

### **Looking Forward:** An Insight into the 2025 ADA Standards of Care in Diabetes

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Nagesh Sharma, PharmD PGY-1 Pharmacy Resident Memorial Hospital of South Bend

Preceptor: Kaitlyn Marie DeWeerd, PharmD, BCPS Clinical Pharmacy Coordinator & PGY1 Pharmacy Residency Coordinator Memorial Hospital, South Bend, Indiana

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### Objectives

Recall

Recall changes in medication recommendations and glycemic targets outlined in the 2025 ADA Standard of Care in Diabetes

Identify

Identify a pharmacologic treatment plan for a patient with Type 2 diabetes and cardiovascular disease based on the recommendation from the 2025 ADA Standards on the use of GLP-1 receptor agonists

### Recognize

Recognize strategies to implement screening protocols for specific comorbidities in the clinic setting based upon the revised ADA standards

### Contents



Summary of General Changes Specific Changes to Sections Self-Assessment Questions

### General Changes

• The non-guideline specific changes were focused on: OPerson-first care oInclusivity OSocial Determinants of Health • Recognizing the individual at the center of diabetes care • Applying terminology that empowers people with diabetes

### General Changes

 Although levels of evidence for several recommendations have been updated, these additions will not be covered in this presentation

### Abbreviations

T1DM- Type 1 diabetes mellitus

T2DM- Type 2 diabetes mellitus

HR- Hazard ratio

CI- Confidence interval

**RSV-** Respiratory Syncytial Virus

NAFLD- Nonalcoholic fatty liver disease

NASH- Nonalcoholic steatohepatitis

MASH- Metabolic dysfunction associated steatohepatitis

**CSII-** Continuous subcutaneous insulin infusion

BGM- Blood glucose monitoring

CGM- Continuous glucose monitoring

AID- Automated insulin delivery

**GIP/GLP-1 RA-** Dual glucose-dependent insulinotropic polypeptide and glucagon like peptide-1 receptor agonist **GLP-1 RA-** Glucagon like peptide-1 receptor agonist **SGLT-** Sodium-glucose cotransporter-2 FIB-4- Fibrosis-4 **LSM-** Liver stiffness **ELF-** Enhanced liver fibrosis **HFpEF-** Heart failure with preserved ejection fraction **CKD-** Chronic kidney disease **ACE-** Angiotensin-converting enzyme **ARB-** Angiotensin receptor blockers **MRA-** Mineralocorticoid receptor antagonist

BOHB- b-hydroxybutyrate

### Definitions

GLP-1 RA: Semaglutide, dulaglutide etc. SGLT inhibitors: Dapagliflozin etc. GIP/GLP-RA: Tirzepatide MRAs: Spironolactone etc. ACE inhibitors: Lisinopril etc. ARBs: Losartan etc.

Stages of T1DM:

Stage 1			Stage 2		Stage 3	
•	Normoglycemia	•	Dysglycemia	•	Dysglycemia	
•	Presymptomatic	•	Presymptomatic	•	Symptomatic	
•	Autoantibodies present	•	Autoantibodies present	•	Autoantibodies present	

### Definitions: Diabetic Ketoacidosis

Mild	Moderate	Severe
• Blood glucose: >250 mg/dL	• Blood glucose >250 mg/dL	• Blood glucose >250 mg/dL
• Urine ketones: +	• Urine ketones: +	• Urine ketones: +
∘ BOHB: >3 mmol/L	∘ BOHB: >3 mmol/L	∘ BOHB: >3 mmol/L
∘ pH: 7.25-7.3	• pH: 7.00-7.24	• pH: <7.00
• AGAP: >10	• AGAP: >12	• AGAP: >12
<ul> <li>Sodium bicarbonate: 15-18 mEq/L</li> </ul>	° Sodium bicarbonate: 15-18 mEq/L	• Sodium bicarbonate: <10 mEq/L
<ul> <li>Mental Status: Alert</li> </ul>	<ul> <li>Mental Status: Drowsy</li> </ul>	<ul> <li>Mental Status: Coma</li> </ul>

Hyperosmolar Hyperglycemia Syndrome (HHS): Characterized as hyperglycemia (>600 mg/dL) without ketoacidosis

Source: "Diabetic Ketoacidosis - Criteria | BMJ Best Practice US." Bestpractice.bmj.com, bestpractice.bmj.com/topics/en-us/162/criteria

## Epidemiology of Diabetes

• U.S. population estimates from 2021:

