Executive Summary: Guidelines and Recommendations for Laboratory Analysis in the Diagnosis and Management of Diabetes Mellitus

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BACKGROUND

Numerous laboratory tests are used in the diagnosis and management of patients with diabetes mellitus. The quality of the scientific evidence supporting the use of these assays varies substantially. An expert committee compiled evidence-based recommendations for laboratory analysis in patients with diabetes. The overall quality of the evidence and the strength of the recommendations were evaluated. The draft consensus recommendations were evaluated by invited reviewers and presented for public comment. Suggestions were incorporated as deemed appropriate by the authors (see Acknowledgments in the full version of the guideline). The guidelines were reviewed by the Evidence Based Laboratory Medicine Committee and the Board of Directors of the American Association of Clinical Chemistry and by the Professional Practice Committee of the American Diabetes Association.

CONTENT

Diabetes can be diagnosed by demonstrating increased concentrations of glucose in venous plasma or increased hemoglobin A_{1c} (HbA_{1c}) in the blood. Glycemic control is monitored by the patients measuring their own blood glucose with meters and/or with continuous interstitial glucose monitoring devices and also by laboratory analysis of HbA_{1c}. The potential roles of noninvasive glucose monitoring; genetic testing; and measurement of ketones, autoantibodies, urine albumin, insulin, proinsulin, and C-peptide are addressed.

SUMMARY

The guidelines provide specific recommendations based on published data or derived from expert consensus. Several analytes are found to have minimal clinical value at the present time, and measurement of them is not recommended.

Diabetes mellitus is a group of metabolic disorders of carbohydrate metabolism in which glucose is both underutilized and overproduced, resulting in hyperglycemia. The disease is classified conventionally into several clinical categories. Type 1 diabetes mellitus is usually caused by autoimmune destruction of the pancreatic islet β-cells, rendering the pancreas unable to synthesize and secrete insulin (1). Type 2 diabetes mellitus results from a combination of insulin resistance and inadequate insulin

secretion (2,3). Gestational diabetes mellitus (GDM) develops during approximately 17% of pregnancies, usually remits after delivery, and is a major risk factor for the development of type 2 diabetes later in life. Type 2 is the most common form of diabetes, accounting for 85% to 95% of diabetes in developed countries.

Diabetes is a common disease. Worldwide prevalence in 2021 was estimated to be approximately 537 million (10.5% of the global population) and is forecast to reach 783 million by 2045 (4). Based on 2017–2020 National Health and Nutrition Examination Survey data and 2018–2019 National Health Interview Survey data, the U.S. Centers for Disease Control and Prevention estimated that there were 37.3 million people (11.3% of the U.S. population) with diabetes (5). The number of adults with diabetes has also increased in other parts of the world. For example, China and India were thought to have 140.9 and 74.2 million adults with diabetes in 2021 and are expected to have 174.4 and 124.9 million, respectively, by 2045 (4). Approximately 45% of people with diabetes worldwide are thought to be undiagnosed (4).

The cost of diabetes in the U.S. in 2012 was approximately $245 billion and increased to $327 billion by 2017 (6). The mean annual per capita health care costs for an individual with diabetes are approximately 2.3-fold higher than those for individuals who do not have diabetes (7). Worldwide spending in 2021 was thought to be $966 billion. The high costs of diabetes are attributable primarily to the chronic debilitating microvascular and macrovascular complications (6), which make diabetes the fourth most common cause of death in the developed world (8). About 6.7 million adults worldwide were thought to have died of diabetes-related causes in 2021 (4).

The American Association of Clinical Chemistry and American Diabetes Association issued "Guidelines and Recommendations for Laboratory Analysis in the Diagnosis and Management of Diabetes Mellitus" in 2002 (9,10) and 2011 (11,12). Here we review and update these recommendations using an evidence-based approach, especially in those areas where new evidence has emerged since the 2011 publications (13). The guideline committee, whose membership was predominantly from the U.S., included clinical, laboratory, and evidence-based guideline methodology experts. Members of the guideline committee have disclosed any financial, personal, or professional relationships that may constitute conflicts of interest with this guideline and received no direct funding related to the development of the recommendations. The perspectives and views of various international and national organizations, as well as other potential stakeholders (e.g., health care providers, people with diabetes, policymakers, regulatory bodies, health insurance companies, researchers, and industry), were taken into account during the public consultation process. The system developed in 2011 to grade both the overall quality of the evidence (Table 1) and the strength of recommendations (Table 2) was used, and the key steps and evidence summaries are detailed in the guideline and in the Supplementary Material that accompanies the online version of this report (13). The literature was reviewed to the end of 2021.

