# Pre-presentation Survey

**Please fill out the very brief pre-presentation survey via the URL or QR Code below.**

**https://www.pcmg-us.org/survey/pre/owi7**


**Thank you so much.**

# What Primary Care Clinicians Need to Know About Once-Weekly Insulins


***Scott Urquhart, PA-C, DFAAPA***

Co-Chair: Cardio Renal Metabolic/Endocrine Assembly (CaRMA)

Past Chair / founder: Metabolic and Endocrine Disease Summit (MEDS)

American Society of Endocrine PA's

Diabetes and Thyroid Associates, Fredericksburg, VA

# Faculty, Sponsorship and Support

This presentation is sponsored by

ILLINOIS ACADEMY OF FAMILY PHYSICIANS

PRIMARY CARE EDUCATION CONSORTIUM

and supported by an educational grant from Novo Nordisk, Inc.

# In collaboration with


FREE to JOIN!

PCMG

Primary Care Metabolic Group

Join at **https://www.pcmg-us.org** for free CME, discounts on conferences and resources for clinicians interested in metabolic disorders.

# Faculty Disclosure Information

Primary Care Education Consortium adheres to the conflict-of-interest policy of the ACCME and the AMA. It is the policy of PCEC to ensure balance, independence, objectivity, and scientific rigor in all its educational activities. All individuals in a position to control the content in our programs are expected to disclose any relationships they may have with commercial companies whose products or services may be mentioned so that participants may evaluate the objectivity of the presentations. In addition, any discussion of off-label, experimental, or investigational use of drugs or devices will be disclosed by the faculty. Only those participants who have no conflict of interest or who agree to an identified resolution process prior to their participation were involved in the CME activity.

# Disclosures

- **Scott Urquhart, PA-C, DFAAPA,** has disclosed that he is on the advisory board Dexcom, Novo Nordisk, and Ascencia; and is on the speakers bureau for Dexcom and Novo Nordisk.
- **Austin Ulrich, PharmD,** Editorial Support, and **Michael Hanak, MD,** disclose no relevant financial relationship or interest with a proprietary entity producing, marketing, reselling or distributing health care goods or services.
- All relevant financial relationships have been mitigated.
- This CME activity includes discussion about medications not approved by the US Food and Drug Administration and uses of medications outside of their approved labeling.

# Learning Objectives

| Participants in this activity should be able to… |
| --- |
| Initiate basal insulin therapy without unnecessary delays for patients with T2D who are indicated for insulin treatment. |
| Review the clinical efficacy and safety data for new and emerging ultra-long acting once weekly insulins. |
| Compare and contrast the potential benefits and risks of once weekly insulins compared to traditional basal insulins. |

# Introduction

# Type 2 Diabetes (T2D)

- T2D is a serious public health concern globally and in the United States (US)[1]
- Associated with significant morbidity due to microvascular and macrovascular complications resulting from elevated blood glucose[3,4]
  - Diminished functional capacity, lower quality of life, and premature death

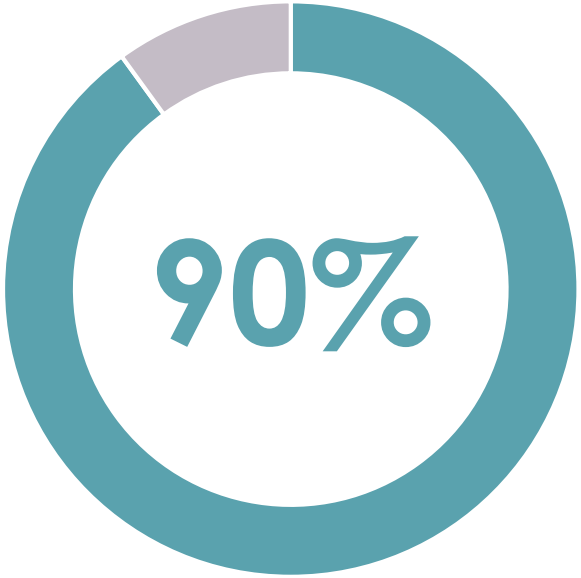
**1 in 10**

**Americans have diabetes; most have T2D[2]**

1. Khan MAB, et al. *J Epidemiol Glob Health*. 2020;10(1):107-111. 2. Centers for Disease Control and Prevention. About type 2 diabetes. Updated May 15, 2024. Accessed June 20, 2024. https://www.cdc.gov/diabetes/about/about-type-2-diabetes.html. 3. American Diabetes Association Professional Practice Committee, et al. *Diabetes Care*. 2024;47(Suppl_1):S179-S218. 4. American Diabetes Association Professional Practice Committee, et al. *Diabetes Care*. 2024;47(Suppl_1):S219-S230.

# The Primary Care Clinician's Role

- Primary care clinicians (PCCs) treat most patients in the US with T2D[1,2]
  - Often the first clinicians to diagnose T2D
- Some patients with T2D may see an endocrinologist
  - Projections indicate current and future shortages of endocrinologists[2,3]




**of patients with T2D are treated by PCCs**

**PCCs play a critical role in the management of patients with T2D, which often involves the use of basal insulin**

1. Davidson JA. *Mayo Clin Proc*. 2010;85(12 Suppl):S3-S4. 2. Shrivastav M, et al. *Diabetes Spectr.* 2018;31(3):279-287. 3. Vigersky RA, et al. *J Clin Endocrinol Metab*. 2014;99(9):3112-3121.

