

Summary of Revisions: Standards of Medical Care in Diabetes—2022

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General Changes

 The field of diabetes care is rapidly changing as new research, technology, and treatments that can improve the health and wellbeing of people with diabetes continue to emerge.
 With annual updates since 1989, the American Diabetes

Association (ADA) has long been a leader in producing guidelines that capture the most current state of the field.

General Changes

- Although levels of evidence for several recommendations have been updated, these changes are not outlined below where the clinical recommendation has remained the same.
- That is, changes in evidence level from, for example, E to C are not noted below.
- The 2022 Standards of Care contains, in addition to many minor changes that clarify recommendations or reflect new evidence, the following more substantive revisions.

Section Changes

Section 1. Improving Care and Promoting Health in Populations

- Additional information has been included on online platforms to support behavior change and well-being.
- The renamed "Cost Considerations for Medication-Taking Behaviors" subsection has been expanded to include more discussion about costs of medications and treatment goals.
 Up to 25% of patients who are prescribed insulin report costrelated insulin underuse

- The concept of health numeracy and its role in diabetes prevention and management was added to the newly named "Health Literacy and Numeracy" subsection.
- The community health workers content was expanded.

Section 2. Classification and Diagnosis of Diabetes

- A recommendation about adequate carbohydrate intake prior to oral glucose tolerance testing as a screen for diabetes was added, with supportive references added to the text (Recommendations 2.4 and 2.12).
- 2.4 Adequate carbohydrate intake (at least 150 g/day) should be assured for 3 days prior to oral glucose tolerance testing as a screen for diabetes. A

The discussion regarding use of point-of-care A1C assays for the diagnosis of diabetes has been revised.

Point-of-care A1C assays may be NGSP certified and cleared by the U.S. Food and Drug Administration (FDA) for use in monitoring glycemic control in people with diabetes in both Clinical Laboratory Improvement Amendments (CLIA)-regulated and CLIAwaived settings. Point-of-care A1C assays have not been prospectively studied for the diagnosis of diabetes and are not recommended for diabetes diagnosis; if used, they should be confirmed with a validated measure.

More information has been added to the "Race/Ethnicity/Hemoglobinopathies" subsection.

Age

- The epidemiologic studies that formed the basis for recommending A1C to diagnose diabetes included only adult populations.
- We However, recent ADA clinical guidance concluded that A1C, FPG, or 2-h PG can be used to test for prediabetes or type 2 diabetes in children and adolescents.

Race/Ethnicity/Hemoglobinopathies

Warked discrepancies between measured A1C and plasma glucose levels should prompt consideration that the A1C assay may not be reliable for that individual.

For patients with a hemoglobin variant but normal red blood cell turnover, such as those with the sickle cell trait, an A1C assay without interference from hemoglobin variants should be used.

An updated list of A1C assays with interferences is available at www.ngsp.org/interf.asp. The "Type 1 Diabetes" subsection and the recommendations within have been updated based on the publication of "The Management of Type 1 Diabetes in Adults. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

- Under "Classification," immune checkpoint inhibitors have been added as a cause of medication-induced diabetes.
- Additional evidence and discussion have been added to the subsection "Screening for Type 1 Diabetes Risk."
- Recommendation 2.9 has been revised to recommend that, for all people, screening for prediabetes and diabetes should begin at age 35 years.

Recommendation 2.24 regarding genetic testing for those who do not have typical characteristics of type 1 or type 2 diabetes has been revised based on the publication of "The Management of Type 1 Diabetes in Adults. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)" 2.24 Children and young adults who do not have typical characteristics of type 1 or type 2 diabetes and who often have a family history of diabetes in successive generations (suggestive of an autosomal dominant pattern of inheritance) should have genetic testing for maturity-onset diabetes of the young. A

2.25 In both instances, consultation with a center specializing in diabetes genetics is recommended to understand the significance of genetic mutations and how best to approach further evaluation, treatment, and genetic counseling. E The gestational diabetes mellitus recommendations have been revised with changes made regarding preconception and early pregnancy screening for diabetes and abnormal glucose metabolism, with supporting evidence added to the text.

In women who are planning pregnancy, screen those with risk factors B and consider testing all women for undiagnosed diabetes. E

Section 3. Prevention or Delay of Type 2 Diabetes and Associated Comorbidities

- The title has been changed to "Prevention or Delay of Type 2 Diabetes and Associated Comorbidities."
- Recommendation 3.1 has been modified to better individualize monitoring for the development of type 2 diabetes in those with prediabetes.
- Adults with overweight/obesity are recommended to be referred to an intensive lifestyle behavior change program (Recommendation)

3.2).

- Additional considerations have been added to the recommendation regarding metformin therapy (Recommendation 3.6).
 - S.6 Metformin therapy for prevention of type 2 diabetes should be considered in adults with prediabetes, as typified by the Diabetes Prevention Program, especially those aged 25–59 years with BMI ≥35 kg/m2, higher fasting plasma glucose (e.g., ≥110 mg/dL), and higher A1C (e.g., ≥6.0%), and in women with prior gestational diabetes mellitus. A
- More discussion was added on vitamin D supplementation in the "Pharmacologic Interventions" subsection.
 - There is a new subsection and recommendation on patient-centered care aimed at weight loss or prevention of weight gain, minimizing progression of hyperglycemia, and attention to cardiovascular risk and associated comorbidities.

Section 4. Comprehensive Medical Evaluation and Assessment of Comorbidities

- The "Immunizations" subsection has been revised, and more information and evidence on the influenza vaccine for people with diabetes and cardiovascular disease has been added to the "Influenza" subsection.
 Within this subsection, coronavirus disease 2019 (COVID-19) vaccination information has been added based on evolving evidence.
- The COVID-19 vaccine will likely become a routine part of the annual preventive schedule for people with diabetes.



From: 4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes—2022

DECISION CYCLE FOR PATIENT-CENTERED GLYCEMIC MANAGEMENT IN TYPE 2 DIABETES

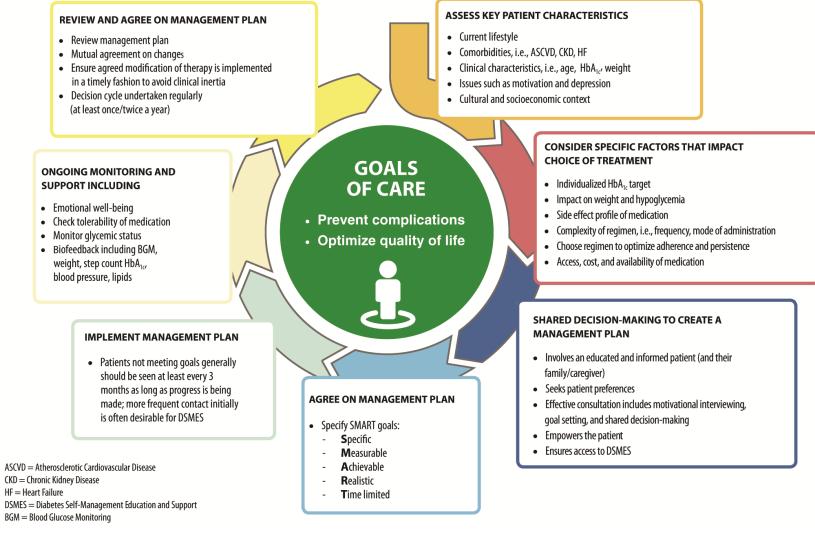


Figure Legend:

Decision cycle for patient-centered glycemic management in type 2 diabetes. Adapted from Davies et al. (104).

