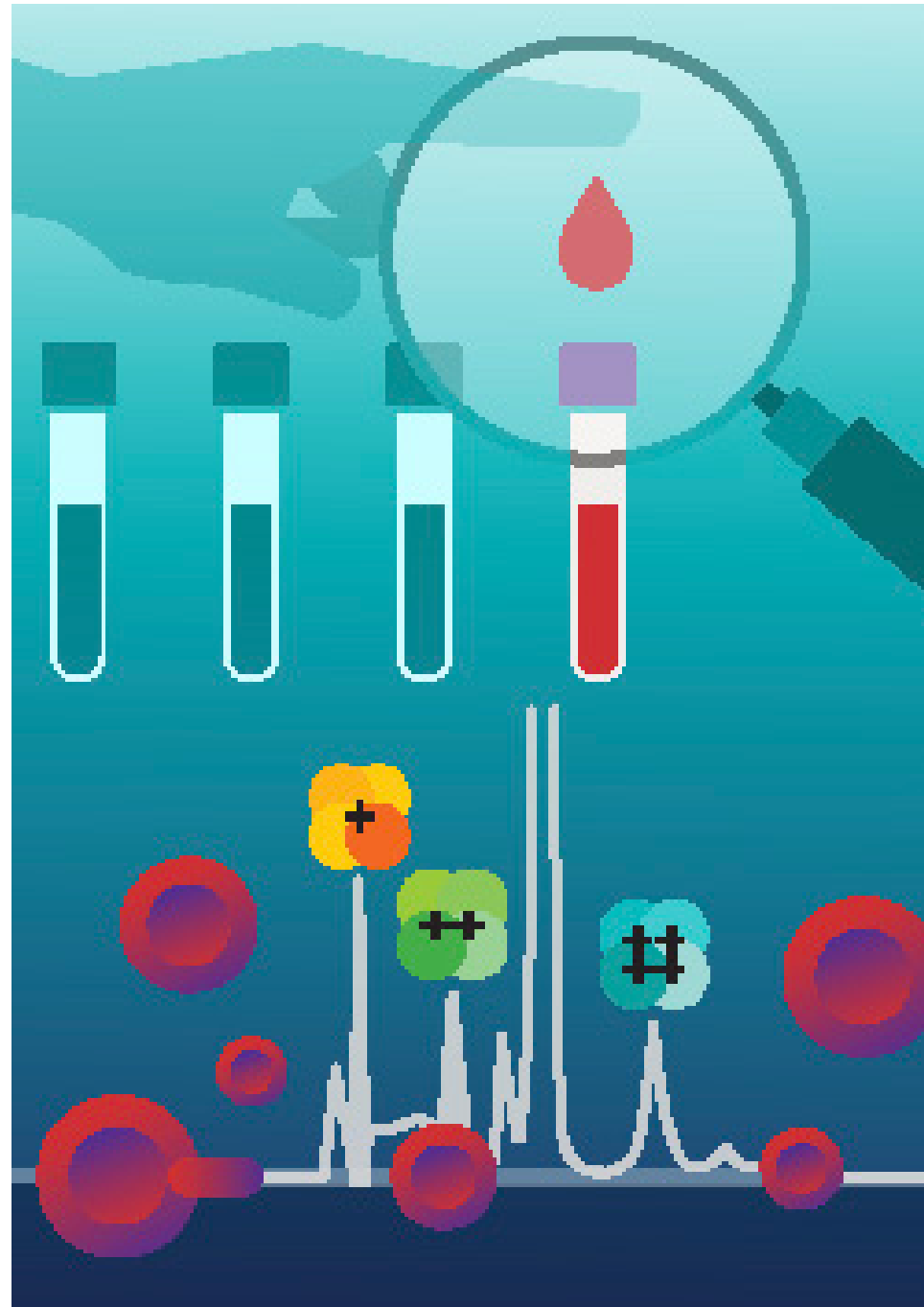


Keeping You Informed

The importance of hemoglobin A1c testing in the screening, diagnosis, and monitoring of patients living with diabetes

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Quick Take Aways

- Prevalence of diabetes continues to increase, with many cases going undiagnosed
- Following American Diabetes Association (ADA) screening guidelines, such as starting testing at age 35, allows for early detection and treatment to avoid worsening of complications caused by diabetes
- DCCT and UKPDS set HbA1c analysis as the standard that should be used to manage patients with diabetes
- The ADA recommends HbA1c methods that are certified by the NGSP (formerly: the National Glycohemoglobin Standardization Program)