This guideline focuses on the practical aspects of care in order to assist with decisions regarding the use or interpretation of laboratory tests while screening, diagnosing, or monitoring patients with diabetes. It covers the rationale, preanalytical, analytical, postanalytical, and, where applicable, emerging considerations, which alert the reader to ongoing studies and potential future aspects relevant to each analyte. The recommendations intend to supplement the American Diabetes Association guidelines and thus do not address any issues related to the clinical management of patients. The full version of this guideline and its accompanying supplements are available as a Special Report (13). Key recommendations are summarized.

These recommendations primarily target laboratory professionals, general practitioners, physicians, nurses, and other health care practitioners involved in the care of people with diabetes. The guidelines can be used by individuals with diabetes (where relevant, e.g., self-monitoring of blood glucose), policymakers, and payers for health care, as well as by researchers and manufacturers. Although recommendations were developed for national and international use and are intended to be generic, certain recommendations may not reflect views that are universally held or may have limited applicability in health care settings with differing organizational, cultural, and economic backgrounds. The guideline committee therefore advises users to adapt recommendations to local settings.

RECOMMENDATIONS

Capital letters denote the grade of recommendations and categories in parentheses refer to the quality of the underlying body of evidence supporting each recommendation. The grading system is described in Tables 1 and 2.

1. Glucose

a. Fasting glucose should be measured in venous plasma when used to establish the diagnosis of diabetes, with a value >7.0 mmol/L (>126 mg/dL) diagnostic of diabetes. **A (high)**
b. Screening by hemoglobin A_{1c} (HbA_{1c}), fasting plasma glucose (FPG), or 2-h oral glucose tolerance test is recommended for individuals who are at high risk of diabetes. If HbA_{1c} is <5.7% (<39 mmol/mol), FPG is <5.6 mmol/L (<100 mg/dL), and/or 2-h plasma glucose is <7.8 mmol/L (<140 mg/dL), testing should be repeated at 3-year intervals. **B (moderate)**
c. Glucose should be measured in venous plasma when used for screening of high-risk individuals. **B (moderate)**
d. Plasma glucose should be measured in an accredited laboratory when used for diagnosis of or screening for diabetes. **Good Practice Point (GPP)**
e. Routine measurement of plasma glucose concentrations in a laboratory is not recommended as the primary means of monitoring or evaluating therapy in individuals with diabetes. **B (moderate)**
f. Blood for fasting plasma glucose analysis should be drawn in the morning after the subject has fasted overnight (at least 8 h). **B (low)**
g. To minimize glycolysis, a tube containing a rapidly effective glycolytic inhibitor such as granulated citrate buffer should be used for collecting the sample. If this cannot be achieved, the sample tube should immediately be placed in an ice-water slurry and subjected to centrifugation to remove the cells within 15–30 min. Tubes with only enolase inhibitors such as sodium fluoride should not be relied on to prevent glycolysis. **B (moderate)**
h. Based on biological variation, glucose measurement should have analytical imprecision ≤2.4%, bias ≤2.1%, and total error ≤6.1%. To avoid misclassification

Table 1—Rating scale for the quality of the evidence

High: Further research is very unlikely to change our confidence in the estimate of effect. The body of evidence comes from high high-level individual studies which are sufficiently powered; provide precise, consistent, and directly applicable results in a relevant population.
Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate and the recommendation. The body of evidence comes from high/moderate moderate-level individual studies which are sufficient to determine effects, but the strength of the evidence is limited by the number, quality, or consistency of the included studies; generalizability of results to routine practice; or indirect nature of the evidence.
Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate and the recommendation. The body of evidence is of low level and comes from studies with serious design flaws, or evidence is indirect.
Very low: Any estimate of effect is very uncertain. Recommendation may change when higher quality evidence becomes available. Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information.

of individuals, the goal for glucose analysis should be to minimize total analytical error, and methods should be without measurable bias. **B (moderate)**

2. Glucose Meters

a. Portable glucose meters should not be used in the diagnosis of diabetes, including gestational diabetes. **B (moderate)**

b. Frequent blood glucose monitoring (BGM) is recommended for all people with diabetes who use intensive insulin regimens (with multiple daily injections