Vaccination	Age-group recommendations	Frequency
Hepatitis B	<60 years of age; ≥60 years of age discuss with health care provider	Two- or three-dose series
Human papilloma virus (HPV)	≤26 years of age; 27–45 years of age may also be vaccinated against HPV after a discussion with health care provider	Three doses over 6 months
Influenza	All patients; advised not to receive live attenuated influenza vaccine	Annual
Pneumonia (PPSV23	19–64 years of age, vaccinate with Pneumovax	One dose
[Pneumovax])	≥65 years of age, obtain second dose of Pneumovax, at least 5 years from prior Pneumovax vaccine	One dose; if PCV13 has been given, then give PPSV23 ≥1 year after PCV13 and ≥5 years after any PPSV23 at age <65 years

Vaccination	Age-group recommendations	Frequency
	Adults ≥19 of age, with an immunocompromising condition (e.g., chronic renal failure), cochlear implant, or cerebrospinal fluid leak	One dose
Pneumonia (PCV13 [Prevnar])	19–64 years of age, immunocompetent, no recommendation	None
	≥65 years of age, immunocompetent, have shared decision-making discussion with health care provider	One dose
Tetanus, diphtheria, pertussis (TDAP)	All adults; pregnant women should have an extra dose	Booster every 10 years
Zoster	≥50 years of age	Two-dose Shingrix, even if previously vaccinated

Table 4.6, management of patients with nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH), and Table 4.7, summary of published NAFLD guidelines, reproduced from "Preparing for the NASH Epidemic: A Call to Action" provide more information on how to manage these diseases.

Developed following an American Gastroenterological Association conference on the burden, screening, risk stratification, diagnosis, and management of individuals with NAFLD, the Call to Action informed other revisions to the "Nonalcoholic Fatty Liver Disease" subsection.

Table 4.6—Management of patients with nonalcoholic fatty liver disease and nonalcoholic steatohepatitis

Variable	Lifestyle intervention ^a	Liver-directed pharmacotherapy	Diabetes care (in individuals with diabetes)	Cardiovascular risk reduction
NAFLD	Yes	No	Standard of care	Yes
NASH with fibrosis stage 0 or 1 (F0, F1)	Yes	No	Standard of care	Yes
NASH with fibrosis stage 2 or 3 (F2, F3)	Yes	Yes	Yes Pioglitazone, GLP-1 Yes receptor agonists ^b	
NASH cirrhosis (F4)	Yes	Yes	Individualize ^c	Yes

NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis. ^aAll patients require regular physical activity and healthy diet and to avoid excess alcohol intake; weight loss recommended. ^bAmong glucagon-like peptide 1 (GLP-1) receptor agonists, semaglutide has the best evidence of benefit in patients with NASH and fibrosis. ^cEvidence for efficacy of pharmacotherapy in patients with NASH cirrhosis is very limited and should be individualized and used with caution. Adapted from "Preparing for the NASH Epidemic: A Call to Action" (62).

Section 5. Facilitating Behavior Change and Well-being to Improve Health Outcomes

- Recommendation 5.5 has been added to the "Diabetes Self-Management Education and Support" subsection to address digital coaching and digital self-management interviews as effective methods of education and support.
- 5.5 Digital coaching and digital self-management interventions can be effective methods to deliver diabetes self-management education and support. B
- In the "Carbohydrates" subsection, more emphasis has been placed on the quality of carbohydrates selected. In Recommendation 5.15, a fiber goal has been added for additional clarity.
- 5.15 Carbohydrate intake should emphasize nutrient-dense carbohydrate sources that are high in fiber (at least 14 g fiber per 1,000 kcal) and minimally processed. Eating plans should emphasize nonstarchy vegetables, fruits, and whole grains, as well as dairy products, with minimal added sugars. B
- Evidence on consumption of mixed meals, insulin dosing, and impact on glycemia has also been added to this subsection.

Торіс	Recommendation	
Effectiveness of nutrition therapy	5.9 An individualized medical nutrition therapy program as needed to achieve treatment goals, provided by a registered dietitian nutritionist (RD/RDN), preferably one who has comprehensive knowledge and experience in diabetes care, is recommended for all people with type 1 or type 2 diabetes, prediabetes, and gestational diabetes mellitus. A	
	5.10 Because diabetes medical nutrition therapy can result in cost savings B and improved outcomes (e.g., A1C reduction, reduced weight, decrease in cholesterol) A , medical nutrition therapy should be adequately reimbursed by insurance and other payers. E	
Energy balance	5.11 For all patients with overweight or obesity, behavioral modification to achieve and maintain a minimum weight loss of 5% is recommended. A	
	5.12 There is no ideal macronutrient pattern for people with diabetes; meal plans should be individualized while keeping total calorie and metabolic goals in mind. E	
Eating patterns and	5.13 A variety of eating patterns can be considered for the management of type 2 diabetes and to prevent diabetes in individuals with prediabetes. B	
macronutrient distribution	5.14 Reducing overall carbohydrate intake for individuals with diabetes has demonstrated the most evidence for improving glycemia and may be applied in a variety of eating patterns that meet individual needs and preferences. B	
	5.15 Carbohydrate intake should emphasize nutrient-dense carbohydrate sources that are high in fiber (at least 14 g fiber per 1,000 kcal) and minimally processed. Eating plans should emphasize nonstarchy vegetables, fruits, and whole grains, as well as dairy products, with minimal added sugars. B	
Carbohydrates	5.16 People with diabetes and those at risk are advised to replace sugar-sweetened beverages (including fruit juices) with water as much as possible in order to control glycemia and weight and reduce their risk for cardiovascular disease and fatty liver B and should minimize the consumption of foods with added sugar that have the capacity to displace healthier, more nutrient-dense food choices. A	
	5.17 When using a flexible insulin therapy program, education on the glycemic impact of carbohydrate A, fat, and protein B should be tailored to an individual's needs and preferences and used to optimize mealtime insulin dosing.	
	5.18 When using fixed insulin doses, individuals should be provided education about consistent pattern of carbohydrate intake with respect to time and amount, while considering the insulin action time, as it can result in improved glycemia and reduce the risk for hypoglycemia. B	
Protein	5.19 In individuals with type 2 diabetes, ingested protein appears to increase insulin response without increasing plasma glucose concentrations. Therefore, carbohydrate sources high in protein should be avoided when trying to treat or prevent hypoglycemia. B	
Dietary fat	5.20 An eating plan emphasizing elements of a Mediterranean-style eating pattern rich in monounsaturated and polyunsaturated fats may be considered to improve glucose metabolism and lower cardiovascular disease risk. B	
	5.21 Eating foods rich in long-chain n-3 fatty acids, such as fatty fish (EPA and DHA) and nuts and seeds (ALA), is recommended to prevent or treat cardiovascular disease. B	
Micronutrients and herbal supplements	5.22 There is no clear evidence that dietary supplementation with vitamins, minerals (such as chromium and vitamin D), herbs, or spices (such as cinnamon or aloe vera) can improve outcomes in people with diabetes who do not have underlying deficiencies, and they are not generally recommended for glycemic control. C	
	5.23 Adults with diabetes who drink alcohol should do so in moderation (no more than one drink per day for adult women and no more than two drinks per day for adult men). C	
Alcohol	5.24 Educating people with diabetes about the signs, symptoms, and self-management of delayed hypoglycemia after drinking alcohol, especially when using insulin or insulin secretagogues, is recommended. The importance of glucose monitoring after drinking alcoholic beverages to reduce hypoglycemia risk should be emphasized. B	
Sodium	5.25 Sodium consumption should be limited to <2,300 mg/day. B	
Nonnutritive sweeteners	5.26 The use of nonnutritive sweeteners as a replacement for sugar-sweetened products may reduce overall calorie and carbohydrate intake as long as there is not a compensatory increase of energy intake from other sources. Overall, people are encouraged to decrease both sweetened and nonnutritive-sweetened beverages, with an emphasis on water intake. B	

