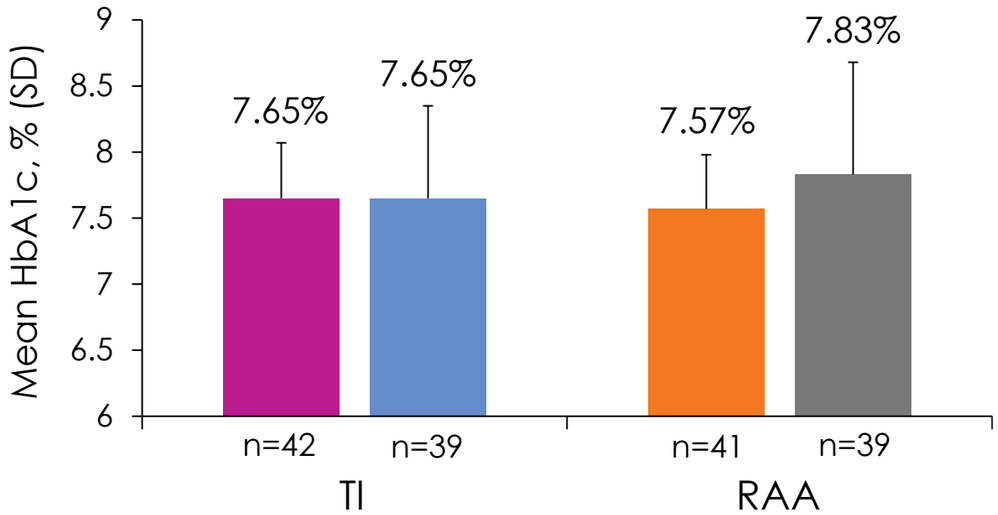
CI, confidence interval; HbA1c, hemoglobin A1c; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; TI, Technosphere Insulin.

Haller MJ, Kanapka L, Monzavi R, et al. *Diabetes Care*. 2026;49(1):179-187.

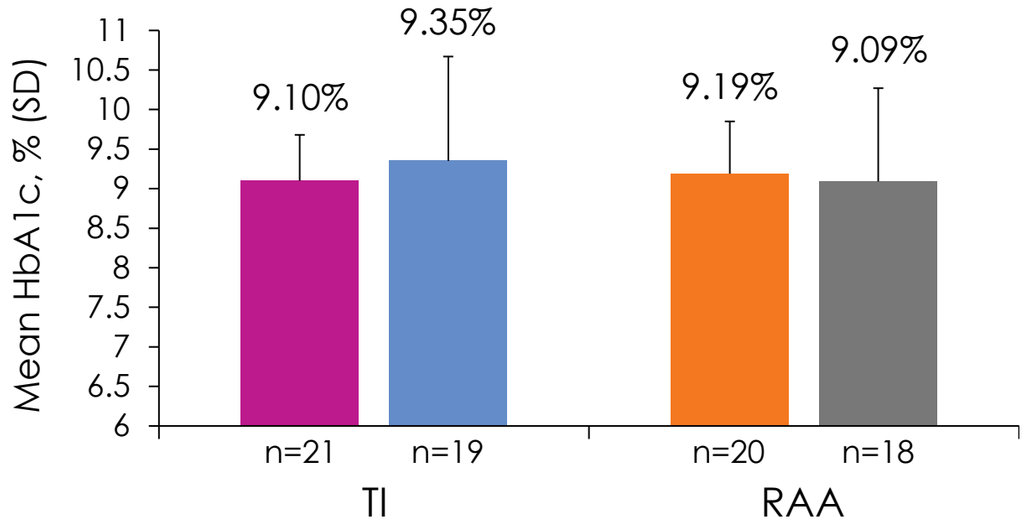
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HbA1c: Outcomes by Age and Baseline A1c

Age ≥13 years/HbA1c <8.5%
Adjusted Difference (95% CI):
-0.17 (-0.56 to 0.22)



Age ≥13 years/HbA1c ≥8.5%
Adjusted Difference (95% CI):
0.17 (-0.61 to 0.94)

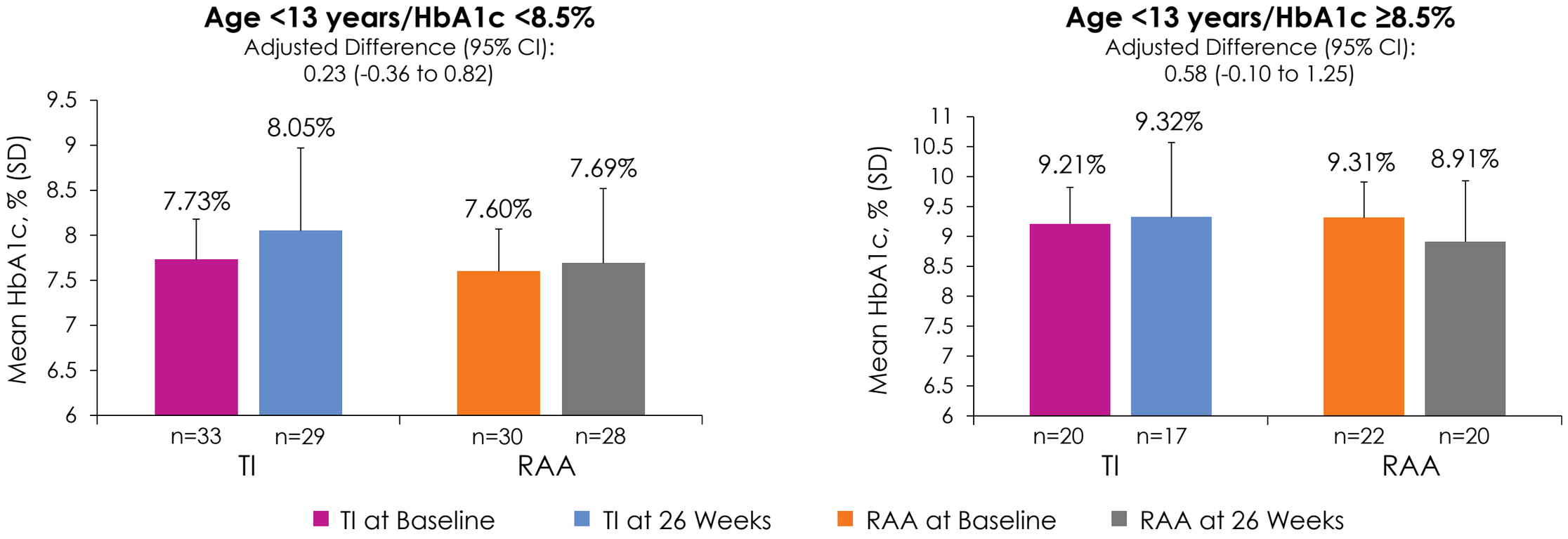


TI at Baseline | TI at 26 Weeks | RAA at Baseline | RAA at 26 Weeks

CI, confidence interval; HbA1c, hemoglobin A1c; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.
Haller MJ, Kanapka L, Monzavi R, et al. *Diabetes Care*. 2026;49(1):179-187.

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HbA1c: Outcomes by Age and Baseline A1c

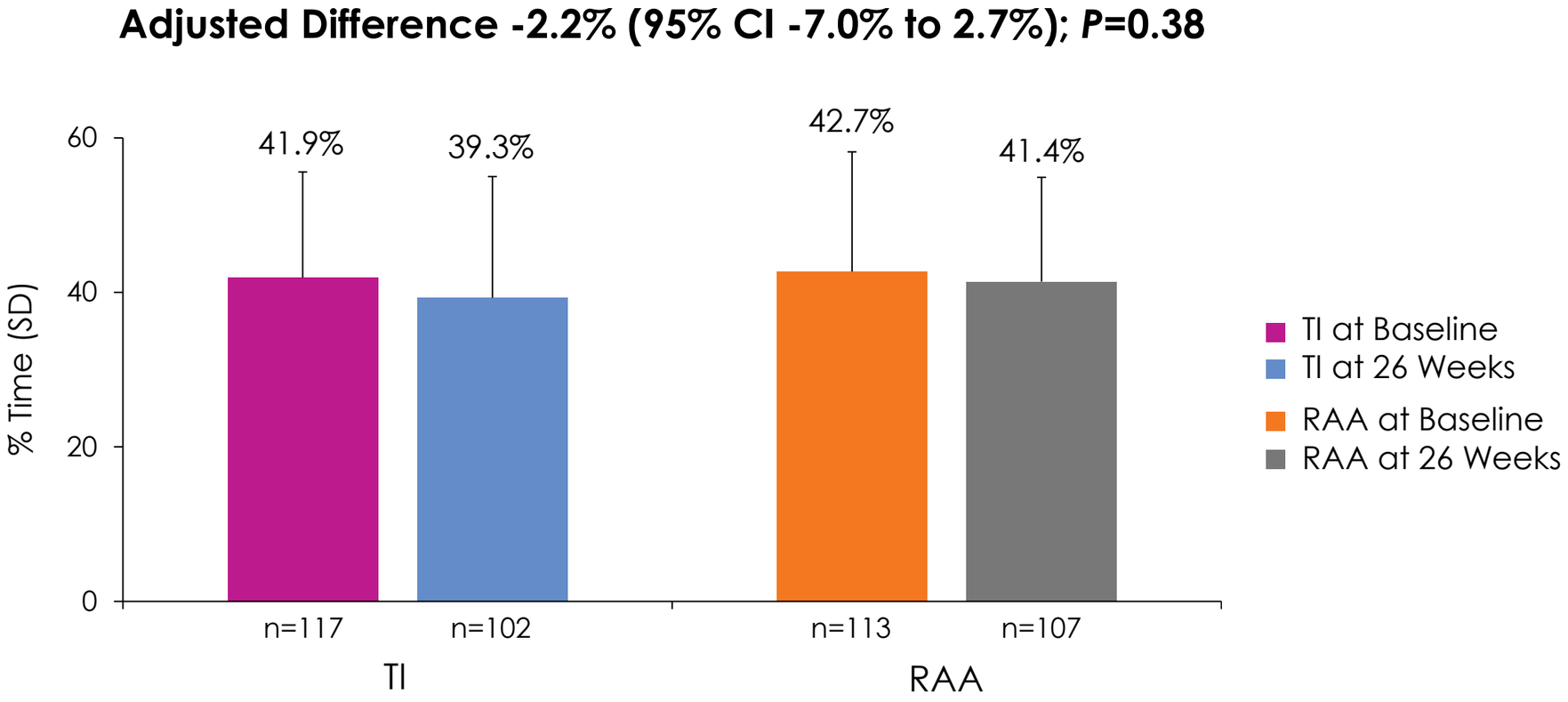


CI, confidence interval; HbA1c, hemoglobin A1c; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.

Haller MJ, et al. *Diabetes Care*. 2026;49(1):179-187.

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CGM Time-in-Range 70-180 mg/dL



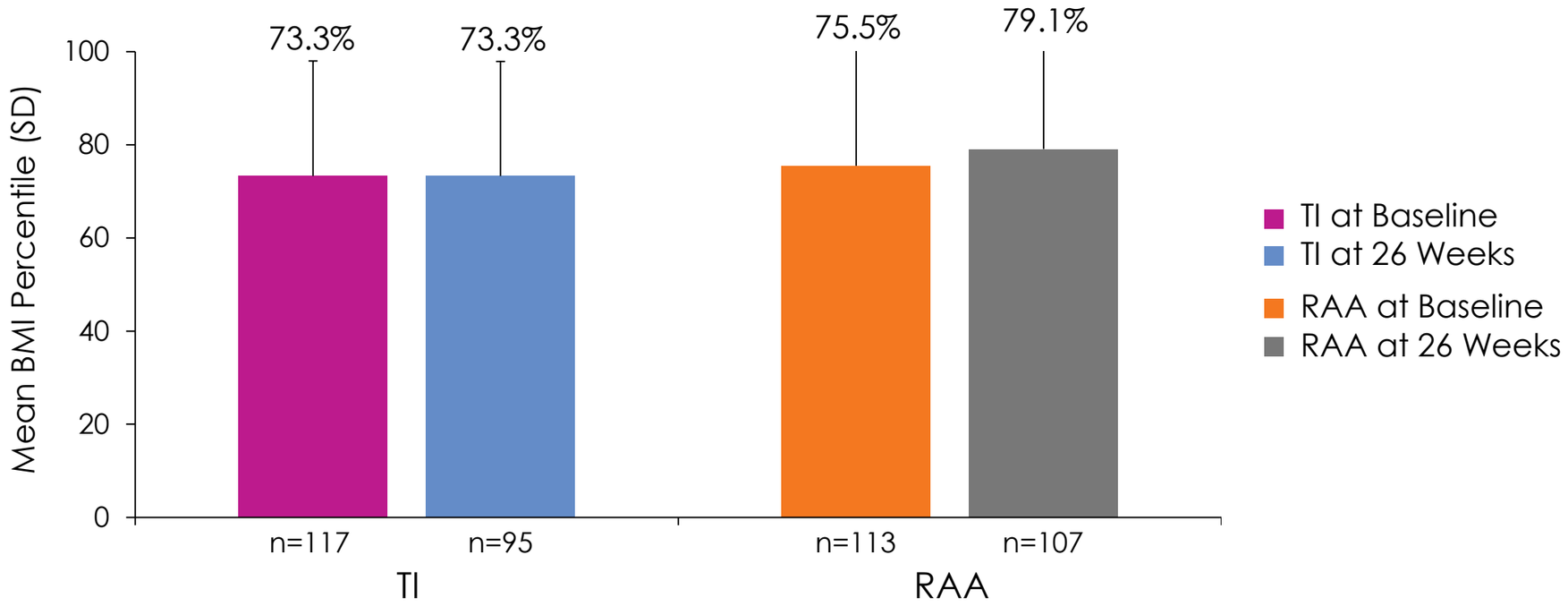
CGM, continuous glucose monitoring; CI, confidence interval; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.
Haller MJ, et al. *Diabetes Care*. 2026;49(1):179-187.

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Body Mass Index

Change in BMI Percentile from Baseline to 26 Weeks

Treatment group difference -4.2 (95% CI -7.4 to -0.9); *P*=0.009

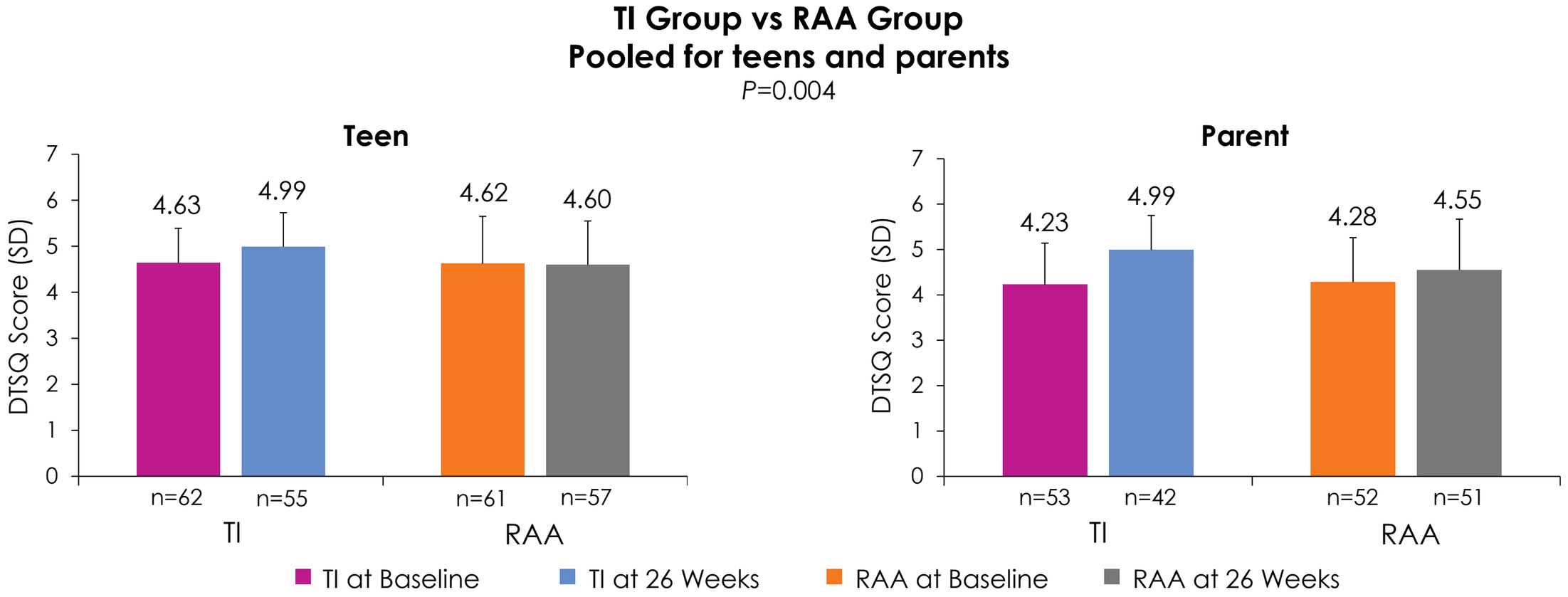


BMI, body mass index; CI, confidence interval; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.

Haller MJ, et al. *Diabetes Care*. 2026;49(1):179-187.

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Diabetes Treatment Satisfaction Questionnaire (DTSQ)



DTSQ, diabetes treatment satisfaction questionnaire; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.

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INHALE-1 AEs

Summary of AEs	TI (n=117)	RAA (n=113)
All AEs, N Events	240	195
# of Participants with ≥ 1 AE	88 (75%)	74 (65%)
Severe Hypoglycemia Events	2*	1
Diabetic Ketoacidosis Events	0	1
Other Serious Adverse Events	1[a]	2[b]

[a]Spinal operation; [b]Osteomyelitis and suicide attempt in one participant.

*One event was unlikely related (no TI dose for several hours prior to the event, and site investigator and medical monitor noted an increase in glargine dose as a potential cause); the other event was due to an accidental inhalation of double the intended TI supplemental dose.

TEAEs Possibly, Probably, or Definitely Related to TI	N of participants
Cough	20
Oropharyngeal pain	9
Pulmonary function test abnormal	5
Dysgeusia	2
Hypoglycemia	1
Dyspnea	1
Chest discomfort	1
Anxiety	1
Bronchospasm	1
Ketosis	1
Fatigue	1
Headache	1
Nausea	1
Pain	1
Wheezing	1
Chest Pain	1

Cough with inhalation - 20/117 (17%)

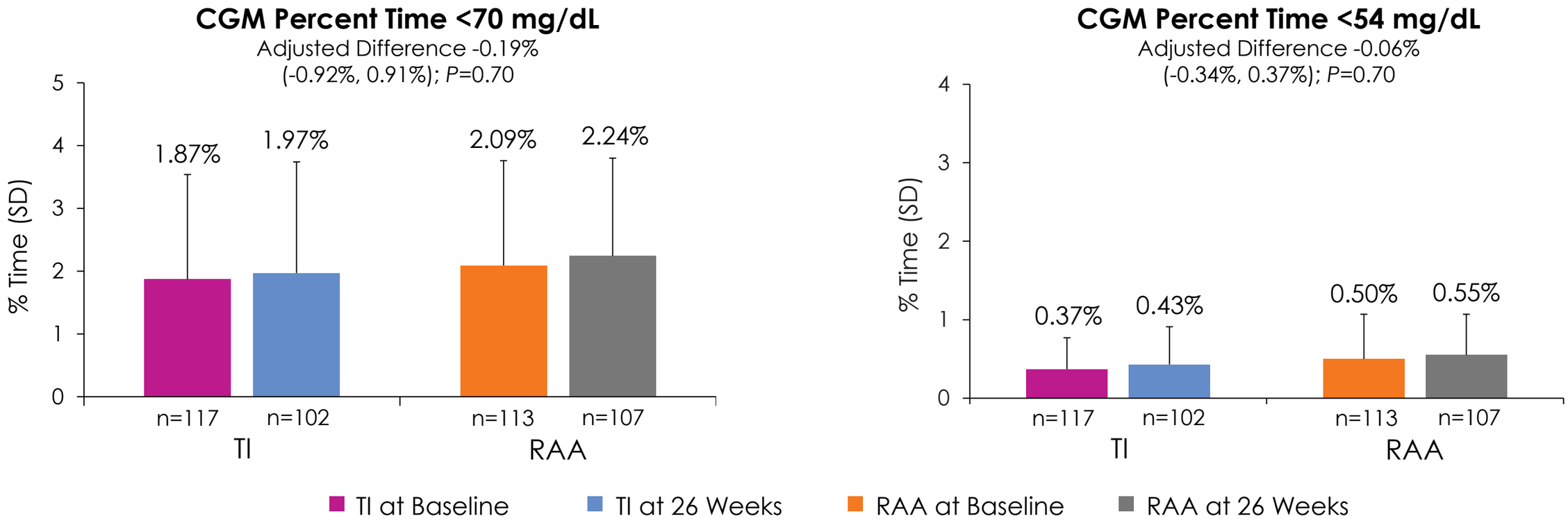
- Typically, mild at time of inhalation (sip of water prior to inhalation mitigates)
- Frequency consistent with adult studies

AE, adverse event; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; TEAE, treatment-emergent adverse events; TI, Technosphere Insulin.

