



2. Classification and Diagnosis of Diabetes: *Standards of Medical Care in Diabetes—2022*

American Diabetes Association
Professional Practice Committee*

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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/dc22-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/dc22-SINT>). Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

CLASSIFICATION

Diabetes can be classified into the following general categories:

1. Type 1 diabetes (due to autoimmune β -cell destruction, usually leading to absolute insulin deficiency, including latent autoimmune diabetes of adulthood)
2. Type 2 diabetes (due to a progressive loss of adequate β -cell insulin secretion frequently on the background of insulin resistance)
3. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation)
4. Gestational diabetes mellitus (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation)

This section reviews most common forms of diabetes but is not comprehensive. For additional information, see the American Diabetes Association (ADA) position statement “Diagnosis and Classification of Diabetes Mellitus” (1).

Type 1 diabetes and type 2 diabetes are heterogeneous diseases in which clinical presentation and disease progression may vary considerably. Classification is important for determining therapy, but some individuals cannot be clearly classified as having type 1 or type 2 diabetes at the time of diagnosis. The traditional paradigms of type 2 diabetes occurring only in adults and type 1 diabetes only in children are no longer accurate, as both diseases occur in both age-groups. Children with type 1 diabetes often present with the hallmark symptoms of polyuria/polydipsia, and

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approximately half present with diabetic ketoacidosis (DKA) (2–4). The onset of type 1 diabetes may be more variable in adults; they may not present with the classic symptoms seen in children and may experience temporary remission from the need for insulin (5–7). The features most useful in discrimination of type 1 diabetes include younger age at diagnosis (<35 years) with lower BMI (<25 kg/m²), unintentional weight loss, ketoacidosis, and glucose >360 mg/dL (20 mmol/L) at presentation (8). Occasionally, patients with type 2 diabetes may present with DKA (9,10), particularly ethnic and racial minorities (11). It is important for the provider to realize that classification of diabetes type is not always straightforward at presentation and that misdiagnosis is common (e.g., adults with type 1 diabetes misdiagnosed as having type 2 diabetes; individuals with maturity-onset diabetes of the young [MODY] misdiagnosed as having type 1 diabetes, etc.). Although difficulties in distinguishing diabetes type may occur in all age-groups at onset, the diagnosis becomes more obvious over time in people with β -cell deficiency.

In both type 1 and type 2 diabetes, various genetic and environmental factors can result in the progressive loss of β -cell mass and/or function that manifests clinically as hyperglycemia. Once hyperglycemia occurs, people with all forms of diabetes are at risk for developing the same chronic complications, although rates of progression may differ. The identification of individualized therapies for diabetes in the future will be informed by better characterization of the many paths to β -cell demise or dysfunction (12). Across the globe many groups are working on combining

clinical, pathophysiological, and genetic characteristics to more precisely define the subsets of diabetes that are currently clustered into the type 1 diabetes versus type 2 diabetes nomenclature with the goal of optimizing personalized treatment approaches. Many of these studies show great promise and may soon be incorporated into the diabetes classification system (13).

Characterization of the underlying pathophysiology is more precisely developed in type 1 diabetes than in type 2 diabetes. It is now clear from prospective studies that the persistent presence of two or more islet autoantibodies is a near certain predictor of clinical diabetes (14). The rate of progression is dependent on the age at first detection of autoantibody, number of autoantibodies, autoantibody specificity, and autoantibody titer. Glucose and A1C levels rise well before the clinical onset of diabetes, making diagnosis feasible well before the onset of DKA. Three distinct stages of type 1 diabetes can be identified (Table 2.1) and serve as a framework for future research and regulatory decision-making (12,15). There is debate as to whether slowly progressive autoimmune diabetes with an adult onset should be termed latent autoimmune diabetes in adults (LADA) or type 1 diabetes. The clinical priority with detection of LADA is awareness that slow autoimmune β -cell destruction can occur in adults leading to a long duration of marginal insulin secretory capacity. For the purpose of this classification, all forms of diabetes mediated by autoimmune β -cell destruction are included under the rubric of type 1 diabetes. Use of the term LADA is common and acceptable in clinical practice and has the practical impact of heightening awareness of a population of adults

likely to have progressive autoimmune β -cell destruction (16), thus accelerating insulin initiation prior to deterioration of glucose control or development of DKA (6,17).

The paths to β -cell demise and dysfunction are less well defined in type 2 diabetes, but deficient β -cell insulin secretion, frequently in the setting of insulin resistance, appears to be the common denominator. Type 2 diabetes is associated with insulin secretory defects related to genetics, inflammation, and metabolic stress. Future classification schemes for diabetes will likely focus on the pathophysiology of the underlying β -cell dysfunction (12,13,18–20).

DIAGNOSTIC TESTS FOR DIABETES

Diabetes may be diagnosed based on plasma glucose criteria, either the fasting plasma glucose (FPG) value or the 2-h plasma glucose (2-h PG) value during a 75-g oral glucose tolerance test (OGTT), or A1C criteria (21) (Table 2.2).

Generally, FPG, 2-h PG during 75-g OGTT, and A1C are equally appropriate for diagnostic screening. It should be noted that the screening tests do not necessarily detect diabetes in the same individuals. The efficacy of interventions for primary prevention of type 2 diabetes (22,23) has mainly been demonstrated among individuals who have impaired glucose tolerance (IGT) with or without elevated fasting glucose, not for individuals with isolated impaired fasting glucose (IFG) or for those with prediabetes defined by A1C criteria.

The same tests may be used to screen for and diagnose diabetes and to detect individuals with prediabetes (Table 2.2 and Table 2.5) (24). Diabetes may be identified anywhere along the spectrum of clinical scenarios—in

Table 2.1—Staging of type 1 diabetes (12,15)

	Stage 1	Stage 2	Stage 3
Characteristics	<ul style="list-style-type: none">• Autoimmunity• Normoglycemia• Presymptomatic	<ul style="list-style-type: none">• Autoimmunity• Dysglycemia• Presymptomatic	<ul style="list-style-type: none">• Autoimmunity• Overt hyperglycemia• Symptomatic
Diagnostic criteria	<ul style="list-style-type: none">• Multiple islet autoantibodies• No IGT or IFG	<ul style="list-style-type: none">• Islet autoantibodies (usually multiple)• Dysglycemia: IFG and/or IGT• FPG 100–125 mg/dL (5.6–6.9 mmol/L)• 2-h PG 140–199 mg/dL (7.8–11.0 mmol/L)• A1C 5.7–6.4% (39–47 mmol/mol) or \geq10% increase in A1C	<ul style="list-style-type: none">• Autoantibodies may become absent• Diabetes by standard criteria

FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; 2-h PG, 2-h plasma glucose.

Table 2.2—Criteria for the diagnosis of diabetesFPG ≥ 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

2-h PG ≥ 200 mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

OR

A1C $\geq 6.5\%$ (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L).

DCCT, Diabetes Control and Complications Trial; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; WHO, World Health Organization; 2-h PG, 2-h plasma glucose. *In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in two separate test samples.

seemingly low-risk individuals who happen to have glucose testing, in individuals screened based on diabetes risk assessment, and in symptomatic patients. For additional details on the evidence used to establish the criteria for the diagnosis of diabetes, prediabetes and abnormal glucose tolerance (OFG, IGT), see the ADA position statement “Diagnosis and Classification of Diabetes Mellitus” (1) and other reports (21,25,26).

Fasting and 2-Hour Plasma Glucose

The FPG and 2-h PG may be used to diagnose diabetes (Table 2.2). The concordance between the FPG and 2-h PG tests is imperfect, as is the concordance between A1C and either glucose-based test. Compared with FPG and A1C cut points, the 2-h PG value diagnoses more people with prediabetes and diabetes (27). In people in whom there is discordance between A1C values and glucose values, FPG and 2-h PG are more accurate (28).

A1C

Recommendations

- 2.1** To avoid misdiagnosis or missed diagnosis, the A1C test should be performed using a method that is certified by the NGSP and standardized to the Diabetes Control and Complications Trial (DCCT) assay. **B**
- 2.2** Marked discordance between measured A1C and plasma glucose levels should raise

the possibility of A1C assay interference and consideration of using an assay without interference or plasma blood glucose criteria to diagnose diabetes. **B**

- 2.3** In conditions associated with an altered relationship between A1C and glycemia, such as hemoglobinopathies including sickle cell disease, pregnancy (second and third trimesters and the postpartum period), glucose-6-phosphate dehydrogenase deficiency, HIV, hemodialysis, recent blood loss or transfusion, or erythropoietin therapy, only plasma blood glucose criteria should be used to diagnose diabetes. (See OTHER CONDITIONS ALTERING THE RELATIONSHIP OF A1C AND GLYCEMIA below for more information.) **B**
- 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 A1C test should be performed using a method that is certified by the NGSP (www.ngsp.org) and standardized or traceable to the Diabetes Control and Complications Trial (DCCT) reference assay. 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 CLIA-waived 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. In the U.S., point-of-care A1C is a laboratory test that limits CLIA regulation. As discussed in Section 6, “Glycemic Targets” (<https://doi.org/10.2337/dc22-S006>), point-of-care A1C assays may be more generally applied for assessment of glycemic control in the clinic.

A1C has several advantages compared with FPG and OGTT, including greater convenience (fasting not required), greater preanalytical stability, and less day-to-day perturbations during stress, changes in diet, or illness. However, these advantages may be offset by the lower sensitivity of A1C at the designated cut point, greater cost, limited availability of A1C testing in certain regions of the developing world, and the imperfect correlation between A1C and average glucose in certain individuals. The A1C test, with a diagnostic threshold of $\geq 6.5\%$ (48 mmol/mol), diagnoses only 30% of the diabetes cases identified collectively using A1C, FPG, or 2-h PG, according to National Health and Nutrition Examination Survey (NHANES) data (29). Despite these limitations with A1C, in 2009 the International Expert Committee added A1C to the diagnostic criteria with the goal of increased screening (21).

When using A1C to diagnose diabetes, it is important to recognize that A1C is an indirect measure of average blood glucose levels and to take other factors into consideration that may impact hemoglobin glycation independently of glycemia, such as hemodialysis, pregnancy, HIV treatment (30,31), age, race/ethnicity, genetic background, and anemia/hemoglobinopathies. (See OTHER CONDITIONS ALTERING THE RELATIONSHIP OF A1C AND GLYCEMIA below for more information.)

Age

The epidemiologic studies that formed the basis for recommending A1C to diagnose diabetes included only adult populations (29). 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 (see SCREENING AND TESTING FOR PREDIABETES AND TYPE 2 DIABETES IN CHILDREN AND ADOLESCENTS below for additional information) (32).

Race/Ethnicity/Hemoglobinopathies

Hemoglobin variants can interfere with the measurement of A1C, although most assays in use in the U.S. are unaffected by the most common variants. Marked 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.

African Americans heterozygous for the common hemoglobin variant HbS may have, for any given level of mean glycemia, lower A1C by about 0.3% compared with those without the trait (33). Another genetic variant, X-linked glucose-6-phosphate dehydrogenase G202A, carried by 11% of African Americans, was associated with a decrease in A1C of about 0.8% in homozygous men and 0.7% in homozygous women compared with those without the variant (34). For example, in Tanzania, where there is a high likelihood of hemoglobinopathies in people with HIV, A1C may be lower than expected based on glucose, limiting its usefulness for screening (35).

Even in the absence of hemoglobin variants, A1C levels may vary with race/ethnicity independently of glycemia (36–38). For example, African Americans may have higher A1C levels than non-Hispanic Whites with similar fasting and postglucose load glucose levels (39). Though conflicting data exists, African Americans may also have higher levels of fructosamine and glycated albumin and lower levels of 1,5-anhydroglucitol, suggesting that their glycemic burden (particularly postprandially) may be higher (40,41). Similarly, A1C levels may be higher for a given mean glucose concentration when measured with continuous glucose monitoring (42). A

recent report in Afro-Caribbean people demonstrated a lower A1C than predicted by glucose levels (43). Despite these and other reported differences, the association of A1C with risk for complications appears to be similar in African Americans and non-Hispanic Whites (44,45). In the Taiwanese population, age and sex have been reported to be associated with increased A1C in men (46); the clinical implications of this finding are unclear at this time.

Other Conditions Altering the Relationship of A1C and Glycemia

In conditions associated with increased red blood cell turnover, such as sickle cell disease, pregnancy (second and third trimesters), glucose-6-phosphate dehydrogenase deficiency (47,48), hemodialysis, recent blood loss or transfusion, or erythropoietin therapy, only plasma blood glucose criteria should be used to diagnose diabetes (49). A1C is less reliable than blood glucose measurement in other conditions such as the postpartum state (50–52), HIV treated with certain protease inhibitors (PIs) and nucleoside reverse transcriptase inhibitors (NRTIs) (30), and iron-deficient anemia (53).

Confirming the Diagnosis

Unless there is a clear clinical diagnosis (e.g., patient in a hyperglycemic crisis or with classic symptoms of hyperglycemia and a random plasma glucose ≥ 200 mg/dL [11.1 mmol/L]), diagnosis requires two abnormal screening test results, either from the same sample (54) or in two separate test samples. If using two separate test samples, it is recommended that the second test, which may either be a repeat of the initial test or a different test, be performed without delay. For example, if the A1C is 7.0% (53 mmol/mol) and a repeat result is 6.8% (51 mmol/mol), the diagnosis of diabetes is confirmed. If two different tests (such as A1C and FPG) are both above the diagnostic threshold when analyzed from the same sample or in two different test samples, this also confirms the diagnosis. On the other hand, if a patient has discordant results from two different tests, then the test result that is above the diagnostic cut point should be repeated, with careful consideration of the possibility of A1C assay interference. The

diagnosis is made on the basis of the confirmatory screening test. For example, if a patient meets the diabetes criterion of the A1C (two results $\geq 6.5\%$ [48 mmol/mol]) but not FPG (<126 mg/dL [7.0 mmol/L]), that person should nevertheless be considered to have diabetes.

Each of the screening tests has pre-analytic and analytic variability, so it is possible that a test yielding an abnormal result (i.e., above the diagnostic threshold), when repeated, will produce a value below the diagnostic cut point. This scenario is likely for FPG and 2-h PG if the glucose samples remain at room temperature and are not centrifuged promptly. Because of the potential for preanalytic variability, it is critical that samples for plasma glucose be spun and separated immediately after they are drawn. If patients have test results near the margins of the diagnostic threshold, the health care professional should discuss signs and symptoms with the patient and repeat the test in 3–6 months.

People should consume a mixed diet with at least 150 g of carbohydrate on the 3 days prior to oral glucose tolerance testing (55–57). Fasting and carbohydrate restriction can falsely elevate glucose level with an oral glucose challenge.

Diagnosis

In a patient with classic symptoms, measurement of plasma glucose is sufficient to diagnose diabetes (symptoms of hyperglycemia or hyperglycemic crisis plus a random plasma glucose ≥ 200 mg/dL [11.1 mmol/L]). In these cases, knowing the plasma glucose level is critical because, in addition to confirming that symptoms are due to diabetes, it will inform management decisions. Some providers may also want to know the A1C to determine the chronicity of the hyperglycemia. The criteria to diagnose diabetes are listed in **Table 2.2**.

