Endocrine Update: Diabetes Care

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2019 Statewide Conference

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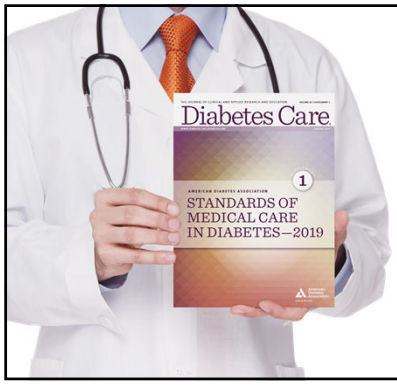
Objectives

1. The participant will be able to discuss current recommendations for the comprehensive medical evaluation of patients with Diabetes- ***2019 clinical update.***
2. The participant will be able to discuss the mechanisms of action of newer agents for the treatment of diabetes – a brief review.
3. The participant will be able to select drugs for the treatment of diabetes based upon the patient profile and individual characteristics.

Comprehensive Medical Evaluation

2019 - update



Standards of Medical Care in Diabetes – 2019

Standards of Care Resources.

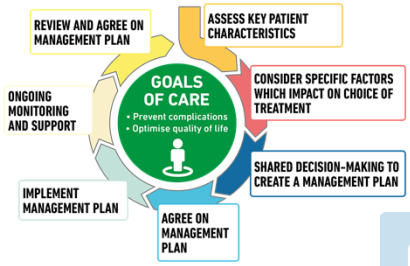
- Full version available
- Abridged version for PCPs
- Free app, with interactive tools
- Pocket cards with key figures
- Free webcast for continuing education credit

Professional.Diabetes.org/SOC

Key Updates

- New cyclic picture guide added
- New suggestions re: Language
- New revisions on who should be on the Multidisciplinary Team
- New Assessment Recommendations
- New recommendation regarding when to test for fatty liver disease

Decision Cycle for Patient-Centered Glycemic Management in Type 2 Diabetes



The diabetes care decision cycle was added to emphasize the need for ongoing assessment and shared decision making to achieve the goals of health care and avoid clinical inertia.

Patient-Centered Collaborative Care

Language

A patient-centered communication style that uses person-centered and strength-based language and active listening, elicits patient preferences and beliefs, and assesses literacy, numeracy, and potential barriers to care should be used to optimize patient and health outcomes and health-related quality of life.

Use of Empowering Language.

1. Language that is neutral, nonjudgmental, and based on facts, actions, or physiology/biology;
2. Use language that is free from stigma;
3. Use language that is strength based, respectful, and inclusive and that imparts hope;
4. Use language that fosters collaboration between patients and providers;
5. Use language that is person centered

Language Update

Negative Connotation	Suggested Replacement	Rationale
Compliant/Compliance Noncompliant/Noncompliance	Engagement, Participation, Involvement - He takes medication about ½ the time - She takes her insulin when she can afford it - He eats fruits and vegetables a few times/week	Compliance and adherence imply doing what someone else wants, as opposed to the patient making choices. Focus on strengths
Diabetic Person	Person with Diabetes	Put person first
How long have you ***been*** diabetic?	How long have you ***had*** diabetes?	Avoid using the disease to describe the person
Refused	Declined	Respect right to make decisions
Difficult patient	I'm having a difficult time with Ms. Smith	Describes behavior rather than label the patient
Unmotivated, unwilling	John is afraid to start insulin due to fear of weight gain	Focus on perceived obstacles
You will end up blind or on dialysis	More people are living longer with diabetes…with effective care plans	Scare tactics are rarely effective, work on specific achievable goals

The Multidisciplinary Team

- Diabetes Care Team:
  - primary care physicians
  - subspecialty physicians
  - nurse practitioners
  - physician assistants
  - nurses
  - dietitians
  - exercise specialists **
  - pharmacists **
  - dentists
  - podiatrists - ophthalmologist
  - mental health professionals

Assessment and Planning Update

Assess risk of diabetes complications -update

•• ASCVD and heart failure history
•• ASCVD risk factors and 10-year ASCVD risk assessment
•• Staging of chronic kidney disease
•• Hypoglycemia risk

