



American Diabetes Association

4. Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Medical Care in Diabetes—2020*

Diabetes Care 2020;43(Suppl. 1):S37–S47 | <https://doi.org/10.2337/dc20-S004>

The American Diabetes Association (ADA) “Standards of Medical Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee, a multidisciplinary expert committee (<https://doi.org/10.2337/dc20-SPPC>), are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations, please refer to the Standards of Care Introduction (<https://doi.org/10.2337/dc20-SINT>). Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

PATIENT-CENTERED COLLABORATIVE CARE

Recommendations

- 4.1 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 health outcomes and health-related quality of life. **B**
- 4.2 Diabetes care should be managed by a multidisciplinary team that may draw from primary care physicians, subspecialty physicians, nurse practitioners, physician assistants, nurses, dietitians, exercise specialists, pharmacists, dentists, podiatrists, and mental health professionals. **E**

A successful medical evaluation depends on beneficial interactions between the patient and the care team. The Chronic Care Model (1–3) (see Section 1 “Improving Care and Promoting Health in Populations,” <https://doi.org/10.2337/dc20-S001>) is a patient-centered approach to care that requires a close working relationship between the patient and clinicians involved in treatment planning. People with diabetes should receive health care from an interdisciplinary team that may include physicians, nurse practitioners, physician assistants, nurses, dietitians, exercise specialists, pharmacists, dentists, podiatrists, and mental health professionals. Individuals with diabetes must assume an active role in their care. The patient, family or support people, physicians, and health care team should together formulate the management plan, which includes lifestyle management (see Section 5 “Facilitating Behavior Change and Well-being to Improve Health Outcomes,” <https://doi.org/10.2337/dc20-S005>).

The goals of treatment for diabetes are to prevent or delay complications and optimize quality of life (**Fig. 4.1**). Treatment goals and plans should be created with patients based

Suggested citation: American Diabetes Association. 4. Comprehensive medical evaluation and assessment of comorbidities: Standards of Medical Care in Diabetes—2020. Diabetes Care 2020;43(Suppl. 1):S37–S47

© 2020 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. More information is available at <http://www.diabetesjournals.org/content/license>.

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

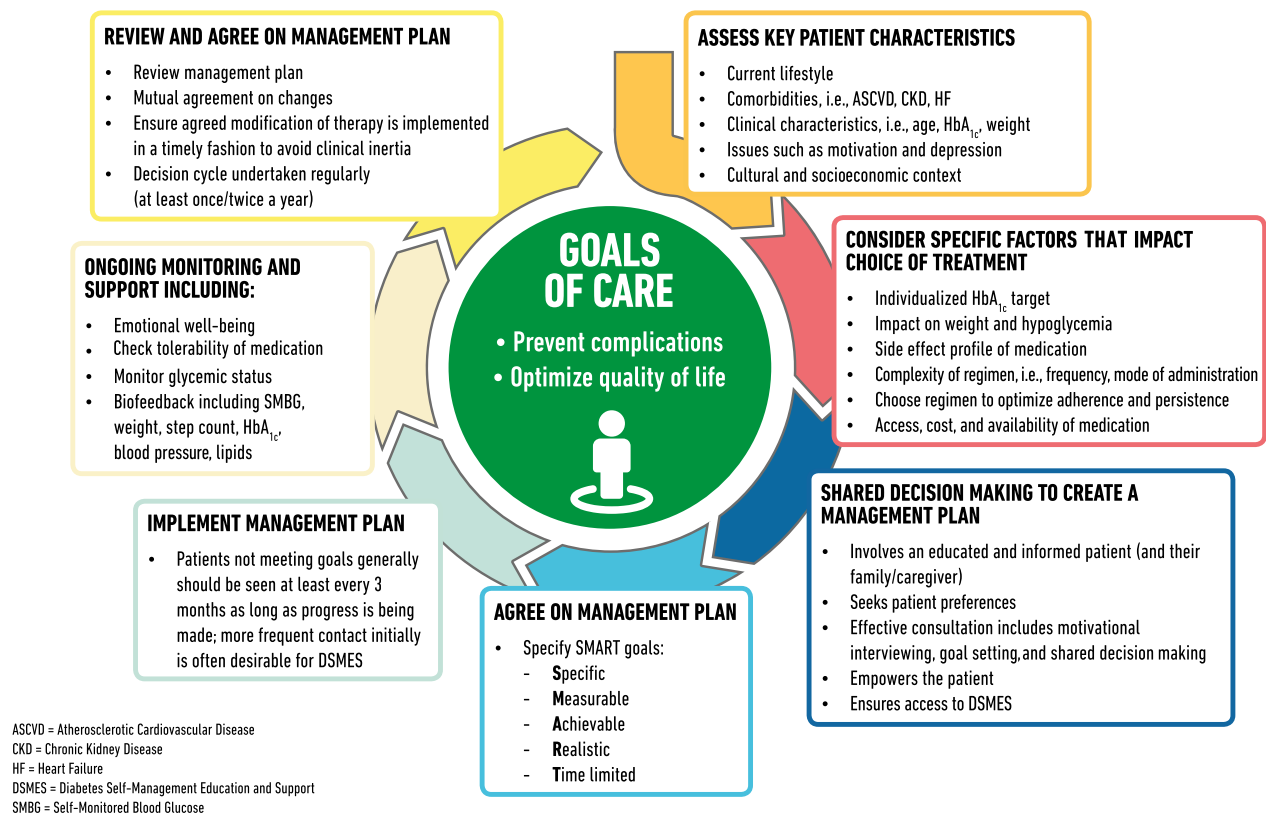


Figure 4.1—Decision cycle for patient-centered glycemic management in type 2 diabetes. Reprinted from Davies et al. (99).

on their individual preferences, values, and goals. The management plan should take into account the patient's age, cognitive abilities, school/work schedule and conditions, health beliefs, support systems, eating patterns, physical activity, social situation, financial concerns, cultural factors, literacy and numeracy (mathematical literacy), diabetes complications and duration of disease, comorbidities, health priorities, other medical conditions, preferences for care, and life expectancy. Various strategies and techniques should be used to support patients' self-management efforts, including providing education on problem-solving skills for all aspects of diabetes management.

Provider communication with patients and families should acknowledge that multiple factors impact glycemic management but also emphasize that collaboratively developed treatment plans and a healthy lifestyle can significantly improve disease outcomes and well-being (4–7). Thus, the goal of provider-patient communication is to establish a collaborative relationship and to assess and address self-management barriers without blaming patients for “noncompliance” or

“nonadherence” when the outcomes of self-management are not optimal (8). The familiar terms “noncompliance” and “nonadherence” denote a passive, obedient role for a person with diabetes in “following doctor's orders” that is at odds with the active role people with diabetes take in directing the day-to-day decision-making, planning, monitoring, evaluation, and problem-solving involved in diabetes self-management. Using a nonjudgmental approach that normalizes periodic lapses in self-management may help minimize patients' resistance to reporting problems with self-management. Empathizing and using active listening techniques, such as open-ended questions, reflective statements, and summarizing what the patient said, can help facilitate communication. Patients' perceptions about their own ability, or self-efficacy, to self-manage diabetes are one important psychosocial factor related to improved diabetes self-management and treatment outcomes in diabetes (9–13) and should be a target of ongoing assessment, patient education, and treatment planning.

