



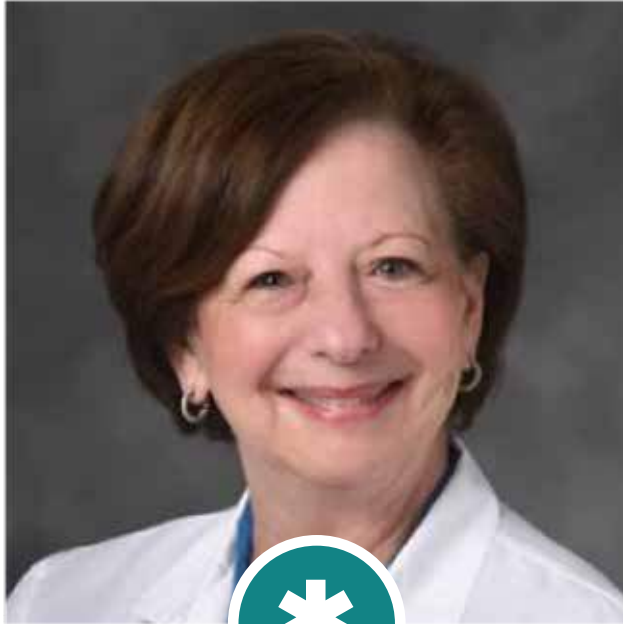
 **EXPERT  
PERSPECTIVES  
AND DISCUSSIONS**

# BREAKING THROUGH INERTIA:

**How To Initiate and Maintain  
Insulin Therapy in Patients  
with Type 2 Diabetes**



# Welcome & Introductions



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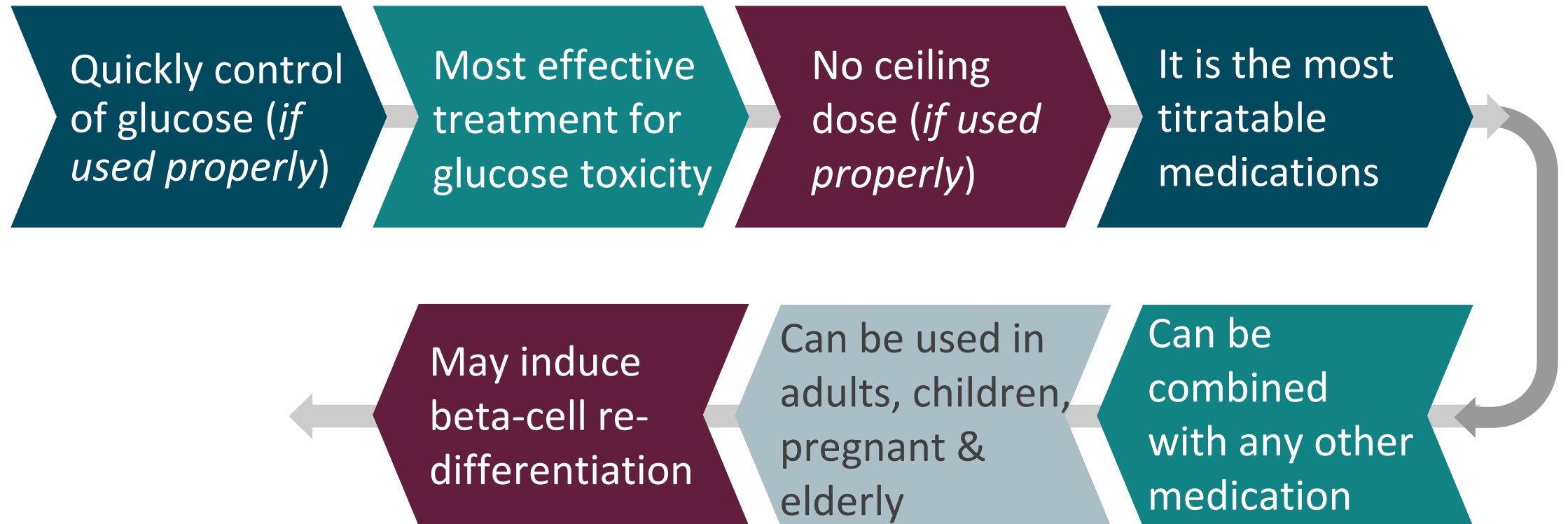


**JAY H. SHUBROOK, DO, FAAFP, FACOFP**  
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Diabetologist  
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# Overview of Insulin Therapy in T2DM

Jay H. Shubrook, DO, FAAFP, FACOFP

# Goals and Benefits of Insulin Therapy



# Pre-Test | Question 1

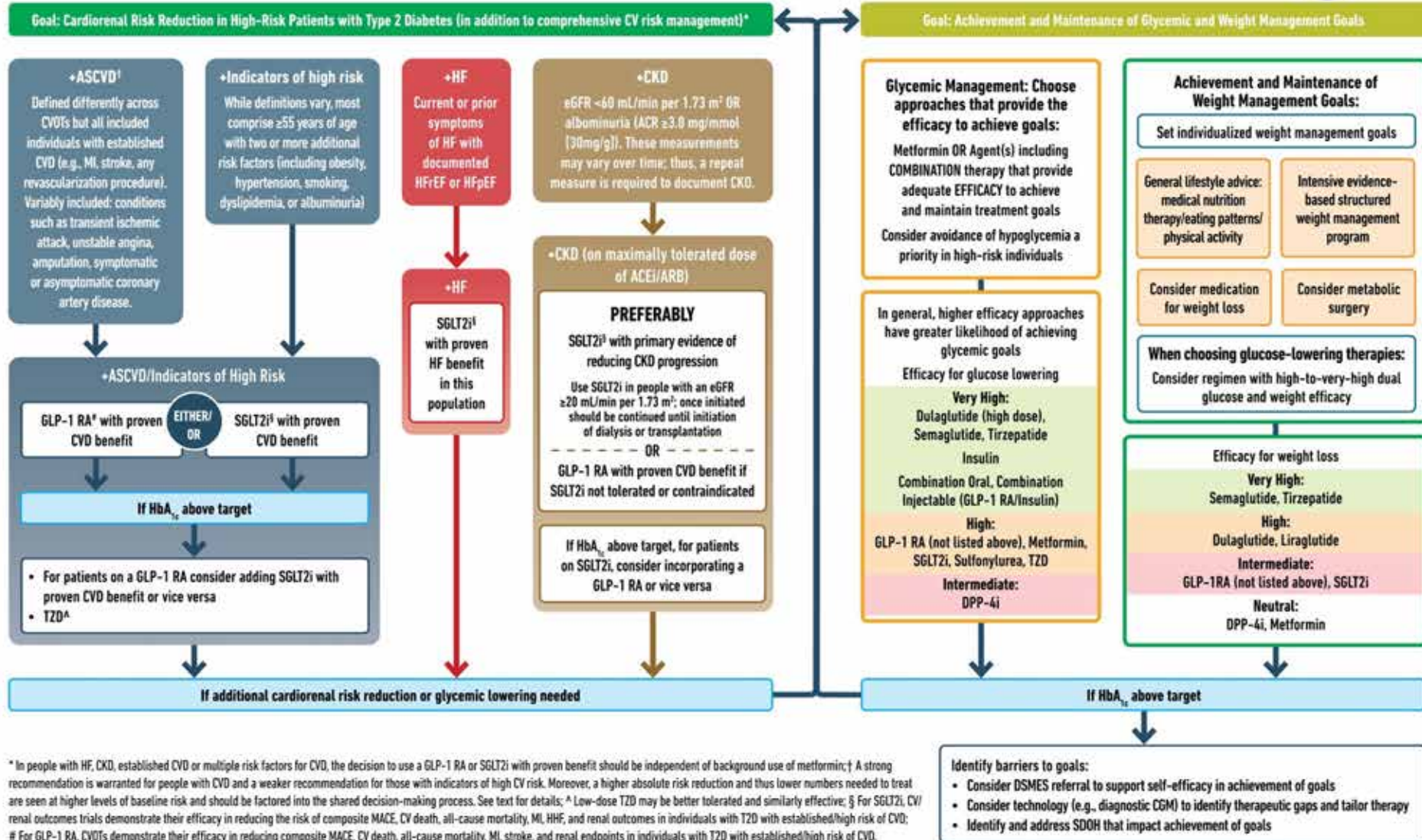
**Which is the most appropriate to start insulin therapy?**

- a. At diagnosis – both type 1 and type 2 diabetes
- b. Any time the patient presents with catabolic symptoms (fasting Bg >200mg/dl, Random BG 300mg/dl, A1c >10% , Polys
- c. If a patient presents with a random BG of >300mg/dl and an A1c of 8.5%
- d. After all other anti-hyperglycemic medications have been tried

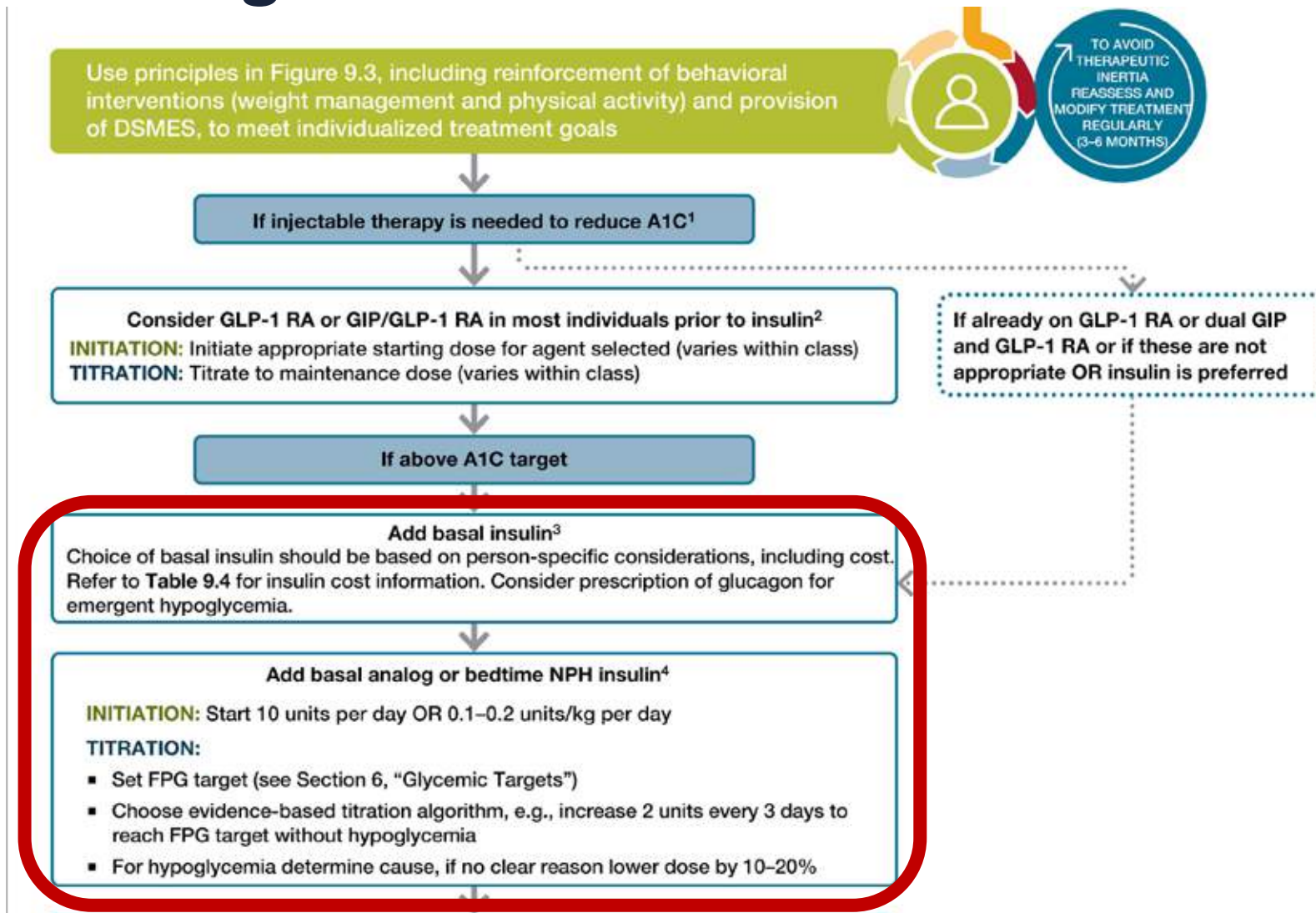
# USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES



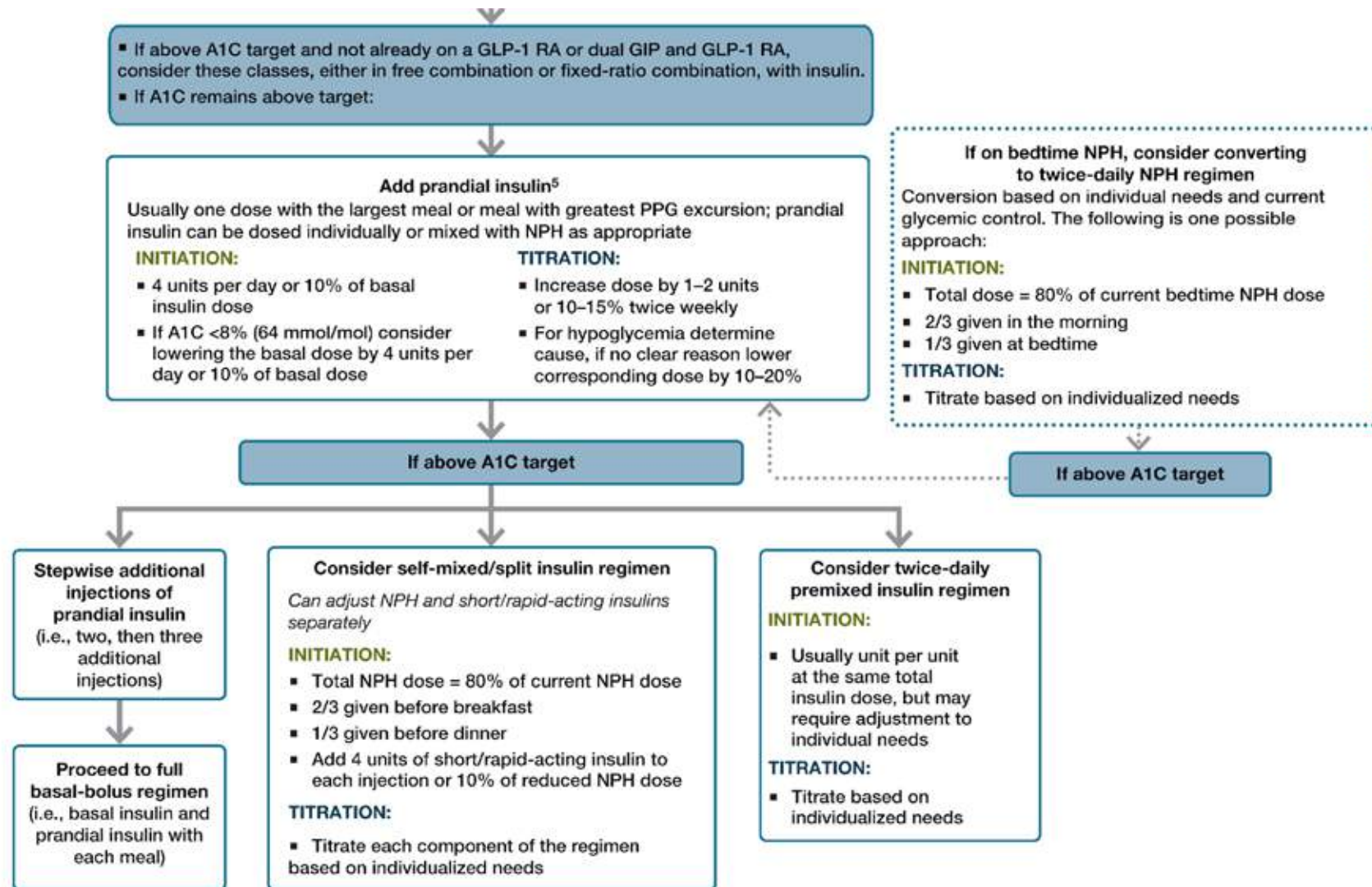
HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)



# ADA Injection Algorithm Part 1

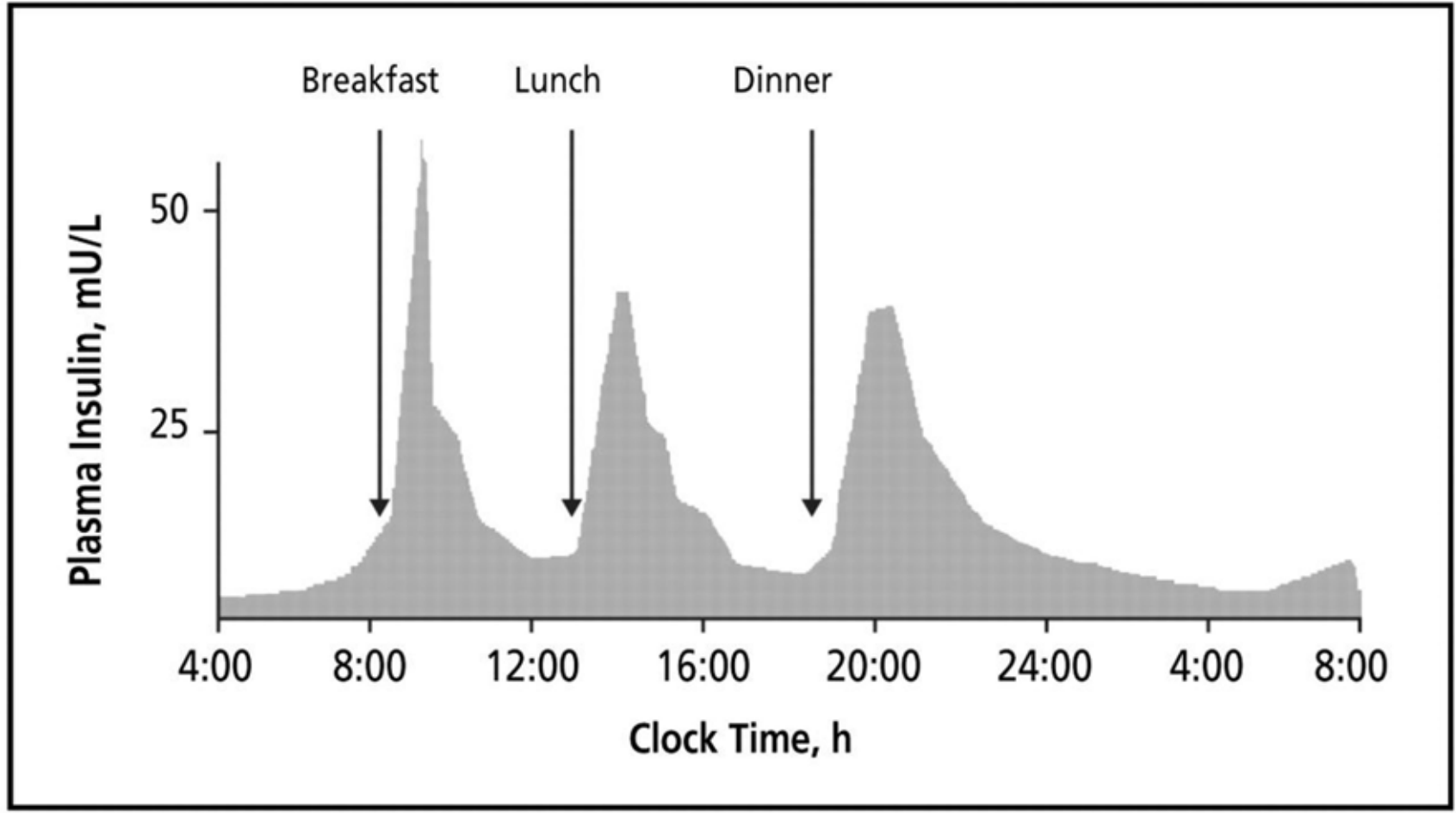


# ADA Injection Algorithm Part 2





# Physiologic Insulin Release



# Components of Insulin Action

## Basal Insulin

- ✓ Required for resting metabolic needs
- ✓ Suppresses glucose production at night and between meals
- ✓ Stays relatively constant
- ✓ Usually is half of total daily insulin needs

