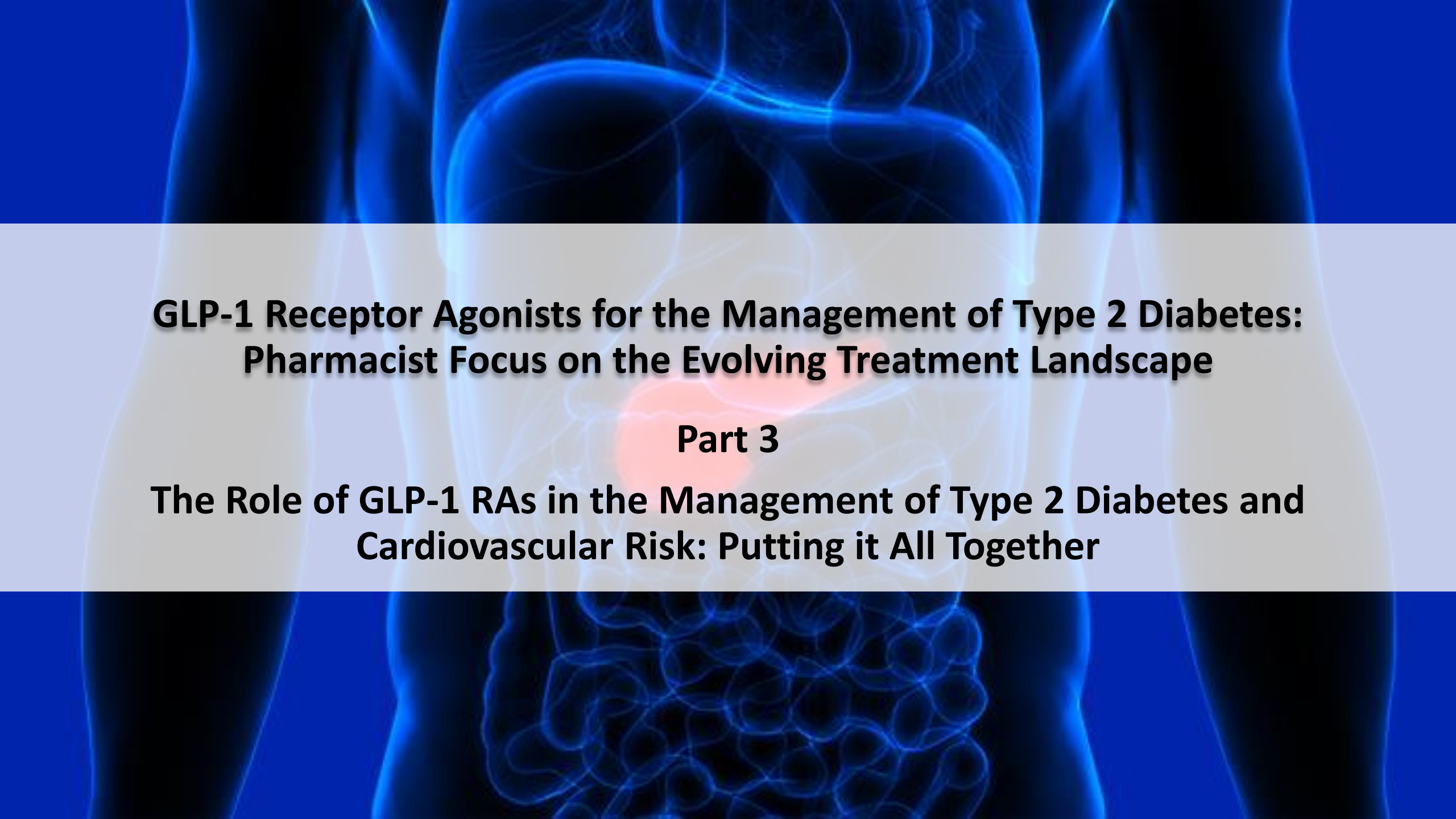

GLP-1 Receptor Agonists for the Management of Type 2 Diabetes: Pharmacist Focus on the Evolving Treatment Landscape

Part 3

The Role of GLP-1 RAs in the Management of Type 2 Diabetes and Cardiovascular Risk: Putting it All Together

This educational activity is sponsored by Postgraduate Healthcare Education, LLC and supported by an educational grant from Novo Nordisk Inc.

Faculty

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Josh's research interests involve the management of diabetes and prevention of adverse drug events during transitions in care. Josh was awarded the 2016 Albert B. Prescott Pharmacy Leadership Award for his work in diabetes care.

Disclosures

Dr. Neumiller has no actual or potential conflicts of interest in relation to this program.

The clinical reviewer, Heather P. Whitley, PharmD, BCPS, CDE has no actual or potential conflicts of interest in relation to this program.

Susanne Batesko, RN, BSN, Robin Soboti, RPh, and the planners, managers, and other individuals, not previously disclosed, who are in a position to control the content of Postgraduate Healthcare Education (PHE) continuing education activities hereby state that they have no relevant conflicts of interest and no financial relationships or relationships to products or devices during the past 12 months to disclose in relation to this activity. PHE is committed to providing participants with a quality learning experience and to improve clinical outcomes without promoting the financial interests of a proprietary business.

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- **UAN:** 0430-0000-20-001-L01-P
- **Credits:** 1.25 hour (0.125 ceu)
- **Activity Type:** Application

Learning Objectives

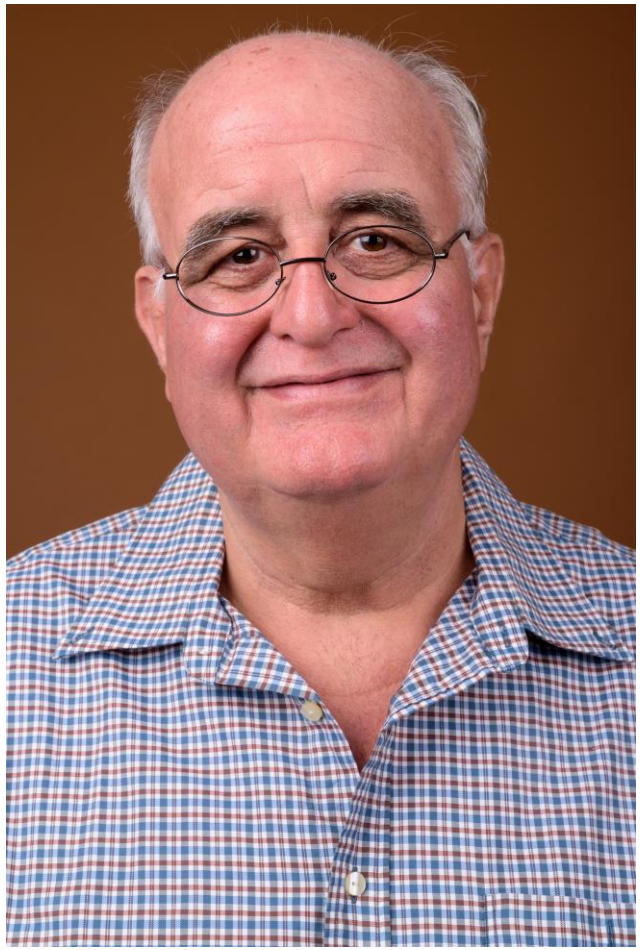
- **Discuss** current clinical recommendations for the use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) in the management of type 2 diabetes mellitus (T2DM)
- **Review** dosing, administration, and safety considerations for agents within the GLP-1 RA class
- **Formulate** a comprehensive management plan for a patient with T2DM and established atherosclerotic cardiovascular disease (ASCVD)

Case Study

Case Scenario: JM

JM is a 65-year-old gentleman with T2DM of 8 years duration

JM presents to the pharmacotherapy clinic today following referral by his primary care provider for a diabetes/medication regimen evaluation



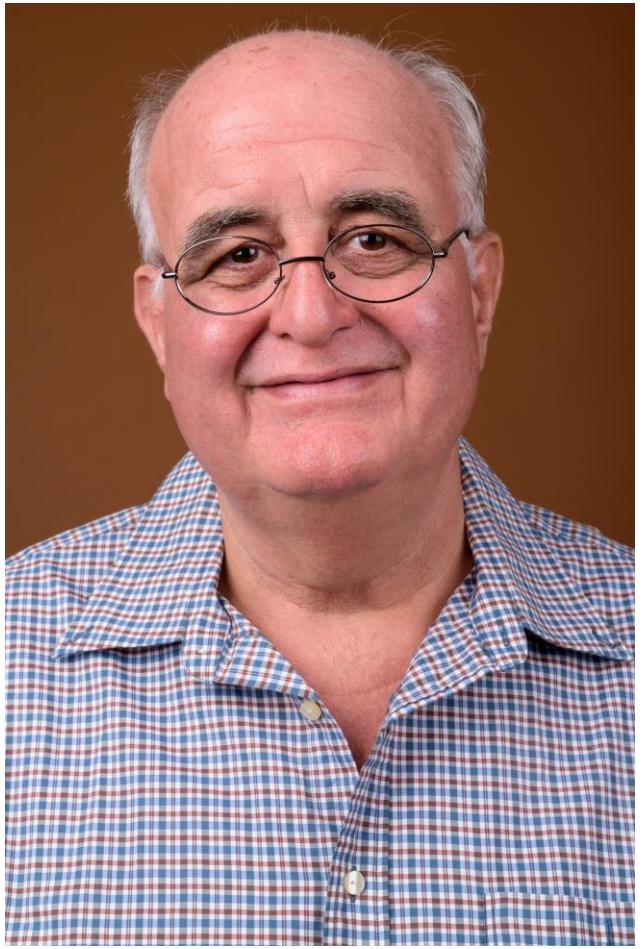
Case Scenario: JM

Past medical history:

- T2DM
- Hypertension
- Hypercholesterolemia
- Hx CABG (January 2019)
- Peripheral vascular disease
- Obesity

Current medications:

- Metformin ER 1000 mg twice daily
- Linagliptin 5 mg once daily
- Rosuvastatin 20 mg once daily
- Lisinopril 20 mg once daily
- Amlodipine 10 mg once daily
- ASA 81 mg once daily
- MVI once daily

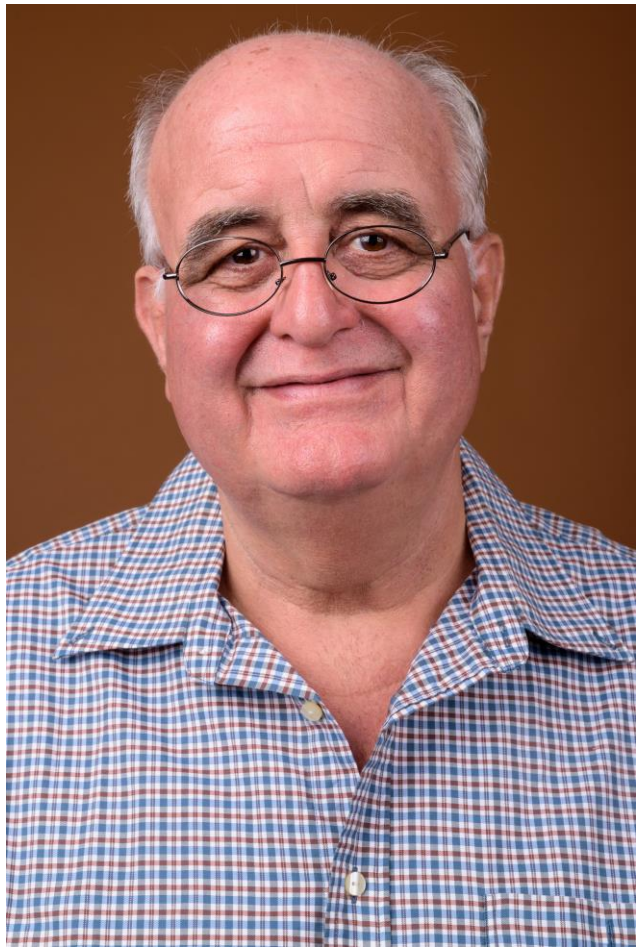


ASA, acetylsalicylic acid (aspirin); CABG, coronary artery bypass graft; ER, extended release; MVI, multivitamin.