TYPE 1 DIABETES

Recommendations

2.5 Screening for presymptomatic type 1 diabetes using screening tests that detect autoantibodies to insulin, glutamic acid decarboxylase (GAD), islet antigen 2, or zinc transporter

8 is currently recommended in the setting of a research study or can be considered an option for first-degree family members of a proband with type 1 diabetes. **B**

- 2.6** Development of and persistence of multiple islet autoantibodies is a risk factor for clinical diabetes and may serve as an indication for intervention in the setting of a clinical trial or screening for stage 2 type 1 diabetes. **B**

Immune-Mediated Diabetes

This form, previously called “insulin-dependent diabetes” or “juvenile-onset diabetes,” accounts for 5–10% of diabetes and is due to cellular-mediated autoimmune destruction of the pancreatic β -cells. Autoimmune markers include islet cell autoantibodies and autoantibodies to GAD (glutamic acid decarboxylase, GAD65), insulin, the tyrosine phosphatases islet antigen 2 (IA-2) and IA-2 β , and zinc transporter 8. Numerous clinical studies are being conducted to test various methods of preventing type 1 diabetes in those with evidence of islet autoimmunity (www.clinicaltrials.gov and www.trialnet.org/our-research/prevention-studies) (14,17,58–61). Stage 1 of type 1 diabetes is defined by the presence of two or more of these autoimmune markers. The disease has strong HLA associations, with linkage to the *DQB1* and *DRB1* haplotypes, and genetic screening has been used in some research studies to identify high risk populations. Specific alleles in these genes can be either predisposing or protective (**Table 2.1**).

The rate of β -cell destruction is quite variable, being rapid in some individuals (particularly but not exclusively in infants and children) and slow in others (mainly but not exclusively adults) (62,63). Children and adolescents often present with DKA as the first manifestation of the disease, and the rates in the U.S. have increased dramatically over the past 20 years (2–4). Others have modest fasting hyperglycemia that can rapidly change to severe hyperglycemia and/or DKA with infection or other stress. Adults may retain sufficient β -cell function to prevent DKA for many years; such individuals may have remission or decreased

insulin needs for months or years and eventually become dependent on insulin for survival and are at risk for DKA (5–7,64,65). At this latter stage of the disease, there is little or no insulin secretion, as manifested by low or undetectable levels of plasma C-peptide. Immune-mediated diabetes is the most common form of diabetes in childhood and adolescence, but it can occur at any age, even in the 8th and 9th decades of life.

Autoimmune destruction of β -cells has multiple genetic factors and is also related to environmental factors that are still poorly defined. Although patients do not typically have obesity when they present with type 1 diabetes, obesity is increasingly common in the general population; as such, obesity should not preclude testing for type 1 diabetes. People with type 1 diabetes are also prone to other autoimmune disorders such as Hashimoto thyroiditis, Graves disease, celiac disease, Addison disease, vitiligo, autoimmune hepatitis, myasthenia gravis, and pernicious anemia (see Section 4, “Comprehensive Medical Evaluation and Assessment of Comorbidities,” <https://doi.org/10.2337/dc22-S004>). Type 1 diabetes can be associated with monogenic polyglandular autoimmune syndromes including immune dysregulation, polyendocrinopathy, enteropathy, and X-linked (IPEX) syndrome, which is an early-onset systemic autoimmune genetic disorder caused by mutation of the forkhead box protein 3 (*FOXP3*) gene, and another caused by the autoimmune regulator (*AIRE*) gene mutation (66,67). As indicated by the names, these disorders are associated with other autoimmune and rheumatological diseases.

Introduction of immunotherapy, specifically checkpoint inhibitors, for cancer treatment has led to unexpected adverse events including immune system activation precipitating autoimmune disease. Fulminant onset of type 1 diabetes can develop, with DKA and low or undetectable levels of C-peptide as a marker of endogenous β -cell function (68,69). Fewer than half of these patients have autoantibodies that are seen in type 1 diabetes, supporting alternate pathobiology. This immune-related adverse event occurs in just under 1% of checkpoint inhibitor-treated patients but most commonly occurs with agents that block the programmed cell death protein 1/programmed cell death ligand 1 pathway

alone or in combination with other checkpoint inhibitors (70). To date, risk cannot be predicted by family history or autoantibodies, so all providers administering these medications should be mindful of this adverse effect and educate patients appropriately.

Idiopathic Type 1 Diabetes

Some forms of type 1 diabetes have no known etiologies. These patients have permanent insulinopenia and are prone to DKA but have no evidence of β -cell autoimmunity. However, only a minority of patients with type 1 diabetes fall into this category. Individuals with autoantibody-negative type 1 diabetes of African or Asian ancestry may suffer from episodic DKA and exhibit varying degrees of insulin deficiency between episodes (possibly ketosis-prone diabetes [71]). This form of diabetes is strongly inherited and is not HLA associated. An absolute requirement for insulin replacement therapy in affected patients may be intermittent. Future research is needed to determine the cause of β -cell destruction in this rare clinical scenario.

Screening for Type 1 Diabetes Risk

The incidence and prevalence of type 1 diabetes are increasing (72). Patients with type 1 diabetes often present with acute symptoms of diabetes and markedly elevated blood glucose levels, and 40–60% are diagnosed with life-threatening DKA (2–4). Multiple studies indicate that measuring islet autoantibodies in relatives of those with type 1 diabetes (15) or in children from the general population (73,74) can effectively identify those who will develop type 1 diabetes. A study reported the risk of progression to type 1 diabetes from the time of seroconversion to autoantibody positivity in three pediatric cohorts from Finland, Germany, and the U.S. Of the 585 children who developed more than two autoantibodies, nearly 70% developed type 1 diabetes within 10 years and 84% within 15 years (14). These findings are highly significant because while the German group was recruited from offspring of parents with type 1 diabetes, the Finnish and American groups were recruited from the general population. Remarkably, the findings in all three groups were the same, suggesting that the same sequence of events led to

Table 2.4—Risk-based screening for type 2 diabetes or prediabetes in asymptomatic children and adolescents in a clinical setting (254)

Screening should be considered in youth* who have overweight (≥ 85 th percentile) or obesity (≥ 95 th percentile) **A** and who have one or more additional risk factors based on the strength of their association with diabetes:

- Maternal history of diabetes or GDM during the child's gestation **A**
- Family history of type 2 diabetes in first- or second-degree relative **A**
- Race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander) **A**
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight) **B**

GDM, gestational diabetes mellitus. *After the onset of puberty or after 10 years of age, whichever occurs earlier. If tests are normal, repeat testing at a minimum of 3-year intervals (or more frequently if BMI is increasing or risk factor profile deteriorating) is recommended. Reports of type 2 diabetes before age 10 years exist, and this can be considered with numerous risk factors.

IGT and/or A1C 5.7–6.4% (39–47 mmol/mol) (**Table 2.5**). Prediabetes should not be viewed as a clinical entity in its own right, but rather as risk factor for progression to diabetes and cardiovascular disease (CVD). Criteria for screening for diabetes or prediabetes in asymptomatic adults are outlined in **Table 2.3**. Prediabetes is associated with obesity (especially abdominal or visceral obesity), dyslipidemia with high triglycerides and/or low HDL cholesterol, and hypertension. The presence of prediabetes should prompt comprehensive screening for cardiovascular risk factors.

Diagnosis

IFG is defined as FPG levels from 100 to 125 mg/dL (from 5.6 to 6.9 mmol/L) (82,83) and IGT as 2-h PG levels during 75-g OGTT from 140 to 199 mg/dL (from 7.8 to 11.0 mmol/L) (25). It should be noted that the World Health Organization and numerous other diabetes organizations define the IFG lower limit at 110 mg/dL (6.1 mmol/L).

As with the glucose measures, several prospective studies that used A1C to predict the progression to diabetes as

defined by A1C criteria demonstrated a strong, continuous association between A1C and subsequent diabetes. In a systematic review of 44,203 individuals from 16 cohort studies with a follow-up interval averaging 5.6 years (range 2.8–12 years), those with A1C between 5.5% and 6.0% (between 37 and 42 mmol/mol) had a substantially increased risk of diabetes (5-year incidence from 9% to 25%). Those with an A1C range of 6.0–6.5% (42–48 mmol/mol) had a 5-year risk of developing diabetes between 25% and 50% and a relative risk 20 times higher compared with A1C of 5.0% (31 mmol/mol) (84). In a community-based study of African American and non-Hispanic White adults without diabetes, baseline A1C was a stronger predictor of subsequent diabetes and cardiovascular events than fasting glucose (85). Other analyses suggest that A1C of 5.7% (39 mmol/mol) or higher is associated with a diabetes risk similar to that of the high-risk participants in the Diabetes Prevention Program (DPP) (86), and A1C at baseline was a strong predictor of the development of glucose-defined diabetes during the DPP and its follow-up (87).

Table 2.5—Criteria defining prediabetes*

FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG)

OR

2-h PG during 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT)

OR

A1C 5.7–6.4% (39–47 mmol/mol)

FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; 2-h PG, 2-h plasma glucose. *For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at the higher end of the range.

Hence, it is reasonable to consider an A1C range of 5.7–6.4% (39–47 mmol/mol) as identifying individuals with prediabetes. Similar to those with IFG and/or IGT, individuals with A1C of 5.7–6.4% (39–47 mmol/mol) should be informed of their increased risk for diabetes and CVD and counseled about effective strategies to lower their risks (see Section 3, "Prevention or Delay of Type 2 Diabetes and Associated Comorbidities," <https://doi.org/10.2337/dc22-S003>). Similar to glucose measurements, the continuum of risk is curvilinear, so as A1C rises, the diabetes risk rises disproportionately (84). Aggressive interventions and vigilant follow-up should be pursued for those considered at very high risk (e.g., those with A1C $> 6.0\%$ [42 mmol/mol]).

Table 2.5 summarizes the categories of prediabetes and **Table 2.3** the criteria for screening for prediabetes. The ADA diabetes risk test is an additional option for assessment to determine the appropriateness of screening for diabetes or prediabetes in asymptomatic adults (**Fig. 2.1**) (diabetes.org/socrisktest). For additional background regarding risk factors and screening for prediabetes, see SCREENING AND TESTING FOR PREDIABETES AND TYPE 2 DIABETES IN ASYMPTOMATIC ADULTS and also SCREENING AND TESTING FOR PREDIABETES AND TYPE 2 DIABETES IN CHILDREN AND ADOLESCENTS below. For details regarding individuals with prediabetes most likely to benefit from a formal behavioral or lifestyle intervention, see Section 3, "Prevention or Delay of Type 2 Diabetes and Associated Comorbidities" (<https://doi.org/10.2337/dc22-S003>).

Type 2 Diabetes

Type 2 diabetes, previously referred to as "noninsulin-dependent diabetes" or "adult-onset diabetes," accounts for 90–95% of all diabetes. This form encompasses individuals who have relative (rather than absolute) insulin deficiency and have peripheral insulin resistance. At least initially, and often throughout their lifetime, these individuals may not need insulin treatment to survive.

There are various causes of type 2 diabetes. Although the specific etiologies are not known, autoimmune destruction of β -cells does not occur, and patients do not have any of the other known causes of diabetes. Most,



Are you at risk for type 2 diabetes?

Diabetes Risk Test:

- 1. How old are you?**
 Less than 40 years (0 points)
 40–49 years (1 point)
 50–59 years (2 points)
 60 years or older (3 points)
- 2. Are you a man or a woman?**
 Man (1 point) Woman (0 points)
- 3. If you are a woman, have you ever been diagnosed with gestational diabetes?**
 Yes (1 point) No (0 points)
- 4. Do you have a mother, father, sister or brother with diabetes?**
 Yes (1 point) No (0 points)
- 5. Have you ever been diagnosed with high blood pressure?**
 Yes (1 point) No (0 points)
- 6. Are you physically active?**
 Yes (0 points) No (1 point)
- 7. What is your weight category?**
See chart at right.

WRITE YOUR SCORE
IN THE BOX.

ADD UP
YOUR SCORE.

Height	Weight (lbs.)		
4' 10"	119–142	143–190	191+
4' 11"	124–147	148–197	198+
5' 0"	128–152	153–203	204+
5' 1"	132–157	158–210	211+
5' 2"	136–163	164–217	218+
5' 3"	141–168	169–224	225+
5' 4"	145–173	174–231	232+
5' 5"	150–179	180–239	240+
5' 6"	155–185	186–246	247+
5' 7"	159–190	191–254	255+
5' 8"	164–196	197–261	262+
5' 9"	169–202	203–269	270+
5' 10"	174–208	209–277	278+
5' 11"	179–214	215–285	286+
6' 0"	184–220	221–293	294+
6' 1"	189–226	227–301	302+
6' 2"	194–232	233–310	311+
6' 3"	200–239	240–318	319+
6' 4"	205–245	246–327	328+
	1 point	2 points	3 points

If you weigh less than the amount in the left column: 0 points

Adapted from Bang et al., Ann Intern Med 151:775–783, 2009 • Original algorithm was validated without gestational diabetes as part of the model.

If you scored 5 or higher:

You are at increased risk for having type 2 diabetes. However, only your doctor can tell for sure if you do have type 2 diabetes or prediabetes, a condition in which blood glucose levels are higher than normal but not yet high enough to be diagnosed as diabetes. Talk to your doctor to see if additional testing is needed.

Type 2 diabetes is more common in African Americans, Hispanics/Latinos, Native Americans, Asian Americans, and Native Hawaiians and Pacific Islanders.

Higher body weight increases diabetes risk for everyone. Asian Americans are at increased diabetes risk at lower body weight than the rest of the general public (about 15 pounds lower).

Lower Your Risk

The good news is you can manage your risk for type 2 diabetes. Small steps make a big difference in helping you live a longer, healthier life.

If you are at high risk, your first step is to visit your doctor to see if additional testing is needed.

Visit diabetes.org or call 1-800-DIABETES (800-342-2383) for information, tips on getting started, and ideas for simple, small steps you can take to help lower your risk.

Learn more at diabetes.org/risktest | 1-800-DIABETES (800-342-2383)

Figure 2.1—ADA risk test (diabetes.org/socrisktest).

but not all, patients with type 2 diabetes have overweight or obesity. Excess weight itself causes some degree of insulin resistance. Patients who do not have obesity or overweight by traditional weight criteria may have an increased percentage of body fat

distributed predominantly in the abdominal region.

DKA seldom occurs spontaneously in type 2 diabetes; when seen, it usually arises in association with the stress of another illness such as infection, myocardial infarction, or with the use of

certain drugs (e.g., corticosteroids, atypical antipsychotics, and sodium–glucose cotransporter 2 inhibitors) (88,89). Type 2 diabetes frequently goes undiagnosed for many years because hyperglycemia develops gradually and, at earlier stages, is often not severe enough for

the patient to notice the classic diabetes symptoms caused by hyperglycemia, such as dehydration or unintentional weight loss. Nevertheless, even undiagnosed patients are at increased risk of developing macrovascular and microvascular complications.

Patients with type 2 diabetes may have insulin levels that appear normal or elevated, yet the failure to normalize blood glucose reflects a relative defect in glucose-stimulated insulin secretion. Thus, insulin secretion is defective in these patients and insufficient to compensate for insulin resistance. Insulin resistance may improve with weight reduction, exercise, and/or pharmacologic treatment of hyperglycemia but is seldom restored to normal. Recent interventions with intensive diet and exercise or surgical weight loss have led to diabetes remission (90–96) (see Section 8, “Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes,” <https://doi.org/10.2337/dc22-S008>).