Table 2—Grading the strength of recommendations

A. STRONGLY RECOMMEND

a. adoption when:
- There is high high-quality evidence and strong or very strong agreement of experts that the intervention improves important health outcomes and that benefits substantially outweigh harms; or
- There is moderate moderate-quality evidence and strong or very strong agreement of experts that the intervention improves important health outcomes and that benefits substantially outweigh harms.

b. against adoption when:
- There is high high-quality evidence and strong or very strong agreement of experts that the intervention is ineffective or that benefits are closely balanced with harms, or that harms clearly outweigh benefits; or
- There is moderate moderate-quality evidence and strong or very strong agreement of experts that the intervention is ineffective or that benefits are closely balanced with harms, or that harms outweigh benefits.

B. RECOMMEND

a. adoption when:
- There is moderate moderate-quality evidence and level of agreement of experts that the intervention improves important health outcomes and that benefits outweigh harms; or
- There is low low-quality evidence but strong or very strong agreement and high level of confidence of experts that the intervention improves important health outcomes and that benefits outweigh harms; or
- There is very low-quality evidence but very strong agreement and a very high level of confidence of experts that the intervention improves important health outcomes and that benefits outweigh harms.

b. against adoption when:
- There is moderate moderate-quality evidence and level of agreement of experts that the intervention is ineffective or that benefits are closely balanced with harms, or that harms outweigh benefits; or
- There is low low-quality evidence but strong or very strong agreement and a high level of confidence of experts that the intervention is ineffective or that benefits are closely balanced with harms, or that harms outweigh benefits; or
- There is very low-quality evidence but very strong agreement and very high levels of confidence of experts that the intervention is ineffective or that benefits are closely balanced with harms, or that harms outweigh benefits.

C. THERE IS INSUFFICIENT INFORMATION TO MAKE A RECOMMENDATION

Grade C is applied in the following circumstances:
- Evidence is lacking or scarce or of very low quality, and the balance of benefits and harms cannot be determined, and there is no or very low level of agreement of experts for or against adoption of the recommendation.
- At any level of evidence—particularly if the evidence is heterogeneous or inconsistent, indirect, or inconclusive—if there is no agreement of experts for or against adoption of the recommendation.

GPP. GOOD PRACTICE POINT

Good Practice Points (GPPs) are recommendations mostly driven by expert consensus and professional agreement and are based on the information listed below listed information and/or professional experience, or widely accepted standards of best practice. This category mostly applies to technical (e.g., preanalytical, analytical, postanalytical), organizational, economic, or quality management aspects of laboratory practice. In these cases, evidence often comes from observational studies, audit reports, case series or case studies, nonsystematic reviews, guidance or technical documents, non-evidence–based guidelines, personal opinions, expert consensus, or position statements. Recommendations are often based on empirical data, usual practice, quality requirements and standards set by professional or legislative authorities or accreditation bodies, etc.

or insulin pump therapy) and who are not using continuous glucose monitoring (CGM). **A (high)**

c. Routine use of BGM is not recommended for people with type 2 diabetes treated with diet and/or oral agents alone. **A (high)**

d. Individuals with diabetes should be instructed in the correct use of glucose meters, including technique of sample collection and use of quality control. **GPP**

e. Glucose meters should report the glucose concentrations in plasma rather than in whole blood to facilitate comparison with plasma results of assays performed in accredited laboratories. **GPP**

f. Glucose meters should meet relevant accuracy standards of the U.S. Food and Drug Administration in the U.S. or comparable analytical performance specifications in other locations. **GPP**

g. In hospitals and acute-care facilities, point-of-care testing personnel, including nurses, should use glucose meters that are intended for professional use. **GPP**

h. When testing newborns, personnel should use only meters that are intended for use in newborns. **GPP**

i. Unless CGM is used, people using multiple daily injections of insulin should be encouraged to perform BGM at a frequency appropriate for their insulin dosage regimen, typically at least 4 times per day. **B (moderate)**

j. Manufacturers should continue to improve the analytical performance of meters. **GPP**