Case Scenario: JM

Social history:

- Lives with his wife of 36 years
- Works full time as a software engineer
- No history of tobacco use
- Consumes alcohol infrequently
- Self-reports that he “could eat better”
- Engages in limited physical activity



Case Scenario: JM

Vitals:

Weight: 232 lbs (BMI = 34 kg/m^2)

BP: 128/84 mmHg (avg, 3 seated readings)

BG: 116 mg/dL (fasting)

POC A1C: 7.1%

Laboratory findings (fasting, December 2019):

SCr: 1.5 mg/dL

eGFR (MDRD): 50 mL/min/1.73 m^2

Na: 139 mEq/L

K: 4.9 mEq/L

UACR: 60 mg/g

LDL-C: 88 mg/dL

HDL-C: 40 mg/dL

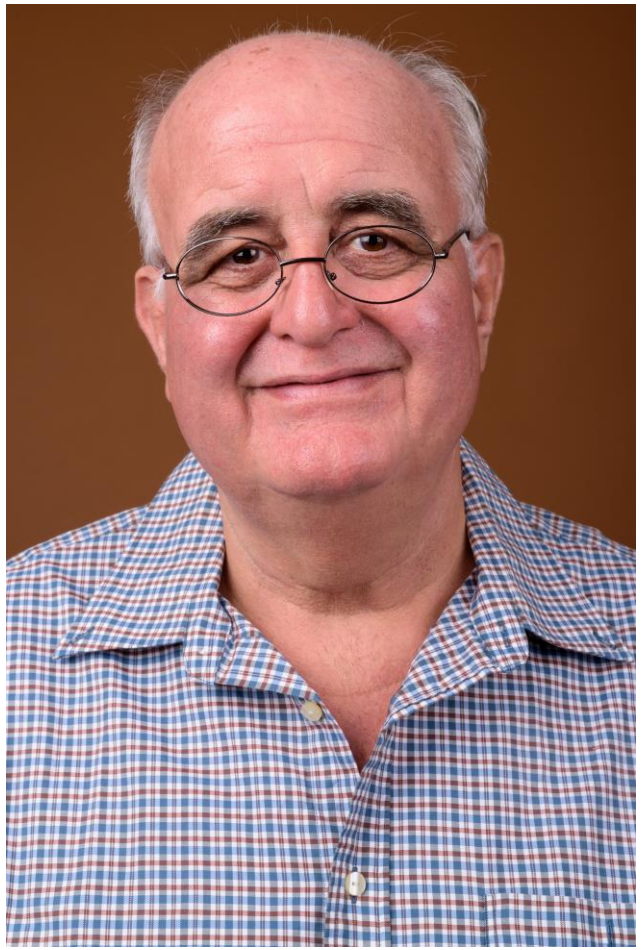
Trig: 148 mg/dL

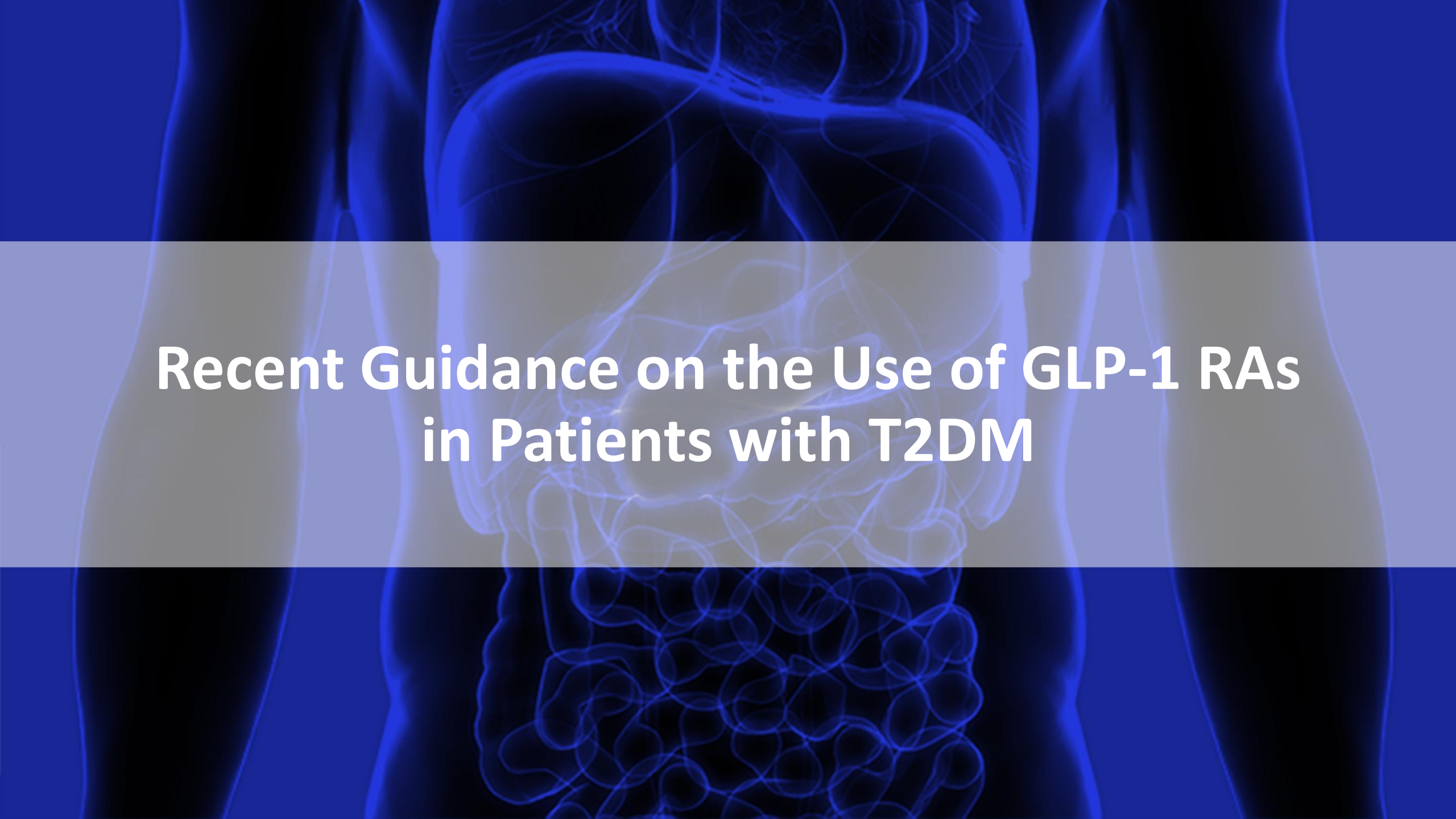
A1C, glycated hemoglobin; BP, blood pressure; BG, blood glucose; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; K, potassium; LDL-C, low-density lipoprotein cholesterol; Na, sodium; POC, point of care; SCr, serum creatinine; Trig, triglycerides; UACR, urine albumin-to-creatinine ratio.

JM: Questions to Consider

Based on the information available:

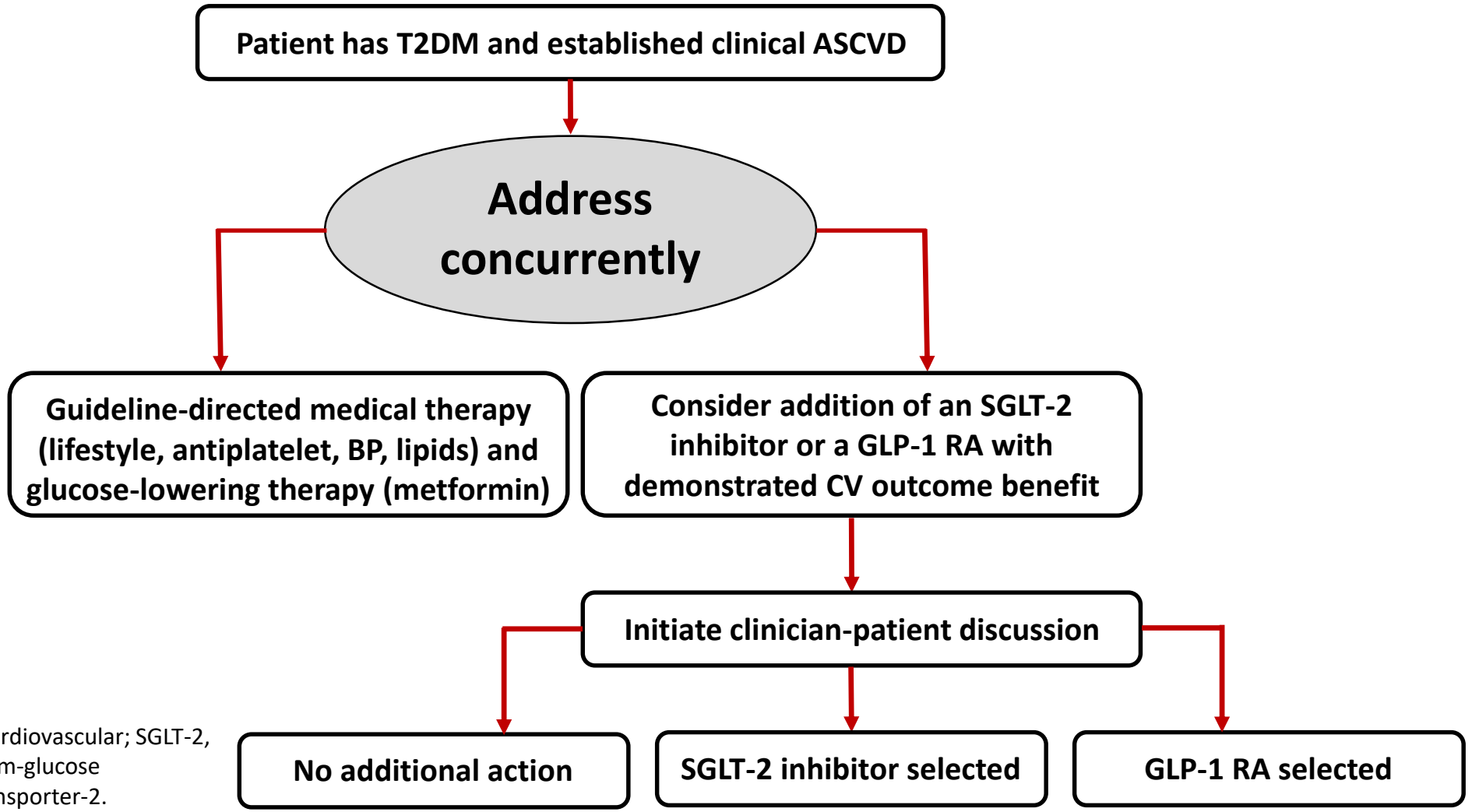
- Is his current glycemic control adequate?
- Is his current glucose-lowering regimen appropriate? Should any changes be considered?
- What interventions could be considered to improve his overall care?





Recent Guidance on the Use of GLP-1 RAs in Patients with T2DM

2018 American College of Cardiology (ACC) Expert Consensus Decision Pathway



CV, cardiovascular; SGLT-2, sodium-glucose cotransporter-2.