- $\circ$  38.4 million people of all ages had diabetes (11.6% of the population)
- 0 38.1 million people aged 18 years or older (14.7% of all U.S. adults)
- 8.7 million people aged 18 years or older met laboratory criteria for diabetes but were not aware/did not report having diabetes
- 0 Diabetes was the eighth leading cause of death in the United States
- Financial impact:
  - The total direct and indirect estimated costs of diagnosed diabetes in the United States in 2022 was \$413 billion
  - o Total direct estimated costs of diagnosed diabetes increased from \$227 billion in 2012 to \$307 billion in 2022



### Section 1: Improving Care and Promoting Health

• Addition of Table 1.1: Considerations for engaging interprofessional members of a comprehensive, personcentered diabetes care team to identify and meet the needs of people with diabetes across the life span

Subpopulation of a person with diabetes	Team members to engage in care	Unique care considerations
All adults with diabetes	Primary care clinician, CDCES, RDN, and other specialists as available and appropriate to treat comorbidities ( <b>Table 4.1</b> )	Assess for and address social determinants of health.
Adults treated with intensive insulin therapy, including multiple daily injections of insulin and insulin pump therapy	Clinicians and other health care team members experienced in advanced diabetes management, including technology use	
All youth with diabetes	Primary care clinician, pediatric endocrinologist, CDCES, RDN, other specialists as available and appropriate to treat comorbidities ( <b>Table 14.1</b> ), daycare or school nurse or other professional, behavioral health professional (as needed), and parent(s) or caregiver(s)	<ul> <li>Assess for and address social determinants of health and barriers to safety, well-being, and academic performance in school.</li> <li>Engage professionals within the school and extracurricular/after-school activities to ensure safe diabetes management. An individualized diabetes medical management plan should be developed in collaboration with school professionals and parent(s) or caregiver(s).</li> <li>Support gradual developmentally appropriate transfer of self-management from caregivers to the youth with diabetes.</li> </ul>

# Section 2: Diagnosis and Classification of Diabetes

### **Recommendation 2.7:** Autoantibody-based screening

for presymptomatic type 1 diabetes should be offered to those with a family history of type 1 diabetes or otherwise known elevated genetic risk Addition of Table 2.3: Considerations related to the use and interpretation of laboratory measurements of glucose and A1C

	Glucose	A1C
Cost	Inexpensive and available in most laboratories across the world	More expensive than glucose and not as widely available globally
Time frame of hyperglycemia	Acute measure	Chronic measure of glucose exposure over the past $\sim$ 2–3 months
Preanalytic stability	Poor; plasma must be separated immediately or samples must be kept on ice to prevent glycolysis	Good
Sample	Measurement can vary depending on sample type (plasma, serum, whole blood) and source (capillary, venous, arterial)	Requires whole-blood sample
Assay standardization	Not standardized	Well standardized
Fasting	Fasting or timed samples required	Nonfasting test; no participant preparation is needed
Within-person variability	High	Low
Acute factors that can affect levels	Food intake, stress, recent illness, activity	Unaffected by recent food intake, stress, illness, activity
Other individual factors that can affect test results	Diurnal variation, medications, alcohol, smoking, bilirubin	Altered erythrocyte turnover (e.g., anemia, iron status, splenectomy, blood loss, transfusion, hemolysis, glucose-6- phosphate dehydrogenase deficiency, erythropoietin), HIV, cirrhosis, renal failure, dialysis, pregnancy
Test interferences	Depends on specific assay: sample handling/ processing time, hemolysis, severe hypertriglyceridemia, severe hyperbilirubinemia	Depends on specific assay: hemoglobin variants, severe hypertriglyceridemia, severe hyperbilirubinemia

### Section 3: Prevention or Delay of Diabetes and Associated Comorbidities

### • Sleep Characteristics Associated With Increased Risk of Type 2 Diabetes

#### • Duration:

o Short (typically defined as <6 h) and long (typically defined as >9 h) sleep duration having up to a 50% increase in the risk of type 2 diabetes

### • Quality:

0 Poor sleep quality was associated with a 40-84% increased risk of developing type 2 diabetes in a meta-analysis

### • Chronotype

• Those with a preference for evenings (i.e., going to bed late and getting up late), there was a 2.5-fold higher odds ratio for type 2 diabetes than for those with a preference for mornings (i.e., going to bed early and getting up early)