# The Role of Basal Insulin in T2D

# Basal Insulin: History and Indications

- Insulin is still an essential and effective glucose-lowering treatment for many patients[1]
  - Advances in molecular biology and drug delivery technologies seen in recent years
- The goal of insulin therapy is to replicate as closely as possible a normal glycemic profile without unacceptable weight gain or hypoglycemia[2]
- For patients with T2D, initiating insulin therapy should start with basal insulin with a preference for basal insulin analogs.[2]

**ADA Recommendations for initiating basal insulin in T2D[2]**

| Consider as the first injectable therapy when a patient has: |
| --- |
| • Blood glucose ≥300 mg/dL |
| • HbA1c >10% |
| • Symptomatic hyperglycemia or signs of catabolism due to glucotoxicity |

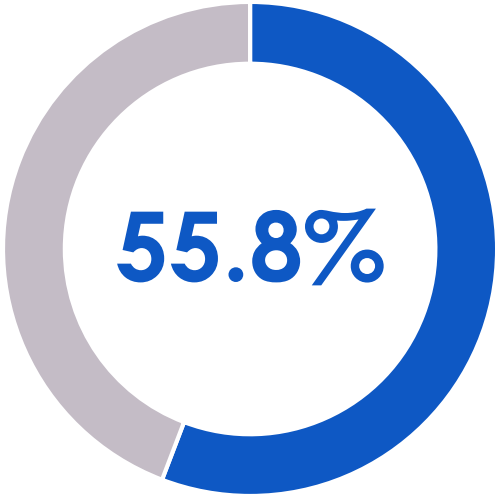
ADA, American Diabetes Association.

1. Rosenstock J, et al. *Metabolism*. 2022;126:154924. 2. American Diabetes Association Professional Practice Committee, et al. *Diabetes Care*. 2024;47(Suppl_1):S158-S178.

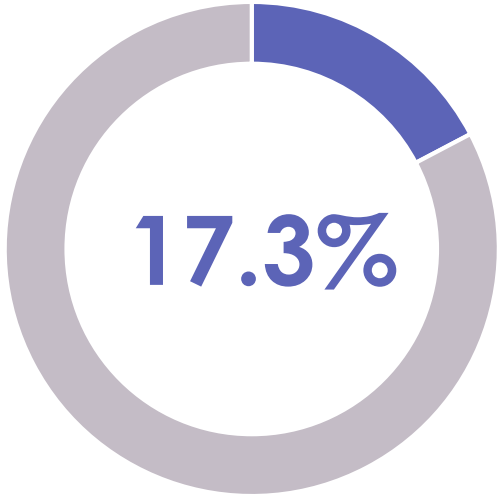
# Failure to Reach Targets in T2D

- Many patients with T2D do not achieve glycemic control
- Few achieve simultaneous control of associated cardiovascular risk factors

## NHANES Data 2013-2016[1]




patients reached target HbA1c




patients reached targets for composite of HbA1c, blood pressure, and lipids


patients reached targets for composite of HbA1c, blood pressure, lipids, and BMI

NHANES, National Health and Nutrition Examination Survey; BMI, body mass index.

1. Andary R, et al. *Am J Cardiol*. 2019;124(4):522-527.

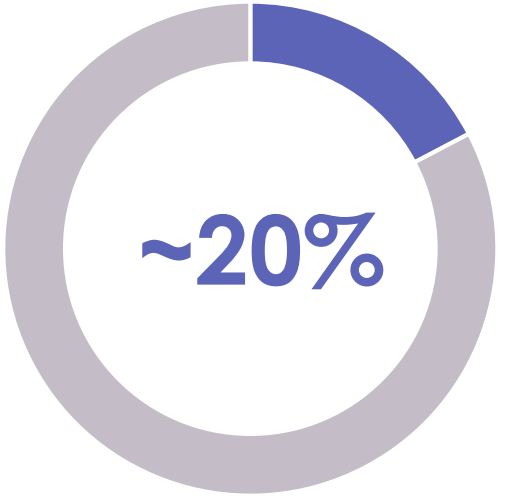
# Patient Perspectives on Insulin

- Acceptability of insulin is low among patients with T2D, leading to reluctance to initiate and continue insulin therapy[1]

- A large proportion of patients interrupt or discontinue treatment shortly after initiation[2]

**~7.4 million**

**Americans use one or more form(s) of insulin to manage diabetes[3]**




of patients initiating basal insulin continued with insulin treatment within the year after initiation

1. Brod M, et al. *Qual Life Res*. 2009;18(1):23-32. 2. Perez-Nieves M, et al. *Curr Med Res Opin*. 2016;32(4):669-680. 3. Cefalu WT, et al. *Diabetes Care*. 2018;41(6):1299-1311.

# Clinical Inertia in T2D

**Clinical inertia: lack of treatment initiation or intensification, resulting in failure to achieve glycemic goals[1]**

- Clinical inertia in the US:
  - Common reason for poor glycemic control[1]
  - **Fewer than 50%** of patients with T2D and a high HbA1c had their treatment appropriately intensified[2]
  - **Seen in more than 26%** of patients who had an HbA1c of ≥7%, and **more than 18%** of patients with an HbA1c of ≥8%; these patients also failed to have intensification of medications after a median follow-up of 4.2 years[3]
  - Results in **inadequate glycemic control in 40% to 60%** of patients with T2D[4,5]

1. Khunti S, et al. *Ther Adv Endocrinol Metab*. 2019;10:2042018819844694. 2. Shah BR, et al. *Diabetes Care*. 2005;28(3):600-606. 3. Mata-Cases M, et al. *Diabetes Obes Metab*. 2018;20(1):103-112. 4. Blonde L, et al. *Diab Vasc Dis Res*. 2017;14(3):172-183. 5. Pantalone KM, et al. *Diabetes Care*. 2018;41(7):e113-e114.

