

SOCIEDAD PUERTORRIQUEÑA DE
ENDOCRINOLOGIA Y DIABETOLOGIA

Use of BeAM and AGP to Determine the Next Anti-Glycemic Therapy

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Disclosures

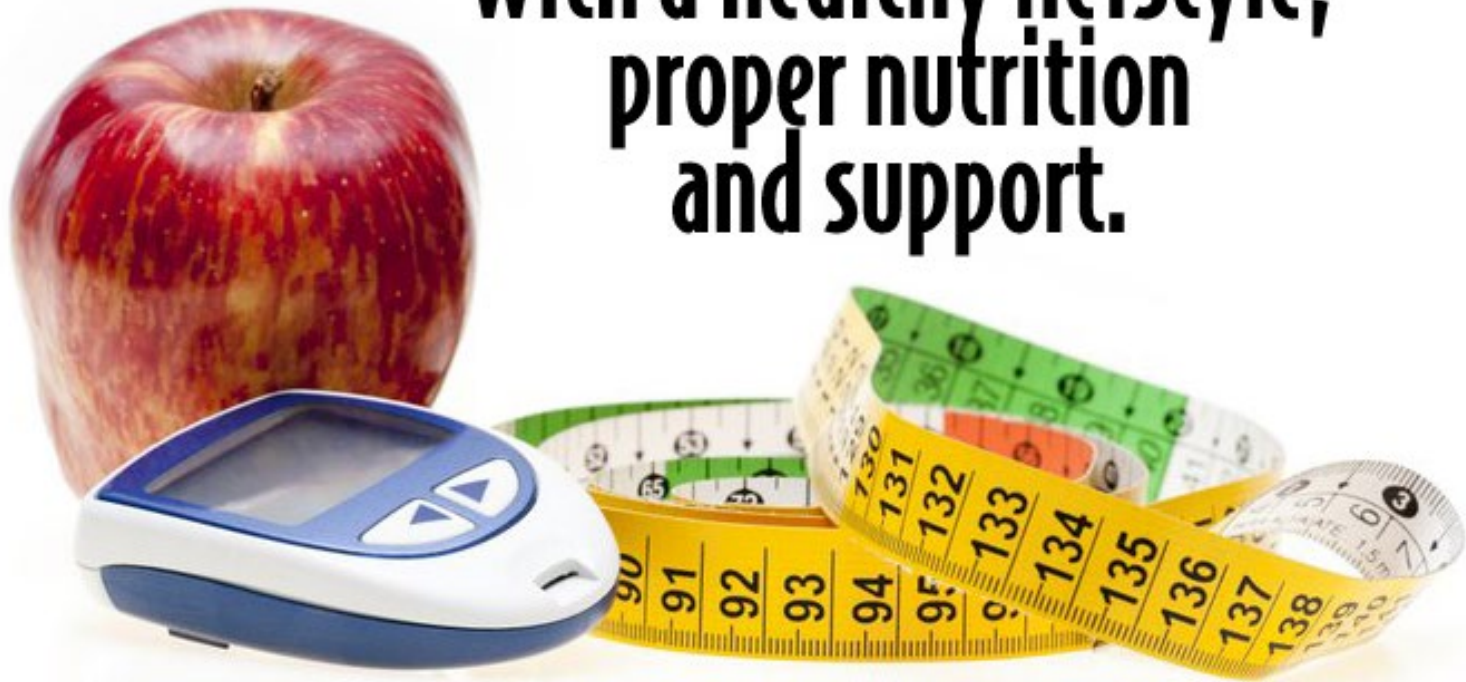
Dr. Zisman is member of the speaker bureau and receives honoraria for lectures from *Sanofi* and *Novo Nordisk*.

Learning Objectives

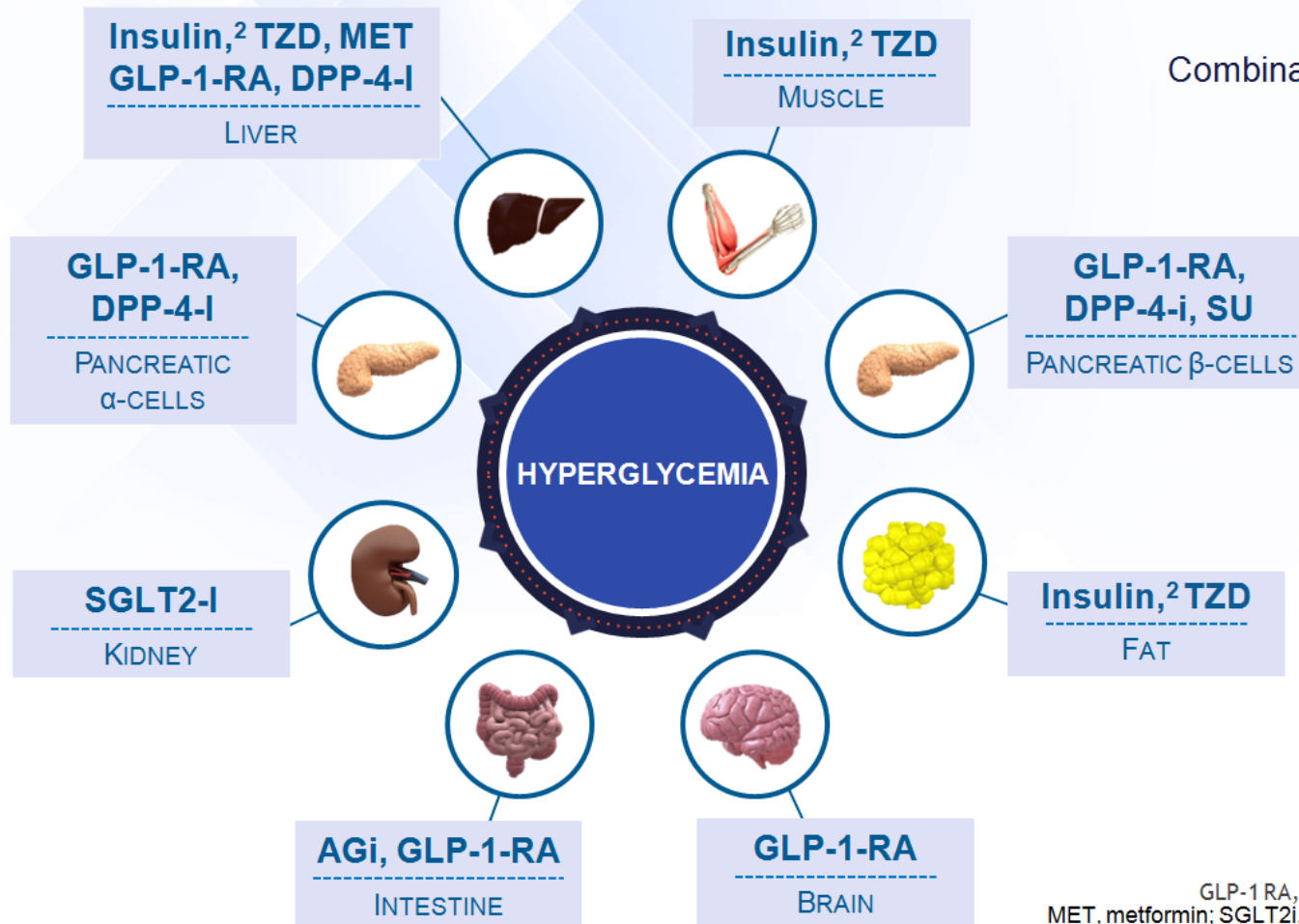
- To recognize persistent clinician inertia in advancing therapies as diabetes evolves
- To understand the BeAM value concept
- To identify utility of BeAM value to decide therapies in patients with type 2 diabetes on basal insulin
- To appreciate the role of Ambulatory Glucose Profiles (AGP) in determining the most appropriate therapeutic interventions to follow

True, but Not That Simple...

**YOU can control diabetes
with a healthy lifestyle,
proper nutrition
and support.**



Pathophysiology of type 2 diabetes and complimentary effects of current medications



Combinations of oral and injectable therapies may address multiple pathophysiologic abnormalities linked to T2DM.¹

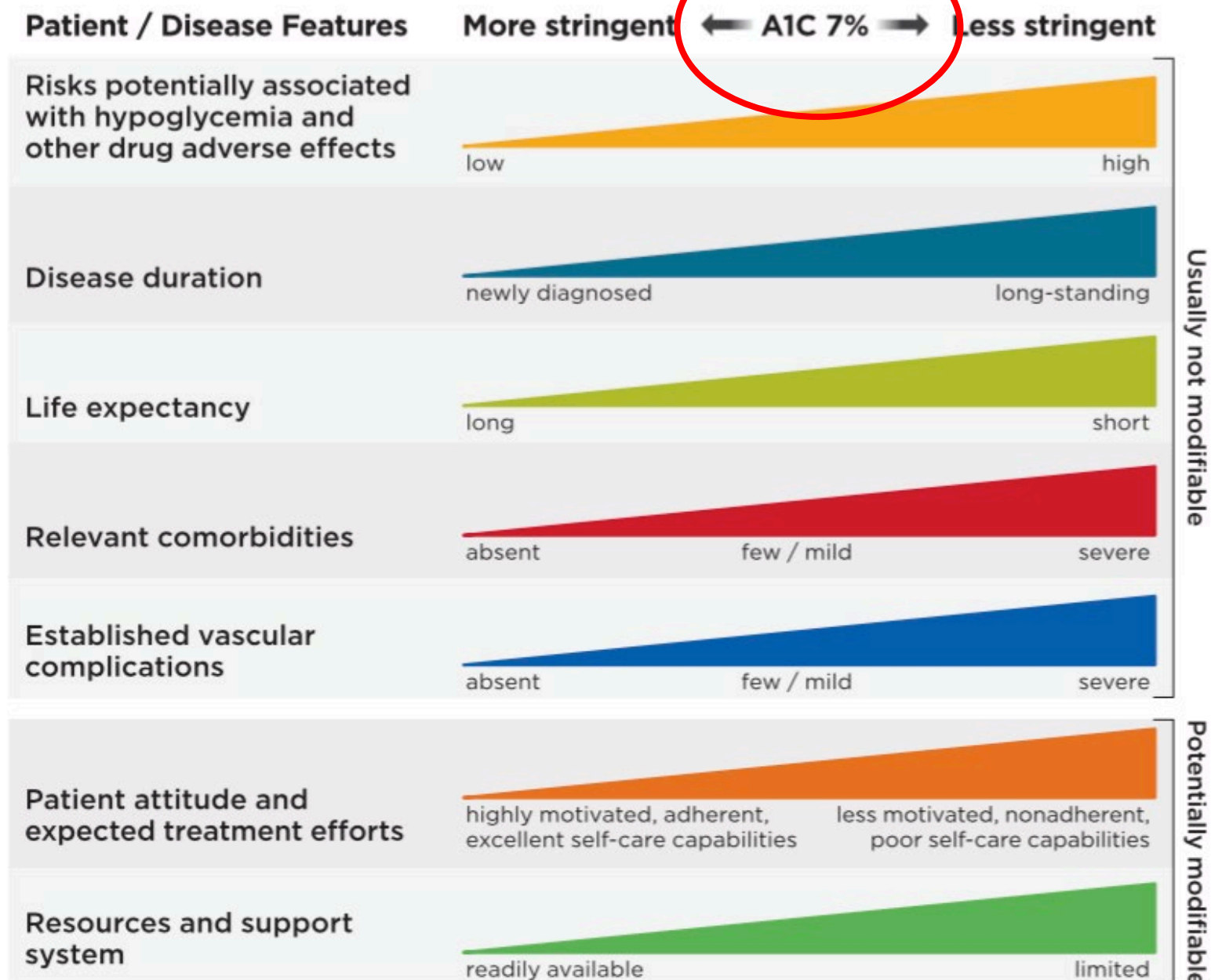
Most classes have multiple sites of action leading to increased antihyperglycemic efficacy.^{2,a}

AGi, α -glucosidase inhibitor;
DPP4i, dipeptidyl peptidase-4 inhibitor;
GLP-1 RA, glucagon-like peptide-1 receptor agonist;
MET, metformin; SGLT2i, sodium-glucose co-transporter-2 inhibitor;
SU, sulfonylurea; TZD, thiazolidinedione.