The risk of developing type 2 diabetes increases with age, obesity, and lack of physical activity (97,98). It occurs more frequently in women with prior gestational diabetes mellitus (GDM) or polycystic ovary syndrome. It is also more common in people with hypertension or dyslipidemia and in certain racial/ethnic subgroups (African American, Native American, Hispanic/Latino, and Asian American). It is often associated with a strong genetic predisposition or family history in first-degree relatives (more so than type 1 diabetes). However, the genetics of type 2 diabetes are poorly understood and under intense investigation in this era of precision medicine (18). In adults without traditional risk factors for type 2 diabetes and/or of younger age, consider islet autoantibody testing (e.g., GAD65 autoantibodies) to exclude the diagnosis of type 1 diabetes (8).

Screening and Testing for Prediabetes and Type 2 Diabetes in Asymptomatic Adults

Screening for prediabetes and type 2 diabetes risk through an informal assessment of risk factors (Table 2.3) or with an assessment tool, such as the ADA risk test (Fig. 2.1) ([online at diabetes.org/socrisktest](https://www.diabetes.org/socrisktest)), is recommended to guide providers on whether performing

a diagnostic test (Table 2.2) is appropriate. Prediabetes and type 2 diabetes meet criteria for conditions in which early detection via screening is appropriate. Both conditions are common and impose significant clinical and public health burdens. There is often a long presymptomatic phase before the diagnosis of type 2 diabetes. Simple tests to detect preclinical disease are readily available (99). The duration of glycemic burden is a strong predictor of adverse outcomes. There are effective interventions that prevent progression from prediabetes to diabetes. It is important to individualize risk/benefit of formal intervention for patients with prediabetes and consider patient-centered goals. Risk models have explored the benefit, in general finding higher benefit of intervention in those at highest risk (100) (see Section 3, “Prevention or Delay of Type 2 Diabetes and Associated Comorbidities,” <https://doi.org/10.2337/dc22-S003>) and reduce the risk of diabetes complications (101) (see Section 10, “Cardiovascular Disease and Risk Management,” <https://doi.org/10.2337/dc22-S010>, Section 11, “Chronic Kidney Disease and Risk Management,” <https://doi.org/10.2337/dc22-S011>, and Section 12, “Retinopathy, Neuropathy, and Foot Care,” <https://doi.org/10.2337/dc22-S012>). In the most recent National Institutes of Health (NIH) Diabetes Prevention Program Outcomes Study (DPPOS) report, prevention of progression from prediabetes to diabetes (102) resulted in lower rates of developing retinopathy and nephropathy (103). Similar impact on diabetes complications was reported with screening, diagnosis, and comprehensive risk factor management in the U.K. Clinical Practice Research Datalink database (101). In that report, progression from prediabetes to diabetes augmented risk of complications.

Approximately one-quarter of people with diabetes in the U.S. and nearly half of Asian and Hispanic Americans with diabetes are undiagnosed (82,83). Although screening of asymptomatic individuals to identify those with prediabetes or diabetes might seem reasonable, rigorous clinical trials to prove the effectiveness of such screening have not been conducted and are unlikely to occur. Clinical conditions, such as hypertension, hypertensive pregnancy, and obesity, enhance risk (104). Based on a population estimate, diabetes in women

of childbearing age is underdiagnosed (105). Employing a probabilistic model, Peterson et al. (106) demonstrated cost and health benefits of preconception screening.

A large European randomized controlled trial compared the impact of screening for diabetes and intensive multifactorial intervention with that of screening and routine care (107). General practice patients between the ages of 40 and 69 years were screened for diabetes and randomly assigned by practice to intensive treatment of multiple risk factors or routine diabetes care. After 5.3 years of follow-up, CVD risk factors were modestly but significantly improved with intensive treatment compared with routine care, but the incidence of first CVD events or mortality was not significantly different between the groups (25). The excellent care provided to patients in the routine care group and the lack of an unscreened control arm limited the authors’ ability to determine whether screening and early treatment improved outcomes compared with no screening and later treatment after clinical diagnoses. Computer simulation modeling studies suggest that major benefits are likely to accrue from the early diagnosis and treatment of hyperglycemia and cardiovascular risk factors in type 2 diabetes (108); moreover, screening, beginning at age 30 or 45 years and independent of risk factors, may be cost-effective (<\$11,000 per quality-adjusted life year gained—2010 modeling data) (109). Cost-effectiveness of screening has been reinforced in cohort studies (110,111).

Additional considerations regarding testing for type 2 diabetes and prediabetes in asymptomatic patients include the following.

Age

Age is a major risk factor for diabetes. Testing should begin at no later than age 35 years for all patients (111a). Screening should be considered in adults of any age with overweight or obesity and one or more risk factors for diabetes.

BMI and Ethnicity

In general, BMI ≥ 25 kg/m² is a risk factor for diabetes. However, data suggest that the BMI cut point should be lower

for the Asian American population (112,113). The BMI cut points fall consistently between 23 and 24 kg/m² (sensitivity of 80%) for nearly all Asian American subgroups (with levels slightly lower for Japanese Americans). This makes a rounded cut point of 23 kg/m² practical. An argument can be made to push the BMI cut point to lower than 23 kg/m² in favor of increased sensitivity; however, this would lead to an unacceptably low specificity (13.1%). Data from the World Health Organization also suggest that a BMI of ≥ 23 kg/m² should be used to define increased risk in Asian Americans (114). The finding that one-third to one-half of diabetes in Asian Americans is undiagnosed suggests that testing is not occurring at lower BMI thresholds (97,115).

Evidence also suggests that other populations may benefit from lower BMI cut points. For example, in a large multiethnic cohort study, for an equivalent incidence rate of diabetes, a BMI of 30 kg/m² in non-Hispanic Whites was equivalent to a BMI of 26 kg/m² in African Americans (116).

Medications

Certain medications, such as glucocorticoids, thiazide diuretics, some HIV medications (30), and atypical antipsychotics (90), are known to increase the risk of diabetes and should be considered when deciding whether to screen.

HIV

Individuals with HIV are at higher risk for developing prediabetes and diabetes on antiretroviral (ARV) therapies, so a screening protocol is recommended (117). The A1C test may underestimate glycemia in people with HIV; it is not recommended for diagnosis and may present challenges for monitoring (31). 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 used in patients without HIV is critical to reduce the risks of microvascular and macrovascular complications. Diabetes risk is increased with certain PIs and 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 (118).

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. 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 (119). 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.

Testing Interval

The appropriate interval between screening tests is not known (120). The rationale for the 3-year interval is that with this interval, the number of false-positive tests that require confirmatory testing will be reduced and individuals with false-negative tests will be retested before substantial time elapses and complications develop (120). In especially high-risk individuals, particularly with weight gain, shorter intervals between screening may be useful.

Community Screening

Ideally, screening should be carried out within a health care setting because of the need for follow-up and treatment. Community screening outside a health care setting is generally not recommended because people with positive tests may not seek, or have access to, appropriate follow-up testing and care. However, in specific situations where an adequate referral system is established beforehand for positive tests, community screening may be considered. Community screening may also be poorly targeted; i.e., it may fail to reach the groups most at risk and inappropriately test those at very low risk or even those who have already been diagnosed (121).

Screening in Dental Practices

Because periodontal disease is associated with diabetes, the utility of screening in a dental setting and referral to primary care as a means to improve the diagnosis of prediabetes and diabetes has been explored (122–124), with one study estimating

that 30% of patients ≥ 30 years of age seen in general dental practices had dysglycemia (124,125). A similar study in 1,150 dental patients >40 years old in India reported 20.69% and 14.60% meeting criteria for prediabetes and diabetes, respectively, using random blood glucose. Further research is needed to demonstrate the feasibility, effectiveness, and cost-effectiveness of screening in this setting.

Screening and Testing for Prediabetes and Type 2 Diabetes in Children and Adolescents

In the last decade, the incidence and prevalence of type 2 diabetes in children and adolescents has increased dramatically, especially in racial and ethnic minority populations (72). See **Table 2.4** for recommendations on risk-based screening for type 2 diabetes or prediabetes in asymptomatic children and adolescents in a clinical setting (32). See **Table 2.2** and **Table 2.5** for the criteria for the diagnosis of diabetes and prediabetes, respectively, that apply to children, adolescents, and adults. See Section 14, “Children and Adolescents” (<https://doi.org/10.2337/dc22-S014>) for additional information on type 2 diabetes in children and adolescents.

Some studies question the validity of A1C in the pediatric population, especially among certain ethnicities, and suggest OGTT or FPG as more suitable diagnostic tests (126). However, many of these studies do not recognize that diabetes diagnostic criteria are based on long-term health outcomes, and validations are not currently available in the pediatric population (127). The ADA acknowledges the limited data supporting A1C for diagnosing type 2 diabetes in children and adolescents. Although A1C is not recommended for diagnosis of diabetes in children with cystic fibrosis or symptoms suggestive of acute onset of type 1 diabetes and only A1C assays without interference are appropriate for children with hemoglobinopathies, the ADA continues to recommend A1C and the criteria in **Table 2.2** for diagnosis of type 2 diabetes in this cohort to decrease barriers to screening (128,129).

CYSTIC FIBROSIS–RELATED DIABETES

Recommendations

- 2.16** Annual screening for cystic fibrosis–related diabetes with an oral glucose tolerance test should begin by age 10 years in all patients with cystic fibrosis not previously diagnosed with cystic fibrosis–related diabetes. **B**
- 2.17** A1C is not recommended as a screening test for cystic fibrosis–related diabetes. **B**
- 2.18** People with cystic fibrosis–related diabetes should be treated with insulin to attain individualized glycemic goals. **A**
- 2.19** Beginning 5 years after the diagnosis of cystic fibrosis–related diabetes, annual monitoring for complications of diabetes is recommended. **E**

Cystic fibrosis–related diabetes (CFRD) is the most common comorbidity in people with cystic fibrosis, occurring in about 20% of adolescents and 40–50% of adults (130). Diabetes in this population, compared with individuals with type 1 or type 2 diabetes, is associated with worse nutritional status, more severe inflammatory lung disease, and greater mortality. Insulin insufficiency is the primary defect in CFRD. Genetically determined β -cell function and insulin resistance associated with infection and inflammation may also contribute to the development of CFRD. Milder abnormalities of glucose tolerance are even more common and occur at earlier ages than CFRD. Whether individuals with IGT should be treated with insulin replacement has not currently been determined. Although screening for diabetes before the age of 10 years can identify risk for progression to CFRD in those with abnormal glucose tolerance, no benefit has been established with respect to weight, height, BMI, or lung function. OGTT is the recommended screening test; however, recent publications suggest that an A1C cut point threshold of 5.5% (5.8% in a second study) would detect more than 90% of cases and reduce patient screening burden (131,132). Ongoing studies are underway to validate this approach, and

A1C is not recommended for screening (133). Regardless of age, weight loss or failure of expected weight gain is a risk for CFRD and should prompt screening (131,132). The Cystic Fibrosis Foundation Patient Registry (134) evaluated 3,553 cystic fibrosis patients and diagnosed 445 (13%) with CFRD. Early diagnosis and treatment of CFRD was associated with preservation of lung function. The European Cystic Fibrosis Society Patient Registry reported an increase in CFRD with age (increased 10% per decade), genotype, decreased lung function, and female sex (135,136). Continuous glucose monitoring or HOMA of β -cell function (137) may be more sensitive than OGTT to detect risk for progression to CFRD; however, evidence linking these results to long-term outcomes is lacking, and these tests are not recommended for screening outside of the research setting (138).

CFRD mortality has significantly decreased over time, and the gap in mortality between cystic fibrosis patients with and without diabetes has considerably narrowed (139). There are limited clinical trial data on therapy for CFRD. The largest study compared three regimens: premeal insulin aspart, repaglinide, or oral placebo in cystic fibrosis patients with diabetes or abnormal glucose tolerance. Participants all had weight loss in the year preceding treatment; however, in the insulin-treated group, this pattern was reversed, and patients gained 0.39 (\pm 0.21) BMI units ($P = 0.02$). The repaglinide-treated group had initial weight gain, but it was not sustained by 6 months. The placebo group continued to lose weight (139). Insulin remains the most widely used therapy for CFRD (140). The primary rationale for the use of insulin in patients with CFRD is to induce an anabolic state while promoting macronutrient retention and weight gain.

Additional resources for the clinical management of CFRD can be found in the position statement “Clinical Care Guidelines for Cystic Fibrosis–Related Diabetes: A Position Statement of the American Diabetes Association and a Clinical Practice Guideline of the Cystic Fibrosis Foundation, Endorsed by the Pediatric Endocrine Society” (141) and in the International Society for Pediatric and Adolescent Diabetes 2018 clinical practice consensus guidelines (130).

POSTTRANSPLANTATION DIABETES MELLITUS

Recommendations

- 2.20** After organ transplantation, screening for hyperglycemia should be done. A formal diagnosis of posttransplantation diabetes mellitus is best made once the individual is stable on an immunosuppressive regimen and in the absence of an acute infection. **B**
- 2.21** The oral glucose tolerance test is the preferred test to make a diagnosis of posttransplantation diabetes mellitus. **B**
- 2.22** Immunosuppressive regimens shown to provide the best outcomes for patient and graft survival should be used, irrespective of posttransplantation diabetes mellitus risk. **E**

Several terms are used in the literature to describe the presence of diabetes following organ transplantation (142). “New-onset diabetes after transplantation” (NODAT) is one such designation that describes individuals who develop new-onset diabetes following transplant. NODAT excludes patients with pretransplant diabetes that was undiagnosed as well as posttransplant hyperglycemia that resolves by the time of discharge (143). Another term, “posttransplantation diabetes mellitus” (PTDM) (143,144), describes the presence of diabetes in the posttransplant setting irrespective of the timing of diabetes onset.

Hyperglycemia is very common during the early posttransplant period, with ~90% of kidney allograft recipients exhibiting hyperglycemia in the first few weeks following transplant (143–146). In most cases, such stress- or steroid-induced hyperglycemia resolves by the time of discharge (146,147). Although the use of immunosuppressive therapies is a major contributor to the development of PTDM, the risks of transplant rejection outweigh the risks of PTDM and the role of the diabetes care provider is to treat hyperglycemia appropriately regardless of the type of immunosuppression (143). Risk factors for PTDM include both general diabetes

risks (such as age, family history of diabetes, etc.) as well as transplant-specific factors, such as use of immunosuppressant agents (148–150). Whereas post-transplantation hyperglycemia is an important risk factor for subsequent PTDM, a formal diagnosis of PTDM is optimally made once the patient is stable on maintenance immunosuppression and in the absence of acute infection (146–148,151). In a recent study of 152 heart transplant recipients, 38% had PTDM at 1 year. Risk factors for PTDM included elevated BMI, discharge from the hospital on insulin, and glucose values in the 24 h prior to hospital discharge (152). In an Iranian cohort, 19% had PTDM after heart and lung transplant (153). The OGTT is considered the gold-standard test for the diagnosis of PTDM (1 year posttransplant) (143,144, 154,155). Pretransplant elevation in hs-CRP was associated with PTDM in the setting of renal transplant (156,157). However, screening patients with fasting glucose and/or A1C can identify high-risk patients requiring further assessment and may reduce the number of overall OGTTs required.