Diabetes Prevalence

The prevalence of diabetes continues to increase. The International Diabetes Federation (IDF) estimates that 10% of the world's population presently is affected by diabetes. By 2045, nearly 800 million adults will be living with diabetes.¹ Because type 2 diabetes may not have symptoms in its early stages, type 2 diabetes may go undiagnosed for several years. Currently 1 in approximately every 2 people with diabetes is not diagnosed.¹

Diabetes Complications

As diabetes progresses, it causes long-term damage to various organs, including the eyes, kidneys, nerves, heart, liver, and blood vessels. Screening for diabetes is important for early detection to allow for prompt treatment to slow the progression of the disease and its complications. Improved glucose control reduces the risk of complications in persons with type 1 diabetes or type 2 diabetes.²⁻⁴

HbA1c Testing

Hemoglobin A1c tests measure the patient's average plasma glucose over the past ~90 days. A HbA1c value taken every 2–3 months serves as an indicator of glucose control over those months, providing an objective view of the patient's control between checkups. HbA1c is more advantageous than other methods of glycemia (glucose) assessment because the patient does not need to fast or consume a glucose challenge drink before testing.

In an individual with no abnormalities of glucose metabolism, HbA1c values are normally less than 5.7% (39 mmol/mol); in a patient with diabetes, this concentration may double or even triple depending upon the degree of hyperglycemia. With early detection of diabetes, proper therapy, and the normalization of plasma glucose levels in patients with diabetes, HbA1c values can often gradually approach normal concentrations.

The ADA recommends that methods used to measure HbA1c should be standardized to the Diabetes Control and Complications Trial (DCCT) assay and certified by the NGSP. NGSP-reported results are now standardized by comparison to the reference method as described by the International Federation of Clinical Chemistry (IFCC).⁵

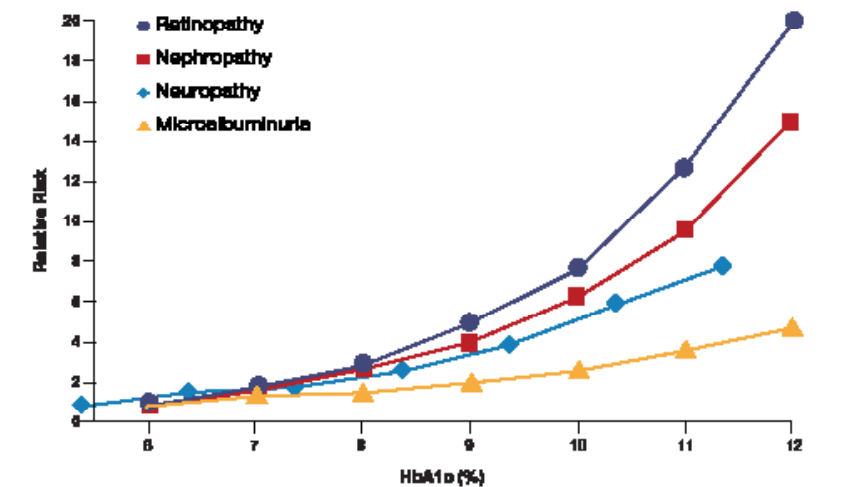
Value of HbA1c Testing in Diabetes Management

Demonstrated by DCCT and UKPDS

The landmark nine-year Diabetes Control and Complications Trial (DCCT) carried out in persons with type 1 diabetes used a high-performance liquid chromatography (HPLC) method to measure HbA1c concentrations. This study showed that the risk for development and progression of the chronic microvascular and neuropathic complications of type 1 diabetes was closely related to the degree of glycemic control.² Thus, the DCCT results have been used to establish specific diabetes treatment goals using HbA1c as an index of a patient's average plasma glucose. The United Kingdom Prospective Diabetes Study (UKPDS) used HbA1c values to show that lowering plasma glucose levels also reduced the incidence of complications in individuals with type 2 diabetes.³

The results of the DCCT and UKPDS demonstrated the importance of HbA1c testing in managing patients living with diabetes. The DCCT and UKPDS also illustrated how HbA1c tests can predict a patient's risk for complications. The greater a patient's HbA1c value, the higher their risk of complication.⁴

Correlation between HbA1c level and risk for diabetic complications



Using HbA1c to Screen for Diabetes

The World Health Organization, the International Expert Committee, and the ADA recommend the use of HbA1c to screen for and diagnose diabetes.⁶⁻⁸ Under defined circumstances, certain groups of children and adults (and all adults aged 35 and older) should be screened for type 2 diabetes.⁸