## Prandial Insulin

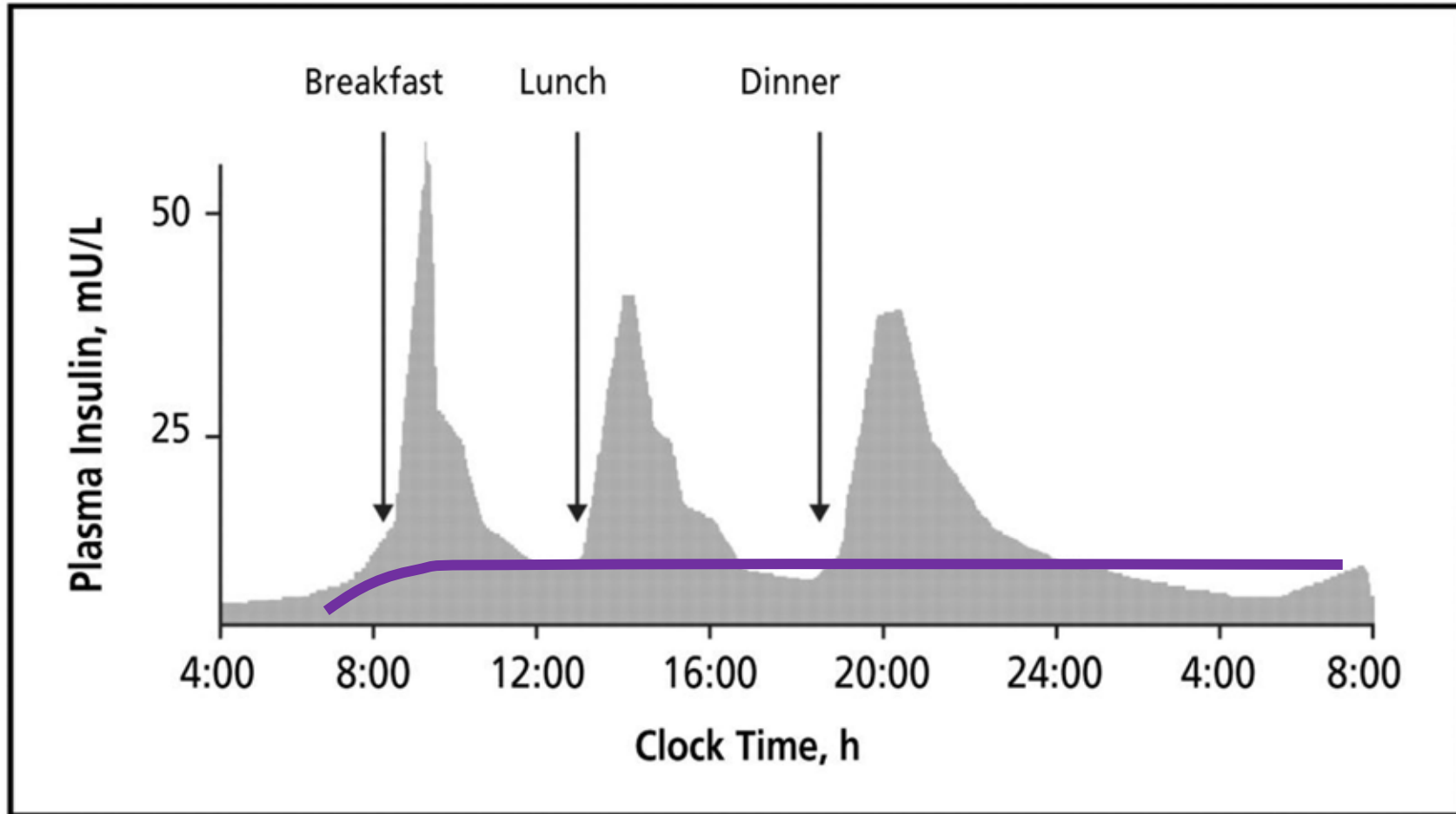
- ✓ Limits/prevent post-prandial hyperglycemia
- ✓ Physiologic two-phase release
  - First phase immediate and lasts 1-2 hours
  - Delayed slower to peak second phase
- ✓ Each meal about 10-20% of daily insulin needs

## Pre-Test | Question 2

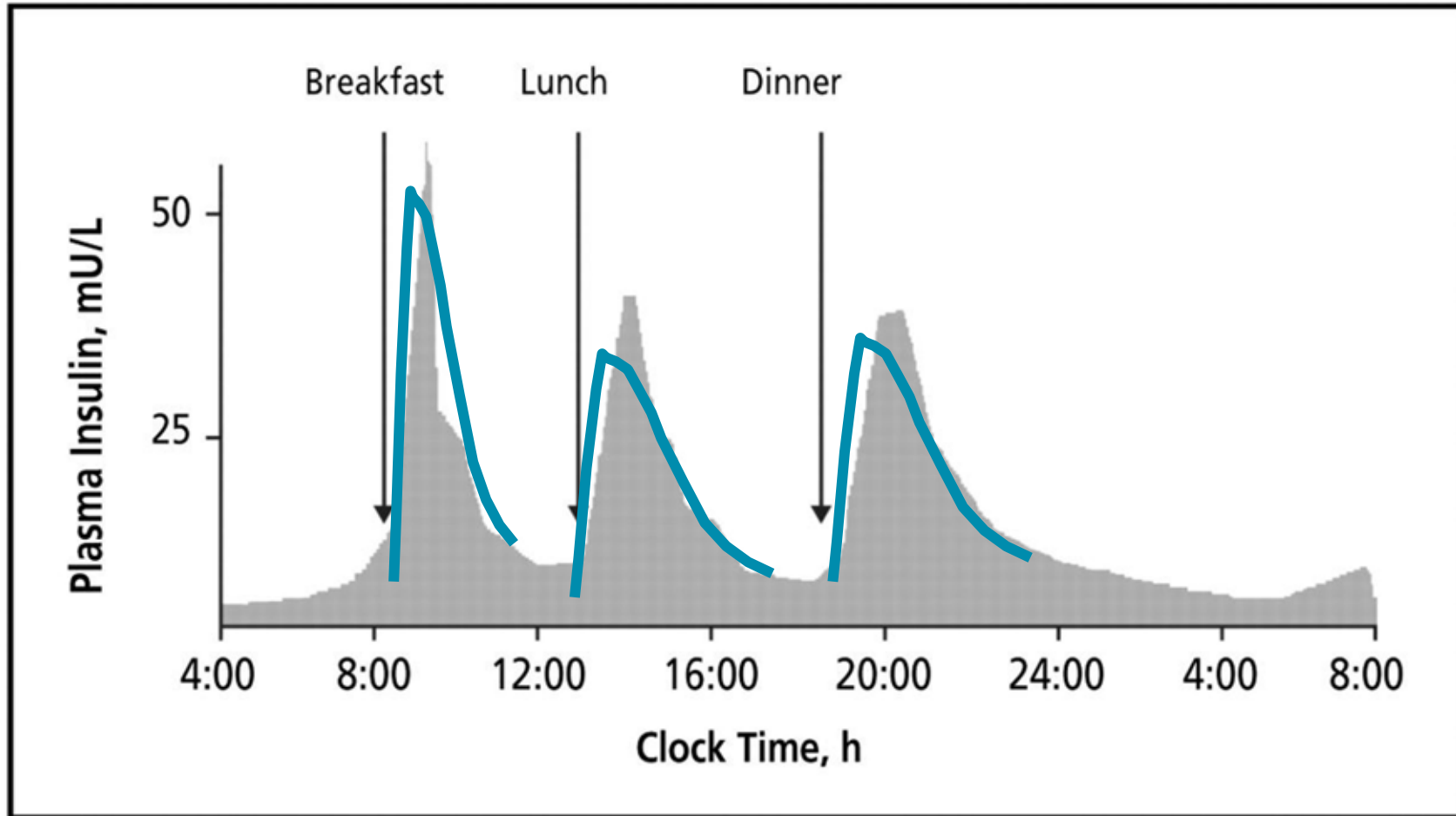
**Which of the following is a best practice in using basal insulin in type 2 diabetes?**

- a) Start with 0.2/0.3 units per KG of body weight or 10 units once daily
- b) Start 10 units per day in people with type 2 and 20 units per day in people with type 1
- c) The maximum daily dose is 1.0 units per KG of body weight daily
- d) Start with injections every other day if person is nervous about injections