Das SR, et al. *J Am Coll Cardiol.* 2018;72(24):3200-23.

2018 ACC Expert Consensus Decision Pathway

Recommended opportunities to initiate a GLP-1 RA or an SGLT-2 inhibitor with demonstrated benefit in patients with clinical ASCVD and T2DM:

- In a patient with T2DM and ASCVD
- At the time of diagnosis of clinical ASCVD in a patient with T2DM on a drug regimen that does not include a GLP-1 RA or an SGLT-2 inhibitor with CV benefit
- At the time of diagnosis of T2DM in a patient with clinical ASCVD
- At hospital discharge after admission for an ASCVD- or diabetes-related clinical event

Das SR, et al. *J Am Coll Cardiol.* 2018;72(24):3200-23.

2018 ACC Expert Consensus Decision Pathway

Consider using a **GLP-1 RA** first when patient and clinician priorities include:	Consider using an **SGLT-2 inhibitor** first when patient and clinician priorities include:
Reducing MACE and CV death	Reducing MACE and CV death
Substantial weight loss	Preventing heart failure hospitalization
Once-weekly dosing	Reducing blood pressure
When eGFR is consistently < 45 mL/min/1.73 m^2	Orally administered therapy
Consider alternative agents if: • Persistent nausea, even at low doses • History of pancreatitis • History of gastroparesis • History of MEN2 or medullary thyroid cancer • History of proliferative retinopathy (semaglutide)	Consider alternative agents if: • Significant CKD • History of prior amputation, severe PAD, neuropathy, or foot ulcers (canagliflozin) • History of recurrent genital candidiasis • History of diabetic ketoacidosis • History of osteoporosis (canagliflozin)

CKD, chronic kidney disease; MACE, major adverse cardiovascular event; MEN2, multiple endocrine neoplasia type 2; PAD, peripheral arterial disease.

Das SR, et al. *J Am Coll Cardiol.* 2018;72(24):3200-23.

ARS Question #1

Which of the following is NOT a scenario in which the 2020 American Diabetes Association (ADA) Standards of Medical Care in Diabetes recommend consideration of a GLP-1 RA for use in patients with T2DM?

A. When there is a compelling need to minimize weight gain or promote weight loss
B. When there is a compelling need to minimize hypoglycemia
C. To decrease cardiovascular risk in patients with established ASCVD
D. When drug cost is a major consideration
E. Unsure

ADA Standards of Medical Care in Diabetes

- Beginning with the 2018 ADA Standards of Medical Care in Diabetes, the Standards document became a “living” document in which notable updates are incorporated into the Standards
- Updates will be made in response to important events inclusive of, but not limited to:
  - Approval of new treatments (medications or devices) with the potential to impact patient care;
  - Publication of new findings that support a change to a recommendation and/or evidence level of a recommendation; or
  - Publication of a consensus document endorsed by the ADA that necessitates an update of the Standards to align content of the documents

American Diabetes Association. http://care.diabetesjournals.org/living-standards.

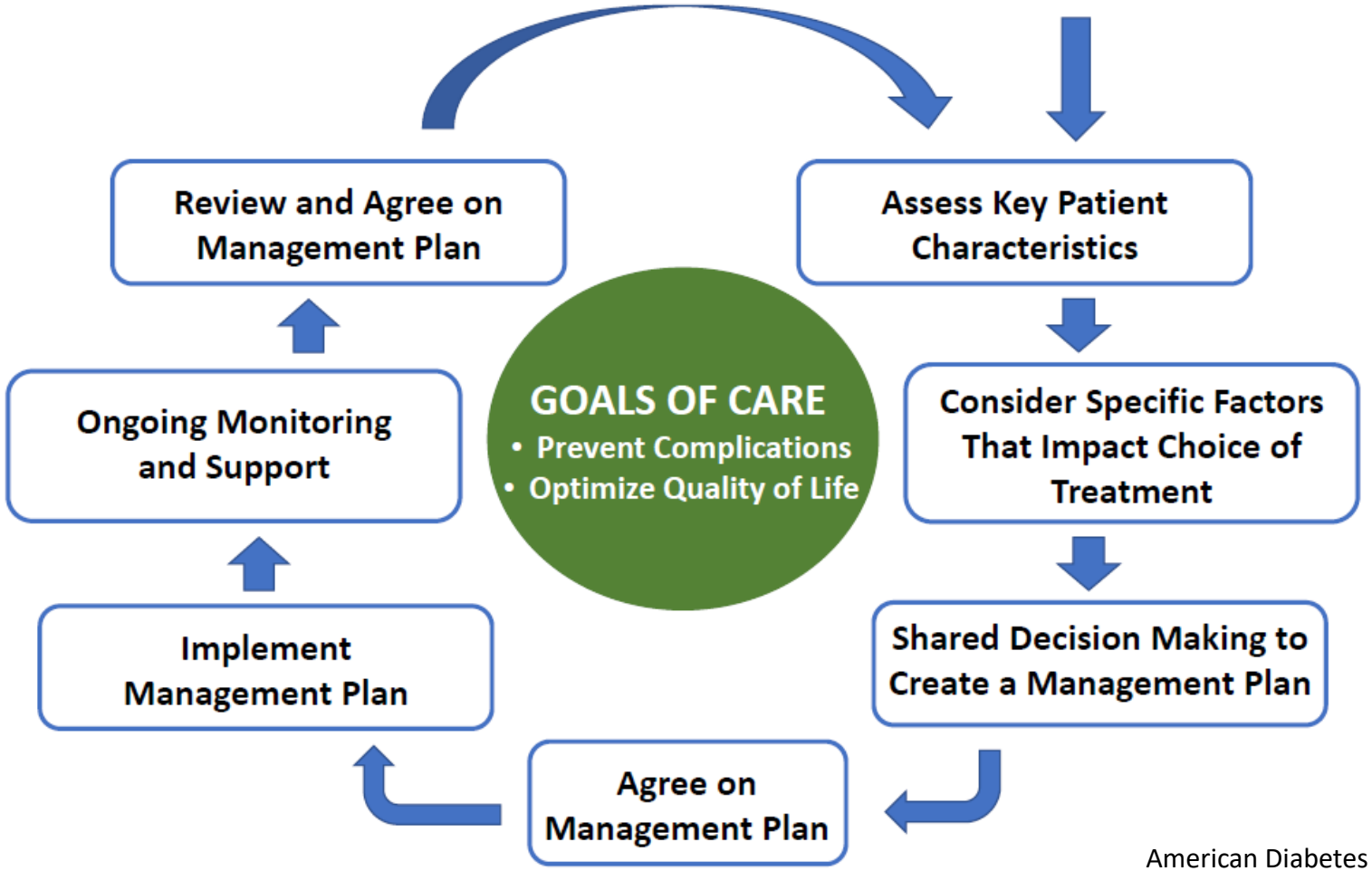
Glycemic Recommendations for Many Nonpregnant Adults with Diabetes

Measure	Target
Hemoglobin A1c (A1C)	< 7.0%*
Preprandial (fasting) glucose	80-130 mg/dL*
Peak postprandial glucose (1-2 h)	< 180 mg/dL*

More or less stringent glycemic goals may be appropriate for individual patients

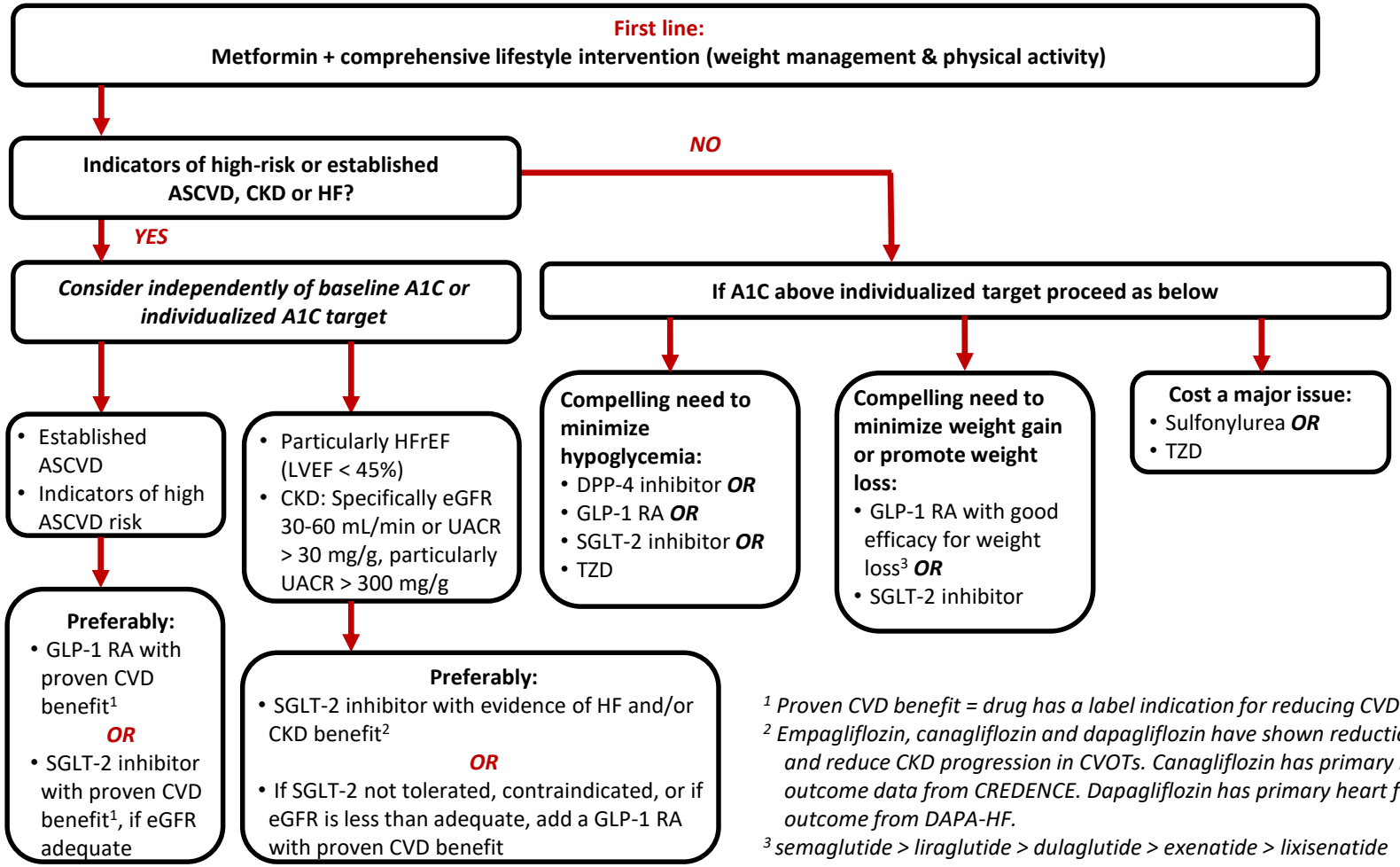
American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S66-76.

Decision Cycle for Patient-Centered Glycemic Management in T2DM



American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S37-47.

Glucose-Lowering Medication Use in T2DM



[1] Proven CVD benefit = drug has a label indication for reducing CVD events

[2] Empagliflozin, canagliflozin and dapagliflozin have shown reduction in HF and reduce CKD progression in CVOTs. Canagliflozin has primary renal outcome data from CREDENCE. Dapagliflozin has primary heart failure outcome from DAPA-HF.

[3] semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide

CVD, cardiovascular disease; CVOT, cardiovascular outcome trial; DPP-4, dipeptidyl peptidase-4; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; TZD, thiazolidinedione.

American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S98-110.; Buse JB, et al. *Diabetologia.* 2019.

