Intensifying Diabetes Therapies to Achieve Personalized Treatment Goals

AACE

Commercial Support

AACE®

Disclosures

Faculty

- Radica Alicic, MD, FHM, FACP, Bayer, research funding, advisory board member; Boehringer Ingelheim, consultant; Eli Lilly, consultant

- Diana Isaacs, PharmD, BCPS, BCACP, BC-ADM, CDCES, FADCES, FCCP, Abbott, Speakers' Bureau; Dexcom, Speakers' Bureau; Medtronic, Speakers' Bureau, Consultant; Insulet, Speakers' Bureau; Eli Lilly, Speaker's Bureau, Consultant; Novo Nordisk, Speakers' Bureau; Cequr, Speakers' Bureau; Sanofi, Consultant; Lifescan, Consultant

- Madhuri Vasudevan, MD, MPH, no relationships to disclose.

All of the relevant financial relationships listed for these individuals have been mitigated.

Planners

- Diane Alberson, MEd, CAE, mo relationships to disclose

- Amy Ogunsunlade, no relationships to disclose

- Audrey Shively, MSHSE, MCHES, CHPD, no relationships to disclose

AACE®

Learning Objectives

Recognize the connection between managing T2D and how other serious complications, such as cardiovascular and chronic kidney disease, can also be avoided.

Identify methods to intensify therapies to reach timely, sustained glycemic control targets (GLP-1 RA info).

Apply shared decision-making strategies with sustained glycemic control targets and personalized treatment/management as critical goals in persons with diabetes to prevent long-term health implications.

AACE.

Overview of Enduring

Complications-Centric Treatment of Type 2 Diabetes: Scope of the Problem

- 30 - 40% of adults with T2D develop chronic kidney disease (CKD), a leading cause of kidney failure requiring dialysis and transplant worldwide

- Majority of patients die from cardiovascular disease (CVD) before progressing to kidney failure

- The triad of T2D, heart failure (HF) and CKD drives high rates of death, poor quality of life and hospital admission

AACE

Complications-Centric Glycemic Control

- Sodium glucose cotransporter 2 inhibitors (SGLT2i), and glucagon-like peptide-1 receptor agonists (GLP-1RAs) changed treatment paradigm in patients with T2D complicated by CKD and/or CVD

- Treatment focus in this population transitioned from gluco-centric to complications-centric (organ protection)

- In the large cardiovascular outcomes (CVOTs) and following kidney and heart failure trails, SGLT2i and GLP-1RAs demonstrated kidney and heart protection

AACE.

# 2023 AACE Complications-Centric Treatment Algorithm

- SGLT2i are used as a first line therapy, independent of the need for A1C lowering, for slowing down CKD progression and reducing risks of HF in all patients with eGFR≥20 mL/min/1.73m^2

- GLP-1RAs are used as first line therapy for risk reduction of atherosclerotic CVD, and kidney disease outcomes

- For patients with CKD requiring additional glucose lowering beyond SGLT2 inhibition long-acting GLP-1RA are preferential agents

AACE

Characteristics of Diabetes Distress

- Diabetes distress is present in nearly 50% of patients with diabetes

- Diabetes distress manifests in many forms including denial, frustration, and low motivation

- Discussing patient goals and barriers to success helps to better understand how to achieve recommended glycemic targets