Few randomized controlled studies have reported on the short- and long-term use of antihyperglycemic agents in the setting of PTDM (148,158,159). Most studies have reported that transplant patients with hyperglycemia and PTDM after transplantation have higher rates of rejection, infection, and rehospitalization (146,148,160). Insulin therapy is the agent of choice for the management of hyperglycemia, PTDM, and preexisting diabetes and diabetes in the hospital setting. After discharge, patients with preexisting diabetes could go back on their pretransplant regimen if they were in good control before transplantation. Those with previously poor control or with persistent hyperglycemia should continue insulin with frequent home self-monitoring of blood glucose to determine when insulin dose reductions may be needed and when it may be appropriate to switch to noninsulin agents.

No studies to date have established which noninsulin agents are safest or most efficacious in PTDM. The choice of agent is usually made based on the side effect profile of the medication and possible interactions with the patient's immunosuppression regimen (148).

Drug dose adjustments may be required because of decreases in the glomerular filtration rate, a relatively common complication in transplant patients. A small short-term pilot study reported that metformin was safe to use in renal transplant recipients (161), but its safety has not been determined in other types of organ transplant. Thiazolidinediones have been used successfully in patients with liver and kidney transplants, but side effects include fluid retention, heart failure, and osteopenia (162,163). Dipeptidyl peptidase 4 inhibitors do not interact with immunosuppressant drugs and have demonstrated safety in small clinical trials (164,165). Well-designed intervention trials examining the efficacy and safety of these and other antihyperglycemic agents in patients with PTDM are needed.

MONOGENIC DIABETES SYNDROMES

Recommendations

- 2.23** Regardless of current age, all people diagnosed with diabetes in the first 6 months of life should have immediate genetic testing for neonatal diabetes. **A**
- 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**

Monogenic defects that cause β -cell dysfunction, such as neonatal diabetes and MODY, represent a small fraction of patients with diabetes (<5%). **Table 2.6** describes the most common causes of monogenic diabetes. For a

comprehensive list of causes, see *Genetic Diagnosis of Endocrine Disorders* (166).

Neonatal Diabetes

Diabetes occurring under 6 months of age is termed “neonatal” or “congenital” diabetes, and about 80–85% of cases can be found to have an underlying monogenic cause (8,167–170). Neonatal diabetes occurs much less often after 6 months of age, whereas autoimmune type 1 diabetes rarely occurs before 6 months of age. Neonatal diabetes can either be transient or permanent. Transient diabetes is most often due to overexpression of genes on chromosome 6q24, is recurrent in about half of cases, and may be treatable with medications other than insulin. Permanent neonatal diabetes is most commonly due to autosomal dominant mutations in the genes encoding the Kir6.2 subunit (*KCNJ11*) and SUR1 subunit (*ABCC8*) of the β -cell K_{ATP} channel. A recent report details a de novo mutation in *EIF2B1* affecting eIF2 signaling associated with permanent neonatal diabetes and hepatic dysfunction, similar to Wolcott-Rallison syndrome but with few severe comorbidities (171). The recent ADA-European Association for the Study of Diabetes type 1 diabetes consensus report makes the recommendation that regardless of current age, individuals diagnosed under 6 months of age should have genetic testing (8). Correct diagnosis has critical implications because 30–50% of people with K_{ATP} -related neonatal diabetes will exhibit improved glycemic control when treated with high-dose oral sulfonylureas instead of insulin. Insulin gene (*INS*) mutations are the second most common cause of permanent neonatal diabetes, and, while intensive insulin management is currently the preferred treatment strategy, there are important genetic counseling considerations, as most of the mutations that cause diabetes are dominantly inherited.

Maturity-Onset Diabetes of the Young

MODY is frequently characterized by onset of hyperglycemia at an early age (classically before age 25 years, although diagnosis may occur at older ages). MODY is characterized by impaired insulin secretion with minimal or no defects in insulin

Table 2.6—Most common causes of monogenic diabetes (166)

	Gene	Inheritance	Clinical features
MODY	<i>GCK</i>	AD	GCK-MODY: higher glucose threshold (set-point) for glucose-stimulated insulin secretion, causing stable, nonprogressive elevated fasting blood glucose; typically does not require treatment; microvascular complications are rare; small rise in 2-h PG level on OGTT (<54 mg/dL [3 mmol/L])
	<i>HNF1A</i>	AD	HNF1A-MODY: progressive insulin secretory defect with presentation in adolescence or early adulthood; lowered renal threshold for glucosuria; large rise in 2-h PG level on OGTT (>90 mg/dL [5 mmol/L]); sensitive to sulfonylureas
	<i>HNF4A</i>	AD	HNF4A-MODY: progressive insulin secretory defect with presentation in adolescence or early adulthood; may have large birth weight and transient neonatal hypoglycemia; sensitive to sulfonylureas
	<i>HNF1B</i>	AD	HNF1B-MODY: developmental renal disease (typically cystic); genitourinary abnormalities; atrophy of the pancreas; hyperuricemia; gout
Neonatal diabetes	<i>KCNJ11</i>	AD	Permanent or transient: IUGR; possible developmental delay and seizures; responsive to sulfonylureas
	<i>INS</i>	AD	Permanent: IUGR; insulin requiring
	<i>ABCC8</i>	AD	Permanent or transient: IUGR; rarely developmental delay; responsive to sulfonylureas
	6q24 (<i>PLAGL1</i> , <i>HYMA1</i>)	AD for paternal duplications	Transient: IUGR; macroglossia; umbilical hernia; mechanisms include UPD6, paternal duplication, or maternal methylation defect; may be treatable with medications other than insulin
	<i>GATA6</i>	AD	Permanent: pancreatic hypoplasia; cardiac malformations; pancreatic exocrine insufficiency; insulin requiring
	<i>EIF2AK3</i>	AR	Permanent: Wolcott-Rallison syndrome: epiphyseal dysplasia; pancreatic exocrine insufficiency; insulin requiring
	<i>EIF2B1</i>	AD	Permanent diabetes: can be associated with fluctuating liver function (171)
	<i>FOXP3</i>	X-linked	Permanent: immunodysregulation, polyendocrinopathy, enteropathy X-linked (IPEX) syndrome: autoimmune diabetes, autoimmune thyroid disease, exfoliative dermatitis; insulin requiring

AD, autosomal dominant; AR, autosomal recessive; IUGR, intrauterine growth restriction; OGTT, oral glucose tolerance test; UPD6, uniparental disomy of chromosome 6; 2-h PG, 2-h plasma glucose.

action (in the absence of coexistent obesity). It is inherited in an autosomal dominant pattern with abnormalities in at least 13 genes on different chromosomes identified to date (172). The most commonly reported forms are GCK-MODY (MODY2), HNF1A-MODY (MODY3), and HNF4A-MODY (MODY1).

For individuals with MODY, the treatment implications are considerable and warrant genetic testing (173,174). Clinically, patients with GCK-MODY exhibit mild, stable fasting hyperglycemia and do not require antihyperglycemic therapy except commonly during pregnancy. Patients with HNF1A- or HNF4A-MODY usually respond well to low doses of sulfonylureas, which are considered first-line therapy; in some instances insulin will be required over time. Mutations or deletions in *HNF1B* are associated with renal cysts and uterine malformations (renal cysts and diabetes [RCAD] syndrome). Other extremely rare forms of MODY have been reported to involve other transcription factor genes including *PDX1* (*IPF1*) and *NEUROD1*.

Diagnosis of Monogenic Diabetes

A diagnosis of one of the three most common forms of MODY, including GCK-MODY, HNF1A-MODY, and HNF4A-MODY, allows for more cost-effective therapy (no therapy for GCK-MODY; sulfonylureas as first-line therapy for HNF1A-MODY and HNF4A-MODY). Additionally, diagnosis can lead to identification of other affected family members. Genetic screening is increasingly available and cost-effective (171,174).

A diagnosis of MODY should be considered in individuals who have atypical diabetes and multiple family members with diabetes not characteristic of type 1 or type 2 diabetes, although admittedly “atypical diabetes” is becoming increasingly difficult to precisely define in the absence of a definitive set of tests for either type of diabetes (168–170,173–179). In most cases, the presence of autoantibodies for type 1 diabetes precludes further testing for monogenic diabetes, but the presence of autoantibodies in patients with monogenic diabetes has been reported

(180). Individuals in whom monogenic diabetes is suspected should be referred to a specialist for further evaluation if available, and consultation can be obtained from several centers. Readily available commercial genetic testing following the criteria listed below now enables a cost-effective (181), often cost-saving, genetic diagnosis that is increasingly supported by health insurance. A biomarker screening pathway such as the combination of urinary C-peptide/creatinine ratio and antibody screening may aid in determining who should get genetic testing for MODY (182). It is critical to correctly diagnose one of the monogenic forms of diabetes because these patients may be incorrectly diagnosed with type 1 or type 2 diabetes, leading to suboptimal, even potentially harmful, treatment regimens and delays in diagnosing other family members (183). The correct diagnosis is especially critical for those with GCK-MODY mutations, where multiple studies have shown that no complications ensue in the absence of glucose-

perinatal mortality, small-for-gestational-age births, and neonatal intensive care unit admission (208). If women are not screened prior to pregnancy, universal early screening at <15 weeks of gestation for undiagnosed diabetes may be considered over selective screening (Table 2.3), particularly in populations with high prevalence of risk factors and undiagnosed diabetes in women of childbearing age. Strong racial and ethnic disparities exist in the prevalence of undiagnosed diabetes. Therefore, early screening provides an initial step to identify these health disparities so that they can begin to be addressed (204–207). Standard diagnostic criteria for identifying undiagnosed diabetes in early pregnancy are the same as those used in the nonpregnant population (see Table 2.2). Women found to have diabetes by the standard diagnostic criteria used outside of pregnancy should be classified as having diabetes complicating pregnancy (most often type 2 diabetes, rarely type 1 diabetes or monogenic diabetes) and managed accordingly.

Early abnormal glucose metabolism, defined as fasting glucose threshold of 110 mg/dL (6.1 mmol/L) or an A1C of 5.9% (39 mmol/mol) may identify women who are at higher risk of adverse pregnancy and neonatal outcomes (pre-eclampsia, macrosomia, shoulder dystocia, perinatal death), are more likely to need insulin treatment, and are at high risk of a later GDM diagnosis (209–215). An A1C threshold of 5.7% has not been shown to be associated with adverse perinatal outcomes (216,217).

If early screening is negative, women should be rescreened for GDM between 24 and 28 weeks of gestation (see Section 15, “Management of Diabetes in Pregnancy,” <https://doi.org/10.2337/dc22-S015>). The International Association of the Diabetes and Pregnancy Study Groups (IADPSG) GDM diagnostic criteria for the 75-g OGTT as well as the GDM screening and diagnostic criteria used in the two-step approach were not derived from data in the first half of pregnancy and should not be used for early screening (218). To date, most randomized controlled trials of treatment of early abnormal glucose metabolism have been underpowered for outcomes. Therefore, the benefits of treatment for

early abnormal glucose metabolism remain uncertain. Nutrition counseling and periodic “block” testing of glucose levels weekly to identify women with high glucose levels are suggested. Testing frequency may proceed to daily, and treatment may be intensified, if the fasting glucose is predominantly >110 mg/dL, prior to 18 weeks of gestation.

Both the fasting glucose and A1C are low-cost tests. An advantage of the A1C is its convenience, as it can be added to the prenatal laboratories and does not require an early-morning fasting appointment. Disadvantages include inaccuracies in the presence of increased red blood cell turnover and hemoglobinopathies (usually reads lower), and higher values with anemia and reduced red blood cell turnover (219). A1C is not reliable to screen for GDM or for preexisting diabetes at 15 weeks of gestation or later. See Recommendation 2.3 above.

GDM is often indicative of underlying β -cell dysfunction (220), which confers marked increased risk for later development of diabetes, generally but not always type 2 diabetes, in the mother after delivery (221,222). As effective prevention interventions are available (223,224), women diagnosed with GDM should receive lifelong screening for prediabetes to allow interventions to

reduce diabetes risk and for type 2 diabetes to allow treatment at the earliest possible time (225).

Diagnosis

GDM carries risks for the mother, fetus, and neonate. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study (226), a large-scale multinational cohort study completed by more than 23,000 pregnant women, demonstrated that risk of adverse maternal, fetal, and neonatal outcomes continuously increased as a function of maternal glycemia at 24–28 weeks of gestation, even within ranges previously considered normal for pregnancy. For most complications, there was no threshold for risk. These results have led to careful reconsideration of the diagnostic criteria for GDM.

GDM diagnosis (Table 2.7) can be accomplished with either of two strategies:

1. The “one-step” 75-g OGTT derived from the IADPSG criteria, or
2. The older “two-step” approach with a 50-g (nonfasting) screen followed by a 100-g OGTT for those who screen positive, based on the work of Carpenter and Coustan’s interpretation of the older O’Sullivan (227) criteria.

Table 2.7—Screening for and diagnosis of GDM

One-step strategy

Perform a 75-g OGTT, with plasma glucose measurement when patient is fasting and at 1 and 2 h, at 24–28 weeks of gestation in women not previously diagnosed with diabetes. The OGTT should be performed in the morning after an overnight fast of at least 8 h. The diagnosis of GDM is made when any of the following plasma glucose values are met or exceeded:

- Fasting: 92 mg/dL (5.1 mmol/L)
- 1 h: 180 mg/dL (10.0 mmol/L)
- 2 h: 153 mg/dL (8.5 mmol/L)

Two-step strategy

Step 1: Perform a 50-g GLT (nonfasting), with plasma glucose measurement at 1 h, at 24–28 weeks of gestation in women not previously diagnosed with diabetes.

If the plasma glucose level measured 1 h after the load is ≥ 130 , 135, or 140 mg/dL (7.2, 7.5, or 7.8 mmol/L, respectively), proceed to a 100-g OGTT.

Step 2: The 100-g OGTT should be performed when the patient is fasting.

The diagnosis of GDM is made when at least two* of the following four plasma glucose levels (measured fasting and at 1, 2, and 3 h during OGTT) are met or exceeded (Carpenter-Coustan criteria [244]):

- Fasting: 95 mg/dL (5.3 mmol/L)
- 1 h: 180 mg/dL (10.0 mmol/L)
- 2 h: 155 mg/dL (8.6 mmol/L)
- 3 h: 140 mg/dL (7.8 mmol/L)

GDM, gestational diabetes mellitus; GLT, glucose load test; OGTT, oral glucose tolerance test. *American College of Obstetricians and Gynecologists notes that one elevated value can be used for diagnosis (240).

Different diagnostic criteria will identify different degrees of maternal hyperglycemia and maternal/fetal risk, leading some experts to debate, and disagree on, optimal strategies for the diagnosis of GDM.