# Clinical Inertia in T2D (cont)

- Retrospective cohort study of >80,000 patients[1]
  - Median time to intensification with insulin was **longer than 7 years** for those not achieving glycemic goals on oral therapies alone

- Study of clinical inertia in patients with T2D in primary care practice[2]
  - Clinicians waited an **average of 9 years** before insulin initiation
    - Average HbA1c was 9.5% and complications were present
  - Even after initiation, insulin was **not titrated adequately**
    - Average HbA1c remained at 7.9% after 4 years of treatment

1. Khunti K, et al. *Diabetes Care*. 2013;36(11):3411-3417. 2. Harris SB, et al. *Can Fam Physician*. 2010;56(12):e418-e424.

# Clinical Inertia in T2D (cont)

- The prevalence of clinical inertia is remarkable, considering the focus of guidelines on the importance of glycemic control
  - Increased attention is needed to achieve glycemic targets in patients with T2D
- Newer formulations of basal insulins, such as ultra-long acting once-weekly insulins, are nearing FDA approval
- Provided that potential risks are properly addressed, once-weekly basal insulins are predicted to[1]:
  - Increase treatment adherence **SURVEY KNOWLEDGE Q**
  - Decrease clinical inertia
  - Improve patient quality of life

1. Rosenstock J, et al. *Metabolism*. 2022;126:154924.

# Patient Case Scenario

59-year-old woman with a 20-year history of T2D presents to her PCC for a follow up visit 3 months after starting basal insulin once daily

- Despite her hesitation to agree to an injectable medication

After one month of titrating her basal insulin dose via twice weekly phone appointments, she had reached:

- 45 units of insulin glargine once daily (0.5 units/kg)
- Fasting glucose level ranging from 130 mg/dL to 140 mg/dL
- No hypoglycemic episodes

Since then, she says that she has a difficult time remembering to do her daily injections on her own

She also doesn't like having to give herself an injection every day

# Patient Case Scenario (cont)

Today's visit:

- Fasting blood glucose: 195 mg/dL
- HbA1c: 9.6% (improved from 10.3% three months ago)

Other antihyperglycemic medications include:

- Metformin 2000 mg daily
- Oral semaglutide 14 mg once daily

States that she would like to try and work on her diet and exercise to get her HbA1c lower, toward her goal of <8%.

**Is this patient at risk for clinical inertia?**
**How might a once-weekly basal insulin be helpful for this patient?**

# Patient Case Scenario (cont)

- The patient originally responded well to basal insulin therapy, with fasting blood glucose values that indicated improvement in overall glucose control
  - After she was no longer under close follow up, she began to miss doses
- She is at risk for clinical inertia, raising her risk of complications that can result from hyperglycemia
- This patient may be a good candidate for receiving a once-weekly basal insulin (if approved) to improve her adherence and overall glucose control, and due to her preference for fewer injections

# New and Emerging Once-Weekly Insulins

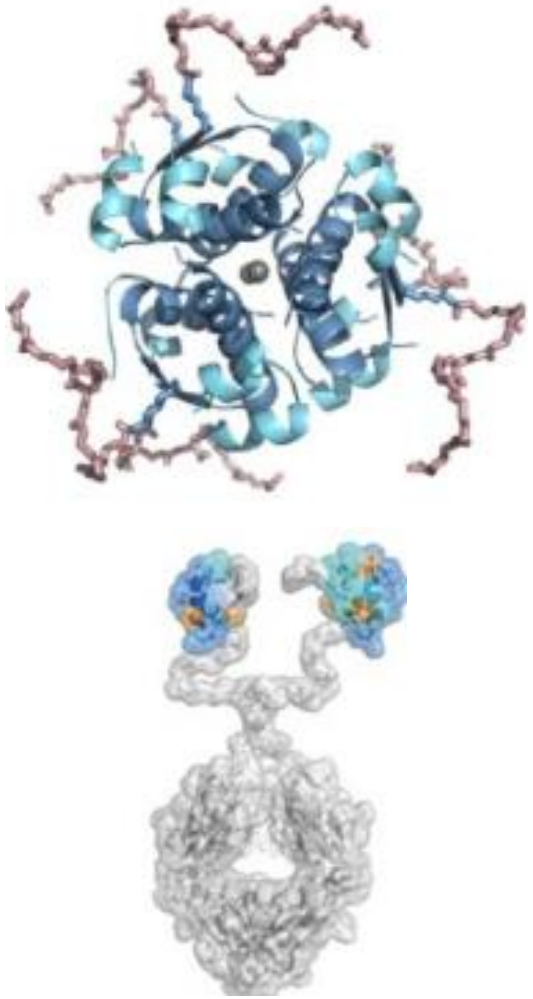
# The Emergence of Weekly Insulins

- Innovative insulin formulations and delivery systems have resulted in an expansion of choices that include basal insulins, rapid-acting insulins, and intermediate-acting formulations[1]

- Once-weekly basal insulin formulations are in late-stage development, with insulin icodec receiving a recommendation for marketing approval in Europe and an FDA decision is hoped for in late 2024/2025.