Goal setting

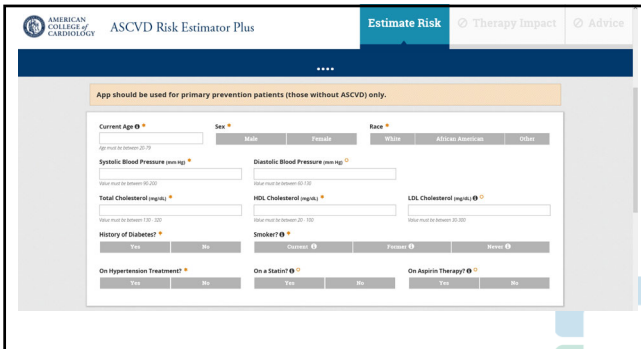
•• Set A1C/blood glucose target
•• If hypertension present, establish blood pressure target
•• Diabetes self-management goals (e.g., monitoring frequency)

Therapeutic treatment plan

•• Lifestyle management
•• Pharmacologic therapy (glucose lowering)
•• Pharmacologic therapy (cardiovascular disease risk factors and renal)
•• Use of glucose monitoring and insulin delivery devices
•• Referral to diabetes education and medical specialists (as needed)

ASCVD risk factors and 10-year ASCVD risk assessment

- **For Optimal Use:**
- Estimate patient's 10-year ASCVD risk at an initial visit to establish a reference point.
- Forecast the potential impact of different interventions on patient risk.
- Reassess ASCVD risk at follow-up visits.
  - Follow up risk incorporates change in risk factor levels over time and requires both initial and follow up values.
- Use the information above to help with clinician-patient discussions on risk and risk-lowering interventions.



http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/

Staging of chronic kidney disease

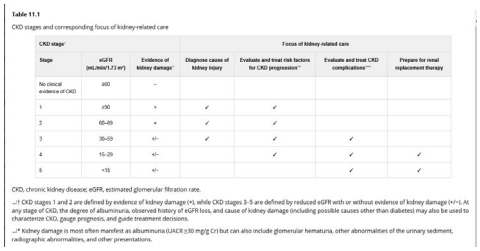


Table 11.1

CKD stages and corresponding focus of kidney-related care

CKD stage*			Focus of kidney related care			
Stage	eGFR (mL/min/1.73 m²)	Evidence of kidney damage*	Diagnose cause of kidney injury	Evaluate and treat risk factors for CKD progression††	Evaluate and treat CKD complications†††	Prepare for renal replacement therapy
No clinical evidence of CKD	≥60	–				
1	≥90	+	✓	✓		
2	60–89	+	✓	✓		
3	30–59	+/-	✓	✓	✓	
4	15–29	+/-		✓	✓	✓
5	<15	+/-			✓	✓

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

...† CKD stages 1 and 2 are defined by evidence of kidney damage (+), while CKD stages 3–5 are defined by reduced eGFR with or without evidence of kidney damage (+/-). At any stage of CKD, the degree of albuminuria, observed history of eGFR loss, and cause of kidney damage (including possible causes other than diabetes) may also be used to characterize CKD, gauge prognosis, and guide treatment decisions.

...* Kidney damage is most often manifest as albuminuria (UACR ≥30 mg/g Cr) but can also include glomerular hematuria, other abnormalities of the urinary sediment, radiographic abnormalities, and other presentations.

Hypoglycemia risk

Table 4.3—Assessment of hypoglycemia risk

Factors that increase risk of treatment-associated hypoglycemia

- Use of insulin or insulin secretagogues (i.e., sulfonylureas, meglitinides)
- Impaired kidney or hepatic function
- Longer duration of diabetes
- Frailty and older age
- Cognitive impairment
- Impaired counterregulatory response, hypoglycemia unawareness
- Physical or intellectual disability that may impair behavioral response to hypoglycemia
- Alcohol use
- Polypharmacy (especially ACE inhibitors, angiotensin receptor blockers, nonselective β-blockers)

See references 114–118.