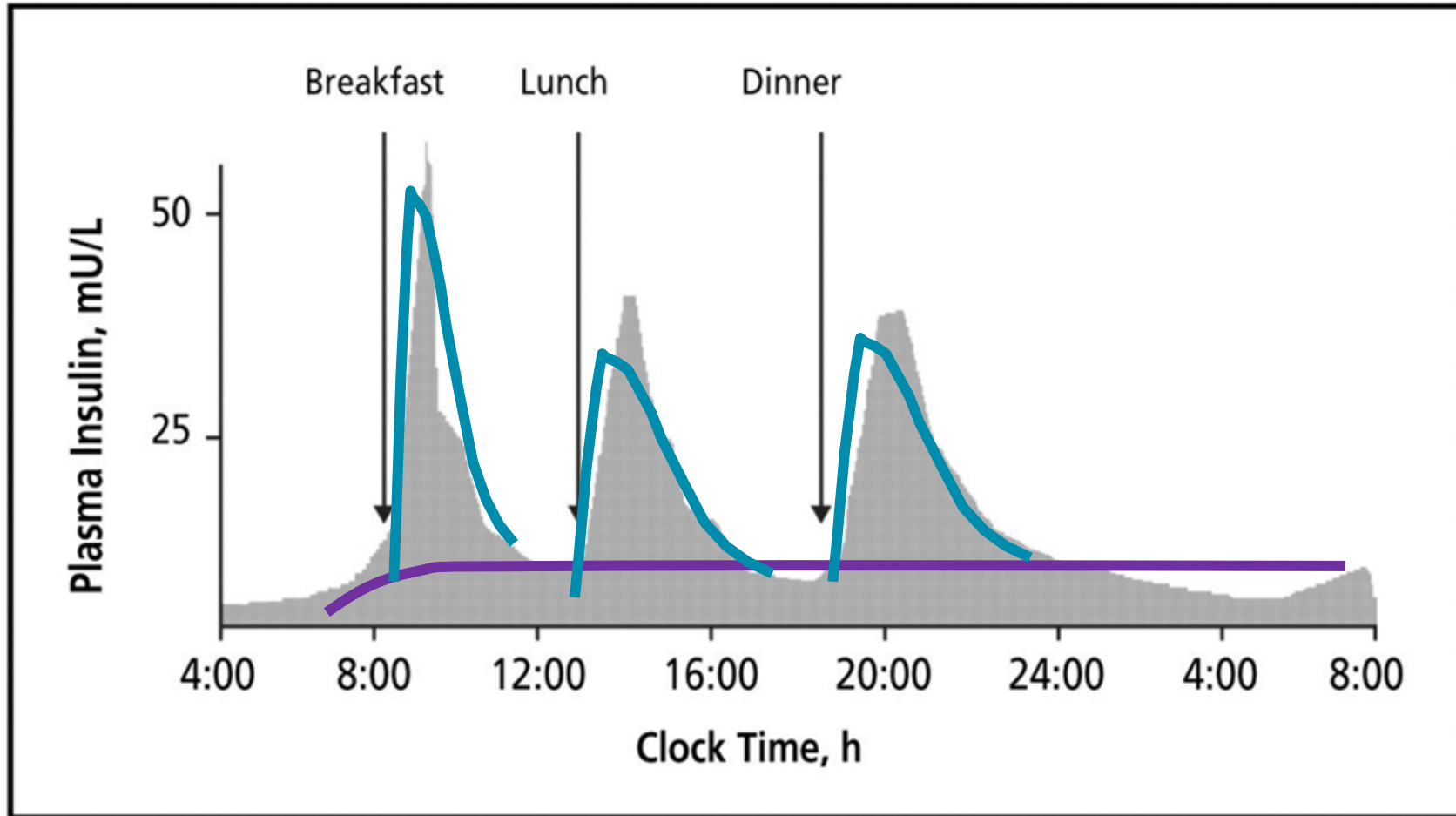
# Basal Insulin



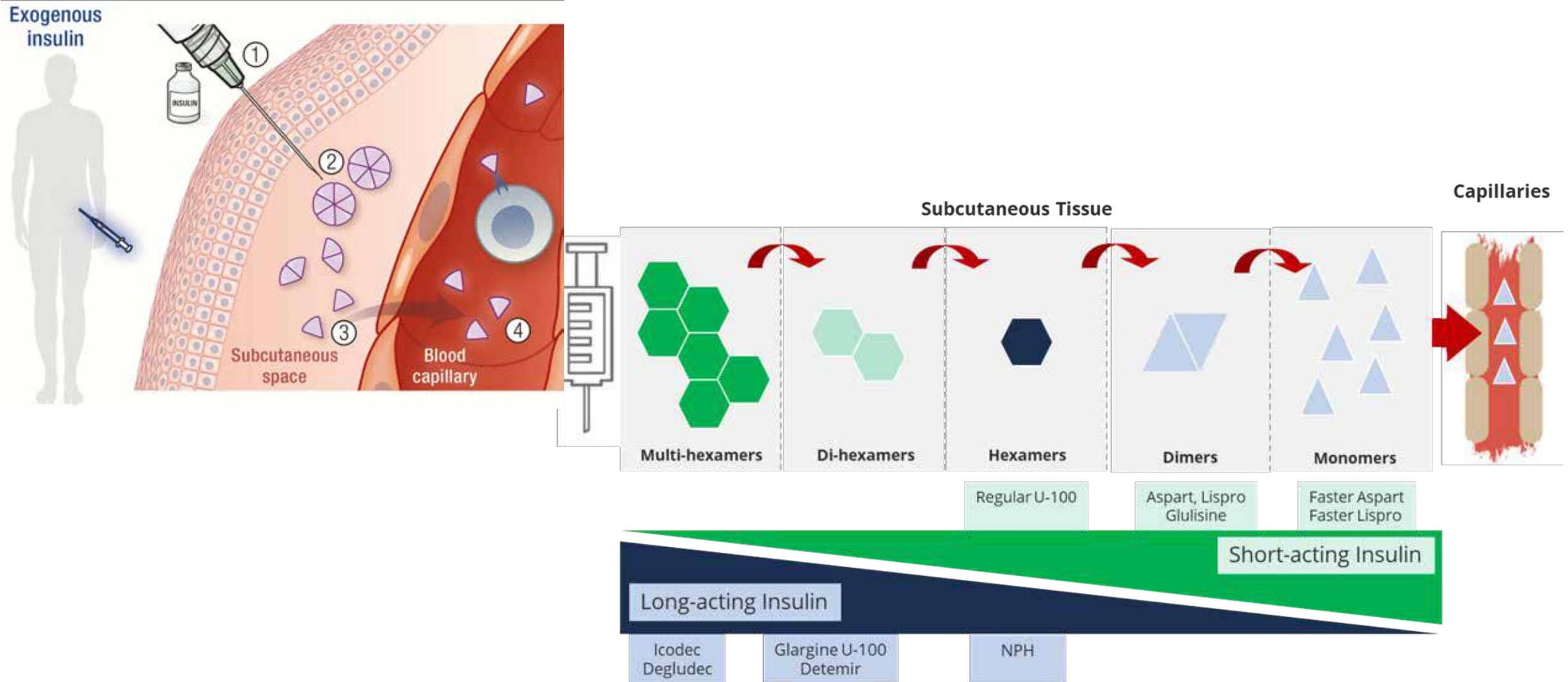
# Prandial Insulin



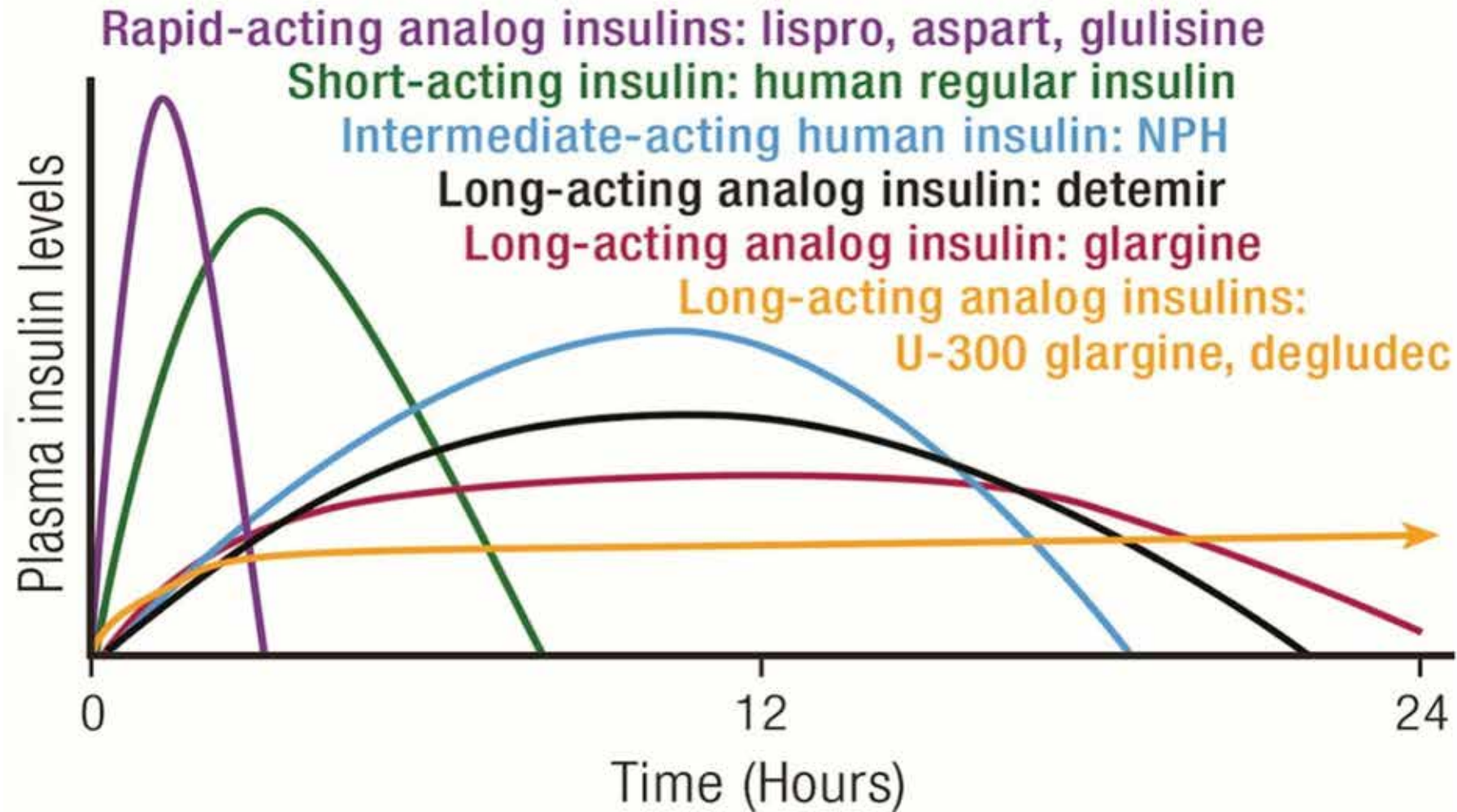
# Basal + Prandial (bolus) insulin



# Pharmacologic Modifications of Insulin



# Spectrum of Available Injectable Insulins





# Traditional Insulin Delivery Options



Syringes

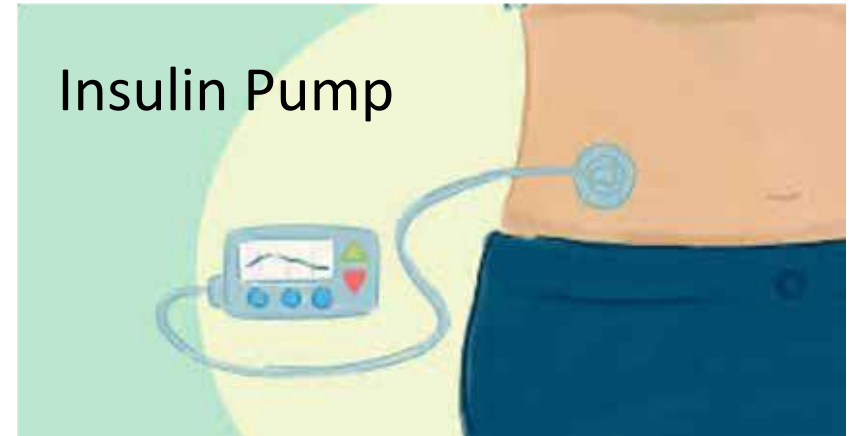


Insulin Pens

Inhaled  
Insulin



Insulin Pump



# Spectrum of Basal Insulins

	Branded Names	Onset	Peak	Duration	Notes
NPH	HumuLIN	1-2 hours	4-8 hours	6-12 hours	Pens, Vials
	NovoLIN				Pens, Vials
	ReliON				Vials
Glargine (U100)	Lantus	1-4 hours	No peak	24 hours	Vials
	Basaglar				Pens
	Semglee				Pens Only
Detemir	Levemir	1-4 hours	No peak	20-23 hours	Vials
					Pens
Glargine U300	Toujeo	6 hours	No peak	24 hours	Pens only
	Toujeo Max				
Degludec U100, U200	Tresiba	1 hour	No peak	42 hours	Pens only

# Spectrum of Rapid and Regular insulin

	Branded Names	Onset	Peak	Duration	Notes
Regular (R)	HumuLIN	30-45 minutes	2-4 hours	4-8 hours	Pens, Vials
	NovoLIN				
	ReliON				Vials Only
Aspart Faster acting aspart	NovoLOG	15 minutes	1-2 hours	2-4 hours	Pens, Vials
Glulisine	FIASP	15 minutes	1-2 hours	2-4 hours	Vials
	Apidra				
Lispro	Humalog	15 minutes	1-2 hours	2-4 hours	Pens, Vials
	Admelog				
Lispro aabb	Lyumjev				

# Inhaled Insulin Technospheres



4-units



8-units



12-units



Rapid acting inhaled human insulin indicated to improve glycemic control in adult patients with diabetes mellitus



Not recommended to be used in patients who smoke or recently stopped smoking



Contraindicated in chronic lung disease such as asthma or COPD



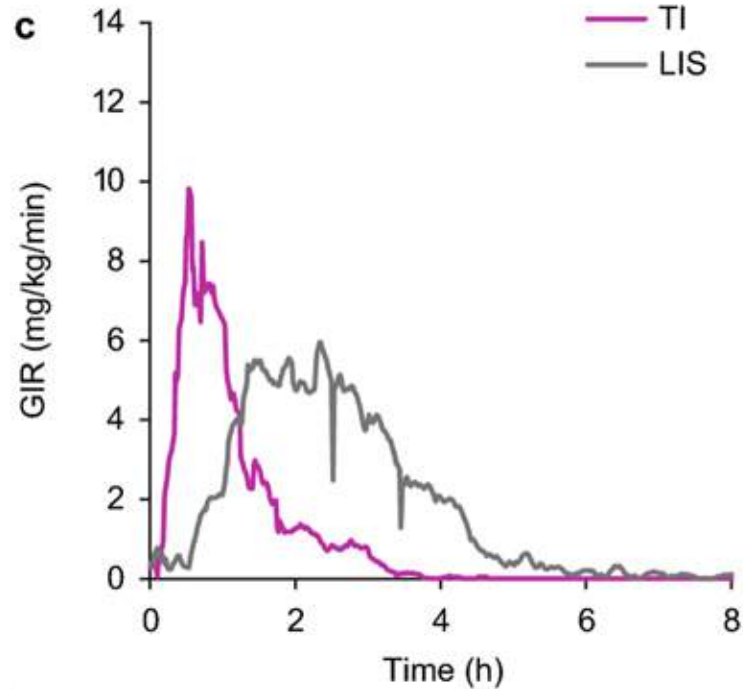
Perform FEV1 spirometry before initiating, 6 months after therapy, and annually thereafter. Discontinue if greater than or equal to 20% decline in FEV1



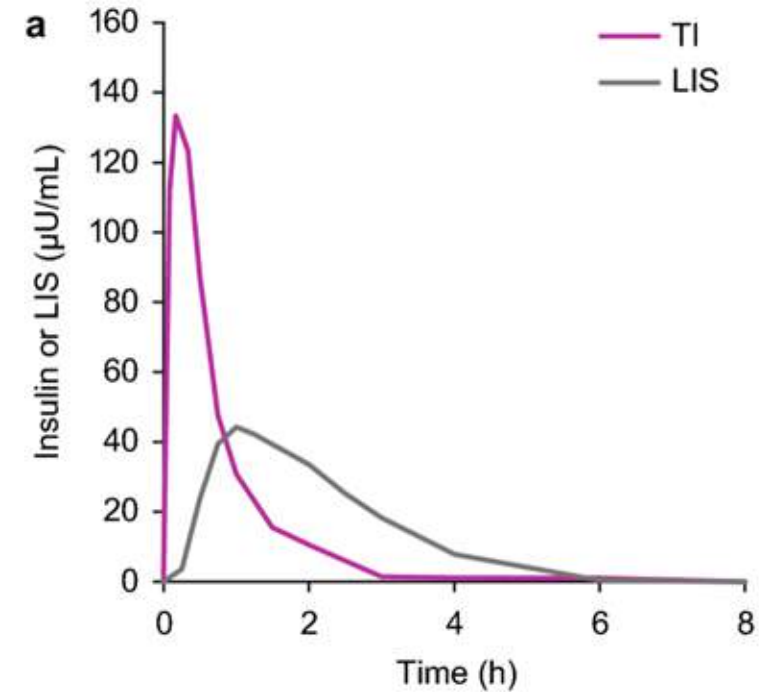
Administer at the beginning of the meal  
Doses available 4 units, 8 units, and 12 units

# PK/PD Compared to Insulin Lispro

## Pharmacodynamics



## Pharmacokinetics



# Ultra Rapid Acting Insulins

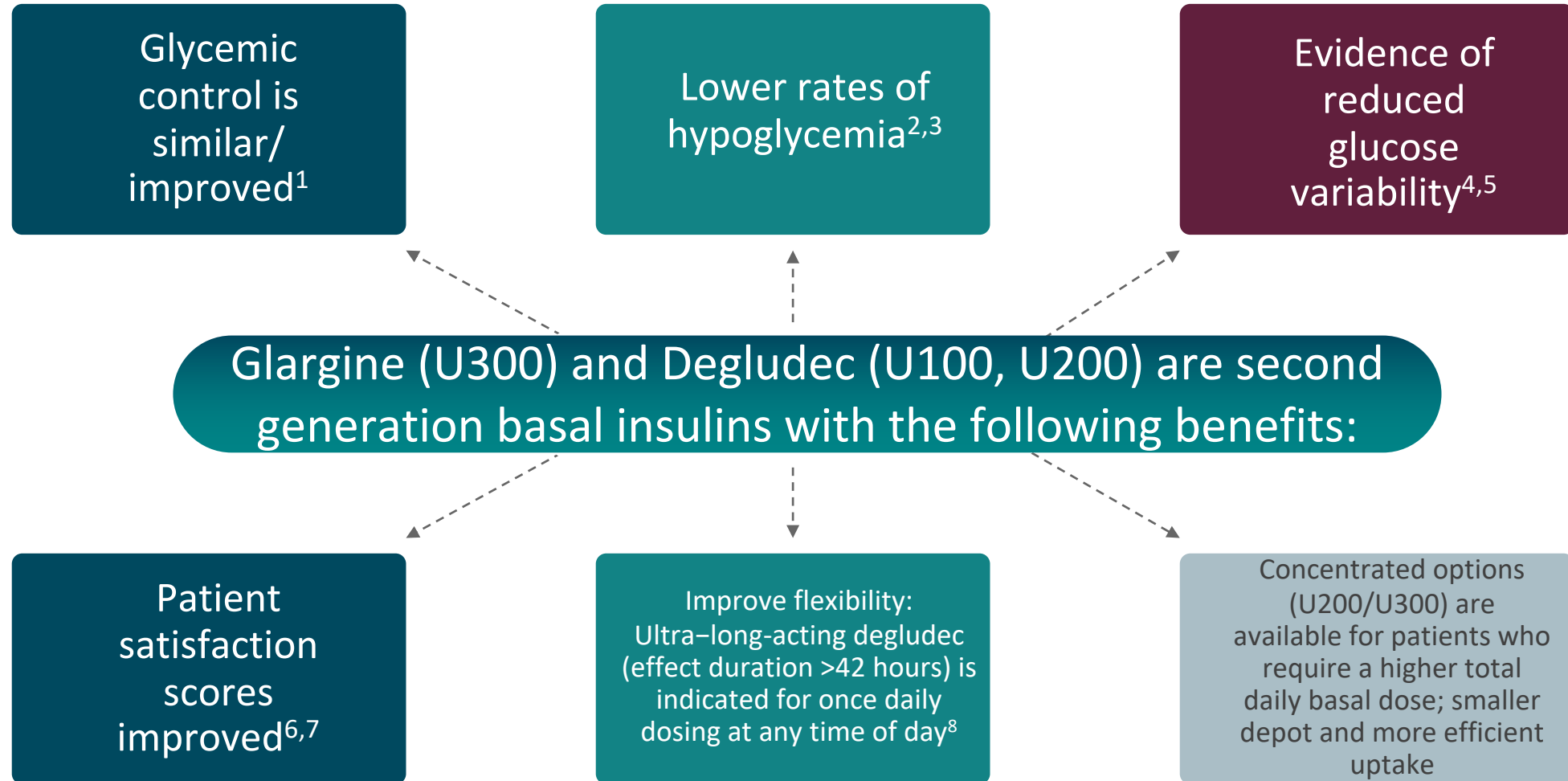
Ultra-rapid insulins have been modified to:

- ✓ Better mimic physiologic insulin secretion
- ✓ Have a faster onset of action and shorter duration of effect
- ✓ Improve PPG control
- ✓ Reduce hypoglycemia

Phase 3 clinical trials in both T1D and T2D showed that faster aspart and ultra-rapid lispro are associated with:

- ✓ A reduction of PPG excursions
- ✓ Similar or marginally superior A1c levels compared with those of first-generation rapid-acting insulin aspart and insulin lispro

# Ultra Long-acting Basal Insulins



# Best Practices in Insulin Therapy

## Type 1 Diabetes

- ✓ Basal plus bolus regimens (MDI or CSII)  
Individualize treatment
  - Carb ratio
- ✓ -Individually calculated correction scale
  - Meal time insulin BEFORE meals (default)

## Type 2 Diabetes

- ✓ Basal insulin first
- ✓ Basal plus 1 is as good as basal-bolus
- ✓ Keep basal insulin once daily
- ✓ Carb ratios often not needed

✓ Teach injections in person with first injection observed

✓ Always look and feel injection sites

✓ Regularly ask about hypoglycemia

Technology helps insulin therapy

- ✓
  - CGMs
  - Smart pens
  - Insulin pumps



# Basal Insulin: A Deeper Dive

Jay H. Shubrook, DO, FAAFP, FACOFP

## Pre-Test | Question 3

**Which of the following is a best practice in titrating basal insulin in type 2 diabetes?**

- a. Make sure all insulin titrations occur at a face-to-face visit
- b. Titrate daily 2-3 units daily
- c. Stop titrating at 1.0 units per KG of body weight daily
- d. Once you achieve the target glucose, you can start down-titrating

# Best Practices When Starting Insulin

Do not use insulin as a weapon



Utilize targeted glucose readings for insulin titration

Insulin does not have to be a lifetime medication



First injection in the office

Start a weight-based dose of basal insulin



If needed ask patients to demonstrate injections

Provide patient with a titration plan



Always look at injection sites

# What is Challenging Regarding Insulin Use

“Insulin is a sign of failure”

“Insulin is scary” (for clinician and patient)

“Insulin means my diabetes is real and serious”

Insulin prescribing is “complicated and dangerous”

Insulin can be expensive



# Insulin Use Inertia

ADA recommends treatment intensification every 3-6 months if not at A1c goal

- Timely intensification and use of insulin if A1c is above 10%
- Most people would be on insulin between 1-2 years if not at goal
- Mean time to insulin was 4.3 years

Only 31% of eligible T2D patients had treatments intensified

(Khunti et al  
Diabetes, Obes,  
Metab)

Another study found that those who did not achieve target glucose at 3 months were less likely to achieve at 24 months.

(Maurico et al)

# Insulin: Action without Benefit

A systematic review of 218 randomized trials 39% of patients with type 2 diabetes treated with basal insulin achieved A1C <7.0%

(Esposito et al Diab, Obes, Metab)

A study of real-world data from a large United States electronic medical record database found that 38% of patients achieved A1C target <7% within 12 months of initiating basal insulin and only 8% more achieved target after 24 months

(Blonde et al, Diabetes Ther)

Disparities exist in access to insulin

- African-American (23%) & Latino American (34%) patients less likely to get insulin

(Pilla et al JGIM)

# Insulin in the Real World (What is the Barrier?)



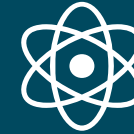
Patient and Providers set individualized HbA1c target (DUNE study)



Patients started or titrated basal insulin  
At week 12 only 27% achieved the agreed upon target



Insulin dose increased very little  
-9 units in new users (from 14-23 units)  
-5 units in continued users (23 -28 units)

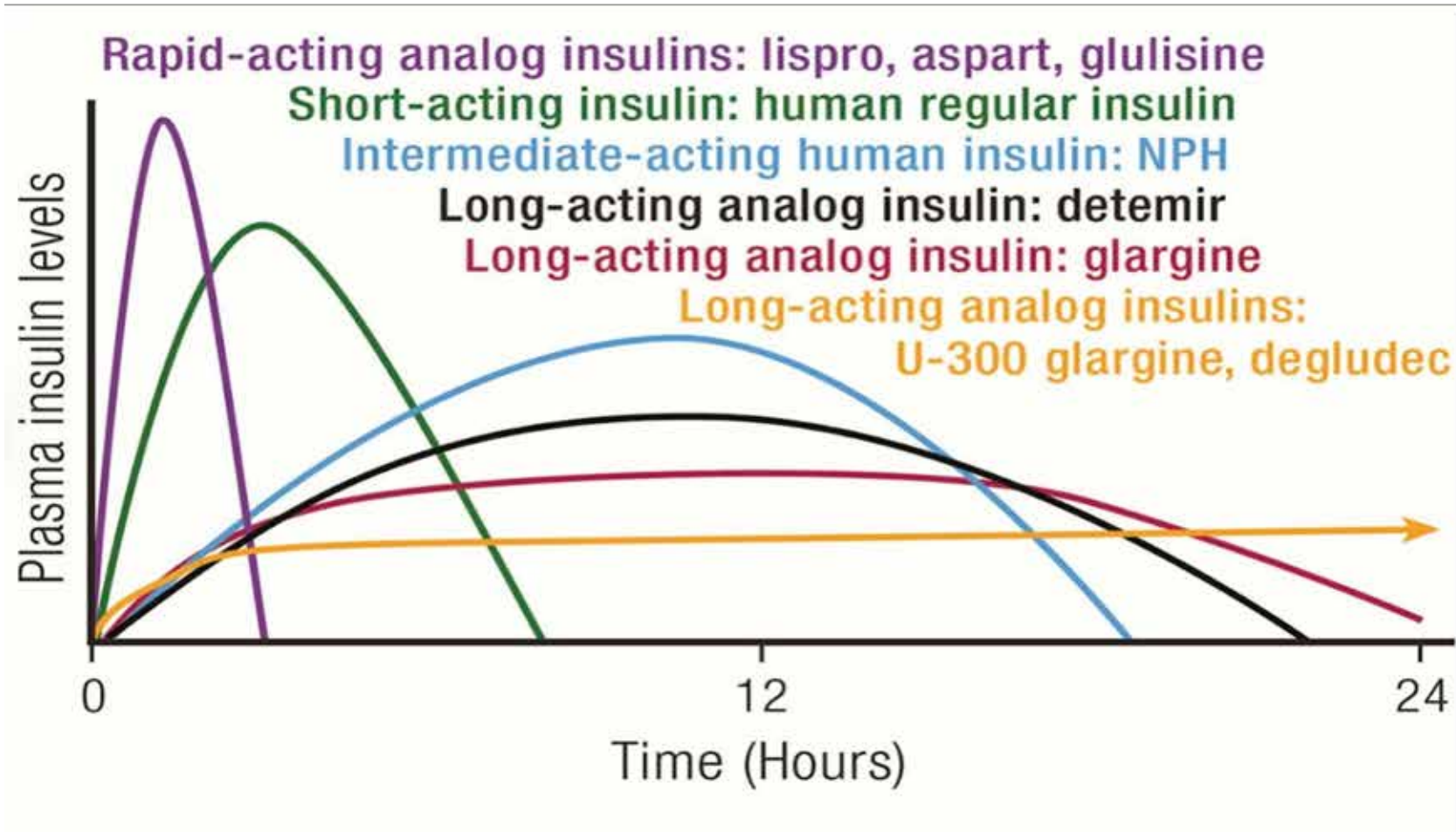


Failure to titrate insulin results in patient not getting to goal and ultimately stopping the treatment