Language has a strong impact on perceptions and behavior. The use of empowering

language in diabetes care and education can help to inform and motivate people, yet language that shames and judges may undermine this effort. The American Diabetes Association (ADA) and the American Association of Diabetes Educators consensus report, “The Use of Language in Diabetes Care and Education,” provides the authors' expert opinion regarding the use of language by health care professionals when speaking or writing about diabetes for people with diabetes or for professional audiences (14). Although further research is needed to address the impact of language on diabetes outcomes, the report includes five key consensus recommendations for language use:

- Use language that is neutral, nonjudgmental, and based on facts, actions, or physiology/biology.
- Use language free from stigma.
- Use language that is strength based, respectful, and inclusive and that imparts hope.
- Use language that fosters collaboration between patients and providers.
- Use language that is person centered (e.g., “person with diabetes” is preferred over “diabetic”).

COMPREHENSIVE MEDICAL EVALUATION

Recommendations

4.3 A complete medical evaluation should be performed at the initial visit to:

- Confirm the diagnosis and classify diabetes. **B**
- Evaluate for diabetes complications and potential comorbid conditions. **B**
- Review previous treatment and risk factor control in patients with established diabetes. **B**
- Begin patient engagement in the formulation of a care management plan. **B**
- Develop a plan for continuing care. **B**

4.4 A follow-up visit should include most components of the initial comprehensive medical evaluation, including interval medical history, assessment of medication-taking behavior and intolerance/side effects, physical examination, laboratory evaluation as appropriate to assess attainment of A1C and metabolic targets, and assessment of risk for complications, diabetes self-management behaviors, nutrition, psychosocial health, and the need for referrals, immunizations, or other routine health maintenance screening. **B**

4.5 Ongoing management should be guided by the assessment of diabetes complications and shared decision-making to set therapeutic goals. **B**

4.6 The 10-year risk of a first atherosclerotic cardiovascular disease event should be assessed using the race- and sex-specific Pooled Cohort Equations to better stratify atherosclerotic cardiovascular disease risk. **B**

The comprehensive medical evaluation includes the initial and follow-up evaluations, assessment of complications, psychosocial assessment, management of comorbid conditions, and engagement of the patient throughout the process. While a comprehensive list is provided in **Table 4.1**, in clinical practice the provider may need to prioritize the components of the medical evaluation given the available resources and time. The goal is to provide the health care team information so it can optimally

support a patient. In addition to the medical history, physical examination, and laboratory tests, providers should assess diabetes self-management behaviors, nutrition, and psychosocial health (see Section 5 “Facilitating Behavior Change and Well-being to Improve Health Outcomes,” <https://doi.org/10.2337/dc20-S005>) and give guidance on routine immunizations. The assessment of sleep pattern and duration should be considered; a recent meta-analysis found that poor sleep quality, short sleep, and long sleep were associated with higher A1C in people with type 2 diabetes (15). Interval follow-up visits should occur at least every 3–6 months, individualized to the patient, and then annually.

Lifestyle management and psychosocial care are the cornerstones of diabetes management. Patients should be referred for diabetes self-management education and support, medical nutrition therapy, and assessment of psychosocial/emotional health concerns if indicated. Patients should receive recommended preventive care services (e.g., immunizations, cancer screening, etc.); smoking cessation counseling; and ophthalmological, dental, and podiatric referrals.

The assessment of risk of acute and chronic diabetes complications and treatment planning are key components of initial and follow-up visits (**Table 4.2**). The risk of atherosclerotic cardiovascular disease and heart failure (Section 10 “Cardiovascular Disease and Risk Management,” <https://doi.org/10.2337/dc20-S010>), chronic kidney disease staging (Section 11 “Microvascular Complications and Foot Care,” <https://doi.org/10.2337/dc20-S011>), and risk of treatment-associated hypoglycemia (**Table 4.3**) should be used to individualize targets for glycemia (Section 6 “Glycemic Targets,” <https://doi.org/10.2337/dc20-S006>), blood pressure, and lipids and to select specific glucose-lowering medication (Section 9 “Pharmacologic Approaches to Glycemic Treatment,” <https://doi.org/10.2337/dc20-S009>), antihypertension medication, and statin treatment intensity.

Additional referrals should be arranged as necessary (**Table 4.4**). Clinicians should ensure that individuals with diabetes are appropriately screened for complications and comorbidities. Discussing and implementing an approach to glycemic control with the patient is a part, not the sole goal, of the patient encounter.

Immunizations

Recommendations

4.7 Provide routinely recommended vaccinations for children and adults with diabetes as indicated by age. **C**

4.8 Annual vaccination against influenza is recommended for all people ≥ 6 months of age, especially those with diabetes. **C**

4.9 Vaccination against pneumococcal disease, including pneumococcal pneumonia, with 13-valent pneumococcal conjugate vaccine (PCV13) is recommended for children before age 2 years. People with diabetes ages 2 through 64 years should also receive 23-valent pneumococcal polysaccharide vaccine (PPSV23). At age ≥ 65 years, regardless of vaccination history, additional PPSV23 vaccination is necessary. **C**

4.10 Administer a 2- or 3-dose series of hepatitis B vaccine, depending on the vaccine, to unvaccinated adults with diabetes ages 18 through 59 years. **C**

4.11 Consider administering a 3-dose series of hepatitis B vaccine to unvaccinated adults with diabetes ≥ 60 years of age. **C**

Children and adults with diabetes should receive vaccinations according to age-appropriate recommendations (16,17). The Centers for Disease Control and Prevention (CDC) provides vaccination schedules specifically for children, adolescents, and adults with diabetes at [cdc.gov/vaccines/schedules/](https://www.cdc.gov/vaccines/schedules/).

People with diabetes are at higher risk for hepatitis B infection and are more likely to develop complications from influenza and pneumococcal disease. The CDC Advisory Committee on Immunization Practices (ACIP) recommends influenza, pneumococcal, and hepatitis B vaccinations specifically for people with diabetes. Vaccinations against tetanus-diphtheria-pertussis, measles-mumps-rubella, human papillomavirus, and shingles are also important for adults with diabetes, as they are for the general population.