CGMS in DM

MATCHING GLUCOSE MONITORING OPTION TO COMPLEXITY OF ANTIHYPERGLYCEMIC REGIMENS
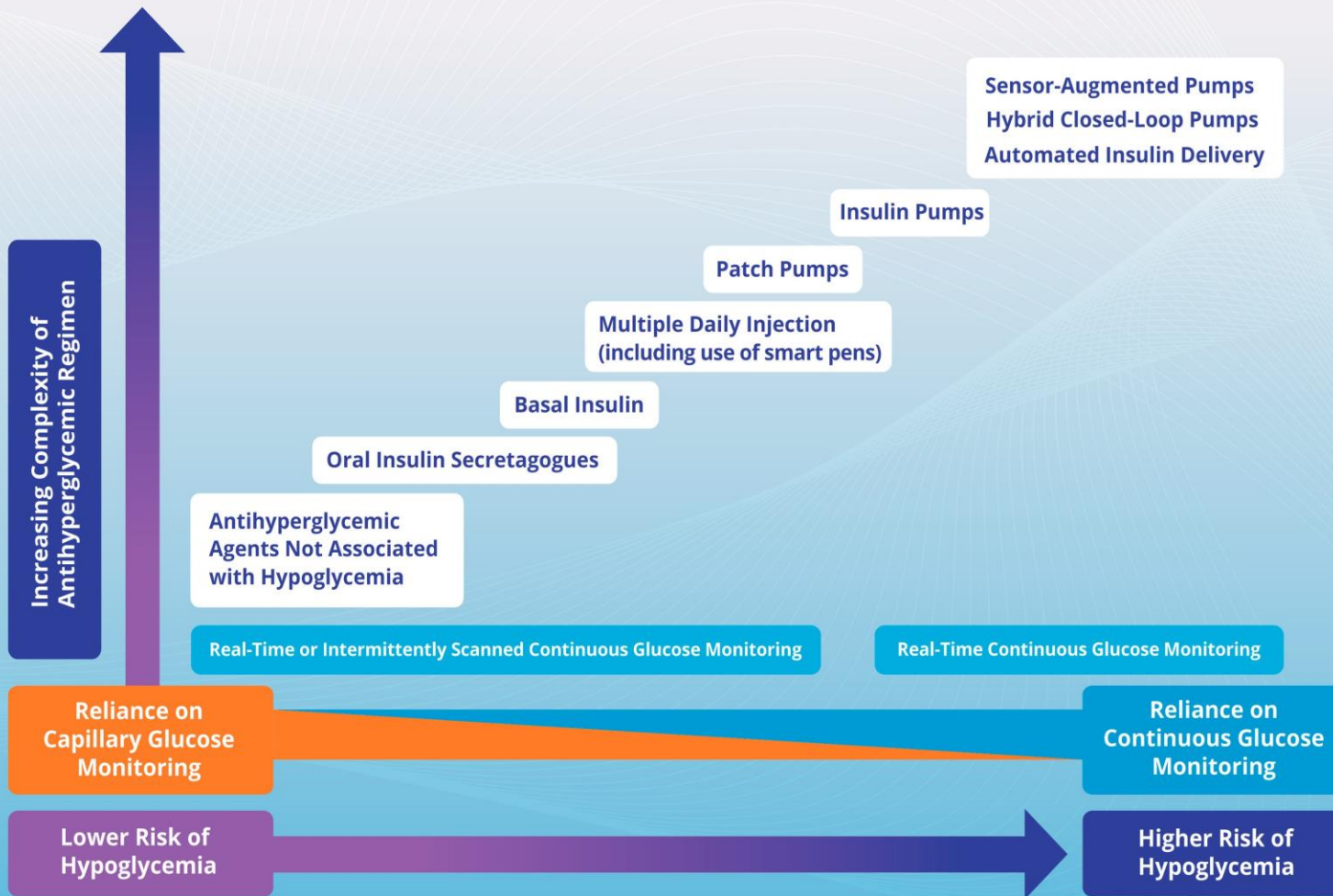
CGMS indication for patients with DM with:

- Increasing complexity of DM treatment regimen
- At higher risk for hypoglycemia

Case Discussions

CASE 1

- 73-year-old female with T2DM x 14 years, HTN, HLD

- A1C=7.5%, Weight=210lbs, BMI=42kg/m^2

- DM Meds:
  - Metformin 1000mg twice daily
  - Insulin degludec 38 units daily
  - Insulin lispro 8 units at meals 3 times daily before meals + correction factor

GLUCOSE STATISTICS AND TARGETS

May 12, 2022 - May 25, 2022	14 Days
% Time CGM is Active	87%

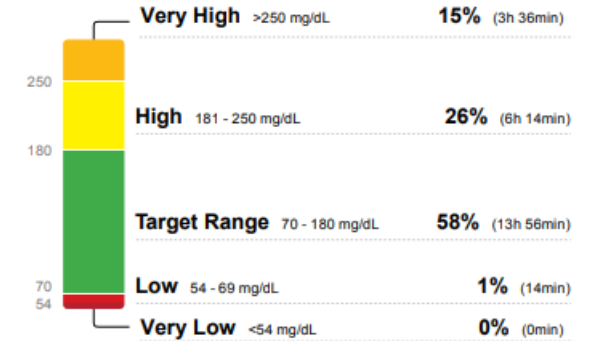| Ranges And Targets For	Type 1 or Type 2 Diabetes
Glucose Ranges Target Range 70-180 mg/dL	**Targets** % of Readings (Time/Day) Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (6h)
Above 250 mg/dL	Less than 5% (1h 12min)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

Average Glucose	179 mg/dL
Glucose Management Indicator (GMI)	7.6%
Glucose Variability	39.2%
Defined as percent coefficient of variation (%CV)	