### Section 3: Prevention or Delay of Diabetes and Associated Comorbidities

### Vitamin D Therapy

- Several meta-analyses studies have suggested a modest potential benefit in specific populations
- Many of the included studies lacked statistical significance
- Supplemental dosing varied between 15-20 mcg daily; no recommendations provided
- No evidence of safety concerns
- Clinical judgment encouraged

## Teplizumab-mzwv Infusion

#### Teplizumab-mzwv Infusion

- O Acknowledged the potential of teplizumab to delay the onset of stage 3 T1DM with selected individuals ≥ 8 years of age with stage 2 T1DM
- The first and only approved immunomodulator to delay the onset of Stage 3 T1DM in patients 8 years and older with Stage 2 T1DM
- For patients with stage 2 T1DM, the 5-year risk of developing stage 3 is about 75%, and the lifetime risk approaches 100%

## Teplizumab-mzwv Infusion

- Mechanism of Action:
  - In type 1 diabetes, CD8+ T cells infiltrate the pancreas and attack the insulin-producing beta cells
  - Teplizumab helps to deactivate these autoreactive T cells reducing the immune system's attack
  - Teplizumab binds to CD3 on T cells leading to their deactivation rather than a full activation response
  - Teplizumab may also increase the proportion of regulatory T cells, which help to suppress the immune response and promote tolerance



Source: Herold, K.C, et al. An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes. New England Journal of Medicine, [online] 381(7), pp.603–613.

## Teplizumab-mzwv Infusion

• TN-10 Study Design:

o Randomized, double-blind, event-driven, placebo-controlled study

0 76 patients (teplizumab group N=44, placebo group N=32), 8 to 49 years of age, with Stage 2 T1DM

• The primary efficacy endpoint: time from randomization to stage 3 T1DM diagnosis

• Results:

• Teplizumab group: delayed progression to stage 3 T1DM by ~4 years (50 months)

○ Placebo group: delayed progression to stage 3 T1DM by ~2 years (25 months)

○ HR: 0.41; 95% confidence interval, 0.22-0.78, P= 0.0066

### Teplizumab-mzwv Clinical Pearls

#### Dosing (IV)

- Day 1: 65 mcg/m<sup>2</sup>
- $\circ$  Day 2: 125 mcg/m<sup>2</sup>
- $\circ \quad Day \ 3:250 \ mcg/m^2$
- $\circ$  Day 4: 500 mcg/m<sup>2</sup>
- $\circ$  Days 5 14: 1,030 mcg/m<sup>2</sup>
- ∘ Infuse over  $\geq$ 30 minutes

#### Premedication

- To mitigate risk of cytokine release syndrome
- Acetaminophen
- Antihistamine
- Antiemetic
- ° First 5 days of therapy

#### **Adverse Effects**

- Skin reactions
- Leukopenia/lymphocytopenia
- Diarrhea/nausea
- Cytokine release syndrome
- Serious infection

### Vaccine Recommendations:

- Pneumococcal vaccine
  - 0 Age group updated to all immunocompetent adults 50 years or older (previously 65 years of age)
  - o Administer PCV15, PCV20, or PCV21
  - 0 If PCV15 is used, administer a dose of PPSV23 one year later
  - $\circ$  If PCV20 or PCV21 is used, a dose of PPSV23 isn't indicated
- Influenza vaccine
  - All people with diabetes advised to receive a trivalent influenza vaccine (or another inactivated influenza vaccine)
- $\circ$  RSV

 $\circ$  Adults aged  $\geq$ 75 years and those aged  $\geq$ 60 years and at high risk may receive a single dose of an RSV vaccine

- Screening for Male and Female Sexual Dysfunction—No specific guidelines are available for treatment
- **Recommendation 4.20:** In women with diabetes or prediabetes, inquire about sexual health particularly in those who experience depression and/or anxiety and those with recurrent urinary tract infections
- **Recommendation 4.21:** In postmenopausal women with diabetes or prediabetes, screen for symptoms and/or signs of genitourinary syndrome of menopause, including vaginal dryness

- The terminology for nonalcoholic fatty liver disease (NAFLD) was updated to metabolic dysfunction-associated steatotic liver disease (MASLD)
- Nonalcoholic steatohepatitis (NASH) was updated to metabolic dysfunction-associated steatohepatitis (MASH)
- **Recommendation 4.26:** GIP/GLP-1 RA was added due to potential benefits in MASH for weight loss in adults with type 2 diabetes, MASLD, and overweight or obesity