Influenza

Influenza is a common, preventable infectious disease associated with high

Table 4.1 – Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PAST MEDICAL AND FAMILY HISTORY	Diabetes history			
	▪ Characteristics at onset (e.g., age, symptoms)	✓		
	▪ Review of previous treatment regimens and response	✓		
	▪ Assess frequency/cause/severity of past hospitalizations	✓		
	Family history			
	▪ Family history of diabetes in a first-degree relative	✓		
	▪ Family history of autoimmune disorder	✓		
	Personal history of complications and common comorbidities			
	▪ Macrovascular and microvascular	✓		✓
	▪ Common comorbidities (e.g., obesity, OSA)	✓		✓
	▪ Hypoglycemia: awareness/frequency/causes/timing of episodes	✓	✓	✓
	▪ Presence of hemoglobinopathies or anemias	✓		✓
	▪ High blood pressure or abnormal lipids	✓		✓
LIFESTYLE FACTORS	▪ Last dental visit	✓		✓
	▪ Last dilated eye exam	✓		✓
	▪ Visits to specialists	✓	✓	✓
MEDICATIONS AND VACCINATIONS	Interval history			
	▪ Changes in medical/family history since last visit		✓	✓
	▪ Eating patterns and weight history	✓	✓	✓
	▪ Physical activity and sleep behaviors	✓	✓	✓
	▪ Tobacco, alcohol, and substance use	✓		✓
TECHNOLOGY USE	▪ Current medication regimen	✓	✓	✓
	▪ Medication-taking behavior	✓	✓	✓
	▪ Medication intolerance or side effects	✓	✓	✓
BEHAVIORAL AND DIABETES SELF-MANAGEMENT SKILLS	▪ Complementary and alternative medicine use	✓	✓	✓
	▪ Vaccination history and needs	✓		✓
	▪ Assess use of health apps, online education, patient portals, etc.	✓		✓
	▪ Glucose monitoring (meter/CGM): results and data use	✓	✓	✓
	▪ Review insulin pump settings and use	✓	✓	✓
	Psychosocial conditions			
	▪ Screen for depression, anxiety, and disordered eating; refer for further assessment or intervention if warranted	✓		✓
BEHAVIORAL AND DIABETES SELF-MANAGEMENT SKILLS	▪ Identify existing social supports	✓		✓
	▪ Consider assessment for cognitive impairment*	✓		✓
	Diabetes self-management education and support			
	▪ History of dietitian/diabetes educator visits/classes	✓	✓	✓
	▪ Assess diabetes self-management skills and barriers	✓		✓
BEHAVIORAL AND DIABETES SELF-MANAGEMENT SKILLS	▪ Assess familiarity with carbohydrate counting (type 1 diabetes)	✓		
	Pregnancy planning			
BEHAVIORAL AND DIABETES SELF-MANAGEMENT SKILLS	▪ For women with childbearing capacity, review contraceptive needs and preconception planning	✓	✓	✓

Continued on p. S41

Table 4.1 (cont.)—Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PHYSICAL EXAMINATION	▪ Height, weight, and BMI; growth/pubertal development in children and adolescents	✓	✓	✓
	▪ Blood pressure determination	✓	✓	✓
	▪ Orthostatic blood pressure measures (when indicated)	✓		
	▪ Fundoscopic examination (refer to eye specialist)	✓		✓
	▪ Thyroid palpation	✓		✓
	▪ Skin examination (e.g., acanthosis nigricans, insulin injection or insertion sites, lipodystrophy)	✓	✓	✓
	▪ Comprehensive foot examination			
	• Visual inspection (e.g., skin integrity, callous formation, foot deformity or ulcer, toenails)**	✓		✓
	• Screen for PAD (pedal pulses—refer for ABI if diminished)	✓		✓
	• Determination of temperature, vibration or pinprick sensation, and 10-g monofilament exam	✓		✓
LABORATORY EVALUATION	▪ A1C, if the results are not available within the past 3 months	✓	✓	✓
	▪ If not performed/available within the past year	✓		✓
	• Lipid profile, including total, LDL, and HDL cholesterol and triglycerides [#]	✓		✓ [^]
	• Liver function tests [#]	✓		✓
	• Spot urinary albumin-to-creatinine ratio	✓		✓
	• Serum creatinine and estimated glomerular filtration rate [*]	✓		✓
	• Thyroid-stimulating hormone in patients with type 1 diabetes [#]	✓		✓
	• Vitamin B12 if on metformin (when indicated)	✓		✓
	• Serum potassium levels in patients on ACE inhibitors, ARBs, or diuretics [*]	✓		✓

ABI, ankle-brachial pressure index; ARBs, angiotensin receptor blockers; CGM, continuous glucose monitors; OSA, obstructive sleep apnea; PAD, peripheral arterial disease

^{*}at 65 years of age or older

⁺may be needed more frequently in patients with known chronic kidney disease or with changes in medications that affect kidney function and serum potassium (see Table 11.1)

[#]may also need to be checked after initiation or dose changes of medications that affect these laboratory values (i.e., diabetes medications, blood pressure medications, cholesterol medications, or thyroid medications)

[^]in people without dyslipidemia and not on cholesterol lowering therapy, testing may be less frequent.

^{**}should be performed at every visit in patients with sensory loss, previous foot ulcers, or amputations

mortality and morbidity in vulnerable populations, including youth, older adults, and people with chronic diseases. Influenza vaccination in people with diabetes has been found to significantly reduce influenza and diabetes-related hospital admissions (18).

Pneumococcal Pneumonia

Like influenza, pneumococcal pneumonia is a common, preventable disease. People with diabetes are at increased risk for the bacteremic form of pneumococcal infection and have been reported to have a high risk of nosocomial bacteremia,

with a mortality rate as high as 50% (19). The ADA endorses recommendations from the CDC ACIP that adults age ≥ 65 years, who are at higher risk for pneumococcal disease, receive an additional 23-valent pneumococcal polysaccharide vaccine (PPSV23), regardless of prior pneumococcal vaccination history. See detailed recommendations at www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/pneumo.html.

Hepatitis B

Compared with the general population, people with type 1 or type 2 diabetes have higher rates of hepatitis B. This may

be due to contact with infected blood or through improper equipment use (glucose monitoring devices or infected needles). Because of the higher likelihood of transmission, hepatitis B vaccine is recommended for adults with diabetes age < 60 years. For adults age ≥ 60 years, hepatitis B vaccine may be administered at the discretion of the treating clinician based on the patient's likelihood of acquiring hepatitis B infection.

ASSESSMENT OF COMORBIDITIES

Besides assessing diabetes-related complications, clinicians and their patients

Table 4.2—Assessment and treatment plan*

Assessing risk of diabetes complications

- ASCVD and heart failure history
- ASCVD risk factors and 10-year ASCVD risk assessment
- Staging of chronic kidney disease (see **Table 11.1**)
- Hypoglycemia risk (**Table 4.3**)

Goal setting

- Set A1C/blood glucose target
- If hypertension is present, establish blood pressure target
- Diabetes self-management goals

Therapeutic treatment plans

- 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, atherosclerotic cardiovascular disease. *Assessment and treatment planning are essential components of initial and all follow-up visits.

need to be aware of common comorbidities that affect people with diabetes and may complicate management (20–24). Diabetes comorbidities are conditions that affect people with diabetes more often than age-matched people without diabetes. This section discusses many of the common comorbidities observed in patients with diabetes but is not necessarily inclusive of all the conditions that have been reported.

Autoimmune Diseases**Recommendations**

- 4.12** Patients with type 1 diabetes should be screened for autoimmune thyroid disease soon after diagnosis and periodically thereafter. **B**
- 4.13** Adult patients with type 1 diabetes should be screened for celiac disease in the presence of gastrointestinal symptoms, signs, or laboratory manifestations suggestive of celiac disease. **B**

People with type 1 diabetes are at increased risk for other autoimmune

diseases, with thyroid disease, celiac disease, and pernicious anemia (vitamin B12 deficiency) being among the most common (25). Other associated conditions include autoimmune hepatitis, primary adrenal insufficiency (Addison disease), dermatomyositis, and myasthenia gravis (26–29). Type 1 diabetes may also occur with other autoimmune diseases in the context of specific genetic disorders or polyglandular autoimmune syndromes (30). Given the high prevalence, nonspecific symptoms, and insidious onset of primary hypothyroidism, routine screening for thyroid dysfunction is recommended for all patients with type 1 diabetes. Screening for celiac disease should be considered in adult patients with suggestive symptoms (e.g., diarrhea, malabsorption, abdominal pain) or signs (e.g., osteoporosis, vitamin deficiencies, iron deficiency anemia) (31,32). Measurement of vitamin B12 levels should be considered for patients with type 1 diabetes and peripheral neuropathy or unexplained anemia.

