ECHO Diabetes
Diagnosis of Diabetes
Review of ADA Standards of Care

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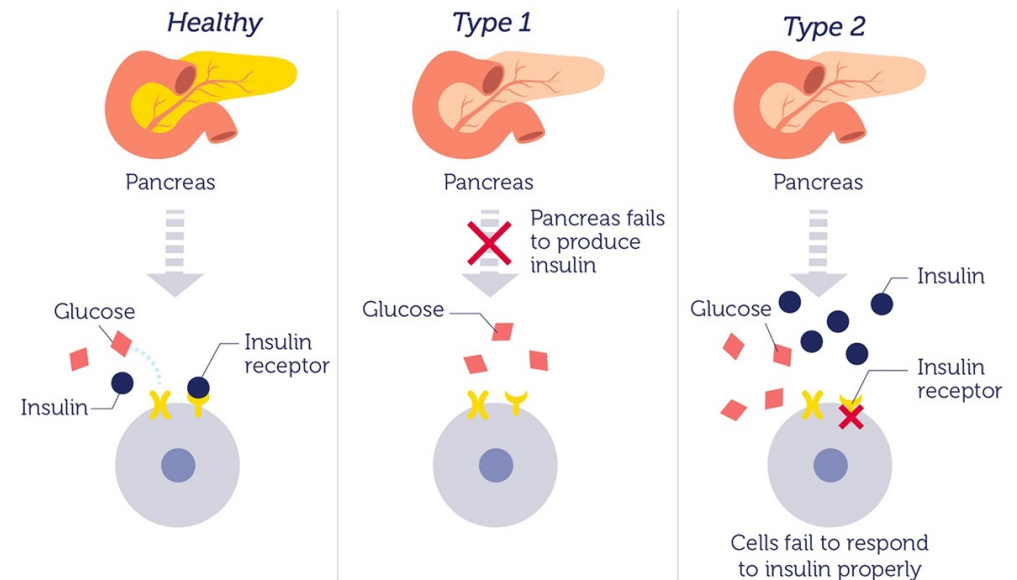
Pre-Question (pick one answer that is most correct)

The Diagnosis of Diabetes

A. Must be confirmed by a 2-hour oral glucose tolerance test (OGTT)
B. Can be made based on a fingerstick blood glucose
C. Can be made in a person with classic hyperglycemic symptoms and a venous blood glucose level =/>200 mg/dl
D. Can be established based on CGM (Continuous Glucose Monitoring) results

What is diabetes

- Diabetes mellitus refers to a group of diseases that affect how the body uses blood sugar (glucose).
  - It is a metabolic disorder in which the body has **high sugar levels** for prolonged periods of time

- From the ADA
  - Diabetes mellitus is a *group of metabolic disorders of carbohydrate metabolism* in which glucose is both
    - *underutilized* as an energy source &
    - *overproduced* due to inappropriate gluconeogenesis and glycogenolysis[*hepatic glucose production/output*],

  resulting in **hyperglycemia**.