1. Ferrannini E et al. *Eur Heart J*. 2015;36(34):2288-2296.

2. ADA. *Diabetes Care*. 2017;40(suppl 1):S1-S135.

Approach to the Management of Hyperglycemia



Patient-Centered Approach Guides Pharmacologic Choices

- Pathophysiology
- Efficacy
- Potential side effects (Safety)
 - especially hypoglycemia and weight gain
- Comorbidities
- Anticipated added benefits
 - Weight loss
 - Cardiovascular protection
- Cost
- Patients preferences and abilities

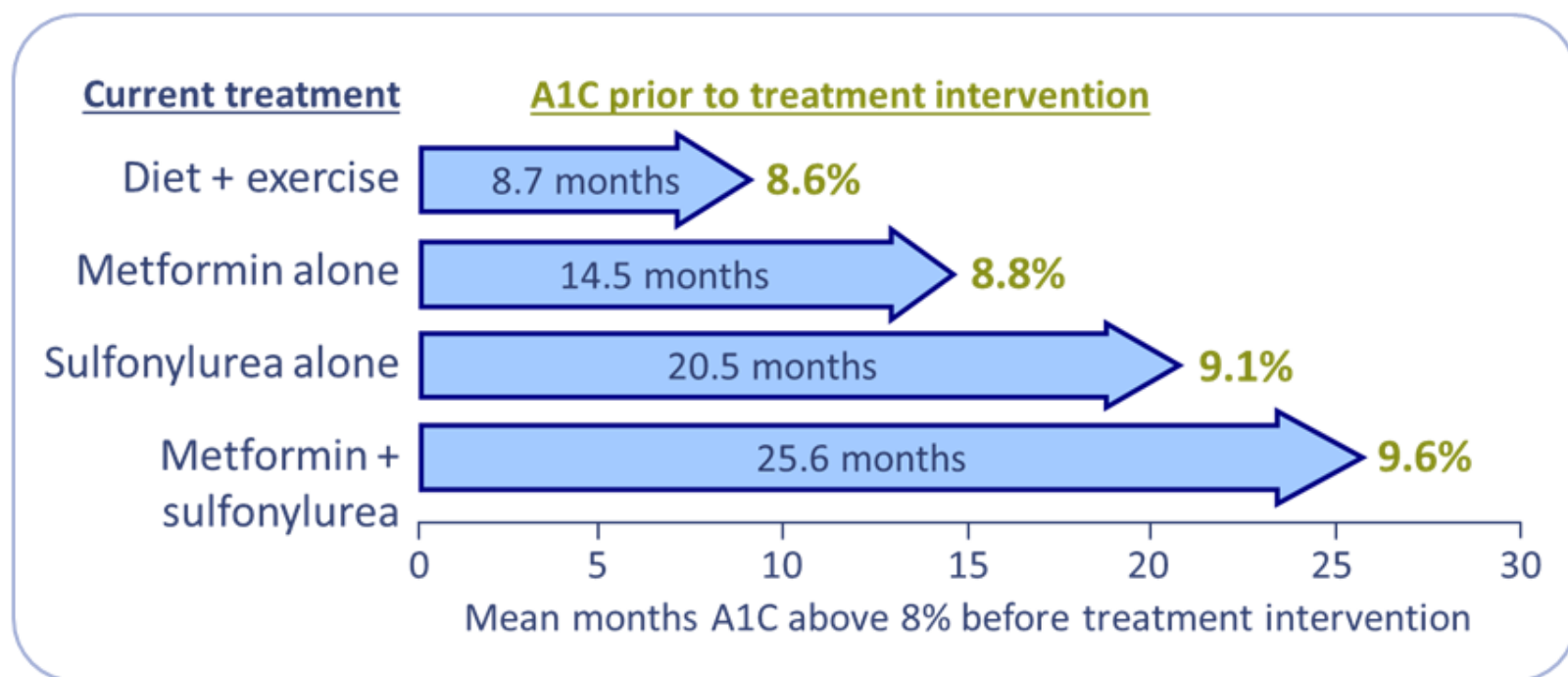
Overcoming Clinician Inertia

Time is Not Our Friend

- Diabetes is a progressive disease
- ADA recommends assessment every 3 months
 - Assess — Identify — Intensify
- We typically take too long to intensify therapy

Are we waiting too long to make an impact?

Delay in Changing Therapy After Failure of Oral Medications



Study Design: A prospective, population-based study using retrospective observational data. All 7208 complete courses of treatment with nondrug therapy, sulfonylurea monotherapy, metformin monotherapy, and combination oral antihyperglycemic therapy between 1994 and 2002 were identified among members of the Kaiser Permanente Northwest Region. Mean cumulative glycemic burden, defined as A1C-months >8.0%, was calculated for each treatment. Intervention was defined as abandonment or change in therapy.

Overcoming Clinician Inertia

Are We Taking Too Long?

VA Study:

- Recent Veterans Administration 5-year study
- Metformin monotherapy was satisfactory in 50%
- For those who intensified beyond metformin:
 - SU (79%) – 11 months
 - TZD (6%) – 13 months
 - Insulin (8%) – 13 months
- Better historically, but still too long

ADA guidelines for the management of T2DM: General recommendations

Start with Monotherapy unless:

A1C is greater than or equal 9%, **consider Dual Therapy**.

A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, **consider Combination Injectable Therapy** (see next slide).

Monotherapy

Metformin

Lifestyle Management

EFFICACY	high
HYPO RISK	low risk
WEIGHT	neutral/loss
SIDE EFFECTS	GI/lactic acidosis
COSTS	low

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- & disease-specific factors):

Dual Therapy

Metformin +

Lifestyle Management

	Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
EFFICACY	high	high	intermediate	intermediate	high	highest
HYPO RISK	moderate risk	low risk	low risk	low risk	low risk	high risk
WEIGHT	gain	gain	neutral	loss	loss	gain
SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GU, dehydration, fxs	GI	hypoglycemia
COSTS	low	low	high	high	high	high

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- & disease-specific factors):

Triple Therapy

Metformin +

Lifestyle Management

Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal) +
TZD	SU	SU	SU	SU	TZD
or DPP-4-i	or DPP-4-i	or TZD	or TZD	or TZD	or DPP-4-i
or SGLT2-i	or SGLT2-i	or SGLT2-i	or DPP-4-i	or SGLT2-i	or SGLT2-i
or GLP-1-RA	or GLP-1-RA	or Insulin (usually basal)	or GLP-1-RA	or Insulin (usually basal)	or GLP-1-RA
or Insulin (usually basal)	or Insulin (usually basal)		or Insulin (usually basal)		

If A1C target not achieved after approximately 3 months of triple therapy and patient (1) on oral combination, move to basal insulin or GLP-1 RA, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1 RA or mealtime insulin. Metformin therapy should be maintained, while other oral agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (ie, adding a fourth antihyperglycemic agent).

Combination Injectable Therapy

Initiate Basal Insulin

Usually with metformin +/- other noninsulin agent

Start: 10 U/day or 0.1–0.2 U/kg/day

Adjust: 10–15% or 2–4 units once or twice weekly to reach FBG target

For hypo: Determine & address cause; if no clear reason for hypo,
↓ dose by 4 units or 10–20%

If A1C not controlled, **consider
combination injectable therapy**

What Can We Learn from CBG records?

Review of CBG records (MET, DPP-4 inhibitor, basal insulin qHS):

aBkfst	pBkfst	aLunch	pLunch	aDinner	pDinner	Bedtime
128		146		168		211
122	166			184		193
108		158		146	194	188
98			171	163		194

- Is there a particular pattern to these readings?
- What can you learn from the CBG review regarding the next therapeutic decision to make?

The BeAM value:

- Many patients with T2DM require therapies to correct postprandial glycemic excursions to attain control
- It is unclear when basal insulin is optimized and/or when additional intervention should be added:
 - Based on FBG levels?
 - Based on total daily insulin dose used?
- There is a need for simplified, clinically-relevant methods to help determine which patients using basal insulin need intensification of prandial coverage.