Diagnosing Diabetes

There are different ways to diagnose diabetes, including the measurement of HbA1c concentrations.⁸ In symptomatic subjects (e.g., persons who report polyuria, polydipsia and/or unexplained weight loss) or in the setting of a diabetic crisis (e.g., diabetic ketoacidosis or hyperglycemic hyperosmolar state), a single finding of hyperglycemia is sufficient to diagnose diabetes. To diagnose diabetes in asymptomatic subjects, hyperglycemia should be observed twice on a single day (assessed using two different measures such as an elevated fasting plasma glucose and an elevated HbA1c). Alternatively, in asymptomatic subjects, diabetes can be diagnosed by observing hyperglycemia on two separate days. The diagnosis of diabetes in pregnancy continues to evolve and a thorough discussion of this topic is available in the latest ADA guidelines.⁸

ADA Hyperglycemia Criteria⁸

Defining Criteria	Prediabetes	Hyperglycemia
Fasting Plasma Glucose	100–125 mg/dL 5.6–6.9 mmol/L	≥126 mg/dL ≥7.0 mmol/L
2h Plasma Glucose during 75g OGTT	140–199 mg/dL 7.8–11.0 mmol/L	≥200 mg/dL ≥11.1 mmol/L
HbA1c	5.7%–6.4% 39–47 mmol/mol	≥6.5% ≥48 mmol/mol
Random plasma glucose – patient with classic symptoms of hyperglycemia	Not applicable	≥200 mg/dL ≥11.1 mmol/L

When using a HbA1c testing method, it is important to keep in mind that certain factors (e.g., hemoglobinopathies or alterations in the lifespan of red blood cells, etc.) may falsely increase or decrease HbA1c results.⁹⁻¹³ Therefore, it could be considered good medical practice for physicians to evaluate the HbA1c result alongside a complete blood count, patient history, and other tests that may help identify potential biases. To ensure that accurate HbA1c results are obtained for all patients, it is important to know if a patient has a hemoglobin variant and how that variant can affect his or her HbA1c.¹⁹

At a Glance^{8,14,15}

Condition	HbA1c	HbA1c Testing Per Year
Adult with diabetes meeting glycemic goals	<7% (<53 mmol/mol) <ul style="list-style-type: none"> A lower HbA1c goal may be acceptable if significant hypoglycemia or other adverse consequences of treatment can be avoided A less stringent goal such as <8% (<64 mmol/mol) may be appropriate when life expectancy is limited or the harms of treatment exceed the benefits 	2x
Adult with diabetes not meeting glycemic goals and/or therapy has recently changed	≥7% (≥53 mmol/mol)	4x
Children with diabetes meeting glycemic goals	<7% (<53 mmol/mol) <ul style="list-style-type: none"> A lower goal such as <6.5% (<48 mmol/mol) may be acceptable in various circumstances A less stringent goal such as <7.5% (<58 mmol/mol) or <8% (<64 mmol/mol) may be acceptable in various circumstances 	2x
Prediabetes has been diagnosed	5.7–6.4% (39–47 mmol/mol)	1x
Patients with normal HbA1c values*	<5.7% (<39 mmol/mol)	Every 3 years

*See hyperglycemia table

Monitoring Patients Living with Diabetes

The ADA guidelines state that the therapeutic goal in caring for patients with diabetes should be the normalization of blood glucose levels when considered in the context of the risk of hypoglycemia, life expectancy, and the balance of the benefits versus the risk of improved control. Numerous investigations have shown a strong correlation between HbA1c levels and glycemic control as assessed by traditional glucose assays.¹⁶⁻¹⁸



ADA Criteria for Screening Diabetes

Screening for diabetes should be considered in the following circumstances:⁸

- Patients 35 years of age or older
- Patients with HIV
- Adults who are overweight (BMI >25 kg/m²) and have one or more of the following risk factors:
 - Physical inactivity
 - Relatives with diabetes
 - High-risk ethnicity
 - History of cardiovascular disease
 - HDL cholesterol <35 mg/dL (<0.90 mmol/L) and/or a triglyceride level >250 mg/dL (>2.82 mmol/L)
 - Hypertension (≥140/90 mmHg or on therapy)
 - Women with polycystic ovary syndrome
 - Conditions associated with insulin resistance

Screening Follow-Up Frequency⁸

- If results are normal, testing should be repeated at a minimum of 3-year intervals with consideration for more frequent testing depending on initial results and risk status
- Patients with prediabetes should be retested yearly
- Women diagnosed with gestational diabetes mellitus should have lifelong testing at least every 3 years
- Patients meeting treatment goals and with stable glycemic control should be monitored with an HbA1c test at least 2 times a year
- Patients whose therapy has changed or who are not meeting glycemic goals, should be monitored with an HbA1c test performed quarterly

See also At a Glance in the Diagnosing section.

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