A new subsection on cognitive capacity/impairment has been added, with recommendations for monitoring (Recommendation 5.51) and referral (Recommendation 5.52) for formal assessment, and a discussion of the evidence regarding cognitive impairment and diabetes.

5.51 Cognitive capacity should be monitored throughout the life span for all individuals with diabetes, particularly in those who have documented cognitive disabilities, those who experience severe hypoglycemia, very young children, and older adults. B

5.52 If cognitive capacity changes or appears to be suboptimal for provider-patient decision-making and/or behavioral self-management, referral for a formal assessment should be considered. E

Section 6. Glycemic Targets

Time in range has been more fully incorporated into the "Glycemic Assessment" subsection.

Time in range thresholds were removed from Recommendation 6.4, and the reader is directed to Table 6.2 for those values.

Standardized CGM metrics for clinical care

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Å.	1. Number of days CGM device is worn (recommend 14 days)	
2. Percentage of time CGM device is active (recommend 70% of data from 14		
2	days)	
<u>ک</u> ر	3. Mean glucose	
∱.	4. Glucose management indicator	
7	 Glycemic variability (%CV) target ≤36%[*] 	
۲ کا	6. TAR: % of readings and time >250 mg/dL (>13.9 mmol/L)	Level 2 hyperglycemia
, ↓ ↓	7. TAR: % of readings and time 181–250 mg/dL (10.1–13.9 mmol/L)	Level 1 hyperglycemia
'. 1	8. TIR: % of readings and time 70–180 mg/dL (3.9–10.0 mmol/L)	In range
5	9. TBR: % of readings and time 54–69 mg/dL (3.0–3.8 mmol/L)	Level 1 hypoglycemia
↓ A	10. TBR: % of readings and time <54 mg/dL (<3.0 mmol/L)	Level 2 hypoglycemia
2		



From: 6. Glycemic Targets: Standards of Medical Care in Diabetes—2022

AGP Report: Continuous Glucose Monitoring

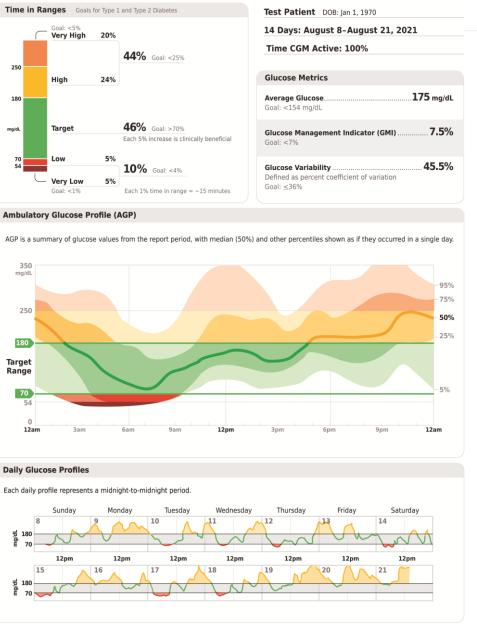


Figure Legend:

Key points included in standard ambulatory glucose profile (AGP) report. Reprinted from Holt et al. (33).



From: 6. Glycemic Targets: Standards of Medical Care in Diabetes—2022

Approach to Individualization of Glycemic Targets

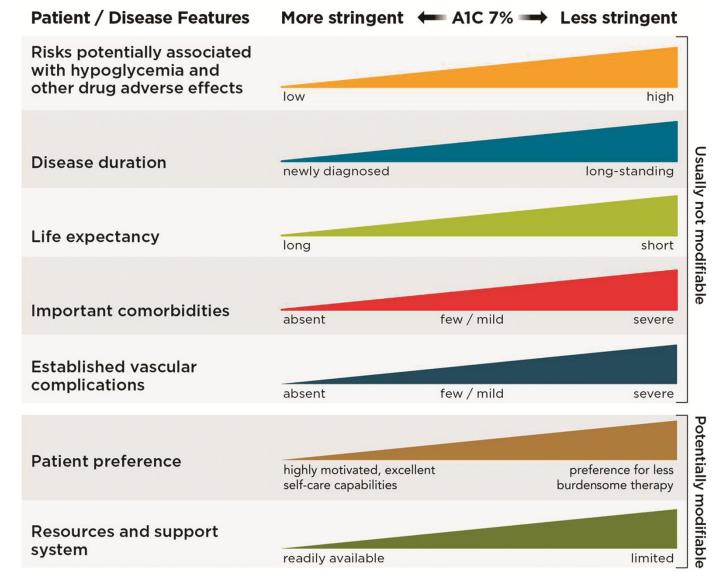


Figure Legend:

Patient and disease factors used to determine optimal glycemic targets. Characteristics and predicaments toward the left justify more stringent efforts to lower A1C; those toward the right suggest less stringent efforts. A1C 7% = 53 mmol/mol. Adapted with permission from Inzucchi et al. (68).

Glucose variability and the association of hypoglycemia was added to the "Hypoglycemia" subsection, as well as information on hypoglycemia prevention, including the Blood Glucose Awareness Training, Dose Adjusted for Normal Eating (DAFNE), and DAFNEplus programs.

Section 7. Diabetes Technology

General recommendations on the selection of technology based on individual and caregiver preferences (Recommendation 7.1), ongoing education on use of devices (Recommendation 7.2), continued access to devices across payers (Recommendation) 7.3), support of students using devices in school settings (Recommendation 7.4), and early initiation of technology (Recommendation 7.5) now introduce the technology section, when previously these concepts were distributed throughout the section.

Self-monitoring of blood glucose (SMBG)" was replaced with the more commonly used "blood glucose monitoring (BGM)" throughout, and more information based on the U.S. Food and Drug Administration recommendation regarding when an individual might need access to BGM was added to the "Blood Glucose Monitoring" subsection. 7.7 People who are on insulin using blood glucose monitoring should be encouraged to check when appropriate based on their insulin regimen. This may include checking when fasting, prior to meals and snacks, at bedtime, prior to exercise, when low blood glucose is suspected, after treating low blood glucose levels until they are normoglycemic, and prior to and while performing critical tasks such as driving. B

7.9 Although blood glucose monitoring in individuals on noninsulin therapies has not consistently shown clinically significant reductions in A1C, it may be helpful when altering diet, physical activity, and/or medications (particularly medications that can cause hypoglycemia) in conjunction with a treatment adjustment program. E The recommendations regarding use of continuous glucose monitoring (CGM) were divided between adults (Recommendations 7.11 and 7.12) and youth (Recommendations 7.13 and 7.14), and the recommendation regarding periodic use of CGM or the use of professional CGM has been simplified (Recommendation 7.17).