The BeAM value:

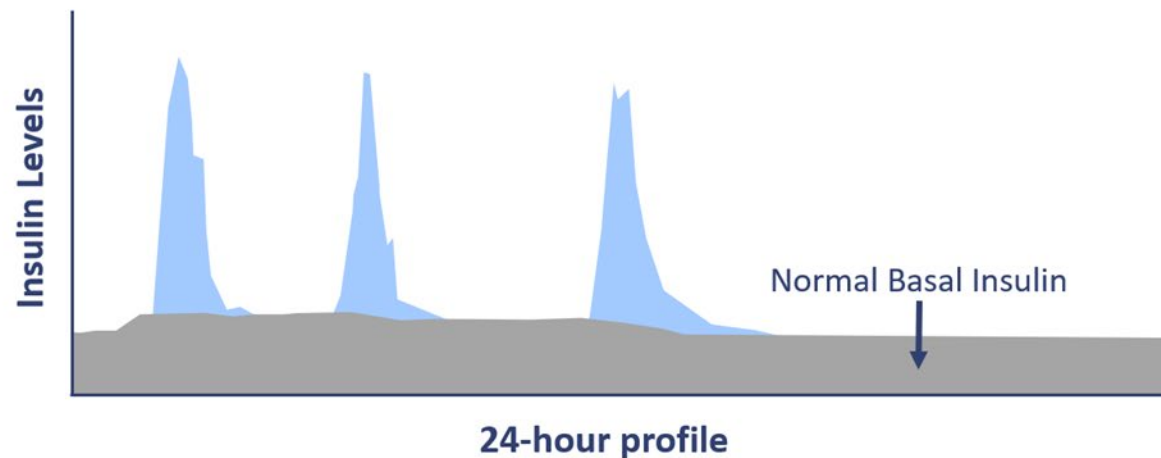
BeAM value = Bedtime glucose – AM (fasting) glucose

- Simple
- Readily Accessible
- Useful

Replacing Insulin Secretion:

Physiologic insulin secretion includes basal and prandial components

Conceptual Action Profile of Physiologic Insulin Secretion

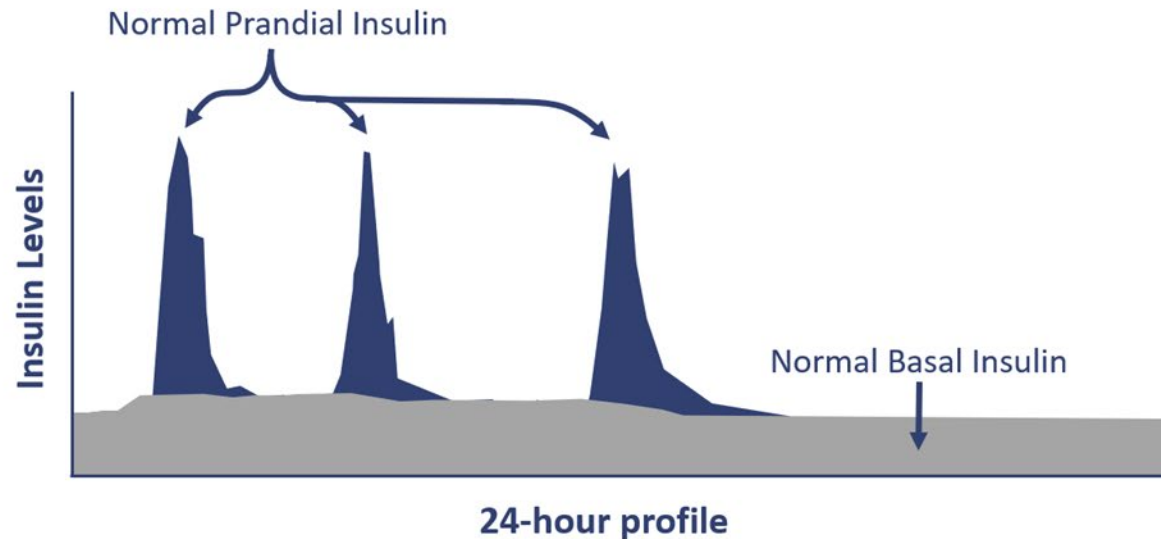


Basal insulin is secreted 24 hours a day and accounts for approximately 50% of daily insulin secretion

Replacing Insulin Secretion:

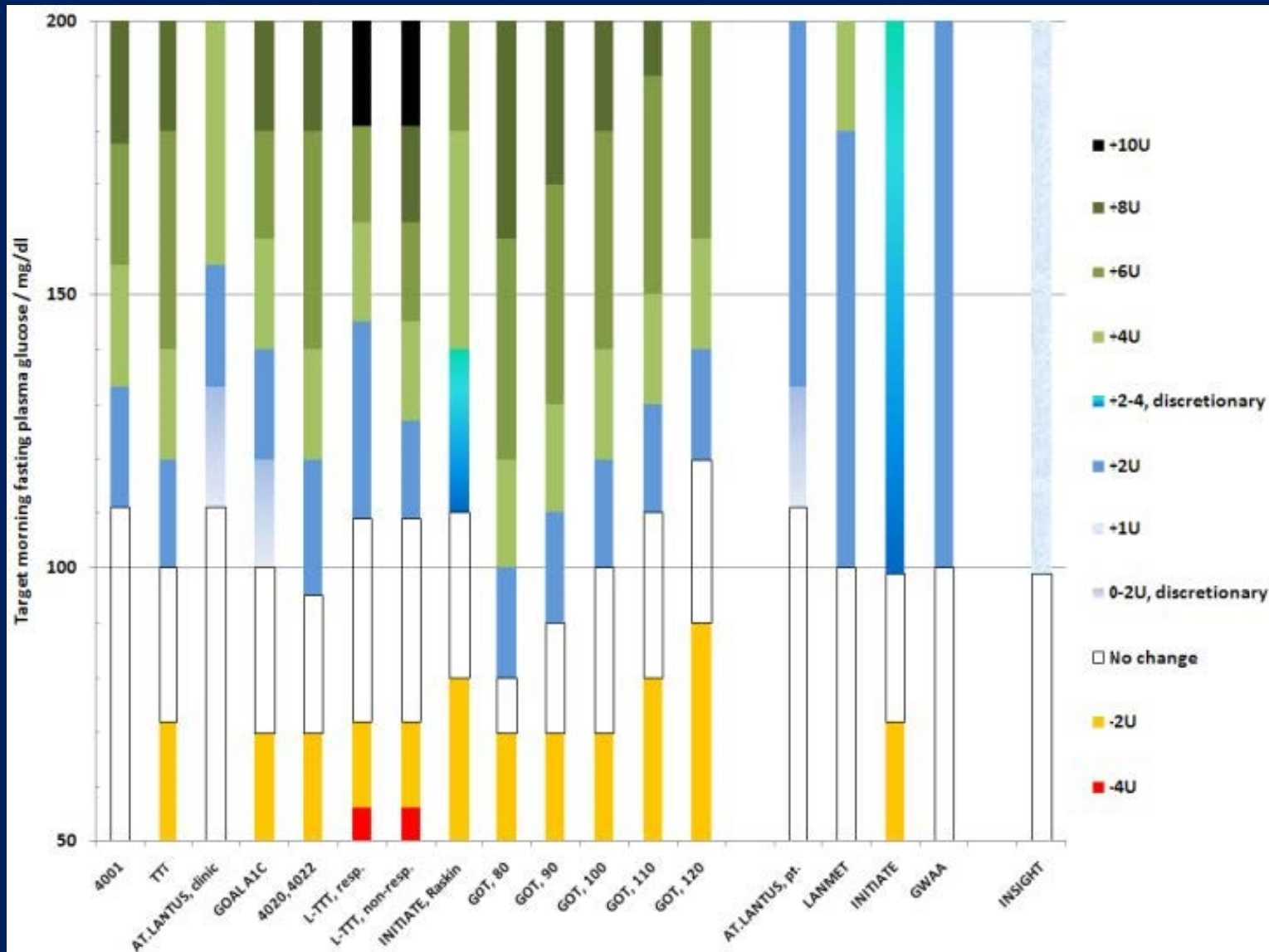
Physiologic insulin secretion includes basal and prandial components

Conceptual Action Profile of Physiologic Insulin Secretion



Basal insulin is secreted 24 hours a day and accounts for approximately 50% of daily insulin secretion

Insulin Titration Algorithms for Basal Insulin



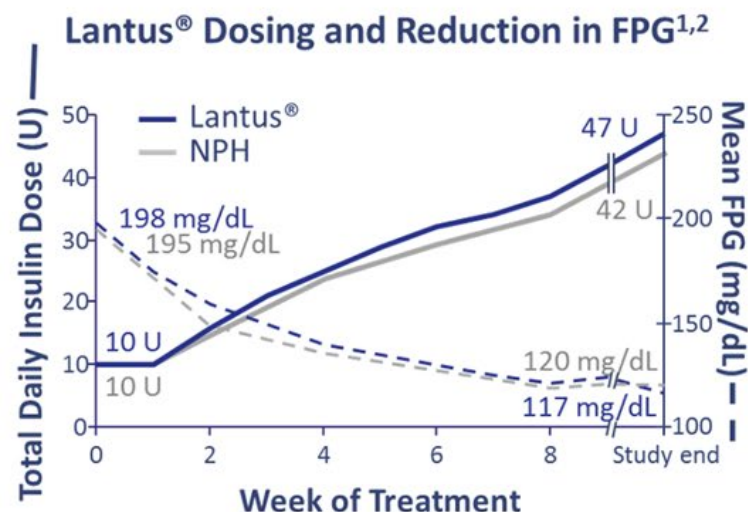
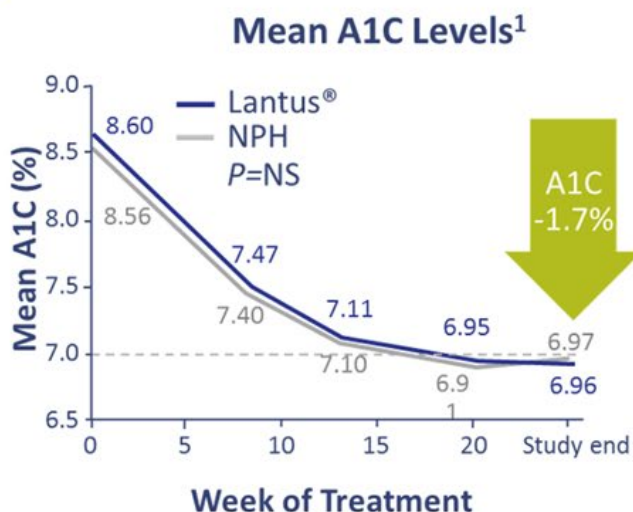
Insulin Titration Algorithms for Basal Insulin

Treat-to-Target Study

Appropriate dose and titration helps achieve glycemic targets

Results

24-week treat-to-target trial of Lantus® (insulin glargine [rDNA origin] injection) vs NPH



- Insulin starting dose and forced titration schedule were determined by the study protocol
- 58% of patients randomized to Lantus® achieved A1C goals
- Titration is required to achieve FPG target

Please see Important Safety Information for Lantus® at the beginning of this section.
Please see provided full Prescribing Information for Lantus® available at this event.