Hypoglycemic Emergency UpDate

- ***Baqsimi*** – approved July 2019
- nasal glucagon: the first-ever severe hypoglycemia emergency treatment that does not require an injection

Liver Disease

Review of Mechanisms of Action

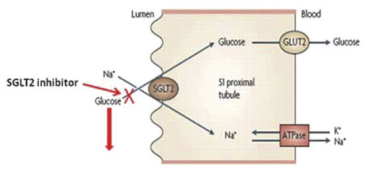
SGLT2-Inhibition
GLP1- Receptor Agonist

Newer Agents for DM Care

SGLT Inhibitors

GLP-1 mimetics

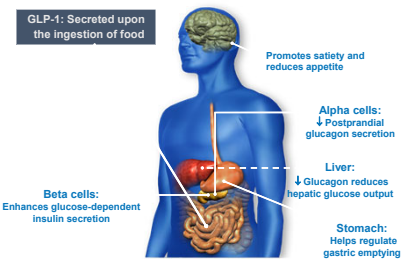
Glucose reabsorption by the proximal convoluted tubule



Dokken B. Diabetes Spectr 2012;25:29-36.

American Diabetes Association.

GLP-1 Modulates Numerous Functions in Humans



Select Agents: Patient Profile

Considerations: Profiling

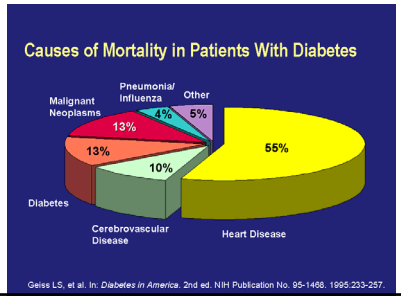
- Cardiovascular Risk Reduction-
  - Medications that are FDA approved to reduce CV risk (CV events and/or CV death)
- Low Hypoglycemia Risk
  - Medications associated with a low risk of hypoglycemia are ranked in a recommended order of utilization
- Weight Loss
  - Medications associated with weight loss (or neutrality) are ranked in a recommended order of utilization, medications associated with greater weight loss appear at the top of the list
- Cost
  - A list of low cost medications, for patients without insurance and/or limited resources, are ranked in a recommended order of utilization
- A1C lowering
  - Medication classes associated with more robust A1C reductions are ranked in a recommended order of utilization, medication classes associated with greater A1C reductions appear at the top of the list

Individualize Goals

- A higher A1C goal (<8%) may be more appropriate for those with:
  - Established CV disease
  - Elderly
  - Renal failure
  - Recurrent hypoglycemia
  - Hypoglycemia unawareness
- A lower A1C goal may be more appropriate for younger/healthy individuals who will experience a longer duration of disease
  - If it can be achieved safely

Cardiovascular and Renal Risk Reduction

Causes of Mortality in Patients With Diabetes



Cardiovascular Risk Reduction

- Among patients with type 2 diabetes who have established atherosclerotic cardiovascular disease
  - Both sodium–glucose cotransporter 2 inhibitors **(SGLT2 inhibitors)**, and glucagon-like peptide 1 receptor agonists **(GLP1-RA)** have demonstrated cardiovascular disease benefit and are now recommended as part of the anti-hyperglycemic regimen

Pharmacologic Approaches to Glycemic Treatment: *Standards of Medical Care in Diabetes - 2019. Diabetes Care* 2019;42(Suppl. 1):S90-S102

Heart Failure Risk Reduction

- Among patients with atherosclerotic cardiovascular disease at high risk of heart failure or in whom heart failure coexists
  - sodium–glucose cotransporter 2 inhibitors are preferred

Pharmacologic Approaches to Glycemic Treatment: *Standards of Medical Care in Diabetes - 2019. Diabetes Care* 2019;42(Suppl. 1):S90-S102

Key Clinical Trials

Empagliflozin (Jardiance)
Liraglutide (Victoza)

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

EMPA-REG OUTCOME TRIAL

- A total of 7020 patients were treated (median observation time, 3.1 years).
- There were no significant between-group differences in the rates of myocardial infarction or stroke, but in the empagliflozin group vs. placebo, there were significantly lower rates of
  - death from cardiovascular causes
  - hospitalization for heart failure
  - death from any cause
  - there was no significant between-group difference in the key secondary outcome
  - among patients receiving empagliflozin, there was an increased rate of genital infection but no increase in other adverse events.

Zinman B, Wanner C, Lachin JM, et al.; EMPA-REG OUTCOME Investigators.
Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med 2015;373:2117

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

EMPA-REG OUTCOME TRIAL

Trial Conclusion

- Patients with type 2 diabetes at high risk for cardiovascular events who received empagliflozin, as compared with placebo, had a lower rate of the primary composite cardiovascular outcome and of death from any cause when the study drug was added to standard care.