Frequency of sensor use has also been added to the text of the "Continuous Glucose Monitoring Devices" subsection, as well as a restructuring of the text in this section based on study design. Smart pens" are now referred to as "connected insulin pens," and more discussion and evidence has been added to the insulin pens content.

The discussion of automated insulin delivery (AID) systems has been combined with the insulin pumps subsection and is separate from the "Do-It-Yourself Closed-Loop Systems" subsection.



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Recommendation 7.29 has been modified to include outpatient procedures and the consideration that people should be allowed continued use of diabetes devices during inpatient or outpatient procedures when they can safely use them and supervision is available.

7.29 Patients who are in a position to safely use diabetes devices should be allowed to continue using them in an inpatient setting or during outpatient procedures when proper supervision is available. E

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

- Evidence has been added regarding the importance of addressing obesity, as both obesity and diabetes increase risk for more severe COVID-19 infections.
- The concept of weight distribution and weight gain pattern and trajectory, in addition to weight and BMI, has been added to the "Assessment" subsection.

Recommendation 8.12 and its associated text discussion added to the "Diet, Physical Activity, and Behavioral Therapy" subsection address the lack of clear evidence that dietary supplements are effective for weight loss.

- 8.12 There is no clear evidence that dietary supplements are effective for weight loss. A
- The "Medical Devices for Weight Loss" subsection has been revised to include more information on a newly approved oral hydrogel.

Recently, an oral hydrogel (Plenity) has been approved for long-term use in those with BMI >25 kg/m2 to simulate the space-occupying effect of implantable gastric balloons. Taken with water 30 min before meals, the hydrogel expands to fill a portion of the stomach volume to help decrease food intake during meals. Though average weight loss is relatively small (2– 3% greater than placebo), the subgroup of participants with prediabetes or diabetes at baseline had improved weight loss outcomes (8.1% weight loss) compared with the overall treatment (6.4% weight loss) and placebo (4.4% weight loss) groups

Recommendation 8.21 has been revised to include behavioral support and routine monitoring of metabolic status.

- 8.21 People who undergo metabolic surgery should receive long-term medical and behavioral support and routine monitoring of micronutrient, nutritional, and metabolic status. B
- A new recommendation (Recommendation 8.22) and discussion on postbariatric
 hypoglycemia, its causes, diagnosis, and management have been added.
 Table 8.2, medications approved by the FDA for the treatment of obesity, has been
 - updated to include semaglutide.

8.22 If postbariatric hypoglycemia is suspected, clinical evaluation should exclude other potential disorders contributing to hypoglycemia, and management includes education, medical nutrition therapy with a dietitian experienced in postbariatric hypoglycemia, and medication treatment, as needed. A

Continuous glucose monitoring should be considered as an important adjunct to improve safety by alerting patients to hypoglycemia, especially for those with severe hypoglycemia or hypoglycemia unawareness. E

Section 9. Pharmacologic Approaches to Glycemic Treatment

- Recommendation 9.3 has been revised to include fat and protein content, in addition to carbohydrates, as part of education on matching mealtime insulin dosing.
- 9.1 Most individuals with type 1 diabetes should be treated with multiple daily injections of prandial and basal insulin, or continuous subcutaneous insulin infusion. A
- 9.2 Most individuals with type 1 diabetes should use rapid-acting insulin analogs to reduce hypoglycemia risk. A
 - 9.3 Individuals with type 1 diabetes should receive education on how to match mealtime insulin doses to carbohydrate intake, fat and protein content, and anticipated physical activity. B

Fig. 9.1, "Choices of insulin regimens in people with type 1 diabetes," Fig. 9.2, "Simplified overview of indications for β-cell replacement therapy in people with type 1 diabetes," and Table 9.1, "Examples of subcutaneous insulin regimens," from "The Management of Type 1 Diabetes in Adults. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)" (https://doi.org/10.2337/dci21-0043), have been added to the "Pharmacologic Therapy for Adults with Type 1 Diabetes" subsection.

PHARMACOLOGIC APPROACHES TO GLYCEMIC TREATMENT

Two daily injections with NPH + short-acting (regular)

insulin or premixed

Representative relative attributes of insulin delivery approaches in people with type 1 diabetes¹

Injected insulin regimens	Flexibility	Lower risk of hypoglycemia	Higher costs
MDI with LAA + RAA or URAA	+++	+++	+++
Less-preferred, alternative injected insulin regimens			
MDI with NPH + RAA or URAA	++	++	++
MDI with NPH + short-acting (regular) insulin	++	+	+

Continuous insulin infusion regimens	Flexibility	Lower risk of hypoglycemia	Higher costs
Hybrid closed-loop technology	+++++	+++++	++++++
Insulin pump with threshold/ predictive low-glucose suspend	++++	++++	+++++
Insulin pump therapy without automation	+++	+++	++++

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Pharmacologic Approaches to Glycemic Management: *Standards of Medical Care in Diabetes -2022*; 45(Suppl. 1):S125-S143



Simplified overview of indications for β-cell replacement therapy in people with type 1 diabetes

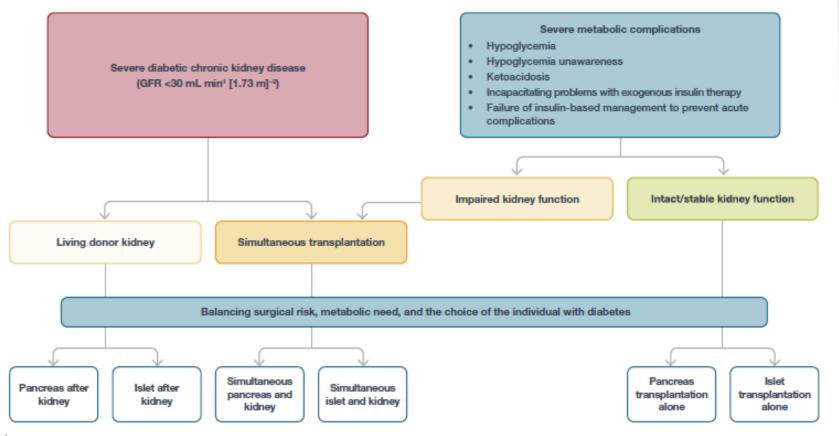


Figure 9.2—Simplified overview of indications for β -cell replacement therapy in people with type 1 diabetes. The two main forms of β -cell replacement therapy are whole-pancreas transplantation or islet cell transplantation. β -Cell replacement therapy can be combined with kidney transplantation if the individual has end-stage renal disease, which may be performed simultaneously or after kidney transplantation. All decisions about transplantation must balance the surgical risk, metabolic need, and the choice of the individual with diabetes. GFR, glomerular filtration rate. Reprinted from Holt et al. (5).

Pharmacologic Approaches to Glycemic Management: Standards of Medical Care in Diabetes - 2022. Diabetes Care 2022;45(Suppl. 1):S125-S143



Pharmacologic Therapy for Adults with Type 2 Diabetes

Recommendation 9.4 has been revised and is now two recommendations (Recommendations 9.4a and 9.4b) on first-line therapies and initial therapies, all based on comorbidities, patientcentered treatment factors, and management needs.