TIME IN RANGES

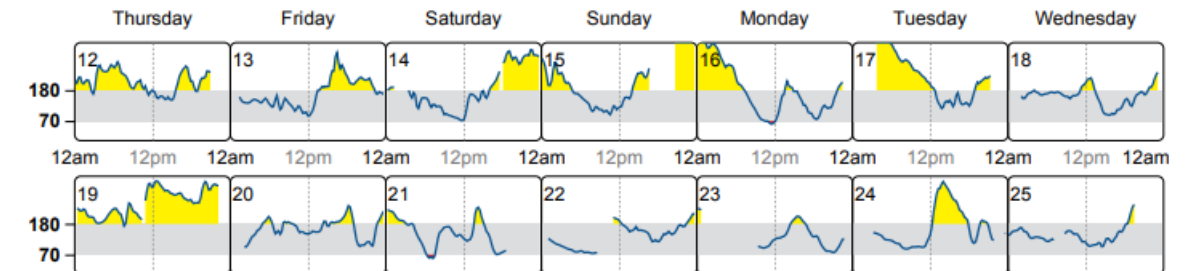|		
Very High >250 mg/dL	15%	(3h 36min)
High 181 - 250 mg/dL	26%	(6h 14min)
Target Range 70 - 180 mg/dL	58%	(13h 56min)
Low 54 - 69 mg/dL	1%	(14min)
Very Low <54 mg/dL	0%	(0min)

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/dci19-0028.
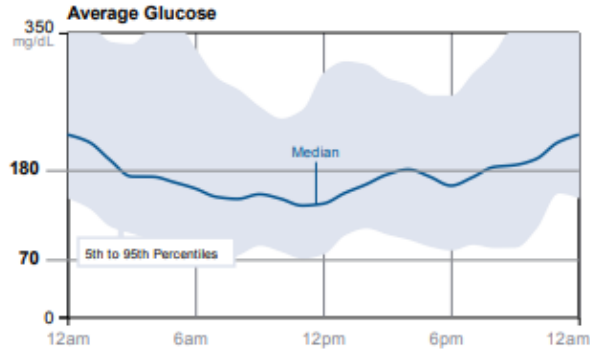
Snapshot

📱 Glucose

GMI **7.6**% or **60** mmol/mol

AVERAGE GLUCOSE **179** mg/dL

% above target	**42** %
% in target	**57** %
% below target	**1** %

Average Glucose

350 mg/dL

Median

180

5th to 95th Percentiles

70

0

12am   6am   12pm   6pm   12am

LOW GLUCOSE EVENTS **2**

Average duration **76** Min

Low Glucose Events

100
90
80
70
60
50
40

12am   6am   12pm   6pm   12am
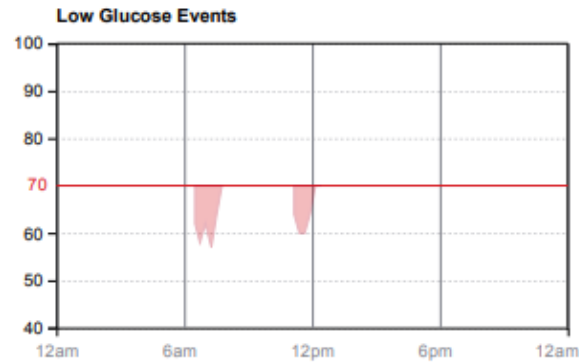
📶 Sensor Usage

% TIME SENSOR IS ACTIVE **87** %

Average scans/views **5 / Day**

% Time Sensor is Active

100%
50%
0%

12am   6am   12pm   6pm   12am

Mon
May 16

350
180
70
0

12am   6am   12pm   6pm   12am
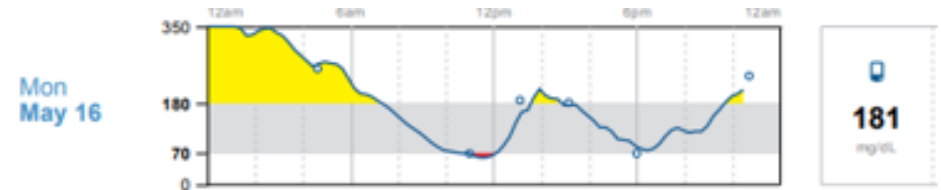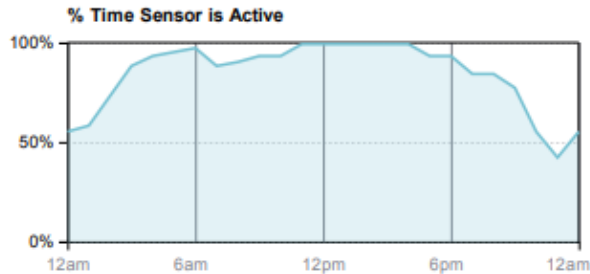
📱 **181** mg/dL