Cancer

Diabetes is associated with increased risk of cancers of the liver, pancreas,

endometrium, colon/rectum, breast, and bladder (33). The association may result from shared risk factors between type 2 diabetes and cancer (older age, obesity, and physical inactivity) but may also be due to diabetes-related factors (34), such as underlying disease physiology or diabetes treatments, although evidence for these links is scarce. Patients with diabetes should be encouraged to undergo recommended age- and sex-appropriate cancer screenings and to reduce their modifiable cancer risk factors (obesity, physical inactivity, and smoking). New onset of atypical diabetes (lean body habitus, negative family history) in a middle-aged or older patient may precede the diagnosis of pancreatic adenocarcinoma (35). However, in the absence of other symptoms (e.g., weight loss, abdominal pain), routine screening of all such patients is not currently recommended.

Cognitive Impairment/Dementia**Recommendation**

- 4.14** In the presence of cognitive impairment, diabetes treatment regimens should be simplified as much as possible and tailored to minimize the risk of hypoglycemia. **B**

Diabetes is associated with a significantly increased risk and rate of cognitive decline and an increased risk of dementia (36,37). A recent meta-analysis of prospective observational studies in people with diabetes showed 73% increased risk of all types of dementia, 56% increased risk of Alzheimer dementia, and 127% increased risk of vascular dementia compared with individuals without diabetes (38). The reverse is also true: people with Alzheimer dementia are more likely to develop diabetes than people without Alzheimer dementia. In a 15-year prospective study of community-dwelling people >60 years of age, the presence of diabetes at baseline significantly increased the age- and sex-adjusted incidence of all-cause dementia, Alzheimer dementia, and vascular dementia compared with rates in those with normal glucose tolerance (39).

Hyperglycemia

In those with type 2 diabetes, the degree and duration of hyperglycemia are

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 100–104.

Table 4.4—Referrals for initial care management

- Eye care professional for annual dilated eye exam
- Family planning for women of reproductive age
- Registered dietitian nutritionist for medical nutrition therapy
- Diabetes self-management education and support
- Dentist for comprehensive dental and periodontal examination
- Mental health professional, if indicated

related to dementia. More rapid cognitive decline is associated with both increased A1C and longer duration of diabetes (38). The Action to Control Cardiovascular Risk in Diabetes (ACCORD) study found that each 1% higher A1C level was associated with lower cognitive function in individuals with type 2 diabetes (40). However, the ACCORD study found no difference in cognitive outcomes in participants randomly assigned to intensive and standard glycemic control, supporting the recommendation that intensive glucose control should not be advised for the improvement of cognitive function in individuals with type 2 diabetes (41).

Hypoglycemia

In type 2 diabetes, severe hypoglycemia is associated with reduced cognitive function, and those with poor cognitive function have more severe hypoglycemia. In a long-term study of older patients with type 2 diabetes, individuals with one or more recorded episodes of severe hypoglycemia had a stepwise increase in risk of dementia (42). Likewise, the ACCORD trial found that as cognitive function decreased, the risk of severe hypoglycemia increased (43). Tailoring glycemic therapy may help to prevent hypoglycemia in individuals with cognitive dysfunction.

Nutrition

In one study, adherence to the Mediterranean diet correlated with improved cognitive function (44). However, a recent Cochrane review found insufficient evidence to recommend any dietary change for the prevention or treatment of cognitive dysfunction (45).

Statins

A systematic review has reported that data do not support an adverse effect of statins on cognition (46). The U.S. Food and Drug Administration postmarketing surveillance databases have also revealed a

low reporting rate for cognitive-related adverse events, including cognitive dysfunction or dementia, with statin therapy, similar to rates seen with other commonly prescribed cardiovascular medications (46). Therefore, fear of cognitive decline should not be a barrier to statin use in individuals with diabetes and a high risk for cardiovascular disease.

Nonalcoholic Fatty Liver Disease

Recommendation

4.15 Patients with type 2 diabetes or prediabetes and elevated liver enzymes (ALT) or fatty liver on ultrasound should be evaluated for presence of nonalcoholic steatohepatitis and liver fibrosis. **C**

Diabetes is associated with the development of nonalcoholic fatty liver disease, including its more severe manifestations of nonalcoholic steatohepatitis, liver fibrosis, cirrhosis, and hepatocellular carcinoma (47). Elevations of hepatic transaminase concentrations are associated with higher BMI, waist circumference, and triglyceride levels and lower HDL cholesterol levels. Noninvasive tests, such as elastography or fibrosis biomarkers, may be used to assess risk of fibrosis, but referral to a liver specialist and liver biopsy may be required for definitive diagnosis (48). Interventions that improve metabolic abnormalities in patients with diabetes (weight loss, glycemic control, and treatment with specific drugs for hyperglycemia or dyslipidemia) are also beneficial for fatty liver disease (49,50). Pioglitazone and vitamin E treatment of biopsy-proven nonalcoholic steatohepatitis have been shown to improve liver histology, but effects on longer-term clinical outcomes are not known (51,52). Treatment with liraglutide and with sodium–glucose cotransporter 2 inhibitors (dapagliflozin and empagliflozin) has also shown some promise in preliminary studies, although benefits may be

mediated, at least in part, by weight loss (53–55).

Hepatitis C Infection

Infection with hepatitis C virus (HCV) is associated with a higher prevalence of type 2 diabetes, which is present in up to one-third of individuals with chronic HCV infection. HCV may impair glucose metabolism by several mechanisms, including directly via viral proteins and indirectly by altering proinflammatory cytokine levels (56). The use of newer direct-acting antiviral drugs produces a sustained virological response (cure) in nearly all cases and has been reported to improve glucose metabolism in individuals with diabetes (57). A meta-analysis of mostly observational studies found a mean reduction in A1C levels of 0.45% (95% CI –0.60 to –0.30) and reduced requirement for glucose-lowering medication use following successful eradication of HCV infection (58).

Pancreatitis

Recommendation

4.16 Islet autotransplantation should be considered for patients requiring total pancreatectomy for medically refractory chronic pancreatitis to prevent postsurgical diabetes. **C**

Diabetes is linked to diseases of the exocrine pancreas such as pancreatitis, which may disrupt the global architecture or physiology of the pancreas, often resulting in both exocrine and endocrine dysfunction. Up to half of patients with diabetes may have some degree of impaired exocrine pancreas function (59). People with diabetes are at an approximately twofold higher risk of developing acute pancreatitis (60).

Conversely, prediabetes and/or diabetes has been found to develop in approximately one-third of patients after an episode of acute pancreatitis (61); thus, the relationship is likely bidirectional. Postpancreatitis diabetes may include either new-onset disease or previously unrecognized diabetes (62). Studies of patients treated with incretin-based therapies for diabetes have also reported that pancreatitis may occur more frequently with these medications, but results have been mixed (63,64).