Recommendation 9.5 has been updated with other considerations for the continuation of metformin therapy after patients have been initiated on insulin.

- 9.4a First-line therapy depends on comorbidities, patient-centered treatment factors, and management needs and generally includes metformin and comprehensive lifestyle modification. A
- 9.4b Other medications (glucagon-like peptide 1 receptor agonists, sodium–glucose cotransporter 2 inhibitors), with or without metformin based on glycemic needs, are appropriate initial therapy for individuals with type 2 diabetes with or at high risk for atherosclerotic cardiovascular disease, heart failure, and/or chronic kidney disease (Fig. 9.3). A
 - 9.5 Metformin should be continued upon initiation of insulin therapy (unless contraindicated or not tolerated) for ongoing glycemic and metabolic benefits. A

A new recommendation has been added regarding the use of insulin and combination therapy with a glucagon-like peptide 1 (GLP-1) receptor agonist for greater efficacy and durability (Recommendation 9.11).

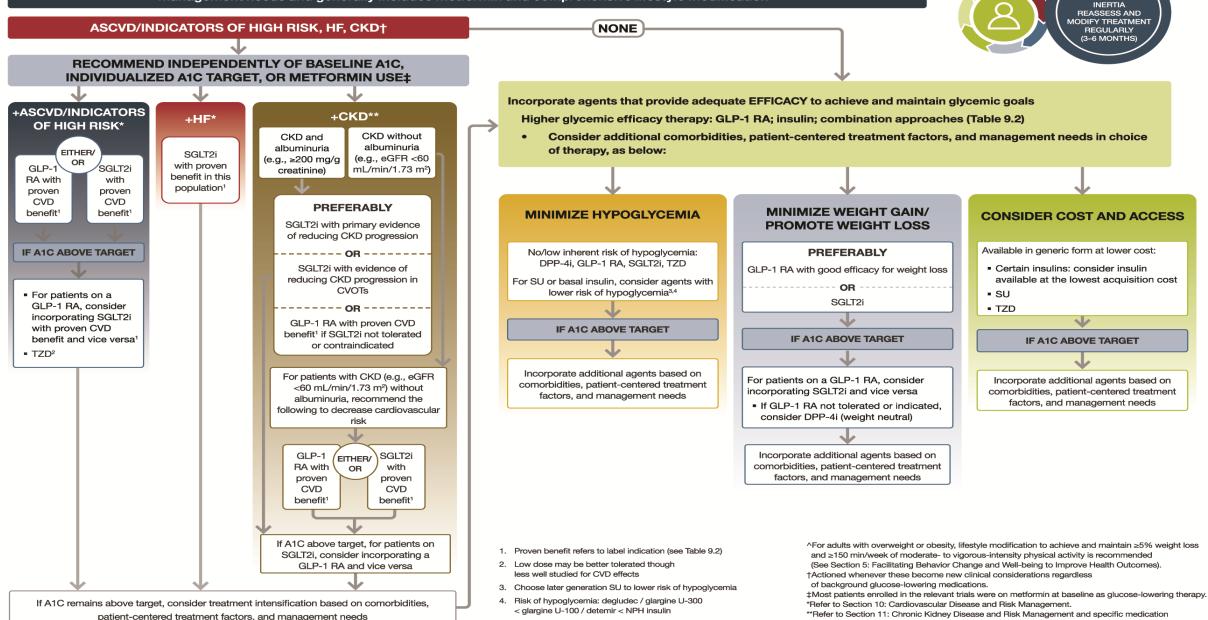
9.11 If insulin is used, combination therapy with a glucagon-like peptide 1 receptor agonist is recommended for greater efficacy and durability of treatment effect. A The section now concludes with an overview of changes made to Fig. 9.3, "Pharmacologic treatment of hyperglycemia in adults with type 2 diabetes," to reconcile emerging evidence and support harmonization of guidelines recognizing alternative initial treatment approaches to metformin as acceptable, depending on comorbidities, patient-centered treatment factors, and glycemic and comorbidity management needs. The principle of medication incorporation is emphasized throughout Fig. 9.3—not all treatment intensification results in sequential add-on therapy, and instead may involve switching therapy or weaning current therapy to accommodate therapeutic changes.

PHARMACOLOGIC TREATMENT OF HYPERGLYCEMIA IN ADULTS WITH TYPE 2 DIABETES

TO AVOID

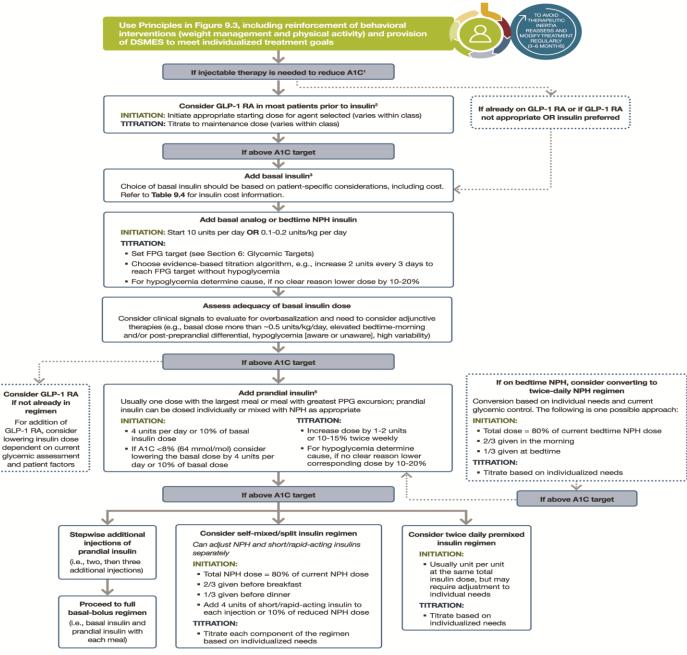
THERAPEUTIC





5. Consider country- and region-specific cost of drugs

label for eGFR criteria.



1. Consider insulin as the first injectable if evidence of ongoing catabolism, symptoms of hyperglycemia are present, when A1C levels (>10% [86 mmol/mol]) or blood glucose levels (>300 mg/dL [16.7 mmol/L]) are very high, or a diagnosis of type 1 diabetes is a possibility.