Haller MJ, et al. *Diabetes Care*. 2026;49(1):179-187.

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CGM Metrics: Hypoglycemia



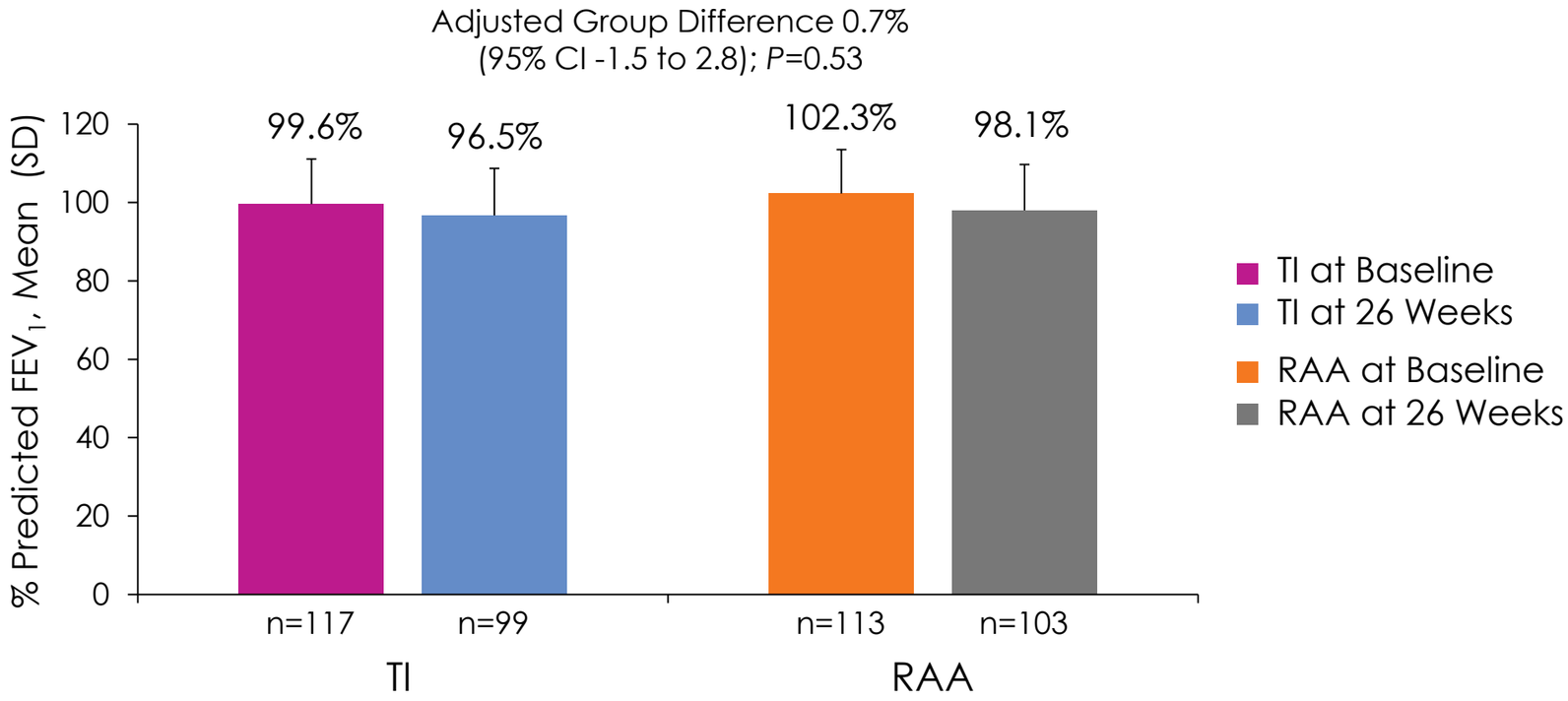
CGM, continuous glucose monitoring; RAA, rapid-acting insulin analog; SD, standard deviation; RCT, randomized controlled trial; TI, Technosphere Insulin.

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Pulmonary Function

Percent Predicted FEV_1 Results

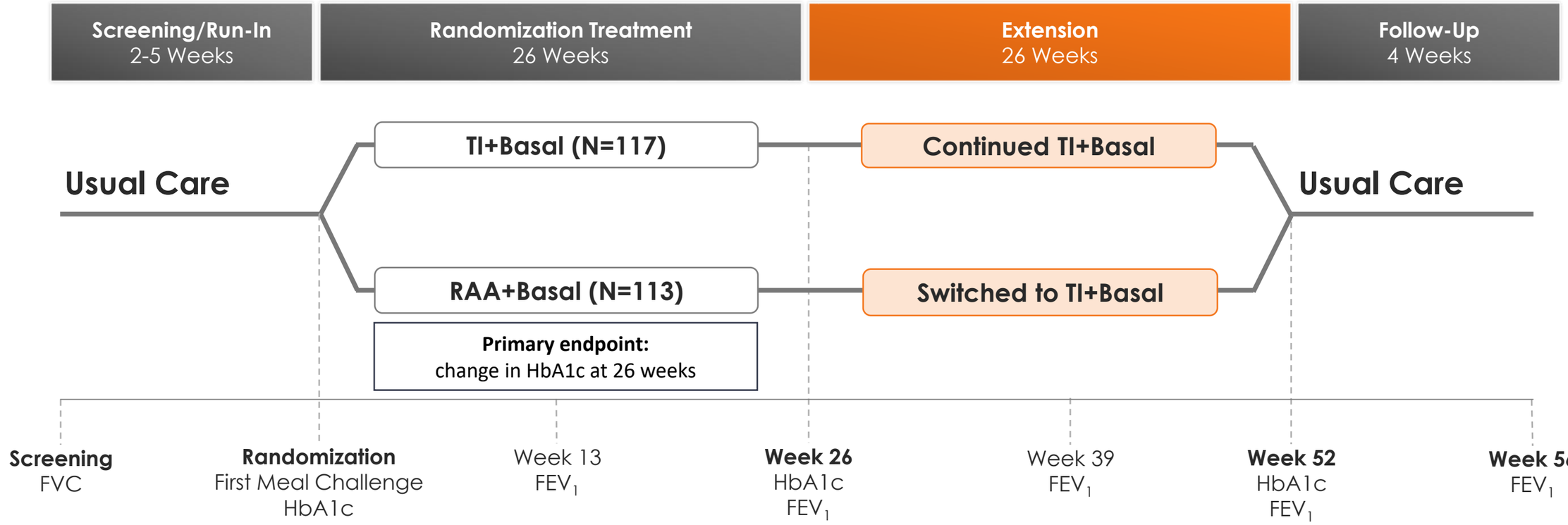


CI, confidence interval; FEV_1, forced expiratory volume in 1 second; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.

Haller MJ, Kanapka L, Monzavi R, et al. *Diabetes Care*. 2026;49(1):179-187.

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INHALE-1 Study - Extension[1,2]



FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; HbA1c; hemoglobin A1c; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; TI, Technosphere Insulin.

1. Haller MJ, et al. *Diabetes Care.* 2026;49(1):179-187. 2. Data on File (MKC-TI-155, Clinical Study Report, 2025). MannKind Corporation.

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Baseline Characteristics and Diabetes History

	TI n=80	RAA Crossover n=88
Age, years		
Mean (SD)	12.7 (3.1)	12.4 (3.1)
Range	6.0-17.0	4.0-17.0
4 to <13 (%)	36 (45)	42 (48)
13 to <18 (%)	44 (55)	46 (52)
Female (%)	26 (33)	28 (32)
Diabetes type, n (%)		
T1DM	77 (96)	88 (100)
T2DM	3 (4)	0
Diabetes duration (yrs)		
Mean (SD)	4.5 (3.4)	4.5 (3.2)
Range	0.5-14.0	0.6-14.0
Central lab HbA1c, %	**N=80**	**N=87**
Mean (SD)	8.1 (0.8)	8.1 (1.1)
<7.0 (<53 mmol/mol)	1 (1)	9 (10)
7.0-8.4 (53-68 mmol/mol)	52 (65)	52 (60)
8.5-9.9 (69-85 mmol/mol)	25 (31)	20 (23)
≥10.0 (≥86 mmol/mol)	2 (3)	6 (7)

	TI n=80	RAA Crossover n=88
BMI		
Mean Percentile/ ≥95th %	72.3 (20)	73.1 (17)
Annual household income (USD), %		
<50,000	10 (13)	13 (15)
50,000 to <100,000	25 (31)	25 (28)
100,000 to <200,000	23 (29)	25 (28)
≥200,000	9 (11)	11 (13)
Unknown or not reported	13 (16)	14 (16)
Parent's highest completed education level, %		
Less than high school	2 (3)	0
High school graduate/diploma/GED	12 (15)	21 (24)
Associate degree/technical/vocational	25 (31)	17 (19)
Bachelor's degree	23 (29)	34 (39)
Advanced degree	15 (19)	14 (16)
Unknown or not reported	3 (4)	2 (2)

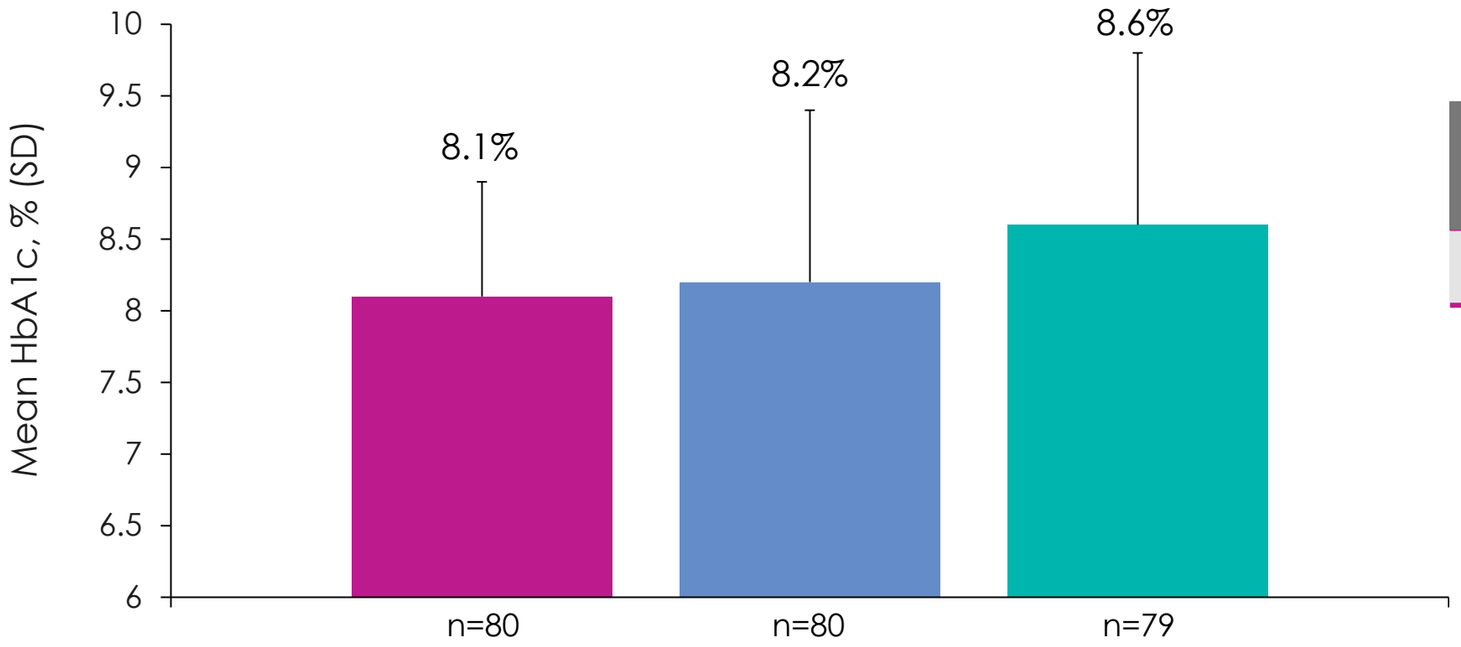
BMI, body mass index; HbA1c, hemoglobin A1c; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; SD, standard deviation; T1DM, Type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; TI, Technosphere Insulin.

Beck RW, et al. *Diabetes Technol Ther.* Published online February 4, 2026. doi:10.1177/15209156261420176

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TI Group: Change in HbA1c

Change in Mean HbA1c from Baseline to 52 weeks



Change from baseline to 52 weeks (95% CI) [P-value]	Change from 26 to 52 weeks (95% CI) [P-value]
0.46 (0.22, 0.71) [0.001]	0.38 (0.08, 0.67) [0.003]

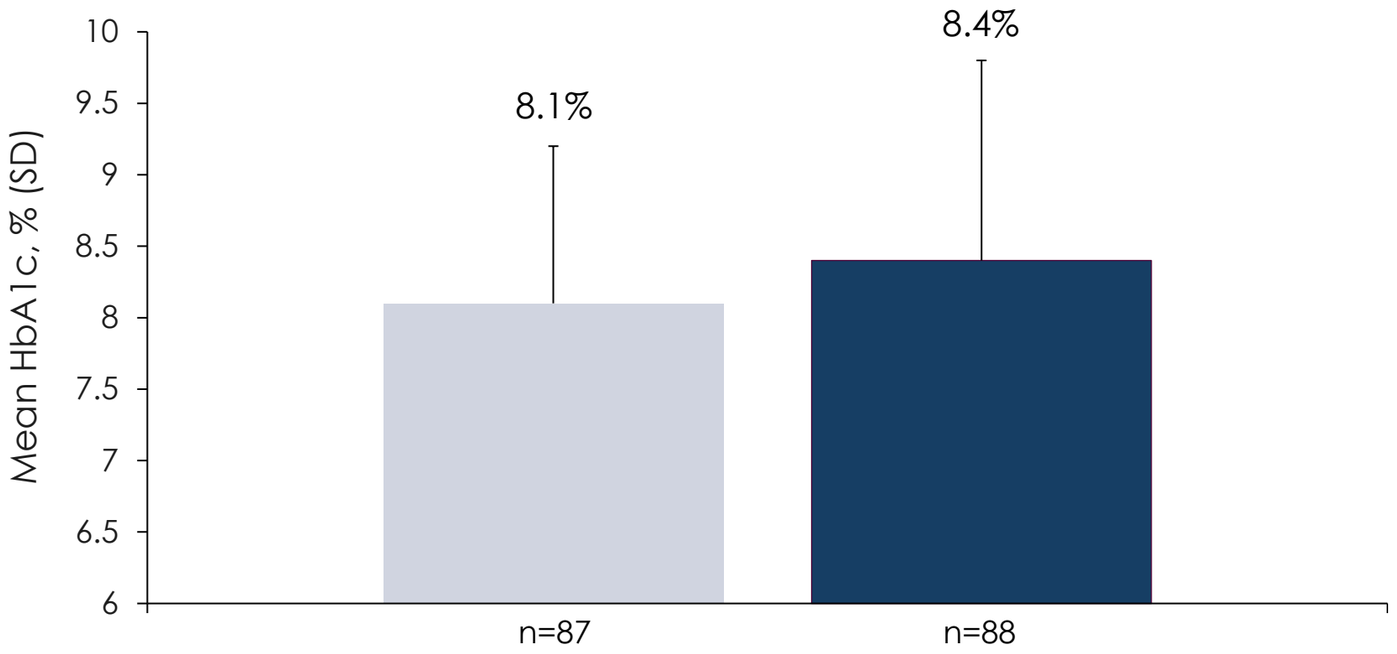
- TI at Baseline
- TI at 26 Weeks
- TI to TI at 52 Weeks

CI, confidence interval; HbA1c, hemoglobin A1c; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.
Beck RW, et al. *Diabetes Technol Ther*. Published online February 4, 2026. doi:10.1177/15209156261420176

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RAA Crossover Group: Change in HbA1c

Change in Mean HbA1c from 26 to 52 weeks



Change from 26 to 52 weeks (95% CI) [P-value]
0.31 (-0.02, 0.64) [0.08]

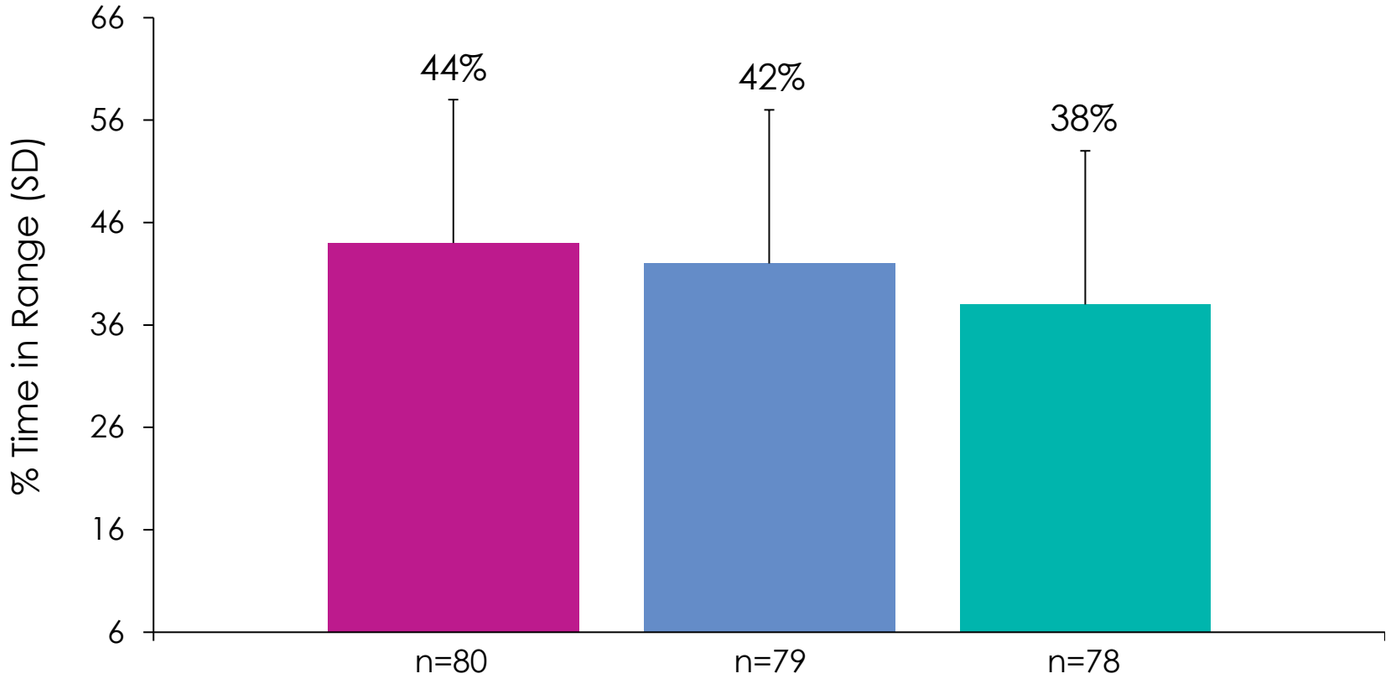
- RAA at 26 Weeks (TI initiation baseline)
- RAA to TI at 52 Weeks

CI, confidence interval; HbA1c, hemoglobin A1c; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.