**When starting basal insulin, we have 3 months to achieve the goal!**



# Basal Insulin



# Pre-Test | Question 4

**Which of the following is true regarding basal insulin dosing?**

- a) A dose  $> 0.7$  units/kg/day has diminishing returns and more hypoglycemia
- b) Is titrated by looking at the post-prandial glucose data
- c) Must be titrated by the healthcare clinician
- d) Once started will be a lifetime medication

# Basal insulin Actions and Mechanisms

	Branded Names	Onset	Peak	Duration	Notes
NPH	HumuLIN	1-2 hours	4-8 hours	6-12 hours	Utilizes Zinc and protamination to extend duration
	NovoLIN				
	ReliON				
Glargine (U100)	Lantus	1-4 hours	No peak	24 hours	Acidic pH, AA substitution
	Basaglar				
	Semglee				
Detemir	Levemir	1-4 hours	No peak	20-23 hours	AA substitution Binds to Albumin FFA
Glargine U300	Toujeo	6 hours	No peak	24 hours	Acidic pH, AA substitution
	Toujeo Max				
Degludec U100, U200	Tresiba	1 hour	No peak	42 hours	AA substitution Binds to Albumin FFA Makes chains of hexamers

# Best Practices When Starting Basal Insulin

## “Fix the fasting first”

- ✓ Shared decision-making A1c goal target
- ✓ Discuss the corresponding fasting glucose goal
- ✓ Focus on am glucose monitoring

## Use a weight-based dose

- ✓ 0.2-0.3 units/kg/day-starting dose (long-acting analog)
- ✓ 0.1 units/kg given before breakfast and dinner/bedtime if NPH
- ✓ Package insert states 10 units/day in type 2 diabetes

# Best Practices When Starting Basal Insulin

## Set the titration schedule with patient (any schedule will do)

- ✓ 1 unit/day increase
- ✓ 3 units increase twice weekly (ADA 2-4 units)
- ✓ 5-7 units increase weekly

## Set parameters when to stop titration

- ✓ Achieved am glucose goal
- ✓ Had a hypoglycemic episode
- ✓ Reached 0.5 units/kg/day (Ceiling dose)
- ✓ Always set the next appt to reassess

# Guidelines Regarding Insulin Basal Insulin Dosing/Titration

Initiation Stage	ADA <sup>1,2</sup>	AACE <sup>3</sup>	
Initial Dose	10 u/day OR 0.1-0.2 u/kg/day	HbA1c <8%  0.1-0.2 u/kg/day	HbA1c >8%  0.2-0.3 u/kg/day
Titration	Set FPG goal	Goal: HbA1c <7%, FPG <110 mg/dL	
	Choose evidence-based algorithm to reach goal without hypoglycemia (eg, increase dose 2 units every 3 days; increase 1 unit per day; increase 5-7 units weekly)	Titration every 2-3 days	
		Fixed regimen: increase dose by 2 units	
		Adjustable regimen: FPG >180 mg/dL: add 20% of TDD FPG 140-180 mg/dL: add 10% of TDD FPG 110-139 mg/dL: add 1 U	
Hypoglycemia: reduce dose 10%-20% if no clear cause is evident	If hypoglycemia, reduce TDD by: 10%-20% if BG <70 mg/dL 20%-40% if BG <40 mg/dL		

BG, blood glucose; FPG, fasting plasma glucose; TDD, total daily dose.

1. ADA. Diabetes Care. 2022;45(supp 1): S1-S264. 2. Shubrook JH, Pfothenauer KM. Prim Care Clin Office Pract. 2022;49:301-313.

3. Garber AJ et al. Endocr Pract. 2020 Jan;26(1):107-139.

# Best Practices in Using Basal Insulin

## Be careful to not over-basalize

- ✓ 0.5 units/kg/day- good time to stop and “look up”
- ✓ Look at stability of the fasting glucose
- ✓ Look at bedtime to am change (BeAM)
- ✓ If stable move to meal-time glucose monitoring
- ✓ Basal insulin doses > 0.7 units/kg/day has diminishing returns and more hypoglycemia

(Meneghini et al, Reid et al)

## Once you achieve the fasting goal

- Move glucose readings to pre and post meal (instead of fasting)
- Allows you to see about meal-time excursions

## Pre-Test | Question 5

**Which of the following is true regarding mealtime insulin in type 2 diabetes?**

- a) Must be started at all three meals to be effective.
- b) Start with one meal ( biggest/first), and 0.1 unit per kg of body weight
- c) Should be taken 10-15 minutes after eating the meal
- d) Must be injected in the abdomen



# What To Do After Basal Insulin

## If you are considering insulin

- ✓ Start with basal plus 1
- ✓ One mealtime insulin injection at a meal (first, biggest)
- ✓ Start with 0.1 unit/kg/dose

## Insulin disadvantages

- ✓ Costs
- ✓ Weight Gain
- ✓ Hypoglycemia

# What To Do After Basal Insulin

## If you are considering an injection, think GLP-1RA agonist first

- ✓ Better efficacy than mealtime insulin
- ✓ Less hypoglycemia
- ✓ Benefits of weight loss
- ✓ Non-glycemic benefits

## GLP-1 RA disadvantages

- ✓ COST
- ✓ Coverage
- ✓ Product warnings (pancreatitis, gastroparesis, MTC)

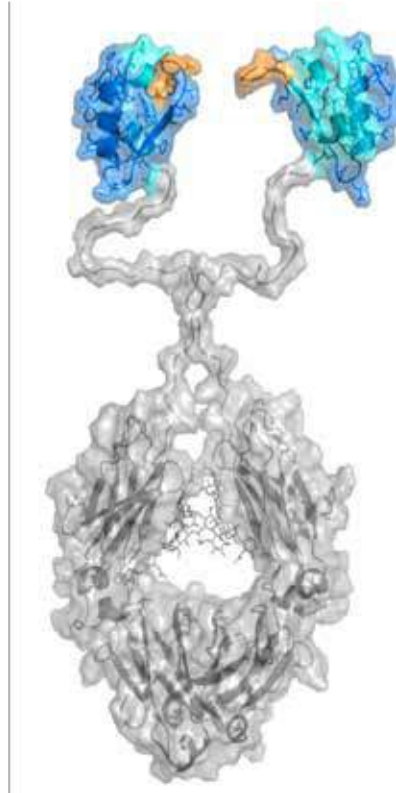
# The Future of Basal Insulin

## Pre-Test | Question 6

**Which of the following applies to the new once-weekly insulins in clinical trials?**

- a) The once-weekly insulins have more hypoglycemia than the once-daily basal insulins
- b) The once-weekly insulins have higher rates of hypoglycemia than once-daily basal insulins
- c) The once-weekly insulins achieve lower A1c levels than once-daily basal insulins
- d) The once-weekly insulins have similar A1c reductions, safety and hypoglycemia rates as the once-daily insulins

# Weekly Basal Insulin Candidate

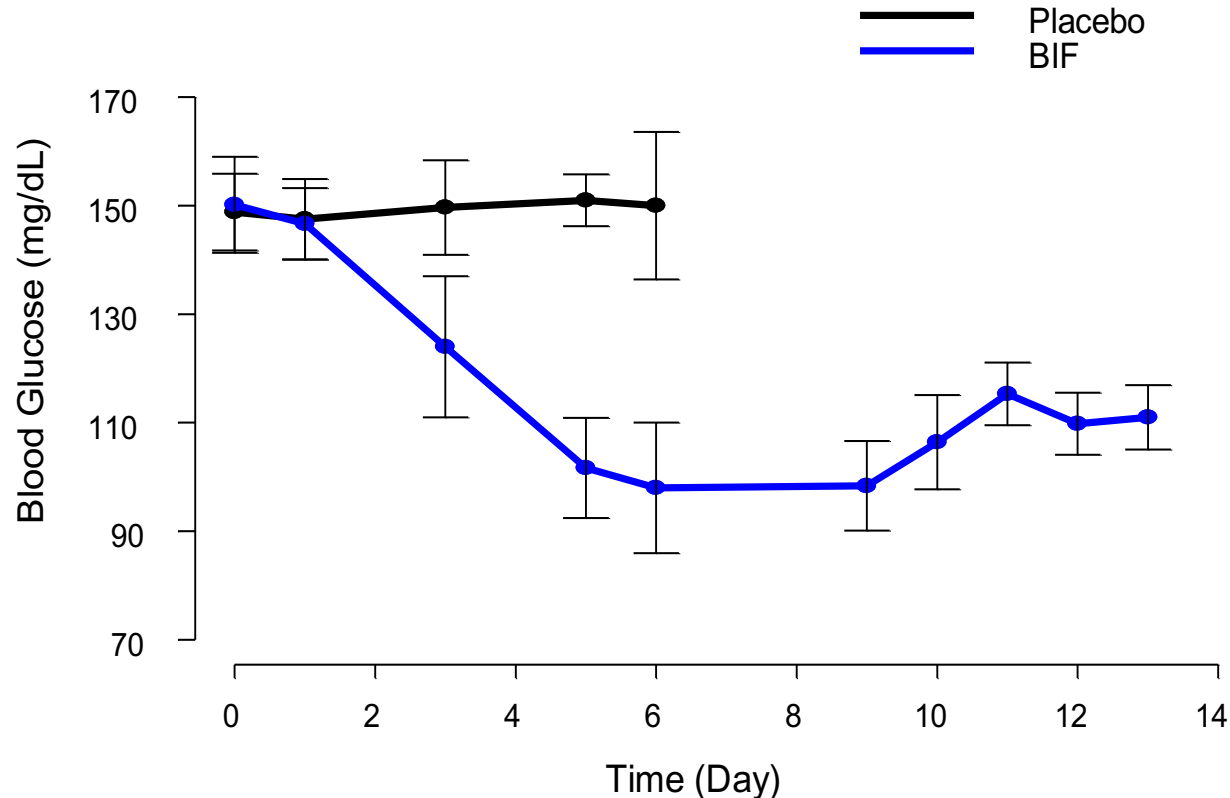


Eli Lilly

Courtesy of Stefano Del Prato, MD | University of Pisa, Pisa, Italy | ADA 2020 Scientific Sessions

# Insulin BIF Glucose Efficacy

Fasting glucose in patients with T2DM



Prolonged glucose lowering for up to 10 days after a single dose of BIF

Glucose control comparable to conventional basal insulins

Low incidence of hypoglycemia with multiple doses

- No severe hypoglycemia
- All hypoglycemic episodes recovered spontaneously or with oral carbohydrate
- Profile similar to insulin glargine

No clinically significant injection site reactions

Very low rate of anti-drug antibodies

Abbreviations: BIF, weekly basal insulin Fc; T2DM, type 2 diabetes mellitus.

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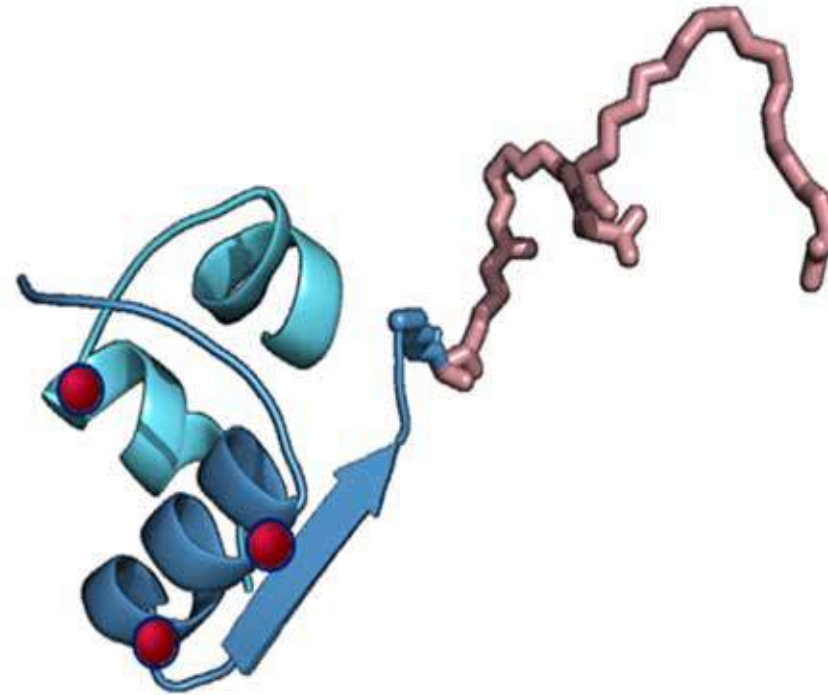
# Summary – Insulin BIF

Novel once weekly insulin receptor agonist utilizing well-established Fc platform

- Potent glucose lowering
- Safety profile comparable to conventional insulins
  - No safety or tolerability findings to preclude from moving to next stage of development
  - Low mitogenicity potential
  - Low immunogenicity potential, very low rate of anti-drug antibodies
  - Most hypoglycemic episodes recovered spontaneously or with oral carbohydrate
- Potential to decrease number of hypoglycemic events beyond conventional insulins due to low peak-to-trough ratio

A large phase 2 program exploring the efficacy and safety of BIF in a broad patient population, including T1DM, is being conducted.

# Weekly Basal Insulin Candidate

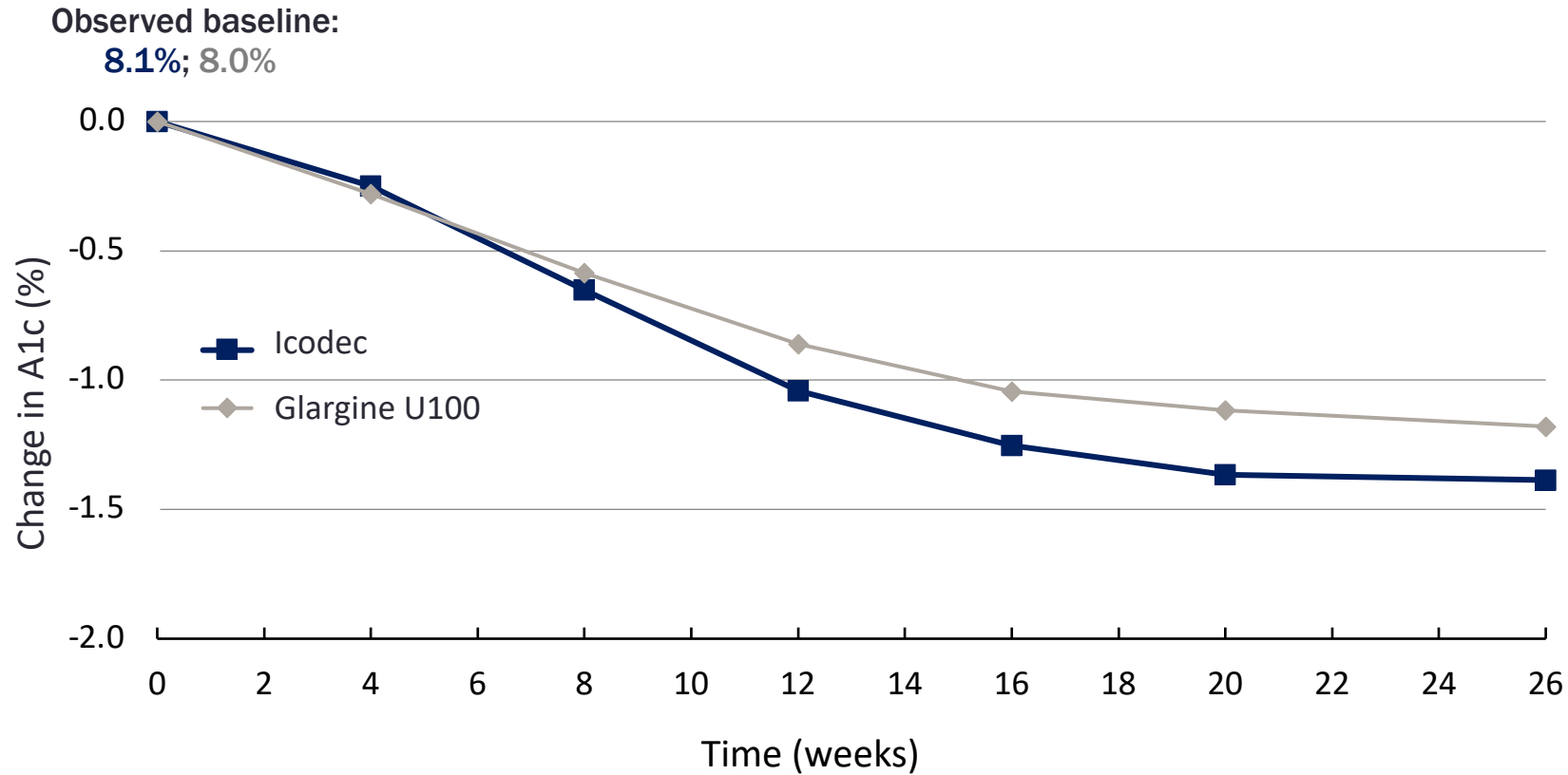


Novo Nordisk

Courtesy of Stefano Del Prato, MD | University of Pisa, Pisa, Italy | ADA 2020 Scientific Sessions



# Weekly Insulin Icodec: A1C Changes Over Time



Supportive Statistical Analysis	
Estimated mean A1c at week 26	
6.9%	<b>6.7%</b>
Estimated mean change from baseline to week 26 in A1c	
-1.15%	<b>-1.33%</b>
ETD (Icodec – Glargine U100): -0.18% [95%CI 0.38; 0.02] p= 0.08	

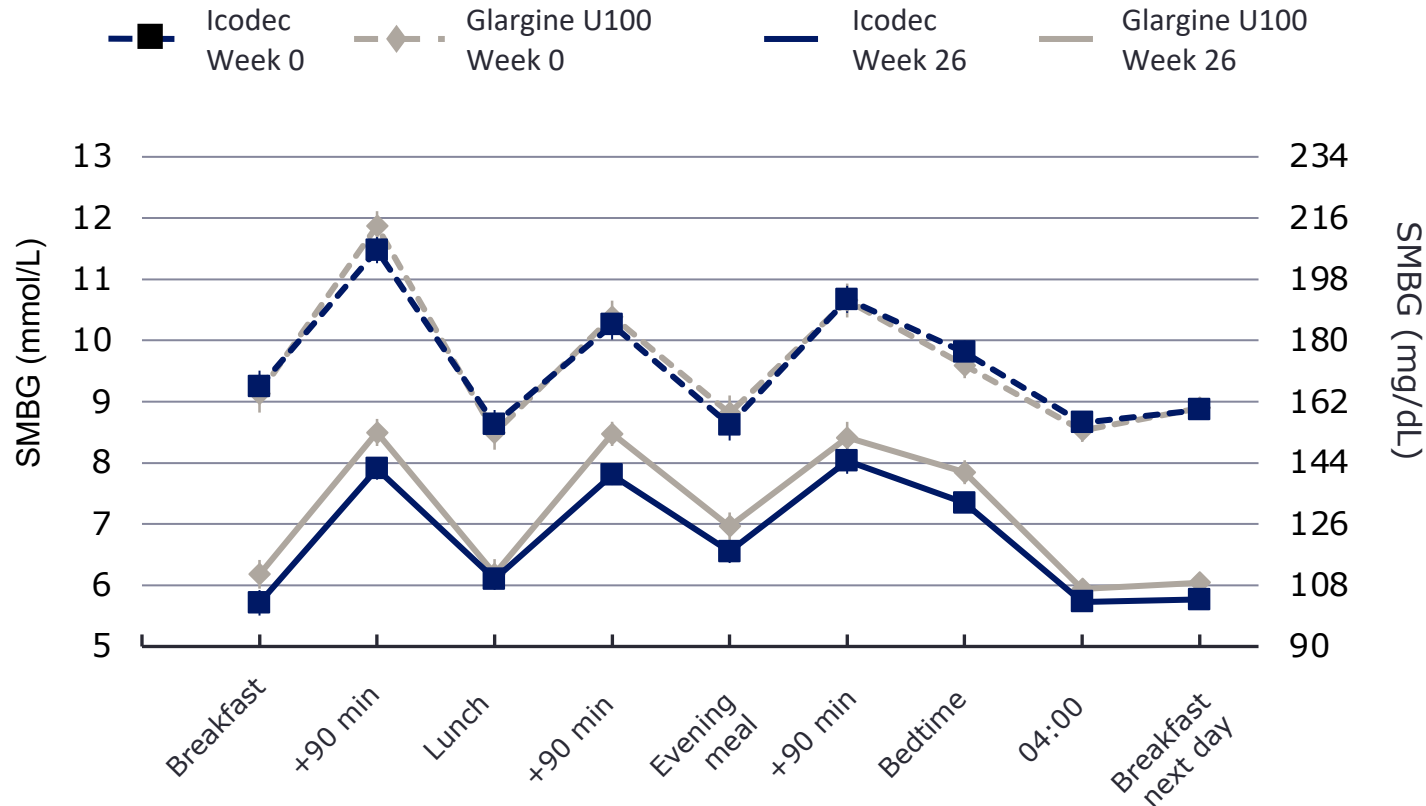
Full analysis set. Observed data are mean (symbol) ± SEM (error bars) on-treatment without ancillary treatment.