Glucose-Lowering Medication Use in T2DM

First line:
Metformin + comprehensive lifestyle intervention (weight management & physical activity)

9.4 Metformin is the preferred initial pharmacologic agent for the treatment of T2DM. **A**

9.5 Once initiated, metformin should be continued as long as it is tolerated and not contraindicated; other agents, including insulin, should be added to metformin. **A**

9.6 Early combination therapy can be considered in some patients at treatment initiation to extend the time to treatment failure. **A**

American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S98-110.

Glucose-Lowering Medication Use in T2DM

First line:
Metformin + comprehensive lifestyle intervention (weight management & physical activity)

↓

Indicators of high-risk or established ASCVD, CKD or HF?*

Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications

American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S98-110.

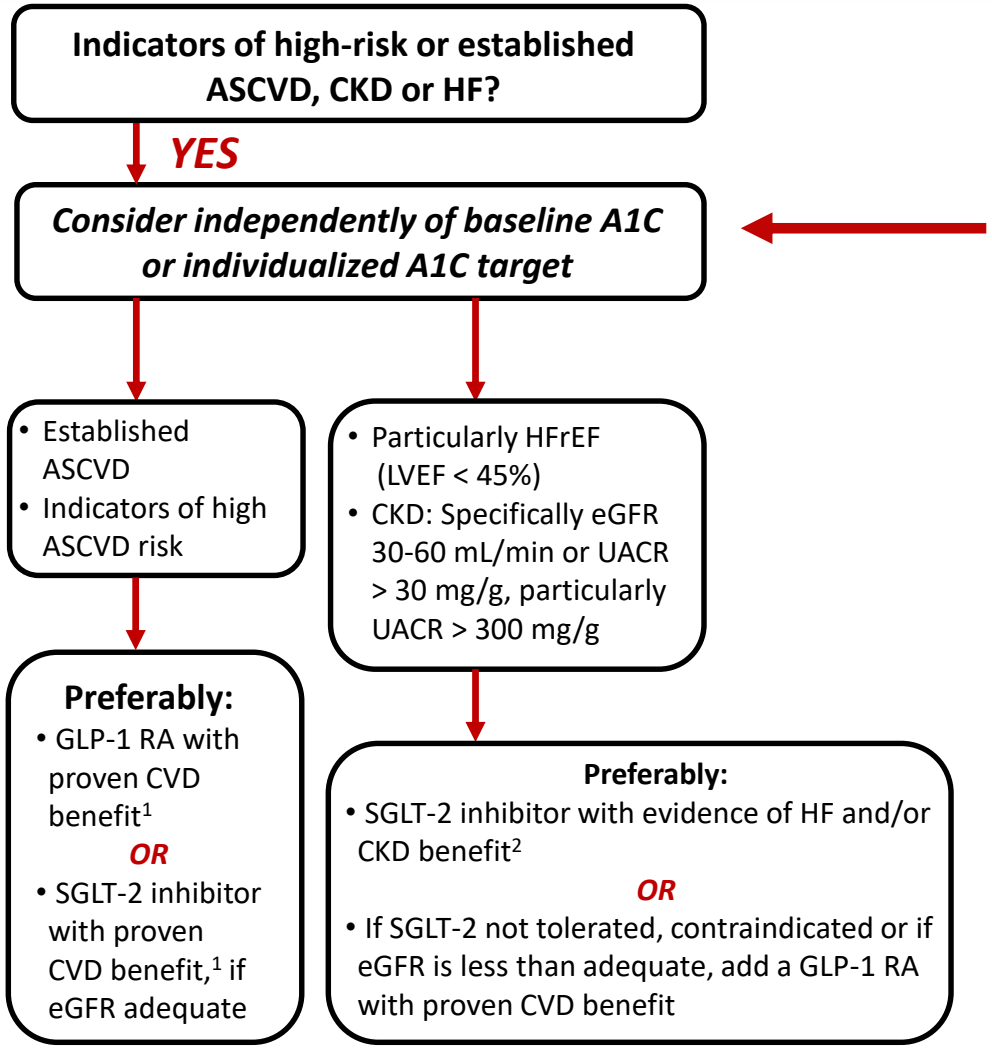
Glucose-Lowering Medication Use in T2DM

9.8 A patient-centered approach should be used to guide the choice of pharmacologic agents. Considerations include cardiovascular comorbidities, hypoglycemia risk, impact on weight, cost, risk for side effects, and patient preferences. **E**

9.9 Among patients with T2DM who have established ASCVD or indicators of high risk, established kidney disease, or heart failure, an SGLT-2 inhibitor or a GLP-1 RA with demonstrated CVD benefit is recommended as part of the glucose-lowering regimen independent of A1C and in consideration of patient-specific factors. **A**

American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S98-110.

Glucose-Lowering Medication Use in T2DM



Key Change in 2020:

- For patients with indicators of high-risk or established ASCVD, CKD or HF – use of agents with established evidence for risk reduction should be considered ***independently*** of current A1C and/or A1C target

American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S98-110.

Glucose-Lowering Medication Use in T2DM

9.8 A patient-centered approach should be used to guide the choice of pharmacologic agents. Considerations include cardiovascular comorbidities, hypoglycemia risk, impact on weight, cost, risk for side effects, and patient preferences. **E**

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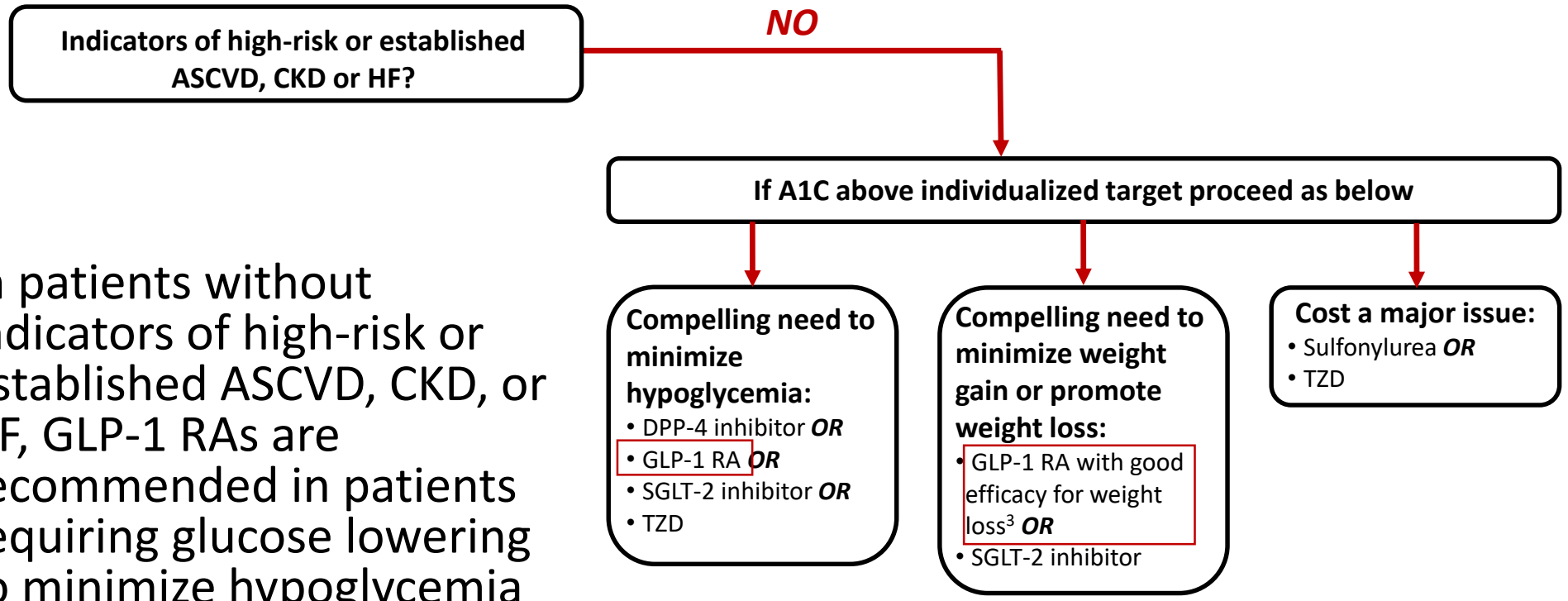
American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S98-110.

Glucose-Lowering Medication Use in T2DM



In patients without indicators of high-risk or established ASCVD, CKD, or HF, GLP-1 RAs are recommended in patients requiring glucose lowering to minimize hypoglycemia and minimize weight gain/ promote weight loss

American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S98-110.

Glucose-Lowering Medication Use in T2DM

Compelling need to minimize weight gain or promote weight loss:

- GLP-1 RA with good efficacy for weight loss[3] ***OR***
- SGLT-2 inhibitor

[3] *semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide*

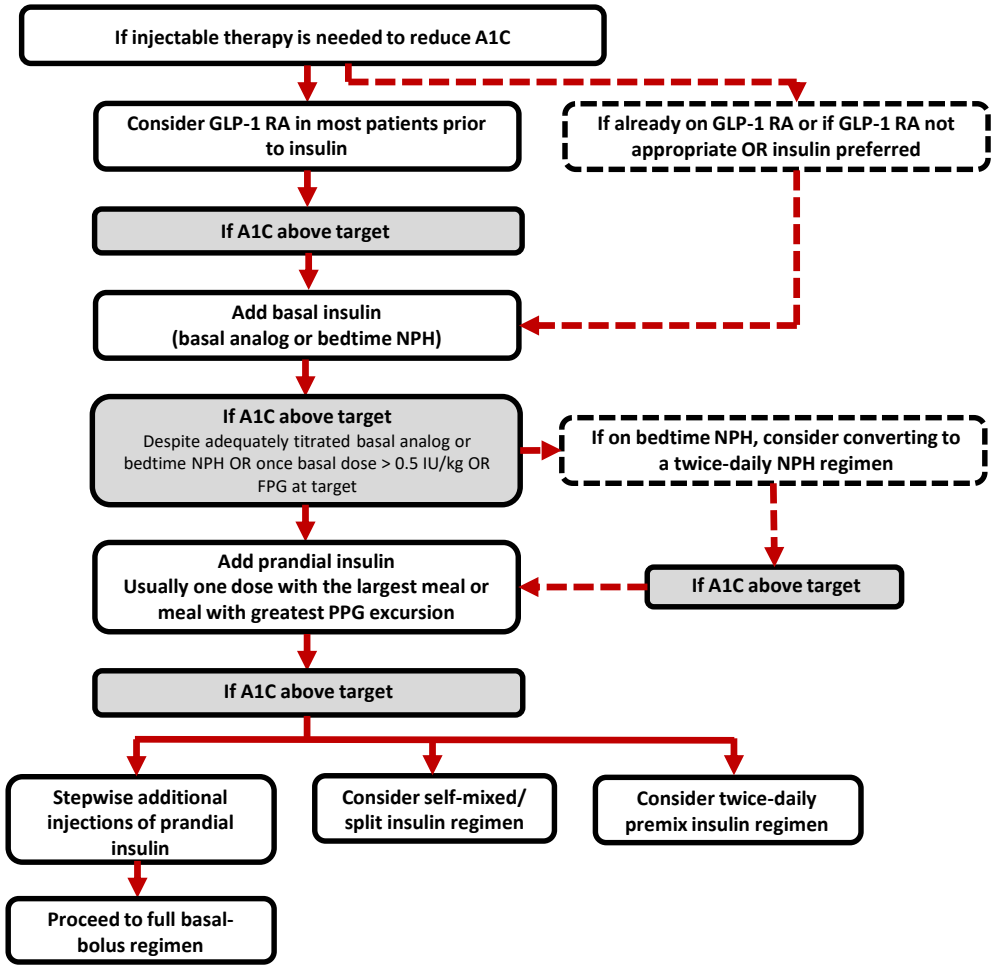
American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S98-110.