DIABETES MELLITUS

Healthy — Pancreas — Glucose — Insulin — Insulin receptor

Type 1 — Pancreas — Pancreas fails to produce insulin — Glucose

Type 2 — Pancreas — Glucose — Insulin — Insulin receptor — Cells fail to respond to insulin properly
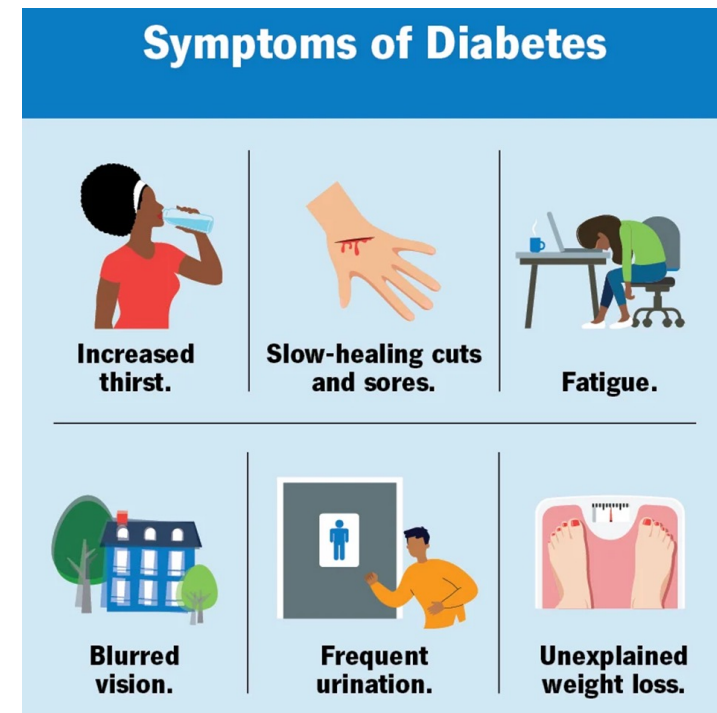
Diagnose Diabetes

- 2.1a Diagnose diabetes based on
  - **A1C** or
  - **Plasma glucose criteria**, either
    - the fasting plasma glucose (FPG) value,
    - 2-h plasma glucose (2-h PG) value during a 75-g oral glucose tolerance test (OGTT), or
    - random glucose value accompanied by classic hyperglycemic symptoms/crises criteria. A

- 2.1b In the absence of unequivocal hyperglycemia (e.g., hyperglycemic crises), *diagnosis requires **confirmatory testing***. A

  - The same tests may be used to screen for and diagnose diabetes and to detect individuals with *prediabetes*

Prediabetes Diagnosis Criteria

Fasting PG 100-125 mg/dL	2hr PG 75 g OGTT 140-199 mg/dL	A1c 5.7-6.4%

Diabetes Diagnosis Criteria

Fasting PG ≥ 126 mg/dL	2hr PG 75 g OGTT ≥200 mg/dL	A1c ≥6.5%

Random PG ≥200 mg/dL + hyperglycemic symptoms

Definitions

PG = Plasma Glucose	OGTT = Oral Glucose Tolerance Test	Hyperglycemic Symptoms: Polydipsia (↑ thirst), Polyuria (↑ urination), Polyphagia (↑ hunger)

Presenting with Classic Hyperglycemic Symptoms* or Hyperglycemic Crisis

- In this scenario, measurement of **random plasma glucose is sufficient** to diagnose diabetes (symptoms of hyperglycemia or hyperglycemic crisis plus random **plasma glucose ≥200 mg/dL**).
  - 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*.
  - Does *not* require a second test to confirm the diagnosis of diabetes , but health care professionals may also want to know the **A1C** to determine the *chronicity of hyperglycemia*.

- *classic hyperglycemic symptoms (e.g., polyuria, polydipsia, and unexplained weight loss)

Symptoms of Diabetes

Increased thirst.

Slow-healing cuts and sores.

Fatigue.

Blurred vision.

Frequent urination.

Unexplained weight loss.

In Asymptomatic Individuals – Who & How to Screen

- 2.9 Screening for **prediabetes and type 2 diabetes** with an **assessment of risk factors or validated risk calculator** should be done in asymptomatic adults. B

- 2.10a Testing for prediabetes or type 2 diabetes in asymptomatic people should be considered in *adults of any age* with **overweight or obesity** who have **one or more risk factors** (Table 2.4). B

- 2.10b For all other people, screening should begin at age 35 years. B

- 2.11 If tests are normal, **repeat screening** recommended at a minimum of 3-year intervals is reasonable, sooner with symptoms or change in risk (e.g., weight gain). C

- 2.12 To screen for prediabetes and type 2 diabetes, **FPG, 2-h PG during 75-g OGTT, and A1C** are each appropriate. B [increasing research on using 1-h PG during 75-g OGTT]

- 2.13 When using OGTT as a screen for prediabetes or diabetes, adequate carbohydrate intake (at least 150 g/day) should be assured for 3 days prior to testing. A

ADA Risk Calculator for T2D

American Diabetes Association
Connected for Life

Are you at risk for type 2 diabetes?