One-Step Strategy

The IADPSG defined diagnostic cut points for GDM as the average fasting, 1-h, and 2-h PG values during a 75-g OGTT in women at 24–28 weeks of gestation who participated in the HAPO study at which odds for adverse outcomes reached 1.75 times the estimated odds of these outcomes at the mean fasting, 1-h, and 2-h PG levels of the study population. This one-step strategy was anticipated to significantly increase the incidence of GDM (from 5–6% to 15–20%), primarily because only one abnormal value, not two, became sufficient to make the diagnosis (228). Many regional studies have investigated the impact of adopting the IADPSG criteria on prevalence and have seen a roughly one- to threefold increase (229). The anticipated increase in the incidence of GDM could have a substantial impact on costs and medical infrastructure needs and has the potential to “medicalize” pregnancies previously categorized as normal. A recent follow-up study of women participating in a blinded study of pregnancy OGTTs found that 11 years after their pregnancies, women who would have been diagnosed with GDM by the one-step approach, as compared with those without, were at 3.4-fold higher risk of developing prediabetes and type 2 diabetes and had children with a higher risk of obesity and increased body fat, suggesting that the larger group of women identified by the one-step approach would benefit from the increased screening for diabetes and prediabetes that would accompany a history of GDM (230,231). The ADA recommends the IADPSG diagnostic criteria with the intent of optimizing gestational outcomes because these criteria are the only ones based on pregnancy outcomes rather than end points such as prediction of subsequent maternal diabetes.

The expected benefits of using IADPSG criteria to the offspring are inferred from intervention trials that focused on women with lower levels of hyperglycemia than identified using older GDM diagnostic criteria. Those

trials found modest benefits including reduced rates of large-for-gestational-age births and preeclampsia (232,233). It is important to note that 80–90% of women being treated for mild GDM in these two randomized controlled trials could be managed with lifestyle therapy alone. The OGTT glucose cutoffs in these two trials overlapped with the thresholds recommended by the IADPSG, and in one trial (233), the 2-h PG threshold (140 mg/dL [7.8 mmol/L]) was lower than the cutoff recommended by the IADPSG (153 mg/dL [8.5 mmol/L]). No randomized controlled trials of treating versus not treating GDM diagnosed by the IADPSG criteria but not the Carpenter-Coustan criteria have been published to date. However, a recent randomized trial of testing for GDM at 24–28 weeks of gestation by the one-step method using IADPSG criteria versus the two-step method using a 1-h 50-g glucose loading test (GLT) and, if positive, a 3-h OGTT by Carpenter-Coustan criteria identified twice as many women with GDM using the one-step method compared with the two-step. Despite treating more women for GDM using the one-step method, there was no difference in pregnancy and perinatal complications (234).

The one-step method identifies the long-term risks of maternal prediabetes and diabetes and offspring abnormal glucose metabolism and adiposity. Post hoc GDM in women diagnosed by the one-step method in the HAPO cohort was associated with higher prevalence of IGT; higher 30-min, 1-h, and 2-h glucoses during the OGTT; and reduced insulin sensitivity and oral disposition index in their offspring at 10–14 years of age compared with offspring of mothers without GDM. Associations of mother's fasting, 1-h, and 2-h values on the 75-g OGTT were continuous with a comprehensive panel of offspring metabolic outcomes (231,235). In addition, HAPO Follow-up Study (HAPO FUS) data demonstrate that neonatal adiposity and fetal hyperinsulinemia (cord C-peptide), both higher across the continuum of maternal hyperglycemia, are mediators of childhood body fat (236).

Data are lacking on how the treatment of mother's hyperglycemia in pregnancy affects her offspring's risk for obesity, diabetes, and other metabolic disorders.

Additional well-designed clinical studies are needed to determine the optimal intensity of monitoring and treatment of women with GDM diagnosed by the one-step strategy (237,238).

Two-Step Strategy

In 2013, the NIH convened a consensus development conference to consider diagnostic criteria for diagnosing GDM (239). The 15-member panel had representatives from obstetrics and gynecology, maternal-fetal medicine, pediatrics, diabetes research, biostatistics, and other related fields. The panel recommended a two-step approach to screening that used a 1-h 50-g GLT followed by a 3-h 100-g OGTT for those who screened positive. The American College of Obstetricians and Gynecologists (ACOG) recommends any of the commonly used thresholds of 130, 135, or 140 mg/dL for the 1-h 50-g GLT (240). A systematic review for the U.S. Preventive Services Task Force compared GLT cutoffs of 130 mg/dL (7.2 mmol/L) and 140 mg/dL (7.8 mmol/L) (241). The higher cutoff yielded sensitivity of 70–88% and specificity of 69–89%, while the lower cutoff was 88–99% sensitive and 66–77% specific. Data regarding a cutoff of 135 mg/dL are limited. As for other screening tests, choice of a cutoff is based upon the trade-off between sensitivity and specificity. The use of A1C at 24–28 weeks of gestation as a screening test for GDM does not function as well as the GLT (242).

Key factors cited by the NIH panel in their decision-making process were the lack of clinical trial data demonstrating the benefits of the one-step strategy and the potential negative consequences of identifying a large group of women with GDM, including medicalization of pregnancy with increased health care utilization and costs. Moreover, screening with a 50-g GLT does not require fasting and is therefore easier to accomplish for many women. Treatment of higher-threshold maternal hyperglycemia, as identified by the two-step approach, reduces rates of neonatal macrosomia, large-for-gestational-age births (243), and shoulder dystocia without increasing small-for-gestational-age births. ACOG currently supports the two-step approach but notes that one elevated value, as opposed to two, may

be used for the diagnosis of GDM (240). If this approach is implemented, the incidence of GDM by the two-step strategy will likely increase markedly. ACOG recommends either of two sets of diagnostic thresholds for the 3-h 100-g OGTT—Carpenter-Coustan or National Diabetes Data Group (244,245). Each is based on different mathematical conversions of the original recommended thresholds by O’Sullivan (227), which used whole blood and nonenzymatic methods for glucose determination. A secondary analysis of data from a randomized clinical trial of identification and treatment of mild GDM (246) demonstrated that treatment was similarly beneficial in patients meeting only the lower thresholds per Carpenter-Coustan (244) and in those meeting only the higher thresholds per National Diabetes Data Group (245). If the two-step approach is used, it would appear advantageous to use the Carpenter-Coustan lower diagnostic thresholds as shown in step 2 in **Table 2.7**.

Future Considerations

The conflicting recommendations from expert groups underscore the fact that there are data to support each strategy. A cost-benefit estimation comparing the two strategies concluded that the one-step approach is cost-effective only if patients with GDM receive postdelivery counseling and care to prevent type 2 diabetes (247). The decision of which strategy to implement must therefore be made based on the relative values placed on factors that have yet to be measured (e.g., willingness to change practice based on correlation studies rather than intervention trial results, available infrastructure, and importance of cost considerations).

As the IADPSG criteria (“one-step strategy”) have been adopted internationally, further evidence has emerged to support improved pregnancy outcomes with cost savings (248), and IADPSG may be the preferred approach. Data comparing populationwide outcomes with one-step versus two-step approaches have been inconsistent to date (234,249–251). In addition, pregnancies complicated by GDM per the IADPSG criteria, but not recognized as such, have outcomes comparable to pregnancies with diagnosed GDM by the more stringent two-step criteria (252,253). There remains strong consensus

that establishing a uniform approach to diagnosing GDM will benefit patients, caregivers, and policy makers. Longer-term outcome studies are currently underway.

References

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2014;37(Suppl. 1):S81–S90
2. Rewers A, Dong F, Slover RH, Klingensmith GJ, Rewers M. Incidence of diabetic ketoacidosis at diagnosis of type 1 diabetes in Colorado youth, 1998–2012. *JAMA* 2015;313:1570–1572
3. Alonso GT, Coakley A, Pyle L, Manseau K, Thomas S, Rewers A. Diabetic ketoacidosis at diagnosis of type 1 diabetes in Colorado children, 2010–2017. *Diabetes Care* 2020;43:117–121
4. Jensen ET, Stafford JM, Saydah S, et al. Increase in prevalence of diabetic ketoacidosis at diagnosis among youth with type 1 diabetes: the SEARCH for Diabetes in Youth Study. *Diabetes Care* 2021;44:1573–1578
5. Humphreys A, Bravis V, Kaur A, et al. Individual and diabetes presentation characteristics associated with partial remission status in children and adults evaluated up to 12 months following diagnosis of type 1 diabetes: an ADDRESS-2 (After Diagnosis Diabetes Research Support System-2) study analysis. *Diabetes Res Clin Pract* 2019;155:107789
6. Thomas NJ, Lynam AL, Hill AV, et al. Type 1 diabetes defined by severe insulin deficiency occurs after 30 years of age and is commonly treated as type 2 diabetes. *Diabetologia* 2019;62:1167–1172
7. Hope SV, Wienand-Barnett S, Shepherd M, et al. Practical Classification Guidelines for Diabetes in patients treated with insulin: a cross-sectional study of the accuracy of diabetes diagnosis. *Br J Gen Pract* 2016;66:e315–e322
8. Holt RIG, DeVries JH, Hess-Fischl A, et al. 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). *Diabetes Care*. 11 October 2021 [Epub ahead of print]. DOI: 10.2337/dci21-0043
9. Zhong VW, Juhaeri J, Mayer-Davis EJ. Trends in hospital admission for diabetic ketoacidosis in adults with type 1 and type 2 diabetes in England, 1998–2013: a retrospective cohort study. *Diabetes Care* 2018;41:1870–1877
10. Lawrence JM, Slezak JM, Quesenberry C, et al. Incidence and predictors of type 1 diabetes among younger adults aged 20–45 years: the Diabetes in Young Adults (DiYA) study. *Diabetes Res Clin Pract* 2021;171:108624
11. Newton CA, Raskin P. Diabetic ketoacidosis in type 1 and type 2 diabetes mellitus: clinical and biochemical differences. *Arch Intern Med* 2004;164:1925–1931
12. Skyler JS, Bakris GL, Bonifacio E, et al. Differentiation of diabetes by pathophysiology, natural history, and prognosis. *Diabetes* 2017;66:241–255
13. Lynam AL, Dennis JM, Owen KR, et al. Logistic regression has similar performance to optimised machine learning algorithms in a clinical setting: application to the discrimination between type 1 and type 2 diabetes in young adults. *Diagn Progn Res* 2020;4:6

14. Ziegler AG, Rewers M, Simell O, et al. Seroconversion to multiple islet autoantibodies and risk of progression to diabetes in children. *JAMA* 2013;309:2473–2479
15. Insel RA, Dunne JL, Atkinson MA, et al. Staging presymptomatic type 1 diabetes: a scientific statement of JDRF, the Endocrine Society, and the American Diabetes Association. *Diabetes Care* 2015;38:1964–1974
16. Zhu Y, Qian L, Liu Q, et al. Glutamic acid decarboxylase autoantibody detection by electrochemiluminescence assay identifies latent autoimmune diabetes in adults with poor islet function. *Diabetes Metab J* 2020;44:260–266
17. Lynam A, McDonald T, Hill A, et al. Development and validation of multivariable clinical diagnostic models to identify type 1 diabetes requiring rapid insulin therapy in adults aged 18–50 years. *BMJ Open* 2019;9:e031586
18. Chung WK, Erion K, Florez JC, et al. Precision medicine in diabetes: a consensus report from the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care* 2020;43:1617–1635
19. Gale EA. Declassifying diabetes. *Diabetologia* 2006;49:1989–1995
20. Schwartz SS, Epstein S, Corkey BE, Grant SFA, Gavin JR 3rd, Aguilar RB. The time is right for a new classification system for diabetes: rationale and implications of the β -cell-centric classification schema. *Diabetes Care* 2016;39:179–186
21. International Expert Committee. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. *Diabetes Care* 2009;32:1327–1334
22. Knowler WC, Barrett-Connor E, Fowler SE, et al.; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;346:393–403
23. Tuomilehto J, Lindström J, Eriksson JG, et al.; Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001;344:1343–1350
24. Chadha C, Pittas AG, Lary CW, et al.; D2d Research Group. Reproducibility of a prediabetes classification in a contemporary population. *Metabol Open* 2020;6:100031
25. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 1997;20:1183–1197
26. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 2003;26(Suppl. 1):S5–S20
27. Meijnikman AS, De Block CEM, Dirinck E, et al. Not performing an OGTT results in significant underdiagnosis of (pre)diabetes in a high risk adult Caucasian population. *Int J Obes* 2017;41:1615–1620
28. Gonzalez A, Deng Y, Lane AN, et al. Impact of mismatches in HbA_{1c} vs glucose values on the diagnostic classification of diabetes and prediabetes. *Diabet Med* 2020;37:689–696
29. Cowie CC, Rust KF, Byrd-Holt DD, et al. Prevalence of diabetes and high risk for diabetes