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TI Group: CGM Time-in-Range 70-180 mg/dL



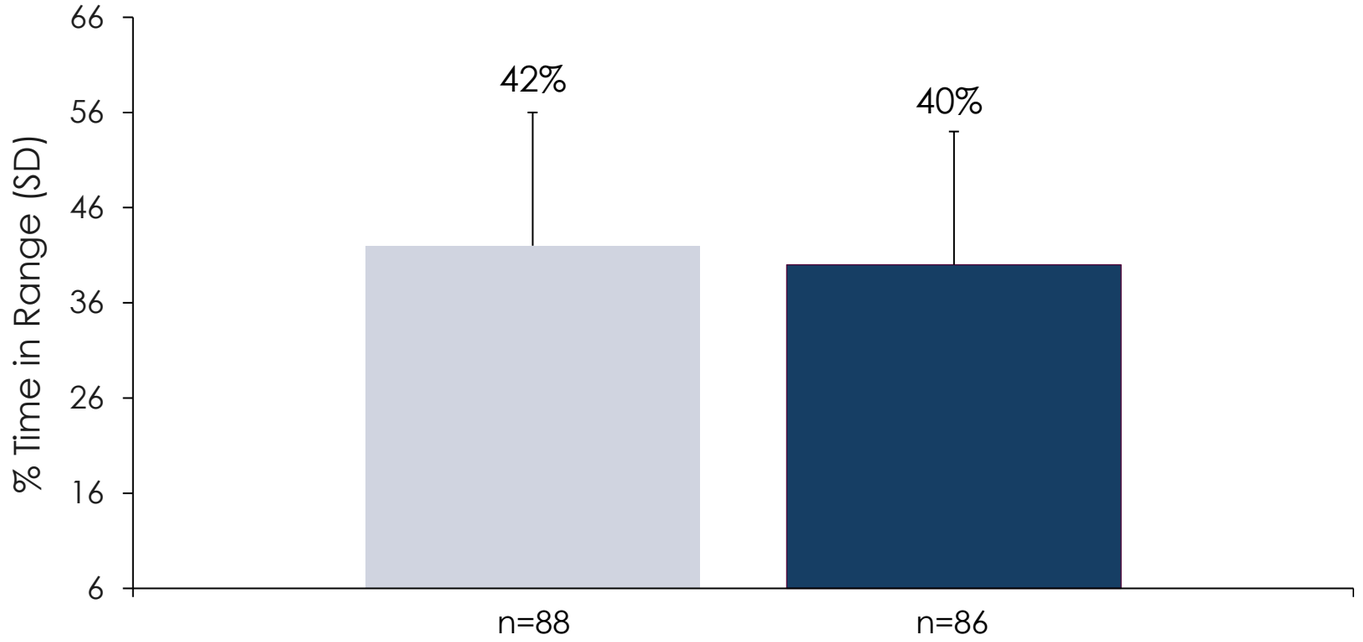
Change from baseline to 52 weeks (95% CI) [P-value]	Change from 26 to 52 weeks (95% CI) [P-value]
-5.0% (-8.9%, -1.2%) [0.03]	-3.1% (-7.1%, 0.9%) [0.15]

- TI at Baseline
- TI at 26 Weeks
- TI to TI at 52 Weeks

CGM, continuous glucose monitoring; CI, confidence interval; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.
Beck RW, et al. *Diabetes Technol Ther*. Published online February 4, 2026. doi:10.1177/15209156261420176

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RAA Crossover Group: CGM Time-in-Range 70-180 mg/dL



Change from 26 to 52 weeks (95% CI) [P-value]
-2.0% (-6.2%, 2.2%) [0.35]

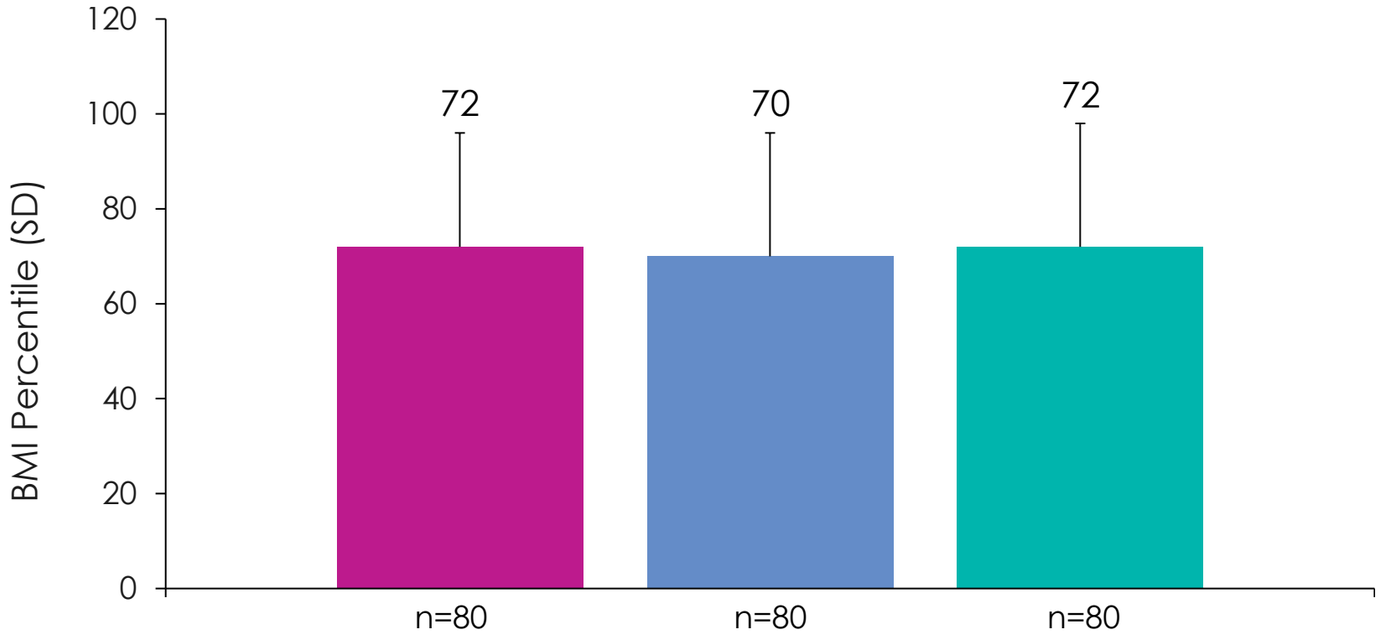
- RAA at 26 Weeks (TI initiation baseline)
- RAA to TI at 52 Weeks

CGM, continuous glucose monitoring; CI, confidence interval; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.
Haller M, et al. Abstract and oral presentation at International Society for Pediatric and Adolescent Diabetes 51st Annual Conference; November 2025; Montreal, Canada

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TI Group: Body Mass Index

Change in BMI Percentile from Baseline to 52 weeks



Change from baseline to 52 weeks (95% CI) [P-value]	Change from 26 to 52 weeks (95% CI) [P-value]
-0.4 (-2.9, 2.2) [0.78]	1.7 (-0.1, 3.4) [0.07]

- TI at Baseline
- TI at 26 Weeks
- TI to TI at 52 Weeks

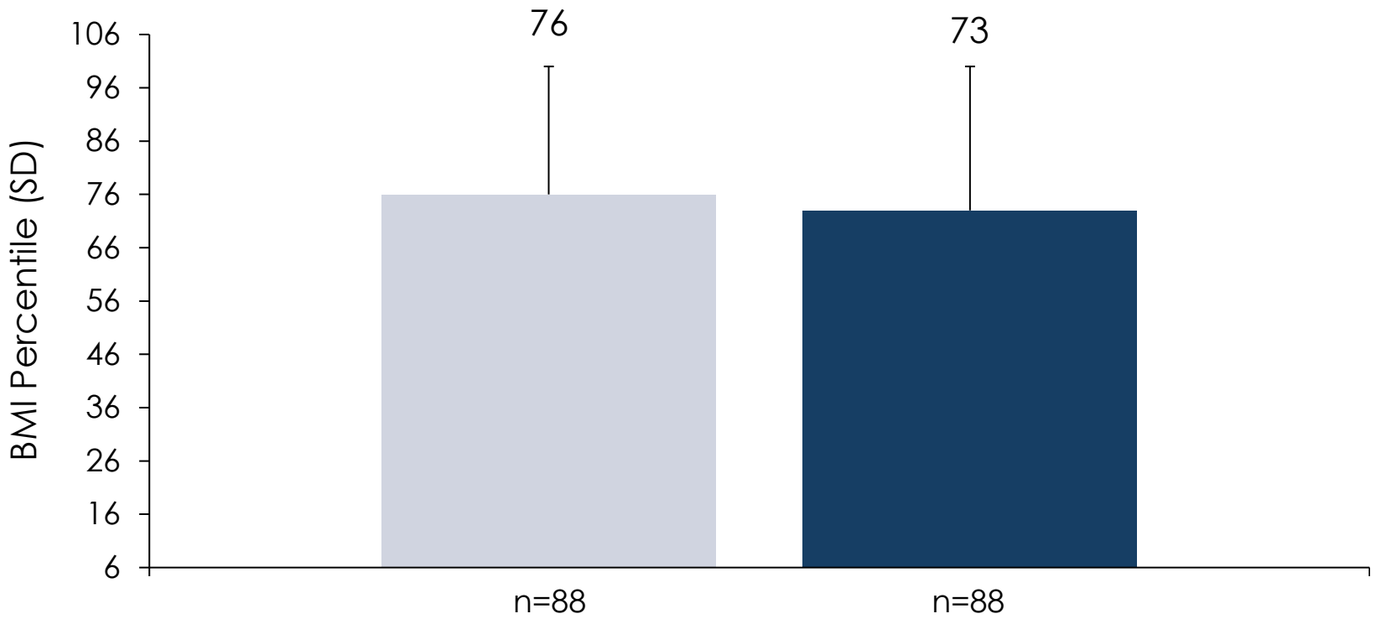
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RAA Crossover Group: Body Mass Index

Change in BMI Percentile from 26 to 52 weeks



Change from 26 to 52 weeks (95% CI) [P-value]
-2.8 (-4.6, -1.1) [0.002]

RAA at 26 Weeks (TI initiation baseline)
RAA to TI at 52 Weeks

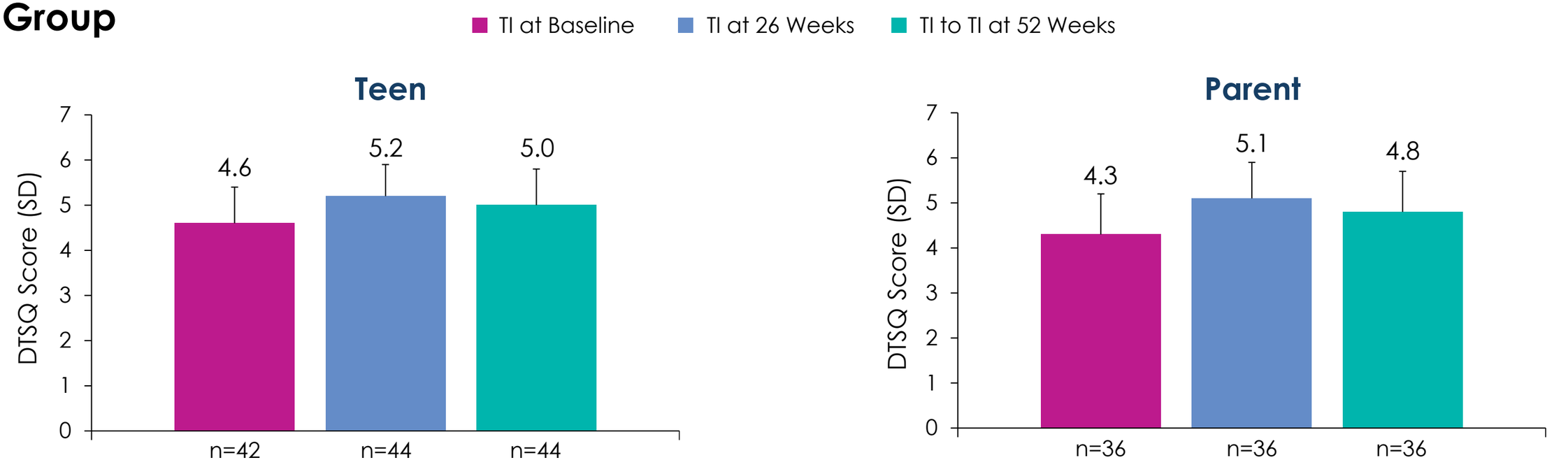
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Diabetes Treatment Satisfaction Questionnaire (DTSQ)

TI Group



Change from baseline to 52 weeks (95% CI) [P-value]	Change from 26 to 52 weeks (95% CI) [P-value]
0.44 (0.09, 0.78) [0.02]	-0.19 (-0.44, 0.06) [0.14]

Change from baseline to 52 weeks (95% CI) [P-value]	Change from 26 to 52 weeks (95% CI) [P-value]
0.47 (0.06, 0.87) [0.02]	-0.25 (-0.68, 0.19) [0.22]

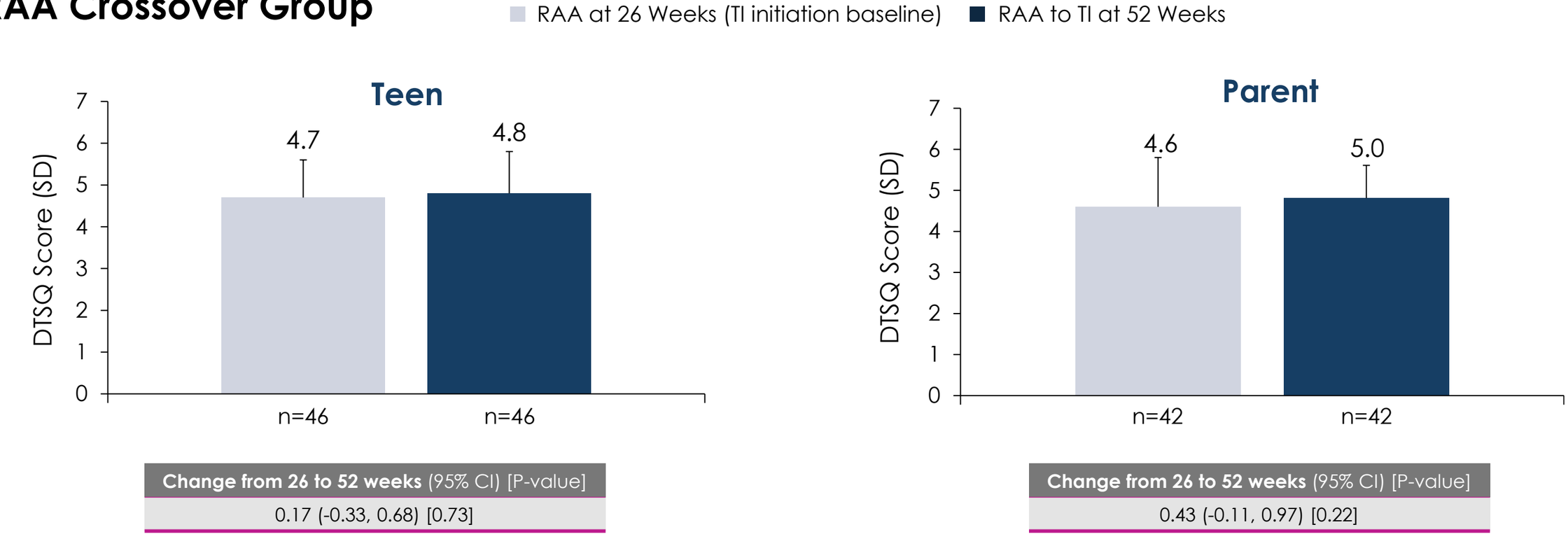
CI, confidence interval; DTSQ, diabetes treatment satisfaction questionnaire; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.

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Diabetes Treatment Satisfaction Questionnaire (DTSQ)

RAA Crossover Group



Change from 26 to 52 weeks (95% CI) [P-value]
0.17 (-0.33, 0.68) [0.73]

Change from 26 to 52 weeks (95% CI) [P-value]
0.43 (-0.11, 0.97) [0.22]

CI, confidence interval; DTSQ, diabetes treatment satisfaction questionnaire; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.

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Study-Drug-Related TEAEs since Entering the Treatment Extension

	TI to TI (n=90)	RAA to TI (n=103)
Subjects with ≥1 TEAE related to Study Drug, N Events	11 (12.2)	35 (34.0)
Cough	1 (1.1)	18 (17.5)
Hypoglycemia Events	1 (1.1)	1 (1.0)
Diabetic Ketoacidosis Events	0 (0)	1 (1.0)
Subjects with any severe TEAE, N Events	5 (5.6)	11 (10.7)
Hypoglycemia Events	1 (1.1)	1 (1.0)
Diabetic Ketoacidosis Events	0 (0)	2 (1.9)

RAA, rapid-acting insulin analog; RCT, randomized controlled trial; TEAE, treatment-emergent adverse event; TI, Technosphere Insulin.
Data on File (MKC-TI-155, Clinical Study Report, 2025). MannKind Corporation.