Diabetes Risk Test:

WRITE YOUR SCORE IN THE BOX.

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.

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.

Diabetes Risk Test | American Diabetes Association®

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

Table 2.4 Criteria for screening for diabetes or prediabetes in asymptomatic adults

1.Testing should be considered in **adults with overweight or obesity** (BMI ≥25 kg/m2 or ≥23 kg/m2 in Asian American individuals) who have one or more of the following risk factors:

- First-degree relative with diabetes
- High-risk race and ethnicity (e.g., African American, Latino, **Native American**, Asian American, Pacific Islander)
- History of cardiovascular disease
- Hypertension (≥130/80 mmHg or on therapy for hypertension)
- HDL cholesterol level <35 mg/dL (<0.9 mmol/L) and/or a triglyceride level >250 mg/dL (>2.8 mmol/L)
- Individuals with polycystic ovary syndrome
- Physical inactivity
- Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)

2. People with **prediabete**s (A1C ≥5.7%, IGT, or IFG) should be **tested yearly**.

3. People who were diagnosed with **GDM** should have lifelong testing **at least every 3 years**.

4. For all other people, testing should begin at age 35 years.

5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.

6. People with HIV, exposure to high-risk medicines, history of pancreatitis

When to Screen for T2D in Youth

2.14 Risk-based screening for prediabetes or type 2 diabetes should
 be considered after the onset of puberty or after 10 years of age,
whichever occurs earlier, in children and adolescents with
overweight (BMI ≥85th percentile) or obesity (BMI ≥95th percentile)
and who have one or more risk factors for diabetes. B

Screening should be considered in youth who have overweight (≥85th percentile) or obesity (≥95th 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 and ethnicity (e.g., **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**

Diagnostic Screening

- In people *without* symptoms, FPG, 2-h PG during 75-g OGTT, and A1C are appropriate for diagnostic screening.
  - **Detection rates of different screening tests vary** in both populations and individuals.
    - FPG, 2-h PG, and A1C *reflect different aspects of glucose metabolism*, and diagnostic cut points for the different tests will **identify different groups of people**.
  - Compared with FPG and A1C cut points, the **2-h PG value diagnoses more people with prediabetes and diabetes. (Gold Standard)**
    - the 2-h PG (OGTT) testing protocol may identify individuals with diabetes who may otherwise be missed (e.g., those with cystic fibrosis–related diabetes, post-transplantation diabetes mellitus, PCOS, hepatogenous diabetes [cirrhosis])
  - In the absence of classic hyperglycemic symptoms, **repeat testing is required to *confirm* the diagnosis regardless of the test used**

  - *There is presently insufficient evidence to support the use of continuous glucose monitoring (CGM) for screening or diagnosis of prediabetes or diabetes.*
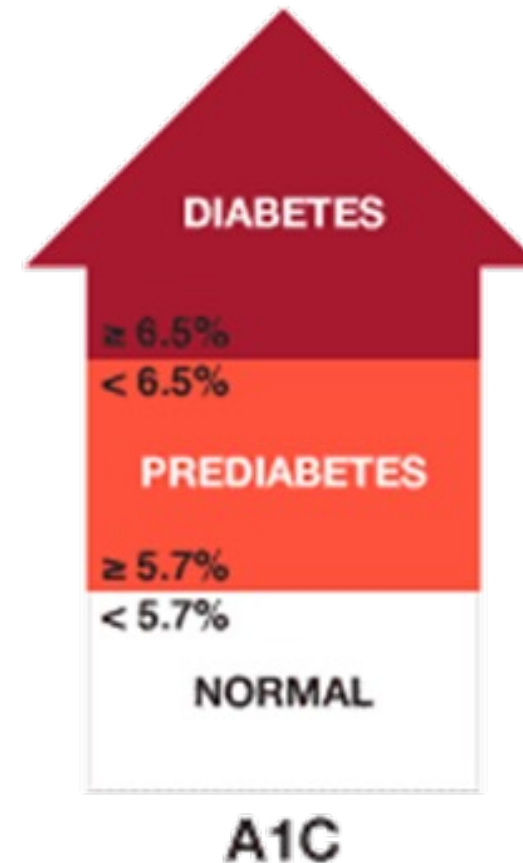
Use of A1C for Screening and Diagnosis of Diabetes