- Recommendation 4.27a: Adults with type 2 diabetes and biopsy-proven MASH or those at high risk for liver fibrosis, use of pioglitazone or a GLP-1 RA or a dual GIP and GLP-1 RA is preferred for glycemic management due to potential beneficial effects on MASH
- Recommendation 4.27b: Combination therapy with pioglitazone and a GLP-1 RA can be considered for treatment of hyperglycemia in adults with type 2 diabetes with biopsy-proven MASH or those at high risk of liver fibrosis because of potential beneficial effects of such a combination on MASH

### A Placebo-Controlled Trial of Subcutaneous Semaglutide in Nonalcoholic Steatohepatitis

• Study design:

- o Double-blind, randomized, placebo-controlled, parallel-group international trial
- 320 patients (semaglutide 0.1-mg group n=80, 0.2-mg group n=80, 0.4-mg group n=80, placebo group n=80), biopsy confirmed NASH and liver fibrosis
- Primary efficacy endpoint: resolution of NASH with no worsening fibrosis

#### • Results:

- $\circ$  Semaglutide 0.1-mg group= 40%
- $\circ$  Semaglutide 0.2-mg group= 36%
- $\circ$  Semaglutide 0.4-mg group = 59%
- $\circ$  Placebo group= 17%
- $\odot$  P<0.001 for semaglutide 0.4-mg vs. placebo

- Revision of figure 4.2
   FIB-4- Fibrosis-4
   LSM- Liver stiffness
   ELF- Enhanced liver fibrosis
   CV- Cardiovascular risk
- **ALT** Alanine transaminase

#### Diagnostic Algorithm for the Prevention of Cirrhosis in People With Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)



### Section 5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes

- **Recommendation 5.23:** Emphasizes screening for malnutrition (Malnutrition Universal Screening Tool), in those who have undergone metabolic surgery and for those being treated with **weight management pharmacological therapies**
- **Recommendation 5.26:** Addressed the issue of sodium–glucose cotransporter (SGLT) inhibition being associated with euglycemic diabetic ketoacidosis
  - Avoid ketogenic eating patterns
  - 0 Avoid fasting
  - 0 Maintain appropriate insulin therapy

### Section 5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes

- **Recommendation 5.33:** Optimize treatment plan for people with diabetes partaking in religious fasting to reduce risk of hypoglycemia, dehydration, hyperglycemia, and/or ketoacidosis
- **Recommendation 5.42:** Advise individuals with type 1 diabetes and those at risk for diabetic ketoacidosis (DKA) not to use recreational cannabis in any form due to the risk of cannabis hyperemesis syndrome

### Section 5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes

• Addition of Table 5.7 and 5.8: Psychosocial concerns and their association with diabetes-related outcomes in adults with type 1 and type 2 diabetes, example below:

T2DM	Increased A1C	Increased B P	Dyslipidemia	Microvascular complications	Macrovascular complications	Decreased QOL	Increased Mortality
Anxiety	+++	++	+	+	+++	+++	+++
Depression	+++	++	+++	+++	+++	+++	+++
Eating Disorders	+/-	5	5	?	5	+++	;
Cognitive Impairment	+++	+++	+++	+++	+++	+++	+++

+++= Strong Evidence, ++=Moderate Evidence, += Limited Evidence, +/-=Inconclusive, ?=No Data

## Section 6. Glycemic Goals and Hypoglycemia

#### Table 6.9-Risk factors for hyperglycemic crises

Type 1 diabetes/absolute insulin deficiency

Younger age

Prior history of hyperglycemic crises

Prior history of hypoglycemic crises

Presence of other diabetes complications

Presence of other chronic health conditions (particularly in people with type 2 diabetes)

Presence of behavioral health conditions (e.g., depression, bipolar disorder, and eating disorders)

Alcohol and/or substance use

High A1C level

Social determinants of health

#### Table 6.10-Clinical presentation in people with diabetes with DKA and HHS

DKA	HHS			
Develops over hours to days	Develops over days to a week			
Usually alert	Change in cognitive state common			
Polyuria, polydipsia, weight loss, and dehydration				
Nausea, vomiting, and abdominal pain	Often copresenting with other acute illnes			
Kussmaul respiration				

One-third of hyperglycemic emergencies have a hybrid DKA-HHS presentation

### Section 7. Diabetes Technology

Insulin administered by syringe, pen, patch devices, CSII (Omnipod<sup>®</sup>), BGM (Contour<sup>®</sup>) or CGM (Dexcom<sup>®</sup>), and AID (Tandem<sup>®</sup>) systems that use CGM-informed algorithms to modulate insulin delivery