1. Hirsch IB, et al. *Endocr Rev*. 2020;41(5):733-755.

# The Emergence of Weekly Insulins (cont)





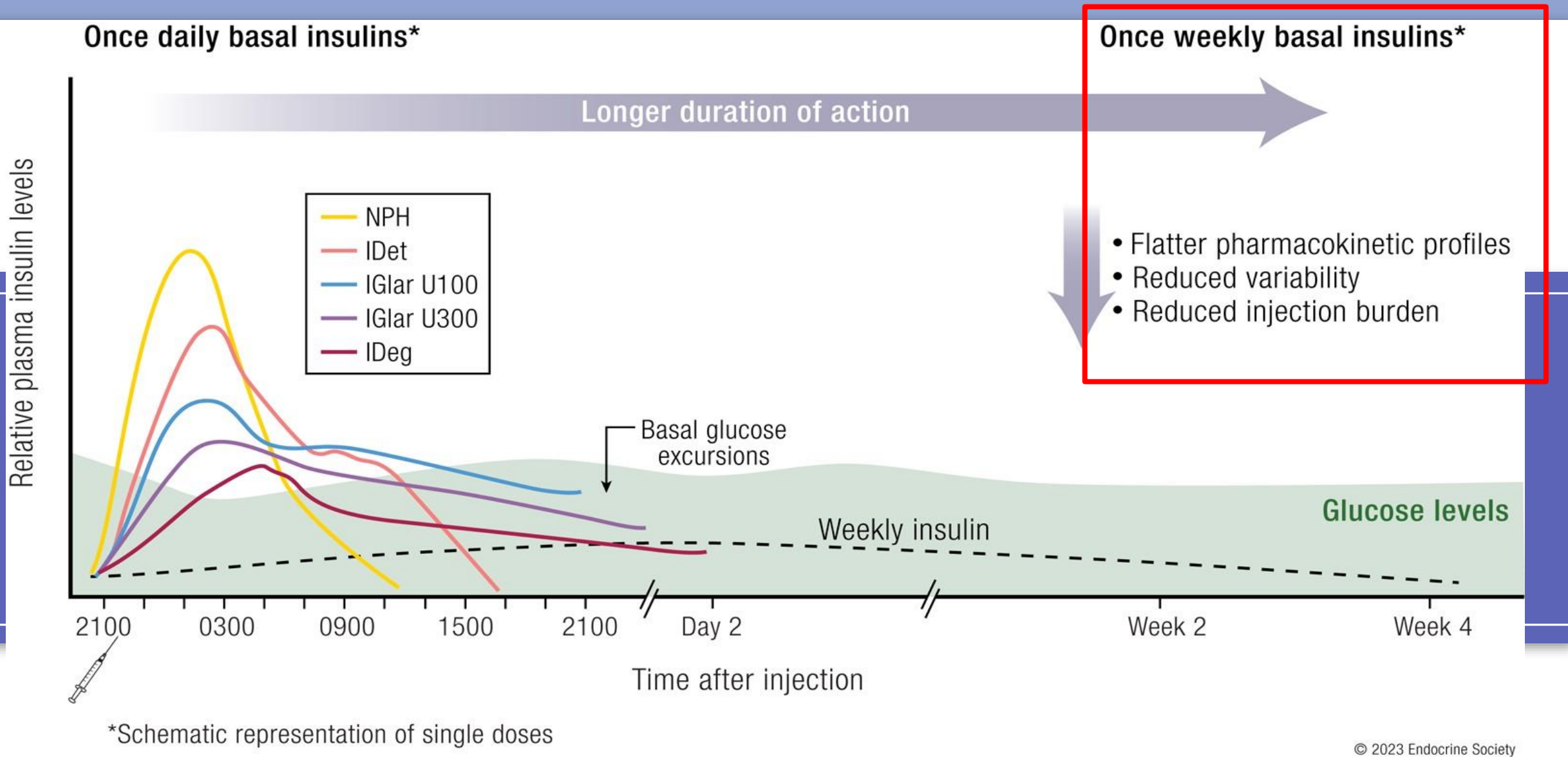
**Insulin icodec**

- A novel once-weekly basal insulin analog that has a prolonged half-life through strong reversible binding to albumin, reduced enzymatic degradation, and slow receptor-mediated clearance[1]

**Basal insulin Fc (BIF, insulin efsitora)**

- A novel, once-weekly long-acting IgG Fc–fusion protein[2]

1. Bajaj HS, et al. *Diabetes Care*. 2021;44(7):1586-1594. 2. Frias J, et al. *Lancet Diabetes Endocrinol*. 2023;11(3):158-168.




IDeg, insulin degludec; IDet, insulin detemir; IGlar, insulin glargine; NPH, neutral protamine hagedorn.

Rosenstock J, Juneja R, Beals JM, Moyers JS, Ilag L, McCrimmon RJ. The basis for weekly insulin therapy: evolving evidence with insulin icodec and insulin efsitora alfa. Endocr Rev. 2024;45(3):379-413. 

# Overview of Weekly Insulins Late-Stage Trials

- While once-weekly insulins are not yet clinically available, evidence supports their comparable efficacy and safety in patients with T2D
- Insulin icodec has been evaluated in five phase 3 randomized trials in patients with T2D
- BIF (insulin efsitora) has been evaluated in four phase 3 randomized trials in patients with T2D

# Phase 3 Trials for Insulin Icodec in T2D

| Trial | Design | Patients (with T2D) | Comparator | Baseline treatment | Duration (weeks) |
|---|---|---|---|---|---|
| **ONWARDS 1**[1] | Open label | Insulin-naïve N = 984 | Glargine U100 | Any non-insulin drugs | 78 |
| **ONWARDS 2**[2] | Open label | Insulin-treated N = 526 | Degludec | Basal insulins ± non-insulin glucose-lowering agents | 26 |
| **ONWARDS 3**[3] | Double blind | Insulin-naïve N = 588 | Degludec | Any non-insulin drugs | 26 |
| **ONWARDS 4**[4] | Open label | Insulin-treated N = 582 | Glargine U100 | Multiple daily insulin injections ± non-insulin drugs | 26 |
| **ONWARDS 5**[5] | Open label | Insulin-naïve N = 1085 | Glargine U100/300 and degludec | Any non-insulin drugs | 52 |

1. Rosenstock J, et al. *N Engl J Med*. 2023;389(4):297-308. 2. Philis-Tsimikas A, et al. *Lancet Diabetes Endocrinol*. 2023;11(6):414-425. 3. Lingvay I, et al. *JAMA*. 2023;330(3):228. 4. Mathieu C, et al. *Lancet*. 2023;401(10392):1929-1940. 5. Bajaj HS, et al. *Ann Intern Med*. 2023;176(11):1476-1485.