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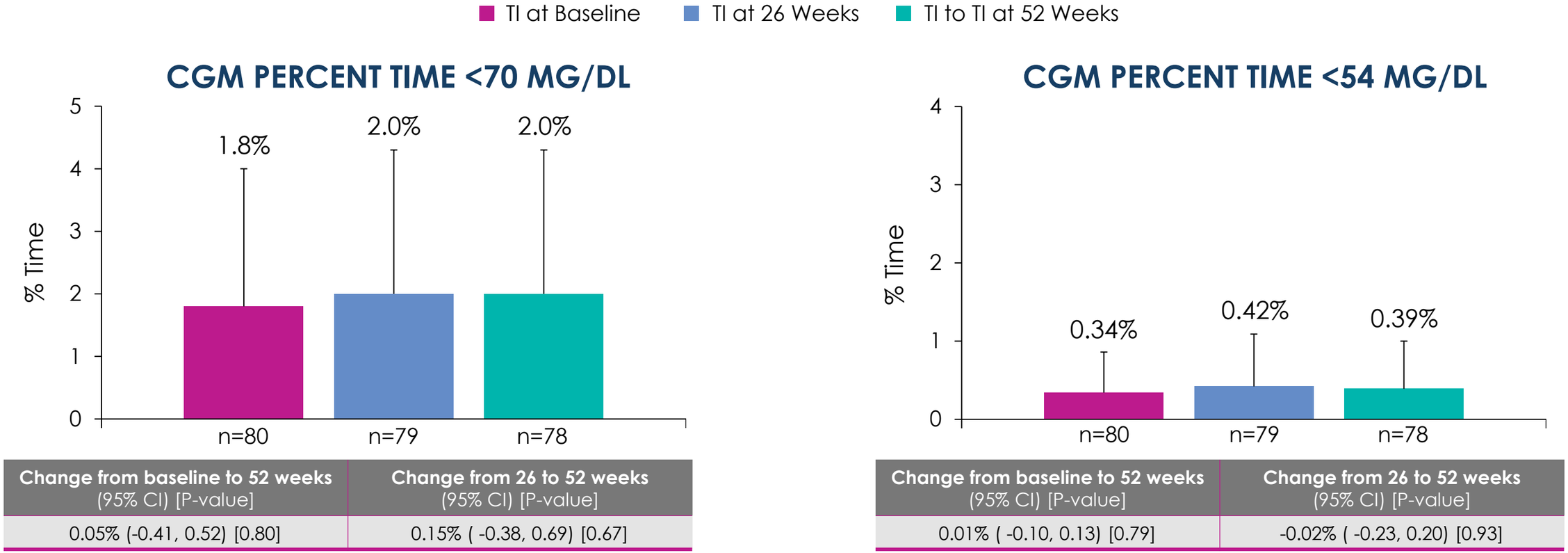
INHALE-1 Extension TEAEs

TEAEs Possibly, Probably, or Definitely Related to TI During the Extension No. of Participants (No. of Events)	TI n=12 events	RAA Crossover n=45 events
Cough	1 (1)	18 (19)
Pulmonary function test abnormal	9 (10)	5 (5)
Oropharyngeal pain	0	4 (4)
Chest discomfort	0	3 (3)
Dysgeusia	0	3 (3)
Chest pain	0	2 (2)
Dyspnea	0	2 (2)
Hypoglycemia	1 (1)	0
Retching	0	1 (1)
Anxiety	0	1 (1)
Dry throat	0	1 (1)
Bronchospasm	0	1 (1)
Ketosis	0	1 (1)
Diabetic ketoacidosis	0	1 (1)
Dry mouth	0	1 (1)

RAA, rapid-acting insulin analog; RCT, randomized controlled trial; TEAE, treatment-emergent adverse event; TI, Technosphere Insulin.
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TI Group: Hypoglycemia



Change from baseline to 52 weeks (95% CI) [P-value]	Change from 26 to 52 weeks (95% CI) [P-value]
0.05% (-0.41, 0.52) [0.80]	0.15% (-0.38, 0.69) [0.67]

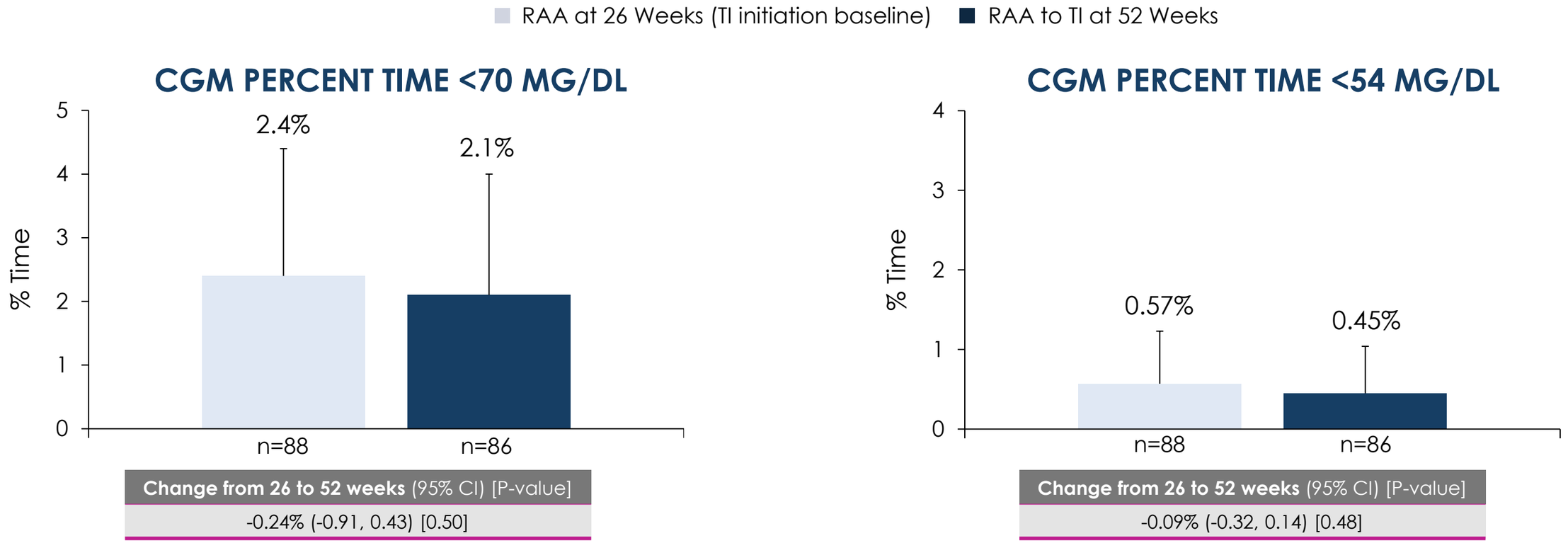
Change from baseline to 52 weeks (95% CI) [P-value]	Change from 26 to 52 weeks (95% CI) [P-value]
0.01% (-0.10, 0.13) [0.79]	-0.02% (-0.23, 0.20) [0.93]

CGM, continuous glucose monitoring; CI, confidence interval; HbA1c, hemoglobin A1c; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.

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RAA Crossover Group: Hypoglycemia



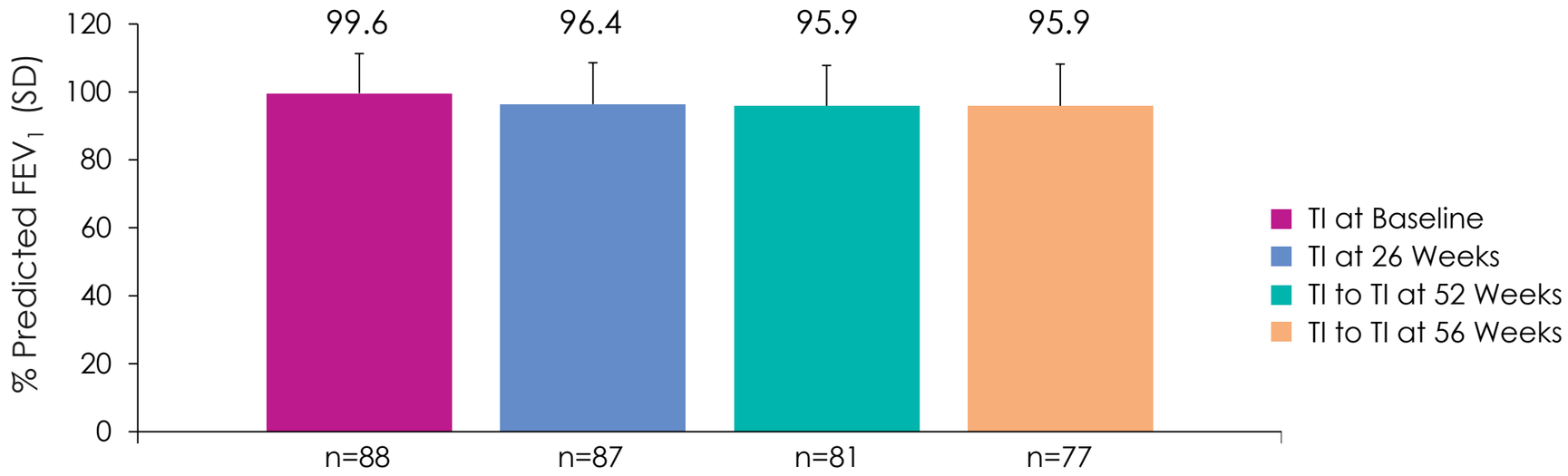
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TI Group: Pulmonary Function

Change in Percent Predicted FEV_1 from Baseline to 56 weeks



Change from baseline to 26 weeks (95% CI) [P-value]	Change from baseline to 52 weeks (95% CI) [P-value]	Change from baseline to 56 weeks (95% CI) [P-value]
-3.0 (-4.7, -1.3) [<0.001]	-3.7 (-5.5, -1.9) [<0.001]	-3.1 (-5.3, -0.8) [0.008]

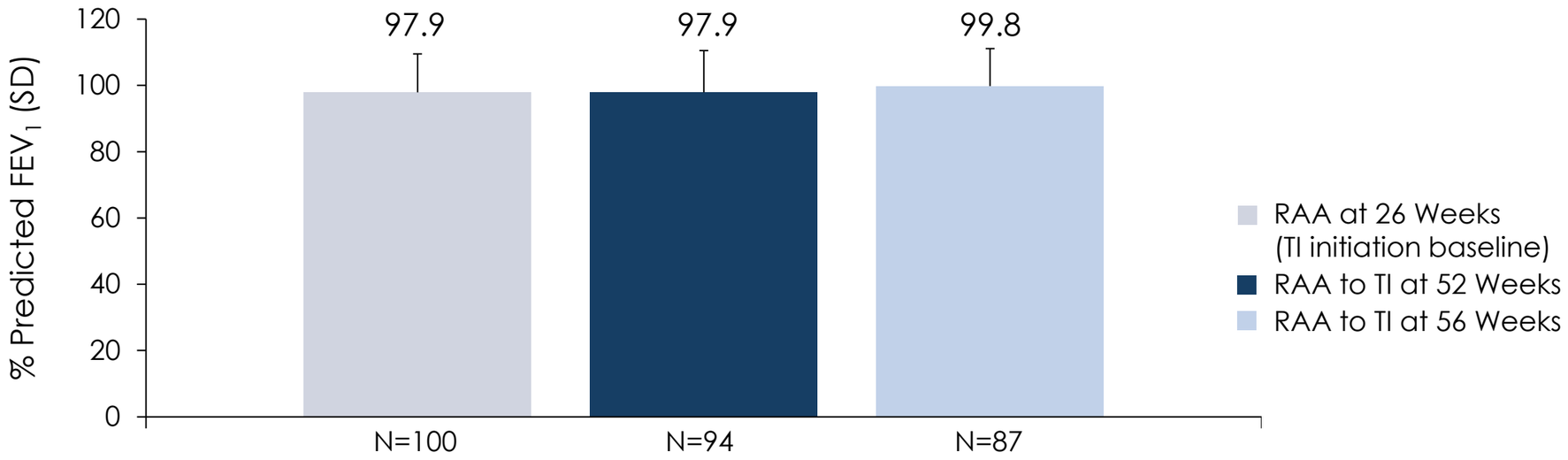
CI, confidence interval; FEV_1, forced expiratory volume in 1 second; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.

Beck RW, et al. *Diabetes Technol Ther.* Published online February 4, 2026. doi:10.1177/15209156261420176

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RAA Crossover Group: Pulmonary Function

Change in Percent Predicted FEV_1 from 26 weeks to 56 weeks



Change from 26 to 52 weeks (95% CI) [P-value]
0.5 (-0.9, 2.0) [0.46]
Change from 52 to 56 weeks (95% CI) [P-value]
2.1 (0.9, 3.4) [0.001]
Change from 26 to 56 weeks (95% CI) [P-value]
1.9 (0.3, 3.5) [0.02]

CI, confidence interval; FEV_1, forced expiratory volume in 1 second; RAA, rapid-acting insulin analog; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.

Beck RW, et al. *Diabetes Technol Ther.* Published online February 4, 2026. doi:10.1177/15209156261420176

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INHALE-3 (Adult)

INHALE-3 trial[1] (17 weeks)

- Randomized Phase 4 trial in adults with type 1 diabetes
- Evaluated inhaled insulin plus long-acting basal insulin (degludec) vs usual insulin therapy (AID systems, pump, or MDI) for 17 weeks
- Builds on previous trials (DOS, ABC)[2-4] to further demonstrate the safety and efficacy

INHALE-3 extension phase (13 weeks) followed the initial 17-week study

- Assessed whether glycemic outcomes achieved with the inhaled insulin–degludec regimen could be maintained over an additional 13 weeks
- Also assessed outcomes in patients who switched at 17 weeks from usual care to inhaled insulin–degludec regimen for 13 weeks



INHALE-3 RCT >
INHALE-3 extension phase >

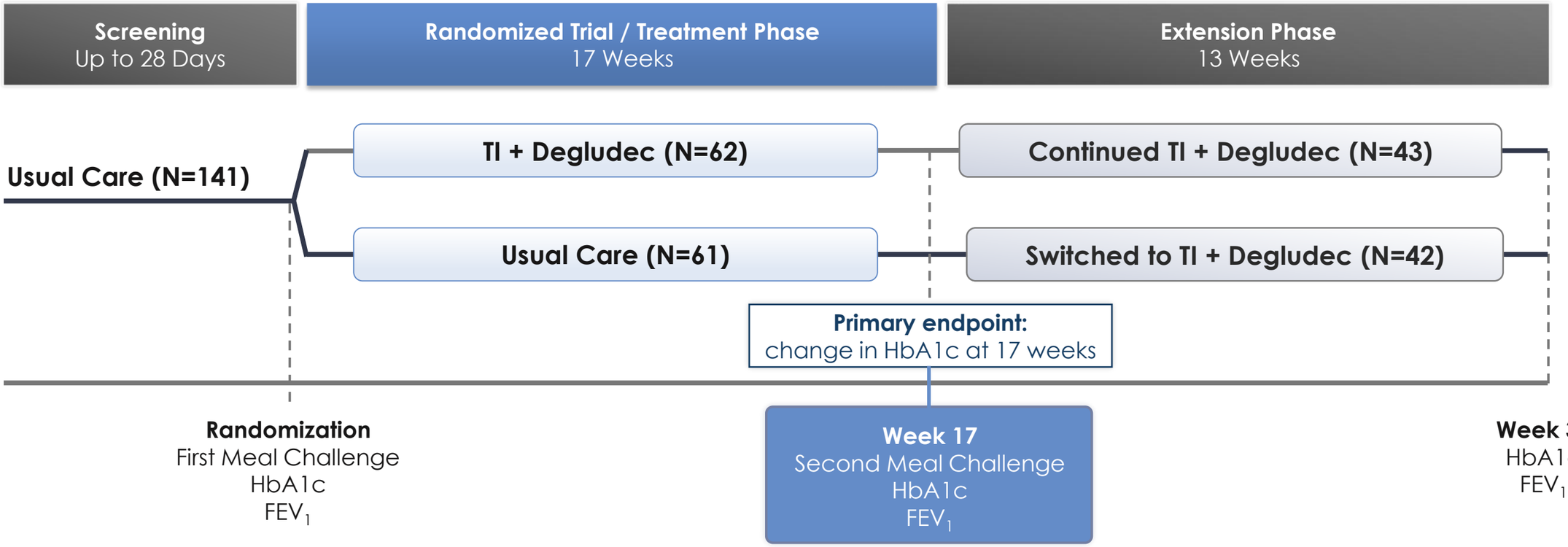
ABC, Afrezza with Basal Combination study; AID, automated insulin delivery; DOS, Dose Optimization Study; MDI, multiple daily injections; RCT, randomized controlled trial.

1. Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360. 2. Kaiserman K, et al. *J Diabetes Sci Technol*. 2024;18(2):397-401 3. Jacobson C, et al. *Diabetes Ther*. 2025;16(8):1695-1705. 4. Kaiserman K, et al. *J Diabetes Sci Technol*. Published online November 11, 2025. doi:10.1177/19322968251388128

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INHALE-3 Study

19 US Sites
≥18 years old
with T1D



FEV_1, forced expiratory volume in 1 second; HbA1c, hemoglobin A1c; RCT, randomized controlled trial; T1D, type 1 diabetes; TI, Technosphere Insulin.

1. Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360. 2. ClinicalTrials.gov identifier: NCT05904743. Accessed May 26, 2026. https://clinicaltrials.gov/study/NCT05904743

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INHALE-3 Dosing Protocol

TI Titration Protocol

- Subjects were advised to add 4 units of TI for a larger-than-usual meal and to decrease by 4 TI units for a smaller-than-usual meal

	Glucose Level	Recommended TI Dose Titration
Adjustments Based on 1-hour Post-prandial CGM Readings	>140 mg/dL	+ 4 units
	>200 mg/dL	+ 8 units
Adjustments Based on Pre-Meal CGM Glucose	140-200 mg/dL	+ 4 units
	>200 mg/dL	+ 8 units

TI Correction Dosing

- Subjects were instructed to administer a correction dose of TI as early as 60-90 minutes after the previous dose of 4 TI units

Glucose Level	Time of Day	Units Given
140-200 mg/dL	Day/Bedtime	+ 4 units
>200 mg/dL	Day/Bedtime	+ 8 units
>200 mg/dL	Overnight	+ 4 units

CGM, continuous glucose monitoring; RCT, randomized controlled trial; TI, Technosphere Insulin.

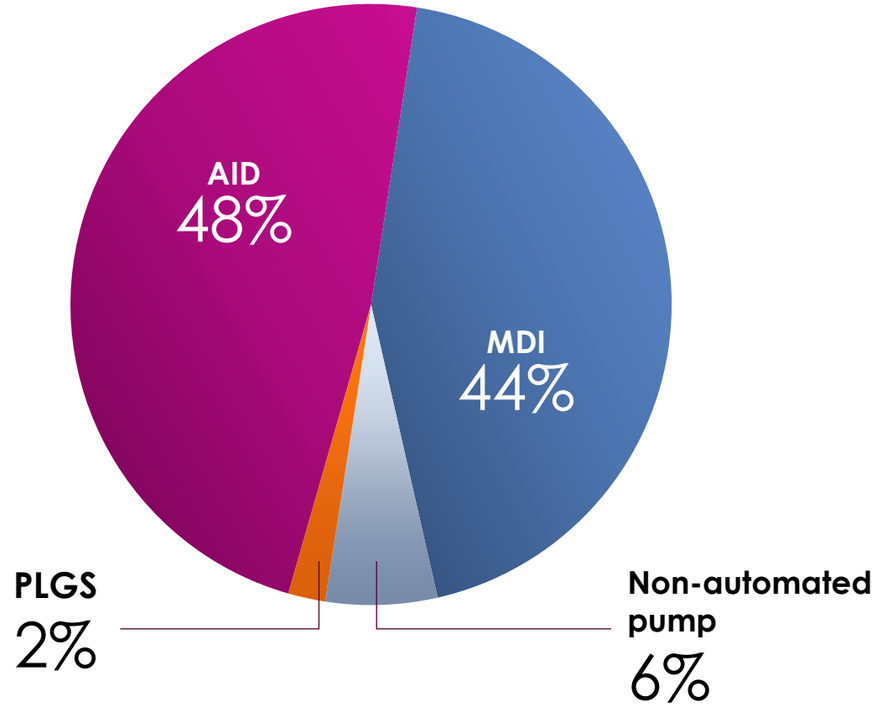
Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360.

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Participant Characteristics[1,2]

Baseline Characteristics (N=123)	
Mean Age (years)	45 (range 18-77)
Female (%)	54
Mean BMI (kg/m²)	27.9
AID System Type (n=59)	
Control-IQ	39
Omnipod 5	17
780G	3

Insulin Delivery Modality



AID, automated insulin delivery; BMI, body mass index; MDI, multiple daily injections; PLGS, predictive low-glucose suspend; RCT, randomized controlled trial.