ARS Question #2

The 2020 ADA Standards of Medical Care in Diabetes recommend which of the following be considered as the first injectable agent in most patients requiring an injectable agent to meet individualized A1C goals?

A. Basal insulin
B. Injectable GLP-1 RA
C. Rapid-acting insulin
D. Premix insulin product
E. Unsure

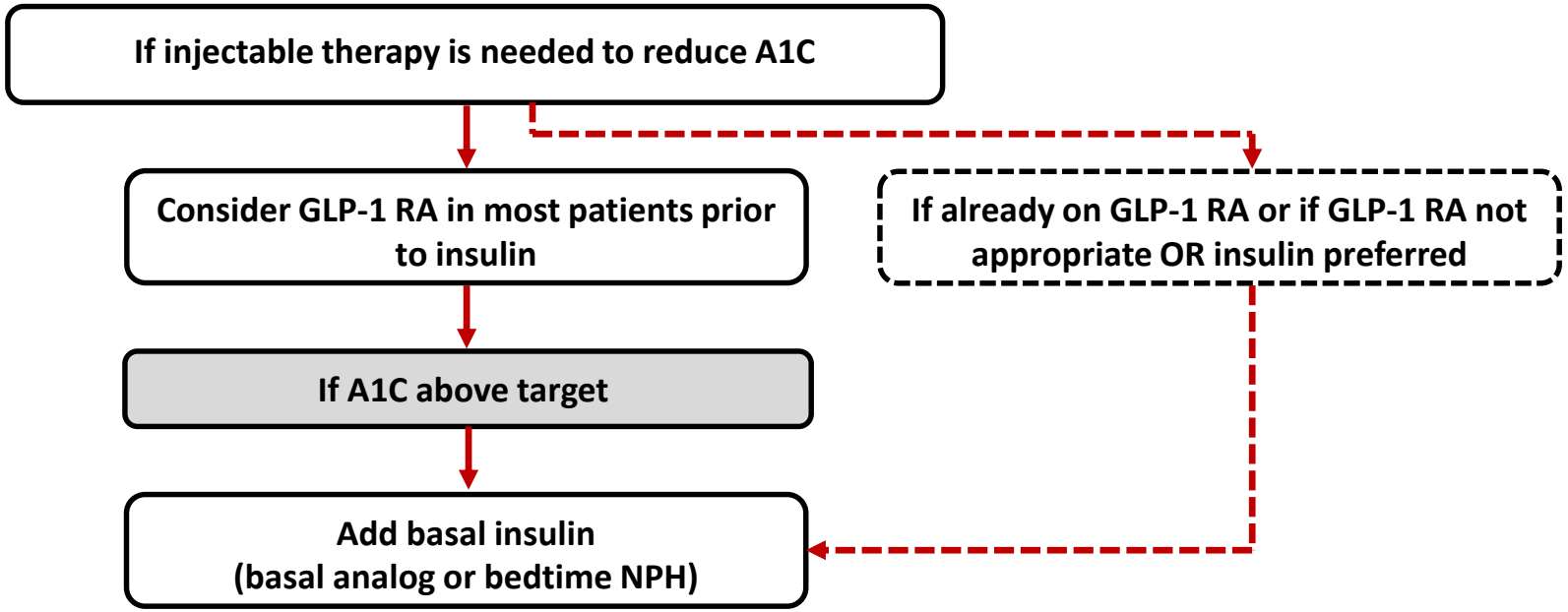
Use of Injectable Glucose-Lowering Agents in T2DM



FPG, fasting plasma glucose;
PPG, postprandial glucose.

American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S98-110.

Use of Injectable Glucose-Lowering Agents in T2DM



9.10 In patients with T2DM who need greater glucose lowering than can be obtained with oral agents, GLP-1 RAs are preferred to insulin when possible. **B**

American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S98-110.

Insulin Glargine/Lixisenatide

Fixed-dose combination product

- Insulin glargine (U-100)
- Lixisenatide (short-acting GLP-1 RA) – 33 mcg/mL

- Initiation:
  - **For patients naïve to components, on a GLP-1 RA, or on < 30 units basal insulin:**
    - 15 units insulin glargine U-100 (5 mcg lixisenatide)
  - **For patients on 30 - 60 units basal insulin:**
    - 30 units insulin glargine U-100 (10 mcg lixisenatide)
- Administration: within 1 hour before the first meal of the day
- Titration: titrate by 2 - 4 units (insulin glargine U-100 component) once weekly based on FPG or hypoglycemia

Soliqua [prescribing information]. 2019.

Insulin Degludec/Liraglutide

- **Fixed-dose combination product**
  - Insulin degludec (U-100)
  - Liraglutide (once-daily GLP-1 RA) – 3.6 mg/mL
- Initiation:
  - **Naïve to basal insulin or GLP-1 RA:**
    - 10 units insulin degludec (0.36 mg liraglutide) once daily
  - **Currently taking a basal insulin or GLP-1 RA:**
    - 16 units insulin degludec (0.58 mg liraglutide) once daily
- Administration: same time once daily (with or without food)
- Titration: Titrate by 2 units (insulin degludec) every 3 - 4 days based on FPG or hypoglycemia

Xultophy [prescribing information]. 2019.

Fixed-Ratio GLP-1 RA + Basal Insulin Products

Insulin glargine/lixisenatide

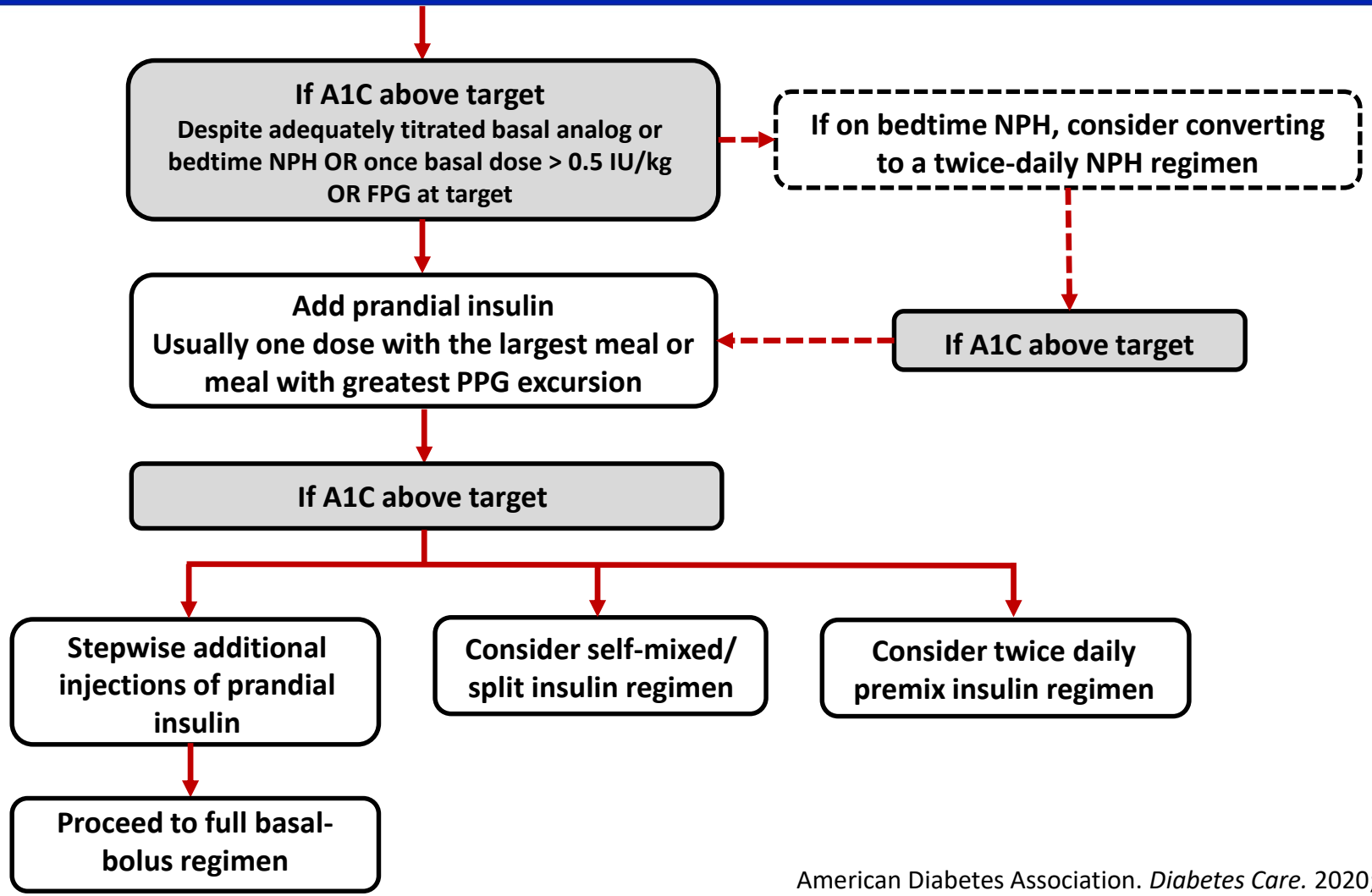
- Unit dose markings from 0 to 2 for priming
- No markings from 3 to 14 units
- Dose unit markings from 15 to 60 units

Insulin degludec/liraglutide

- Dosing unit "line" at 2 units for priming
- No markings until 10 units
- Dose unit markings from 10 to 50 units

Soliqua [prescribing information]. 2019.;
Xultophy [prescribing information]. 2019.

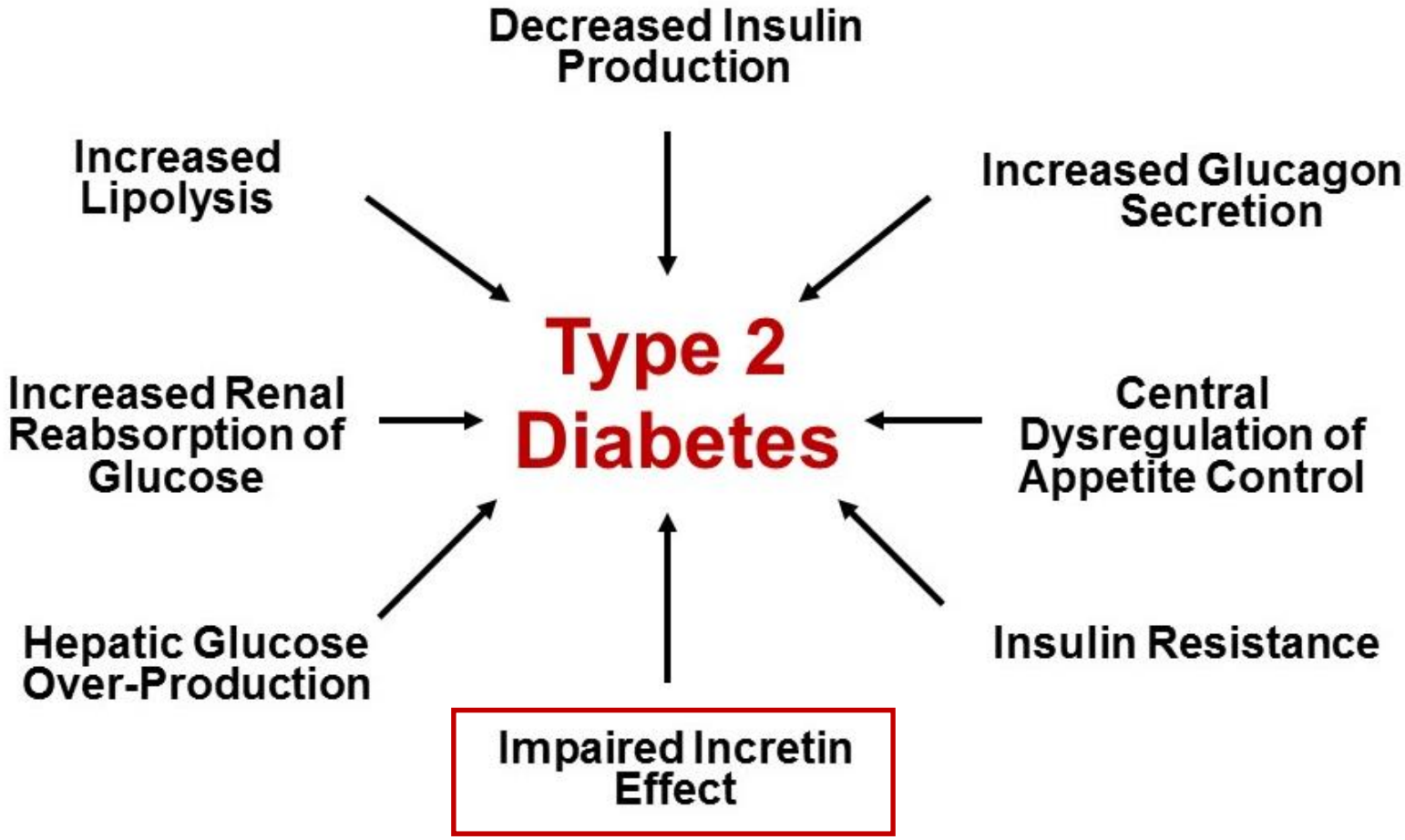
Use of Injectable Glucose-Lowering Agents in T2DM