# Results and Hypoglycemic Events in ONWARDS Trials of Insulin Icodec in T2D

| Trial | Main results | Hypoglycemic events |
|---|---|---|
| **ONWARDS 1**[1] | Icodec compared to glargine:<br>• A1c reduction: -0.2%<br>• Increase in patients at target A1c without significant hypoglycemia: 10%<br>• TIR: increased 4.3% | Icodec: 226 episodes in 61 patients (12.4%); 1 episode severe<br>Glargine: 114 episodes in 66 patients (13.4%); 7 episodes severe |
| **ONWARDS 2**[2] | Icodec demonstrated noninferiority and superiority to degludec in reducing HbA1c from baseline | No significant differences in hypoglycemia rates |
| **ONWARDS 3**[3] | Icodec compared to degludec:<br>• A1c reduction: -0.2%<br>• Increase in patients at target A1c without significant hypoglycemia: 15% | Icodec: 53 episodes in 26 patients (9%); 0 episodes severe<br>Degludec: 23 episodes in 17 patients (6%); 2 episodes severe |

1. Rosenstock J, et al. *N Engl J Med*. 2023;389(4):297-308. 2. Philis-Tsimikas A, et al. *Lancet Diabetes Endocrinol*. 2023;11(6):414-425. 3. Lingvay I, et al. *JAMA*. 2023;330(3):228.

# Results and Hypoglycemic Events in ONWARDS Trials of Insulin Icodec in T2D (cont)

| Trial | Main results | Hypoglycemic events |
|---|---|---|
| **ONWARDS 4**[1] | Icodec compared to glargine:<br>• Mean change in A1c: -1.16% in the icodec group (baseline 8.29%); -1.18% in the glargine group (baseline 8.31%) | Icodec: 35 episodes in 22 (8%) patients<br>Glargine: 33 episodes in 25 (9%) patients |
| **ONWARDS 5**[2] | Icodec in conjuction with the dosing guide app demonstrated noninferiority and superiority compared to basal insulin analogues in reducing mean A1c from baseline | No significant differences in hypoglycemia rates |

1. Mathieu C, et al. *Lancet*. 2023;401(10392):1929-1940. 2. Bajaj HS, et al. *Ann Intern Med*. 2023;176(11):1476-1485.

# Phase 3 Trials for Insulin Efsitora in T2D

| Trial | Design | Patients (with T2D) | Comparator | Baseline treatment | Duration (weeks) |
|---|---|---|---|---|---|
| **QWINT-1 NCT05662332** | Open label | Insulin-naïve N = 670 | Glargine U100 | At least 1 glucose-lowering medication | 52 |
| **QWINT-2 NCT05362058** | Open label | Insulin-naïve N = 912 | Degludec | At least 1 glucose-lowering medication | 52 |
| **QWINT-3 NCT05275400** | Open label | Insulin-treated N = 986 | Degludec | Basal insulins ± up to 3 non-insulin drugs (except SUs) | 78 |
| **QWINT-4 NCT05462756** | Open label | Insulin-treated N = 670 | Glargine U100 | Multiple daily insulin injections | 26 |

# Results and Hypoglycemic Events in QWINT Trials of Insulin Efsitora in T2D[1]

| Trial | Results | Hypoglycemic events |
|---|---|---|
| **QWINT-1[1] (52 weeks)** | Efsitora compared to glargine:<br>• A1c reduction: -0.04%<br>• Noninferior in A1c change | Severe or clinically significant hypoglycemic events per patient year:<br>• 0.50 with efsitora<br>• 0.88 with glargine |
| **QWINT-2[2] (52 weeks)** | Efsitora compared to degludec:<br>• A1c reduction: -0.09%<br>• Noninferior in A1c change<br>• Percent of time glucose level was within target range was 64.3% with efsitora and 61.2% with degludec (95% CI, 0.1 to 6.1) | Severe or clinically significant hypoglycemic events per patient year:<br>• 0.58 with efsitora<br>• 0.45 with degludec |

1. Lilly. News release. September 5, 2024, Accessed September 20, 2024. https://investor.lilly.com/news-releases/news-release-details/first-its-kind-fixed-dose-study-once-weekly-insulin-efsitora. 2. Wysham C, et al. *N Engl J Med*. 2024;Sep 10. doi:10.1056/NEJMoa2403953

# Results and Hypoglycemic Events in QWINT Trials of Insulin Efsitora in T2D[1]

| Trial | Results | Hypoglycemic events |
|---|---|---|
| **QWINT-3[1] (78 weeks)** | Efsitora compared to degludec:<br>• A1c reduction: -0.11%<br>• Noninferior in A1c change<br>• 2 hours more time in range per day for weeks 22–26, compared to baseline | Severe or clinically significant hypoglycemic events per patient year:<br>• 0.84 with efsitora<br>• 0.74 with degludec |
| **QWINT-4[2] (26 weeks)** | Efsitora compared to glargine:<br>• A1c reduction: both reduced A1c by 1.07%<br>• Noninferior A1c reduction | Severe or clinically significant hypoglycemic events per patient year:<br>• 6.6 with efsitora<br>• 5.9 with glargine |

1. Lilly. News release. September 5, 2024, Accessed September 20, 2024. https://investor.lilly.com/news-releases/news-release-details/first-its-kind-fixed-dose-study-once-weekly-insulin-efsitora. 2. Lilly. News release. May 16, 2024, Accessed August 17, 2024. https://investor.lilly.com/news-releases/news-release-details/once-week-dosing-insulin-efsitora-alfa-delivers-a1c-reduction

# Looking to the Future: Once-Weekly Insulins in Clinical Practice

# Preparing for Weekly Insulins

As once-weekly insulin formulations become available, **PCCs will be at the forefront of providing practical strategies** for the integration of these formulations into clinical practice[1]