Reports stacking insulin

Glucose
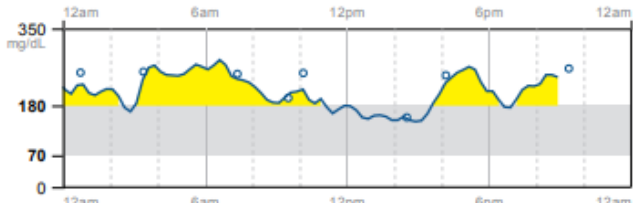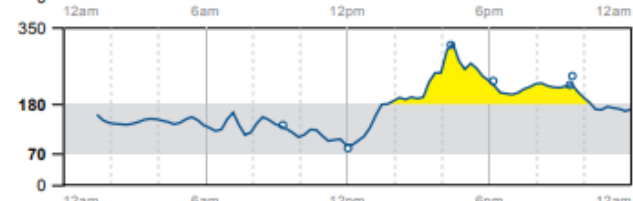
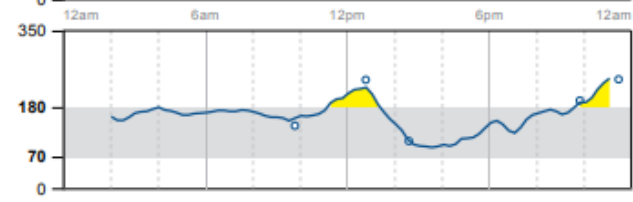|	Average Glucose
Thu May 12	211 mg/dL
Fri May 13	169 mg/dL
Sat May 14	187 mg/dL
Sun May 15	213 mg/dL → Missed dose of lispro
Mon May 16	181 mg/dL
Tue May 17	226 mg/dL
Wed May 18	161 mg/dL → Balanced eating, walked after lunch
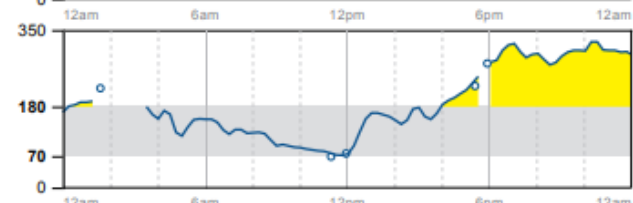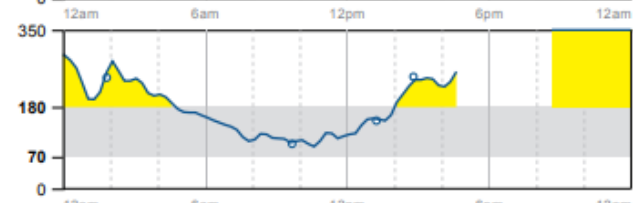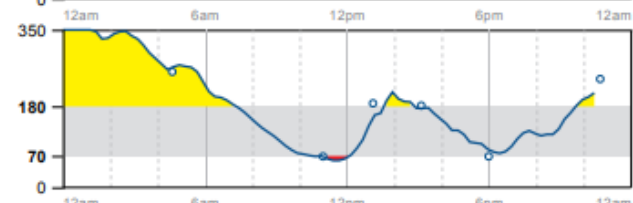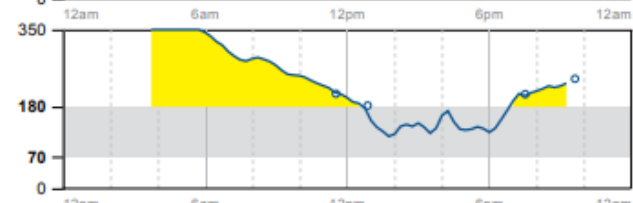
3 weeks later

- She has learned from her data

- Sees the benefits of walking after meals

- Regular coke vs. diet coke

- When she takes her insulin late

- Is she meeting the metrics?

- Time in range?

- Time below range?

- Glucose variability?