American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S98-110.

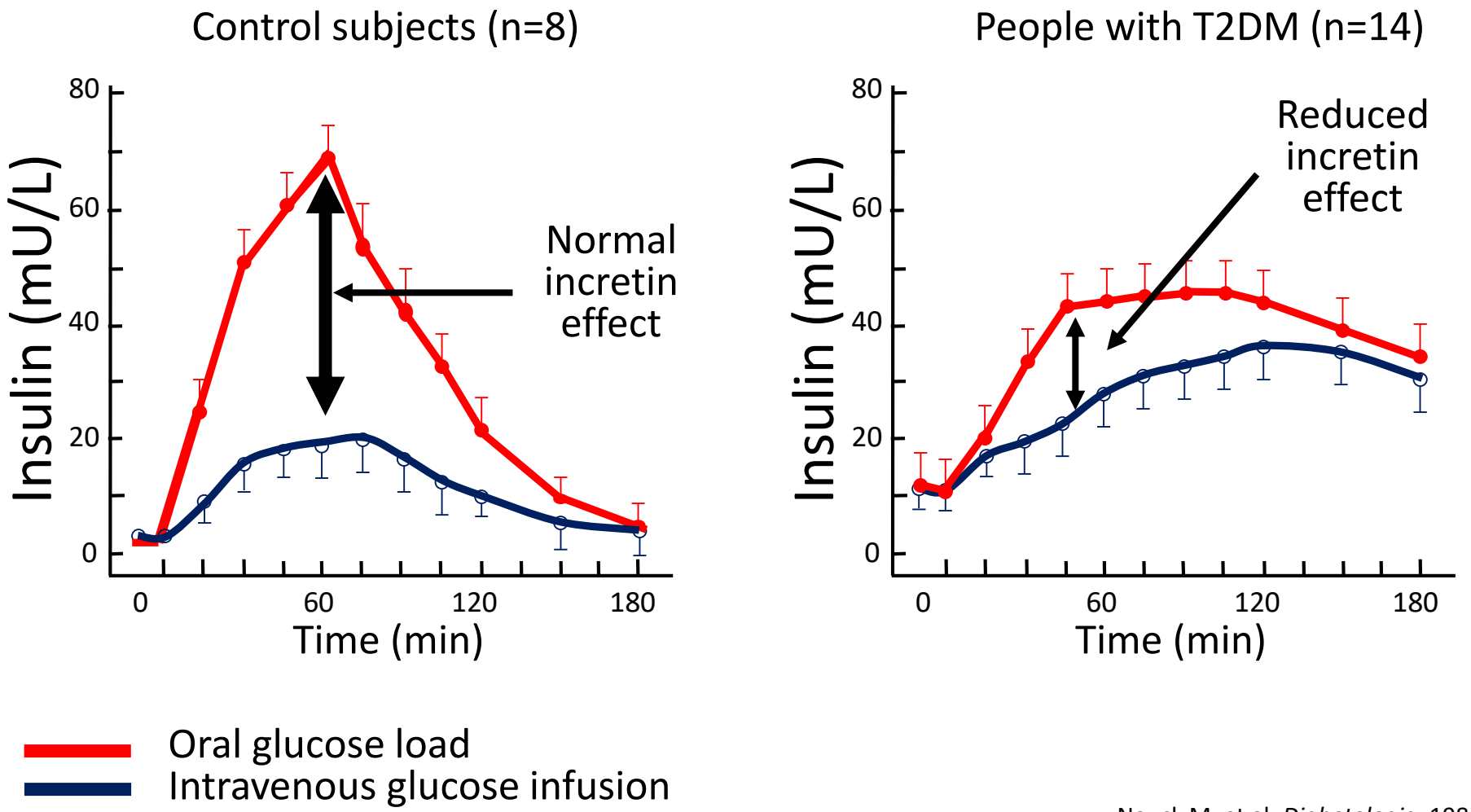
Review of Currently Available GLP-1 RA Products

Pathophysiologic Defects in T2DM



DeFronzo RA. *Diabetes*. 2009;58(4):773-95.

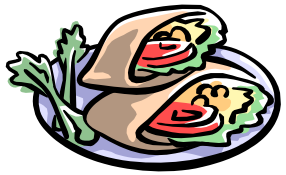
The Incretin Effect



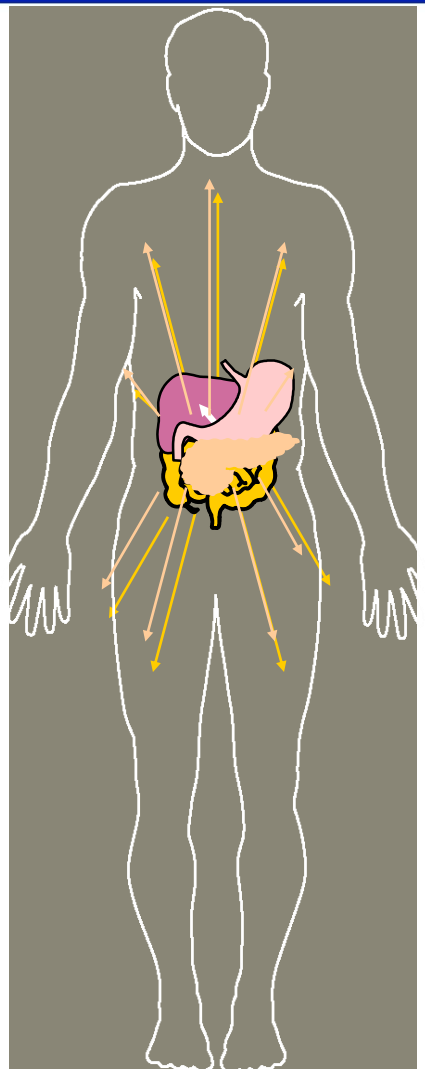
Nauck M, et al. *Diabetologia.* 1986;29(1):46-52.

GLP-1: Effects in Humans

After food ingestion…



GLP-1 is secreted from L-cells of the jejunum and ileum



That, in turn, …

- Stimulates glucose-dependent insulin secretion
- Suppresses glucagon secretion
- Slows gastric emptying
- Leads to a reduction of food intake

Drucker DJ. *Curr Pharm Des.* 2001;7(14):1399-412.;
Drucker DJ. *Mol Endocrinol.* 2003;17(2):161-71.;
Drucker DJ. *Cell Metab.* 2006;3(3):153-65.

Pharmacologic Approaches to Enhancing the Incretin Effect

The incretin effect is blunted in people with T2DM and endogenous GLP-1 has an extremely short half-life

Block DPP-4 to slow the enzymatic degradation of endogenous GLP-1:

- Alogliptin
- Linagliptin
- Saxagliptin
- Sitagliptin

Use GLP-1 analogs with longer half-lives:

- Exenatide
- Lixisenatide
- Liraglutide
- Exenatide XR
- Dulaglutide
- Semaglutide (injectable & oral)

Drucker DJ. *Curr Pharm Des.* 2001;7(14):1399-412.; Drucker DJ. *Mol Endocrinol.* 2003;17(2):161-71.; Drucker DJ. *Cell Metab.* 2006;3(3):153-65.

Currently Available GLP-1 RA Products

	GLP-1 RA "type"	Route of administration	Administration frequency	Half-life	Recommended renal dose adjustment
Short-acting agents					
Exenatide	Exendin-4-based	SC injection	Twice daily	~2.4 h	Not recommended with CrCl < 30 mL/min
Lixisenatide	Exendin-4-based	SC injection	Once daily	~3 h	Not recommended with CrCl < 15 mL/min
Long-acting agents					
Liraglutide	Human-GLP-1-based	SC injection	Once daily	~13 h	No dosage adjustments recommended
Exenatide XR	Exendin-4-Based	SC injection	Once weekly	~1 w	Not recommended with eGFR < 45 mL/min/1.73 m^2 or ESRD
Dulaglutide	Human-GLP-1-based	SC injection	Once weekly	~5 d	No dosage adjustments recommended
Semaglutide	Human-GLP-1-based	SC injection	Once weekly	~1 w	No dosage adjustments recommended
		Oral	Once daily		

CrCl, creatinine clearance; d, days; ESRD, end-stage renal disease; h, hours; SC, subcutaneous; w, weeks.

Adlyxin [prescribing information]. 2016.; Bydureon [prescribing information]. 2018.; Byetta [prescribing information]. 2015.; Ozempic [prescribing information]. 2017.; Rybelsus [prescribing information]. 2019.; Trulicity [prescribing information]. 2017.; Victoza [prescribing information]. 2017.

Currently Available Injectable GLP-1 RA Products

	Short-acting		Long-acting			
	Exenatide	**Lixisenatide**	**Liraglutide**	**Exenatide XR**	**Dulaglutide**	**Semaglutide**
Dose titration	5 mcg twice daily x 1 month; increase to 10 mcg twice daily	10 mcg once daily x 14 days; increase to 20 mcg daily	0.6 mg once daily x 1 week; increase to 1.2 mg daily x 1 week; increase to 1.8 mg daily	2 mg once weekly	0.75 mg once weekly; increase to 1.5 mg once weekly	0.25 mg once weekly x 4 weeks; increase to 0.5 mg x 4 weeks; increase to 1 mg once weekly
Administration timing	Take within 60 minutes before meals	Take within 60 minutes before morning meal	Take at same time each day	Take on same day each week	Take on same day each week	Take on same day each week
Pen availability	Multi-use pen (2 strengths)	Multi-use pen (2 strengths)	Multi-use pen	Single-use pen	Single-use pen (2 strengths)	Multi-use pen (2 pen options)

Adlyxin [prescribing information]. 2016.; Bydureon [prescribing information]. 2018.; Byetta [prescribing information]. 2015.; Ozempic [prescribing information]. 2017.; Rybelsus [prescribing information]. 2019.; Trulicity [prescribing information]. 2017.; Victoza [prescribing information]. 2017.