- Indications for once-weekly insulin are likely to be similar to those for once-daily insulin
- New insulin titration strategies will be needed because glucose-lowering will not achieve a steady state for several weeks after initial dosing
- Clinicians and patients will need to learn these approaches and how to manage dosing and concomitant pre-prandial insulin

1. Rosenstock J, et al. *Metabolism*. 2022;126:152924.

# Potential Patient Selection for Weekly Insulins

- If weekly insulins become approved and available, not all patients with may be appropriate candidates for therapy
- Patients with inadequate glucose control despite multiple therapies and **poor adherence to daily injections** may benefit[1]

**Examples of patients who may benefit from once weekly insulins, if approved[1]**

- Patients with T2D inadequately controlled on multiple glucose-lowering agents who require basal insulin therapy
- Patients who prefer flexibly in dose timing and those who have difficulty with adherence to daily injections

1. Rosenstock J, et al. *Endocr Rev*. 2024;45(3):379-413.

# Potential Benefits of Weekly Insulins

- Injection burden is a major barrier to insulin adherence[1,2]
  - Fewer injections can reduce this burden and **improve the likelihood of treatment adherence**
- When once-weekly insulins reach steady state, a missed dose does not result in immediate loss of efficacy due to their long half-life[1]
- Due to a flatter pharmacokinetic profile of once-weekly insulins, decrease in day-to-day glycemic variability is expected[1]

| Potential Benefits of Weekly Insulins[1] |
| --- |
| Lower injection burden |
| Improved convenience, adherence, and quality of life[3] |
| Increased flexibility in dose timing |
| Better glucose coverage in the case of missed doses |
| Decreased day-to-day glycemic variability |

1. Rosenstock J, et al. *Endocr Rev*. 2024;45(3):379-413. 2. Vijan S, et al. *J Gen Intern Med*. 2005;20(5):479-482. 3. Bajaj HS, et al. *Diabetes Care*. 2021;44(7):1586-1594.

# Potential Concerns of Weekly Insulins

- Patients and clinicians may worry over a "large dose" of insulin injected at once and hypoglycemia management[1]
  - Increased familiarity with weekly insulins may address these concerns
- As with any insulin, hypoglycemia is a potential safety concern

| Potential Concerns of Weekly Insulins[1] |
| --- |
| Lack of familiarity |
| Challenges with dose calculations |
| Clinicians' concerns about hypoglycemia |

1. Rosenstock J, et al. *Endocr Rev*. 2024;45(3):379-413.

# Hypoglycemia Considerations

- Meta-analysis of 7 randomized trials[1]:
  - **Increased risk of hypoglycemic events** with insulin icodec compared to once-daily basal insulins (risk ratio 1.24; 95% CI, 1.02-1.50; P = .03)
  - **Numerically decreased risk of severe hypoglycemia** with insulin icodec compared to once-daily basal insulins (risk ratio 0.81, 95% CI, 0.31-2.08)
- Meta-analysis of insulin icodec's ONWARDS trials in T2D:
  - **Similar incidence but higher rates of clinically significant hypoglycemia** with insulin icodec versus comparators (incidence 17.9% vs 16.2%, odds ratio 1.14; rates 1.15 vs 1.00 episodes/participant-year of exposure, rate ratio 1.51)
  - **Fewer severe hypoglycemic episodes** with insulin icodec than comparators (8 vs 18)

1. Mukhopadhyay P, et al. *Endocr Pract*. 2024;30(2):128-134. 2. Bajaj HS, et al. *Diabetes Obes Metab*. 2024;26(9):3810-3820.

# Hypoglycemia Considerations

- **Managing hypoglycemia with insulin icodec[1,2]:**
  - The fundamental principles are similar to treating typical hypoglycemia episodes in T2D, which include advising the patient to:
    - Consume 15 grams of glucose (or other fast-acting carbohydrate) for a blood glucose value of 70 mg/dL or less
    - Recheck the blood glucose 15 minutes afterward
    - If blood glucose remains at or near 70 mg/dL (or less), or if glucose is not rising, consume an additional 15 grams of fast-acting carbohydrates, repeating the process until glucose rises
    - In the case of continually ongoing hypoglycemia, seek additional care.
  - Insulin icodec has a similar counterregulatory hormone response and recovery compared to insulin glargine

1. Rosenstock J, et al. *Endocr Rev*. 2024;45(3):379-413. 2. American Diabetes Association Professional Practice Committee. *Diabetes Care*. 2024;47(Suppl_1):S111-S125.

# Patient Case Scenario (revisited)

Today's visit:

- Fasting blood glucose: 195 mg/dL
- HbA1c: 9.6% (improved from 10.3% three months ago)

Other antihyperglycemic medications include:

- Metformin 2000 mg daily
- Oral semaglutide 14 mg once daily

States that she would like to try and work on her diet and exercise to get her HbA1c lower, toward her goal of <8%.

**Would this patient be a good candidate for once-weekly insulin?**

# Patient Case Scenario (revisited, cont)

- Revisiting the case scenario, use of a once-weekly insulin would likely help the patient be more adherent to her regimen, because she prefers to avoid daily injections

- With improved adherence to her basal insulin regimen, her blood glucose would likely improve, lowering her risk for cardiometabolic complications associated with hyperglycemia

# Let's revisit Knowledge Question Two

**Which of the following patients would likely be the best candidate to receive a once-weekly insulin?**

A. A 23-year-old man with newly diagnosed T2D, A1c 8.5%

B. A 59-year-old woman with T2D who takes basal insulin along with other glucose-lowering agents and is concerned about weight gain, A1c 7.1%

C. A 41-year-old man with T2D who takes metformin and a once-weekly GLP-1 RA with an A1c of 6.5%

D. A 52-year-old woman with T2D who likes to travel and frequently misses doses of her daily basal insulin, A1c 8.2%

# Additional Case Studies

# Now let's look at another case study…

Mr. A is a 56-year-old man. He works on the line at one of the auto industry plants. He was told he had T2D about 6 years ago.