GLUCOSE STATISTICS AND TARGETS

June 4, 2022 - June 17, 2022 — 14 Days
% Time CGM is Active — 72%

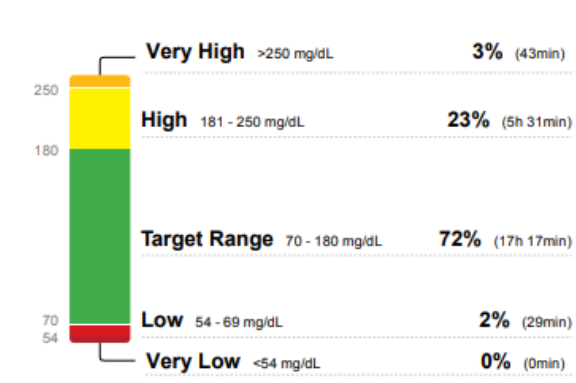| Ranges And Targets For	Type 1 or Type 2 Diabetes
Glucose Ranges	**Targets** % of Readings (Time/Day)
Target Range 70-180 mg/dL	Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (6h)
Above 250 mg/dL	Less than 5% (1h 12min)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

Average Glucose	**144** mg/dL
Glucose Management Indicator (GMI)	**6.8%**
Glucose Variability	**35.5%**
Defined as percent coefficient of variation (%CV)	

TIME IN RANGES

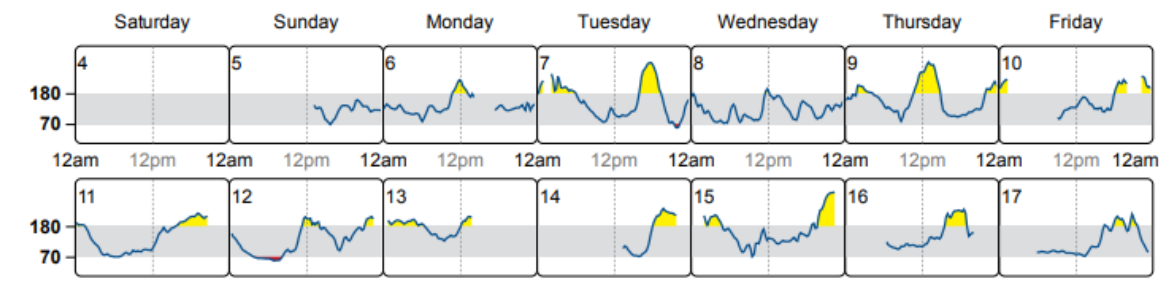|		
Very High >250 mg/dL	**3%**	(43min)
High 181 - 250 mg/dL	**23%**	(5h 31min)
Target Range 70 - 180 mg/dL	**72%**	(17h 17min)
Low 54 - 69 mg/dL	**2%**	(29min)
Very Low <54 mg/dL	**0%**	(0min)

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/dci19-0028.

What Do the Guidelines Say?

GLUCOSE-CENTRIC ALGORITHM FOR GLYCEMIC CONTROL
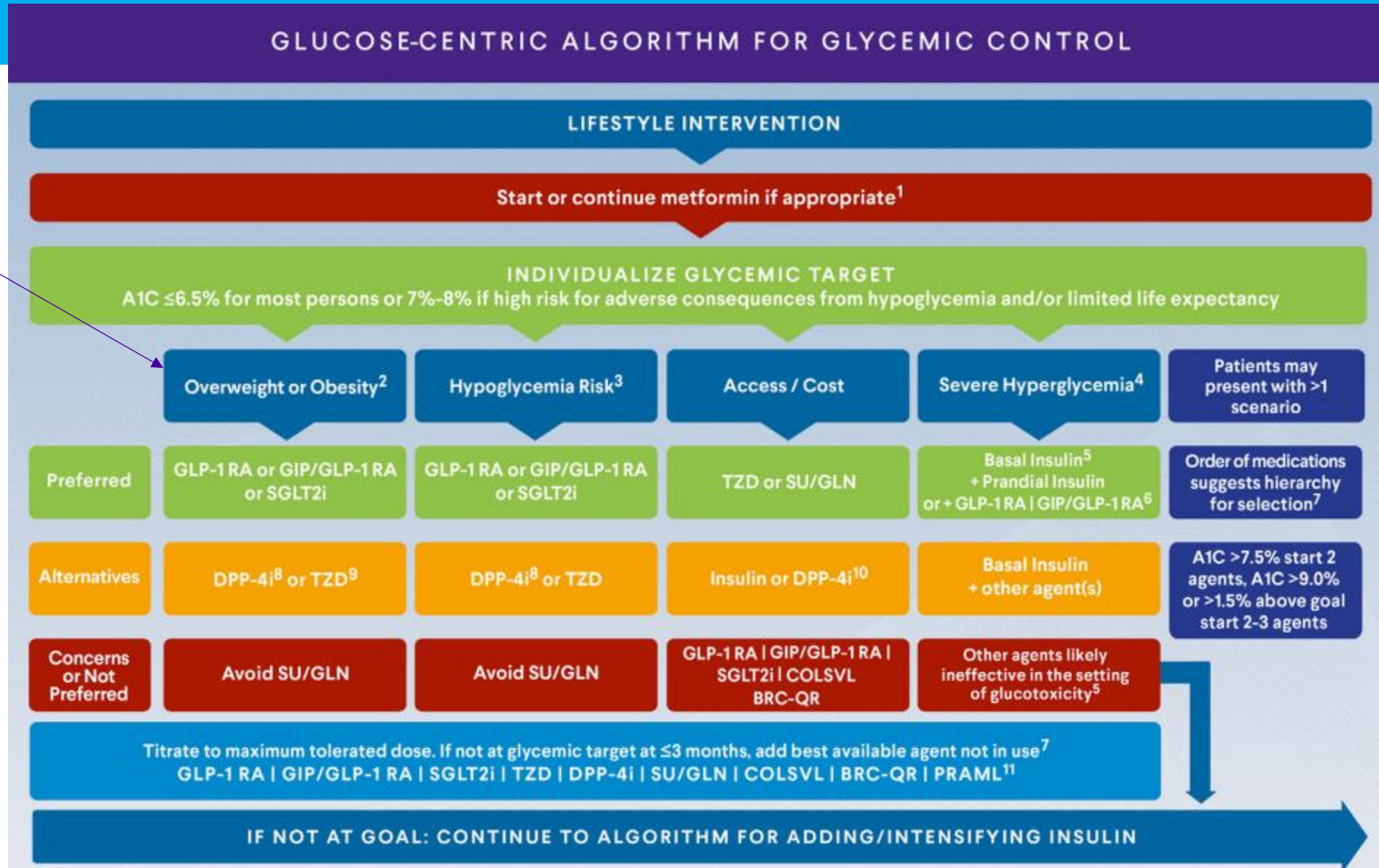
ALGORITHM FOR ADDING/INTENSIFYING INSULIN