### Table 7.2—Common interfering substances and/or conditions that affect glucose meters (for inpatient and outpatient use)

Substance or condition	Effects on glucose values measured by blood glucose meters
Maltose*	Falsely higher blood glucose values
Galactose	Falsely higher blood glucose values
Xylose	Falsely higher blood glucose values
N-Acetylcysteine†	Falsely higher blood glucose values
Acetaminophen	Falsely higher blood glucose values at low blood glucose levels
Dopamine	Falsely higher blood glucose values at low blood glucose levels
Furosemide	Falsely lower blood glucose values
Vitamin C	Falsely lower or higher blood glucose values
Uric acid	Falsely higher blood glucose values at very low or very high glucose levels
Hematocrit (high)	Falsely lower blood glucose values
Hematocrit (low)	Falsely higher blood glucose values

\*Unmodified glucose dehydrogenase method only. †Glucose dehydrogenase monitors using pyrroloquinoline quinone cofactor (GDH/PQQ).

## Section 7. Diabetes Technology

- **Recommendation 7.16:** Consider the use of real-time CGM or intermittently- scanned CGM in adults with T2DM on glucose-lowering agents other than insulin to achieve and maintain individualized glycemic goals
- When prescribing a device, ensure that patients and caregivers receive initial and ongoing education and training, and ongoing evaluation of technique, results, and the ability to utilize data, including uploading or sharing data (if applicable), to monitor and adjust therapy
- Recommend early initiation, including at diagnosis, of CGM, CSII, and AID depending on a person's or caregiver's needs and preferences
- **Recommendation 7.32:** Emphasized the importance of continuing the use of insulin pumps or AID in people with diabetes while hospitalized when clinically appropriate
- Utilize confirmatory point-of-care blood glucose measurements for insulin dose adjustments and hypoglycemia assessment and treatment

# Section 8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes

- **Recommendation 8.18:** Recommends screening for malnutrition for people with diabetes and obesity who have lost significant weight
- **Recommendation 8.19:** Recommends **continuing weight management pharmacotherapy**, as indicated, beyond reaching weight loss goals to maintain health benefits and avoid weight regain and worsening of cardiometabolic abnormalities that often result from sudden discontinuation of weight management pharmacotherapy
- **Recommendation 8.25:** Importance of CGM device use to improve safety in individuals with post-metabolic surgery hypoglycemia
- It is also essential that health care teams are knowledgeable about insurance coverage requirements, eligibility for medication assistance programs, and availability of copayment reduction cards to reduce financial hardship of treatment for individuals

### Section 9. Pharmacologic Approaches to Glycemic Treatment

- Recommendation 9.12: Recommends use of GLP-1 RA in individuals with T2DM, symptomatic HFpEF, and obesity
- Recommendation 9.13: Recommends use of either SGLT2 inhibitor or GLP-1 RA in individuals with T2DM and CKD
- Recommendations 9.15 and 9.16: Recommends treatment of individuals with type 2 diabetes and MASLD or MASH with GLP-1 RA, dual GIP and GLP-1 RA, pioglitazone, or a combination of GLP-1 RA and pioglitazone based on the staging of liver disease risk and need for weight management
- A section was added discussing strategies to deal with medication shortages:
  - o Due to safety, quality, and effectiveness concerns, use of non-FDA-approved compounded products is not recommended
  - o Consider switching to a different FDA-approved medication as clinically appropriate

### Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity

- Study Design:
  - ° Multinational, double-blind, randomized, placebo-controlled trial
  - $\circ$  529 patients (semaglutide n=263, placebo n=266), BMI >30, heart failure with preserved ejection fraction
  - Dual primary efficacy endpoint: change from baseline in the Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS; scores range from 0 to 100, with higher scores indicating fewer symptoms and physical limitations), and changes in body weight
- Results:
  - ° Semaglutide group: mean change in KCCQ-CSS score was 16.6 points
  - Placebo group: mean change in KCCQ-CSS score was 8.7 points
  - Mean difference, of 7.8 points; 95% CI, 4.8 to 10.9; P<0.001

#### Source: Mikhail Kosiborod, et al. "Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity." NEJM, vol. 389, no. 12, 25 Aug. 2023, https://doi.org/10.1056/nejmoa2306963