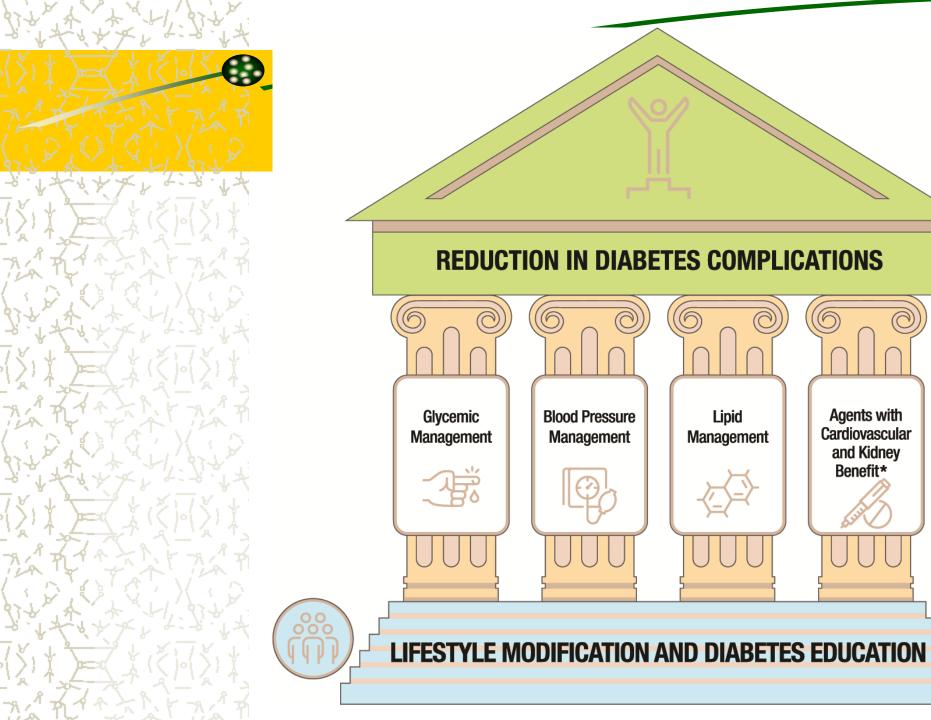
2. When selecting GLP-1 RA, consider patient preference, A1C lowering, weight-lowering effect, or frequency of injection. If CVD, consider GLP-1 RA with proven CVD benefit. Oral or injectable GLP-1 RA are appropriate.

- 3. For patients on GLP-1 RA and basal insulin combination, consider use of a fixed-ratio combination product (IDegLira or iGlarLixi).
- 4. Consider switching from evening NPH to a basal analog if the patient develops hypoglycemia and/or frequently forgets to administer NPH in the evening and would be better managed with an AM dose of a long-acting basal insulin.
- what an am code of a long-actual basal mount. 5. If adding prandial insulin to NPH, consider initiation of a self-mixed or premixed insulin regimen to decrease the number of injections required.

Section 10. Cardiovascular Disease and Risk Management

This section is endorsed for the fourth consecutive year by the American College of Cardiology.

- A new figure (Fig. 10.1) has been added to depict the recommended comprehensive approach to the reduction in risk of diabetes-related complications.
- ➢ Recommendation 10.1 on screening and diagnosis of blood pressure has been revised to include diagnosis of hypertension at a single health care visit for individuals with blood pressure measuring ≥180/110 mmHg and cardiovascular disease.



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I0.1 Blood pressure should be measured at every routine clinical visit. When possible, patients found to have elevated blood pressure (≥140/90 mmHg) should have blood pressure confirmed using multiple readings, including measurements on a separate day, to diagnose hypertension. A Patients with blood pressure ≥180/110 mmHg and cardiovascular disease could be diagnosed with hypertension at a single visit. E
 10.2 All hypertensive patients with diabetes should monitor their blood pressure at home. A

More information on low diastolic blood pressure and blood pressure management has been added to the "Individualization of Treatment Targets" subsection under "Hypertension/Blood Pressure Control."

In the "Treatment Strategies: Lifestyle Interventions" subsection under "Hypertension/Blood Pressure Control," discussion has been added on the use of internet or mobile-based digital platforms to reinforce healthy behaviors and their ability to enhance the efficacy of medical therapy for hypertension.

- 10.3 For patients with diabetes and hypertension, blood pressure targets should be individualized through a shared decision-making process that addresses cardiovascular risk, potential adverse effects of antihypertensive medications, and patient preferences. B
- I0.4 For individuals with diabetes and hypertension at higher cardiovascular risk (existing atherosclerotic cardiovascular disease [ASCVD] or 10-year ASCVD risk ≥15%), a blood pressure target of <130/80 mmHg may be appropriate, if it can be safely attained. B</p>
- 10.5 For individuals with diabetes and hypertension at lower risk for cardiovascular disease (10year atherosclerotic cardiovascular disease risk <15%), treat to a blood pressure target of <140/90 mmHg. A</p>
 - 10.6 In pregnant patients with diabetes and preexisting hypertension, a blood pressure target of 110–135/85 mmHg is suggested in the interest of reducing the risk for accelerated maternal hypertension A and minimizing impaired fetal growth. E

More information on use of ACE inhibitors and angiotensin receptor blocker (ARB) therapy for those with kidney function decline has been added to the "Pharmacologic Interventions" subsection under "Hypertension/Blood Pressure Control.

- Ezetimibe being preferential due to its lower cost has been removed from Recommendation 10.24.
- More discussion was added on use of evolocumab therapy and reduction in all strokes and ischemic stroke.
- A new subsection on statins and bempedoic acid has been added.

Hyperkalemia and Acute Kidney Injury

Treatment with ACE inhibitors or ARBs can cause AKI and hyperkalemia, while diuretics can cause AKI and either hypokalemia or hyperkalemia (depending on mechanism of action).

Detection and management of these abnormalities is important because AKI and hyperkalemia each increase the risks of cardiovascular events and death. Therefore, serum creatinine and potassium should be monitored during treatment with an ACE inhibitor, ARB, or diuretic, particularly among patients with reduced glomerular filtration who are at increased risk of hyperkalemia and AKI. 10.22 In adults with diabetes and 10-year atherosclerotic cardiovascular disease risk of 20% or higher, it may be reasonable to add ezetimibe to maximally tolerated statin therapy to reduce LDL cholesterol levels by 50% or more. C

I0.24 For patients with diabetes and atherosclerotic cardiovascular disease considered very high risk using specific criteria, if LDL cholesterol is ≥70 mg/dL on maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor). A

- Evolocumab therapy also significantly reduced all strokes (1.5% vs. 1.9%; HR 0.79 [95% CI 0.66–0.95]; P = 0.01) and ischemic stroke (1.2% vs. 1.6%; HR 0.75 [95% CI 0.62–0.92]; P = 0.005) in the total population, with findings being consistent in patients with or without a history of ischemic stroke at baseline
 - A pooled analysis suggests that bempedoic acid therapy lowers LDL cholesterol levels by about 23% compared with placebo (114). At this time, there are no completed trials demonstrating a cardiovascular outcomes benefit to use of this medication; however, this agent may be considered for patients who cannot use or tolerate other evidencebased LDL cholesterol–lowering approaches, or for whom those other therapies are inadequately effective

Diabetes Risk With Statin Use

 treatment of 255 patients with statins for 4 years resulted in one additional case of diabetes while simultaneously preventing 5.4 vascular events

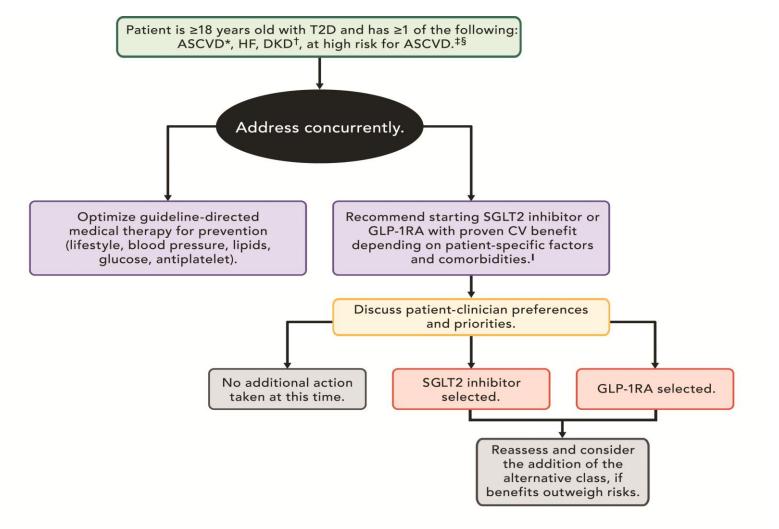
Lipid-Lowering Agents and Cognitive Function

 Therefore, a concern that statins or other lipid-lowering agents might cause cognitive dysfunction or dementia is not currently supported by evidence and should not deter their use in individuals with diabetes at high risk for ASCVD A discussion of the ADAPTABLE (Aspirin Dosing: A Patient-Centric Trial Assessing Benefits and Long-term Effectiveness) trial has been added to the "Aspirin Dosing" subsection.