Estimated mean change values and ETD with 95% CI at week 26 derived based on MMRM (trial product estimand).

A1c, glycated hemoglobin; CI, confidence interval; ETD, estimated treatment difference; MMRM, mixed model for repeated measures; SEM, standard error of the mean.

Courtesy of Stefano Del Prato, MD | University of Pisa, Pisa, Italy | ADA 2020 Scientific Sessions | Rosenstock J et al ADA Scientific Sessions 2020

# Weekly Insulin Icodec: 9-point SMBG Profile



## Supportive Statistical Analysis

Estimated mean change from baseline to week 26 in mean of 9-point SMBG profile

ETD (Icodec – Glargine U100):  
 -7.9 mg/dL [95%CI-14.1; -1.6]  
 p= 0.01

Full analysis set. Observed data are mean (symbol) ± SEM (error bars) on-treatment without ancillary treatment.

Estimated mean change values and ETD with 95% CI at week 26 derived based on MMRM (trial product estimand).

A1C, glycated hemoglobin; CI, confidence interval; ETD, estimated treatment difference; MMRM, mixed model for repeated measures; SEM, standard error of the mean.

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# Hypoglycemia During the On-Treatment Period

## Weekly Insulin Icodec

Hypoglycemia Levels	Icodec (N = 125)		Glargine U100 (N = 122)	
	N (%)	E (R)	N (%)	E (R)
Hypoglycemia Alert Value (Level 1)	67 (53.6)	368 (508.9)	46 (37.7)	148 (210.8)
Severe (Level 3) or Clinically Significant (Level 2) Hypoglycemia	20 (16.0)	38 (52.5)	12 (9.8)	32 (45.6)
Severe Hypoglycemia (Level 3)	1 (0.8)	1 (1.4)	0	

The duration of hypoglycaemia was not longer with Icodec compared to Glargine U100

On-treatment: onset date on or after the first dose of trial product and no later than the first date of either the last follow-up visit (FU2), the last date on trial product + 5 weeks for once-daily insulin and + 6 weeks for once-weekly insulin or the end-date for the in-trial period.

%, percentage of patients with one or more events; E, number of events; N, number of patients with one or more events; R, rate (number of events divided by patient years of exposure multiplied by 100).

Courtesy of Stefano Del Prato, MD | University of Pisa, Pisa, Italy | ADA 2020 Scientific Sessions

# Weekly Insulin Icodec vs Daily Insulin Glargine U100 in Insulin Naïve Patients with T2DM: Summary

Once-weekly insulin Icodec displayed similar glucose-lowering effect and safety profile to once-daily insulin Glargine U100

- No significant differences between treatments in change from baseline in A1C, FPG, or body weight
- Improved mean of the 9-point SMBG profile with insulin Icodec compared with insulin Glargine U100
- Rates of severe (level 3) or clinically significant (level 2) hypoglycemia were low for both insulin treatments
  - No statistically significant differences during the on-treatment period
- No new safety issues were identified in relation to insulin Icodec in this trial

# Once Weekly Insulins

1

Once-weekly insulins will facilitate insulin replacement therapy

2

Once-weekly dosing has the potential to reduce therapeutic inertia, and improve persistence, as has been seen with GLP-1 RAs

3

New implementation strategies (eg, initiation, titration, switching, intensification) will be needed

4

Understanding the risk and management of hypoglycemic events will be important

5

Clinician and patient education will be crucial

6

Offer the potential of a once-weekly insulin/GLP-1RA combination

# Summary



Pharmacologic insulin replacement should try to mimic normal insulin physiology



There is a wide spectrum of basal and prandial insulins that allow for individualization of treatment



Strong knowledge of time action curves improve insulin selection and safety of insulin use



Newer ultra-rapid and ultra long-lasting insulins continue to prove to be safe and effective

# Role of CGM in Insulin Therapy & Minimizing Hypoglycemia with Insulins

DAVIDA F. KRUGER, MSN, APN-BC, BC-ADM

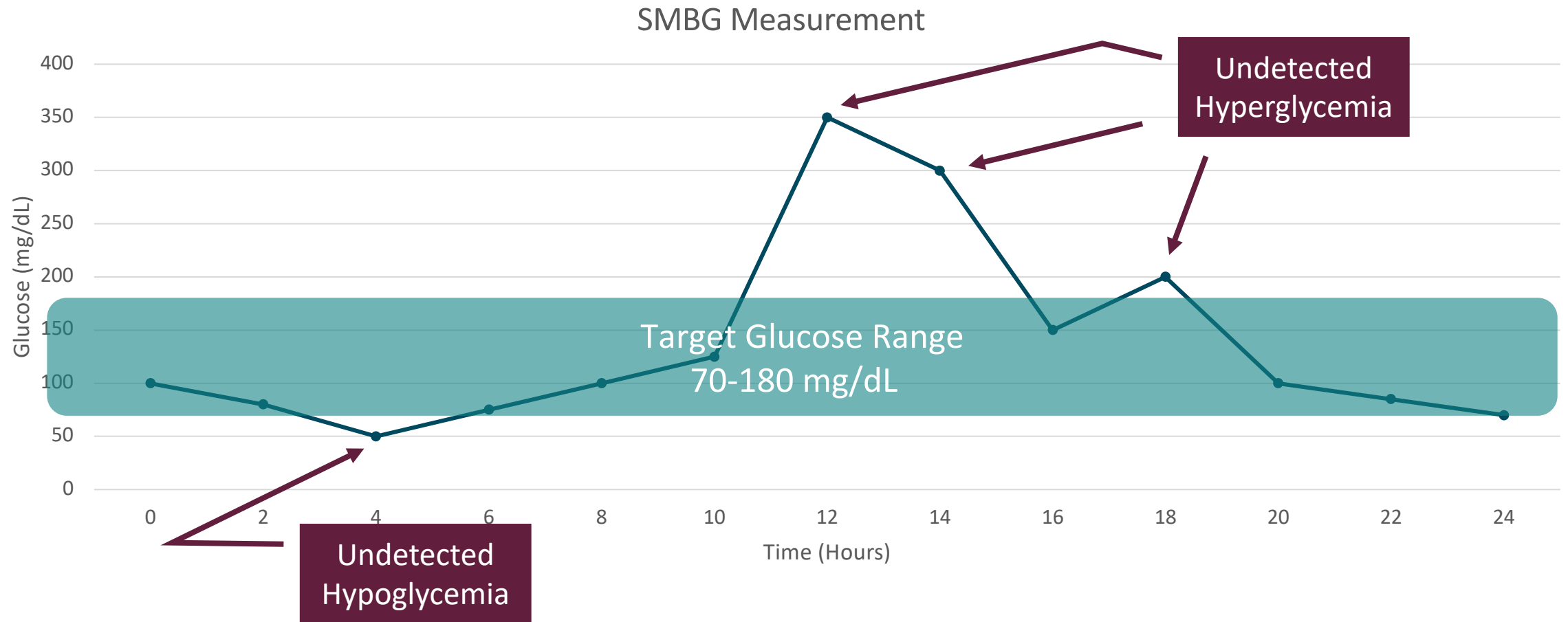
## Pre-Test | Question 7

**Which of the following statements below is TRUE regarding Continuous Glucose Monitoring?**

- a) It is not covered by Medicare for people on insulin
- b) It is not able to accurately identify hypoglycemia
- c) It identifies glycemic patterns that are often missed by finger-stick data
- d) It is widely accepted by all insurance for all people with diabetes



# Glycemic Patterns Are Often Missed by SMBG but Detected With CGM



# Real-Time CGM & Intermittently Scanned CGM

## Real-Time CGM (rtCGM)

CGM systems that measure and display blood glucose continuously every 1 to 5 minutes

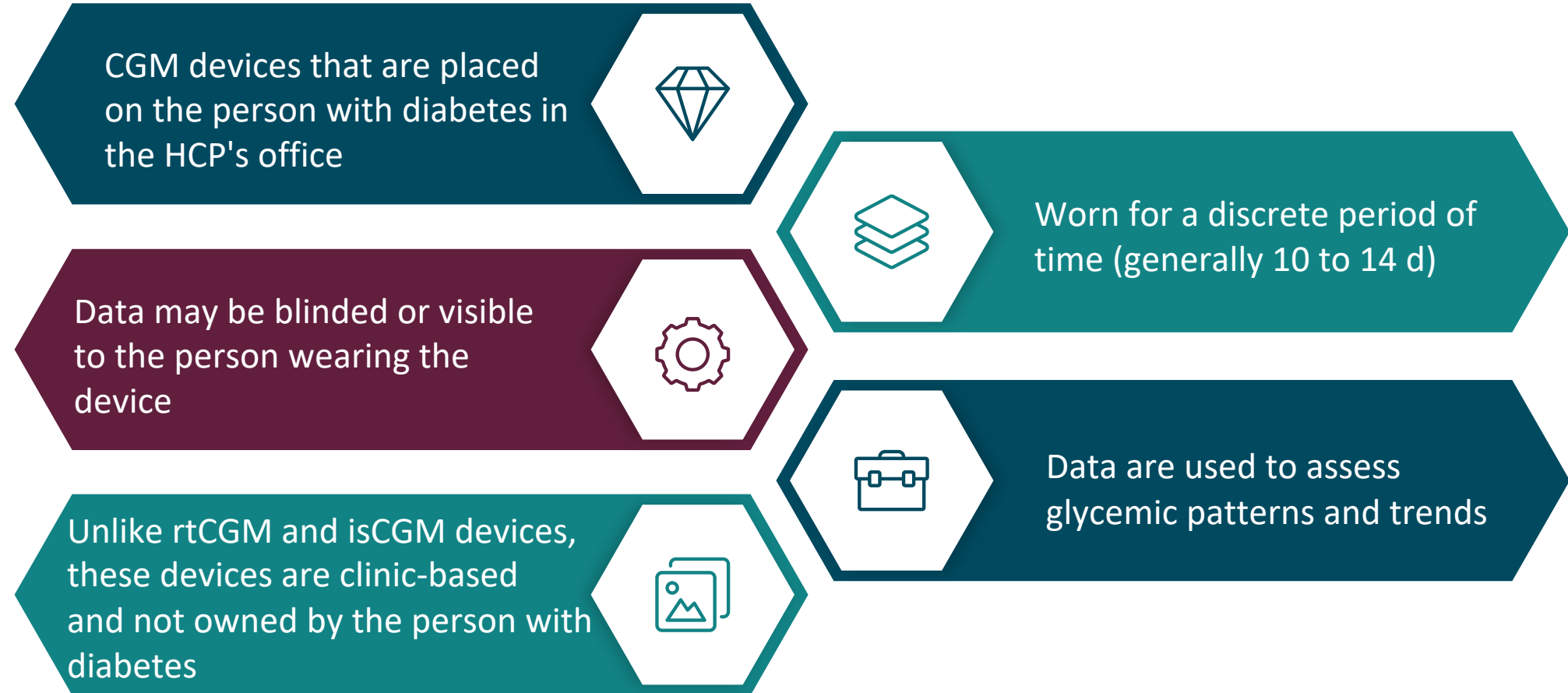
rtCGM, real-time continuous glucose monitoring.  
Elsayed NA, et al. Diabetes Care. 2023;46(suppl):S111-S127.

## Intermittently Scanned CGM (isCGM) with and without alarms

CGM systems that measure glucose levels continuously but require scanning for visualization and storage of glucose values

isCGM, intermittently scanned continuous glucose monitoring.  
Elsayed NA, et al. Diabetes Care. 2023;46(suppl):S111-S127.

# Professional CGM



HCP, healthcare provider.

ElSayed NA, et al. Diabetes Care. 2023;46(suppl):S111-S127.

# Professional CGM Devices

	FreeStyle Libre Pro	G6 Pro
Data type	Blinded	Blinded or unblinded
Frequency of glucose readings	Records glucose every 15 min	Glucose readings sent to patient's smart device every 5 min in unblinded mode; data also sent to HCP Sensor/transmitter returned after 10 days and CGM data uploaded for HCP and patient
Approved ages	≥ 18 y	≥ 2 y
Location for placement	Back of upper arm	Abdomen (also buttocks for patients 2 to 17 y)
Sensor life	14 d	10 d
Calibration	No	No
Warm-up time	1 h	2 h
Potential interfering agents	Ascorbic acid Salicylic acid	Hydroxyurea High-dose acetaminophen (> 1 g every 6 h in adults)
Alerts or alarms	No	Yes (unblinded)

# Personal CGM Devices



	FreeStyle Libre 14-Day isCGM/ 2 isCGM/ 3 rtCGM	G6 / G7 rtCGM	Guardian Sensor 3 & 4 (pump integrated) and Guardian Connect (stand-alone) rtCGM	Eversense 90-Day/ E3 rtCGM
Approved labeling	Replaces fingersticks for treatment decisions; no fingerstick calibration required	Replaces fingersticks for treatment decisions; no fingerstick calibration required	4: Replaces fingersticks for treatment decisions; no fingerstick calibration required 3: Requires $\geq 2$ fingerstick calibrations/d	Replaces fingersticks for treatment decisions; requires $\geq 2$ fingerstick calibrations/d
Age	$\geq 18$ y / $\geq 4$ y / $\geq 4$ y 2 / 3: Use during pregnancy by women with T1D, T2D, or GDM	$\geq 2$ y G 7: Use during pregnancy by women with T1D, T2D, or GDM	Guardian 4: $\geq 7$ y Guardian 3: $\geq 14$ y Connect: $\geq 14$ y	$\geq 18$ y
Medicare coverage	Yes / Yes / yes	Yes / Yes	Sensor 3: Yes / 780 G: Yes / Connect: No	Yes
Wear length	14 d / up to 15 d / up to 15 d	10 d / 10 d + 12 h	7 d	90 d / 180 d
Warm-up	1 h	2 h / up to 30 min	2 h	24 h after implementation
Alarms	No / Yes / Yes	Yes	Yes	Yes
Data display/integration	14 / 2/3: Reader; Android and iOS Apps 2 / 3: CGM for integration with AID systems	Receiver; Android and iOS Apps; smartwatches t:slim X2 pump, Omnipod 5	Connect: Android and iOS Apps Guardian 3: 630G, 670G, 770G Guardian 4: 780G	Android and iOS Apps, smartwatches
Form	Disposable transmitter integrated with sensor patch	G6: Transmitter (3-mo use) separate from sensor/G7 integrated	Transmitter (rechargeable every 6 days) separate from sensor	Transmitter (lasts 1 year, charge daily) separate from sensor
Accuracy*	11.4% / 9.3% / 7.9%	9.0% / 8.2%	9.6% / 9.0% to 11%	8.5% to 9.5%

\*Accuracy measured by MARD (mean absolute relative difference) relative to venous glucose. Lower numbers are more accurate. Accuracy figures and specifications for each device provided by manufacturers. AID, automated insulin delivery; FDA, US Food and Drug Administration; GDM, gestational diabetes mellitus; T1D, type 1 diabetes; T2D, type 2 diabetes.