Islet autotransplantation should be considered for patients requiring total pancreatectomy for medically refractory chronic pancreatitis to prevent postsurgical diabetes. Approximately one-third of patients undergoing total pancreatectomy with islet autotransplantation are insulin free 1 year postoperatively, and observational studies from different centers have demonstrated islet graft function up to a decade after the surgery in some patients (65–69). Both patient and disease factors should be carefully considered when deciding the indications and timing of this surgery. Surgeries should be performed in skilled facilities that have demonstrated expertise in islet autotransplantation.

Fractures

Age-specific hip fracture risk is significantly increased in both people with type 1 diabetes (relative risk 6.3) and those with type 2 diabetes (relative risk 1.7) in both sexes (70). Type 1 diabetes is associated with osteoporosis, but in type 2 diabetes, an increased risk of hip fracture is seen despite higher bone mineral density (BMD) (71). In three large observational studies of older adults, femoral neck BMD T score and the World Health Organization Fracture Risk Assessment Tool (FRAX) score were associated with hip and nonspine fractures. Fracture risk was higher in participants with diabetes compared with those without diabetes for a given T score and age or for a given FRAX score (72). Providers should assess fracture history and risk factors in older patients with diabetes and recommend measurement of BMD if appropriate for the patient's age and sex. Fracture prevention strategies for people with diabetes are the same as for the general population and include vitamin D supplementation. For patients with type 2 diabetes with fracture risk factors, thiazolidinediones (73) and sodium–glucose cotransporter 2 inhibitors (74) should be used with caution.

Sensory Impairment

Hearing impairment, both in high-frequency and low- to mid-frequency ranges, is more common in people with diabetes than in those without, perhaps due to neuropathy and/or vascular disease. In a National Health and Nutrition Examination Survey (NHANES) analysis, hearing impairment was about

twice as prevalent in people with diabetes compared with those without, after adjusting for age and other risk factors for hearing impairment (75). Low HDL, coronary heart disease, peripheral neuropathy, and general poor health have been reported as risk factors for hearing impairment for people with diabetes, but an association of hearing loss with blood glucose levels has not been consistently observed (76). In the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) cohort, time-weighted mean A1C was associated with increased risk of hearing impairment when tested after long-term (>20 years) follow-up (77). Impairment in smell, but not taste, has also been reported in individuals with diabetes (78).

HIV

Recommendation

4.17 Patients with HIV should be screened for diabetes and prediabetes with a fasting glucose test before starting antiretroviral therapy, at the time of switching antiretroviral therapy, and 3–6 months after starting or switching antiretroviral therapy. If initial screening results are normal, fasting glucose should be checked annually. **E**

Diabetes risk is increased with certain protease inhibitors (PIs) and nucleoside reverse transcriptase inhibitors (NRTIs). New-onset diabetes is estimated to occur in more than 5% of patients infected with HIV on PIs, whereas more than 15% may have prediabetes (79). PIs are associated with insulin resistance and may also lead to apoptosis of pancreatic β -cells. NRTIs also affect fat distribution (both lipohypertrophy and lipoatrophy), which is associated with insulin resistance.

Individuals with HIV are at higher risk for developing prediabetes and diabetes on antiretroviral (ARV) therapies, so a screening protocol is recommended (80). The A1C test may underestimate glycemia in people with HIV; it is not recommended for diagnosis and may present challenges for monitoring (81). In those with prediabetes, weight loss through healthy nutrition and physical activity may reduce the progression toward

diabetes. Among patients with HIV and diabetes, preventive health care using an approach similar to that used in patients without HIV is critical to reduce the risks of microvascular and macrovascular complications.

For patients with HIV and ARV-associated hyperglycemia, it may be appropriate to consider discontinuing the problematic ARV agents if safe and effective alternatives are available (82). Before making ARV substitutions, carefully consider the possible effect on HIV virological control and the potential adverse effects of new ARV agents. In some cases, antihyperglycemic agents may still be necessary.

Low Testosterone in Men

Recommendation

4.18 In men with diabetes who have symptoms or signs of hypogonadism, such as decreased sexual desire (libido) or activity, or erectile dysfunction, consider screening with a morning serum testosterone level. **B**

Mean levels of testosterone are lower in men with diabetes compared with age-matched men without diabetes, but obesity is a major confounder (83,84). Treatment in asymptomatic men is controversial. Testosterone replacement in men with symptomatic hypogonadism may have benefits including improved sexual function, well-being, muscle mass and strength, and bone density (85). In men with diabetes who have symptoms or signs of low testosterone (hypogonadism), a morning total testosterone level should be measured using an accurate and reliable assay. In men who have total testosterone levels close to the lower limit, it is reasonable to check sex hormone-binding globulin, as it is often low in diabetes and associated with lower testosterone levels. Further testing (such as luteinizing hormone and follicle-stimulating hormone levels) may be needed to determine if the patient has hypogonadism. Testosterone replacement in older men with hypogonadism has been associated with increased coronary artery plaque volume and, in some studies, an increase in cardiovascular events, which should be considered when assessing the risks and benefits of treatment (86,87).

Obstructive Sleep Apnea

Age-adjusted rates of obstructive sleep apnea, a risk factor for cardiovascular disease, are significantly higher (4- to 10-fold) with obesity, especially with central obesity (88). The prevalence of obstructive sleep apnea in the population with type 2 diabetes may be as high as 23%, and the prevalence of any sleep-disordered breathing may be as high as 58% (89,90). In obese participants enrolled in the Action for Health in Diabetes (Look AHEAD) trial, it exceeded 80% (91). Patients with symptoms suggestive of obstructive sleep apnea (e.g., excessive daytime sleepiness, snoring, witnessed apnea) should be considered for screening (92). Sleep apnea treatment (lifestyle modification, continuous positive airway pressure, oral appliances, and surgery) significantly improves quality of life and blood pressure control. The evidence for a treatment effect on glycemic control is mixed (93).

Periodontal Disease

Periodontal disease is more severe, and may be more prevalent, in patients with diabetes than in those without and has been associated with higher A1C levels (94–96). Longitudinal studies suggest that people with periodontal disease have higher rates of incident diabetes. Current evidence suggests that periodontal disease adversely affects diabetes outcomes, although evidence for treatment benefits remains controversial (24,97). In a randomized clinical trial, intensive periodontal treatment was associated with better glycemic control (A1C 8.3% vs. 7.8% in control subjects and the intensive-treatment group, respectively) and reduction in inflammatory markers after 12 months of follow-up (98).