CVOT Summary of Trials with Injectable GLP-1 RAs

	ELIXA (n = 6068)	LEADER (n = 9340)	SUSTAIN-6 (n = 3297)	EXSCEL (n = 14,752)	REWIND (n = 9901)
Agent	Lixisenatide	Liraglutide	Semaglutide	Exenatide XR	Dulaglutide
Median follow-up (years)	2.1	3.8	2.1	3.2	5.4
Metformin use (%)	66	76	73	77	81
Prior CVD (%)	100	81	60	73.1	32
Mean baseline A1C (%)	7.7	8.7	8.7	8.0	7.4
Primary outcome	4-point MACE 1.02 (0.89–1.17)	**3-point MACE 0.87 (0.78–0.97)**	**3-point MACE 0.74 (0.58–0.95)**	3-point MACE 0.91 (0.83–1.00)	**3-point MACE 0.88 (0.79–0.99)**
Cardiovascular death	0.98 (0.78–1.22)	**0.78 (0.66–0.93)**	0.98 (0.65–1.48)	0.88 (0.76–1.02)	0.91 (0.78–1.06)
MI	1.03 (0.87–1.22)	0.86 (0.73–1.00)	0.74 (0.51–1.08)	0.97 (0.85–1.10)	0.96 (0.79–1.15)
Stroke	1.12 (0.79–1.58)	0.86 (0.71–1.06)	**0.61 (0.38–0.99)**	0.85 (0.70–1.03)	**0.76 (0.61–0.95)**
All-cause mortality	0.94 (0.78–1.13)	**0.85 (0.74–0.97)**	1.05 (0.74–1.50)	**0.86 (0.77–0.97)**	0.90 (0.80–1.01)
Worsening nephropathy	-	**0.78 (0.67–0.92)**	**0.64 (0.46–0.88)**	-	**0.85 (0.77–0.93)**

MI, myocardial infarction.

American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S111-34.

Oral GLP-1 RA Product: Semaglutide

- First orally available GLP-1 RA
- Co-formulated with the absorption enhancer sodium *N*-[8-(2-hydroxylbonzoyl)aminocaprylate] – AKA "**SNAC**"
  - Facilitates transcellular absorption of semaglutide in the stomach
    - Increases local pH around the tablet
    - Increased drug solubility
    - Protection against proteolytic degradation

Bui V, Neumiller JJ. *Clin Diabetes.* 2018;36(4):327-9.

Oral Semaglutide: Administration

- Take at least 30 minutes before the first food, beverage, or other oral medication of the day
  - Take with no more than 4 ounces of plain water only
  - Swallow tablets whole: do not crush or chew
- Dose titration:
  - Start with 3 mg once daily for 30 days
  - Increase to 7 mg once daily for 30 days
  - Increase to 14 mg once daily, if needed, for additional glycemic control

Rybelsus [prescribing information]. 2019.

CVOT Summary for Oral Semaglutide: PIONEER-6

	PIONEER-6 (n = 3183)
Agent	Oral semaglutide
Median follow-up (months)	15.9
Metformin use (%)	77.4
Prior CVD (%)	84.7
Mean baseline A1C (%)	8.2
Primary outcome	3-point MACE 0.79 (0.57–1.11)*
Cardiovascular death	0.49 (0.27–0.92)†
MI	1.18 (0.73–1.90)†
Stroke	0.74 (0.35–1.57)†
All-cause mortality	0.51 (0.31–0.84)†

*P<0.001 for noninferiority; P=0.17 for superiority

†Not controlled for multiple comparisons; interpreted as exploratory

Husain M, et al. *N Engl J Med.* 2019;381(9):841-51.

GLP-1 RAs: Pros & Cons

Pros:

- High efficacy
- Low hypoglycemia risk (monotherapy or combination with metformin)
- Cardiovascular & renal benefits
- Weight loss

Potential cons:

- Cost
- Injectable (most)
- GI intolerance (nausea, vomiting, diarrhea)
- **Rare/serious safety concerns**: thyroid C-cell tumors (long-acting agents), acute pancreatitis

GI, gastrointestinal.

American Diabetes Association. *Diabetes Care.* 2020;43(Suppl. 1):S98-110.

2018 ACC Expert Consensus Decision Pathway

Consider using a **GLP-1 RA** first when patient and clinician priorities include:
Reducing MACE and CV death
Substantial weight loss
Once-weekly dosing
When eGFR is consistently < 45 mL/min/1.73 m^2
Consider alternative agents if: • Persistent nausea, even at low doses • History of pancreatitis • History of gastroparesis • History of MEN2 or medullary thyroid cancer • History of proliferative retinopathy (semaglutide)

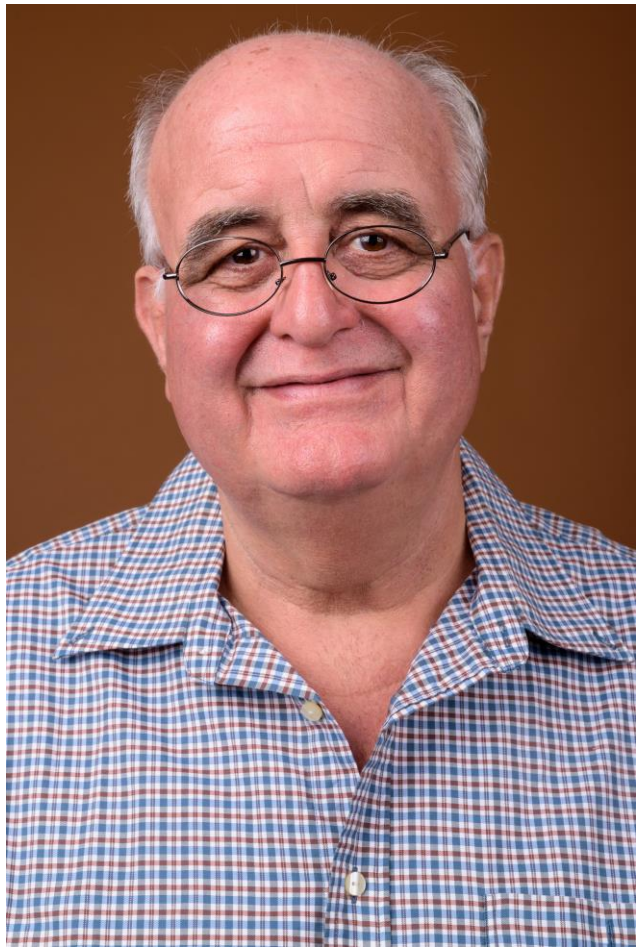
Das SR, et al. *J Am Coll Cardiol* 2018;72(24):3200-23.

Case Study Debrief

Case Scenario: JM

JM is a 65-year-old gentleman with T2DM of 8 years duration

JM presents to the pharmacotherapy clinic today following referral by his primary care provider for a diabetes/medication regimen evaluation



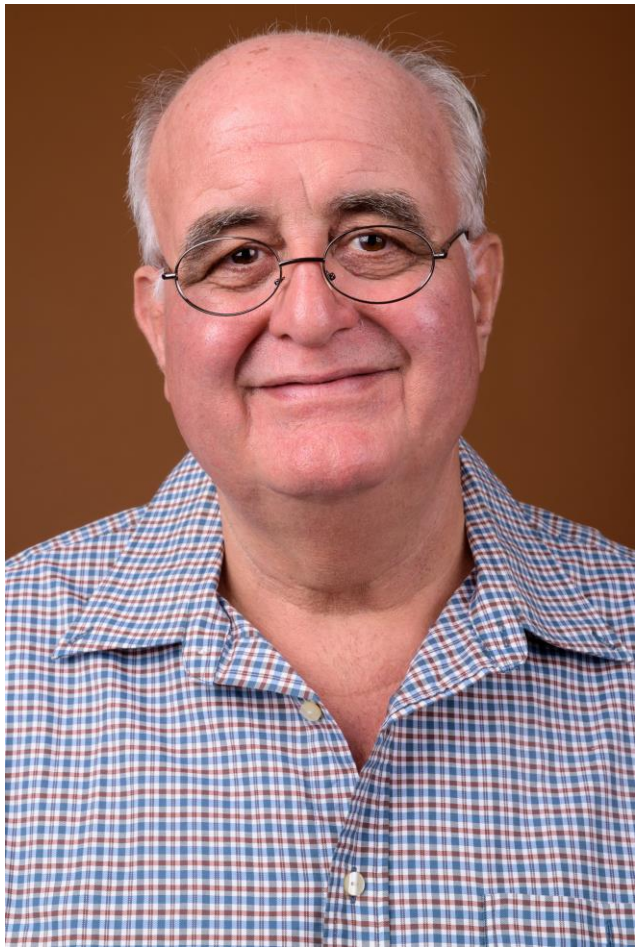
Case Scenario: JM

Past medical history:

- T2DM
- Hypertension
- Hypercholesterolemia
- Hx CABG (January 2019)
- Peripheral vascular disease
- Obesity

Current medications:

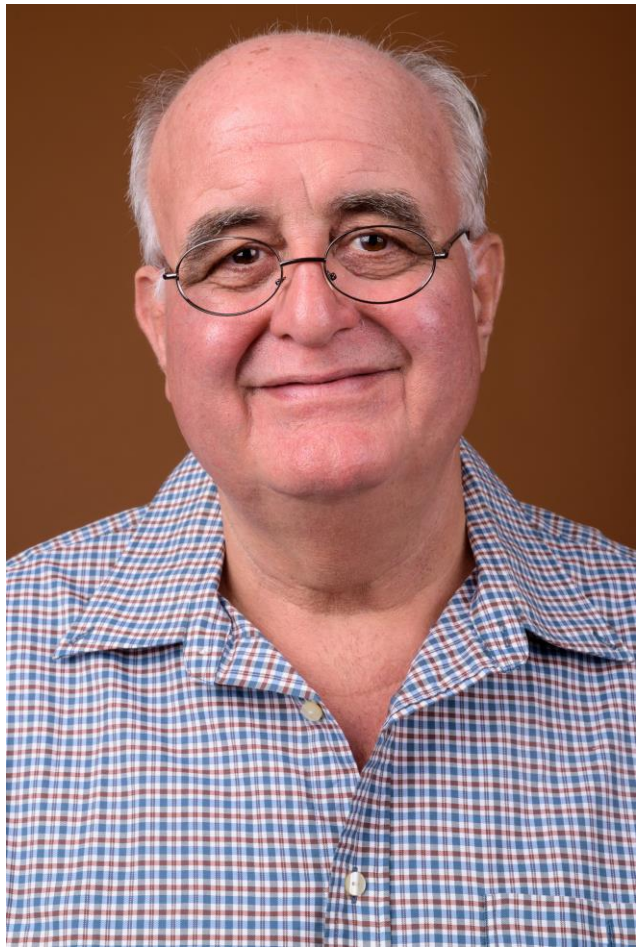
- Metformin ER 1000 mg twice daily
- Linagliptin 5 mg once daily
- Rosuvastatin 20 mg once daily
- Lisinopril 20 mg once daily
- Amlodipine 10 mg once daily
- ASA 81 mg once daily
- MVI once daily



Case Scenario: JM

Social history:

- Lives with his wife of 36 years
- Works full time as a software engineer
- No history of tobacco use
- Consumes alcohol infrequently
- Self-reports that he “could eat better”
- Engages in limited physical activity



Case Scenario: JM

Vitals:

Weight: 232 lbs (BMI = 34 kg/m^2)

BP: 128/84 mmHg (avg, 3 seated readings)

BG: 116 mg/dL (fasting)

POC A1C: 7.1%

Laboratory findings (fasting, December 2019):