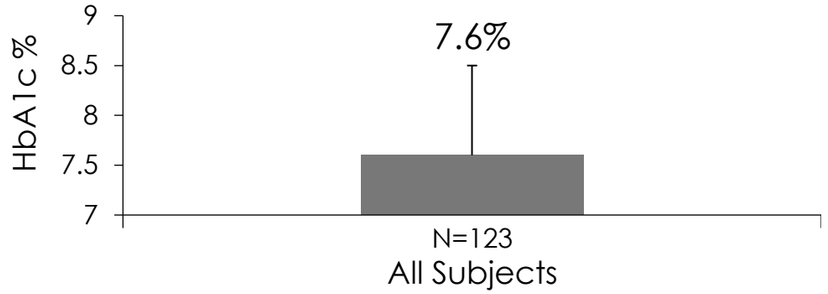
1. Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360. 2. Data on File (INHALE-3 Clinical Study Report, 2026). MannKind Corporation

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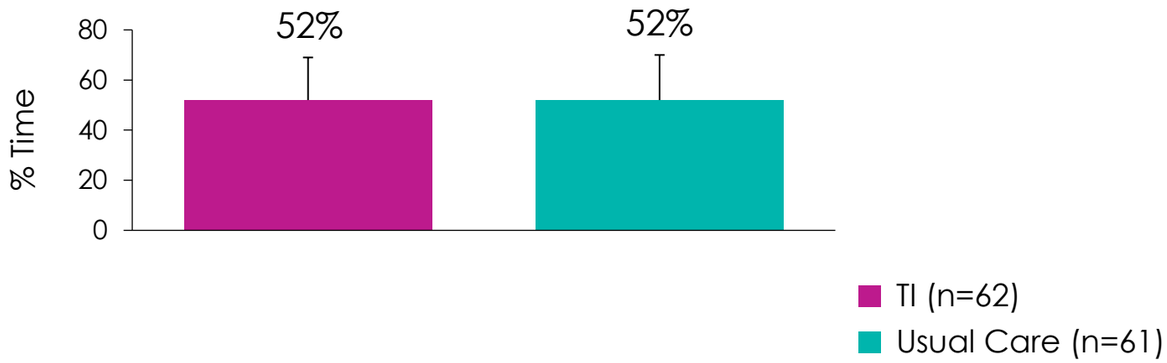
Participant Characteristics[1]

Baseline Glycemic Metrics

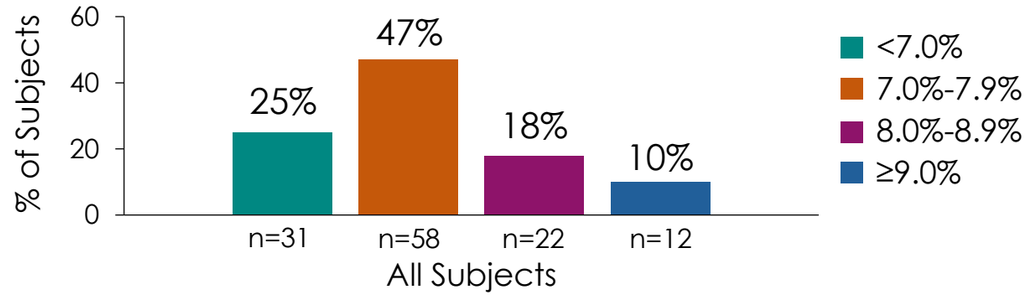
Mean HbA1c



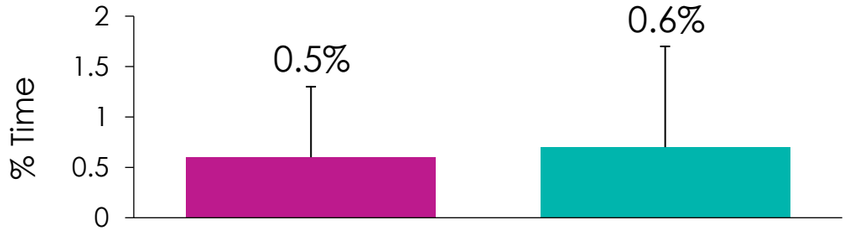
Mean Percent TIR (70-180 mg/dL)[2]



HbA1c Categories



Mean Percent Time <54 mg/dL[2]



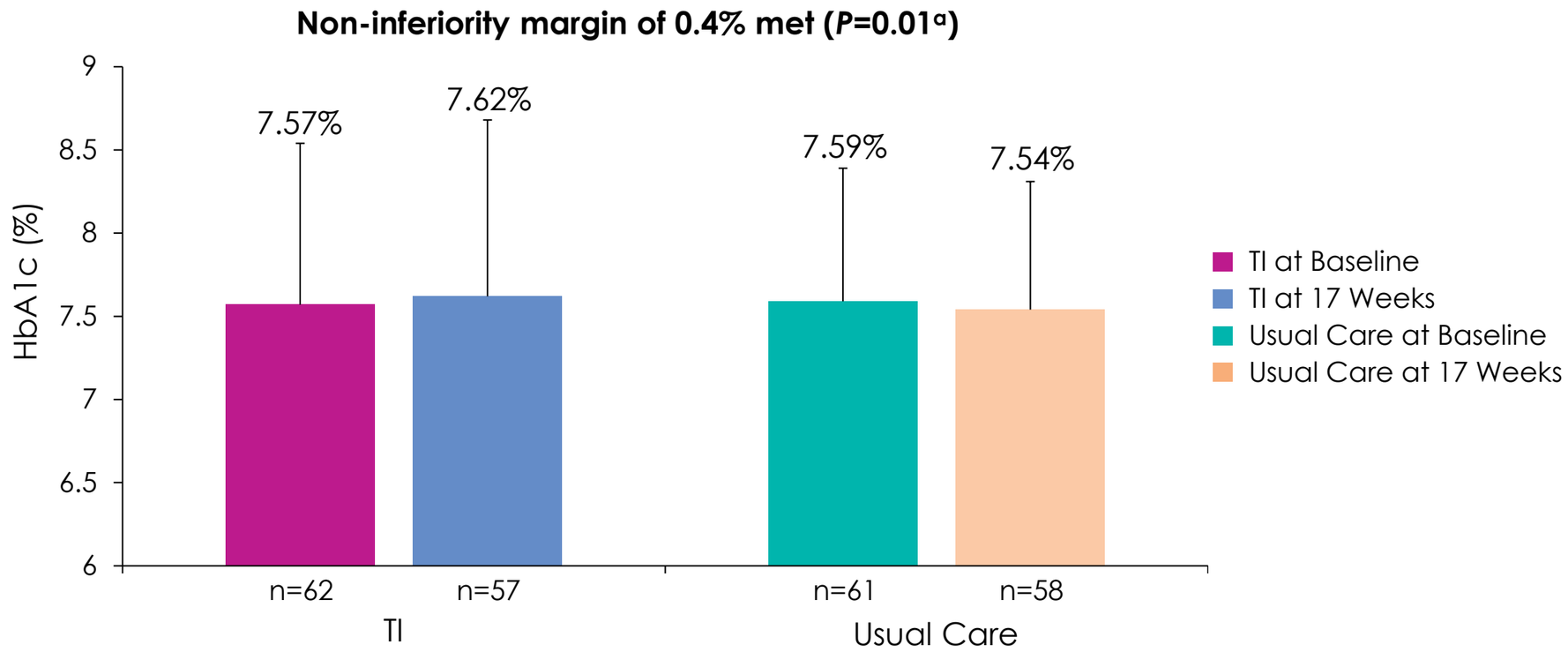
HbA1c, hemoglobin A1c; RCT, randomized controlled trial; TI, Technosphere Insulin; TIR, time in range.

1. Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360. 2. Data on File (INHALE-3 Clinical Study Report, 2026). MannKind Corporation

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HbA1c: Primary Endpoint

Change in HbA1c from Randomization to 17 Weeks



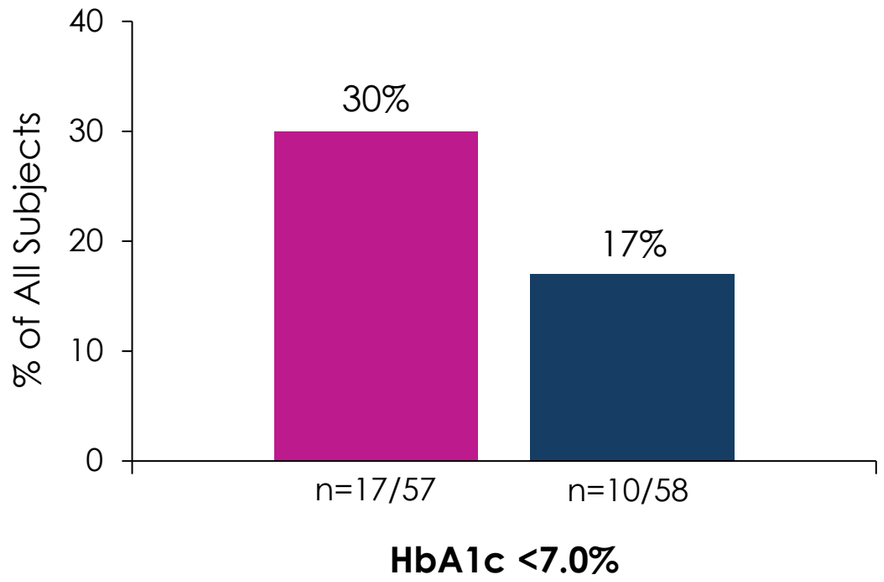
[a]17-week treatment difference between TI and Usual Care (95% CI): 0.11 (-0.10, 0.33).
CI, confidence interval; HbA1c, hemoglobin A1c; RCT, randomized controlled trial; TI, Technosphere Insulin.
Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360.

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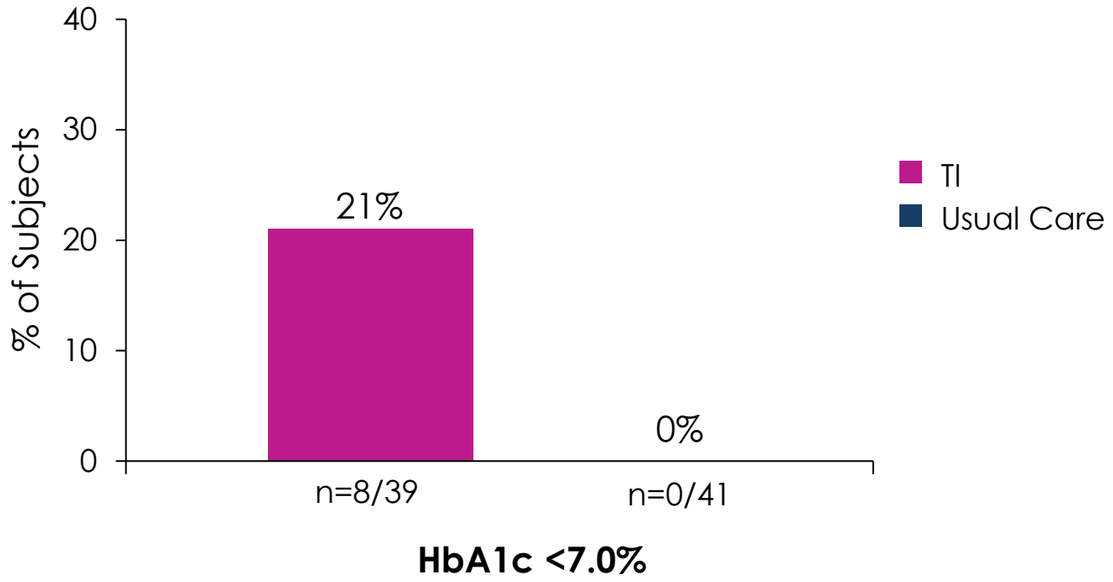
HbA1c: <7.0% at 17 Weeks[1,2]

HbA1c Change in All Subjects

10% (-2%, 24%); *P*=0.10[a]



Subjects with Baseline HbA1c >7.0%



[a]17-week treatment difference between TI and Usual Care (95% CI); P-value.

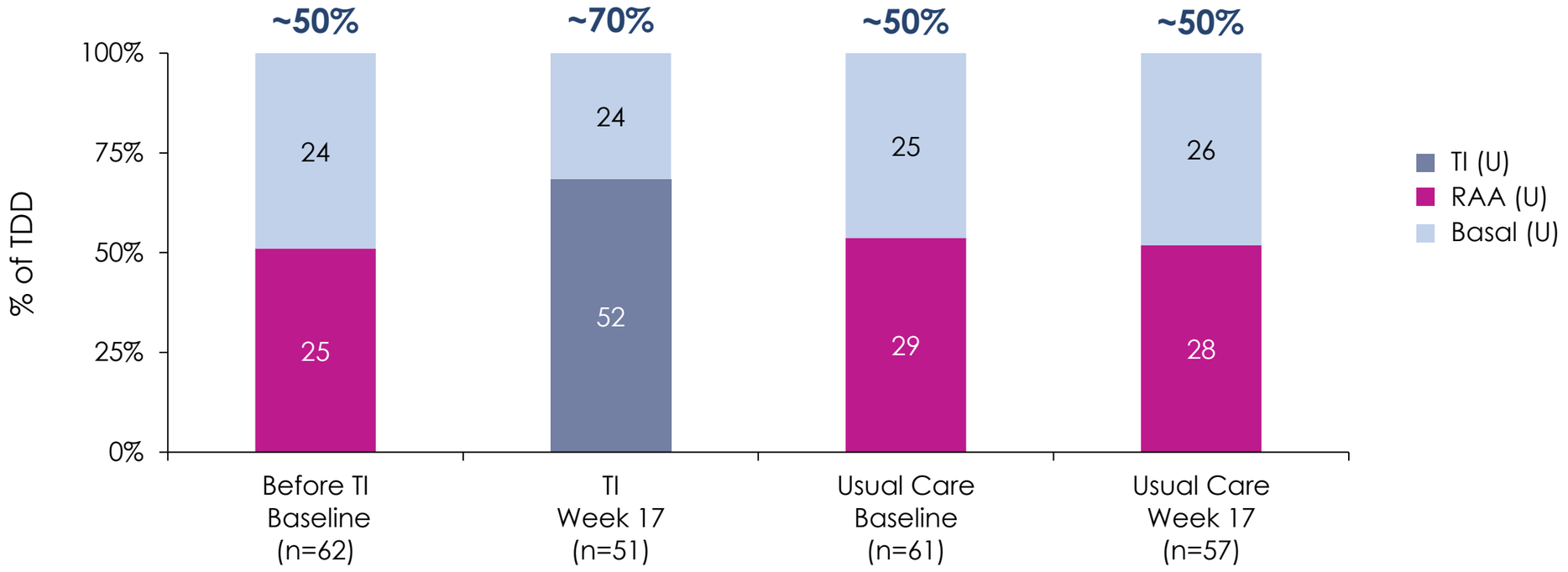
HbA1c, hemoglobin A1c; RCT, randomized controlled trial; TI, Technosphere Insulin.

1. Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360. 2. Data on File (INHALE-3 Clinical Study Report, 2026). MannKind Corporation

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Bolus to Basal Insulin Dose Ratio*

Total Daily Insulin[1,2]



*Percentages represent bolus to total ratio
TI arm used insulin degludec for basal; Usual Care RAA is bolus insulin.
RAA, rapid-acting insulin analog; RCT, randomized controlled trial; TDD, Total Daily Dose; TI, Technosphere Insulin; U, units.
1. Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360. 2. Data on File (INHALE-3 Clinical Study Report, 2024). MannKind Corporation.

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Technosphere Insulin (TI) Dosing

Change in TI Dose From Baseline to 17 Weeks[1]

	Breakfast (Mean ± SD)	Lunch (Mean ± SD)	Dinner (Mean ± SD)	Snack (Mean ± SD)
Prescribed Meal Dose at Randomization (U)	9 ± 5	10 ± 7	12 ± 7	5 ± 2
Actual Meal Dose Week 17 (U)	12 ± 8	14 ± 10	15 ± 9	6 ± 5

Patients may need to adjust TI dosing and timing to attain effective glucose control. Dosing of mealtime TI should be modified based on the patient's metabolic needs, blood glucose monitoring results, and glycemic control goal.[2]

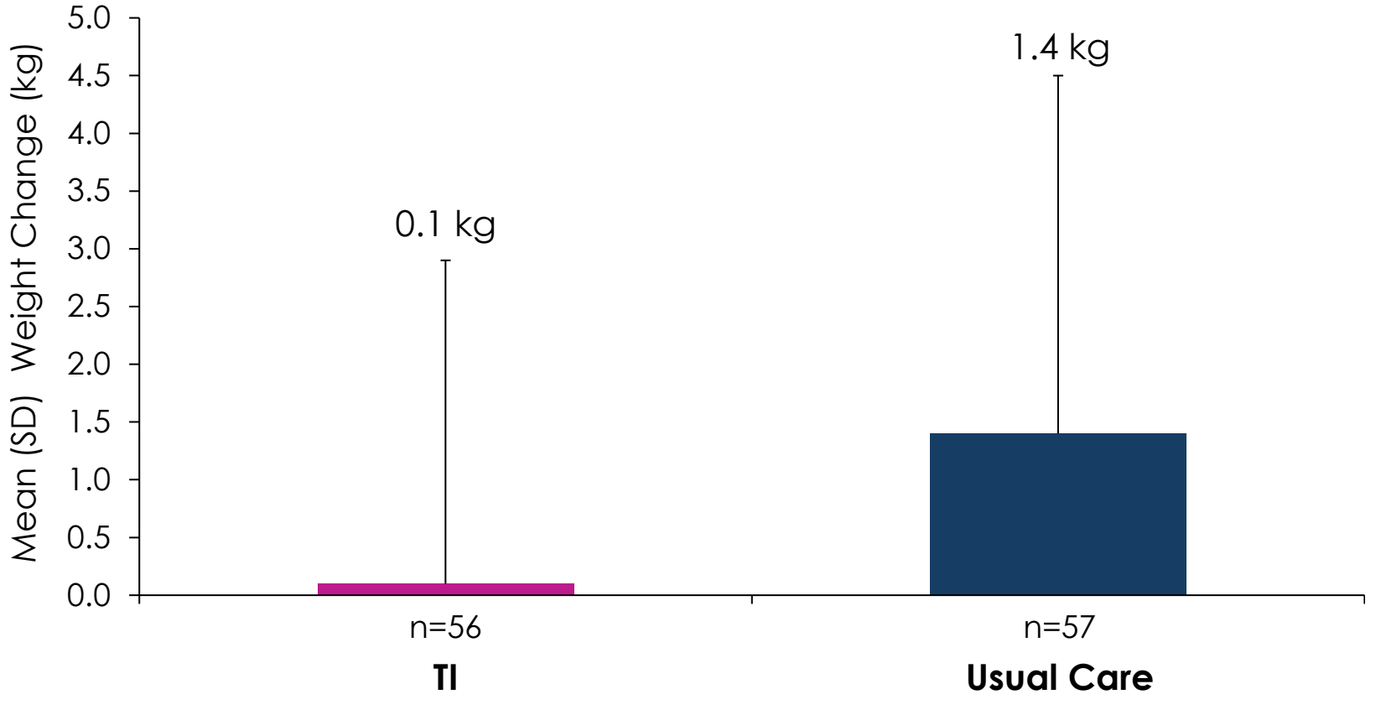
RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin; U, units.