References

1. Stelfox M, Dipnarine K, Stopka C. The chronic care model and diabetes management in US primary care settings: a systematic review. *Prev Chronic Dis* 2013;10:E26
2. Coleman K, Austin BT, Brach C, Wagner EH. Evidence on the Chronic Care Model in the new millennium. *Health Aff (Millwood)* 2009;28:75–85
3. Gabbay RA, Bailit MH, Mauger DT, Wagner EH, Siminerio L. Multipayer patient-centered medical home implementation guided by the chronic care model. *Jt Comm J Qual Patient Saf* 2011;37:265–273
4. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998;352:837–853
5. Nathan DM, Genuth S, Lachin J, et al.; Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;329:977–986
6. Lachin JM, Genuth S, Nathan DM, Zinman B, Rutledge BN; DCCT/EDIC Research Group. Effect of glycemic exposure on the risk of microvascular complications in the Diabetes Control and Complications Trial—revisited. *Diabetes* 2008;57:995–1001
7. White NH, Cleary PA, Dahms W, Goldstein D, Malone J, Tamborlane WV; Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC) Research Group. Beneficial effects of intensive therapy of diabetes during adolescence: outcomes after the conclusion of the Diabetes Control and Complications Trial (DCCT). *J Pediatr* 2001;139:804–812
8. Anderson RM, Funnell MM. Compliance and adherence are dysfunctional concepts in diabetes care. *Diabetes Educ* 2000;26:597–604
9. Sarkar U, Fisher L, Schillinger D. Is self-efficacy associated with diabetes self-management across race/ethnicity and health literacy? *Diabetes Care* 2006;29:823–829
10. King DK, Glasgow RE, Toobert DJ, et al. Self-efficacy, problem solving, and social-environmental support are associated with diabetes self-management behaviors. *Diabetes Care* 2010;33:751–753
11. Nouwen A, Urquhart Law G, Hussain S, McGovern S, Napier H. Comparison of the role of self-efficacy and illness representations in relation to dietary self-care and diabetes distress in adolescents with type 1 diabetes. *Psychol Health* 2009;24:1071–1084
12. Beckerle CM, Lavin MA. Association of self-efficacy and self-care with glycemic control in diabetes. *Diabetes Spectr* 2013;26:172–178
13. Iannotti RJ, Schneider S, Nansel TR, et al. Self-efficacy, outcome expectations, and diabetes self-management in adolescents with type 1 diabetes. *J Dev Behav Pediatr* 2006;27:98–105
14. Dickinson JK, Guzman SJ, Maryniuk MD, et al. The use of language in diabetes care and education. *Diabetes Care* 2017;40:1790–1799
15. Lee SWH, Ng KY, Chin WK. The impact of sleep amount and sleep quality on glycemic control in type 2 diabetes: a systematic review and meta-analysis. *Sleep Med Rev* 2017;31:91–101
16. Robinson CL, Romero JR, Kempe A, Pellegrini C; Advisory Committee on Immunization Practices (ACIP) Child/Adolescent Immunization Work Group. Advisory Committee on Immunization Practices recommended immunization schedule for children and adolescents aged 18 years or younger – United States, 2017. *MMWR Morb Mortal Wkly Rep* 2017;66:134–135
17. Kim DK, Riley LE, Harriman KH, Hunter P, Bridges CB. Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older – United States, 2017. *MMWR Morb Mortal Wkly Rep* 2017;66:136–138
18. Goeijenbier M, van Sloten TT, Slobbe L, et al. Benefits of flu vaccination for persons with diabetes mellitus: a review. *Vaccine* 2017;35:5095–5101
19. Smith SA, Poland GA. Use of influenza and pneumococcal vaccines in people with diabetes. *Diabetes Care* 2000;23:95–108
20. Selvin E, Coresh J, Brancati FL. The burden and treatment of diabetes in elderly individuals in the U.S. *Diabetes Care* 2006;29:2415–2419
21. Grant RW, Ashburner JM, Hong CS, Chang Y, Barry MJ, Atlas SJ. Defining patient complexity from the primary care physician's perspective: a cohort study [published correction appears in *Ann Intern Med* 2012;157:152]. *Ann Intern Med* 2011;155:797–804
22. Tinetti ME, Fried TR, Boyd CM. Designing health care for the most common chronic condition—multimorbidity. *JAMA* 2012;307:2493–2494
23. Sudore RL, Karter AJ, Huang ES, et al. Symptom burden of adults with type 2 diabetes across the disease course: diabetes & aging study. *J Gen Intern Med* 2012;27:1674–1681
24. Borgnakke WS, Ylöstalo PV, Taylor GW, Genco RJ. Effect of periodontal disease on diabetes: systematic review of epidemiologic observational evidence. *J Periodontol* 2013;84(Suppl.):S135–S152
25. Nederstigt C, Uitbeijerse BS, Janssen LGM, Corssmit EPM, de Koning EJP, Dekkers OM. Associated auto-immune disease in type 1 diabetes patients: a systematic review and meta-analysis. *Eur J Endocrinol* 2019;180:135–144
26. De Block CE, De Leeuw IH, Van Gaal LF. High prevalence of manifestations of gastric autoimmunity in parietal cell antibody-positive type 1 (insulin-dependent) diabetic patients. The Belgian Diabetes Registry. *J Clin Endocrinol Metab* 1999;84:4062–4067
27. Triolo TM, Armstrong TK, McFann K, et al. Additional autoimmune disease found in 33% of patients at type 1 diabetes onset. *Diabetes Care* 2011;34:1211–1213
28. Hughes JW, Riddlesworth TD, DiMeglio LA, Miller KM, Rickels MR, McGill JB; T1D Exchange Clinic Network. Autoimmune diseases in children and adults with type 1 diabetes from the T1D Exchange Clinic Registry. *J Clin Endocrinol Metab* 2016;101:4931–4937
29. Kahaly GJ, Hansen MP. Type 1 diabetes associated autoimmunity. *Autoimmun Rev* 2016;15:644–648
30. Eisenbarth GS, Gottlieb PA. Autoimmune polyendocrine syndromes. *N Engl J Med* 2004;350:2068–2079
31. Rubio-Tapia A, Hill ID, Kelly CP, Calderwood AH, Murray JA; American College of Gastroenterology. ACG clinical guidelines: diagnosis and management of celiac disease. *Am J Gastroenterol* 2013;108:656–676; quiz 677
32. Husby S, Murray JA, Katzka DA. AGA clinical practice update on diagnosis and monitoring of celiac disease—changing utility of serology and histologic measures: expert review. *Gastroenterology* 2019;156:885–889
33. Suh S, Kim K-W. Diabetes and cancer: is diabetes causally related to cancer? *Diabetes Metab J* 2011;35:193–198
34. Giovannucci E, Harlan DM, Archer MC, et al. Diabetes and cancer: a consensus report. *CA Cancer J Clin* 2010;60:207–221