# FreeStyle Libre Phone App and Desktop

FreeStyle Libre 14-day sensor, LibreLink for loved ones,  
and LibreView for download reports

Libre 10-day and 14-day Libre 2/3 sensor, LibreView for download reports



# G6/G7 Phone App and Desktop

**G6/G7 10-day sensor**  
**Share for loved ones and Clarity for download reports**



# Guardian Phone App and Desktop

**Guardian System with Connect for loved ones  
and CareLink™ software for downloading reports**





# Eversense Phone App

## Mobile App for iOS and Android



## Educate Patient

- Blood glucose values are changing constantly
- A fingerstick is only a snapshot of a 24-hour period
- CGM provides continuous information to help us with decisions (eg, show them an example of the AGP and discuss TIR)



# Educating Your Patients About Technology

**Explain** how the CGM download or AGP helps us recognize hyper- and hypoglycemia patterns

- Allows us to discuss medication and lifestyle choices and develop a treatment plan using a shared decision-making approach
- "Opens up the conversation"



**Explain** that CGMs are beneficial if patients are having a difficult time reaching or maintaining their glycemic target or HbA1c

Helps them understand how certain foods or activities affect their personal glucose journey



**Show** patients the CGM options available on the market, and explain how they differ. Give them choice, and empower them to make the right decision for themselves personally

**Discuss** hypoglycemia anxiety, and how it affects them and their family members personally. Discuss how it can prevent us from improving HbA1c levels and glycemic control



# Clinical Practice Guidelines on CGM Use in Adults

## AACE Clinical Practice Guidelines 2022<sup>[a]</sup>

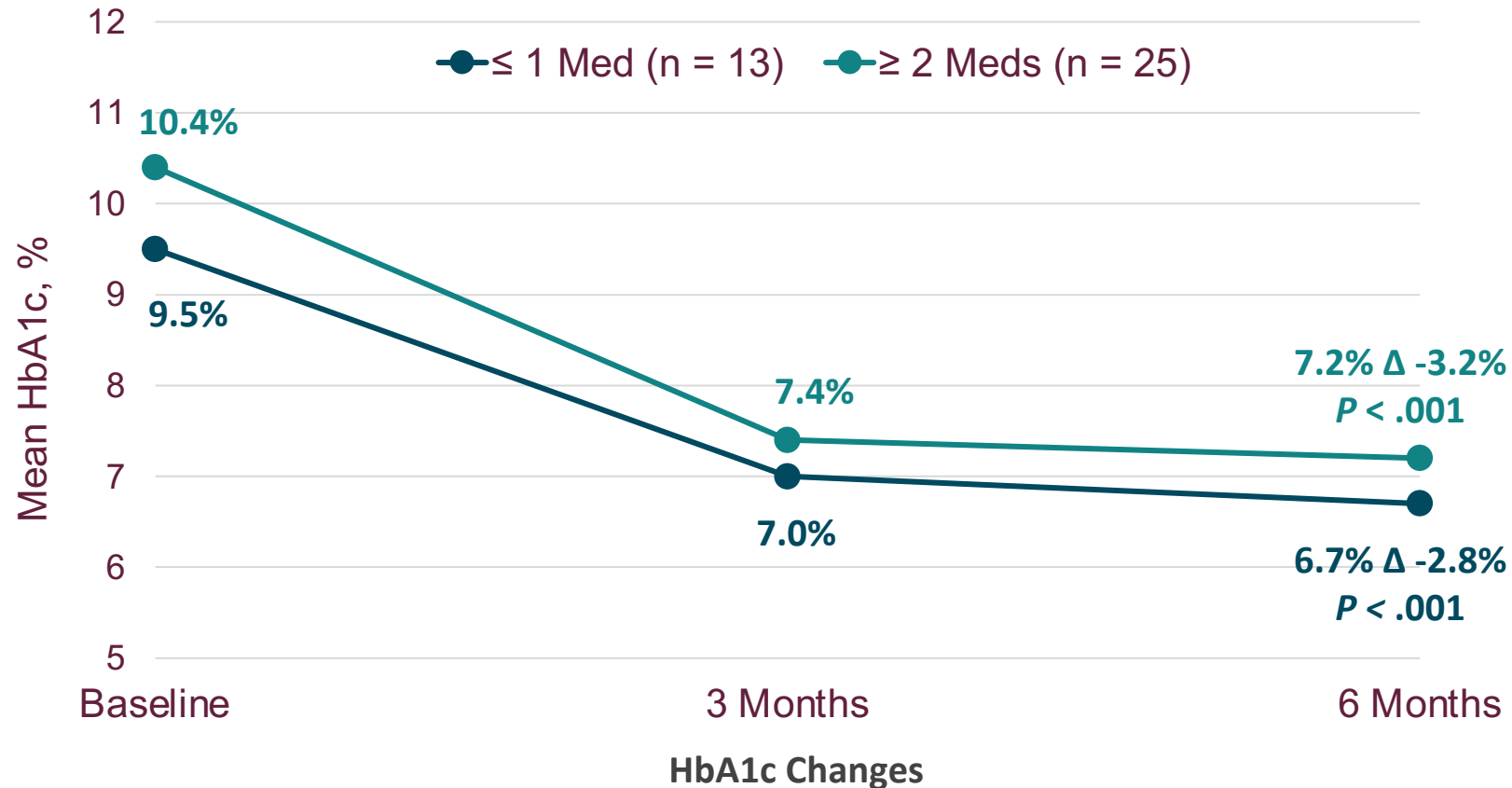
CGM is recommended for persons with T2D who are treated with insulin therapy, or who have high risk of hypoglycemia and/or with hypoglycemia unawareness (**Grade A\***)

## ADA Standards of Care 2023<sup>[b]</sup>

rtCGM (**Grade A<sup>†</sup>**) or isCGM (**Grade B<sup>‡</sup>**) should be offered for diabetes management in adults with diabetes on MDI insulin regimen or CSII, and should be used for diabetes management in adults with diabetes on basal insulin

Initiation of CGM, CSII, or AID early in the treatment of diabetes can be beneficial (**Grade C<sup>§</sup>**)

# Real-World Study



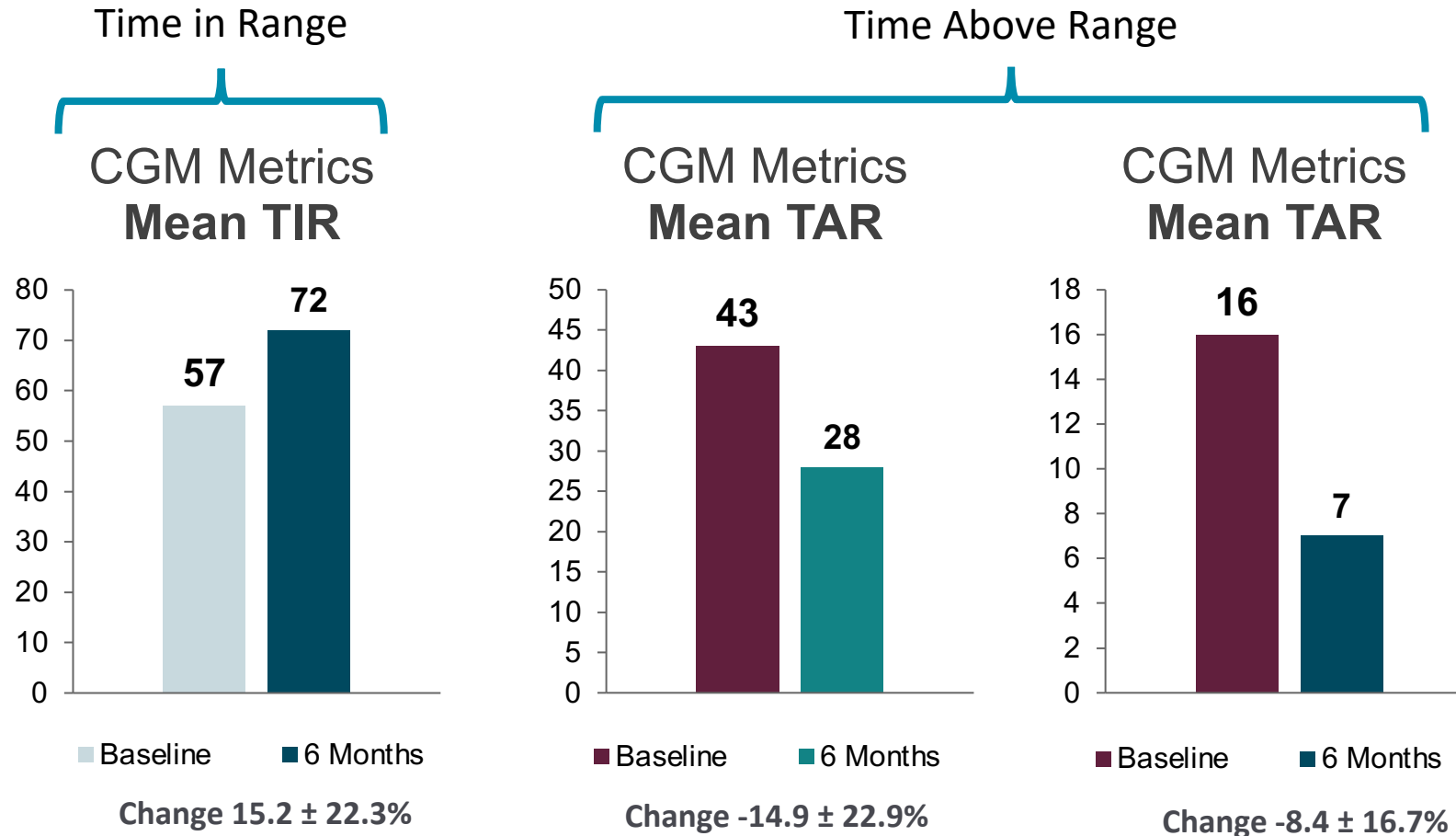
**rtCGM (G6) in T2D  
With/Without Insulin**

N = 38 T2D, prospective, interventional, single-arm study 26 weeks

Primary outcomes: changes in HbA1c, BG, %TIR, %TBR, %TAR

BG, blood glucose; TAR, time above range; TBR, time below range.  
Grace T, et al. Diabetes Technol Ther. 2022;24:26-31.

# Percent Time in Range Changes



## Study Limitations

Findings do not accurately assess the actual changes that occurred relative to glycemic status before rtCGM initiation

Diverse study population

Findings cannot be generalized to the broader T2D population

6-month study duration

# Glycemic Management and Treatment Plan Should Not Be Defined by HbA1c Alone

HbA1c, %	Glucose, mg/dL	95% CI
5	97	(76, 120)
6	126	(100, 152)
<b>7</b>	<b>154</b>	<b>(123, 185)</b>
8	183	(147, 217)
9	212	(170, 249)
10	240	(193, 282)
11	269	(217, 314)
12	298	(240, 347)

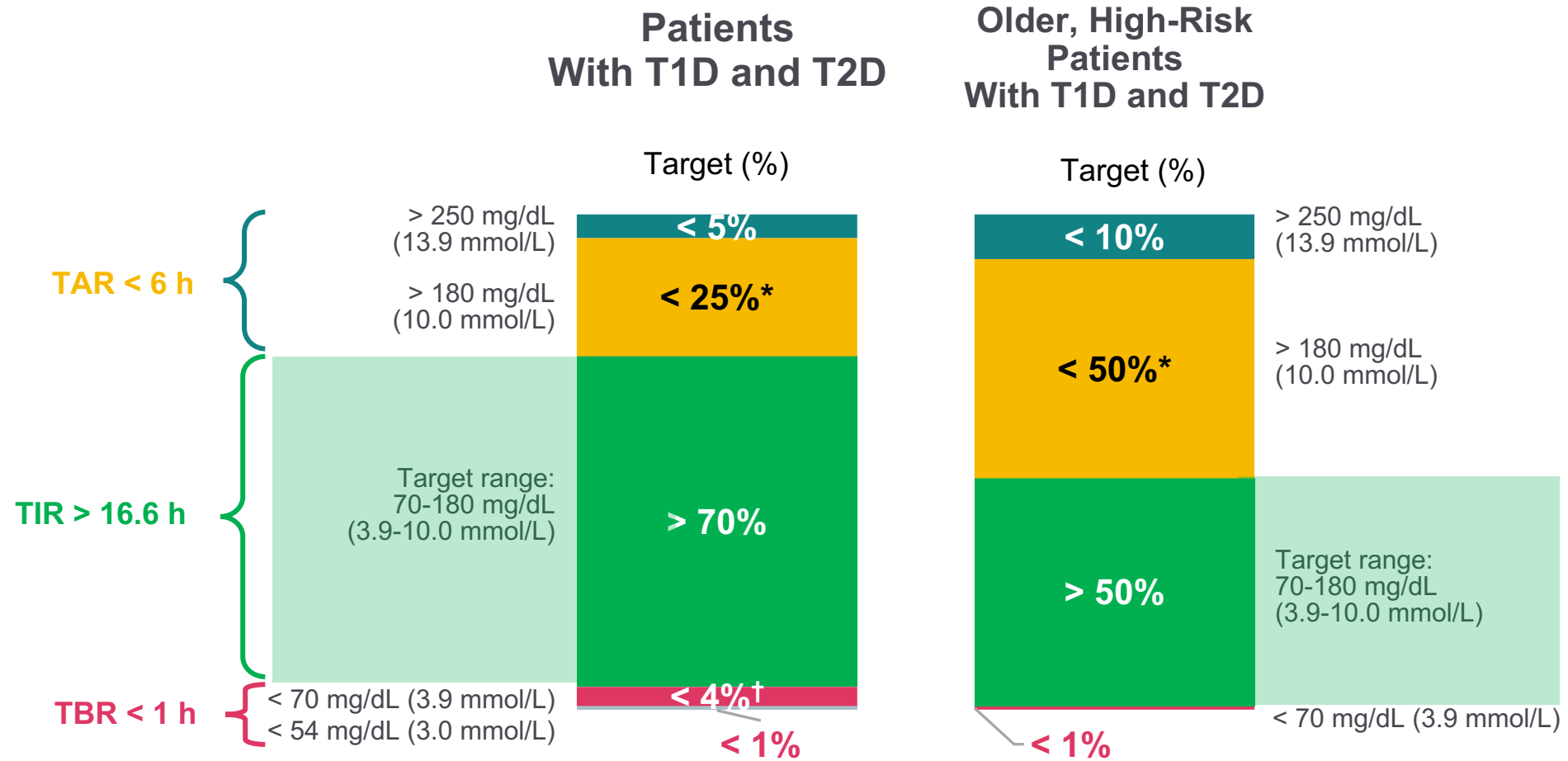
- May underestimate or overestimate average glucose (eg, HbA1c 7% could represent a range between 123 mg/dL and 185 mg/dL)
- Does not indicate extent or timing of hypoglycemia or hyperglycemia
- Does not reveal glycemic variability
- Limited utility for insulin dosing decisions
- Unreliable in patients with hemolytic anemia, hemoglobinopathies, or iron deficiency
- Underestimates in end-stage kidney disease or during pregnancy
- Correlation with mean glucose can vary among races

## Pre-Test | Question 8

**Which of the following is a treatment recommendation for adults with type 2 diabetes who have an A1c goal of < 7.0%**

- a) Time above range should be less than 50%
- b) Time in range should be > 50%
- c) Time in range should be > 70%
- d) Time below range should be < 10%

# Time in Range (TIR) Targets for CGM Data Interpretation

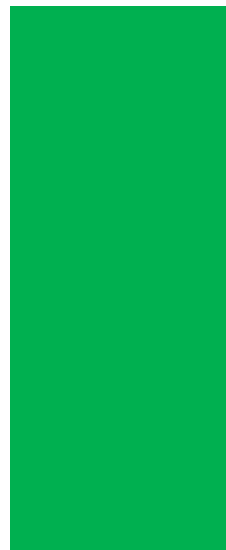


\*Includes percentage of values > 250 mg/dL. †Includes percentage of values < 54 mg/dL.  
 Battelino T, et al. Diabetes Care. 2019;42:1593-1603.

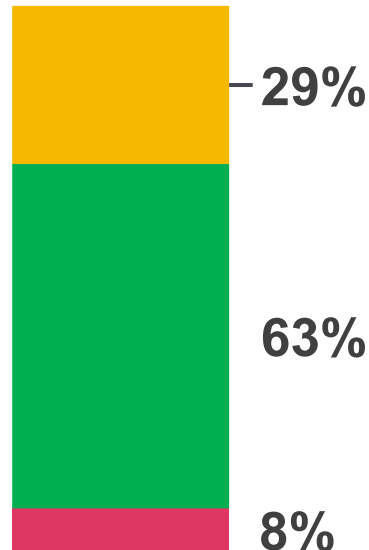


# Equal HbA1c Values Do Not Equal TIR

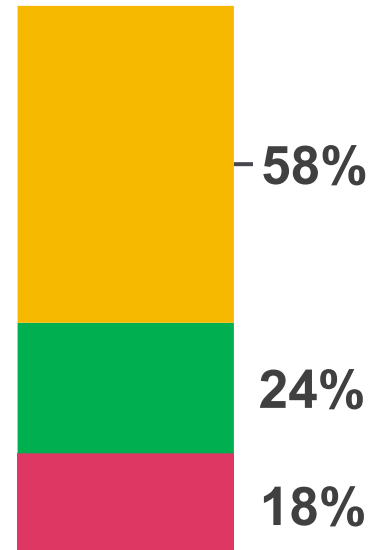
**Patient A**  
HbA1c 7%



**Patient B**  
HbA1c 7%




**Patient C**  
HbA1c 7%



 **In Target Range**  
(70-180 mg/dL)

 **Above Target Range**  
(> 180 mg/dL)

 **Below Target Range**  
(< 70 mg/dL)



HbA1c provides only an average of a patient's glucose history



TIR provides more actionable information than HbA1c alone and should complement HbA1c



Each 5% increase in TIR is clinically beneficial

# The Ambulatory Glucose (AGP) Report Summarizes CGM Data



A single-page, standardized report for interpreting a patient's daily glucose and insulin patterns



Allows "big picture" view of diabetes management



Easily shared with patients and parents/caregivers



Facilitates communication with the diabetes care team

AGP, ambulatory glucose profile.

Johnson ML, et al. Diabetes Technol Ther. 2019;21(suppl):S2-17–S2-25.