### Section 10. Cardiovascular Disease and Risk Management

- **Recommendation 10.13:** ACE inhibitors, angiotensin receptor blockers, MRAs, direct renin inhibitors, and neprilysin inhibitors should be avoided in sexually active individuals of childbearing potential who are not using reliable contraception and are contraindicated in pregnancy
  - o This recommendation was stated throughout the guidelines including the Pregnancy and Special Populations sections
- **Recommendation 10.26:** In most circumstances, lipid lowering agents should be stopped prior to conception and avoided in sexually active individuals of childbearing potential who are not using reliable contraception

### Section 10. Cardiovascular Disease and Risk Management

- Triglyceride thresholds were updated, in adults with hypertriglyceridemia (fasting triglycerides >150 mg/dL) or non-fasting triglycerides >175 mg/dL), clinicians should address and treat lifestyle factors
  - Previously: fasting or non-fasting triglycerides 175–499 mg/dL
- In patients with ASCVD on a statin with controlled LDL cholesterol but elevated triglycerides (150-499 mg/dL), the addition of icosapent ethyl can be considered to reduce cardiovascular risk
- **Recommendation 10.46d:** For individuals with type 2 diabetes, obesity, and symptomatic heart failure with preserved ejection fraction, treatment with a GLP-1 RA is recommended

Source: Cardiovascular Disease and Risk Management: Standards of Care in Diabetes-2025

### Section 11. Chronic Kidney Disease And Risk Management

Table 11.1—Reasons to consider nondiabetic kidney diseases in a person with chronic kidney disease and diabetes

- Type 1 diabetes duration <5 years</li>
- Active urine sediment (e.g., containing red blood cells or cellular casts)
- · Chronically well-managed blood glucose
- Rapidly declining eGFR
- · Rapidly increasing or very high UACR or urine protein/creatinine level
- · No retinopathy in a person with type 1 diabetes

Information adapted from Liang et al. (129). eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio.

#### Table 11.2-Screening for selected complications of chronic kidney disease

Complication	Physical and laboratory evaluation
Blood pressure >130/80 mmHg	Blood pressure, weight, BMI
Volume overload	History, physical examination, weight
Electrolyte abnormalities	Serum electrolytes
Metabolic acidosis	Serum electrolytes
Anemia	Hemoglobin; iron, iron saturation, ferritin testing if indicated
Metabolic bone disease	Serum calcium, phosphate, PTH, vitamin 25(OH)D

Complications of chronic kidney disease (CKD) generally become prevalent when estimated glomerular filtration rate falls below 60 mL/min/1.73 m<sup>2</sup> (stage G3 CKD or greater) and become more common and severe as CKD progresses. Evaluation of elevated blood pressure and volume overload should occur at every clinical contact possible; laboratory evaluations are generally indicated every 6–12 months for stage G3 CKD, every 3–5 months for stage G4 CKD, and every 1–3 months for stage G5 CKD, or as indicated to evaluate symptoms or changes in therapy. 25(OH)D, 25-hydroxyvitamin D; PTH, parathyroid hormone.

### Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes

- Study Design:
  - ° Double-blind, randomized, placebo-controlled, international trial
  - 3533 patients (semaglutide n=1767, placebo n=1766), T2DM, high-risk CKD and were receiving max dose RAS inhibitors
  - ° Primary endpoint: major kidney disease events, a composite of onset of kidney failure
- Results:
  - ° Semaglutide group: 18.7% of patients had a major kidney disease event
  - ° Placebo group: 23.3% of patients had a major kidney disease event
  - HR: 0.76 (95% CI, 0.66-0.88), P=0.0003
  - $^\circ\,$  Difference in mean annual decline in kidney function also favored the semaglutide group by 1.6 mL/min/1.73  $m^2$
  - ∘ 95% CI, 0.86-1.47, P<0.001

### Section 12. Retinopathy, Neuropathy, and Foot Care

- **Recommendation 12.8:** Individuals with preexisting type 1 or type 2 diabetes should receive an eye exam before pregnancy as well as in the first trimester and may need to be monitored every trimester and for 1 year postpartum as indicated by the degree of retinopathy
- **Recommendation 12.22:** Gabapentinoids, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, and sodium channel blockers are recommended as initial pharmacologic treatments for neuropathic pain in diabetes
- Opioids, including tramadol and tapentadol, should not be used for neuropathic pain treatment in diabetes given the potential for adverse events
- **Recommendation 12.29:** Refer individuals who smoke and have a history of prior lower-extremity complications, loss of protective sensation, structural abnormalities, or PAD to foot care specialists for ongoing preventive care and lifelong surveillance