- using A1C criteria in the U.S. population in 1988–2006. *Diabetes Care* 2010;33:562–568
30. Eckhardt BJ, Holzman RS, Kwan CK, Baghdadi J, Aberg JA. Glycated hemoglobin A_{1c} as screening for diabetes mellitus in HIV-infected individuals. *AIDS Patient Care STDS* 2012;26:197–201
 31. Kim PS, Woods C, Georgoff P, et al. A1C underestimates glycemia in HIV infection. *Diabetes Care* 2009;32:1591–1593
 32. Arslanian S, Bacha F, Grey M, Marcus MD, White NH, Zeitler P. Evaluation and management of youth-onset type 2 diabetes: a position statement by the American Diabetes Association. *Diabetes Care* 2018;41:2648–2668
 33. Lacy ME, Wellenius GA, Sumner AE, et al. Association of sickle cell trait with hemoglobin A1c in African Americans. *JAMA* 2017;317:507–515
 34. Wheeler E, Leong A, Liu C-T, et al.; EPIC-CVD Consortium; EPIC-InterAct Consortium; Lifelines Cohort Study. Impact of common genetic determinants of hemoglobin A1c on type 2 diabetes risk and diagnosis in ancestrally diverse populations: a transethnic genome-wide meta-analysis. *PLoS Med* 2017;14:e1002383
 35. Kweka B, Lyimo E, Jeremiah K, et al. Influence of hemoglobinopathies and glucose-6-phosphate dehydrogenase deficiency on diagnosis of diabetes by HbA1c among Tanzanian adults with and without HIV: a cross-sectional study. *PLoS One* 2020;15:e0244782
 36. Ziemer DC, Kolm P, Weintraub WS, et al. Glucose-independent, black-white differences in hemoglobin A1c levels: a cross-sectional analysis of 2 studies. *Ann Intern Med* 2010;152:770–777
 37. Kumar PR, Bhansali A, Ravikiran M, et al. Utility of glycated hemoglobin in diagnosing type 2 diabetes mellitus: a community-based study. *J Clin Endocrinol Metab* 2010;95:2832–2835
 38. Herman WH. Are there clinical implications of racial differences in HbA_{1c}? Yes, to not consider can do great harm! *Diabetes Care* 2016;39:1458–1461
 39. Herman WH, Ma Y, Uwaifo G, et al.; Diabetes Prevention Program Research Group. Differences in A1C by race and ethnicity among patients with impaired glucose tolerance in the Diabetes Prevention Program. *Diabetes Care* 2007;30:2453–2457
 40. Selvin E, Steffes MW, Ballantyne CM, Hoogeveen RC, Coresh J, Brancati FL. Racial differences in glycemic markers: a cross-sectional analysis of community-based data. *Ann Intern Med* 2011;154:303–309
 41. Herman WH, Dungan KM, Wolfenbutter BHR, et al. Racial and ethnic differences in mean plasma glucose, hemoglobin A1c, and 1,5-anhydroglucitol in over 2000 patients with type 2 diabetes. *J Clin Endocrinol Metab* 2009;94:1689–1694
 42. Bergenstal RM, Gal RL, Connor CG, et al.; T1D Exchange Racial Differences Study Group. Racial differences in the relationship of glucose concentrations and hemoglobin A1c levels. *Ann Intern Med* 2017;167:95–102
 43. Khosla L, Bhat S, Fullington LA, Horlyck-Romanovsky MF. HbA_{1c} performance in African descent populations in the United States with normal glucose tolerance, prediabetes, or diabetes: a scoping review. *Prev Chronic Dis* 2021;18:E22
 44. Selvin E, Rawlings AM, Bergenstal RM, Coresh J, Brancati FL. No racial differences in the association of glycated hemoglobin with kidney disease and cardiovascular outcomes. *Diabetes Care* 2013;36:2995–3001
 45. Selvin E. Are there clinical implications of racial differences in HbA_{1c}? A difference, to be a difference, must make a difference. *Diabetes Care* 2016;39:1462–1467
 46. Huang S-H, Huang P-J, Li J-Y, Su Y-D, Lu C-C, Shih C-L. Hemoglobin A1c levels associated with age and gender in Taiwanese adults without prior diagnosis with diabetes. *Int J Environ Res Public Health* 2021;18:3390
 47. Paterson AD. HbA1c for type 2 diabetes diagnosis in Africans and African Americans: personalized medicine NOW! *PLoS Med* 2017;14:e1002384
 48. Cappellini MD, Fiorelli G. Glucose-6-phosphate dehydrogenase deficiency. *Lancet* 2008;371:64–74
 49. Picón MJ, Murri M, Muñoz A, Fernández-García JC, Gomez-Huelgas R, Tinahones FJ. Hemoglobin A_{1c} versus oral glucose tolerance test in postpartum diabetes screening. *Diabetes Care* 2012;35:1648–1653
 50. Göbl CS, Bozkurt L, Yarragudi R, Tura A, Pacini G, Kautzky-Willer A. Is early postpartum HbA1c an appropriate risk predictor after pregnancy with gestational diabetes mellitus? *Acta Diabetol* 2014;51:715–722
 51. Megia A, Näf S, Herranz L, et al. The usefulness of HbA1c in postpartum reclassification of gestational diabetes. *BJOG* 2012;119:891–894
 52. Welsh KJ, Kirkman MS, Sacks DB. Role of glycated proteins in the diagnosis and management of diabetes: research gaps and future directions. *Diabetes Care* 2016;39:1299–1306
 53. Kim C, Bullard KM, Herman WH, Beckles GL. Association between iron deficiency and A1C levels among adults without diabetes in the National Health and Nutrition Examination Survey, 1999–2006. *Diabetes Care* 2010;33:780–785
 54. Selvin E, Wang D, Matsushita K, Grams ME, Coresh J. Prognostic implications of single-sample confirmatory testing for undiagnosed diabetes: a prospective cohort study. *Ann Intern Med* 2018;169:156–164
 55. Klein KR, Walker CP, McFerren AL, Huffman H, Frohlich F, Buse JB. Carbohydrate intake prior to oral glucose tolerance testing. *J Endocr Soc* 2021;5:bvab049
 56. Conn JW. Interpretation of the glucose tolerance test. The necessity of a stand ard preparatory diet. *Am J Med Sci* 1940;199:555–564
 57. Wilkerson HL, Butler FK, Francis JO. The effect of prior carbohydrate intake on the oral glucose tolerance test. *Diabetes* 1960;9:386–391
 58. Ziegler A-G; BABYDIAB-BABYDIET Study Group. Age-related islet autoantibody incidence in offspring of patients with type 1 diabetes. *Diabetologia* 2012;55:1937–1943
 59. Parikka V, Nääntö-Salonen K, Saarinen M, et al. Early seroconversion and rapidly increasing autoantibody concentrations predict prepubertal manifestation of type 1 diabetes in children at genetic risk. *Diabetologia* 2012;55:1926–1936
 60. Steck AK, Vehik K, Bonifacio E, et al.; TEDDY Study Group. Predictors of progression from the appearance of islet autoantibodies to early childhood diabetes: The Environmental Determinants of Diabetes in the Young (TEDDY). *Diabetes Care* 2015;38:808–813
 61. McKeigue PM, Spiliopoulou A, McGurnaghan S, et al. Persistent C-peptide secretion in type 1 diabetes and its relationship to the genetic architecture of diabetes. *BMC Med* 2019;17:165
 62. Bogun MM, Bundy BN, Goland RS, Greenbaum CJ. C-Peptide levels in subjects followed longitudinally before and after type 1 diabetes diagnosis in TrialNet. *Diabetes Care* 2020;43:1836–1842
 63. Greenbaum CJ, Beam CA, Boulware D, et al.; Type 1 Diabetes TrialNet Study Group. Fall in C-peptide during first 2 years from diagnosis: evidence of at least two distinct phases from composite Type 1 Diabetes TrialNet data. *Diabetes* 2012;61:2066–2073
 64. Mishra R, Hodge KM, Cousminer DL, Leslie RD, Grant SFA. A global perspective of latent autoimmune diabetes in adults. *Trends Endocrinol Metab* 2018;29:638–650
 65. Buzzetti R, Zampetti S, Maddaloni E. Adult-onset autoimmune diabetes: current knowledge and implications for management. *Nat Rev Endocrinol* 2017;13:674–686
 66. Ben-Skownronek I. IPEX syndrome: genetics and treatment options. *Genes (Basel)* 2021;12:323
 67. Frommer L, Kahaly GJ. Autoimmune polyendocrinopathy. *J Clin Endocrinol Metab* 2019;104:4769–4782
 68. Smith CJ, Almodallal Y, Jatou A. Rare adverse events with programmed death-1 and programmed death-1 ligand inhibitors: justification and rationale for a systematic review. *Curr Oncol Rep* 2021;23:86
 69. Zhao Z, Wang X, Bao X-Q, Ning J, Shang M, Zhang D. Autoimmune polyendocrine syndrome induced by immune checkpoint inhibitors: a systematic review. *Cancer Immunol Immunother* 2021;70:1527–1540
 70. Stamatouli AM, Quandt Z, Perdigoto AL, et al. Collateral damage: insulin-dependent diabetes induced with checkpoint inhibitors. *Diabetes* 2018;67:1471–1480
 71. Balasubramanyam A, Nalini R, Hampe CS, Maldonado M. Syndromes of ketosis-prone diabetes mellitus. *Endocr Rev* 2008;29:292–302
 72. Dabelea D, Mayer-Davis EJ, Saydah S, et al.; SEARCH for Diabetes in Youth Study. Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. *JAMA* 2014;311:1778–1786
 73. Ziegler A-G, Kick K, Bonifacio E, et al.; Fr1da Study Group. Yield of a public health screening of children for islet autoantibodies in Bavaria, Germany. *JAMA* 2020;323:339–351
 74. McQueen RB, Geno Rasmussen C, Waugh K, et al. Cost and cost-effectiveness of large-scale screening for type 1 diabetes in Colorado. *Diabetes Care* 2020;43:1496–1503
 75. Sosenko JM, Skyler JS, Palmer JP, et al.; Type 1 Diabetes TrialNet Study Group; Diabetes Prevention Trial-Type 1 Study Group. The prediction of type 1 diabetes by multiple autoantibody levels and their incorporation into an autoantibody risk score in relatives of type 1

- diabetic patients. *Diabetes Care* 2013;36:2615–2620
76. Orban T, Sosenko JM, Cuthbertson D, et al.; Diabetes Prevention Trial–Type 1 Study Group. Pancreatic islet autoantibodies as predictors of type 1 diabetes in the Diabetes Prevention Trial–Type 1. *Diabetes Care* 2009;32:2269–2274
77. Jacobsen LM, Larsson HE, Tamura RN, et al.; TEDDY Study Group. Predicting progression to type 1 diabetes from ages 3 to 6 in islet autoantibody positive TEDDY children. *Pediatr Diabetes* 2019;20:263–270
78. Barker JM, Goehrig SH, Barriga K, et al.; DAISY study. Clinical characteristics of children diagnosed with type 1 diabetes through intensive screening and follow-up. *Diabetes Care* 2004;27:1399–1404
79. Elding Larsson H, Vehik K, Gesualdo P, et al.; TEDDY Study Group. Children followed in the TEDDY study are diagnosed with type 1 diabetes at an early stage of disease. *Pediatr Diabetes* 2014;15:118–126
80. Herold KC, Bundy BN, Long SA, et al.; Type 1 Diabetes TrialNet Study Group. An anti-CD3 antibody, teplizumab, in relatives at risk for type 1 diabetes. *N Engl J Med* 2019;381:603–613
81. Sims EK, Bundy BN, Stier K, et al.; Type 1 Diabetes TrialNet Study Group. Teplizumab improves and stabilizes beta cell function in antibody-positive high-risk individuals. *Sci Transl Med* 2021;13:eabc8980
82. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2011;34(Suppl. 1):S62–S69
83. Genuth S, Alberti KGMM, Bennett P, et al.; Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Follow-up report on the diagnosis of diabetes mellitus. *Diabetes Care* 2003;26:3160–3167
84. Zhang X, Gregg EW, Williamson DF, et al. A1C level and future risk of diabetes: a systematic review. *Diabetes Care* 2010;33:1665–1673
85. Selvin E, Steffes MW, Zhu H, et al. Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults. *N Engl J Med* 2010;362:800–811
86. Ackermann RT, Cheng YJ, Williamson DF, Gregg EW. Identifying adults at high risk for diabetes and cardiovascular disease using hemoglobin A1c: National Health and Nutrition Examination Survey 2005–2006. *Am J Prev Med* 2011;40:11–17
87. Diabetes Prevention Program Research Group. HbA_{1c} as a predictor of diabetes and as an outcome in the Diabetes Prevention Program: a randomized clinical trial. *Diabetes Care* 2015;38:51–58
88. Umpierrez G, Korytkowski M. Diabetic emergencies – ketoacidosis, hyperglycaemic hyperosmolar state and hypoglycaemia. *Nat Rev Endocrinol* 2016;12:222–232
89. Fadini GP, Bonora BM, Avogaro A. SGLT2 inhibitors and diabetic ketoacidosis: data from the FDA Adverse Event Reporting System. *Diabetologia* 2017;60:1385–1389
90. Lean ME, Leslie WS, Barnes AC, et al. Primary care-led weight management for remission of type 2 diabetes (DIRECT): an open-label, cluster-randomised trial. *Lancet* 2018;391:541–551
91. Taheri S, Zaghloul H, Chagoury O, et al. Effect of intensive lifestyle intervention on bodyweight and glycaemia in early type 2 diabetes (DIADDEM-1): an open-label, parallel-group, randomised controlled trial. *Lancet Diabetes Endocrinol* 2020;8:477–489
92. Lean MEJ, Leslie WS, Barnes AC, et al. Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DIRECT open-label, cluster-randomised trial. *Lancet Diabetes Endocrinol* 2019;7:344–355
93. Roth AE, Thornley CJ, Blackstone RP. Outcomes in bariatric and metabolic surgery: an updated 5-year review. *Curr Obes Rep* 2020;9:380–389
94. Conte C, Lapeyre-Mestre M, Hanaire H, Ritz P. Diabetes remission and relapse after bariatric surgery: a nationwide population-based study. *Obes Surg* 2020;30:4810–4820
95. Yoshino M, Kayser BD, Yoshino J, et al. Effects of diet versus gastric bypass on metabolic function in diabetes. *N Engl J Med* 2020;383:721–732
96. Cresci B, Cosentino C, Monami M, Mannucci E. Metabolic surgery for the treatment of type 2 diabetes: a network meta-analysis of randomized controlled trials. *Diabetes Obes Metab* 2020;22:1378–1387
97. Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2020: Estimates of Diabetes and Its Burden in the United States. National Diabetes Statistics Report, 2020: Estimates of Diabetes and Its Burden in the United States. Accessed 15 October 2020. Available from <https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf>
98. International Diabetes Federation. IDF Diabetes Atlas, 9th edition. Brussels, Belgium, International Diabetes Federation, 2019. Accessed 15 October 2020. Available from <https://www.diabetesatlas.org/en/>
99. Bardenheier BH, Wu W-C, Zullo AR, Gravenstein S, Gregg EW. Progression to diabetes by baseline glycemic status among middle-aged and older adults in the United States, 2006–2014. *Diabetes Res Clin Pract* 2021;174:108726
100. Sussman JB, Kent DM, Nelson JP, Hayward RA. Improving diabetes prevention with benefit based tailored treatment: risk based reanalysis of Diabetes Prevention Program. *BMJ* 2015;350:h454
101. Palladino R, Tabak AG, Khunti K, et al. Association between pre-diabetes and microvascular and macrovascular disease in newly diagnosed type 2 diabetes. *BMJ Open Diabetes Res Care* 2020;8:e001061
102. Perreault L, Pan Q, Aroda VR, et al.; Diabetes Prevention Program Research Group. Exploring residual risk for diabetes and microvascular disease in the Diabetes Prevention Program Outcomes Study (DPPOS). *Diabet Med* 2017;34:1747–1755
103. Nathan DM, Bennett PH, Crandall JP, et al.; Research Group. Does diabetes prevention translate into reduced long-term vascular complications of diabetes? *Diabetologia* 2019;62:1319–1328
104. Lin C-H, Wei J-N, Fan K-C, et al. Different cutoffs of hypertension, risk of incident diabetes and progression of insulin resistance: a prospective cohort study. *J Formos Med Assoc.* 22 March 2021 [Epub ahead of print]. DOI: 10.1016/j.jfma.2021.02.022
105. Wei Y, Xu Q, Yang H, et al. Preconception diabetes mellitus and adverse pregnancy outcomes in over 6.4 million women: a population-based cohort study in China. *PLoS Med* 2019;16:e1002926
106. Peterson C, Grosse SD, Li R, et al. Preventable health and cost burden of adverse birth outcomes associated with pregestational diabetes in the United States. *Am J Obstet Gynecol* 2015;212:74.e1–74.e9
107. Griffin SJ, Borch-Johnsen K, Davies MJ, et al. Effect of early intensive multifactorial therapy on 5-year cardiovascular outcomes in individuals with type 2 diabetes detected by screening (ADDITION-Europe): a cluster-randomised trial. *Lancet* 2011;378:156–167
108. Herman WH, Ye W, Griffin SJ, et al. Early detection and treatment of type 2 diabetes reduce cardiovascular morbidity and mortality: a simulation of the results of the Anglo-Danish-Dutch Study of Intensive Treatment in People With Screen-Detected Diabetes in Primary Care (ADDITION-Europe). *Diabetes Care* 2015;38:1449–1455
109. Kahn R, Alperin P, Eddy D, et al. Age at initiation and frequency of screening to detect type 2 diabetes: a cost-effectiveness analysis. *Lancet* 2010;375:1365–1374
110. Zhou X, Siegel KR, Ng BP, et al. Cost-effectiveness of diabetes prevention interventions targeting high-risk individuals and whole populations: a systematic review. *Diabetes Care* 2020;43:1593–1616
111. Chatterjee R, Narayan KMV, Lipscomb J, et al. Screening for diabetes and prediabetes should be cost-saving in patients at high risk. *Diabetes Care* 2013;36:1981–1987
- 111a. Chung S, Azar KM, Baek M, Lauderdale DS, Palaniappan LP. Reconsidering the age thresholds for type II diabetes screening in the U.S. *Am J Prev Med* 2014;47:375–381
112. Araneta MRG, Kanaya A, Hsu WC, et al. Optimum BMI cut points to screen Asian Americans for type 2 diabetes. *Diabetes Care* 2015;38:814–820
113. Hsu WC, Araneta MRG, Kanaya AM, Chiang JL, Fujimoto W. BMI cut points to identify at-risk Asian Americans for type 2 diabetes screening. *Diabetes Care* 2015;38:150–158
114. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004;363:157–163
115. Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and trends in diabetes among adults in the United States, 1988–2012. *JAMA* 2015;314:1021–1029
116. Chiu M, Austin PC, Manuel DG, Shah BR, Tu JV. Deriving ethnic-specific BMI cutoff points for assessing diabetes risk. *Diabetes Care* 2011;34:1741–1748
117. 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
118. Monroe AK, Glesby MJ, Brown TT. Diagnosing and managing diabetes in HIV-