# 3 Sections of the AGP Report



## Metrics, Values, Goals

Summary of values to help assess the overall quality of glucose management



## AGP Profile

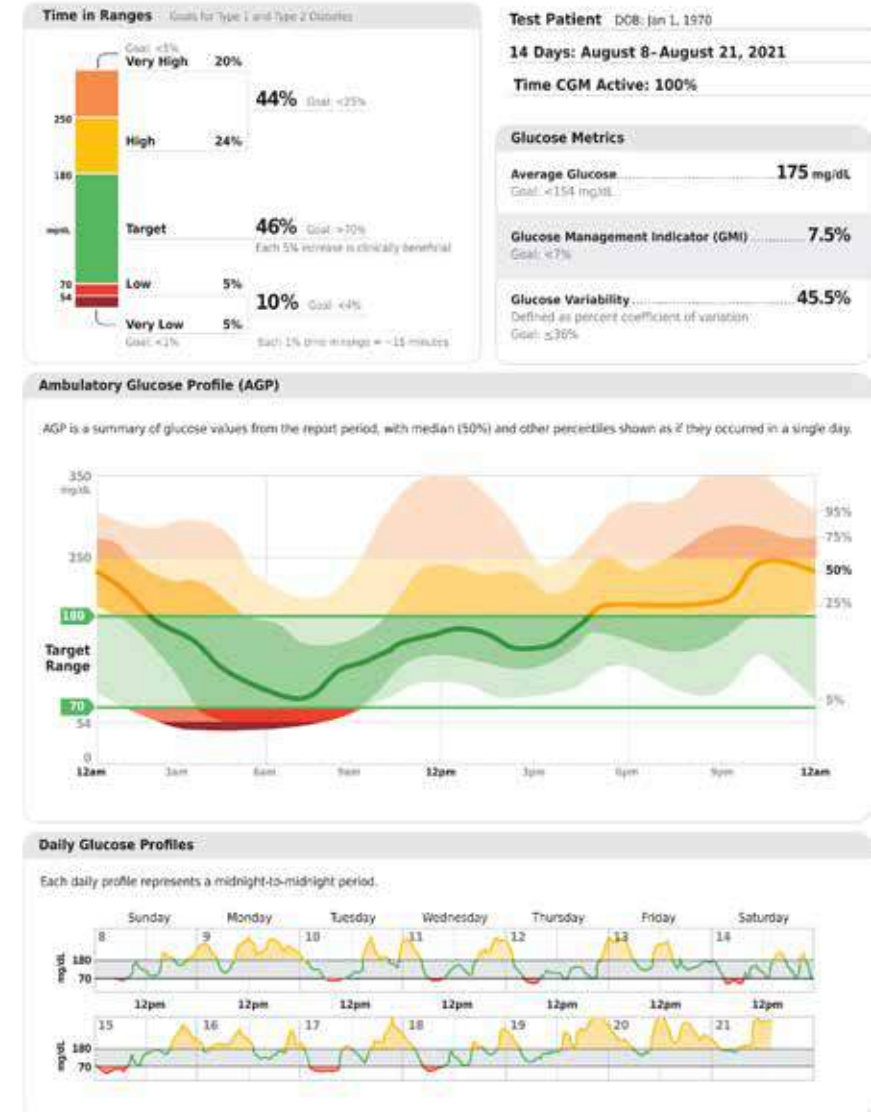
Shows all values as if collected over a single 24-h period. Shows variability in the mean glucose and patterned areas of highs and lows



## Daily Views

Shows daily values -- helpful in determining causes of patterns or exceptions to usual patterns

### AGP Report: Continuous Glucose Monitoring

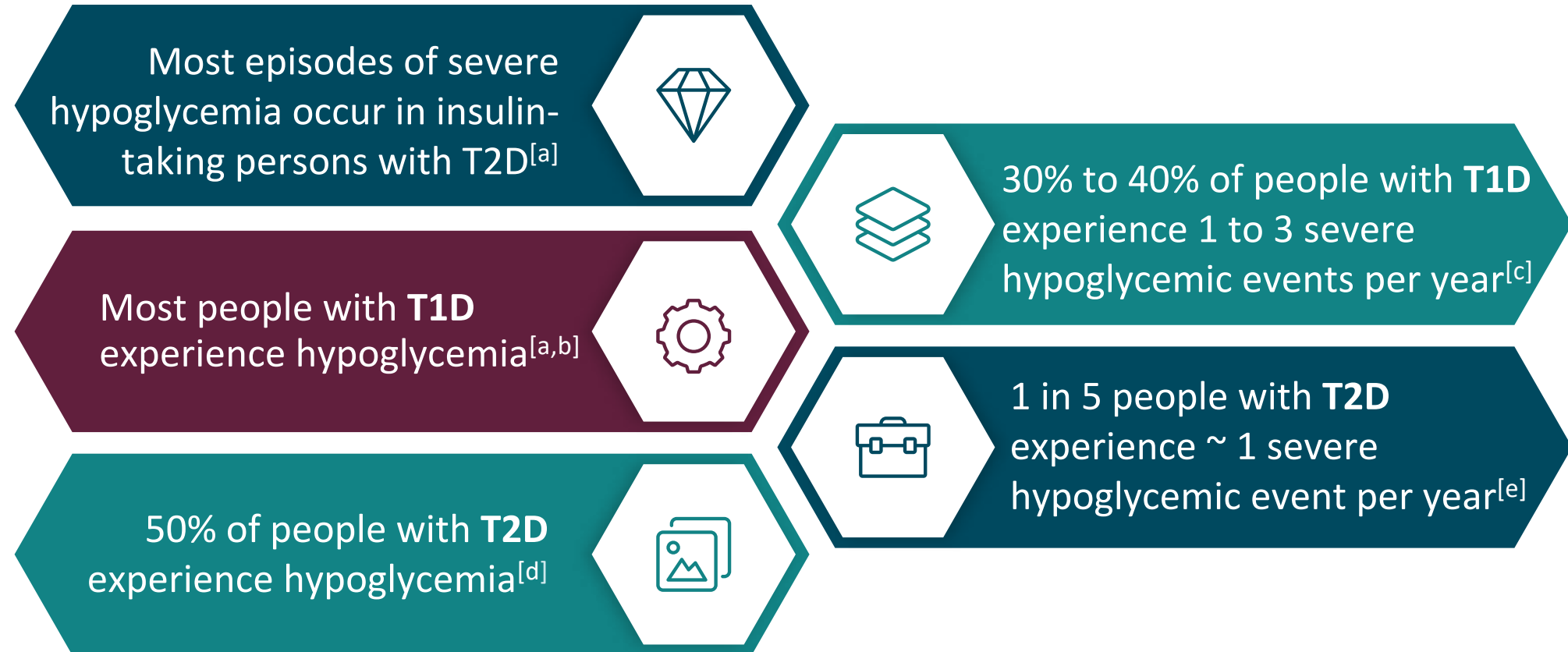


## Pre-Test | Question 9

**Which of the following statements is true regarding hypoglycemia in people with diabetes?**

- a) Hypoglycemia is only seen when the HbA1c is <8%
- b) Is rare in type 2 diabetes
- c) Is equally common in people with an HbA1c levels of <7% and >9%
- d) It is not necessary to provide Glucagon prescriptions for type 2 diabetes on Insulin

# Severe Hypoglycemia Is Common in People With Diabetes

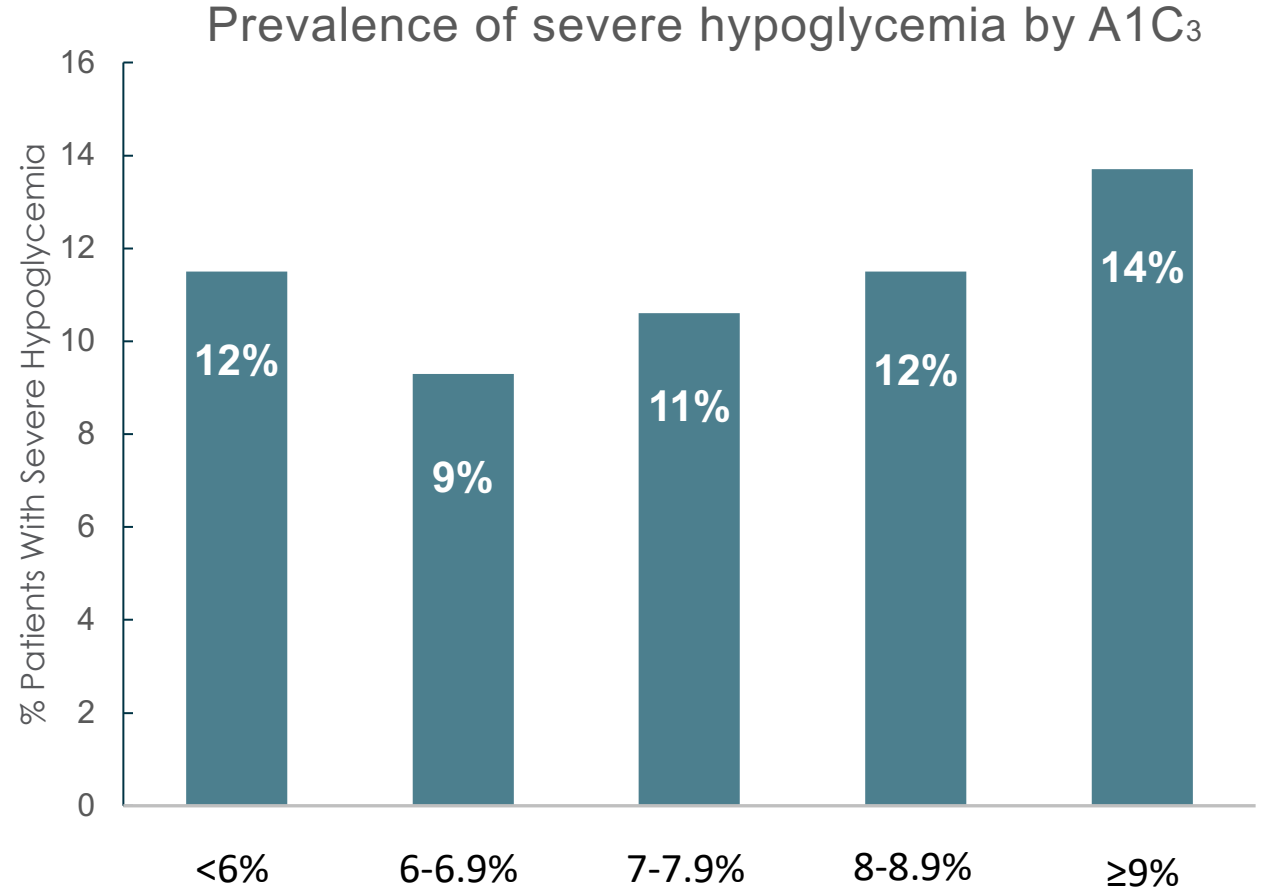


a. Cryer PE. Diabetes. 2008;57:3169-3176; b. Spanakis EK, et al. Endotext. 2018; c. International Hypoglycaemia Study Group. Diabetes Care. 2015;38:1583-1591; d. Gehlert RR, et al. J Diabetes Sci Technol. 2015;9:999-1005; e. Edridge CL, et al. PLoS One. 2015;10:e1026427.

# HbA1C Does Not Reveal Glycemic Variability or Extent or Timing of Hypoglycemia



9094 persons with Type 2 diabetes (ages 30-77 years) in Kaiser Diabetes Registry on glycemic lowering medication surveyed



1. Nathan DM et al. Diabetes Care. 2008;31(8):1473-1478. 2. Lipska KJ et al. Diabetes Care. 2013;36(11):3535-3542 3. Hirsch, I.F. et al. Diabetic Medicine. 2019;36(12):1637-1642

# Burden of Hypoglycemia is Prevalent in T2D Not on Insulin

Retrospective analysis of 2,708,762 Medicare Advantage Beneficiaries

19.4%

Hypoglycemic Related Encounters (HREs)

Prior to the 1<sup>st</sup> HRE

- 26% were using sulfonylurea
- 35.9% had evidence of CKD
- 11.5% had CKD + sulfonylurea

>80%

Occurrence in Ambulatory Care Setting



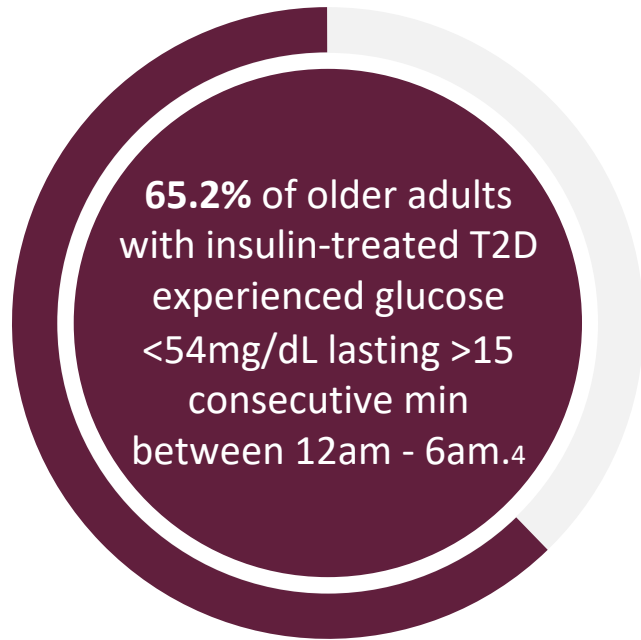
Primary care clinicians should be aware of the latest eligibility criteria for Medicare's coverage of CGM\*

\*Medicare covers Dexcom CGM for non-insulin-requiring patients with hypoglycemia who meet the Medicare coverage criteria. For a list of Medicare coverage criteria, visit the Centers for Medicare and Medicaid Services website

Hannah K. et. Al. Burden of Hypoglycemia in Medicare Advantage Beneficiaries with Type 2 Diabetes Not on Insulin. Presented at ADA Scientific Sessions; June 23-26, 2023; San Diego, CA 06/2023.

# Older Adults have Greater Risk of Hypoglycemia

The percentage of adults with diabetes increases with age, reaching **29.2%** among those aged 65 years or older.<sup>1</sup>



## Level 2 Hypoglycemia



**Hypoglycemia** in this age group is associated with significant morbidities leading to both physical and cognitive dysfunction leading to frailty and disability.<sup>2</sup>



**Severe hypoglycemia** is increased in older adults with diabetes, regardless of diabetes management.<sup>3</sup>



**Recurrent hypoglycemia** is common in older people with diabetes and is likely to be less recognized and under reported by patients and health care professionals.<sup>2</sup>



**Nocturnal Hypoglycemia** is very common and largely undiagnosed in older adults with insulin-treated T2 diabetes.<sup>4</sup>

1. Centers for Disease Control. National Diabetes Statistics Report 2022: Estimates of Diabetes and Its Burden in the United States. <https://www.cdc.gov/diabetes/data/statistics-report/index.html>. (Accessed April 22, 2022).

2. Abdelhafiz AH, et al. Hypoglycemia in older people - a less well recognized risk factor for frailty. *Aging Dis.* 2015 Mar; 10;5(2):156-67. doi: 10.14336/AD.2014.0330.

3. Weinstock RS et al. *J Clin Endocrinol Metab.* 2013;98(8):3411-9. doi: 10.1210/jc.2013-1589.

4. Boureau AS, et al. Nocturnal hypoglycemia is underdiagnosed in older people with insulin-treated type 2 diabetes: The HYPOAGE observational study. *J Am Geriatr Soc.* 2023;1-13. doi: 10.1111/jgs.18341.





# CMS Expanded CGM Coverage in 2023

Effective April 16, 2023 | CMS 2023 Changes

Meet *at least* 1 of the following criteria:

- Treated with **insulin**; or
- Documented **history of problematic hypoglycemia**
- Recurrent level 2 hypoglycemic events (glucose < 54 mg/dL) despite 2 or more attempts to adjust medication or modify treatment plan; or
- A history of **one level 3 hypoglycemic event** (glucose <54 mg/dL) requiring third-party assistance

As long as the beneficiary uses any insulin, the beneficiary is eligible for CGM coverage



# Basics of Billing for CGM

## Who owns the equipment?

- Patient or provider: unique codes for each
- Service occurs over > 1 day
- Minimum of 72 hours of wear
- Download of receiver occurs in office, cloud-based printout, or electronic transfer
- Service can be charged at the day of download or time of analysis

## Interpretation of data

- Minimum of 72 hours of wear time
- Face to face is not required, CPT standalone or with E&M Code
- Limitations of who can bill: physician, NP, PA (those who can prescribe)

# Codes and Descriptions

95249	Personal CGM - Startup/Training: Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 h; patient-provided equipment, sensor placement, hook-up, calibration of monitor, patient training and printout of recording. (Do not report more than once while patient owns device)
95250	Professional CGM - Ambulatory continuous glucose monitoring of interstitial fluid via a subcutaneous sensor for a minimum of 72 h; clinician-provided equipment, sensor placement, hook-up, calibration of monitor, patient training removal of sensor, and printout of recording. (Do not report more than once per mo)
95251	Ambulatory CGM of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72h; interpretation and report. (Do not report more than once per mo)
Evaluation and Management (E/M) Codes 99212-99215	Established patient visit or G0463. (Medicare outpatient clinic visits)
Eversense Only Codes	0446T (creation of subcutaneous pocket with insertion of implantable sensor, including system activation and patient education), 0447T (removal of implantable sensor from subcutaneous pocket via incision), 0448T (removal of sensor with creation of new pocket for new sensor at a different location, including system activation)

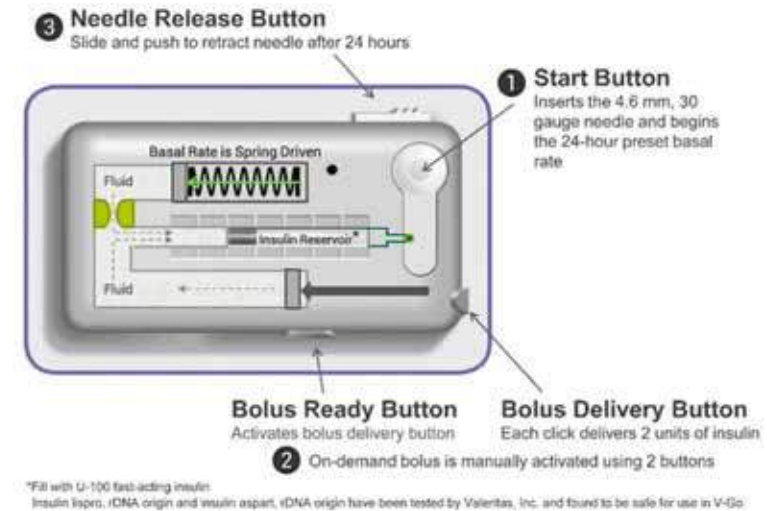
# Disposable Insulin Patch Pumps

## Vgo

- Basal/bolus delivery using rapid-acting analog
- Basal available in 20, 30, or 40 units
- Bolus in 2-unit increments for a maximum bolus of 36 units for the day
- 1-day wear

## CeQur Simplicity

- Delivers mealtime, snack, or correction insulin for hyperglycemia
- Uses rapid-acting analog
- Bolus in 2-unit increments
- Holds 200 units of insulin
- Up to 3 days wear



# Tempo Smart Pen/Button & Platform



This cap is placed on a corresponding pen and can record the dose and time of an insulin injection.

It interfaces with tempo platform.

# NovoPen 6 and NovoPen Echo Plus



Smart pens can record dose and time of injections.  
They can connect with apps to assist in management.

# Pre-Test | Question 10

Betty is a 58-year-old woman with a history of hypertension and dyslipidemia. She also has had Type 2 diabetes for 8 years. She is on medications such as **Atorvastatin 40mg, Lisinopril 20MGZX, semaglutide 2mg** (started 8 months ago (A1c was 9.2% before this and BMI 34)), and **Metformin 1500mg daily**. Her BMI is 32, and her HbA1c is 8.0%. She finds difficulties in reducing her fasting glucose to goal (132-166mg/dl, no lows). She also got a professional CGM, which indicated that in 15 days, 53% of the time, she was in high or very high time in range.

**What is the next best step for Betty to manage her glucose levels?**

- a) Stop semaglutide and start a basal-bolus insulin program.
- b) Stop metformin and semaglutide, start a basal insulin.
- c) Continue metformin and semaglutide, and add a basal Insulin
- d) No changes at this time, work with Diabetes Education to include Medical Nutritional Therapy to get to treatment goal.

# Bringing it All Together: Patient Cases



# Case 1: Betty

- Betty is a 58 y/o female
- She has had type 2 diabetes for 8 years
- History of Hypertension, dyslipidemia
- Medications:
  - Atorvastatin 40 mg
  - Lisinopril 20 MGZX
  - Semaglutide 2mg, started 8 months ago (A1c was 9.2% before this and BMI 34)
  - Metformin 1500 mg daily
- She is happy with her response but cannot seem to get her fasting glucose to goal (132-166 mg/dl, no lows)
- Thought glucose should be easier than BP and lipids—she has these well-managed
- BMI 32, A1c 8.0%
- Professional CGM obtained
  - Treatment Goal : A1c <7% and when available TIR >70% with <5% low BG



# Case 1: Betty

## AGP Report

November 29, 2022 - December 13, 2022 (15 Days)

LibreView

### GLUCOSE STATISTICS AND TARGETS

November 29, 2022 - December 13, 2022 **15 Days**  
 Time CGM Active: **100%**

Ranges And Targets For	Type 1 or Type 2 Diabetes
Glucose Ranges	Targets % of Readings (Time/Day)
Target Range 70-180 mg/dL	Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (6h)
Above 250 mg/dL	Less than 5% (1h 12min)

Each 5% increase in time in range (70-180 mg/dL) is clinically beneficial.