## Section 13. Older Adults

Using the 4Ms Framework of Age-Friendly Health Systems to Address Person-Specific Issues That Can Affect Diabetes Management

#### MENTATION

MOBILITY

- Self-administration of medications
- Ability to use diabetes technology
- · Anxiety, depression, and diabetes distress
- Mild cognitive impairment or dementia
- Coping skills and self-care

Foot complications

Frailty and sarcopenia

Vision and hearing impairment

Functional ability

Leg weakness

Neuropathy



#### MEDICATIONS

- Treatment burden
- Affordability or insurance coverage
- End-organ disease or complications affecting medication choice
- Polypharmacy
- History of adverse medication effects
- Social and family support
- Risk of hypoglycemia, hypoglycemia unawareness, and fear of hypoglycemia

#### WHAT MATTERS MOST

- Discussing goals and expectations
- Symptom and disease burden
- Meal and treatment preferences (e.g., injections and glucose monitoring)
- Risks, burdens, and benefits of treatment
- Loneliness, social isolation, and overall quality of life
- Life expectancy

Figure 13.1: Using the 4Ms framework of age-friendly health systems to address person-specific issues that can affect diabetes management

### Section 13. Older Adults

Selection of glycemic goals should be individualized and should prioritize avoidance of hypoglycemia, with less stringent goals (such as A1C <8.0% and/or time in range (TIR: 70–180 mg/dL) of 50% and time below range (<70 mg/dL) of <1% for those with significant cognitive and/or functional limitations, frailty, severe comorbidities, and a less favorable risk-to benefit ratio of diabetes medications</li>

### Section 14. Children and Adolescents

- Recommendation 14.21: Insulin pumps should be offered to anyone with type 1 diabetes who can use the devices safely
- Recommendation 14.26: Health care professionals may reasonably suggest more stringent A1C goals (such as <6.5%) for selected individuals if they can be achieved without significant hypoglycemia, excessive weight gain, negative impacts on well-being, or undue burden of care or in those who have nonglycemic factors that decrease A1C</li>
- Recommendation 14.41: Consider age-approved statins, in addition to lifestyle changes, for youth with type 1 diabetes who have LDL cholesterol >130 mg/dL
  - $\circ \geq 10$  years of age: atorvastatin, lovastatin, fluvastatin, simvastatin
  - ° ≥8 years of age: rosuvastatin, pravastatin, pitavastatin
- Discourage the use of nicotine and cannabis products

### Section 15. Management of Diabetes in Pregnancy

- **Recommendation 15.12:** CGM metrics may be used in combination with blood glucose monitoring to achieve optimal pre- and postprandial glycemic goals
- Recommendation 15.19: AID systems are recommended if the system has a pregnancy-specific glucose goal for patients with T1DM
  - $\circ$  The CamAPS  $FX^{\circledast}$  is the only FDA approved AID for use in pregnancy
- **Recommendation 15.20:** AID systems may be considered if the system does not have a pregnancy-specific glucose goal or algorithm, for patients with T1DM when used with assistive techniques and working with experienced health care teams
- Pravastatin has been studied in multiple pregnancy trials administering therapy at various time points in gestation with the aim to reduce preeclampsia risk, and although its ability to do so is inconclusive to date, there does not appear to be increased neonatal mortality or morbidity associated with its use during gestation

### Pravastatin Versus Placebo in Pregnancies at High Risk of Term Preeclampsia

• Study design:

- 0 Multicenter, double-blind, placebo-controlled trial
- 1120 patients (pravastatin 20-mg group n=548, placebo group n=543), women with singleton pregnancies at high risk of term preeclampsia
- Primary efficacy endpoint: delivery with preeclampsia at any time after randomization

• Results:

- Preeclampsia occurred in 14.6% (80 of 548) of participants in the pravastatin group and in 13.6% (74 of 543) in the placebo group
- o Hazard ratio for statin/placebo, 1.08 [95% CI, 0.78-1.49]; P=0.65
- There were no significant between-group differences in neonatal adverse outcomes or other adverse events