3. Continuous Glucose Monitoring

a. Real-time CGM should be used in conjunction with insulin as a tool to lower HbA_{1c} concentrations and/or reduce hypoglycemia in teens and adults with type 1 diabetes who are not meeting glycemic targets or have hypoglycemia unawareness and/or episodes of hypoglycemia. **A (high)**

b. Consider using intermittently scanned CGM in conjunction with insulin as a tool to lower HbA_{1c} concentrations and/or reduce hypoglycemia in adults with type 1 diabetes who are not meeting glycemic targets or have hypoglycemia unawareness and/or episodes of hypoglycemia. **B (moderate)**

c. Consider using real-time CGM to improve HbA_{1c} levels, time in range, and neonatal outcomes in pregnant women with type 1 diabetes. **B (moderate)**

d. Consider using real-time CGM and intermittently scanned CGM to lower HbA_{1c} and/or reduce hypoglycemia in adults with type 2 diabetes who are using insulin and not meeting glycemic targets. **B (moderate)**

e. Consider real-time-CGM or intermittently scanned CGM in children with type 1 diabetes, based on regulatory approval, as an additional tool to help improve glucose control and reduce the risk of hypoglycemia. **B (low)**

f. Consider using professional CGM data coupled with diabetes self-management education and medication dose adjustment to identify and address patterns of hyper- and hypoglycemia in people with type 1 or type 2 diabetes. **GPP**

g. For individuals using CGM devices that require calibration by users, a blood glucose meter should be used to calibrate the CGM. Calibration should be done at a time when glucose is not rising or falling rapidly. For all individuals using CGM, BGM should be done during periods when CGM results are not available or are incomplete, or when the CGM results are inconsistent with the clinical state or suspected to be inaccurate. **GPP**

h. CGM data reports should be available in consistent formats that include standard metrics such as time in range, time in hyperglycemia, time in hypoglycemia, mean glucose, and coefficient of variation. **GPP**

4. Noninvasive Glucose Sensing

a. Overall, noninvasive glucose measurement systems cannot be recommended as replacements for either BGM or CGM technologies at this time. **C (very low)**

5. Gestational Diabetes Mellitus

a. All pregnant women with risk factors for diabetes should be tested for undiagnosed prediabetes and diabetes at the first prenatal visit using standard diagnostic criteria. **A (moderate)**

b. All pregnant women not previously known to have diabetes should be evaluated for gestational diabetes mellitus (GDM) at 24 to 28 weeks of gestation. **A (high)**

c. Either the one-step or two-step protocol may be used, depending on regional preferences. **A (moderate)**

d. Women with GDM should perform fasting and postprandial BGM for optimal glucose control. **B (low)**

e. Target glucose values are fasting plasma glucose <5.3 mmol/L (<95 mg/dL) and either 1-h postprandial <7.8 mmol/L (<140 mg/dL) or 2-h postprandial <6.7 mmol/L (<120 mg/dL). **B (low)**

f. Women with GDM should be tested for prediabetes or diabetes 4–12 weeks postpartum using nonpregnant oral glucose tolerance test criteria. **A (moderate)**

g. Lifelong screening for diabetes should be performed in women with a history of GDM using standard nonpregnant criteria at least every 3 years. **A (high)**

h. There is ongoing research, but insufficient evidence at this time, to recommend testing for GDM before 20 weeks of gestation. **C (low)**

6. Urine Glucose

a. Urine glucose testing is not recommended for routine care of patients with diabetes mellitus. **B (low)**

7. Ketone Testing

a. Individuals who are prone to ketosis (those with type 1 diabetes, history of diabetic ketoacidosis [DKA], or treated with sodium-glucose transport protein 2 inhibitors) should measure ketones in urine or blood if they have unexplained hyperglycemia or symptoms of ketosis (abdominal pain, nausea) and implement sick-day rules and/or seek medical advice if urine or blood ketones are increased. **B (moderate)**

b. Specific measurement of β-hydroxybutyrate in blood should be used for diagnosis of DKA and may be used for monitoring during treatment of DKA. **B (moderate)**

c. Blood ketone determinations that rely on the nitroprusside reaction should not be used to monitor treatment of DKA. **B (low)**