- infected patients: current concepts. *Clin Infect Dis* 2015;60:453–462
119. 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
 120. Johnson SL, Tabaei BP, Herman WH. The efficacy and cost of alternative strategies for systematic screening for type 2 diabetes in the U.S. population 45–74 years of age. *Diabetes Care* 2005;28:307–311
 121. Tabaei BP, Burke R, Constance A, et al. Community-based screening for diabetes in Michigan. *Diabetes Care* 2003;26:668–670
 122. Lalla E, Kunzel C, Burkett S, Cheng B, Lamster IB. Identification of unrecognized diabetes and pre-diabetes in a dental setting. *J Dent Res* 2011;90:855–860
 123. Lalla E, Cheng B, Kunzel C, Burkett S, Lamster IB. Dental findings and identification of undiagnosed hyperglycemia. *J Dent Res* 2013;92:888–892
 124. Herman WH, Taylor GW, Jacobson JJ, Burke R, Brown MB. Screening for prediabetes and type 2 diabetes in dental offices. *J Public Health Dent* 2015;75:175–182
 125. Jadhav AN, Tarte PR, Puri SK. Dental clinic: potential source of high-risk screening for prediabetes and type 2 diabetes. *Indian J Dent Res* 2019;30:851–854
 126. Buse JB, Kaufman FR, Linder B, Hirst K, El Ghormli L; HEALTHY Study Group. Diabetes screening with hemoglobin A_{1c} versus fasting plasma glucose in a multiethnic middle-school cohort. *Diabetes Care* 2013;36:429–435
 127. Kapadia C; Drugs and Therapeutics Committee of the Pediatric Endocrine Society. Hemoglobin A_{1c} measurement for the diagnosis of type 2 diabetes in children. *Int J Pediatr Endocrinol* 2012;2012:31
 128. Kester LM, Hey H, Hannon TS. Using hemoglobin A_{1c} for prediabetes and diabetes diagnosis in adolescents: can adult recommendations be upheld for pediatric use? *J Adolesc Health* 2012;50:321–323
 129. Wu E-L, Kazzi NG, Lee JM. Cost-effectiveness of screening strategies for identifying pediatric diabetes mellitus and dysglycemia. *JAMA Pediatr* 2013;167:32–39
 130. Moran A, Pillay K, Becker D, Granados A, Hameed S, Acerini CL. ISPAD Clinical Practice Consensus Guidelines 2018: management of cystic fibrosis-related diabetes in children and adolescents. *Pediatr Diabetes* 2018;19(Suppl. 27):64–74
 131. Gilmour JA. Response to the letter to the editor from Dr. Boudreau et al., “Validation of a Stepwise Approach Using Glycated Hemoglobin Levels to Reduce the Number of Required Oral Glucose Tolerance Tests to Screen for Cystic Fibrosis-Related Diabetes in Adults”. *Can J Diabetes* 2019;43:163
 132. Gilmour JA, Sykes J, Etchells E, Tullis E. Cystic fibrosis-related diabetes screening in adults: a gap analysis and evaluation of accuracy of glycated hemoglobin levels. *Can J Diabetes* 2019;43:13–18
 133. Darukhanavala A, Van Dessel F, Ho J, Hansen M, Kremer T, Alfego D. Use of hemoglobin A_{1c} to identify dysglycemia in cystic fibrosis. *PLoS One* 2021;16:e0250036
 134. Franck Thompson E, Watson D, Benoit CM, Landvik S, McNamara J. The association of pediatric cystic fibrosis-related diabetes screening on clinical outcomes by center: a CF patient registry study. *J Cyst Fibros* 2020;19:316–320
 135. Olesen HV, Drevinek P, Gulmans VA, et al.; ECFSPR Steering Group. Cystic fibrosis related diabetes in Europe: prevalence, risk factors and outcome. *J Cyst Fibros* 2020;19:321–327
 136. Prentice BJ, Chelliah A, Ooi CY, et al. Peak OGTT glucose is associated with lower lung function in young children with cystic fibrosis. *J Cyst Fibros* 2020;19:305–309
 137. Mainguy C, Bellon G, Delaup V, et al. Sensitivity and specificity of different methods for cystic fibrosis-related diabetes screening: is the oral glucose tolerance test still the standard? *J Pediatr Endocrinol Metab* 2017;30:27–35
 138. Ode KL, Moran A. New insights into cystic fibrosis-related diabetes in children. *Lancet Diabetes Endocrinol* 2013;1:52–58
 139. Moran A, Dunitz J, Nathan B, Saeed A, Holme B, Thomas W. Cystic fibrosis-related diabetes: current trends in prevalence, incidence, and mortality. *Diabetes Care* 2009;32:1626–1631
 140. Onady GM, Stolfi A. Insulin and oral agents for managing cystic fibrosis-related diabetes. *Cochrane Database Syst Rev* 2016;4:CD004730
 141. Moran A, Brunzell C, Cohen RC, et al.; CFRD Guidelines Committee. Clinical care guidelines for cystic fibrosis-related diabetes: a position statement of the American Diabetes Association and a clinical practice guideline of the Cystic Fibrosis Foundation, endorsed by the Pediatric Endocrine Society. *Diabetes Care* 2010;33:2697–2708
 142. Shivaswamy V, Boerner B, Larsen J. Post-transplant diabetes mellitus: causes, treatment, and impact on outcomes. *Endocr Rev* 2016;37:37–61
 143. Sharif A, Hecking M, de Vries APJ, et al. Proceedings from an international consensus meeting on posttransplantation diabetes mellitus: recommendations and future directions. *Am J Transplant* 2014;14:1992–2000
 144. Hecking M, Werzowa J, Haidinger M, et al.; European-New-Onset Diabetes After Transplantation Working Group. Novel views on new-onset diabetes after transplantation: development, prevention and treatment. *Nephrol Dial Transplant* 2013;28:550–566
 145. Ramirez SC, Maaske J, Kim Y, et al. The association between glycemic control and clinical outcomes after kidney transplantation. *Endocr Pract* 2014;20:894–900
 146. Thomas MC, Moran J, Mathew TH, Russ GR, Rao MM. Early peri-operative hyperglycaemia and renal allograft rejection in patients without diabetes. *BMC Nephrol* 2000;1:1
 147. Chakkeri HA, Weil EJ, Castro J, et al. Hyperglycemia during the immediate period after kidney transplantation. *Clin J Am Soc Nephrol* 2009;4:853–859
 148. Wallia A, Illuri V, Molitch ME. Diabetes care after transplant: definitions, risk factors, and clinical management. *Med Clin North Am* 2016;100:535–550
 149. Kim HD, Chang J-Y, Chung BH, et al. Effect of everolimus with low-dose tacrolimus on development of new-onset diabetes after transplantation and allograft function in kidney transplantation: a multicenter, open-label, randomized trial. *Ann Transplant* 2021;26:e927984
 150. Cheng C-Y, Chen C-H, Wu M-F, et al. Risk factors in and long-term survival of patients with post-transplantation diabetes mellitus: a retrospective cohort study. *Int J Environ Res Public Health* 2020;17:E4581
 151. Gulsoy Kirnap N, Bozkus Y, Haberal M. Analysis of risk factors for posttransplant diabetes mellitus after kidney transplantation: single-center experience. *Exp Clin Transplant* 2020;18(Suppl. 1):36–40
 152. Munshi VN, Saghaian S, Cook CB, Eric Steidley D, Hardaway B, Chakkeri HA. Incidence, risk factors, and trends for postheart transplantation diabetes mellitus. *Am J Cardiol* 2020;125:436–440
 153. Kgosidialwa O, Blake K, O’Connell O, Egan J, O’Neill J, Hatunic M. Post-transplant diabetes mellitus associated with heart and lung transplant. *Ir J Med Sci* 2020;189:185–189
 154. Sharif A, Moore RH, Baboolal K. The use of oral glucose tolerance tests to risk stratify for new-onset diabetes after transplantation: an underdiagnosed phenomenon. *Transplantation* 2006;82:1667–1672
 155. Hecking M, Kainz A, Werzowa J, et al. Glucose metabolism after renal transplantation. *Diabetes Care* 2013;36:2763–2771
 156. Pham Vu T, Nguyen Thi Thuy D, Truong Quy K, et al. Serum hs-CRP measured prior transplantation predicts of new-onset diabetes after transplantation in renal transplant recipients. *Transpl Immunol* 2021;66:101392
 157. Grundman JB, Wolfsdorf JL, Marks BE. Post-transplantation diabetes mellitus in pediatric patients. *Horm Res Paediatr* 2020;93:510–518
 158. Galindo RJ, Fried M, Breen T, Tamler R. Hyperglycemia management in patients with posttransplantation diabetes. *Endocr Pract* 2016;22:454–465
 159. Jenssen T, Hartmann A. Emerging treatments for post-transplantation diabetes mellitus. *Nat Rev Nephrol* 2015;11:465–477
 160. Thomas MC, Mathew TH, Russ GR, Rao MM, Moran J. Early peri-operative glycaemic control and allograft rejection in patients with diabetes mellitus: a pilot study. *Transplantation* 2001;72:1321–1324
 161. Kurian B, Joshi R, Helmuth A. Effectiveness and long-term safety of thiazolidinediones and metformin in renal transplant recipients. *Endocr Pract* 2008;14:979–984
 162. Budde K, Neumayer H-H, Fritsche L, Sulowicz W, Stompôr T, Eckland D. The pharmacokinetics of pioglitazone in patients with impaired renal function. *Br J Clin Pharmacol* 2003;55:368–374
 163. Luther P, Baldwin D Jr. Pioglitazone in the management of diabetes mellitus after transplantation. *Am J Transplant* 2004;4:2135–2138
 164. Strøm Halden TA, Åsberg A, Vik K, Hartmann A, Jenssen T. Short-term efficacy and safety of sitagliptin treatment in long-term stable renal recipients with new-onset diabetes after transplantation. *Nephrol Dial Transplant* 2014;29:926–933
 165. Lane JT, Odegaard DE, Haire CE, Collier DS, Wrenshall LE, Stevens RB. Sitagliptin therapy in kidney transplant recipients with new-onset