1. Riddle MC et al. *Diabetes Care*. 2003;26(11):3080-3086.

2. Data on file, Sanofi US.

Insulin Titration Algorithms for Basal Insulin

GOT Study:

In the GOT study using forced titration algorithms of basal insulin to five different FBG targets (80, 90, 100, 110, 120), a 20 U dose difference between the extreme groups resulted in only 0.25% difference in A1C

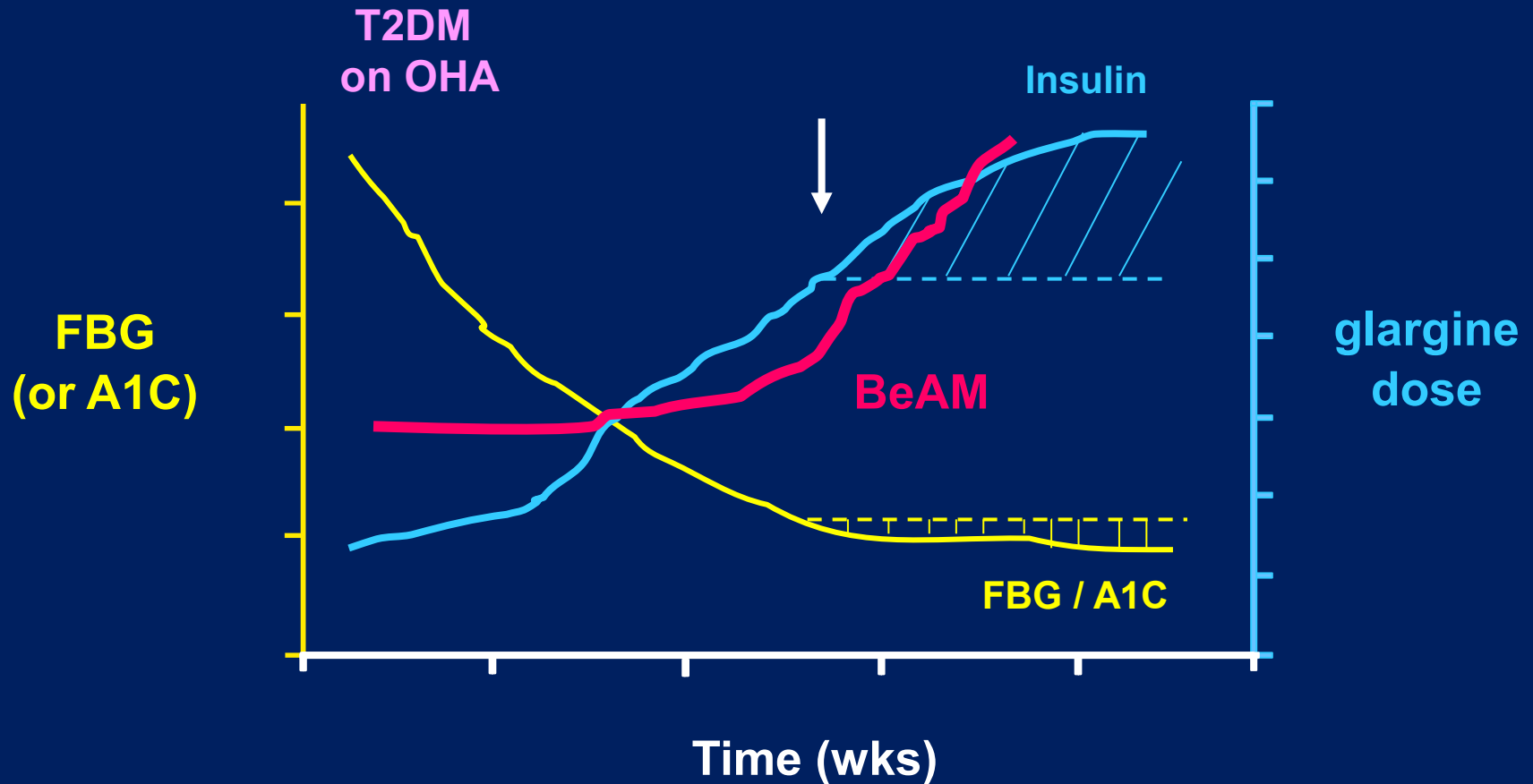
Despite limited benefit in A1C reduction, lower titration targets increased the risk of severe hypoglycemia

Insulin Titration Algorithms for Basal Insulin

Conclusion:

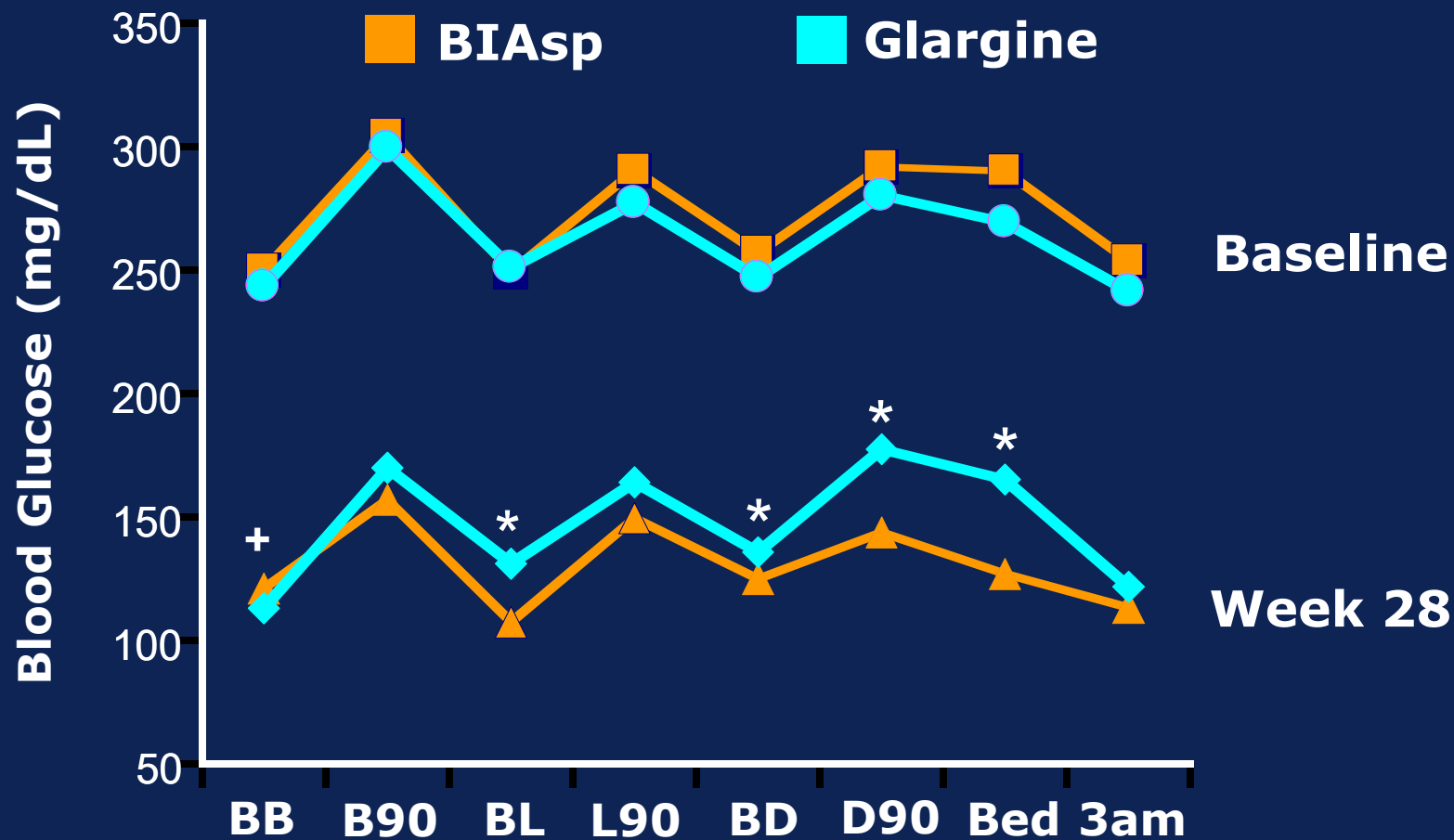
“The increasing average insulin doses after 12 weeks in the face of diminishing incremental returns for glycemic control suggests that introduction of meal insulin after 12 weeks for patients, who are still not in adequate glycemic control, may be a better approach than continued up-titration of the basal insulin.”

Predicted Relationship Between BeAM and the decline in FBG (A1C)



INITIATE:

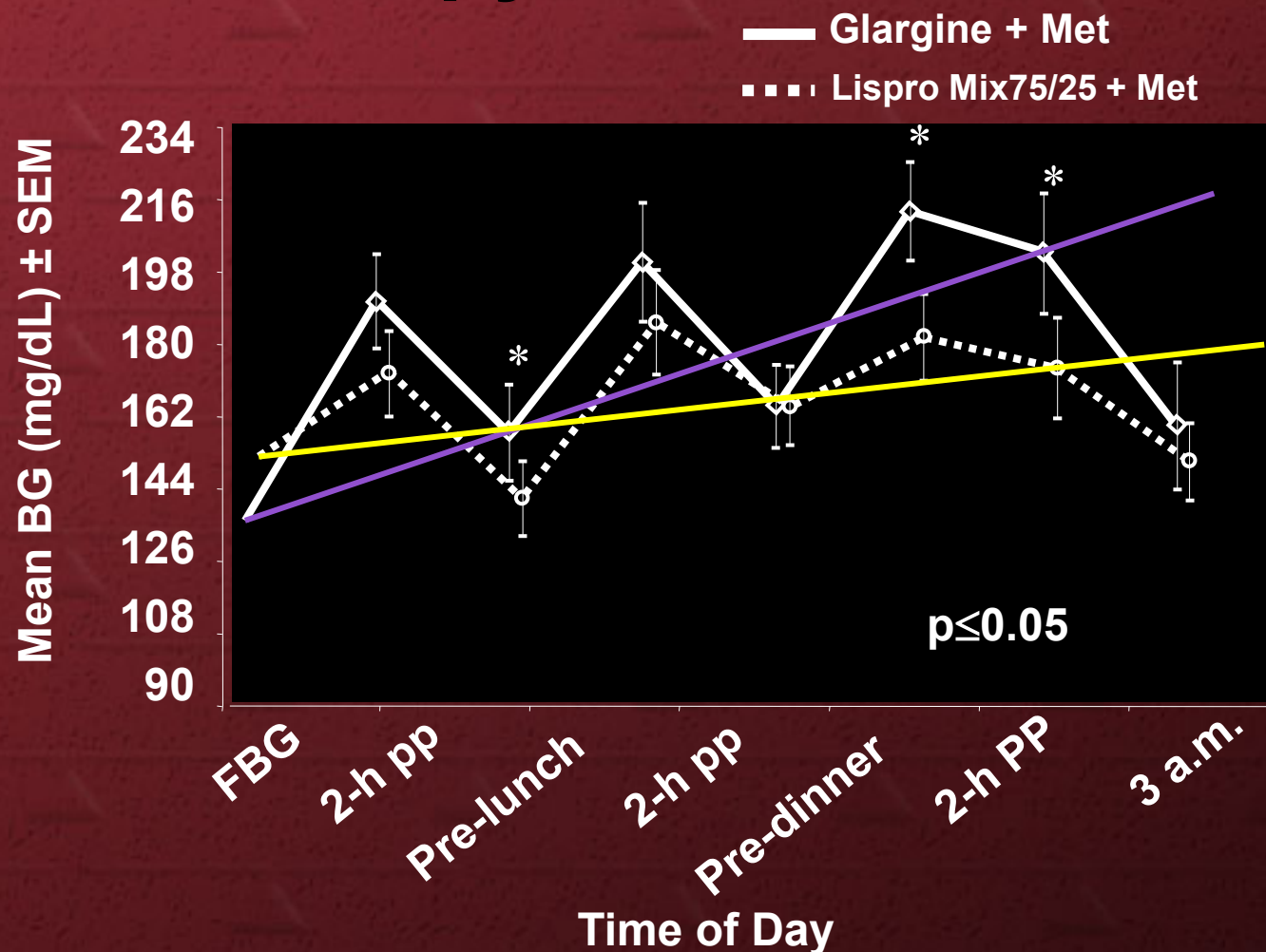
8-Pt BG Profiles - Baseline and Wk 28



* BIAsp 70/30 lower BG vs glargine $P < 0.05$

+ Glargine lower BG vs BIAsp 70/30, $P < 0.05$

PAIR-IN Study: Mean BG Profiles at End of Therapy



**BMJ Open
Diabetes
Research
& Care**

BeAM value: an indicator of the need to initiate and intensify prandial therapy in patients with type 2 diabetes mellitus receiving basal insulin