8. Hemoglobin A_{1c}

a. Laboratory-based HbA_{1c} testing can be used to diagnose (a) diabetes, with a value $\geq 6.5\%$ (≥ 48 mmol/mol) diagnostic

of diabetes, and (b) prediabetes (or high risk for diabetes) with an HbA_{1c} level of 5.7% to 6.4% (39–46 mmol/mol). An NGSP-certified method should be performed in an accredited laboratory. **A (moderate)**

b. Point-of-care HbA_{1c} testing for diabetes screening and diagnosis should be restricted to FDA-approved devices at CLIA-certified laboratories that perform testing of moderate complexity or higher. **B (low)**
c. HbA_{1c} should be measured routinely (usually every 3 months until acceptable, individualized targets are achieved and then no less than every 6 months) in most individuals with diabetes mellitus to document their degree of glycemic control. **A (moderate)**
d. Treatment goals should be based on American Diabetes Association recommendations which include maintaining HbA_{1c} concentrations $<7\%$ (<53 mmol/mol) for many nonpregnant people with diabetes and more stringent goals in selected individuals if this can be achieved without significant hypoglycemia or other adverse effects of treatment. (Note that these values are applicable only if the assay method is certified by the NGSP as traceable to the Diabetes Control and Complications Trial reference.) **A (high)**
e. Higher target ranges are recommended for children and adolescents and are appropriate for individuals with limited life expectancy, extensive comorbid illnesses, a history of severe hypoglycemia, and advanced complications. **A (high)**
f. During pregnancy and in preparation for pregnancy, women with diabetes should try to achieve HbA_{1c} goals that are more stringent than in the nonpregnant state, aiming ideally for $<6.0\%$ (<42 mmol/mol) during pregnancy to protect the fetus from congenital malformations and the baby and mother from perinatal trauma and morbidity owing to large-for-date babies. **A (moderate)**
g. Laboratories should be aware of potential interferences, including hemoglobin variants that may affect HbA_{1c} test results depending on the method used. In selecting assay methods, laboratories should consider the potential for interferences in their particular patient population. **GPP**
h. HbA_{1c} measurements in individuals with disorders that affect red blood cell turnover may provide spurious (generally falsely low) results regardless of the method used, and glucose testing will be necessary for screening, diagnosis, and management. **GPP**
i. Assays of other glycated proteins, such as fructosamine or glycated albumin, may be used in clinical settings where abnormalities in red blood cell turnover, hemoglobin variants, or other interfering factors compromise interpretation of HbA_{1c} test results, although they reflect a shorter period of average glycemia than HbA_{1c}. **GPP**
j. HbA_{1c} cannot be measured and should not be reported in individuals who do not have hemoglobin A, e.g., those with homozygous hemoglobin variants, such as hemoglobin SS or hemoglobin EE; glycated proteins, such as fructosamine or glycated albumin, may be used. **GPP**
k. Laboratories should use only HbA_{1c} assay methods that are certified by the NGSP as traceable to the Diabetes Control and Complications Trial reference. The manufacturers of HbA_{1c} assays should also show traceability to the International Federation of Clinical Chemistry and Laboratory Medicine reference method. **GPP**
l. Laboratories that measure HbA_{1c} should participate in an accuracy-based proficiency-testing program that uses fresh whole blood samples with targets set by the NGSP Laboratory Network. **GPP**
m. The goals for imprecision for HbA_{1c} measurement are intralaboratory CV $<1.5\%$ and interlaboratory CV $<2.5\%$ (using at least 2 control samples with different HbA_{1c} concentrations) and ideally no measurable bias. **B (low)**
n. HbA_{1c} should be reported as a percentage of total hemoglobin or as mmol/mol of total hemoglobin. **GPP**
o. HbA_{1c} may also be reported as estimated average glucose to facilitate comparison with the self-monitoring results obtained by patients and make the interpretation of the HbA_{1c} more accessible to people with diabetes. **GPP**
p. Laboratories should verify by repeat testing specimens with HbA_{1c} results below the lower limit of the reference interval or greater than 15% (140 mmol/mol) HbA_{1c}. **GPP**

9. Genetic Markers

a. Routine determination of genetic markers such as HLA genes or single nucleotide polymorphisms is of no value at this time for the diagnosis or management of patients with type 1 diabetes. Typing for genetic markers and the use of genetic risk scores are recommended for individuals who cannot be clearly classified as having type 1 or type 2 diabetes. **A (moderate)**
b. For selected diabetes syndromes, including neonatal diabetes and maturity-onset diabetes of the young, valuable information including treatment options can be obtained with definition of diabetes-associated mutations. **A (moderate)**
c. There is no role for routine genetic testing in people with type 2 diabetes. These studies should be confined to the research setting and evaluation of specific syndromes. **A (moderate)**