CONSIDER GLP-1 RA IF NOT ALREADY IN USE

SEVERE HYPERGLYCEMIA WITH SYMPTOMS[2], START BASAL INSULIN +/- PRANDIAL INSULIN

IF NOT AT GOAL

Consider fixed-dose basal insulin/GLP-1 RA

START BASAL INSULIN

IF NOT AT GOAL

A1C <8%
TDD 0.1-0.2 U/kg

A1C >8%
TDD 0.2-0.3 U/kg

START PRANDIAL INSULIN

Insulin titration every 2-5 days to reach glycemic goal[1]

Stepwise addition to basal:
- Begin prandial insulin before largest meal (10% of basal or 5 units)
- If not at goal, progress to injections before 2 or 3 meals

Simultaneous addition to basal at all meals:
- TDD is 50% basal and 50% prandial divided by 3 meals

- Rapid-acting analogs preferred over regular insulin

<u>Fixed regimen:</u> Increase TDD by 2 units
<u>Adjustable regimen:</u>
- FBG >180 mg/dL: add 20% of TDD
- FBG 140-180 mg/dL: add 10% of TDD
- FBG 110-139 mg/dL: add 1 unit

If hypoglycemia, reduce TDD by:
- BG <70 mg/dL: 10%-20%
- BG <40 mg/dL: 20%-40%

- Discontinue or reduce SU
- Basal analogs preferred over NPH

Insulin titration every 2-3 days to reach glycemic goal:

HYPERGLYCEMIA
(premeal BG >110-140 mg/dL)
- Increase premeal dose by 10%-20% for the previous meal

HYPOGLYCEMIA
(premeal BG <70 mg/dL)[3]
- Decrease premeal dose by 10%-20% for the previous meal

Glycemic goals unmet
Basal doses >0.5 units/kg/day
BeAM score (bedtime-prebreakfast glucose) >50

ADD PRANDIAL INSULIN

Use of CGM is recommended to reach glycemic goals safely[4]

AACE

What Changes to Make?

A. Continue lifestyle and current meds
B. Add GLP-1 agonist
C. Add SGLT2 inhibitor
D. Add TZD
E. Other agent

Shared decision making also includes a discussion on potential side effects, cost, and administration

Action Plan

- Start semaglutide 0.25mg x 4 weeks, then increase to 0.5mg weekly x 4 weeks, then increase to 1mg weekly x 4 weeks, then 2mg weekly

- Continue insulin degludec 38 units daily

- Stop insulin lispro, change to correction factor before meals only (ICF 50, BG target 150)

AACE

6 Months Later

Insulin degludec 18 units daily

Semaglutide 2mg weekly

A1c = 6.6%

Wt: 190lbs (20lbs loss)

CASE 1 Take Home Points

- CGM can help support positive behavior changes

- GLP-1 agonists or incretin therapies should be considered for their beneficial effects on lowering glucose and decreasing weight

- They can be considered prior to adding basal insulin or meal time insulin.