Ariel Zisman,¹ Francienid Morales,² John Stewart,³ Andreas Stuhr,⁴ Aleksandra Vlajnic,² Rong Zhou⁵

To cite: Zisman A, Morales F, Stewart J, *et al.* BeAM value: an indicator of the need to initiate and intensify prandial therapy in patients with type 2 diabetes mellitus receiving basal insulin. *BMJ Open Diabetes Research and Care* 2016;**4**:e000171. doi:10.1136/bmjdr-2015-000171

AS was at Sanofi US, Inc. at the time this study was conducted.

ABSTRACT

Introduction: In patients with type 2 diabetes mellitus (T2DM) with uncontrolled glycemia despite ongoing upward titration of basal insulin, targeting postprandial hyperglycemia may be required. Nevertheless, the point at which basal insulin is fully optimized and postprandial glucose (PPG) should be targeted with additional treatment remains unclear. We report here on the BeAM value (difference between bedtime and morning blood glucose values) as an indicator of the need to target PPG.

Methods: This study had 3 stages: exploratory, main, and proof-of-concept analyses. For the exploratory and main analyses, data were pooled from phase 3 trials in adults with T2DM adding basal insulin to oral antidiabetic drugs (OADs). The main analysis included

Key messages

- In patients with type 2 diabetes mellitus with uncontrolled glycemia despite optimally titrated basal insulin, targeting postprandial hyperglycemia may be required.
- We report here on the BeAM value (difference between bedtime and morning blood glucose values) as an indicator of the need to target postprandial glucose.
- The BeAM value described in this study is a simple, easy-to-calculate value that may identify patients with type 2 diabetes mellitus using basal insulin whose postprandial glucose needs targeting.

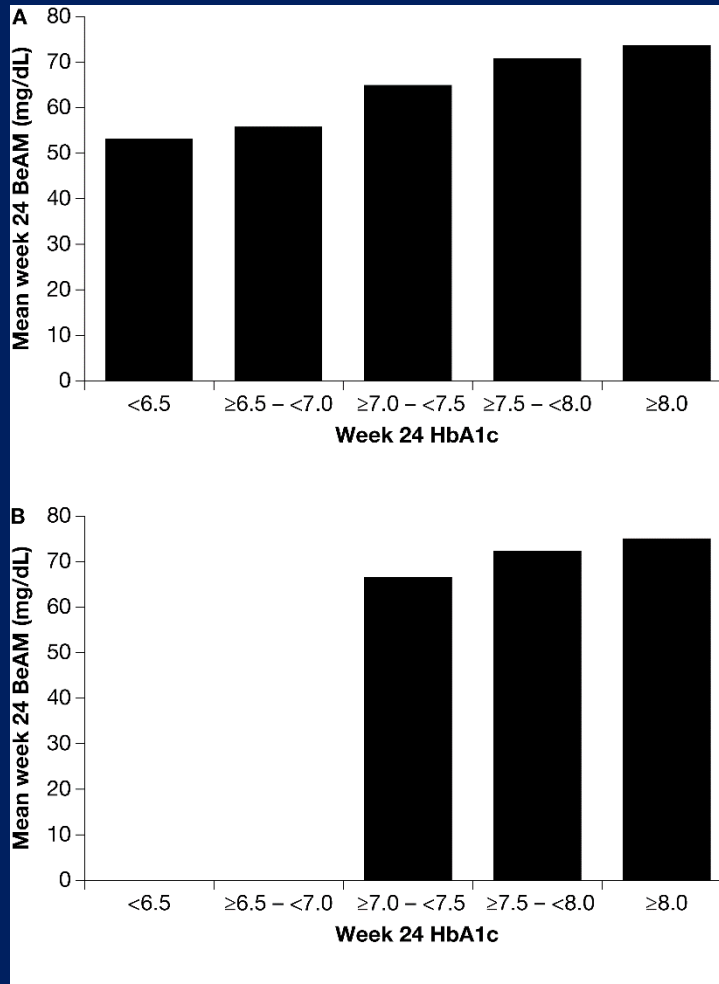
The BeAM value Concept:

- Despite basal insulin titration, A1C and FBG eventually reach a plateau, and primary providers may continue up-titration of basal insulin, causing inadvertent over-insulinization.
- Many patients do not routinely monitor PPG, and it is perceived as being inconvenient and disruptive of their daily routine.
- We propose that bedtime (or 2h postdinner) values, roughly **reflect cumulative daytime postprandial excursions**, and fasting values, provide insights into possible basal insulin overutilization.

The BeAM value:

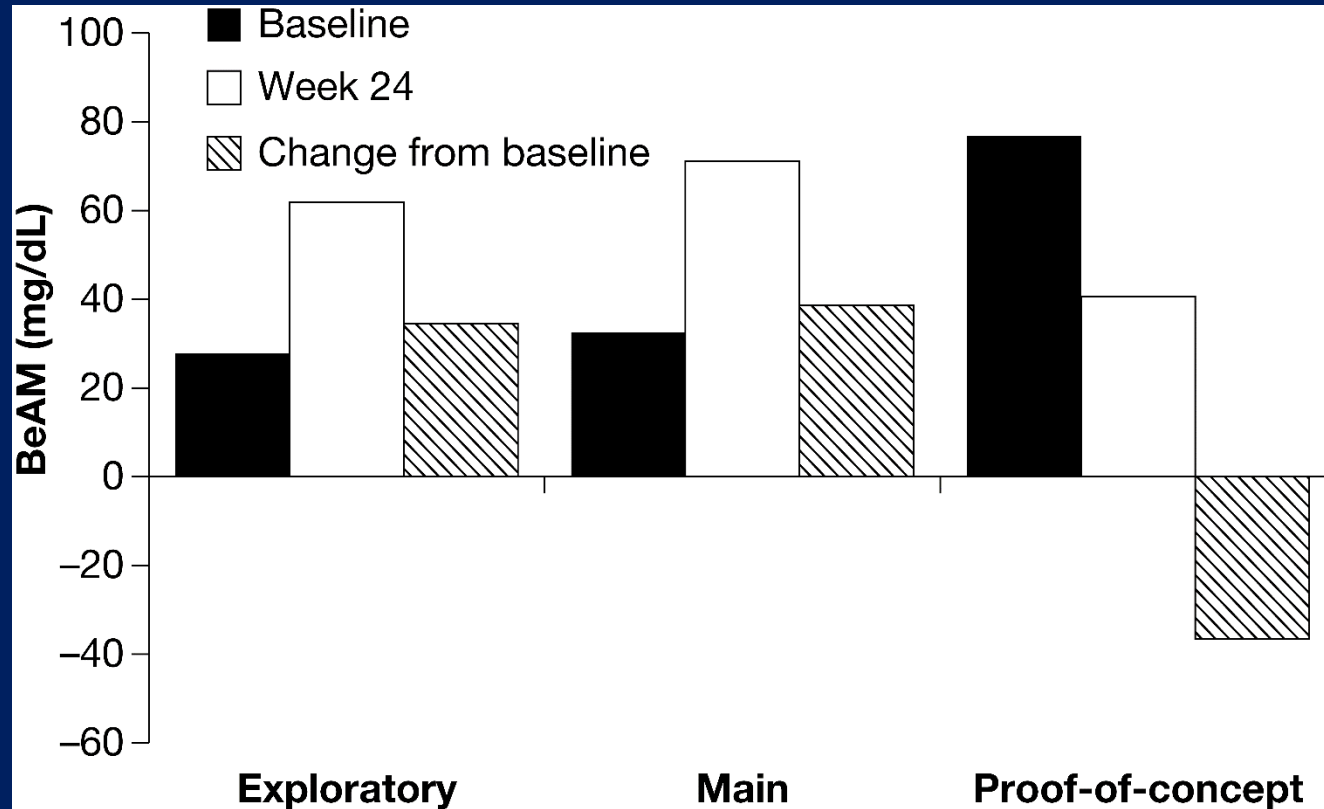
- Pooled data from 6 prospective, phase 3 or 4, RCTs in adults with T2D who had insulin glargine or NPH added to an existing OAD regimen.
 - Involved an *Exploratory analysis* and a *Main analysis*
- For the *proof-of-concept analysis*, data were pooled from three prospective phase 3 RCTs conducted in adults with T2DM who had a single injection of mealtime insulin glulisine added to optimized insulin glargine and an existing OAD regimen

The BeAM value:



- Significant positive correlations:
 - between week 24 BeAM and week 24 A1C ($p < 0.001$)
 - BeAM value and postprandial contributions to hyperglycemia at baseline and at week 24 ($p < 0.001$)

The BeAM value:



- Proof of concept analysis: Adding prandial therapy reduces BeAM value and improves A1C

Relationship between BeAM value and A1C after optimization of Basal Insulin

	A1C, %	BeAM Factor, mg/dL LS Mean (SE)	P Value*
All patients (N = 1,699)	≤ 7.0	38.4 (1.9)	-
	> 7.0 to < 7.5	46.3 (3.1)	0.025
	≥ 7.5 to < 8.0	51.3 (3.5)	0.0007
	≥ 8.0	58.8 (3.6)	< 0.0001
Basal insulin patients (n = 1,261)	≤ 7.0	46.1 (2.2)	-
	> 7.0 to < 7.5	55.2 (3.6)	0.024
	≥ 7.5 to < 8.0	64.1 (4.1)	< 0.0001
	≥ 8.0	69.7 (4.2)	< 0.0001

* LS mean difference from A1C < 7.0%; ANCOVA model includes study number and week 24 A1C category as factors.