A discussion of the TWILIGHT (Ticagrelor With Aspirin or Alone in High-Risk Patients After Coronary Intervention) trial has been added to the "Indications for P2Y12 Receptor Antagonist Use" subsection. ★ Recommendations for using aspirin as primary prevention include both men and women aged ≥50 years with diabetes and at least one additional major risk factor (family history of premature ASCVD, hypertension, dyslipidemia, smoking, or chronic kidney disease/albuminuria) who are not at increased risk of bleeding (e.g., older age, anemia, renal disease). In the ADAPTABLE (Aspirin Dosing: A Patient-Centric Trial Assessing Benefits and Long-term Effectiveness) trial of patients with established cardiovascular disease, 38% of whom had diabetes, there were no significant differences in cardiovascular events or major bleeding between patients assigned to 81 mg and those assigned to 325 mg of aspirin daily Recommendation 10.42c has been added to the "Cardiovascular Disease: Treatment" subsection, providing guidance for patients with type 2 diabetes and established atherosclerotic cardiovascular disease (ASCVD) or multiple risk factors for ASCVD on the use of combined therapy with a sodium– glucose cotransporter 2 (SGLT2) inhibitor with demonstrated cardiovascular benefit and a GLP-1 receptor agonist with demonstrated cardiovascular benefit. 10.42 Among patients with type 2 diabetes who have established atherosclerotic cardiovascular disease or established kidney disease, a sodium–glucose cotransporter 2 inhibitor or glucagonlike peptide 1 receptor agonist with demonstrated cardiovascular disease benefit (Table 10.3B and Table 10.3C) is recommended as part of the comprehensive cardiovascular risk reduction and/or glucose-lowering regimens. A A discussion of the Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) trial, the Effect of Sotagliflozin on Cardiovascular Events in Patients With Type 2 Diabetes Post Worsening Heart Failure (SOLOIST-WHF) trial, and the Effect of Efpeglenatide on Cardiovascular Outcomes (AMPLITUDE-O) have been added, in addition to the results of the Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure (DAPA-HF) trial, the Evaluation of Ertugliflozin Efficacy and Safety Cardiovascular Outcomes Trial (VERTIS CV), and the Effect of Sotagliflozin on Cardiovascular and Renal Events in Patients With Type 2 Diabetes and Moderate Renal Impairment Who Are at Cardiovascular Risk (SCORED) trial, which were added as a Living Standards update in June 2021.

A new subsection, "Clinical Approach," now concludes this section on risk reduction with SGLT2 inhibitors or GLP-1 receptor agonist therapy.

Fig. 10.3 has been reproduced from the ADA-endorsed American College of Cardiology "2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients with Type 2 Diabetes" and outlines the approach to risk reduction with SGLT2 inhibitor or GLP-1 receptor agonist therapy in conjunction with other traditional, guideline-based preventive medical therapies for blood pressure as well as lipid, glycemic, and antiplatelet therapy.



*ASCVD is defined as a history of an acute coronary syndrome or MI, stable or unstable angina, coronary heart disease with or without revascularization, other arterial revascularization, stroke, or peripheral artery disease assumed to be atherosclerotic in origin.

[†]DKD is a clinical diagnosis marked by reduced eGFR, the presence of albuminuria, or both.

⁺ Consider an SGLT2 inhibitor when your patient has established ASCVD, HF, DKD or is at high risk for ASCVD. Consider a GLP-1RA when your patient has established ASCVD or is at high risk for ASCVD.

§ Patients at high risk for ASCVD include those with end organ damage such as left ventricular hypertrophy or retinopathy or with multiple CV risk factors (e.g., age, hypertension, smoking, dyslipidemia, obesity).

¹ Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.

ASCVD = atherosclerotic cardiovascular disease; CV = cardiovascular; DKD = diabetic kidney disease; eGFR = estimated glomerular filtration rate; GLP-1RA = glucagon-like peptide-1 receptor agonist; HF = heart failure; MI = myocardial infarction; SGLT2 = sodium-glucose cotransporter-2; T2D = type 2 diabetes

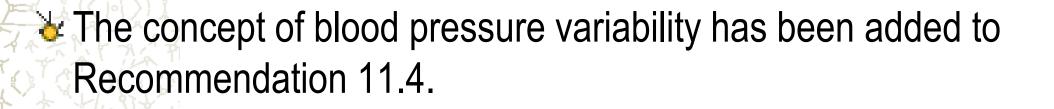
Section 11. Chronic Kidney Disease and Risk Management

- Formerly, Section 11, "Microvascular Complications and Foot Care," contained content on chronic kidney disease, retinopathy, neuropathy, and foot care.
- This section has now been divided into two sections: Section 11, "Chronic Kidney Disease and Risk Management", and Section 12, "Retinopathy, Neuropathy, and Foot Care"

Recommendation 11.3a has been revised to include lower glomular filtration rates and lower urinary albumin as indicators for use of SGLT2 inhibitors to reduce chronic kidney disease (CKD) progression and cardiovascular events.

I1.3a For patients with type 2 diabetes and diabetic kidney disease, use of a sodium–glucose cotransporter 2 inhibitor in patients with an estimated glomerular filtration rate ≥25 mL/min/1.73 m2 and urinary albumin ≥300 mg/g creatinine is recommended to reduce chronic kidney disease progression and cardiovascular events. A

- Recommendation 11.3c has also been revised to include therapy options (nonsteroidal mineralocorticoid receptor antagonist [finerenone]), and a new recommendation has been added (Recommendation 11.3d) regarding reduction of urinary albumin to slow CKD progression.
 - 11.3c In patients with chronic kidney disease who are at increased risk for cardiovascular events or chronic kidney disease progression and are unable to use a sodium–glucose cotransporter 2 inhibitor, a nonsteroidal mineralocorticoid receptor antagonist (finerenone) is recommended to reduce chronic kidney disease progression and cardiovascular events. A
 - 11.3d In patients with chronic kidney disease who have ≥300 mg/g urinary albumin, a reduction of 30% or greater in mg/g urinary albumin is recommended to slow chronic kidney disease progression. B



Wore discussion has been added to the "Acute Kidney Injury" subsection regarding use of ACE inhibitors or ARBs.

Section 12. Retinopathy, Neuropathy, and Foot Care

More discussion was added to the "Diabetic Retinopathy" subsection regarding use of GLP-1 receptor agonists and retinopathy.