At the time, his HbA1c was 8.8% and he was started on metformin 500 mg once daily and titrated to the maximum tolerated dose.

One year ago, a once-weekly GLP-1 RA was added to his T2D regimen.

He is currently taking metformin 1000 mg in the morning and 500 mg in the evening and 2 mg of semaglutide once weekly.

# Mr. A. Case Study (cont)

Today's Visit

Labs:

- Fasting Blood Sugar: 242 HBA1c: 8.2%
- No referrals have been made for Diabetes Self-Management Education(DSME) to include Medical Nutritional Therapy (MNT). No Self Monitoring of Blood Glucose (SMBG) or Continuous Glucose Monitoring (CGM)
- Weight 232 lbs, Height 5'10", BMI 33.3 $kg/m^2$
- Physical activity: His work is active; outside of work he is not very active

# Mr. A. Case Study (cont)

- History of hypertension
  - Takes lisinopril 40 mg once daily
  - Recent blood pressure 128/72 mmHg, pulse is 78 bpm

- History of elevated lipids
  - Taking rosuvastatin 40 mg once daily
  - Recent labs: LDL 68 mg/dL

- Family history of T2D - Mother and one sibling

# Mr. A. Case Study (cont)

- History of hypertension, elevated Lipids, obesity, over 55 years of age
- A1c not at treatment goal ( HbA1c <7% with TIR >70% with <4% low BG)

---

- Discussed need for basal Insulin
- Referred for diabetes self-management education (DSME) and medical nutrition therapy (MNT)
- Discussed physical activity
- Placed professional continuous glucose monitoring (CGM) device
- Discussed potential benefits and risks of insulin; preventing of hypoglycemia
- Continued metformin  and GLP-1 RA
- Patient agrees to start insulin at 20 units daily, with the first injection in the office
- Follow up to support patient and to provide titration and education

# Mr. A. Case Study (cont): Professional CGM

15% Very High
Goal: <5%

43% High

58%
Goal: <25%

42% In Range
Goal: >70%

0% Low

0% Very Low
Goal: <1%

0%
Goal: <4%

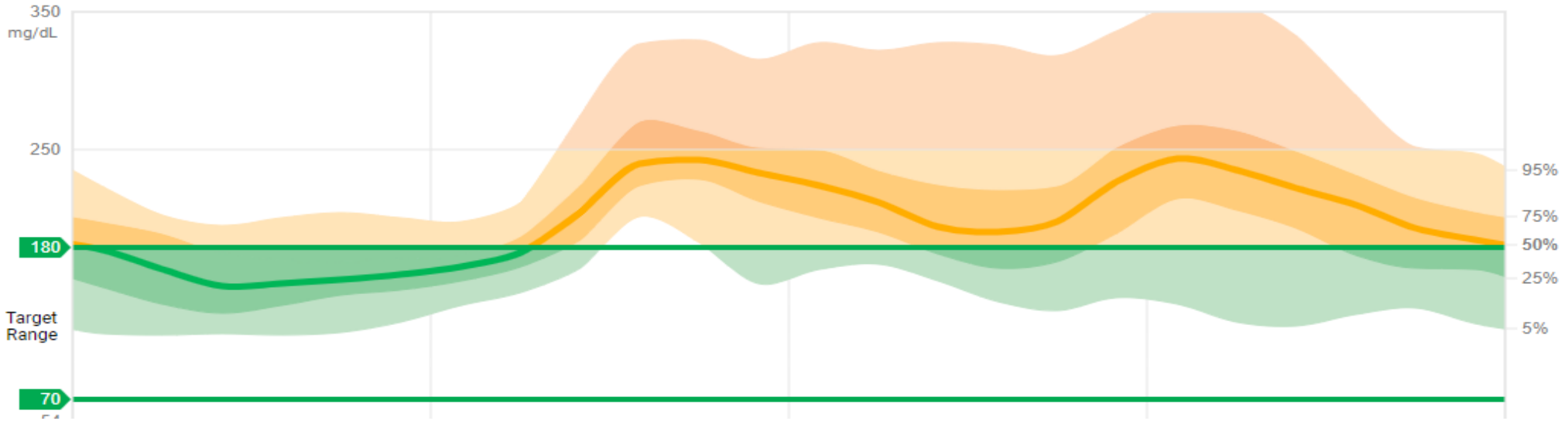
**Target Range:** 70-180 mg/dL
**Very High:** Above 250 mg/dL
**Very Low:** Below 54 mg/dL

## Glucose Metrics

| | |
|---|---|
| Average Glucose<br>Goal: <154 mg/dL | 201 mg/dL |
| GMI<br>Goal: <7% | 8.1% |
| Coefficient of Variation<br>Goal: <36% | 26.1% |
| Time CGM Active | 95.3% |

## Ambulatory Glucose Profile (AGP)

AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if they occurred in a single day.



# Mr. A. Case Study (cont): Three-Month Follow-up

- Continues metformin 1000mg in the morning and 500 mg in the evening; GLP-1 RA at Maximum Dose
- Insulin glargine is taken at 9:00-10:00 every night
  - 40 units of basal insulin
- A1c is 7.6%
- Patient shares that he is doing his best to take insulin daily, but once or twice a week he falls asleep before taking his dose.

**Would this patient be a good candidate for once- weekly Insulin?**

# Considerations

1. The patient is willing to take insulin but forgets to take basal insulin 1-2 days per week.
2. Increased adherence will improve glucose control and decrease the risk of complications.
3. Discussing the risk of hypoglycemia is important with use of all insulin formulations.
4. Diabetes education including MNT will help support the patient to be successful in managing their T2D.