1. Data on File (INHALE-3 Clinical Study Report, 2024). MannKind Corporation. 2. Afrezza® (insulin human) Inhalation Powder Prescribing Information. MannKind Corporation

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Weight

Mean Weight Gain from Baseline to 17 Weeks



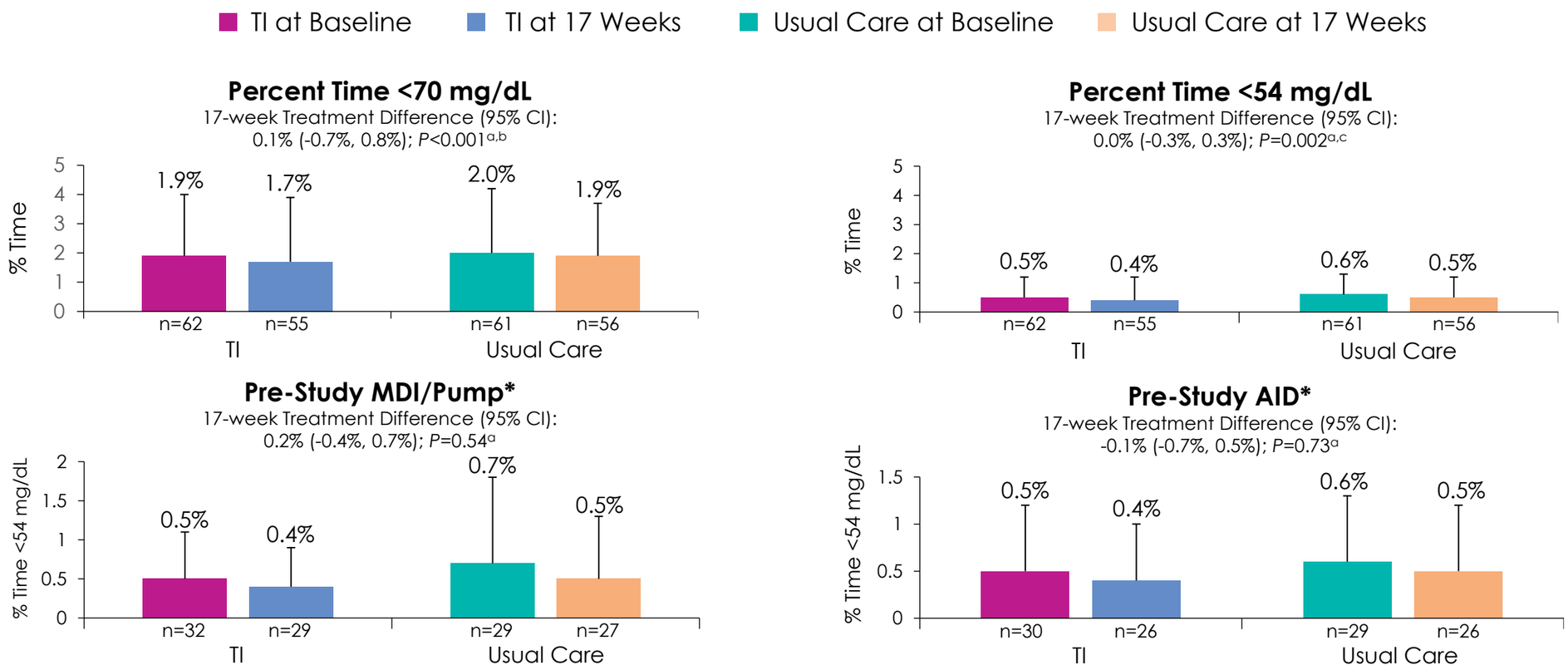
17-week Treatment Difference (95% CI)

TI (n=56)	Usual Care (n=57)
-1.3 kg (-2.4, -0.2); *P*=0.03[a]	

[a]Difference is TI minus Usual Care using only participants that completed 17 weeks.
CI, confidence interval; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin.
Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360.

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CGM Metrics: Hypoglycemia Stratified by Insulin Delivery Method[1,2]



[a] Difference is TI minus Usual Care; [b] Non-inferiority margin = 2.0%; [c] Non-inferiority margin = 0.5%;

*Three Basal-IQ users were excluded from this analysis

On a self-reported log, more BGM in the hypoglycemic or hyperglycemic range were recorded by participants in TI group than Usual Care group [the number of participants submitting a logged BGM during RCT was 27 (44%) and 21 (34%) in TI and Usual Care groups, respectively].

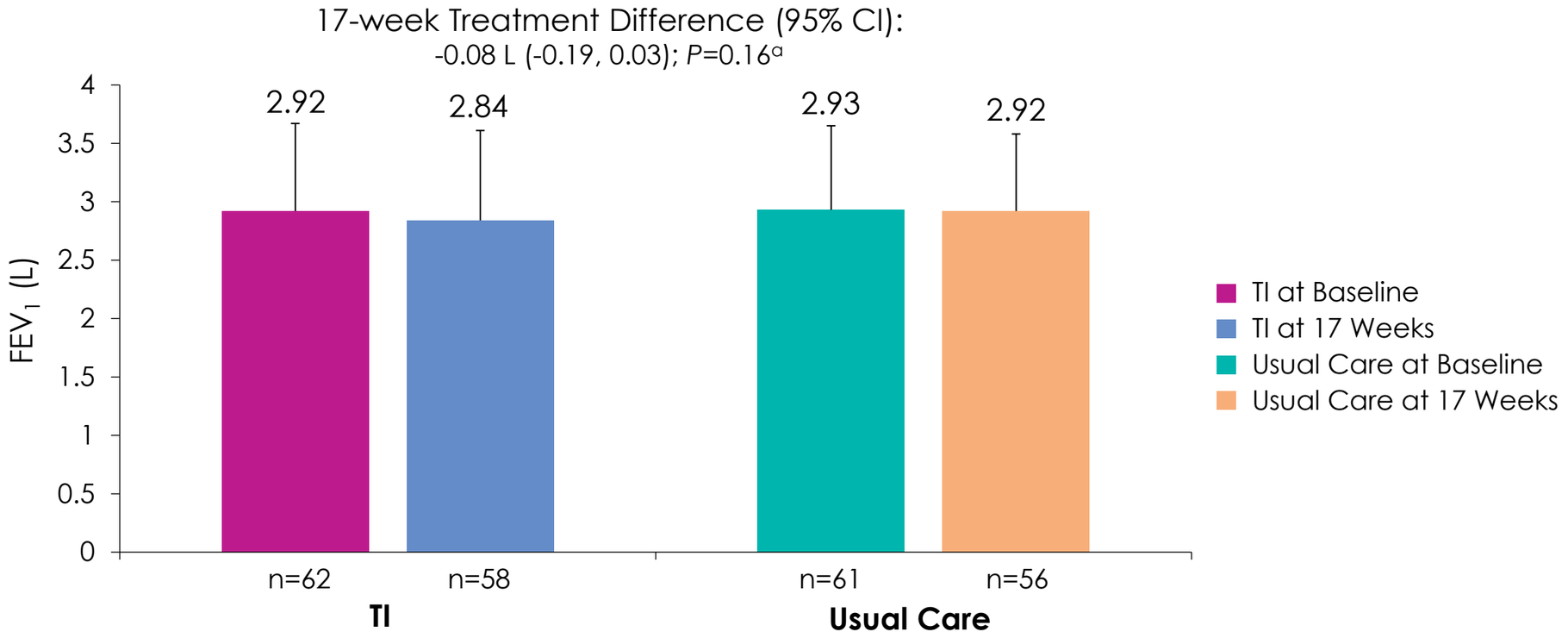
AID, automated insulin delivery; BGM, blood glucose measurements; CGM, continuous glucose monitor; CI, confidence interval; MDI, multiple daily injection; RCT, randomized controlled trial; TI, Technosphere Insulin.

1. Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360. 2. Data on File (INHALE-3 Clinical Study Report, 2024). MannKind Corporation.

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Pulmonary Function

Mean FEV_1 Change from Baseline to 17 Weeks



[a]Difference is TI minus Usual Care.
Note: There were no participants with a ≥20% reduction in FEV_1 from baseline to 17 weeks.
CI, confidence interval; FEV_1, forced expiratory volume in 1 second; RCT, randomized controlled trial; TI, Technosphere Insulin.
Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360.

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Summary of Adverse Events*

	TI (n=62)	Usual Care (n=61)
All AEs, N Events	124	83
# of Participants with ≥1 AE	48 (77%)	39 (64%)
Severe Hypoglycemia Events, n	1[a]	0
Diabetic Ketoacidosis Events, n	0	0
Other Serious Adverse Events, n	0	2[b]

[a]The episode of severe hypoglycemia was associated with excessive alcohol consumption; [b]SAEs: hospitalizations for hyperglycemia/ketosis and for appendectomy; [c]Back pain occurred after prolonged coughing following TI inhalation; [d]Severe hypoglycemia event was considered possibly related to the insulin regimen (degludec) and unlikely related to TI; [e]One participant had one AE for wheezing and then one for physical exam finding of wheezing.

*AEs occurring in each treatment group between randomization and 17 weeks post-randomization

AE, adverse event; RCT, randomized controlled trial; SAE, serious adverse event; TI, Technosphere Insulin.

Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360.

Summary of Treatment Emergent Adverse Events: TI Group*

31 TEAEs were reported in 23 of the 62 (37%) participants in the TI group

	TI n=62
Possibly, Probably, or Definitely Related to TI Regimen - *n*	31
Back pain	1[c]
Bronchospasm	1
Chest pressure	1
Cough	14
Diarrhea	1
Dry mouth	1
Hyperglycemia	1
Rash	1
Severe hypoglycemia	1[d]
Shortness of breath	5
Sore throat	2
Wheezing	3[e]

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INHALE-3 Key Takeaways – 17 Weeks

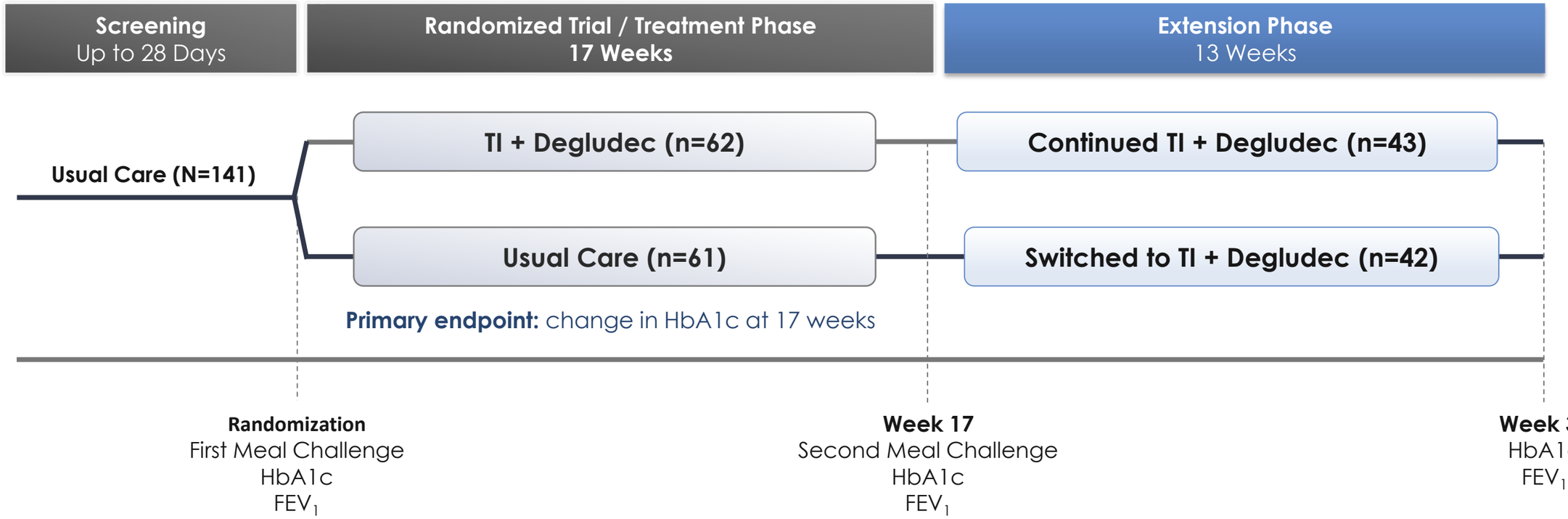
- **Primary endpoint was met for non-inferiority of HbA1c from baseline to 17 weeks (non-inferiority margin of 0.4%)**
  - Usual Care consisted of approximately 50% AID
  - Approximately 25% of all patients had HbA1c <7% at baseline
  - 30% of TI and 17% of Usual Care met HbA1c goal at 17 weeks (<7% HbA1c)
  - 21% of TI and 0% of Usual Care with baseline HbA1c of >7% met HbA1c goal of <7%
- **Improved mealtime glycemic control (standardized meal challenge)**
- **At 17 weeks, bolus to basal insulin dose ratio was ~ 70% : 30% in the TI group**
- **No new pulmonary or glycemic safety signals were identified**

AID, automated insulin delivery; HbA1c, hemoglobin A1c; RCT, randomized controlled trial; TI, Technosphere Insulin.
Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360.

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INHALE-3 Extension Phase[1,2]

19 US Sites
≥18 years old
with T1D



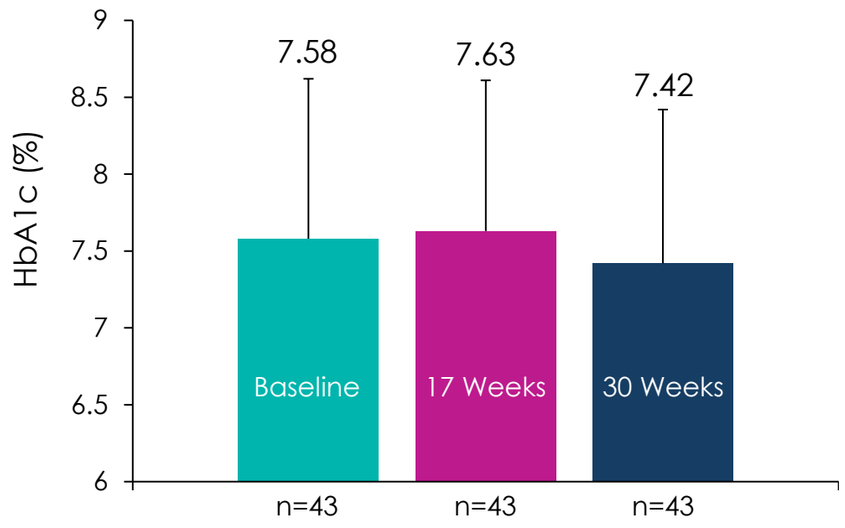
FEV_1, forced expiratory volume in 1 second; HbA1c, hemoglobin A1c; RCT, randomized controlled trial; TI, Technosphere Insulin; T1D, type 1 diabetes.
1. Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360. 2. ClinicalTrials.gov identifier: NCT05904743. Accessed May 26, 2026. https://clinicaltrials.gov/study/NCT05904743

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Change in HbA1c Up to 30 Weeks

TI → TI GROUP[1]

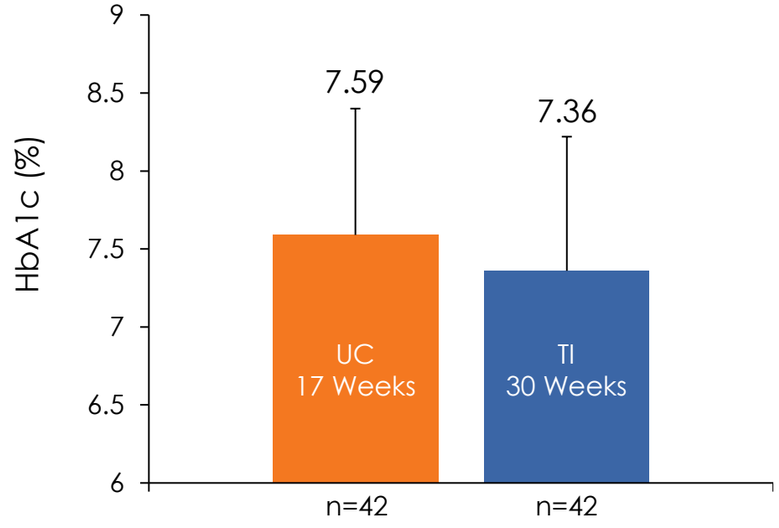
(Exploratory Endpoint)
Mean Change from Baseline to 30 Weeks (95% CI):
-0.17 (-0.41, 0.07); *P*=0.16[a]



Baseline to 30 Weeks

UC → TI SWITCH GROUP[2,3]

Mean Change from 17 to 30 Weeks (95% CI):
-0.23% (-0.42%, -0.04%); *P*=0.02[a]



17 Weeks to 30 Weeks

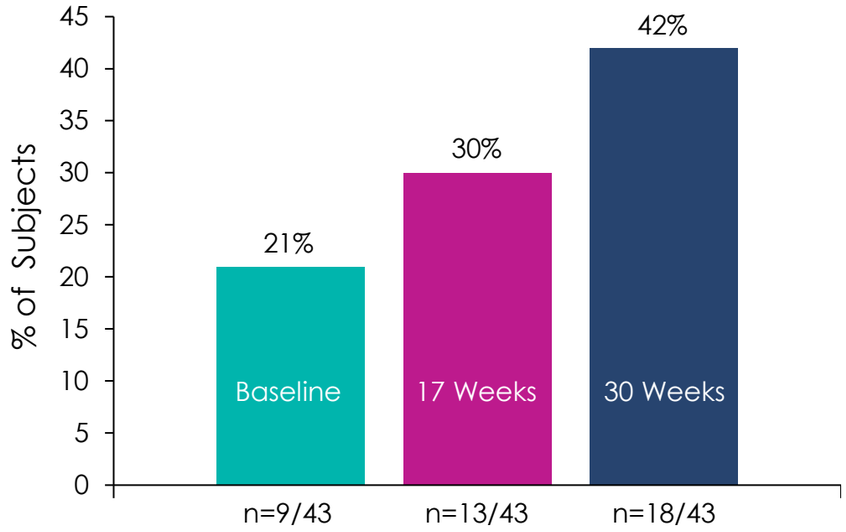
[a]Mean change, 95% CI, and P-value estimated using paired t-test.
CI, confidence interval; HbA1c, hemoglobin A1c; RCT, randomized controlled trial; TI, Technosphere Insulin; UC, usual care.
1. Beck RW, et al. *Diabetes Technol Ther.* 2025;27(3):170-178. 2. Beck RW, et al. *Diabetes Technol Ther.* vol. 2025;27(3):161-169. 3. Data on File (INHALE-3 Clinical Study Report, 2024). MannKind Corporation.

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Participants Meeting HbA1c Target <7.0%

TI → TI GROUP[1,2]

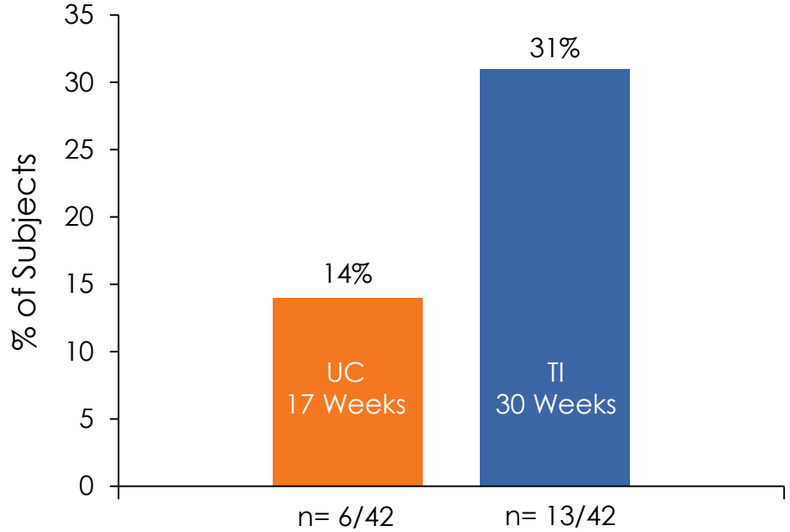
(Exploratory endpoint)
Risk Difference (30 Weeks - Baseline) (95% CI):
21% (4%, 38%); *P*=0.02[a]



Baseline to 30 Weeks

UC → TI SWITCH GROUP[2,3]

Risk Difference (30 Weeks -17 Weeks) (95% CI):
17% (3%, 30%); *P*=0.02[a]



17 Weeks to 30 Weeks

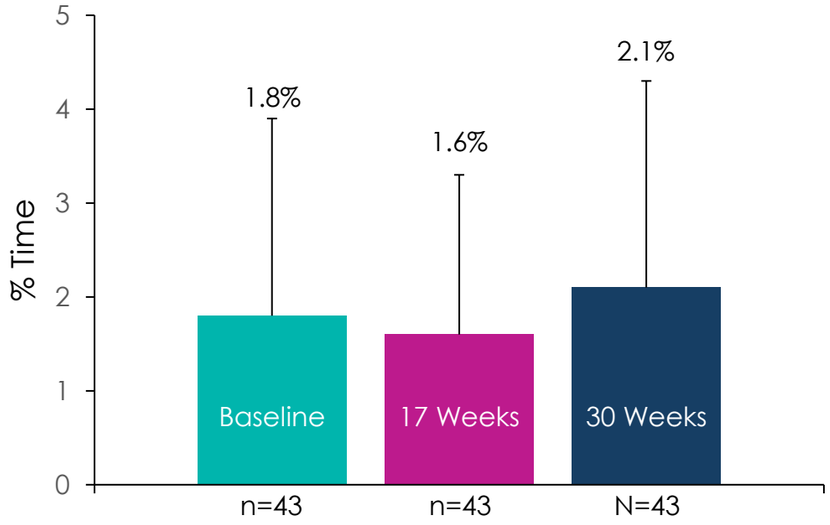
[a]Risk difference, 95% CI, and P-value estimated using McNemar's test.
CI, confidence interval; HbA1c, hemoglobin A1c; RCT, randomized controlled trial; TI, Technosphere Insulin; UC, usual care.
1. Beck RW, et al. *Diabetes Technol Ther.* 2025;27(3):170-178. 2. Data on File (INHALE-3 Clinical Study Report, 2024). MannKind Corporation. 3. Beck RW, et al. *Diabetes Technol Ther.* vol. 2025;27(3):161-169.