35. Aggarwal G, Kamada P, Chari ST. Prevalence of diabetes mellitus in pancreatic cancer compared to common cancers. *Pancreas* 2013;42:198–201
36. Cukierman T, Gerstein HC, Williamson JD. Cognitive decline and dementia in diabetes—systematic overview of prospective observational studies. *Diabetologia* 2005;48:2460–2469
37. Biessels GJ, Staekenborg S, Brunner E, Brayne C, Scheltens P. Risk of dementia in diabetes mellitus: a systematic review. *Lancet Neurol* 2006;5:64–74
38. Gudala K, Bansal D, Schifano F, Bhansali A. Diabetes mellitus and risk of dementia: a meta-analysis of prospective observational studies. *J Diabetes Investig* 2013;4:640–650
39. Ohara T, Doi Y, Ninomiya T, et al. Glucose tolerance status and risk of dementia in the community: the Hisayama study. *Neurology* 2011;77:1126–1134
40. Cukierman-Yaffe T, Gerstein HC, Williamson JD, et al.; Action to Control Cardiovascular Risk in Diabetes-Memory in Diabetes (ACCORD-MIND) Investigators. Relationship between baseline glycemic control and cognitive function in individuals with type 2 diabetes and other cardiovascular risk factors: the Action to Control Cardiovascular Risk in Diabetes-Memory in Diabetes (ACCORD-MIND) trial. *Diabetes Care* 2009;32:221–226
41. Launer LJ, Miller ME, Williamson JD, et al.; ACCORD MIND investigators. Effects of intensive glucose lowering on brain structure and function in people with type 2 diabetes (ACCORD MIND): a randomised open-label substudy. *Lancet Neurol* 2011;10:969–977
42. Whitmer RA, Karter AJ, Yaffe K, Quesenberry CP Jr, Selby JV. Hypoglycemic episodes and risk of dementia in older patients with type 2 diabetes mellitus. *JAMA* 2009;301:1565–1572
43. Punthakee Z, Miller ME, Launer LJ, et al.; ACCORD Group of Investigators; ACCORD-MIND Investigators. Poor cognitive function and risk of severe hypoglycemia in type 2 diabetes: post hoc epidemiologic analysis of the ACCORD trial. *Diabetes Care* 2012;35:787–793
44. Scarmeas N, Stern Y, Mayeux R, Manly JJ, Schupf N, Luchsinger JA. Mediterranean diet and mild cognitive impairment. *Arch Neurol* 2009;66:216–225
45. Ooi CP, Loke SC, Yassin Z, Hamid T-A. Carbohydrates for improving the cognitive performance of independent-living older adults with normal cognition or mild cognitive impairment. *Cochrane Database Syst Rev* 2011;4:CD007220
46. Richardson K, Schoen M, French B, et al. Statins and cognitive function: a systematic review. *Ann Intern Med* 2013;159:688–697
47. El-Serag HB, Tran T, Everhart JE. Diabetes increases the risk of chronic liver disease and hepatocellular carcinoma. *Gastroenterology* 2004;126:460–468
48. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. *Hepatology* 2018;67:328–357
49. American Gastroenterological Association. American Gastroenterological Association medical position statement: nonalcoholic fatty liver disease. *Gastroenterology* 2002;123:1702–1704
50. Cusi K, Orsak B, Bril F, et al. Long-term pioglitazone treatment for patients with nonalcoholic steatohepatitis and prediabetes or type 2 diabetes mellitus: a randomized trial. *Ann Intern Med* 2016;165:305–315
51. Belfort R, Harrison SA, Brown K, et al. A placebo-controlled trial of pioglitazone in subjects with nonalcoholic steatohepatitis. *N Engl J Med* 2006;355:2297–2307
52. Sanyal AJ, Chalasani N, Kowdley KV, et al.; NASH CRN. Pioglitazone, vitamin E, or placebo for nonalcoholic steatohepatitis. *N Engl J Med* 2010;362:1675–1685
53. Armstrong MJ, Gaunt P, Aithal GP, et al.; LEAN trial team. Liraglutide safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): a multicentre, double-blind, randomised, placebo-controlled phase 2 study. *Lancet* 2016;387:679–690
54. Shimizu M, Suzuki K, Kato K, et al. Evaluation of the effects of dapagliflozin, a sodium-glucose co-transporter-2 inhibitor, on hepatic steatosis and fibrosis using transient elastography in patients with type 2 diabetes and non-alcoholic fatty liver disease. *Diabetes Obes Metab* 2019;21:285–292
55. Sattar N, Fitchett D, Hantel S, George JT, Zinman B. Empagliflozin is associated with improvements in liver enzymes potentially consistent with reductions in liver fat: results from randomised trials including the EMPA-REG OUTCOME® trial. *Diabetologia* 2018;61:2155–2163
56. Lecube A, Hernández C, Genescà J, Simó R. Proinflammatory cytokines, insulin resistance, and insulin secretion in chronic hepatitis C patients: a case-control study. *Diabetes Care* 2006;29:1096–1101
57. Hum J, Jou JH, Green PK, et al. Improvement in glycemic control of type 2 diabetes after successful treatment of hepatitis C virus. *Diabetes Care* 2017;40:1173–1180
58. Carnovale C, Pozzi M, Dassano A, et al. The impact of a successful treatment of hepatitis C virus on glyco-metabolic control in diabetic patients: a systematic review and meta-analysis. *Acta Diabetol* 2019;56:341–354
59. Piciocchi M, Capurso G, Archibugi L, Delle Fave MM, Capasso M, Delle Fave G. Exocrine pancreatic insufficiency in diabetic patients: prevalence, mechanisms, and treatment. *Int J Endocrinol* 2015;2015:595649
60. Lee Y-K, Huang M-Y, Hsu C-Y, Su Y-C. Bidirectional relationship between diabetes and acute pancreatitis: a population-based cohort study in Taiwan. *Medicine (Baltimore)* 2016;95:e2448
61. Das SLM, Singh PP, Phillips ARJ, Murphy R, Windsor JA, Petrov MS. Newly diagnosed diabetes mellitus after acute pancreatitis: a systematic review and meta-analysis. *Gut* 2014;63:818–831
62. Petrov MS. Diabetes of the exocrine pancreas: American Diabetes Association-compliant lexicon. *Pancreatol* 2017;17:523–526
63. Thomsen RW, Pedersen L, Møller N, Kahlert J, Beck-Nielsen H, Sørensen HT. Incretin-based therapy and risk of acute pancreatitis: a nationwide population-based case-control study. *Diabetes Care* 2015;38:1089–1098
64. Tkáč I, Raz I. Combined analysis of three large interventional trials with gliptins indicates increased incidence of acute pancreatitis in patients with type 2 diabetes. *Diabetes Care* 2017;40:284–286
65. Bellin MD, Gelrud A, Arreaza-Rubin G, et al. Total pancreatectomy with islet autotransplantation: summary of an NIDDK workshop. *Ann Surg* 2015;261:21–29
66. Sutherland DER, Radosevic DM, Bellin MD, et al. Total pancreatectomy and islet autotransplantation for chronic pancreatitis. *J Am Coll Surg* 2012;214:409–424; discussion 424–426
67. Quartuccio M, Hall E, Singh V, et al. Glycemic predictors of insulin independence after total pancreatectomy with islet autotransplantation. *J Clin Endocrinol Metab* 2017;102:801–809
68. Webb MA, Illouz SC, Pollard CA, et al. Islet auto transplantation following total pancreatectomy: a long-term assessment of graft function. *Pancreas* 2008;37:282–287
69. Wu Q, Zhang M, Qin Y, et al. Systematic review and meta-analysis of islet autotransplantation after total pancreatectomy in chronic pancreatitis patients. *Endocr J* 2015;62:227–234
70. Janghorbani M, Van Dam RM, Willett WC, Hu FB. Systematic review of type 1 and type 2 diabetes mellitus and risk of fracture. *Am J Epidemiol* 2007;166:495–505
71. Vestergaard P. Discrepancies in bone mineral density and fracture risk in patients with type 1 and type 2 diabetes—a meta-analysis. *Osteoporos Int* 2007;18:427–444
72. Schwartz AV, Vittinghoff E, Bauer DC, et al.; Study of Osteoporotic Fractures (SOF) Research Group; Osteoporotic Fractures in Men (MrOS) Research Group; Health, Aging, and Body Composition (Health ABC) Research Group. Association of BMD and FRAX score with risk of fracture in older adults with type 2 diabetes. *JAMA* 2011;305:2184–2192
73. Kahn SE, Zinman B, Lachin JM, et al.; Diabetes Outcome Progression Trial (ADOPT) Study Group. Rosiglitazone-associated fractures in type 2 diabetes: an analysis from A Diabetes Outcome Progression Trial (ADOPT). *Diabetes Care* 2008;31:845–851
74. Taylor SI, Blau JE, Rother KI. Possible adverse effects of SGLT2 inhibitors on bone. *Lancet Diabetes Endocrinol* 2015;3:8–10
75. Bainbridge KE, Hoffman HJ, Cowie CC. Diabetes and hearing impairment in the United States: audiometric evidence from the National Health and Nutrition Examination Survey, 1999 to 2004. *Ann Intern Med* 2008;149:1–10
76. Bainbridge KE, Hoffman HJ, Cowie CC. Risk factors for hearing impairment among U.S. adults with diabetes: National Health and Nutrition Examination Survey 1999–2004. *Diabetes Care* 2011;34:1540–1545
77. Schade DS, Lorenzi GM, Braffett BH, et al.; DCCT/EDIC Research Group. Hearing impairment and type 1 diabetes in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) cohort. *Diabetes Care* 2018;41:2495–2501
78. Rasmussen VF, Vestergaard ET, Hejlesen O, Andersson CUN, Cichosz SL. Prevalence of taste and smell impairment in adults with diabetes: a cross-sectional analysis of data from the National Health and Nutrition Examination Survey (NHANES). *Prim Care Diabetes* 2018;12:453–459
79. Monroe AK, Glesby MJ, Brown TT. Diagnosing and managing diabetes in HIV-infected patients: current concepts. *Clin Infect Dis* 2015;60:453–462
80. Schambelan M, Benson CA, Carr A, et al.; International AIDS Society-USA. Management of metabolic complications associated with