10. Autoimmune Markers

a. Standardized islet autoantibody tests are recommended for classification of diabetes in adults in whom there is phenotypic overlap between type 1 and type 2 diabetes and uncertainty as to the type of diabetes. **GPP**
b. Islet autoantibodies are not recommended for routine diagnosis of diabetes. **B (low)**
c. Longitudinal follow-up of subjects with two or more islet autoantibodies is recommended to stage diabetes into stage 1: two or more islet autoantibodies, normoglycemia, no symptoms; stage 2: two or more islet autoantibodies, dysglycemia, no symptoms; and stage 3: two or more islet autoantibodies, diabetes and symptoms. **GPP**
d. Standardized islet autoantibody tests are recommended in prospective studies of children at increased genetic risk of type 1 diabetes following HLA typing at birth or in first-degree relatives of individuals with type 1 diabetes. **B (low)**
e. Screening for islet autoantibodies in relatives of individuals with type 1 diabetes or in people in the general population is recommended in the setting of a research study or can be offered as an option for first-degree relatives of a proband with type 1 diabetes. **B (low)**

f. Routine screening for islet autoantibodies in people with type 2 diabetes is not recommended at present. **B (low)**
g. There is currently no role for measurement of islet autoantibodies in the monitoring of individuals with established type 1 diabetes. **B (low)**
h. It is important that islet autoantibodies be measured only in an accredited laboratory with an established quality control program and participation in a proficiency testing program. **GPP**

11. Urine Albumin

a. Annual testing for albuminuria should begin in pubertal or post-pubertal individuals 5 years after diagnosis of type 1 diabetes and at the time of diagnosis of type 2 diabetes, regardless of treatment. **A (high)**
b. Urine albumin should be measured annually in adults with diabetes using morning spot urine albumin-to-creatinine ratio (uACR). **A (high)**
c. If estimated glomerular filtration rate is $<$60 mL/min/1.73 m^2 and/or albuminuria is $>$30 mg/g creatinine in a spot urine sample, the uACR should be repeated every 6 months to assess change among people with diabetes and hypertension. **A (moderate)**
d. First morning void urine sample should be used for measurement of albumin-to-creatinine ratio. **A (moderate)**
e. If first morning void sample is difficult to obtain, to minimize variability in test results, all urine collections should be at the same time of day. The individual should be well hydrated and should not have ingested food within the preceding 2 h or have exercised. **GPP**
f. Timed collection for urine albumin should be done only in research settings and should not be used to guide clinical practice. **GPP**
g. The analytical performance goals for urine albumin measurement should be between-day precision $\leq$6%, bias $\leq$7% to 13%, and total allowable error $\leq$24% to 30%. **GPP**
h. Semiquantitative uACR dipsticks can be used to detect early kidney disease and assess cardiovascular risk when quantitative tests are not available. **B (moderate)**
i. Semiquantitative or qualitative screening tests should be positive in $>$85% of individuals with moderately increased albuminuria to be useful for patient screening. **B (moderate)**
j. Practitioners should strictly adhere to manufacturer's instructions when using a semiquantitative uACR dipstick test and repeat it for confirmation to achieve adequate sensitivity for detecting moderately increased albuminuria. **B (moderate)**
k. Positive urine albumin screening results by semiquantitative tests should be confirmed by quantitative analysis in an accredited laboratory. **GPP**
l. Currently available proteinuria dipstick tests should not be used to assess albuminuria. **B (moderate)**

12. Miscellaneous Potentially Important Analytes

a. In most people with diabetes or at risk for diabetes or cardiovascular disease, routine testing for insulin or proinsulin is not recommended. These assays are useful primarily for research purposes. **B (moderate)**
b. Although differentiation between type 1 and type 2 diabetes can usually be made based on the clinical presentation and subsequent course, C-peptide measurements may help distinguish type 1 from type 2 diabetes in ambiguous cases, such as individuals who have a type 2 phenotype but present in ketoacidosis. **B (moderate)**
c. If required by the payer for coverage of insulin pump therapy, measure fasting C-peptide level when simultaneous fasting plasma glucose is 12.5 mmol/L ($<$220 mg/dL). **GPP**
d. Insulin and C-peptide assays should be standardized to facilitate measures of insulin secretion and sensitivity that will be comparable across research studies. **GPP**
e. There is no published evidence to support the use of insulin antibody testing for routine care of people with diabetes. **C (very low)**

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