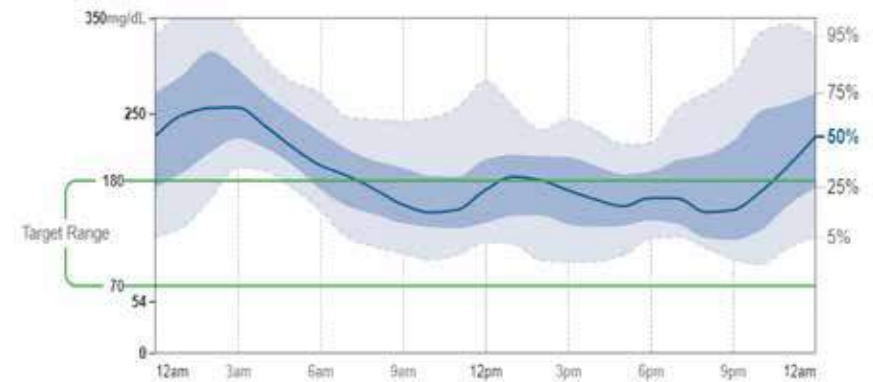
**Average Glucose** **191** mg/dL  
**Glucose Management Indicator (GMI)** **7.9%**  
**Glucose Variability** **31.8%**  
 Defined as percent coefficient of variation (%CV)

### TIME IN RANGES



### AMBULATORY GLUCOSE PROFILE (AGP)

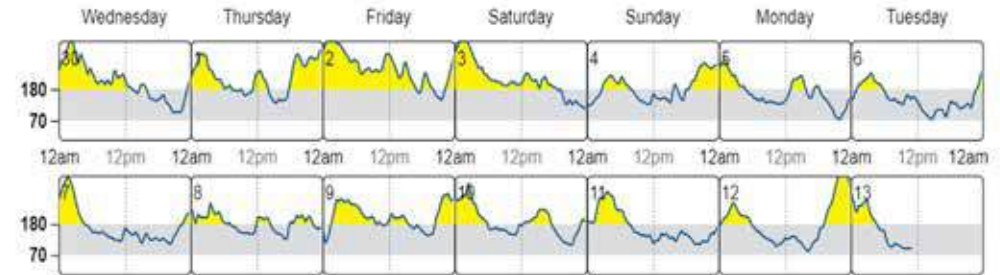
AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if occurring in a single day.



### DAILY GLUCOSE PROFILES

Most recent 14 days. See Weekly Summary report for more days.

Each daily profile represents a midnight to midnight period with the date displayed in the upper left corner.



Source: Battelino, Tadij, et al. "Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range." Diabetes Care, American Diabetes Association, 7 June 2019. <https://doi.org/10.2337/dci.19-0028>

# Case 1: Betty – Case Question

**What would your next steps be for Betty?**

1. Stop semaglutide and start a basal-bolus insulin program.
2. Stop metformin and semaglutide, start a basal insulin.
3. Continue metformin and semaglutide, and add a basal Insulin
4. No changes at this time, work with Diabetes Education to include Medical Nutritional Therapy to get to treatment goal.

# Case 1: Betty - Plan

## Betty's Plan:

- Continue Metformin and Semaglutide
- Refer for Diabetes Education to Include Medical Nutritional Therapy
- Start Basal insulin 20 Units at 9 pm daily
- Titrate Basal Insulin to appropriate Fasting Blood Glucose
- Prescribe Personal CGM
- Discuss prevention and treatment of hypoglycemia
- Prescribe Glucagon therapy



# Case 1: Betty

Betty is feeling back in control.



A1c is now 6.8%



Fasting glucose 80-  
110 mg/dl, random  
80-152 mg/dl

No lows



Meds:  
Metformin 2000 mg  
daily, semaglutide 2  
mg weekly, basal  
insulin 24 units daily



Weight is stable

BMI 32

## Case 2: Javier

- Javier is a 67 years old male who was diagnosed with type 2 diabetes 8 months ago
- He was drinking and urinating more often. He thought it was a prostate problem. Did not want to take injections
- A1c at diagnosis was 12.1%
- Metformin 2000 mg daily (at diagnosis)
- Glimepiride 4 mg daily (at diagnosis)
- Sitagliptin 100 mg daily (1 month ago)
- Empagliflozin 25 mg daily (1 month ago)
- Has started walking 20-30 minutes daily
- Current A1c is 10.1%



## Case 2: Javier

- He is very concerned about controlling his diabetes
  - His dad and uncle had complications from diabetes
  - He is monitoring several times daily
  - Understands need to lower BG and looking for options –not sure these medications are working
- Has met with a Diabetes Educator and received Medical Nutritional Therapy
- Wants to understand why his glucose jumps
- He is trying to “behave”



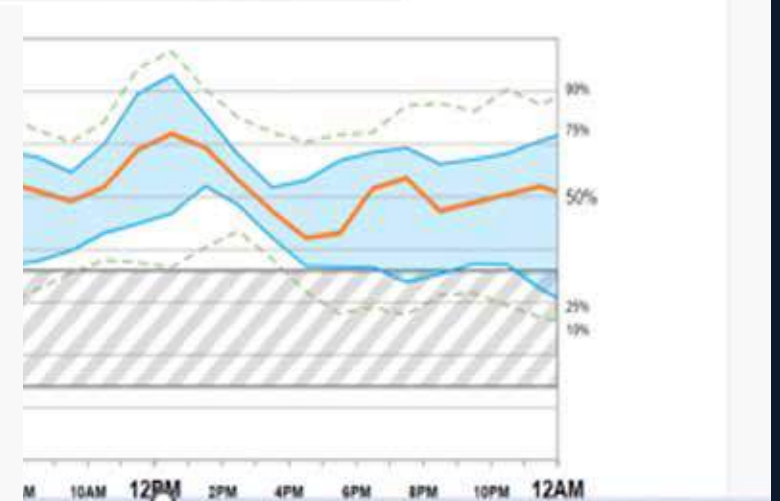
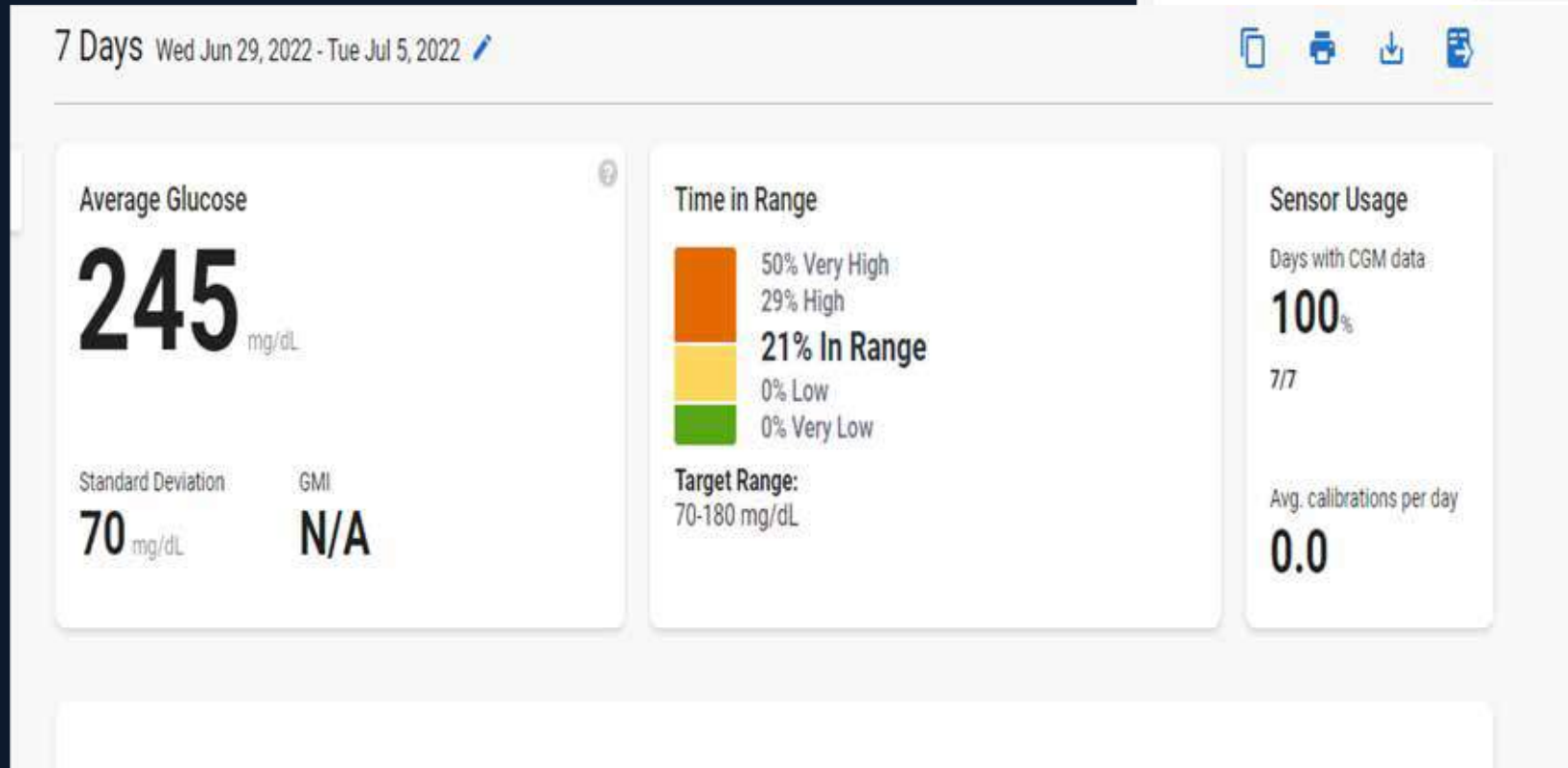
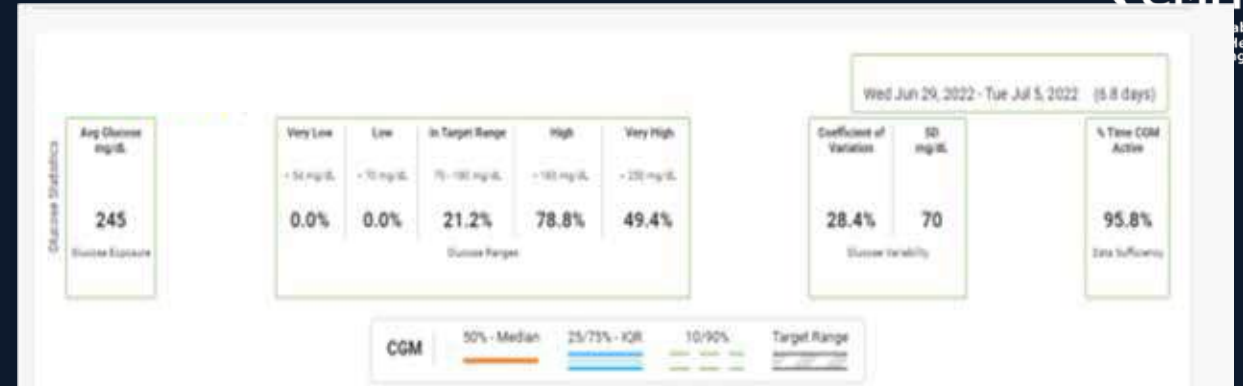
## Case 2: Javier – Case Question

**What do you recommend for Javier to help him understand his glucose patterns?**

- a) 7-point glucose monitoring (fasting, before and after meals and bedtime)
- b) No checking needed– he is not on insulin
- c) Check only in the morning- once the fasting is at goal we can worry about the rest
- d) Offer CGM pro version to wear



# Case 2: Javier – CGM Pro



## Case 2: Javier – Case Question

**What is your next treatment recommendation based upon his CGM?**

- a) Do not change present medications, add basal Insulin
- b) Stop Sitagliptin, keep Metformin and Empagliflozin add basal and bolus Insulin
- c) Do not change present medications, add basal insulin and GLP-1 RA
- d) Stop all medications except Metformin and add basal and bolus insulin

# Case 2: Javier - Plan

## Javier's Plan:

- Metformin 2000 mg daily
- empagliflozin 25 Mg daily
- Glimepiride 4 mg daily
- Stop sitagliptin
- Add a Basal insulin, and titrate to fasting treatment goal
- Prescribe personal CGM
- Prescribe Glucagon



# Case 2: Javier

2 months later | Javier is feeling much better.



Basal insulin 42  
units daily (0.4  
units/kg)



Metformin,  
empagliflozin,  
glimepiride (only  
sometimes makes  
him feel shaky and  
hungry)



Fasting glucose readings  
are 100-130 mg/dl  
  
Post-meal glucose  
readings are 100-220  
mg/dl



A1c is now 8.0%, and he  
has some hypoglycemia  
if he walks rather than  
eating lunch  
  
No severe hypoglycemic  
episodes

## Case 2: Javier – Case Question

**What do you recommend for Javier now?**

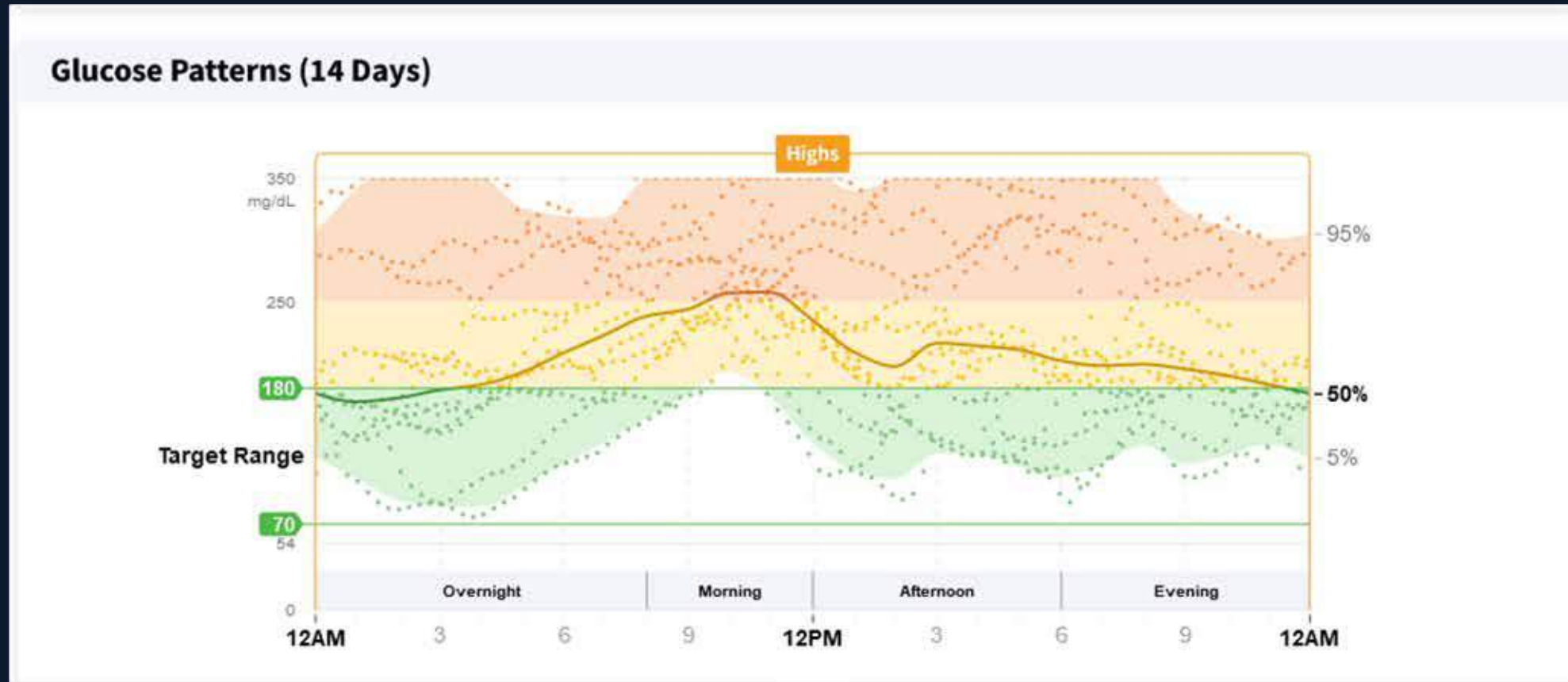
- a) Stop basal insulin
- b) Stop glimepiride
- c) Stop glimepiride and start mealtime insulin
- d) Stop glimepiride and start a GLP-1RA

## Case 3: Trevor

- 43-year-old man with type 2 diabetes for 10 years
- Co-morbidities: HTN, dyslipidemia, MASLD, no microvascular or macrovascular complications
- Meds: Glargine 40 units, Aspart 20 units before meal (may miss lunch dose), Metformin ER 1500 mg daily
- Has not had any diabetes education or medical nutritional therapy since diagnosis
- Wears CGM but does not look at it unless it alarms (and sometimes turns them off)
- A1c 8.6 %



# Case 3: Trevor



# Case 3: Trevor - TM





## Case 3: Trevor – Case Question

**What do you notice on the CGM tracing?**

- a) Persistent first am hypoglycemia
- b) Global hyperglycemia
- c) Morning meals are adequately covered
- d) Lunch time dosing leads to hypoglycemia

## Case 3: Trevor – Case Question

**After reviewing this patient's CGM data what changes would you make to his therapy?**

- a) No changes at this time, A1c is 8.2%, refer to diabetes education
- b) Increase both basal and rapid-acting insulin, add SGLT2 inhibitor, refer to diabetes education
- c) Increase basal insulin only, refer to diabetes education
- d) Increase basal insulin, continue rapid-acting insulin at the present dose add a weekly GLP1 RA, and refer to diabetes education.

# Case 3: Trevor - Plan

## Trevor's Plan

- Increased Glargine to 46 units
- Continued Aspart to 20 units before each meal
- Added a weekly GLP-1 RA
- Referred For Diabetes Education and Medical Nutritional Therapy
- Agreed on a A1c Goal  $<7\%$  (with TIR  $>70\%$  and  $<5\%$  low Blood Glucose)
- Prescribed Glucagon pen
- Asked patient to use CGM more actively to help with insulin dosing



# Case 3: Trevor – Follow Up Data



## Case 3: Trevor – Patient Comments

“It is the CGM that made the real difference. When I ate, I could see what happened to my glucose. If I forgot my meal insulin, wow my glucose really went up and stayed up for a few hours. Even small amounts of activity helped lower my glucose levels.”