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CGM Metrics: Hypoglycemia: Percent Time <70 mg/dL[a]

TI → TI GROUP[1]

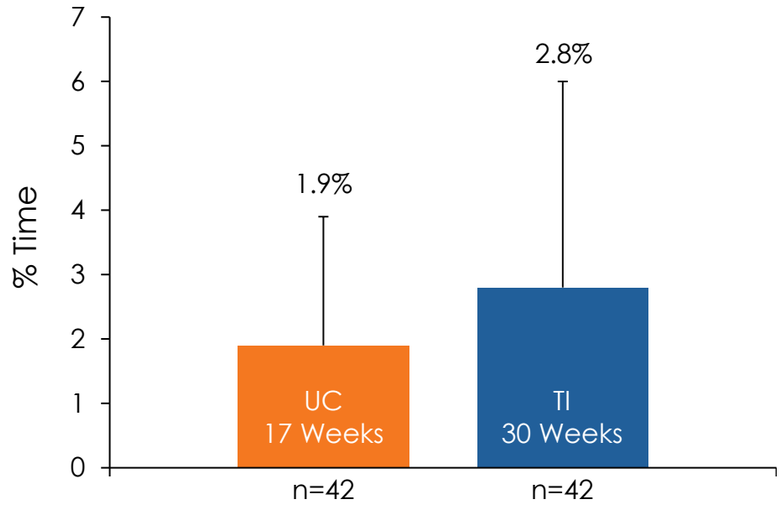
Mean Change from Baseline to 30 Weeks (95% CI):
0.5% (-0.7%, 1.6%); *P*=0.75



Baseline to 30 Weeks

UC → TI SWITCH GROUP[2,3]

Mean Change from 17 Weeks to 30 Weeks (95% CI):
1.1% (-0.2%, 2.4%); *P*=0.18[b]



17 Weeks to 30 Weeks

[a]Mean and SD estimated using maximum likelihood. A generalized linear mixed effects regression model with the t-distribution for the error terms was used to estimate the mean change, 95% CI, and P-value. [b]The mean change, 95% CI, and P-value estimated using a paired t-test.

CGM, continuous glucose monitor; CI, confidence interval; RCT, randomized controlled trial; SD, standard deviation; TI, Technosphere Insulin; UC, usual care.

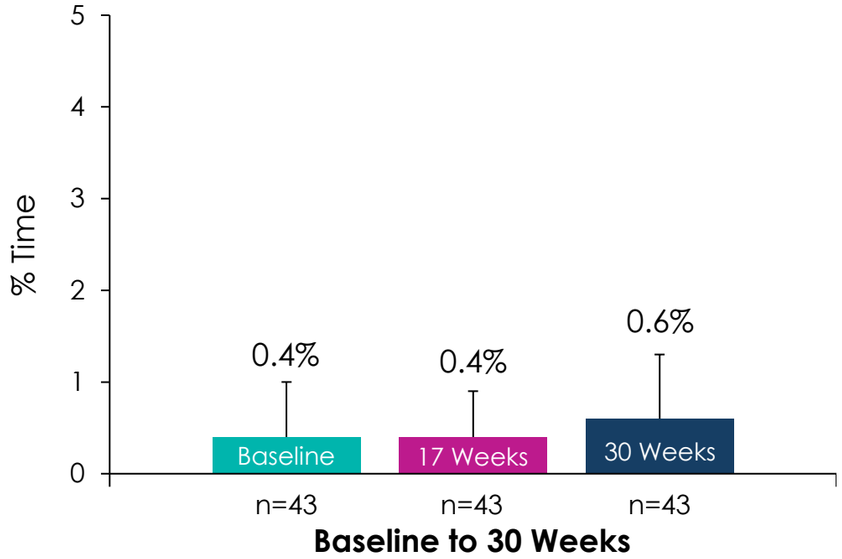
1. Beck RW, et al. *Diabetes Technol Ther.* 2025;27(3):170-178. 2. Beck RW, et al. *Diabetes Technol Ther.* vol. 2025;27(3):161-169. 3. Data on File (INHALE-3 Clinical Study Report, 2026). MannKind Corporation.

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CGM Metrics: Hypoglycemia: Percent Time <54 mg/dL[a]

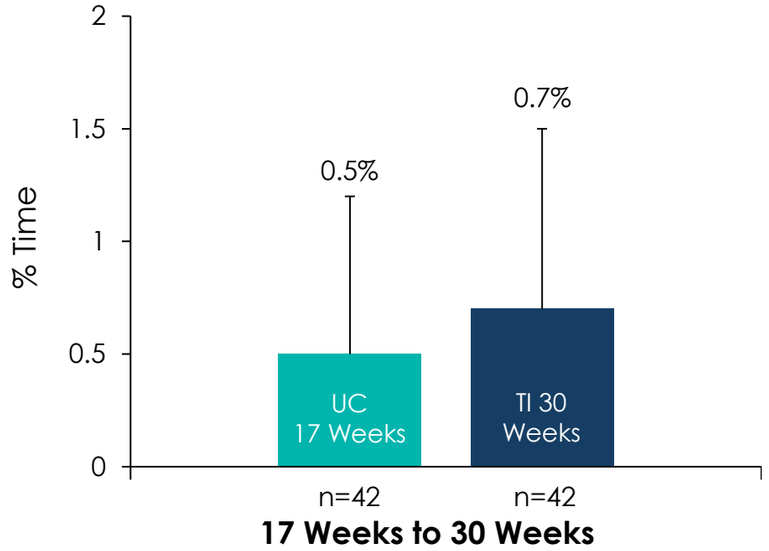
TI → TI GROUP[1]

Mean Change from Baseline to 30 Weeks (95% CI):
0.3% (-0.2%, 0.7%); *P*=0.66



UC → TI SWITCH GROUP[2,3]

Mean Change from 17 Weeks to 30 Weeks (95% CI):
0.2% (-0.2%, 0.7%); *P*=0.30[b]



[a]Mean and standard deviation estimated using maximum likelihood. A generalized linear mixed effects regression model with the t-distribution for the error terms was used to estimate the mean change, 95% CI, and p-value. [b]The mean change, 95% CI, and p-value estimated using a paired t-test.

CGM, continuous glucose monitor; CI, confidence interval; RCT, randomized controlled trial; TI, Technosphere Insulin; UC, usual care.

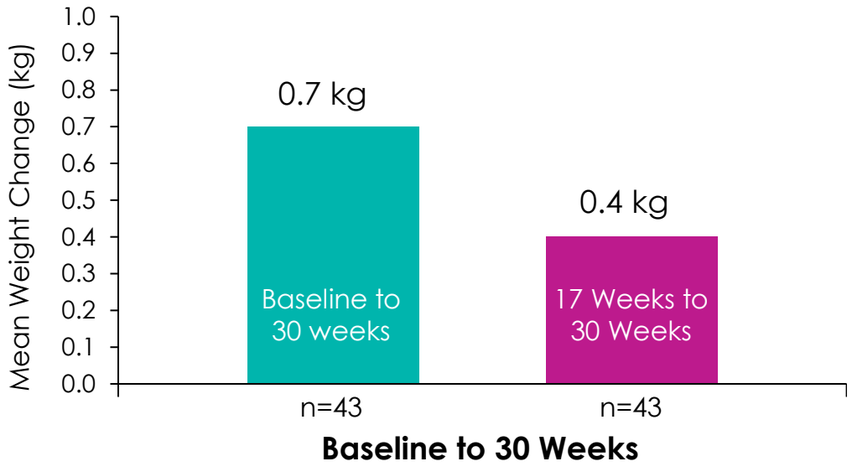
1. Beck RW, et al. *Diabetes Technol Ther.* 2025;27(3):170-178. 2. Beck RW, et al. *Diabetes Technol Ther.* vol. 2025;27(3):161-169. 3. Data on File (INHALE-3 Clinical Study Report, 2026). MannKind Corporation.

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Weight

TI → TI GROUP[1]

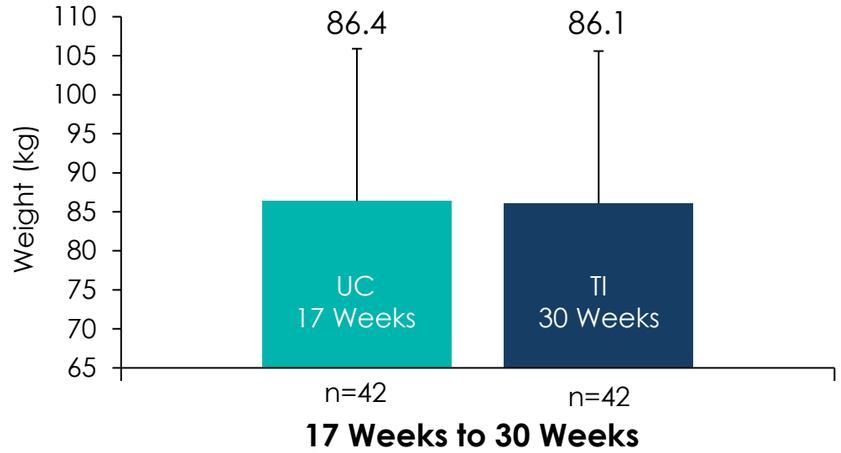
Mean Weight Change from Baseline to 30 Weeks



Mean Change (95% CI) [P-value][b]	
Baseline to 30 Weeks	0.7 (-0.5, 1.9) [0.27]
17 Weeks to 30 Weeks	0.4 (-0.2, 1.0) [0.17]

UC → TI SWITCH GROUP[1,2]

Mean Change from 17 Weeks to 30 Weeks (95% CI): -0.2 (-0.9, 0.4); *P*=0.49[a]



[a]Mean change, 95% CI, and P-value estimated using paired t-test.
CI, confidence interval; RCT, randomized controlled trial; TI, Technosphere Insulin; UC, usual care.
1. Data on File (INHALE-3 Clinical Study Report, 2024). MannKind Corporation. 2. Beck RW, et al. *Diabetes Technol Ther.* vol. 2025;27(3):161-169.

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Participant-Reported Outcomes

TI → TI GROUP[1]

- No significant changes from 17 weeks to 30 weeks were observed on any of the participant-reported outcome surveys

	TI Group Extension Week 30 Percent of participants
Interested in continuing to use TI (n=43)	44%
Prestudy MDI users (n=21)	52%
Prestudy AID users (n=18)	33%
Prestudy nonautomated pump users (n=4)	50%

UC → TI SWITCH GROUP[2]

- No significant changes from week 17 (baseline) to week 30 were observed on any of the participant-reported outcome surveys

	UC Group Extension Week 30 Percent of participants
Interested in continuing to use TI (n=42)	40%
Baseline MDI users (n=23)	43%
Baseline AID users (n=15)	27%
Baseline SAP users (n=2)	100%
Baseline PLGS users (n=2)	50%

AID, automated insulin delivery; MDI, multiple daily injection; PLGS, predictive low-glucose-suspend; RCT, randomized controlled trial; SAP, sensor augmented pump; TI, Technosphere Insulin; UC, usual care.

1. Beck RW, et al. *Diabetes Technol Ther.* 2025;27(3):170-178. 2. Beck RW, et al. *Diabetes Technol Ther.* vol. 2025;27(3):161-169.

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Summary of Adverse Events

TI → TI GROUP[1]

	RCT (Weeks 4-17) n=45	Extension n=45
All AEs, N Events	46	29
# of Participants with ≥ 1AE	29 (64%)	17 (38%)
Severe Hypoglycemia Events, n	1[a]	0
Diabetic Ketoacidosis Events, n	0	0
Other Serious Adverse Events, n Events	0	0

UC → TI SWITCH GROUP[1,2]

	RCT (Weeks 1-13) n=49	Extension n=49
All AEs, N Events	54	45
# of Participants with ≥1 AE	30 (61%)	28 (57%)
Severe Hypoglycemia Events, n	0	1[b]
Diabetic Ketoacidosis Events, n	0	0
Other Serious Adverse Events, n Events	1[c]	0

[a]The episode of severe hypoglycemia was associated with excessive alcohol consumption. [b]This event was associated with both a delay in eating after taking the TI dose and walking several blocks to a restaurant after taking the TI dose. [c]Other serious SAE that occurred during the RCT was appendicitis requiring an appendectomy.

AE, adverse event; RCT, randomized controlled trial; SAE, serious adverse event; TI, Technosphere Insulin; UC, usual care.

1. Data on File (INHALE-3 Clinical Study Report, 2024). MannKind Corporation. 2. Beck RW, et al. *Diabetes Technol Ther.* vol. 2025;27(3):161-169.

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Summary of Treatment-Emergent Adverse Events

TI → TI GROUP[1]

	RCT (Weeks 4-17) n=45	Extension[a] n=45
Possibly, Probably, or Definitely Related to Treatment- *n*	**6 events**	**2 events**
Abnormal weight gain	0	1
Allergic skin reaction	1	0
Back pain	0	0
Bronchospasm	1	0
Chest pressure	0	0
Cough	2	1
Diarrhea	0	0
Dry mouth	0	0
Hyperglycemia	0	0
Rash	0	0
Severe hypoglycemia	1	0
Shortness of breath	0	0
Sore throat	0	0
Wheezing	1	0

- 6 TEAEs were reported in 5 of the 45 (11%) participants during the RCT
- 2 TEAEs were reported during the extension

UC → TI SWITCH GROUP[1,2]

	Extension[a] n=49
Possibly, Probably, or Definitely Related to Treatment- *n*	**19 events**
Abnormal weight gain	1
Chest Burning	1
Cough	9
Glossitis	1
Hypoglycemia[b]	3
Injection-related reaction	1
Injection-site discomfort	1
Pain in ear	1
Sore throat	1

- 19 TEAEs possibly, probably, or definitely related to study treatment were reported for 14 (28%) participants during the extension
- Most common TEAE was cough: 9 events reported for 9 participants

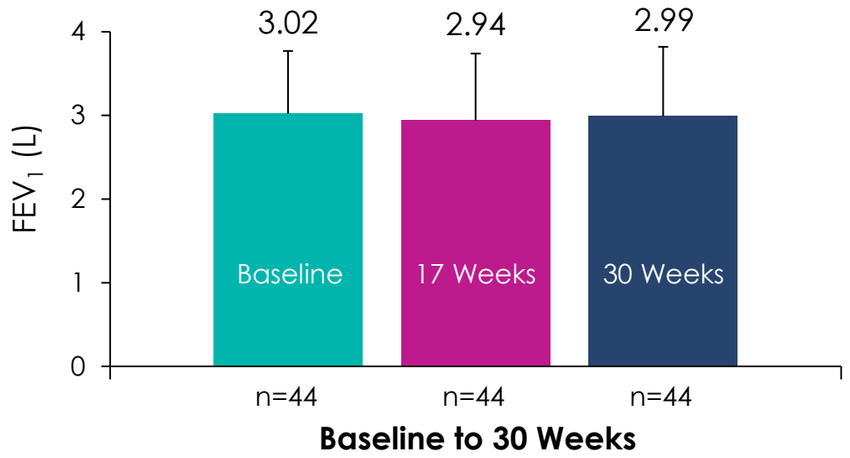
[a]Includes TEAEs with an onset date after the week 17 visit. [b]One hypoglycemic event considered a severe hypoglycemic event.
RCT, randomized controlled trial; TEAE, treatment-emergent adverse event; TI, Technosphere Insulin; UC, usual care.
1. Data on File (INHALE-3 Clinical Study Report, 2024). MannKind Corporation. 2. Beck RW, et al. *Diabetes Technol Ther.* vol. 2025;27(3):161-169.

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Pulmonary Function - Mean FEV_1 Change

TI → TI GROUP[1,2]

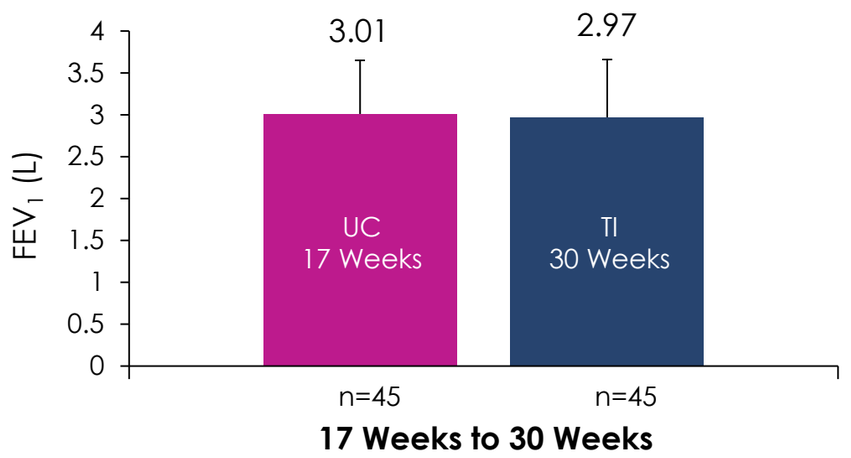
Mean Change from Baseline to 30 Weeks[a]



Mean Change (95% CI) [P-value][b]	
Baseline to 30 Weeks	-0.03 (-0.13, 0.07) [0.58]*
17 Weeks to 30 Weeks	0.05 (-0.03, 0.13) [0.24]*

UC → TI SWITCH GROUP[3]

Mean Change from 17 Weeks to 30 Weeks (95% CI): -0.03 (-0.09, 0.03); *P*=0.30[b]



[a]A repeat FEV_1 measurement was taken at 30 weeks for 1 participant but the original measure was used to calculate means. [b]Mean change, 95% CI, and P-value estimated using a paired t-test. *0% FEV_1 reduction ≥20%.
CI, confidence interval; FEV_1, forced expiratory volume in 1 second; RCT, randomized controlled trial; TI, Technosphere Insulin; UC, usual care.

1. Beck RW, et al. *Diabetes Technol Ther.* 2025;27(3):170-178. 2. Data on File (INHALE-3 Clinical Study Report, 2024). MannKind Corporation. 3. Beck RW, et al. *Diabetes Technol Ther.* vol. 2025;27(3):161-169.

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INHALE-3 Extension Key Takeaways – 30 Weeks

HbA1c improved during the extension period in both groups (UC and TI)

From baseline use of TI to completion of extension, there was an approximate doubling of the number of subjects that achieved the glycemic goal of HbA1c <7.0%

Improved glycemic outcomes in subjects transitioning from MDI and similar outcomes in subjects transitioning from AID to TI + degludec

No new pulmonary or glycemic safety signals were identified

AID, automated insulin delivery; HbA1c, hemoglobin A1c; MDI, multiple daily injection; RCT, randomized controlled trial; TI, Technosphere Insulin; UC, usual care.