Recommendation 12.11 was updated to indicate that intravitreous injections of anti–vascular endothelial growth factor are a reasonable alternative to traditional panretinal laser photocoagulation for some patients with proliferative diabetic retinopathy and also reduce the risk of vision loss in these patients. Recommendation 12.12 was also updated to recommend intravitreous injections of anti–vascular endothelial growth factor as first-line treatment for most eyes with diabetic macular edema that involves the foveal center and impairs visions acuity.

A new recommendation (Recommendation 12.13) was added on macular focal/grid photocoagulation and intravitreal injections of corticosteroid.

Section 13. Older Adults

In the "Hypoglycemia" subsection, glycemic variability and older adults with physical or cognitive limitations was added to the discussion of use of CGM.

The upper threshold of 8.5% (69 mmol/mol) was removed from the example of less stringent goals for those with multiple coexisting chronic illnesses, cognitive impairment, or functional dependence in Recommendation 13.6.

- More discussion was added on classification of older adults in the "Patients With Complications and Reduced Functionality" subsection.
- The benefits of a structured exercise program (as in the Lifestyle Interventions and Independence for Elders [LIFE] Study) was incorporated into the "Lifestyle Management" subsection.
- More discussion of overtreatment was added to the "Pharmacologic Therapy" subsection, as was the consideration that for those taking metformin long term, monitoring vitamin B12 deficiency should be considered. The insulin therapy discussion was also updated with more information on avoidance of hypoglycemia.

Section 14. Children and Adolescents

Table 14.1A and Table 14.1B have been newly created and provide an overview of the recommendations for screening and treatment of complications and related conditions in pediatric type 1 diabetes (Table 14.1A) and type 2 diabetes (Table 14.1B).

The "Diabetes Self-Management Education and Support" subsection now discusses adult caregivers as critical to diabetes self-management in youth, and how they should be engaged to ensure there is not a premature transfer of responsibility for self-management to the youth.

k Recommendation 14.7 has been simplified.

	Thyroid disease	Celiac disease	Hypertension	Dyslipidemia	Nephropathy	Retinopathy	Neuropathy
Corresponding recommendations	14.29 and 14.30	14.31–14.33	14.34–14.37	14.38–14.42	14.45 and 14.46	14.47–14.49	14.50
Method	Thyroid-stimulating hormone; consider antithyroglobulin and antithyroid peroxidase antibodies	IgA tTG if total IgA normal; IgG tTG and deamidated gliadin antibodies if IgA deficient	Blood pressure monitoring	Lipid profile, nonfasting acceptable initially	Albumin-to-creatinine ratio; random sample acceptable initially	Dilated fundoscopy or retinal photography	Foot exam with foot pulses, pinprick, 10-g monofilament sensation tests, vibration, and ankle reflexes
When to start	Soon after diagnosis	Soon after diagnosis	At diagnosis	Soon after diagnosis; preferably after glycemia has improved and ≥2 years old	Puberty or >10 years old, whichever is earlier, and diabetes duration of 5 years	Puberty or ≥11 years old, whichever is earlier, and diabetes duration of 3–5 years	Puberty or ≥10 years old, whichever is earlier, and diabetes duration of 5 years
Follow-up frequency	Every 1–2 years if thyroid antibodies negative; more often if symptoms develop or presence of thyroid antibodies	Within 2 years and then at 5 years after diagnosis; sooner if symptoms develop	Every visit	If LDL ≤100 mg/dL, repeat at 9–11 years old; then, if <100 mg/dL, every 3 years	If normal, annually; if abnormal, repeat with confirmation in two of three samples over 6 months	If normal, every 2 years; consider less frequently (every 4 years) if A1C <8% and eye professional agrees	If normal, annually
Target	NA	NA	<90th percentile for age, sex, and height; if ≥13 years old, <120/80 mmHg	LDL <100 mg/dL	Albumin-to-creatinine ratio <30 mg/g	No retinopathy	No neuropathy
Treatment	Appropriate treatment of underlying thyroid disorder	After confirmation, start gluten-free diet	modification and ACE inhibitor or ARB [*] for hypertension (≥95th	glucose control and medical	Optimize glucose and blood pressure control; ACE inhibitor <u>*</u> if albumin-to- creatinine ratio is elevated in two of three samples over 6 months	Optimize glucose control; treatment per ophthalmology	Optimize glucose control; referral to neurology

Hypertension	Nephropathy	Neuropathy	Retinopathy	Nonalcoholic fatty liver disease	Obstructive sleep apnea	Polycystic ovarian syndrome (for adolescent females)	Dyslipidemia	
Corresponding recom mendations	14.77–14.80	14.81–14.86	14.87 and 14.88	14.89–14.92	14.93 and 14.94	14.95	14.96–14.98	14.100–14.104
Method	Blood pressure monitoring	Albumin-to-creatinine ratio; random sample acceptable initially	Foot exam with foot pulses, pinprick, 10-g monofilament sensation tests, vibration, and ankle reflexes	Dilated fundoscopy	AST and ALT measurement	Screening for symptoms	Screening for symptoms; laboratory evaluation if positive symptoms	Lipid profile
When to start	At diagnosis	At diagnosis	At diagnosis	At/soon after diagnosis	At diagnosis	At diagnosis	At diagnosis	Soon after diagnosis, preferably after glycemia has improved
Follow-up frequency	Every visit	If normal, annually; if abnormal, repeat with confirmation in two of three samples over 6 months	If normal, annually	If normal, annually	Annually	Every visit	Every visit	Annually
Target	<90th percentile for age, sex, and height; if ≥13 years old, <130/80 mmHg	<30 mg/g	No neuropathy	No retinopathy	NA	NA	NA	LDL <100 mg/dL, HDL >35 mg/dL, triglycerides <150 mg/dL
Treatment	Lifestyle modification for elevated blood pressure (90th to <95th percentile for age, sex, and height or, if ≥13 years old, 120– 129/<80 mmHg); lifestyle modification and ACE inhibitor or ARB [*] for hypertension (≥95th percentile for age, sex, and height or, if ≥13 years, ≥130/80 mmHg)	Optimize glucose and blood pressure control; ACE inhibitor <u>*</u> if	Optimize glucose control; referral to neurology	Optimize glucose control; treatment per ophthalmology	Refer to gastroenterology for persistently elevated or worsening transaminases	If positive symptoms, refer to sleep specialist and polysomnogram	If no contra indications, oral contraceptive pills; medical nutrition therapy; metformin	If abnormal, optimize glucose control and medical nutrition therapy; if after 6 months, LDL >130 mg/dL, initiate statin therapy (for those aged >10 years) <u>*</u> ; if triglycerides >400 mg/dL fasting or >1,000 mg/dL nonfasting, begin fibrate

Section 15. Management of Diabetes in Pregnancy

- A new recommendation (Recommendation 15.16) and discussion of the evidence on telehealth visits for pregnant women with gestational diabetes mellitus has been added to the "Management of Gestational Diabetes Mellitus" subsection.
- A new subsection on "Physical Activity" has been added.
- Additional discussion was added regarding insulin as the preferred treatment for type 2 diabetes in pregnancy.

Section 16. Diabetes Care in the Hospital

Additional information has been added on the use of CGM during the COVID-19 pandemic to minimize contact between health care providers and patients, especially those in the intensive care unit.

Section 17. Diabetes Advocacy

Vo changes have been made to this section.



Thank you and hope for a good rain