Patients on basal insulin with a BeAM value >55 mg/dL may not benefit from continued basal insulin titration. Addition of prandial therapy should be considered to correct glucose excursions and achieve glycemic goals.

Clinical Case

Review of CBG records (MET, DPP-4i, titrated basal insulin qHS):

aBkfst	pBkfst	aLunch	pLunch	aDinner	pDinner	Bedtime
128		146		168		211
122	166			184		193
108		158		146	194	188
98			171	163		194

BeAM = 89

BeAM = 85

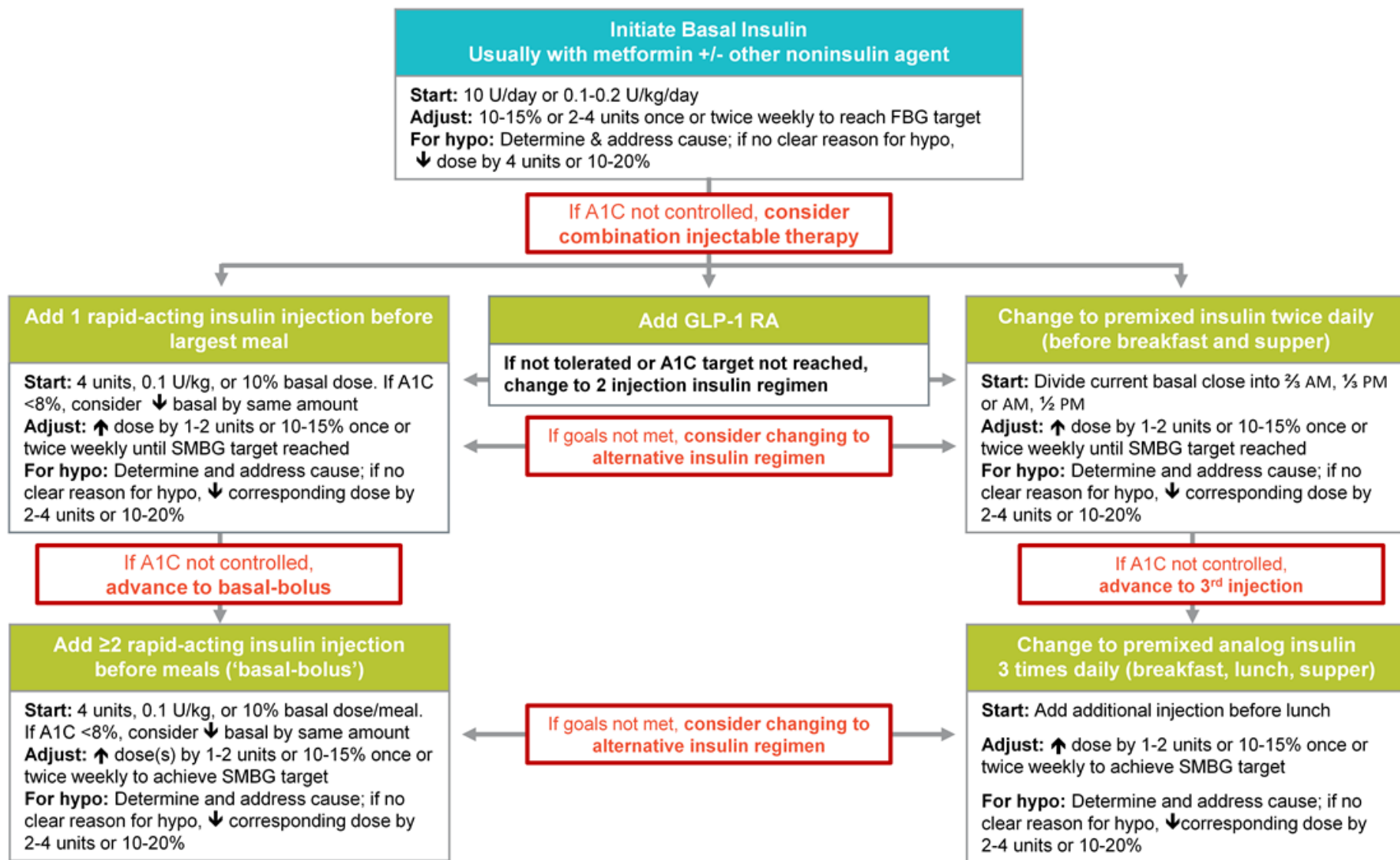
BeAM = 90

BeAM value would suggest to introduce an intervention to address post-prandial control rather than continue up-titration of basal insulin

Evolution of Challenges in the Insulinization of Type 2 Diabetes Patients

- Initiation of Basal insulin **INITIATION**
 - Recognition of Need, Decision, Acceptance
- Titration of Basal insulin **OPTIMIZATION**
 - Goals, Method(s), Frequency, Monitoring Benefits vs. Risks
- Intensification of Basal vs. Adding Prandial **MOVE BEYOND**
 - BeAM, Prandial insulin vs. others, Basal Plus or Basal Bolus
- Basal-Bolus Insulin Regimen
 - Multiple Daily Injections (MDI) vs. Pump therapy, Glucose Sensors

ADA 2017 guidelines for the management of T2DM: Combination injectable therapies



Trend: Delaying the start of prandial insulin

Rationale and support:

- When a patient is on oral therapies and advances to an injection
 - GLP-1 RA are comparable to basal insulin
 - GLP-1 RA often outperform meal-time insulin
 - Less hypoglycemia
 - Weight loss rather than gain
- Cost and GI side effects must be balanced
- Newer co-formulations of basal insulin and GLP-1 RA

Eng C.I, et al. *Lancet*. 2014; 384:2228-2234

FLAT-SUGAR Trial Investigators. *Diabetes Care*. 2016;39:973-981

Rosenstock J, et al. *Diabetes Care*. 2014;37:2317-2325

The BeAM value. Adding GLP-1 RA:

Table 1. BeAM values for iGlar and iGlarLixi groups.

	iGlarLixi (n = 259)	iGlar (n = 258)	<i>P</i> value^a
BeAM values (mg/dL), mean (SD)			
Baseline	58.98 (51.18)	54.21 (48.23)	
Week 30	43.93 (46.45)	55.40 (47.21)	
LS mean change (SE)	-13.52 (2.68)	-0.25 (2.68)	<0.001

^a *P* values determined from analysis of covariance with treatment arms (iGlarLixi, iGlar), analysis variable subgroup, and interaction between treatment and subgroup as fixed effects, and baseline analysis value as a covariate.

- **Learning Points:**

- Early introduction of basal insulin:

- Know when and how to start

- Titration of basal insulin:

- Advance with targets in mind, but know when to stop and shift focus
- BeAM value may be helpful.

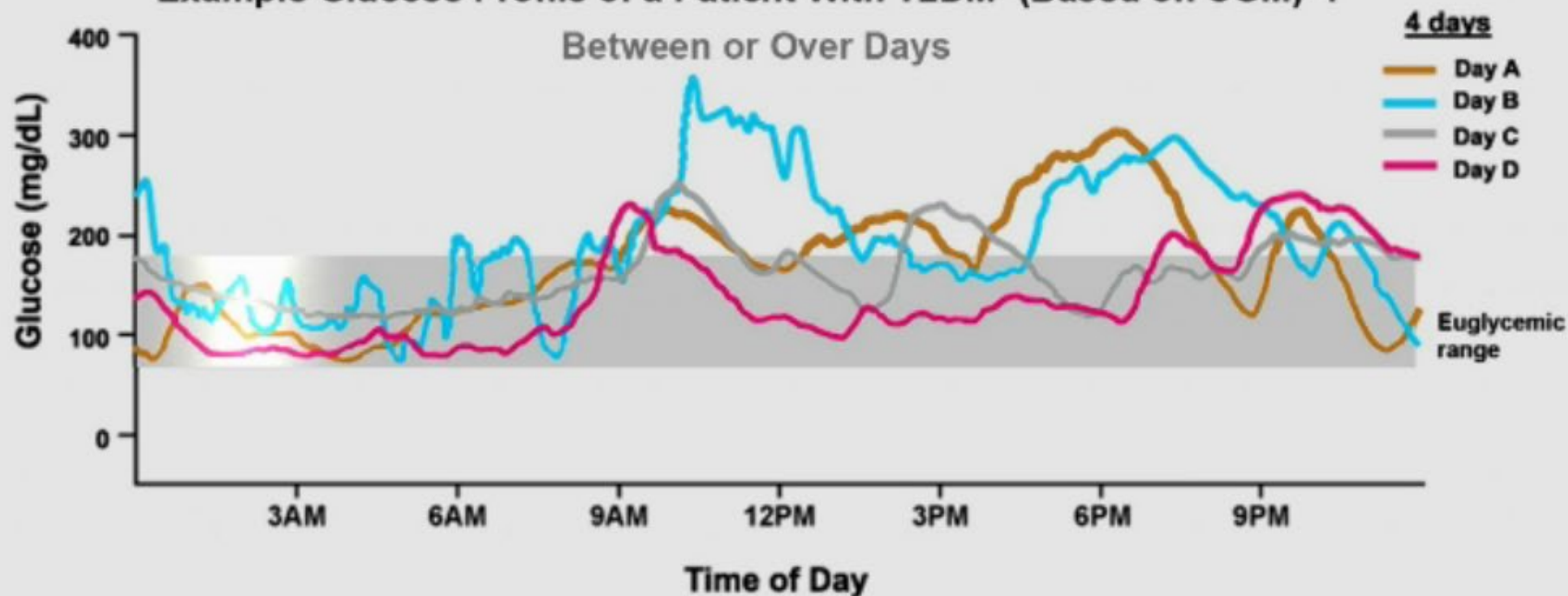
A few words on Hypoglycemia in T2D

- Hypoglycemia is frequently unrecognized in patients with T2D
- It is commonly under-appreciated by providers

Glucose Excursions as a Measure of Daily Glucose Control

- Glucose profiles reflect the frequency and amplitude of blood glucose excursions from peaks to troughs within-day or over longer periods of time (day to day, week to week, etc)⁸⁻¹⁰

Example Glucose Profile of a Patient With T2DM^a (Based on CGM)¹¹:



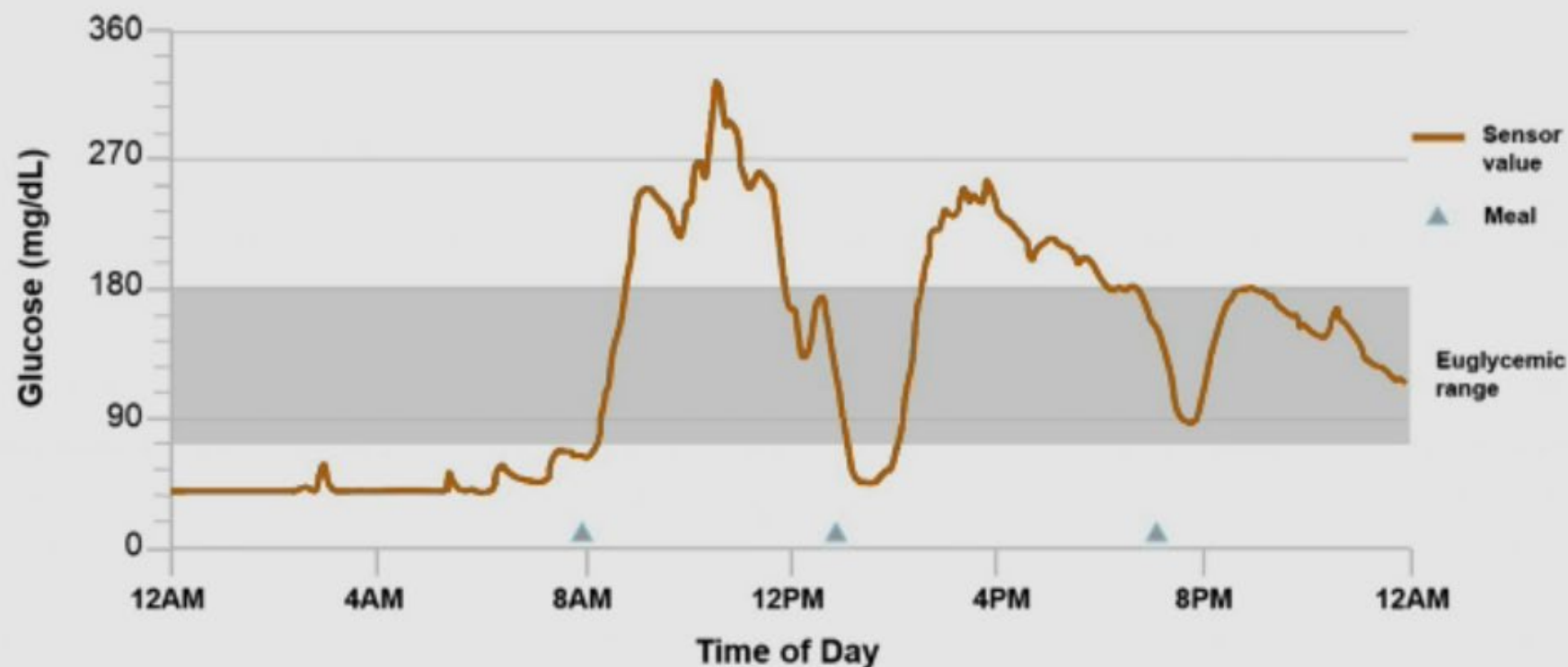
^a62-year-old man with T2DM of 20 years' duration; A1C 9.8%.

8. Monnier L et al. *J Diabetes Sci Technol*. 2008;2(6):1094-1100. 9. van Dijk JW et al. *Diabetes Spectr*. 2015;28(1):24-31.

10. Kilpatrick ES. *J Diabetes Sci Technol*. 2009;3(4):649-655. 11. Adapted from de Oliveira AOT et al. *Diabetes Spectr*. 2013;26(2):120-123.

Patients With T2DM Experience Significant Glucose Fluctuations Despite Being Well Controlled¹²

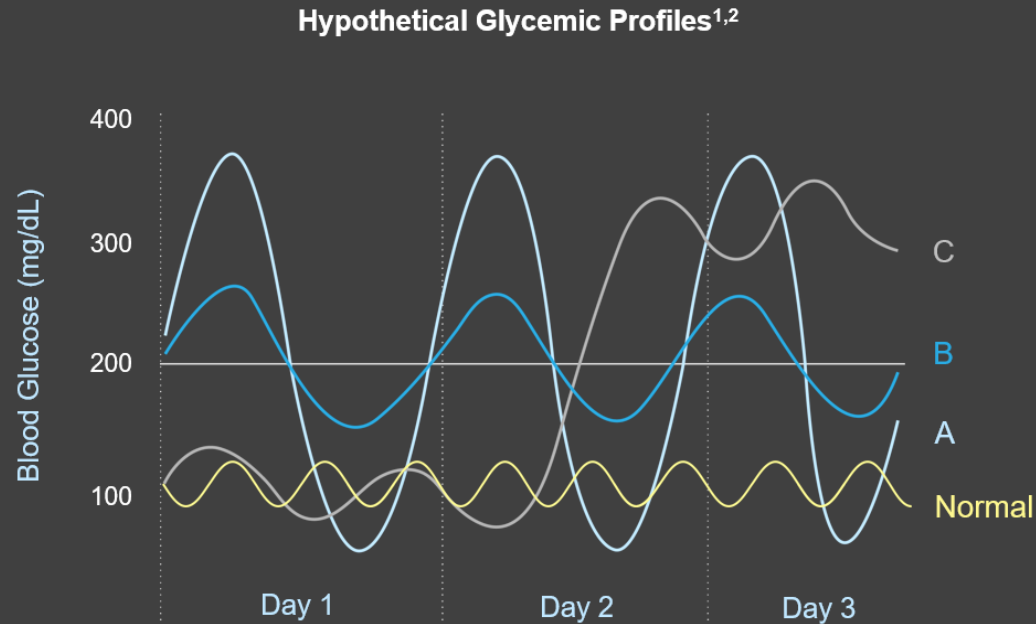
**Typical 24-Hour Tracing of a Patient With T2DM on Oral Medications
From a Group With a Mean Baseline A1C of 6.2% (N=25)**



- Hypoglycemia was defined as a glucose value of ≤ 50 mg/dL with or without symptoms that persisted for at least 15 minutes
- Postprandial hyperglycemia was defined as a glucose value >144 mg/dL 2 hours after the start of any meal

Glycemic Variability

GLYCEMIC VARIABILITY AND GLUCOSE CONTROL



A, B, and C represent hypothetical profiles in patients with diabetes.

1. Adapted from Suh S, Kim JH. *Diabetes Metab J*. 2015;39:273-282. 2. Adapted from Edelman S et al. *Osteopath Med Prim Care*. 2007;1:9.

The Ambulatory Glucose Profile

Metrics and targets

GLUCOSE STATISTICS AND TARGETS

21 Nov 2018–3 Dec 2018

% Time CGM is Active

13 days

99.9%

Glucose Ranges

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 165 mg/dL

Glucose Management Indicator (GMI) 7.3%

Glucose Variability 49.4%

Defined as percent coefficient of variation (%CV): target <36%

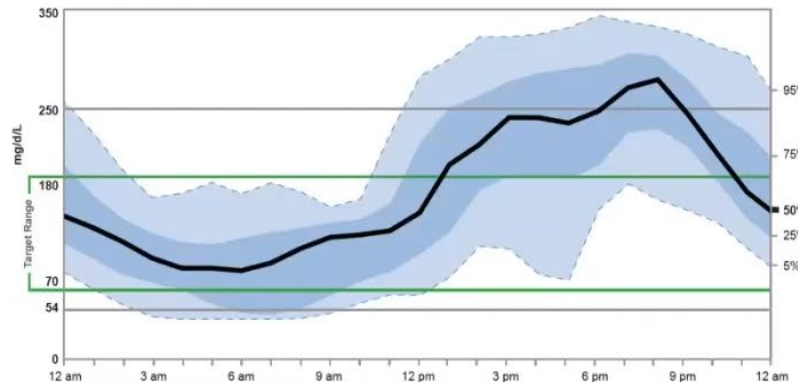
TIME IN RANGES



AGP profile (14 days)

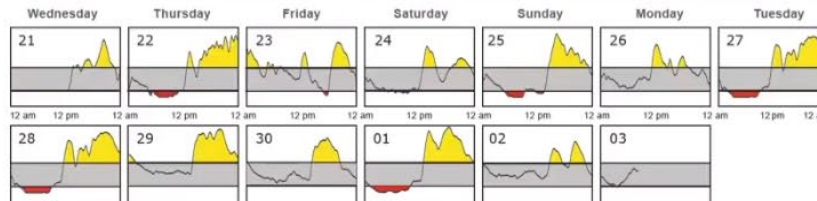
AMBULATORY GLUCOSE PROFILE (AGP)

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 views

DAILY GLUCOSE PROFILES



Each daily profile represents a midnight-to-midnight period.

Patent Pending – HealthPartners Institute dba International Diabetes Center – All Rights Reserved 2019

How an AGP report is organized

AGP Report = CGM data is clearly

- ✓ Standardized
- ✓ Organized
- ✓ User-friendly/single page
- ✓ Analyze

DAVID
DOB: 01/02/1939

MRN: _____
DEVICE: FreeStyle Libre Pro

Dr. Zisman Endocrine
PHONE: 3054669500

PAGE: 1 / 1
GENERATED: 09/25/2020

AGP Report

September 11, 2020 - September 25, 2020 (15 Days)

LibreView

GLUCOSE STATISTICS AND TARGETS

September 11, 2020 - September 25, 2020 **15 Days**
% Time CGM is 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.

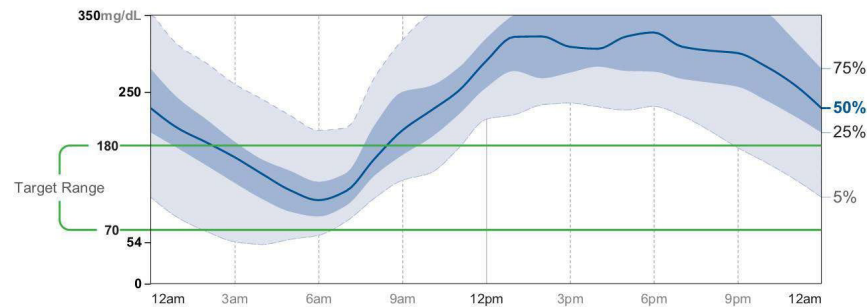
Average Glucose **249** mg/dL
Glucose Management Indicator (GMI) **9.3%**
Glucose Variability **40.6%**
Defined as percent coefficient of variation (%CV); target ≤36%

TIME IN RANGES



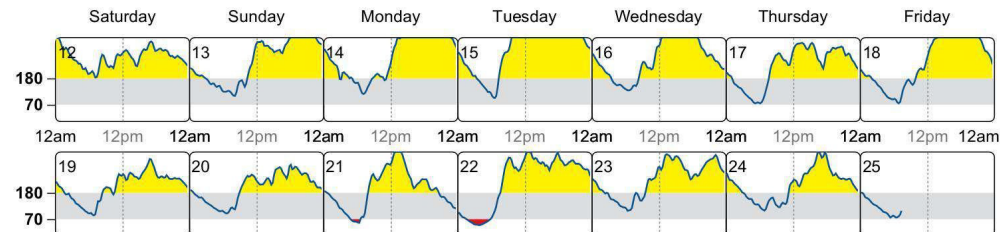
AMBULATORY GLUCOSE PROFILE (AGP)

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

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



Source: Battelino, Tadej, 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/doi19-0028>.