Hirsch IB, et al. *Diabetes Care*. 2025;48(3):353-360.

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Post-Meal Hyperglycemia in Youth With T1D

Post-meal hyperglycemia is common in youth with T1D despite MDI or AID[1]

- Subcutaneous RAAs have delayed onset that mismatches with meal-related glucose rise
- TI has faster onset and faster offset of action compared with RAA
- Prior adult data: TI reduces early post-meal glucose excursion vs RAA
- Pediatric meal challenge data were limited prior to INHALE-1
  - A prior pediatric PK study demonstrated a favorable insulin action profile for TI in children with no safety concerns[2]

AID, automated insulin delivery; MDI, multiple daily injections; PK, pharmacokinetics; RAA, rapid-acting insulin analog; T1D, type 1 diabetes; TI, Technosphere insulin.

1. Ekhlaspour L, et al. *Diabetes Technol Ther*. 2026;0(0). Published online March 14, 2026. doi:10.1177/15209156261432138. 2. Haller MJ, et al. *Diabetes Ther*. 2023;14(1):611-617.

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Meal Challenge Methods: INHALE-1 (vs INHALE-3 as Comparator)

- **INHALE-1: 217 youth (4–17 yrs) with T1D on MDI**
  - Participants fasted ≥8 hours prior to the meal challenge
  - Standardized meal challenge: Clif Bar or BOOST shake (~240–260 cal, 37–43 g carbohydrate)
  - TI dose ≈2× calculated RAA dose, rounded to nearest 4-unit cartridge
  - Optional correction dose at 60–90 min if glucose >160 mg/dL
  - Glucose monitored for 2 hours via Dexcom G6
- **Comparator cohorts from INHALE-3 adults:**
  - TI (n=51)
  - RAA (n=25)
- **Primary metric:** AUC >180 mg/dL
- **Additional metrics:** peak glucose, excursion, time-in-range

AUC, area under the curve; MDI, multiple daily injections; RAA, rapid-acting insulin analog; TI, Technosphere Insulin; T1D, type 1 diabetes; TI, Technosphere insulin

Ekhlaspour L, et al. *Diabetes Technol Ther*. 2026;0(0). Published online March 14, 2026. doi:10.1177/15209156261432138.

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Meal Challenge Results: Glycemic Metrics

- Pediatric TI cohort showed similar post-meal glucose excursion to adult TI cohort (*P*=0.26)
- Compared with adult RAA cohort, pediatric TI cohort demonstrated significantly smaller glucose excursion (*P*<0.001)

	Pediatric TI (INHALE-1; n=217)	Adult TI (INHALE-3; n=51)	Adult RAA (INHALE-3; n=25)
Peak Glucose (mg/dL) mean ± SD	245 ± 74	244 ± 71	287 ± 66
Glucose Excursion (mg/dL) mean ± SD	59 ± 51	73 ± 50	102 ± 45
AUC >180 (mg/dL) mean ± SD	42 ± 50	42 ± 53	69 ± 52
Time-in-Range (70–180 mg/dL) mean ± SD	41% ± 38%	44% ± 39%	23% ± 32%

AUC, area under the curve; RAA, rapid-acting insulin analog; SD, standard deviation; TI, Technosphere insulin.

Ekhlaspour L, et al. *Diabetes Technol Ther*. 2026;0(0). Published online March 14, 2026. doi:10.1177/15209156261432138.

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Safety and Subgroup Analysis

Subgroup analyses by age and baseline HbA1c; safety profile during meal challenge

- Hypoglycemia (<70 mg/dL)
  - Pediatric TI: 6%
  - Adult TI: 2%
  - Adult RAA: 0%
  - Strong association with lower starting glucose (109 vs 193 mg/dL)
  - No hypoglycemia occurred after correction doses
- Age Difference (<13 yrs vs ≥13 yrs)
  - <13 yrs: higher peak glucose (262 vs 230 mg/dL), larger excursion (75 vs 45 mg/dL)
  - Possible factors: inhalation technique, conservative carb ratios, no optimization period
- Baseline HbA1c Subgroup (<8.5% vs ≥8.5%)
  - No significant differences in post-meal glycemic metrics were observed between HbA1c groups

HbA1c, hemoglobin A1c; RAA, rapid-acting insulin analog; TI, Technosphere insulin

Ekhlaspour L, et al. *Diabetes Technol Ther*. 2026;0(0). Published online March 14, 2026. doi:10.1177/15209156261432138.

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Key Takeaways – INHALE-1 Meal Challenge

Key considerations for HCPs integrating TI in diabetes management

- TI demonstrated rapid insulin action with improved early post-meal glucose control in youth with T1D
- Post-meal glycemic metrics in the pediatric TI cohort were similar to those in the adult TI cohort
- Pediatric TI demonstrated significantly improved early post-meal metrics compared with RAA in adults (*P*< 0.001 for excursion, peak glucose, and AUC >180)
- Limitations
  - Basal insulin doses were not optimized for inhaled insulin during the meal challenge
  - No direct pediatric TI vs pediatric RAA comparison; statistical comparison made with adult RAA cohort from INHALE-3

AUC, area under the curve; HCP, healthcare professional; RAA, rapid-acting insulin analog; T1D, type 1 diabetes; TI, Technosphere insulin

Ekhlaspour L, et al. *Diabetes Technol Ther*. 2026;0(0). Published online March 14, 2026. doi:10.1177/15209156261432138.

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Post-Meal Hyperglycemia in Adults With T1D

- Post-meal hyperglycemia is difficult to prevent with subcutaneous RAA insulin, including in people using AID systems
- Technosphere insulin inhalation powder (TI) has a more rapid onset of action and serum insulin levels return to baseline sooner than with RAA insulin
- A standardized in-clinic meal challenge compared TI vs RAA on post-meal glycemia at the start of a multicenter randomized trial in adults with T1D

AID, automated insulin delivery; RAA, rapid-acting insulin analog; T1D, type 1 diabetes; TI, Technosphere insulin

Hirsch IB, et al. *Diabetes Care*. 2024;47(9):1682–1687.

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INHALE-3 Meal Challenge at Randomization Visit

Methods

- Adults with T1D using MDI, nonautomated pump, or AID were randomized 1:1 to bolus with TI (n=61) or their usual RAA insulin (n=61)
- Fasting with no manual insulin bolus for 4 hours prior; pre-meal glucose expected 91–219 mg/dL 15 minutes before meal
- Standardized meal: BOOST shake (~240 calories, 37 g carbohydrate, 10 g protein, 4 g fat)
- RAA dosed 10 ± 5 minutes before meal; TI inhaled at start of meal
- TI dose: rounded usual RAA dose ×2, then rounded down to nearest 4-unit TI dose (max 24 units); no glucose correction
- BG measured at −15, 0, 15, 30, 45, 60, 90, and 120 minutes; 2-hour post-meal glucose used for primary analysis

AID, automated insulin delivery; BG, blood glucose; MDI, multiple daily injections; RAA, rapid-acting insulin analog; T1D, Type 1 diabetes; TI, Technosphere insulin

Hirsch IB, et al. *Diabetes Care*. 2024;47(9):1682–1687.

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INHALE-3 Meal Challenge at Randomization Visit

Postprandial Glycemic Outcomes in first 2 hours

- Primary outcome (AUC180) was lower with TI vs RAA (adjusted group difference −12 mg/dL; 95% CI −22 to −2; *P*=0.02)
- With TI, glucose excursion was smaller (*P*=0.01), peak glucose was lower (*P*=0.01), and time-to-peak glucose was shorter (*P*=0.006)

Outcome (overall)	TI (n=61) Mean ± SD	RAA (n=61) Mean ± SD	Adjusted group difference (95% CI) [P]
Starting glucose (mg/dL)	166 ± 61	163 ± 51	—
AUC180 (mg/dL)	40 ± 44	50 ± 42	−12 (−22, −2) [0.02]
Peak glucose (mg/dL)	248 ± 64	268 ± 58	−22 (−39, −5) [0.01]
Time-to-peak glucose (min)	66 ± 34	81 ± 27	−14 (−24, −4) [0.006]
Excursion (mg/dL)	82 ± 57	105 ± 42	−22 (−39, −5) [0.01]

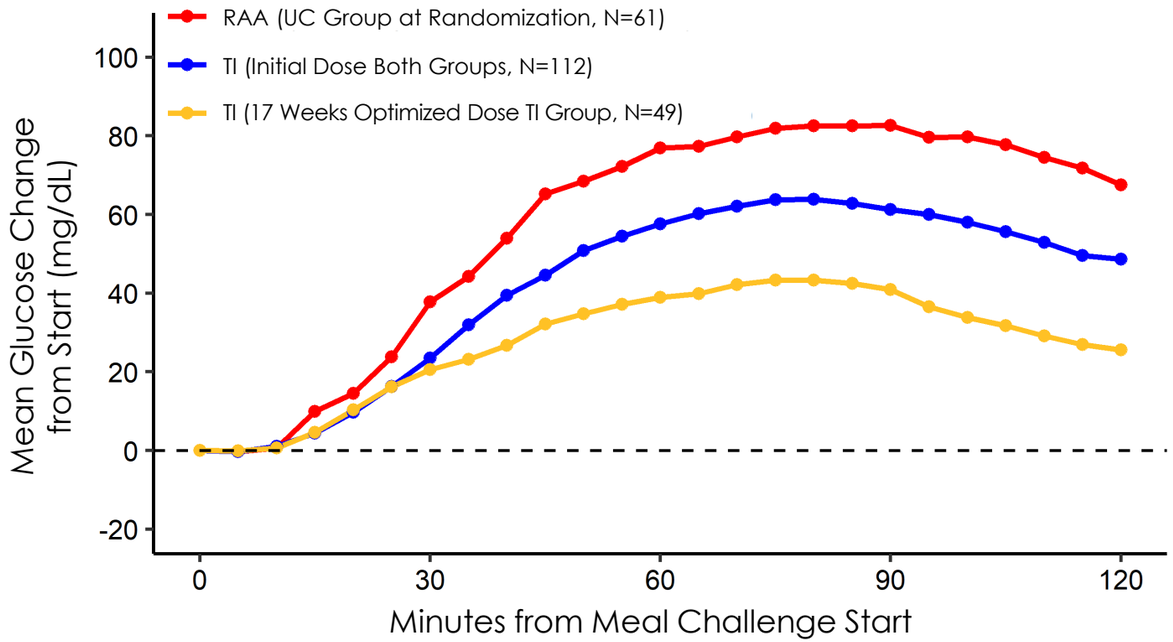
AUC180, area under the curve for glucose >180 mg/dL; RAA, rapid-acting insulin analog; SD, standard deviation; TI, Technosphere insulin

Hirsch IB, et al. Diabetes Care. 2024;47(9):1682–1687.

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INHALE-3 Meal Challenges

Mean Glucose Change from Meal Challenge Start by Insulin Type



TI initial dose combines the TI group at randomization and the Usual Care group using TI at 17 weeks.
TI optimized dose is from the TI group at 17 weeks.

RAA, rapid-acting insulin analog; TI, Technosphere Insulin; UC, usual care.
Data on File (INHALE-3 Clinical Study Report, 2024). MannKind Corporation.

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Safety During the Randomization Visit In-Clinic Meal Challenge

- BG <70 mg/dL occurred in 1 participant in each group during the 2-hour in-clinic procedure
- Additional insulin was given for prolonged hyperglycemia due to an infusion-set failure in 1 RAA participant
- 1 TI participant had a second TI dose after 90 minutes at investigator discretion
- 1 TI participant developed coughing, neck tingling, throat tightness, and breathing difficulties after TI inhalation; symptoms dissipated without intervention
- During the 4-hour post-meal period, mean CGM time <70 mg/dL was low in both groups (TI 0.0% ± 0.0%; RAA 0.2% ± 1.7%)

BG, blood glucose; CGM, continuous glucose monitoring; RAA, rapid-acting insulin analog; TI, Technosphere insulin

Hirsch IB, et al. *Diabetes Care*. 2024;47(9):1682–1687.

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Key Takeaways and Context – INHALE-3 Meal Challenge

TI significantly reduced post-meal hyperglycemia vs RAA insulin in adults with T1D using AID or MDI

- With TI, glucose excursion was smaller, peak glucose was lower, and time-to-peak glucose was shorter vs RAA
- Treatment group difference peaked at ~90 minutes and glucose levels appeared similar by ~3 hours in extended analyses
- Post-meal hypoglycemia during the meal challenge was infrequent and similar between groups
- Study limitations included lack of study CGM data during the meal challenge for some participants; sensitivity analyses using only BG data produced similar results

TI can be dosed at the start of a meal due to rapidity of action, vs 5–15 minutes prior for optimal RAA dosing

- The more rapid dissipation of TI effect allows for repeat bolus after 1 hour without concern for insulin stacking, as would be the case with RAA redosing
- Current labeling bases TI initial dosing on an approximate 1:1 RAA conversion; this study and a prior study indicate that a conversion of at least 2:1 represents a bioequivalent TI dose that can be inhaled safely with substantially greater reduction in post-meal hyperglycemia

AID, automated insulin delivery; BG, blood glucose; CGM, continuous glucose monitoring; MDI, multiple daily injections; RAA, rapid-acting insulin analog; T1D, Type 1 diabetes; TI, Technosphere insulin.

Hirsch IB, et al. *Diabetes Care*. 2024;47(9):1682–1687.

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AFREZZA Prescribing Information[1]

Link to full prescribing information >

Boxed Warning

WARNING: RISK OF ACUTE BRONCHOSPASM IN PATIENTS WITH CHRONIC LUNG DISEASE

- **Acute bronchospasm has been observed in AFREZZA-treated patients with asthma and COPD. (5.1)**
- **AFREZZA is contraindicated in patients with chronic lung disease such as asthma or COPD. (4)**
- **Before initiating AFREZZA, perform a detailed medical history, physical examination, and spirometry (FEV_1) to identify potential lung disease in all patients. (2.1), (5.1)**

COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second.

1. Afrezza® (insulin human) Inhalation Powder Prescribing Information. MannKind Corporation.

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AFREZZA Prescribing Information[1]

Link to full prescribing information >

Contraindications

- During episodes of hypoglycemia *[see Warnings and Precautions (5.3)]*.
- Chronic lung disease, such as asthma or chronic obstructive pulmonary disease (COPD), because of the risk of acute bronchospasm *[see Warnings and Precautions (5.1)]*
- Hypersensitivity to regular human insulin or any of the excipients in AFREZZA *[see Warnings and Precautions (5.7)]*

COPD, chronic obstructive pulmonary disease.

1. Afrezza® (insulin human) Inhalation Powder Prescribing Information. MannKind Corporation.

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AFREZZA Prescribing Information[1]

Link to full prescribing information >

Adverse Reactions

The most common adverse reactions associated with AFREZZA (2% or greater incidence) are hypoglycemia, cough, and throat pain or irritation (6)

The following serious adverse reactions are described below and elsewhere in the labeling:

- Acute bronchospasm in patients with chronic lung disease *[see Warnings and Precautions (5.1)]*
- Hypoglycemia or Hyperglycemia with Changes in Insulin Regimen *[see Warnings and Precautions (5.2)]*
- Hypoglycemia *[see Warnings and Precautions (5.3)]*
- Decline in pulmonary function *[see Warnings and Precautions (5.4)]*
- Lung cancer *[see Warnings and Precautions (5.5)]*
- Diabetic ketoacidosis *[see Warnings and Precautions (5.6)]*
- Hypersensitivity reactions *[see Warnings and Precautions (5.7)]*
- Hypokalemia *[see Warnings and Precautions (5.8)]*
- Fluid Retention and Heart Failure with Concomitant Use of TZDs *[see Warnings and Precautions (5.9)]*

TZDs, Thiazolidinediones.

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Warnings and Precautions

Acute Bronchospasm in Patients with Chronic Lung Disease

Because of the risk of acute bronchospasm, AFREZZA is contraindicated in patients with chronic lung disease such as asthma or COPD. Before initiating therapy with AFREZZA, evaluate all patients with a medical history, physical examination, and spirometry (FEV_1) to identify potential underlying lung disease.

- Acute bronchospasm has been observed in AFREZZA-treated patients with asthma and COPD. In a study of patients with asthma whose bronchodilators were temporarily withheld for assessment, bronchoconstriction and wheezing following AFREZZA dosing was reported in 29% (5 out of 17) and 0% (0 out of 13) of patients with and without a diagnosis of asthma, respectively. In this study, a mean decline in FEV_1 of 400 mL was observed 15 minutes after a single AFREZZA dose in patients with asthma. In a subset study of patients with COPD (n=8), a mean decline in FEV_1 of 200 mL was observed 18 minutes after a single AFREZZA dose.

COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second.

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Warnings and Precautions (continued)

Hypoglycemia or Hyperglycemia with Changes in Insulin Regimen

Carry out under close medical supervision and increase frequency of blood glucose monitoring. For patients with type 2 diabetes mellitus, oral antidiabetic treatment dosage modifications may be needed.

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Warnings and Precautions (continued)

Hypoglycemia (may be life-threatening)

Increase frequency of glucose monitoring in patients at higher risk for hypoglycemia and those who have reduced symptomatic awareness of hypoglycemia.

- Hypoglycemia is the most common adverse reaction associated with insulins, including AFREZZA. Severe hypoglycemia can cause seizures, may be life-threatening, or cause death.

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Warnings and Precautions (continued)

Decline in Pulmonary Function

Assess pulmonary function (e.g., spirometry (FEV_1)) before initiating, after 6 months of therapy, and annually, even in the absence of pulmonary symptoms. In patients who have a decline of ≥ 20% in FEV_1 from baseline, consider discontinuing AFREZZA.

- AFREZZA causes a decline in pulmonary function over time as measured by FEV_1. In clinical trials excluding patients with chronic lung disease and lasting up to 2 years, Afrezza-treated patients experienced a small [40 mL (95% CI: -80, -1)] but greater FEV_1 decline than comparator-treated patients. The FEV_1 decline was noted within the first 3 months, and persisted for the entire duration of therapy (up to 2 years of observation). In this population, the annual rate of FEV_1 decline did not appear to worsen with increased duration of use. The effects of AFREZZA on pulmonary function for treatment duration longer than 2 years has not been established. There are insufficient data in long term studies to draw conclusions regarding reversal of the effect on FEV_1 after discontinuation of Afrezza. The observed changes in FEV_1 were similar in patients with type 1 and type 2 diabetes.

FEV_1, forced expiratory volume in 1 second.

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Warnings and Precautions (continued)

Lung Cancer

In patients with active lung cancer, a prior history of lung cancer, or in patients at risk for lung cancer, consider whether the benefits of AFREZZA use outweigh this potential risk.

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Warnings and Precautions (continued)

Diabetic Ketoacidosis

In patients at risk for DKA, increase the frequency of glucose monitoring and consider changing to alternate route of insulin delivery.

- In clinical trials enrolling patients with type 1 diabetes, diabetic ketoacidosis (DKA) was more common in AFREZZA-treated patients (0.43%; n=13) than in comparator-treated patients (0.14%; n=3). Patients with type 1 diabetes should always use AFREZZA in combination with basal insulin.

DKA, diabetic ketoacidosis.

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Warnings and Precautions (continued)

Hypersensitivity Reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products, including AFREZZA. If hypersensitivity reactions occur, discontinue AFREZZA, treat per standard of care and monitor until symptoms and signs resolve.

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Warnings and Precautions (continued)

Hypokalemia (may be life-threatening)

Monitor potassium levels in patients at risk of hypokalemia.

- All insulin products, including AFREZZA, cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia. Untreated hypokalemia may cause respiratory paralysis, ventricular arrhythmia, and death.

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Warnings and Precautions (continued)

Fluid Retention and Heart Failure with Concomitant Use of Thiazolidinediones (TZDs)

Observe for signs and symptoms of heart failure; consider dosage reduction or discontinuation if heart failure occurs.

TZD, Thiazolidinediones.

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