SCr: 1.5 mg/dL

eGFR (MDRD): 50 mL/min/1.73 m^2

Na: 139 mEq/L

K: 4.9 mEq/L

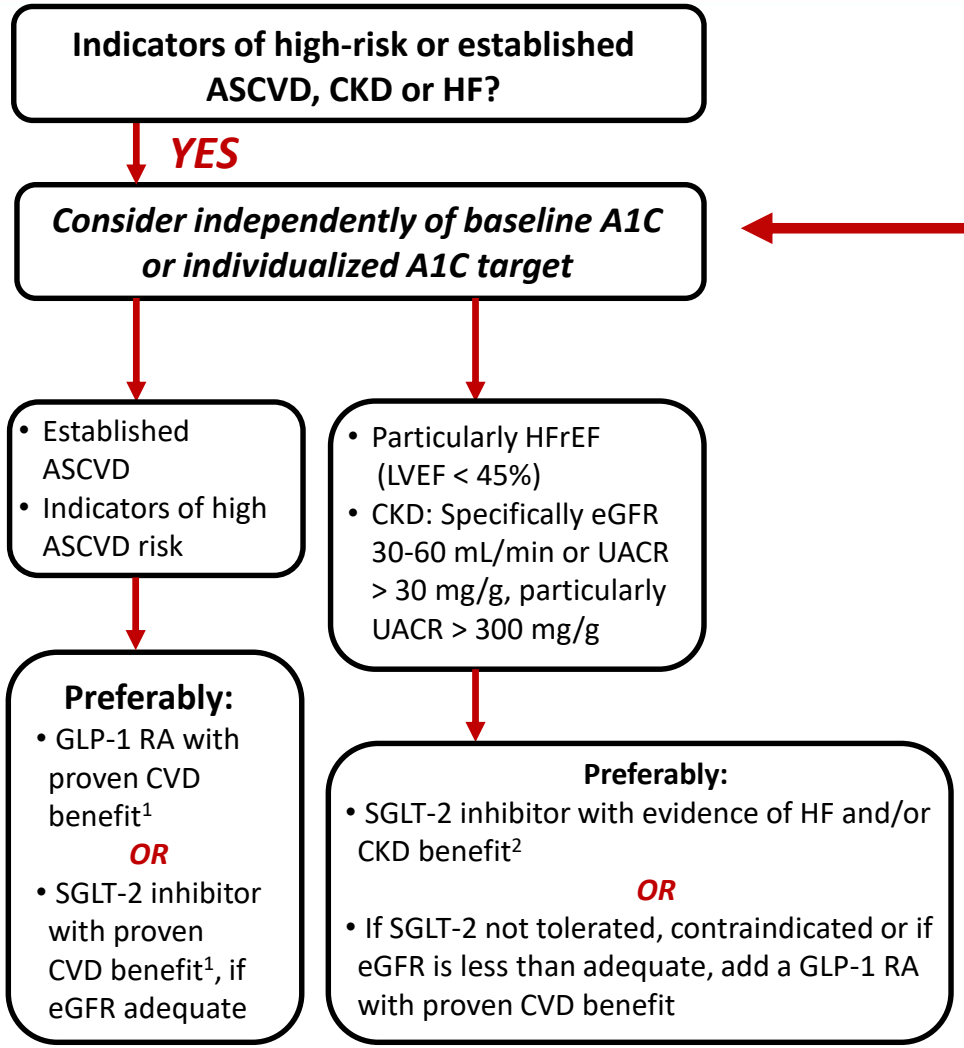
UACR: 60 mg/g

LDL-C: 88 mg/dL

HDL-C: 40 mg/dL

Trig: 148 mg/dL

Glucose-Lowering Medication Use in T2DM



Key Change in 2020:

- For patients with indicators of high-risk or established ASCVD, CKD or HF – use of agents with established evidence for risk reduction should be considered ***independently*** of current A1C and/or A1C target

American Diabetes Association. *Diabetes Care* 2020;43(Suppl. 1):S98-110.

2018 ACC Expert Consensus Decision Pathway

Consider using a **GLP-1 RA** first when patient and clinician priorities include:	Consider using an **SGLT-2 inhibitor** first when patient and clinician priorities include:
Reducing MACE and CV death	Reducing MACE and CV death
Substantial weight loss	Preventing heart failure hospitalization
Once-weekly dosing	Reducing blood pressure
When eGFR is consistently < 45 mL/min/1.73 m^2	Orally administered therapy
Consider alternative agents if: • Persistent nausea, even at low doses • History of pancreatitis • History of gastroparesis • History of MEN2 or medullary thyroid cancer • History of proliferative retinopathy (semaglutide)	Consider alternative agents if: • Significant CKD • History of prior amputation, severe PAD, neuropathy, or foot ulcers (canagliflozin) • History of recurrent genital candidiasis • History of diabetic ketoacidosis • History of osteoporosis (canagliflozin)

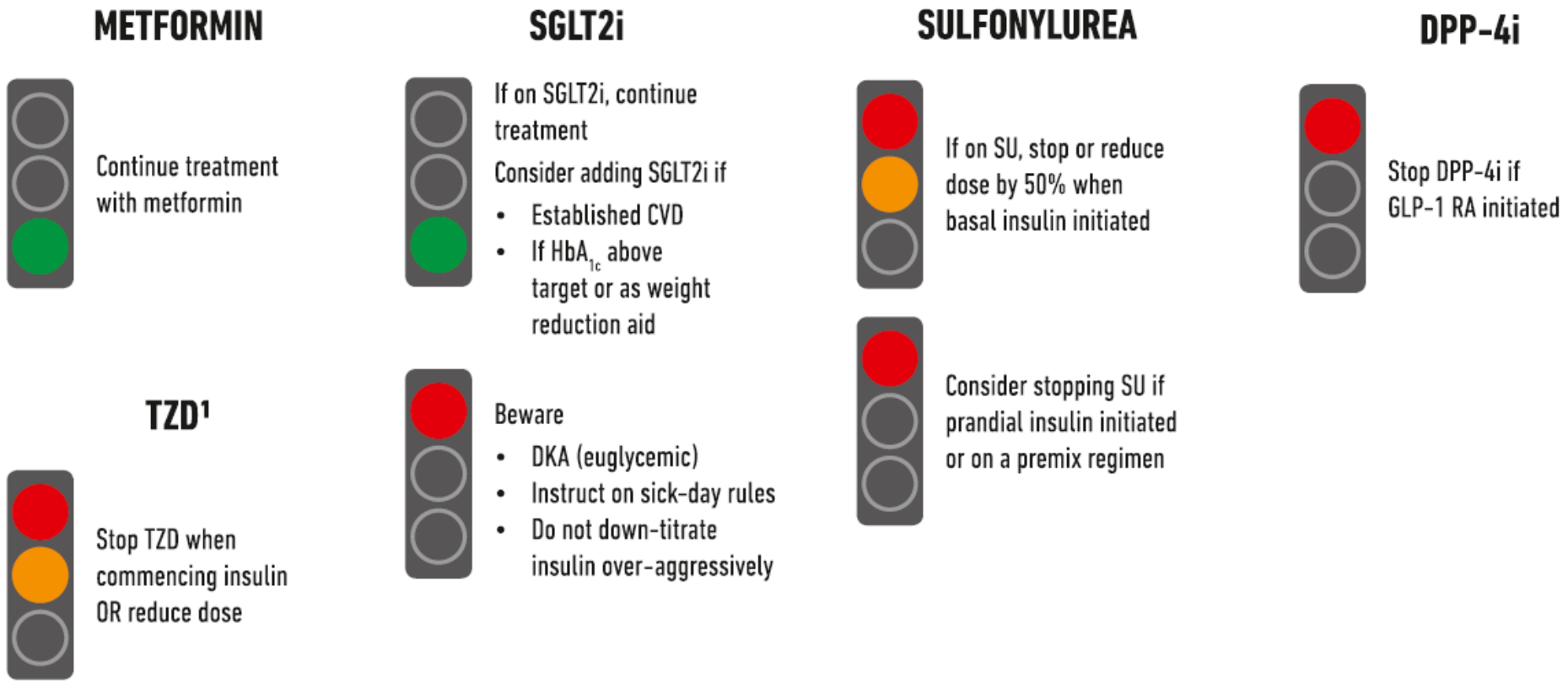
Das SR, et al. *J Am Coll Cardiol.* 2018;72(24):3200-23.

ARS Question #3

If it was decided to add a GLP-1 RA to JM's regimen, what other change would you consider making to his medication regimen?

A. Add an antiemetic medication
B. Start a fixed-dose GLP-1 RA/basal insulin combination product for additional glucose lowering
C. Discontinue his DPP-4 inhibitor
D. Discontinue his statin
E. Unsure

Considering Oral Therapies in Combination with Injectable Therapies



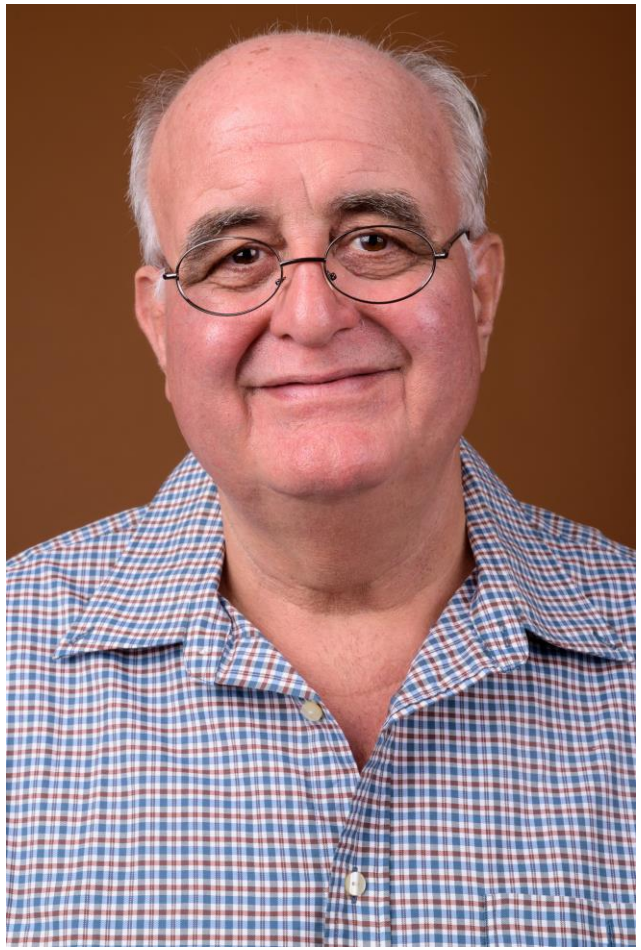
DKA, diabetic ketoacidosis; SU, sulfonylurea.

Davies MJ, et al. *Diabetes Care.* 2018;41(12):2669-701.

Case Scenario: JM

Treatment plan implemented:

- Referred for DSMES
  - Individualized lifestyle counseling
- Add semaglutide 0.25 mg once weekly
  - Counsel on tolerability, self-injection technique
  - Instruct to call clinic with any questions or concerns
- Continue metformin
- Discontinue linagliptin
- Follow-up by phone in 1 week



DSMES, diabetes self-management education and support.

Key Takeaways

- Patient-centered decision-making and consistent efforts at improving diet and physical activity remain the foundation of glycemic management
- The management of hyperglycemia in T2DM has become increasingly complex with the expanding number of glucose-lowering medications available and our expanding understanding of their impact on CV and renal outcomes, with GLP-1 RAs playing an increasingly important role in treatment
- Initial use of metformin, followed by the addition of glucose-lowering medications based on patient comorbidities and preferences, is recommended


Question & Answer

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