AGP Report

November 24, 2020 - December 7, 2020 (14 Days)

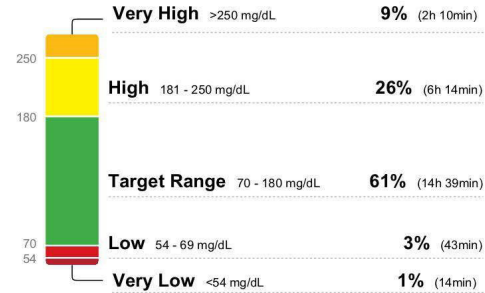
LibreView

GLUCOSE STATISTICS AND TARGETSNovember 24, 2020 - December 7, 2020 **14 Days****% Time CGM is Active** **88%**

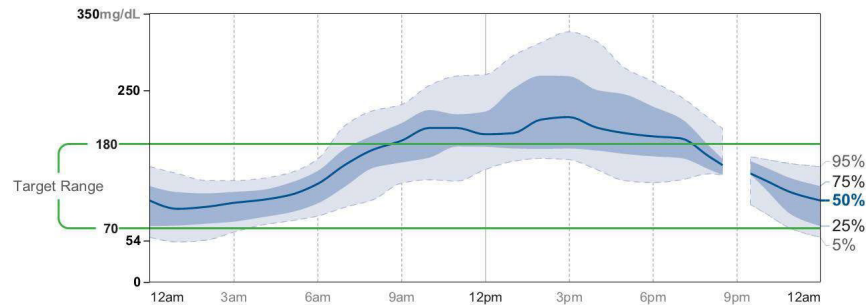
Ranges And Targets For	Type 1 or Type 2 Diabetes
Glucose Ranges	Targets % of Readings (Time/Day)
Target Range 70-180 mg/dL	Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (6h)
Above 250 mg/dL	Less than 5% (1h 12min)
Each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

Average Glucose **160** mg/dL**Glucose Management Indicator (GMI)** **7.1%****Glucose Variability** **37.8%**

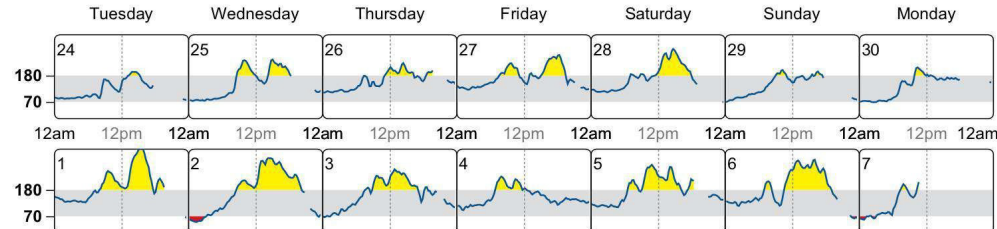
Defined as percent coefficient of variation (%CV); target ≤36%

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**

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



AGP

14 days | Thu Jul 16, 2020 - Wed Jul 29, 2020

Oswaldo

dexcom
CLARITY
DOB: Nov 12, 1945

dexcom | captū^rAGP®

Oswaldo

Thu Jul 16, 2020 - Wed Jul 29, 2020 (13.4 days)

Glucose Statistics	Avg Glucose mg/dL	Very Low < 54 mg/dL	Low < 70 mg/dL	In Target Range 70 - 180 mg/dL	High > 180 mg/dL	Very High > 250 mg/dL	Coefficient of Variation	SD mg/dL	% Time CGM Active
	235	0.0%	0.1%	6.8%	93.1%	33.8%	16.8%	40	75.8%
	Glucose Exposure	Glucose Ranges					Glucose Variability		Data Sufficiency

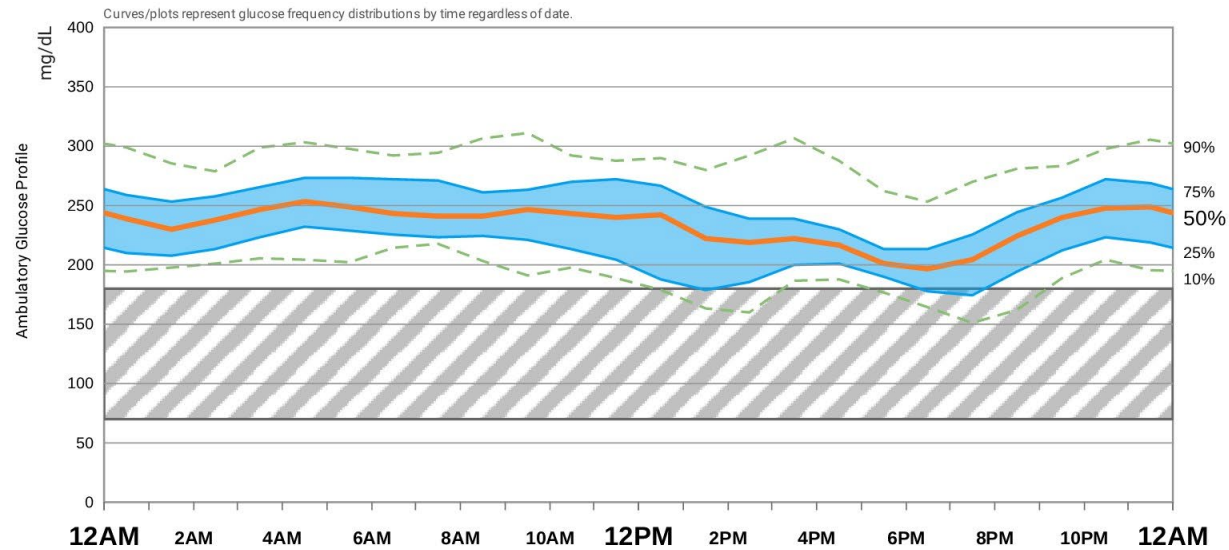
CGM

50% - Median

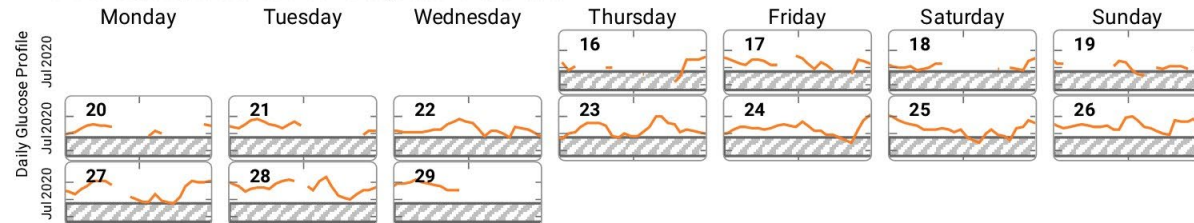
25/75% - IQR

10/90%

Target Range



The Y axis and target range are the same as on the Ambulatory Glucose Profile graph above.



Overview

30 days | Wed Sep 30, 2020 - Thu Oct 29, 2020

Glucose

Average Glucose

114 mg/dL

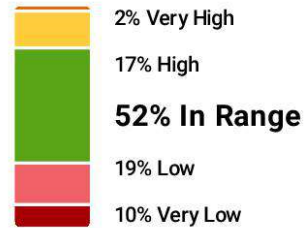
Standard Deviation

57 mg/dL

GMI

6.0%

Time in Range



Target Range:

Day (6:00 AM - 10:00 PM): 70-180 mg/dL

Night (10:00 PM - 6:00 AM): 80-150 mg/dL

Sensor Usage

Days with CGM data

80%

24/30

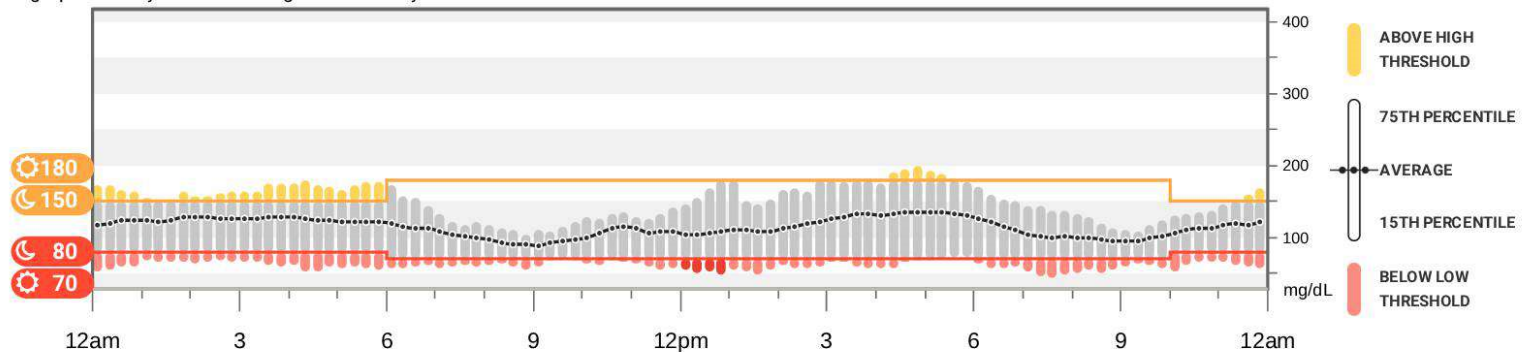
Avg. calibrations per day

0.1

Top Patterns

- 1** ivelisse87 had a pattern of daytime lows
ivelisse87 had a pattern of significant lows between 12:15 PM and 12:50 PM.
- 2** ivelisse87's best glucose day was October 13, 2020
ivelisse87's glucose data was in the target range about 86% of the day.

This graph shows your data averaged over 30 days



Correlation of Glucose Fluctuations to Hypoglycemic Events in T2DM¹³

Number of Hypoglycemic Events^a

Asymptomatic
Hypoglycemic Events
(Number/48-h/Person)



^aAs a function of tertiles of A1C and of glucose variability.

^bGlucose variability measured as SD around mean glucose concentration.

SD=standard deviation.

13. Monnier L et al. *Diabetes Technol Ther.* 2011;13(8):813-818.



**THE SECRET OF GETTING
AHEAD IS GETTING
STARTED.**

MARK TWAIN

Thank You !!!

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