## Section 16. Diabetes Care in the Hospital

- $\circ$  For the treatment of persistent hyperglycemia starting at a threshold of  ${\geq}180~mg/dL$
- Critically Ill Population:
  - Recommendation 16.4a: Insulin should be initiated or intensified for the majority of critically ill individuals
  - Recommendation 16.5a: Glycemic goal of 140–180 mg/dL is recommended
  - **Recommendation 16.8a:** Continuous intravenous insulin infusion is recommended for achieving glycemic goals and avoiding hypoglycemia in critically ill individuals

### • Non-Critically Ill Population:

- Recommendation 16.5b: Glycemic goal of 100–180 mg/dL if it can be achieved without significant hypoglycemia
- **Recommendation 16.4b:** Insulin and/or other glucose-lowering therapies should be initiated or intensified for the majority of noncritically ill individuals

• \*More stringent glycemic goals may be appropriate if it can be achieved without significant hypoglycemia

## Section 16. Diabetes Care in the Hospital

- ° Perioperative Concerns with GLP-1 RA and dual GIP/GLP-1 RA medications:
  - These medications may be associated with nausea, vomiting, and delayed gastric emptying and have the potential to increase the risk of pulmonary aspiration during general anesthesia and deep sedation
  - The American Society of Anesthesiologists recommends holding GLP-1 RAs on the day of the procedure or surgery for daily dose agents and for at least 7 days prior to the procedures or surgery for once-weekly dose agents



Addition of figure 16.1: Treatment pathways for diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS)

### Section 17. Diabetes Advocacy

• Acknowledged the importance of advocating for diabetes management in the following settings:

o School

- Driving (licensing requirements)
- 0 Detention Facilities
- Childcare and Community Settings
- 0 Difficulties with Access and Affordability
- Potential resources with management strategies are listed

### In Summary

- ° The Standards of Care in Diabetes guidelines are updated annually
- ° Incorporated new pharmacotherapy agents into guidelines
  - Teplizumab for patients with stage 2 TID
- ° Broadened the utility of the GLP-1 RA
  - Preferred agent in patients with diabetes and CKD alongside SGLT inhibitors
  - Recommended in patients with diabetes and symptomatic heart failure with preserved ejection fraction and obesity
  - Recommended agent for patients with MASH (including dual GIP and GLP-1 RA agents)
  - Continuing therapy even when weight management/diabetes goals of care are achieved
- Allowed for more patient specific goal directed therapy
- Recognized the benefit of continuous glucose monitoring
- Updated the screening parameters for specific comorbidities and risk factors

## Assessment Question #1

Joe is a 59 year old white male who presents to the clinic for follow-up on uncontrolled type 2 diabetes. PMH: T2DM, HTN, obesity, CKD stage III, Depression, HLD Medications: dapagliflozin 10 mg daily

Based on the information provided what medication would you initiate today?

a. Semaglutide

b. Tirzepatide

c. Insulin

d. Medications are optimized

### Assessment Question #1: Correct Response

Joe is a 59-year-old white male who presents to the clinic for follow-up on uncontrolled type 2 diabetes. PMH: T2DM, HTN, obesity, CKD stage III, sleep apnea, Depression, HLD Medications: dapagliflozin 10 mg daily

Based on the information provided what medication would you initiate today?

a. Semaglutide

b. Tirzepatide

c. Insulin

d. Medications are optimized

## Assessment Question #2

In individuals with ASCVD or other cardiovascular risk factors on a statin with managed LDL cholesterol but elevated triglycerides (150–499 mg/dL), the addition of which agent can be considered to reduce cardiovascular risk

- a. Niacin
- b. Fenofibrate
- c. Icosapent ethyl (Vascepa)
- d. Addition of another statin at high-intensity dosing

### Assessment Question #2: Correct Response

In individuals with ASCVD or other cardiovascular risk factors on a statin with managed LDL cholesterol but elevated triglycerides (150–499 mg/dL), the addition of which agent can be considered to reduce cardiovascular risk

a. Niacin

b. Fenofibrate

c. Icosapent ethyl (Vascepa)

d. Addition of another statin at high-intensity dosing

## Assessment Question #3

True or false, in the 2025 Standards of Care, patients who have lost significant weight in a short period of time or are receiving pharmacotherapy for weight loss should be screened for malnutrition?

a. True

b. False

### Assessment Question #3: Correct Response

True or false, in the 2025 Standards of Care, patients who have lost significant weight in a short period of time or are receiving pharmacotherapy for weight loss should be screened for malnutrition?

#### a. True

b. False

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### Thank you!

Nagesh Sharma, PharmD PGY-1 Pharmacy Resident nsharma2@beaconhealthsystem.org