# Who forgets or skips insulin doses?

This may be a problem with ANY of your patients with diabetes who are treated with insulin.

Studies show that missed insulin doses are recorded for patients with T1D AND T2D.[1]

In both T1D and T2D, missing insulin dosages is a problem that we need to find better ways of addressing.

Once-weekly insulins may help.

1. Robinson S, et al. *Diabetes Technol Ther*. 2021;23(12):844-856.

# Case Study #3: Newly diagnosed

?

- A 48-year-old woman comes to the primary care clinic with complaints of thirst, weight loss and frequent urination. She was recently treated for a yeast infection.
- History of hypertension and elevated lipids – both are well-controlled
- Family history of T2D – mother and an aunt

<u>Today's visit</u>

- Blood glucose 296 mg/dL, HbA1c 10.4%
- Professional CGM placed

# Case Study #3 (cont)

72% Very High
Goal: <5%

21% High

93%
Goal: <25%

7% In Range
Goal: >70%

0% Low

0% Very Low
Goal: <1%

0%
Goal: <4%

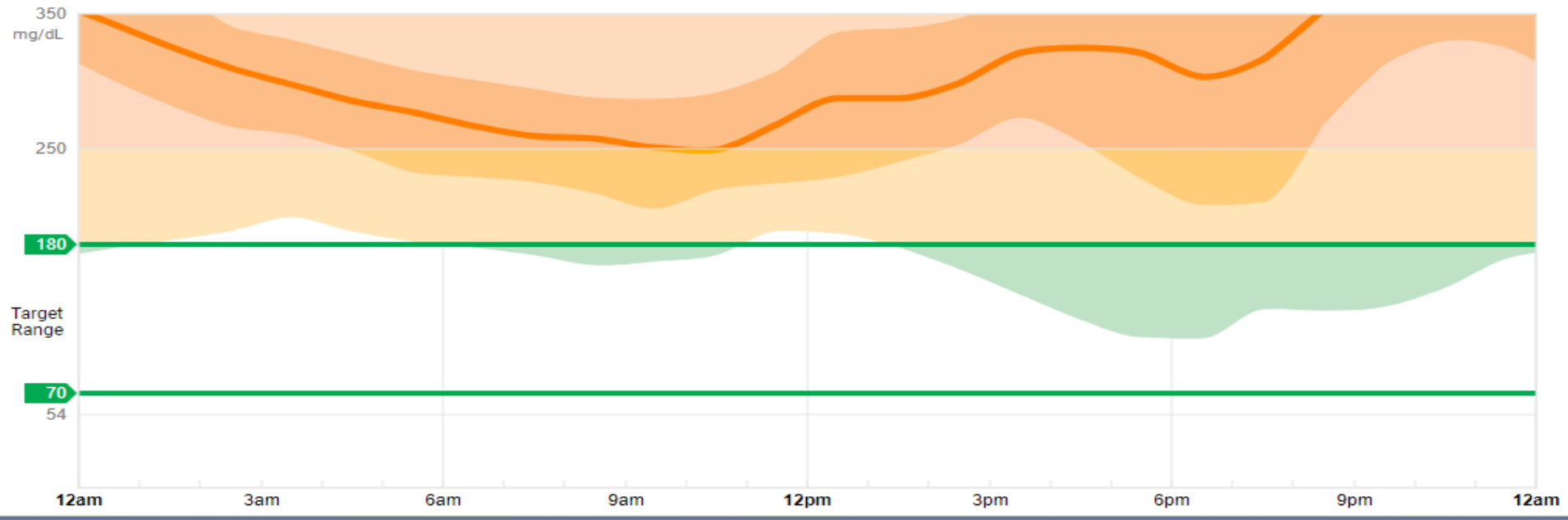
**Target Range:** 70-180 mg/dL
**Very High:** Above 250 mg/dL
**Very Low:** Below 54 mg/dL

## Glucose Metrics

| | |
|---|---|
| Average Glucose<br>Goal: <154 mg/dL | 298 mg/dL |
| GMI<br>Goal: <7% | 10.4% |
| Coefficient of Variation<br>Goal: <36% | 25.4% |
| Time CGM Active | 92.3% |

## Ambulatory Glucose Profile (AGP)

AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if they occurred in a single day.



# Based on the ADA Standards of Care, what therapy would you offer this patient?

- Metformin to maximum dose tolerable
- **BASAL INSULIN**
- Personal CGM
- Diabetes education to include MNT
- Support to titrate basal insulin
- Treatment goal HbA1c <7% with >70% TIR and <4% low blood glucose

**Would this patient benefit from a once-weekly insulin?**

# Key Takeaways

# Key Takeaways

- Basal insulin remains an essential and effective glucose-lowering treatment for many patients with T2D.
- PCCs manage most patients with T2D in the US, including many who receive or are indicated to receive basal insulin therapy.
- Despite insulin's long history in treating diabetes, clinical inertia routinely occurs due to a variety of factors, resulting in treatment delays and suboptimal glucose management.

# Key Takeaways (cont)

- Ultra-long-acting, once-weekly insulins may soon be approved and provide an additional option for basal insulin therapy.

- Once-weekly insulins may improve adherence and persistence, flexibility in administration time, and reduced glycemic variability compared to once-daily basal insulins.

- Potential concerns with once-weekly insulins may include challenges with dose calculations and concerns about hypoglycemia, which may be resolved as clinicians become more familiar with these insulin formulations.

# Resource Toolkit

Visit the website via the QR code to the right or the URL below for more information on this topic and to review the presentation.

**https://www.pcmg-us.org/toolkit/owi**

# Post-presentation Survey

- Please take the post-survey using the QR Code or URL below.

https://www.pcmg-us.org/survey/post/owi7


Thank you

# What Primary Care Clinicians Need to Know About Once-Weekly Insulins

END