Recommendations

- 2.2a The **A1C test** should be performed using a method that is ***certified by the National Glycohemoglobin Standardization Program (NGSP)*** as traceable to the Diabetes Control and Complications Trial (DCCT) reference assay. B

- 2.2b **Point-of-care A1C testing** for diabetes screening and diagnosis should be **restricted to** U.S. Food and Drug Administration (FDA)–approved devices at Clinical Laboratory Improvement Amendments (CLIA)–certified laboratories that perform testing of moderate complexity or higher by trained personnel. B

- 2.3 Marked **discordance between A1C and repeat blood glucose values** should raise the ***possibility of a problem or interference*** with either test. B

- 2.4 In **conditions** associated with an ***altered relationship between A1C and glycemia***, such as some hemoglobin variants, pregnancy (second and third trimesters and the postpartum period), glucose-6-phosphate dehydrogenase deficiency, HIV, hemodialysis, recent blood loss or transfusion, or erythropoietin therapy**, plasma glucose criteria should be used** to diagnose diabetes. B
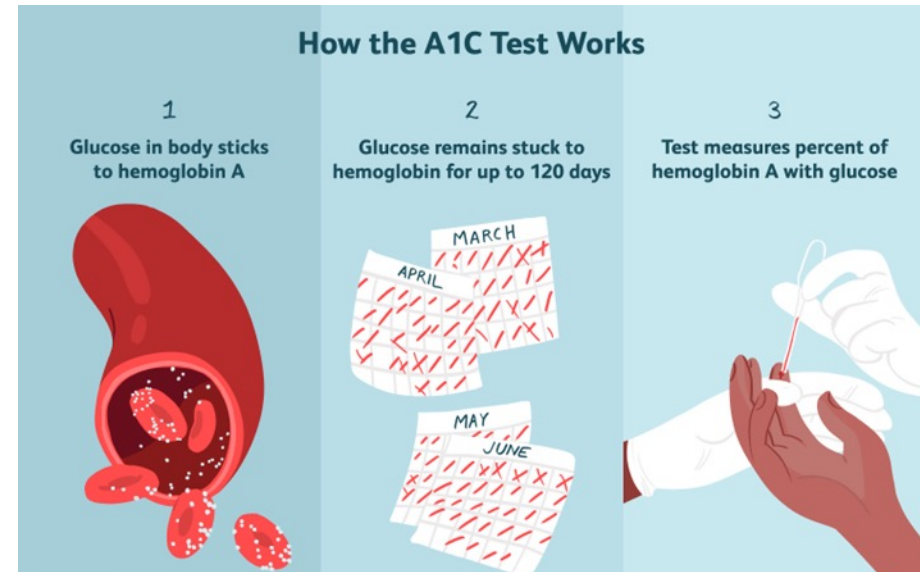
Use of A1C for Screening and Diagnosis of Diabetes

- A1C has several advantages compared with FPG and OGTT, including:
  - greater convenience (fasting not required)
  - greater preanalytical stability
  - fewer day-to-day perturbations during stress, changes in nutrition, or illness.