- antiretroviral therapy for HIV-1 infection: recommendations of an International AIDS Society-USA panel. *J Acquir Immune Defic Syndr* 2002;31:257–275
81. Kim PS, Woods C, Georgoff P, et al. A1C underestimates glycemia in HIV infection. *Diabetes Care* 2009;32:1591–1593
82. Wohl DA, McComsey G, Tebas P, et al. Current concepts in the diagnosis and management of metabolic complications of HIV infection and its therapy. *Clin Infect Dis* 2006;43:645–653
83. Dhindsa S, Miller MG, McWhirter CL, et al. Testosterone concentrations in diabetic and non-diabetic obese men. *Diabetes Care* 2010;33:1186–1192
84. Grossmann M. Low testosterone in men with type 2 diabetes: significance and treatment. *J Clin Endocrinol Metab* 2011;96:2341–2353
85. Bhasin S, Cunningham GR, Hayes FJ, et al.; Task Force, Endocrine Society. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2010;95:2536–2559
86. Budoff MJ, Ellenberg SS, Lewis CE, et al. Testosterone treatment and coronary artery plaque volume in older men with low testosterone. *JAMA* 2017;317:708–716
87. Kloner RA, Carson C III, Dobs A, Kopecky S, Mohler ER III. Testosterone and cardiovascular disease. *J Am Coll Cardiol* 2016;67:545–557
88. Li C, Ford ES, Zhao G, Croft JB, Balluz LS, Mokdad AH. Prevalence of self-reported clinically diagnosed sleep apnea according to obesity status in men and women: National Health and Nutrition Examination Survey, 2005–2006. *Prev Med* 2010;51:18–23
89. West SD, Nicoll DJ, Stradling JR. Prevalence of obstructive sleep apnoea in men with type 2 diabetes. *Thorax* 2006;61:945–950
90. Resnick HE, Redline S, Shahar E, et al.; Sleep Heart Health Study. Diabetes and sleep disturbances: findings from the Sleep Heart Health Study. *Diabetes Care* 2003;26:702–709
91. Foster GD, Sanders MH, Millman R, et al.; Sleep AHEAD Research Group. Obstructive sleep apnea among obese patients with type 2 diabetes. *Diabetes Care* 2009;32:1017–1019
92. Bibbins-Domingo K, Grossman DC, Curry SJ, et al.; US Preventive Services Task Force. Screening for obstructive sleep apnea in adults: US Preventive Services Task Force recommendation statement. *JAMA* 2017;317:407–414
93. Shaw JE, Punjabi NM, Wilding JP, Alberti KGMM, Zimmet PZ; International Diabetes Federation Taskforce on Epidemiology and Prevention. Sleep-disordered breathing and type 2 diabetes: a report from the International Diabetes Federation Taskforce on Epidemiology and Prevention. *Diabetes Res Clin Pract* 2008;81:2–12
94. Khader YS, Dauod AS, El-Qaderi SS, Alkafajei A, Batayha WQ. Periodontal status of diabetics compared with nondiabetics: a meta-analysis. *J Diabetes Complications* 2006;20:59–68
95. Casanova L, Hughes FJ, Preshaw PM. Diabetes and periodontal disease: a two-way relationship. *Br Dent J* 2014;217:433–437
96. Eke PI, Thornton-Evans GO, Wei L, Borgnakke WS, Dye BA, Genco RJ. Periodontitis in US adults: National Health and Nutrition Examination Survey 2009–2014. *J Am Dent Assoc* 2018;149:576–588.e6
97. Simpson TC, Weldon JC, Worthington HV, et al. Treatment of periodontal disease for glycaemic control in people with diabetes mellitus. *Cochrane Database Syst Rev* 2015 11: CD004714
98. D'Aiuto F, Gkranias N, Bhowruth D, et al.; TASTE Group. Systemic effects of periodontitis treatment in patients with type 2 diabetes: a 12 month, single-centre, investigator-masked, randomised trial. *Lancet Diabetes Endocrinol* 2018;6:954–965
99. Davies MJ, D'Alessio DA, Fradkin J, et al. Management of hyperglycemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care* 2018;41:2669–2701
100. Lipska KJ, Ross JS, Wang Y, et al. National trends in US hospital admissions for hyperglycemia and hypoglycemia among Medicare beneficiaries, 1999 to 2011. *JAMA Intern Med* 2014;174:1116–1124
101. Shorr RI, Ray WA, Daugherty JR, Griffin MR. Incidence and risk factors for serious hypoglycemia in older persons using insulin or sulfonylureas. *Arch Intern Med* 1997;157:1681–1686
102. Abdelhafiz AH, Rodríguez-Mañas L, Morley JE, Sinclair AJ. Hypoglycemia in older people - a less well recognized risk factor for frailty. *Aging Dis* 2015;6:156–167
103. Yun J-S, Ko S-H, Ko S-H, et al. Presence of macroalbuminuria predicts severe hypoglycemia in patients with type 2 diabetes: a 10-year follow-up study. *Diabetes Care* 2013;36:1283–1289
104. Chelliah A, Burge MR. Hypoglycaemia in elderly patients with diabetes mellitus: causes and strategies for prevention. *Drugs Aging* 2004;21:511–530