- diabetes after transplantation. *Transplantation* 2011;92:e56–e57
166. Carmody D, Støp J, Greeley SAW, Bell GI, Philipson LH. Chapter 2 – A clinical guide to monogenic diabetes. In *Genetic Diagnosis of Endocrine Disorders*. 2nd ed. Weiss RE, Refetoff S, Eds. Academic Press, 2016, pp. 21–30
 167. De Franco E, Flanagan SE, Houghton JAL, et al. The effect of early, comprehensive genomic testing on clinical care in neonatal diabetes: an international cohort study. *Lancet* 2015;386:957–963
 168. Sanyoura M, Letourneau L, Knight Johnson AE, et al. GCK-MODY in the US Monogenic Diabetes Registry: description of 27 unpublished variants. *Diabetes Res Clin Pract* 2019;151:231–236
 169. Carmody D, Naylor RN, Bell CD, et al. GCK-MODY in the US National Monogenic Diabetes Registry: frequently misdiagnosed and unnecessarily treated. *Acta Diabetol* 2016;53:703–708
 170. Timsit J, Saint-Martin C, Dubois-Laforge D, Bellanné-Chantelot C. Searching for maturity-onset diabetes of the young (MODY): when and what for? *Can J Diabetes* 2016;40:455–461
 171. De Franco E, Caswell R, Johnson MB, et al. De novo mutations in *EIF2B1* affecting eIF2 signaling cause neonatal/early-onset diabetes and transient hepatic dysfunction. *Diabetes* 2020;69:477–483
 172. Valkovicova T, Skopkova M, Stanik J, Gasperikova D. Novel insights into genetics and clinics of the HNF1A-MODY. *Endocr Regul* 2019;53:110–134
 173. Shields BM, Hicks S, Shepherd MH, Colclough K, Hattersley AT, Ellard S. Maturity-onset diabetes of the young (MODY): how many cases are we missing? *Diabetologia* 2010;53:2504–2508
 174. Awa WL, Schober E, Wiegand S, et al. Reclassification of diabetes type in pediatric patients initially classified as type 2 diabetes mellitus: 15 years follow-up using routine data from the German/Austrian DPV database. *Diabetes Res Clin Pract* 2011;94:463–467
 175. Shepherd M, Shields B, Hammersley S, et al.; UNITED Team. Systematic population screening, using biomarkers and genetic testing, identifies 2.5% of the U.K. pediatric diabetes population with monogenic diabetes. *Diabetes Care* 2016;39:1879–1888
 176. SEARCH Study Group. SEARCH for Diabetes in Youth: a multicenter study of the prevalence, incidence and classification of diabetes mellitus in youth. *Control Clin Trials* 2004;25:458–471
 177. Pihoker C, Gilliam LK, Ellard S, et al.; SEARCH for Diabetes in Youth Study Group. Prevalence, characteristics and clinical diagnosis of maturity onset diabetes of the young due to mutations in HNF1A, HNF4A, and glucokinase: results from the SEARCH for Diabetes in Youth. *J Clin Endocrinol Metab* 2013;98:4055–4062
 178. Draznin B (Ed.). *Atypical Diabetes: Pathophysiology, Clinical Presentations, and Treatment Options*. Arlington, VA, American Diabetes Association, 2018
 179. Exeter Diabetes. MODY Probability Calculator. Accessed 15 October 2021. Available from <https://www.diabetesgenes.org/exeter-diabetes-app/ModyCalculator>
 180. Urbanová J, Rypácková B, Procházková Z, et al. Positivity for islet cell autoantibodies in patients with monogenic diabetes is associated with later diabetes onset and higher HbA1c level. *Diabet Med* 2014;31:466–471
 181. Naylor RN, John PM, Winn AN, et al. Cost-effectiveness of MODY genetic testing: translating genomic advances into practical health applications. *Diabetes Care* 2014;37:202–209
 182. Shields BM, Shepherd M, Hudson M, et al.; UNITED study team. Population-based assessment of a biomarker-based screening pathway to aid diagnosis of monogenic diabetes in young-onset patients. *Diabetes Care* 2017;40:1017–1025
 183. Hattersley A, Bruining J, Shield J, Njolstad P, Donaghue KC. The diagnosis and management of monogenic diabetes in children and adolescents. *Pediatr Diabetes* 2009;10(Suppl. 12):33–42
 184. Rubio-Cabezas O, Hattersley AT, Njolstad PR, et al.; International Society for Pediatric and Adolescent Diabetes. ISPAD Clinical Practice Consensus Guidelines 2014. The diagnosis and management of monogenic diabetes in children and adolescents. *Pediatr Diabetes* 2014;15(Suppl. 20):47–64
 185. Steele AM, Shields BM, Shepherd M, Ellard S, Hattersley AT, Pearson ER. Increased all-cause and cardiovascular mortality in monogenic diabetes as a result of mutations in the HNF1A gene. *Diabet Med* 2010;27:157–161
 186. Anök A, Çatlö G, Abacı A, Böber E. Maturity-onset diabetes of the young (MODY): an update. *J Pediatr Endocrinol Metab* 2015;28:251–263
 187. Greeley SAW, Naylor RN, Philipson LH, Bell GI. Neonatal diabetes: an expanding list of genes allows for improved diagnosis and treatment. *Curr Diab Rep* 2011;11:519–532
 188. Le Bodic L, Bignon JD, Raguénès O, et al. The hereditary pancreatitis gene maps to long arm of chromosome 7. *Hum Mol Genet* 1996;5:549–554
 189. Hardt PD, Brendel MD, Kloer HU, Bretzel RG. Is pancreatic diabetes (type 3c diabetes) underdiagnosed and misdiagnosed? *Diabetes Care* 2008;31(Suppl. 2):S165–S169
 190. Woodmansey C, McGovern AP, McCullough KA, et al. Incidence, demographics, and clinical characteristics of diabetes of the exocrine pancreas (type 3c): a retrospective cohort study. *Diabetes Care* 2017;40:1486–1493
 191. Duggan SN, Ewald N, Kelleher L, Griffin O, Gibney J, Conlon KC. The nutritional management of type 3c (pancreatogenic) diabetes in chronic pancreatitis. *Eur J Clin Nutr* 2017;71:3–8
 192. Makuc J. Management of pancreatogenic diabetes: challenges and solutions. *Diabetes Metab Syndr Obes* 2016;9:311–315
 193. Andersen DK, Korc M, Petersen GM, et al. Diabetes, pancreatogenic diabetes, and pancreatic cancer. *Diabetes* 2017;66:1103–1110
 194. Petrov MS, Basina M. Diagnosis of endocrine disease: diagnosing and classifying diabetes in diseases of the exocrine pancreas. *Eur J Endocrinol* 2021;184:R151–R163
 195. 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
 196. Anazawa T, Okajima H, Masui T, Uemoto S. Current state and future evolution of pancreatic islet transplantation. *Ann Gastroenterol Surg* 2018;3:34–42
 197. 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
 198. Huvinen E, Koivusalo SB, Meinilä J, et al. Effects of a lifestyle intervention during pregnancy and first postpartum year: findings from the RADIEL Study. *J Clin Endocrinol Metab* 2018;103:1669–1677
 199. Feig DS, Hwee J, Shah BR, Booth GL, Bierman AS, Lipscombe LL. Trends in incidence of diabetes in pregnancy and serious perinatal outcomes: a large, population-based study in Ontario, Canada, 1996–2010. *Diabetes Care* 2014;37:1590–1596
 200. Peng TY, Ehrlich SF, Crites Y, et al. Trends and racial and ethnic disparities in the prevalence of pregestational type 1 and type 2 diabetes in Northern California: 1996–2014. *Am J Obstet Gynecol* 2017;216:177.e1–177.e8
 201. Jovanović L, Liang Y, Weng W, Hamilton M, Chen L, Wintfeld N. Trends in the incidence of diabetes, its clinical sequelae, and associated costs in pregnancy. *Diabetes Metab Res Rev* 2015;31:707–716
 202. Poltavskiy E, Kim DJ, Bang H. Comparison of screening scores for diabetes and prediabetes. *Diabetes Res Clin Pract* 2016;118:146–153
 203. Mission JF, Catov J, Deihl TE, Feghali M, Scifres C. Early pregnancy diabetes screening and diagnosis: prevalence, rates of abnormal test results, and associated factors. *Obstet Gynecol* 2017;130:1136–1142
 204. Cho NH, Shaw JE, Karuranga S, et al. IDF Diabetes Atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Res Clin Pract* 2018;138:271–281
 205. Britton LE, Hussey JM, Crandell JL, Berry DC, Brooks JL, Bryant AG. Racial/ethnic disparities in diabetes diagnosis and glycemic control among women of reproductive age. *J Womens Health (Larchmt)* 2018;27:1271–1277
 206. Robbins C, Boulet SL, Morgan I, et al. Disparities in preconception health indicators - Behavioral Risk Factor Surveillance System, 2013–2015, and Pregnancy Risk Assessment Monitoring System, 2013–2014. *MMWR Surveill Summ* 2018;67:1–16
 207. Yuen L, Wong VW, Simmons D. Ethnic disparities in gestational diabetes. *Curr Diab Rep* 2018;18:68
 208. Wahabi HA, Fayed A, Esmaeil S, et al. Systematic review and meta-analysis of the effectiveness of pre-pregnancy care for women with diabetes for improving maternal and perinatal outcomes. *PLoS One* 2020;15:e0237571
 209. Zhu W-W, Yang H-X, Wei Y-M, et al. Evaluation of the value of fasting plasma glucose in the first prenatal visit to diagnose gestational diabetes mellitus in China. *Diabetes Care* 2013;36:586–590
 210. Hughes RCE, Moore MP, Gullam JE, Mohamed K, Rowan J. An early pregnancy HbA_{1c} $\geq 5.9\%$ (41 mmol/mol) is optimal for detecting diabetes and identifies women at increased risk of adverse pregnancy outcomes. *Diabetes Care* 2014;37:2953–2959

211. Mañé L, Flores-Le Roux JA, Gómez N, et al. Association of first-trimester HbA1c levels with adverse pregnancy outcomes in different ethnic groups. *Diabetes Res Clin Pract* 2019;150:202–210
212. Boe B, Barbour LA, Allshouse AA, Heyborne KD. Universal early pregnancy glycosylated hemoglobin A1c as an adjunct to Carpenter-Coustan screening: an observational cohort study. *Am J Obstet Gynecol* 2019;124:205–214
213. Immanuel J, Simmons D. Screening and treatment for early-onset gestational diabetes mellitus: a systematic review and meta-analysis. *Curr Diab Rep* 2017;17:115
214. Yefet E, Jeda E, Tzur A, Nachum Z. Markers for undiagnosed type 2 diabetes mellitus during pregnancy—a population-based retrospective cohort study. *J Diabetes* 2020;12:205–214
215. Kattini R, Hummelen R, Kelly L. Early gestational diabetes mellitus screening with glycated hemoglobin: a systematic review. *J Obstet Gynaecol Can* 2020;42:1379–1384
216. Chen L, Pocobelli G, Yu O, et al. Early pregnancy hemoglobin A1C and pregnancy outcomes: a population-based study. *Am J Perinatol* 2019;36:1045–1053
217. Osmundson SS, Zhao BS, Kunz L, et al. First trimester hemoglobin A1c prediction of gestational diabetes. *Am J Perinatol* 2016;33:977–982
218. McIntyre HD, Sacks DA, Barbour LA, et al. Issues with the diagnosis and classification of hyperglycemia in early pregnancy. *Diabetes Care* 2016;39:53–54
219. Cavagnoli G, Pimentel AL, Freitas PAC, Gross JL, Camargo JL. Factors affecting A1C in non-diabetic individuals: review and meta-analysis. *Clin Chim Acta* 2015;445:107–114
220. Buchanan TA, Xiang A, Kjos SL, Watanabe R. What is gestational diabetes? *Diabetes Care* 2007;30(Suppl. 2):S105–S111
221. Noctor E, Crowe C, Carmody LA, et al.; ATLANTIC-DIP investigators. Abnormal glucose tolerance post-gestational diabetes mellitus as defined by the International Association of Diabetes and Pregnancy Study Groups criteria. *Eur J Endocrinol* 2016;175:287–297
222. Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. *Diabetes Care* 2002;25:1862–1868
223. Ratner RE, Christophi CA, Metzger BE, et al.; Diabetes Prevention Program Research Group. Prevention of diabetes in women with a history of gestational diabetes: effects of metformin and lifestyle interventions. *J Clin Endocrinol Metab* 2008;93:4774–4779
224. Aroda VR, Christophi CA, Edelstein SL, et al.; Diabetes Prevention Program Research Group. The effect of lifestyle intervention and metformin on preventing or delaying diabetes among women with and without gestational diabetes: the Diabetes Prevention Program outcomes study 10-year follow-up. *J Clin Endocrinol Metab* 2015;100:1646–1653
225. Wang C, Wei Y, Zhang X, et al. A randomized clinical trial of exercise during pregnancy to prevent gestational diabetes mellitus and improve pregnancy outcome in overweight and obese pregnant women. *Am J Obstet Gynecol* 2017;216:340–351
226. Metzger BE, Lowe LP, Dyer AR, et al.; HAPO Study Cooperative Research Group. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med* 2008;358:1991–2002
227. O'Sullivan JB, Mahan CM. Criteria for the oral glucose tolerance test in pregnancy. *Diabetes* 1964;13:278–285
228. Sacks DA, Hadden DR, Maresh M, et al.; HAPO Study Cooperative Research Group. Frequency of gestational diabetes mellitus at collaborating centers based on IADPSG consensus panel-recommended criteria: the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. *Diabetes Care* 2012;35:526–528
229. Brown FM, Wyckoff J. Application of one-step IADPSG versus two-step diagnostic criteria for gestational diabetes in the real world: impact on health services, clinical care, and outcomes. *Curr Diab Rep* 2017;17:85
230. Lowe WL Jr, Scholtens DM, Lowe LP, et al.; HAPO Follow-up Study Cooperative Research Group. Association of gestational diabetes with maternal disorders of glucose metabolism and childhood adiposity. *JAMA* 2018;320:1005–1016
231. Lowe WL Jr, Scholtens DM, Kuang A, et al.; HAPO Follow-up Study Cooperative Research Group. Hyperglycemia and Adverse Pregnancy Outcome Follow-up Study (HAPO FUS): maternal gestational diabetes mellitus and childhood glucose metabolism. *Diabetes Care* 2019;42:372–380
232. Landon MB, Spong CY, Thom E, et al.; Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. A multicenter, randomized trial of treatment for mild gestational diabetes. *N Engl J Med* 2009;361:1339–1348
233. Crowther CA, Hillier JE, Moss JR, McPhee AJ, Jeffries WS; Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N Engl J Med* 2005;352:2477–2486
234. Hillier TA, Pedula KL, Ogasawara KK, et al. A pragmatic, randomized clinical trial of gestational diabetes screening. *N Engl J Med* 2021;384:895–904
235. Scholtens DM, Kuang A, Lowe LP, et al.; HAPO Follow-up Study Cooperative Research Group. Hyperglycemia and Adverse Pregnancy Outcome Follow-up Study (HAPO FUS): maternal glycemia and childhood glucose metabolism. *Diabetes Care* 2019;42:381–392
236. Josefson JL, Scholtens DM, Kuang A, et al.; HAPO Follow-up Study Cooperative Research Group. Newborn adiposity and cord blood C-peptide as mediators of the maternal metabolic environment and childhood adiposity. *Diabetes Care* 2021;44:1194–1202
237. Tam WH, Ma RCW, Ozaki R, et al. In utero exposure to maternal hyperglycemia increases childhood cardiometabolic risk in offspring. *Diabetes Care* 2017;40:679–686
238. Landon MB, Rice MM, Varner MW, et al.; Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units (MFMU) Network. Mild gestational diabetes mellitus and long-term child health. *Diabetes Care* 2015;38:445–452
239. Vandersten JP, Dodson WC, Espeland MA, et al. NIH consensus development conference: diagnosing gestational diabetes mellitus. *NIH Consens State Sci Statements* 2013;29:1–31
240. Committee on Practice Bulletins—Obstetrics. ACOG practice bulletin no. 190: gestational diabetes mellitus. *Obstet Gynecol* 2018;131:e49–e64
241. Donovan L, Hartling L, Muise M, Guthrie A, Vandermeer B, Dryden DM. Screening tests for gestational diabetes: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med* 2013;159:115–122
242. Khalafallah A, Phuah E, Al-Barazan AM, et al. Glycosylated haemoglobin for screening and diagnosis of gestational diabetes mellitus. *BMJ Open* 2016;6:e011059
243. Horvath K, Koch K, Jeitler K, et al. Effects of treatment in women with gestational diabetes mellitus: systematic review and meta-analysis. *BMJ* 2010;340:c1395
244. Carpenter MW, Coustan DR. Criteria for screening tests for gestational diabetes. *Am J Obstet Gynecol* 1982;144:768–773
245. National Diabetes Data Group. Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes* 1979;28:1039–1057
246. Harper LM, Mele L, Landon MB, et al.; Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units (MFMU) Network. Carpenter-Coustan compared with National Diabetes Data Group criteria for diagnosing gestational diabetes. *Obstet Gynecol* 2016;127:893–898
247. Werner EF, Pettker CM, Zuckerwise L, et al. Screening for gestational diabetes mellitus: are the criteria proposed by the International Association of the Diabetes and Pregnancy Study Groups cost-effective? *Diabetes Care* 2012;35:529–535
248. Duran A, Sáenz S, Torrejón MJ, et al. Introduction of IADPSG criteria for the screening and diagnosis of gestational diabetes mellitus results in improved pregnancy outcomes at a lower cost in a large cohort of pregnant women: the St. Carlos Gestational Diabetes Study. *Diabetes Care* 2014;37:2442–2450
249. Wei Y, Yang H, Zhu W, et al. International Association of Diabetes and Pregnancy Study Group criteria is suitable for gestational diabetes mellitus diagnosis: further evidence from China. *Chin Med J (Engl)* 2014;127:3553–3556
250. Feldman RK, Tieu RS, Yasumura L. Gestational diabetes screening: the International Association of the Diabetes and Pregnancy Study Groups compared with Carpenter-Coustan screening. *Obstet Gynecol* 2016;127:10–17
251. Saccone G, Khalifeh A, Al-Kouaty HB, Sendek K, Berghella V. Screening for gestational diabetes mellitus: one step versus two step approach. A meta-analysis of randomized trials. *J Matern Fetal Neonatal Med* 2020;33:1616–1624
252. Ethridge JK Jr, Catalano PM, Waters TP. Perinatal outcomes associated with the diagnosis of gestational diabetes made by the International Association of the Diabetes and Pregnancy Study Groups criteria. *Obstet Gynecol* 2014;124:571–578
253. Mayo K, Melamed N, Vandenberghe H, Berger H. The impact of adoption of the International Association of Diabetes in Pregnancy Study Group criteria for the screening and diagnosis of gestational diabetes. *Am J Obstet Gynecol* 2015;212:224.e1–224.e9
254. Hutchins J, Barajas RA, Hale D, Escaname E, Lynch J. Type 2 diabetes in a 5-year-old and single center experience of type 2 diabetes in youth under 10. *Pediatr Diabetes* 2017;18:674–677