- If adding an incretin therapy to someone already taking meal time insulin, CGM can be a great tool to help with insulin titration to reduce the risk of hypoglycemia

AACE.

CASE 2

- Patient DR is a 34-year-old man with a history of a single kidney (donated live kidney to his mother), who then developed ketosis prone type 1 DM at the age of 24-years-old. He has had a 10-year history of uncontrolled diabetes. 6 months ago, he developed a non-healing sore on his left toe, underwent debridement, but the infection persisted, and now presents to the ER with fevers, chills, and found to have osteomyelitis of the left foot. He underwent emergency below the knee amputation (BKA). On the day after surgery, blood sugars become uncontrolled, greater than 180 mg/dL in the inpatient setting.

- On post-operative day 2, he appears frustrated, irritable, and the nurses report that he is eating and drinking foods that have not been ordered for him. Upon inspection of the room, empty soda bottles and juice containers are visible.

- Physical Exam: Left BKA with bandage healing well.

- Labs are notable for HbA1C 12%, GFR 54 ml/min

CASE 2

Inpatient endocrinology is consulted. The team approaches the patient, but he appears frustrated and turns his head away from the team, as they approach. The discussion follows as below:

- Specialist: Dear Mr. R, how are you?

- Patient: How do you think? I'm tired, can't move, and I'm frustrated.

- Specialist: I am so sorry. I cannot imagine how you must feel at this time. Are you in any pain?

- Patient: No.

- Specialist: That is good. We are part of the inpatient diabetes team. I have a question for you. Do you have a few minutes for us to talk?

CASE 2

- Patient: Yes.

- Specialist: What are your goals for this admission?

- Patient: I want to be discharged as soon as possible. And I want to be able to walk again after this stump heals.

- Specialist: I am so grateful to you for sharing your thoughts with me, and I support your goals. I would like to help you accomplish these goals. May I share with you a few simple strategies? If you put these activities into place, I hope it will help you accomplish your goals in a safe and effective manner.
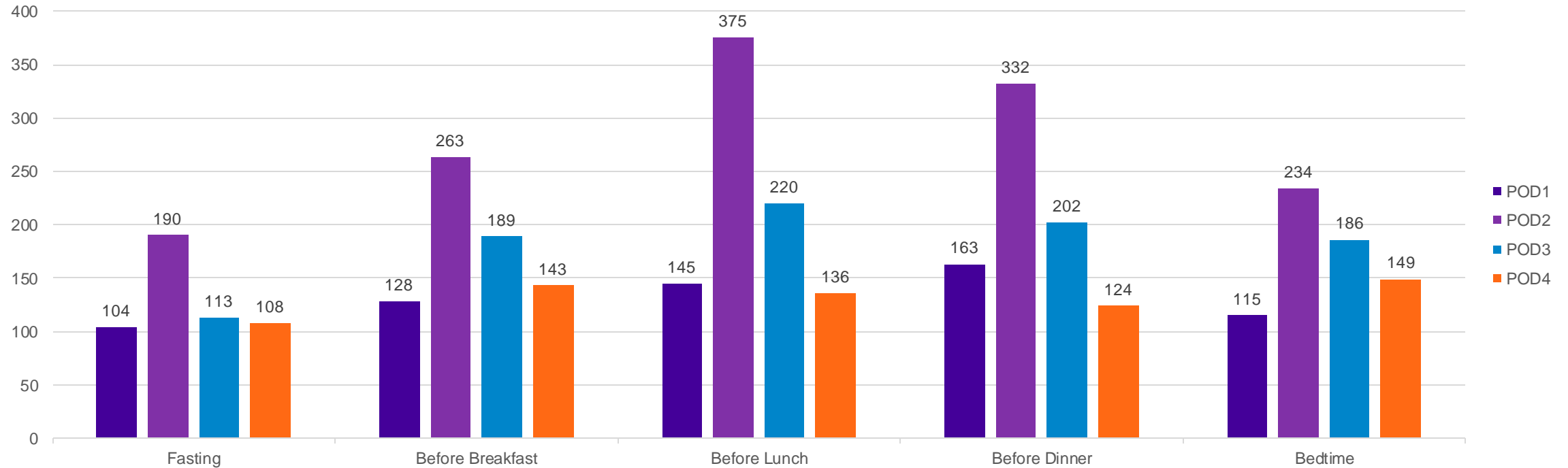
- Patient: Ok.