Zinman B, Wanner C, Lachin JM, et al.; EMPA-REG OUTCOME Investigators.
Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med 2015;373:2117

Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. LEADER TRIAL

METHODS

- In this double-blind trial, patients with type 2 diabetes and high cardiovascular risk were randomly assigned to receive liraglutide or placebo.
- The primary composite outcome in the time-to-event analysis was the first occurrence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.

Marso SP, Daniels GH, Brown-Frandsen K, et al.; LEADER Steering Committee; LEADER Trial Investigators.
Liraglutide and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2016;375:311

Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. LEADER TRIAL

RESULTS

- A total of 9340 patients underwent randomization. The median follow-up was 3.8 years. The primary outcome occurred in significantly fewer patients in the liraglutide group
- Fewer patients died from cardiovascular causes in the liraglutide group
- The rate of death from any cause was lower in the liraglutide group
- The rates of nonfatal myocardial infarction, nonfatal stroke, and hospitalization for heart failure were nonsignificantly lower in the liraglutide group than in the placebo group.
- The most common adverse events leading to the discontinuation of liraglutide were gastrointestinal events.

Marso SP, Daniels GH, Brown-Frandsen K, et al.; LEADER Steering Committee; LEADER Trial Investigators. Liraglutide and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2016;375:311

Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. LEADER TRIAL

CONCLUSIONS

- In the time-to-event analysis, the rate of the first occurrence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke among patients with type 2 diabetes mellitus was lower with liraglutide than with placebo.

Marso SP, Daniels GH, Brown-Frandsen K, et al.; LEADER Steering Committee; LEADER Trial Investigators. Liraglutide and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2016;375:311

Kidney Function

- Both the EMPA-REG OUTCOME TRIAL and LEADER TRIAL examined kidney effects as secondary outcomes

Specifically

- **Empagliflozin** reduced the risk of incident or worsening nephropathy by 39% and the risk of doubling of serum Cr accompanied by eGFR ≤45 mL/min/1.73 m^2 by 44%
- **Liraglutide** reduced the risk of new or worsening nephropathy (a composite of persistent macroalbuminuria, doubling of serum Cr, ESRD, or death from ESRD) by 22%

American Diabetes Association. Diabetes Care 2019 Jan; 42(Supplement 1): S124-S138. https://doi.org/10.2337/dc19-S011

Chronic Kidney Disease Risk Reduction

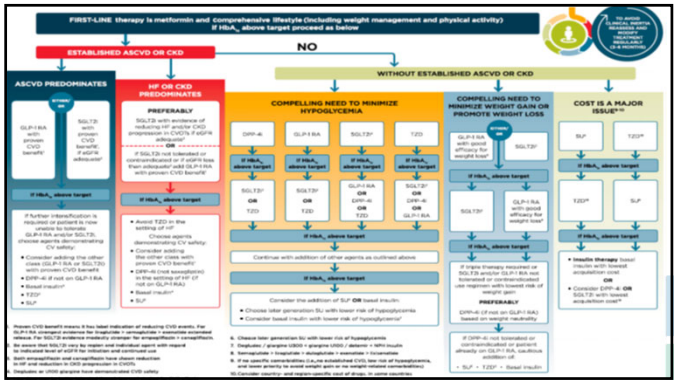
For patients with type 2 diabetes and chronic kidney disease consider

sodium– glucose cotransporter 2 inhibitors or glucagon like peptide 1 receptor agonists shown to reduce risk of chronic kidney disease progression, cardiovascular events, or both.

American Diabetes Association. Diabetes Care 2019 Jan; 42(Supplement 1): S124-S138.
https://doi.org/10.2337/dc19-S011

Agents with Supporting Data for CV and Renal Benefit

- GLP-1 RA
  - Liraglutide
  - Semaglutide
  - Exenatide ER
- SGLT2- inhibitors
  - Empagliflozin
  - Canagliflozin



GLP1 Receptor Agonists

- Byetta/Bydureon (exenatide)
- Victoza (liraglutide)
- Lyxumia/Adlyxin (lixisenatide)
- Tanzeum (albiglutide)
- Trulicity (dulaglutide)
- Ozempic (semaglutide)

Key Takeaways

- Do a comprehensive profile of the patient.
- Keep mortality and morbidity risks in mind not just glucose lowering.
- Consider resources and be cost sensitive.

Cleveland Clinic

Every life deserves world class care.