CASE 2

- Specialist: Thank you. The way I think about diabetes is like riding a car. Speeding comes with risk and consequences. In general, it's safer to drive the speed limit, and know when to push the brakes. In the same line of thinking, it's normal to expect an acceleration in blood sugars for a variety of reasons, including the stress of surgery, physical and emotional stress, side effect of medications and changing insulin requirements. To slow down blood sugar levels, we must first take our foot off the accelerator, so to speak. The trickiest accelerators are carbonated drinks and juices. These escalate the sugar quickly and can compromise wound healing. Therefore, the first step to gaining smoother control of your blood sugars is to avoid these risky beverages – would you be open to giving this strategy a try?

- Patient: I guess… what can I drink instead?

- Specialist: Thank you for being open to the idea. I will request the dietician to bring unsweet tea and water while you are in the hospital.

CASE 2

- Specialist: Thank you. The next step to achieving stable glucose levels is to use insulin as the brakes of a car. This will allow your overall glucose levels to come into a safer range that will allow your tissues to heal to the best possible extent.

- Patient: Ok. Yes, I agree with that. But I'm very afraid of low BG. Is there anything that can be done about that?

- Specialist: I understand your concern, particularly after your surgery, you may be at a higher risk for complications from low blood sugar episodes. I would recommend a continuous glucose. Let's begin the process.

- Patient: Thanks for taking the time to explain it to me like this. No one has ever talked about it like that before. It makes sense to me now.

- Specialist: That is wonderful. I'm very proud of you! Keep up the great work. We will continue to follow you.

AACE®

CASE 2

Inpatient Blood Glucose Trends

Outpatient discharge planning:

- Continue Glargine 20 units once daily

- Continue insulin aspart with meals + correction factor

- Start CGM, Libre 2

CASE 2

Take home points

- Shared decision making requires engagement from patient

- Open-ended questions help the provider understand the patient's health-related goals

- Cultivating trust through patient-centered communication

- Integration of prescriptive dietary counseling with medication adherence optimizes overall glycemic control

- Recognizing patients who would benefit from CGM and providing this in a timely manner

CASE 3

- B.H. is a 55-year-old man with T2D, HTN, CAD, BMI 38 kg/m^2 and CKD stage 3a (eGFR 50 ml/min/1.73m2, UACR 150mg/g)

- Pharmacotherapy: metformin 1000 mg BID, losartan 100 mg QD, atorvastatin 20 mg QD

- His latest A1c is 8.2%

- Social history: He works full time as a clerk, doesn't adhere to diabetic appropriate diet, and checks his blood sugars once a day

- B.H. would like to discuss what changes he can make to improve his health and blood sugar control

CASE 3

KDIGO Heat Map helps with CKD classification and risk stratification (kidney disease progression and cardiovascular risk)

Discuss with B.H.
his moderately increased risk for progression of kidney disease and cardiovascular disease (G3aA2)

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

Persistent albuminuria categories Description and range

				A1 Normal to mildly increased <30 mg/g <3 mg/mmol	A2 Moderately increased 30–300 mg/g 3–30 mg/mmol	A3 Severely increased >300 mg/g >30 mg/mmol
GFR categories (ml/min per 1.73 m²) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); yellow: moderately increased risk; orange: high risk; red, very high risk.

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney inter., Suppl. 2013; 3:1–150.

What do Guidelines Say ?

CASE 3

- Advise patient on importance of exercise (at least 150 minutes per week)

- Make referral for Diabetic education

- Adjust metformin dose to 750 mg BID, and add empagliflozin 10 mg

- Ask patient to check his blood sugars at least twice a day because of increased risk of hypoglycemia with eGFR < 60 ml/min

- Discuss adverse effects associated with empagliflozin and mitigation strategies (stress hygiene of genital area; hold empa during illness; early recognition of DKA)

AACE®

CASE 3

- B.H comes back for follow up visit in 3 months

- His A1c is 7.5 (A1c is reliable measure in CKD 1-3b, target A1C =< 7)

- BMI is improved at 36 kg/m^2

- Labs: eGFR stable at 48ml/min/1.73m^2, UACR down to 100 mg/g

- Patient is very interested in further weight loss

- Add semaglutide 0.5 mg s.c. with plan to titrate dose as tolerated (start low to avoid nausea)

- Decrease metformin to 500 mg BID, with plan to stop once semaglutide dose titrated up

Questions?

For additional resources and copy of slides, please visit https://pro.aace.com/disease-state/diabetes

AACE