- Disadvantages:
  - lower sensitivity of A1C at the designated cut point compared with that of glucose tests
    - the A1C cut point of ≥6.5% identifies one-third fewer cases of undiagnosed diabetes than a fasting glucose cut point of ≥126 mg/dL (NHANES Data) (www.cdc.gov/diabetes/pubs/factsheet11/tables1_2.htm)
  - greater cost
  - limited access in some parts of the world.

DIABETES

≥ 6.5%
< 6.5%

PREDIABETES

≥ 5.7%
< 5.7%

NORMAL

A1C

Use of A1C for Screening and Diagnosis of Diabetes

- A1C reflects glucose bound to hemoglobin over the life span of the erythrocyte (~120 days)
  - It provides a "weighted" average that is *more heavily affected by recent blood glucose* exposure.
    - This means that clinically meaningful changes in A1C can be seen in <120 days.

- ***Factors that affect hemoglobin concentrations or erythrocyte turnover can affect A1C*** (e.g., thalassemia or folate deficiency).
  - A1C may **not be a suitable diagnostic test** in people with anemia, people treated with erythropoietin, or people undergoing hemodialysis or HIV treatment.

How the A1C Test Works

1	2	3
Glucose in body sticks to hemoglobin A	Glucose remains stuck to hemoglobin for up to 120 days	Test measures percent of hemoglobin A with glucose

Conditions Affecting HbA1c Results

Inappropriately Low HbA1c	Inappropriately High HbA1c	Variable Effect on HbA1c+
• Hemolysis	• Iron deficiency	• Fetal hemoglobin
• Certain hemoglobinopathies	• Vitamin B12 deficiency	• Methemoglobin
• Recent blood transfusion	• Alcoholism	• Certain hemoglobinopathies
• Acute blood loss	• Uremia	
• Hypertriglyceridemia	• Hyperbilirubinemia	
• Drugs*	• Drugs*	
• Chronic liver disease		

ngsp.org/interf.asp.

https://www.researchgate.net/publication/230574474_Drugs_affecting_HbA1c_levels

Drugs Affecting HbA1c Results

Postulated Mechanism	Falsely Low HbA1c	Falsely High HbA1c
Increased erythrocyte destruction	Dapsone[11-16] Ribavirin[17] Antiretrovirals[18] Trimethoprim-Sulfamethoxazole[14]	
Altered hemoglobin Altered glycation	Hydroxyurea[19] Vitamin C[10] Vitamin E[10] Aspirin (small doses)[10]	
Interference with assays		Aspirin (large doses)[20] Chronic opiate use[21]

Use of *Plasma Glucose* for Screening & Diagnosis of Diabetes

- **FPG or 2-h PG** can be used for screening and diagnosis of diabetes.
  - Advantages of glucose testing:
    - these assays are inexpensive and widely available.
  - Disadvantages include:
    - High diurnal variation in glucose
    - Fasting requirement (individuals may have difficulty fasting for the full 8-h period or may misreport their fasting status)
    - Recent physical activity, illness, or acute stress can also affect glucose concentrations.
    - Glycolysis is also an important and underrecognized concern with glucose testing.
      - Glucose concentrations will be *falsely low* if samples are not processed promptly or stored properly prior to analysis .

- Protocol:
  - Fasting except for water for 8 hours; should not smoke or consume caffeine containing drinks, such as coffee – for either FPG or 2-h OGTT
  - People should consume a mixed diet with at least 150 g of carbohydrates on the 3 days prior to OGTT.
    - Carbohydrate restriction can *falsely elevate* glucose level with an oral glucose challenge.
  - 75-gram glucose drink ingested in ~5 minutes (nonpregnant adult) (N&V)
  - With OGTT - obtain both FPG and 2-hPG

DIABETES
≥ 126 mg/dl
< 126 mg/dl
PREDIABETES
≥ 100 mg/dl
< 100 mg/dl
NORMAL

FPG

DIABETES
≥ 200 mg/dl
< 200 mg/dl
PREDIABETES
≥ 140 mg/dl
< 140 mg/dl
NORMAL

OGTT
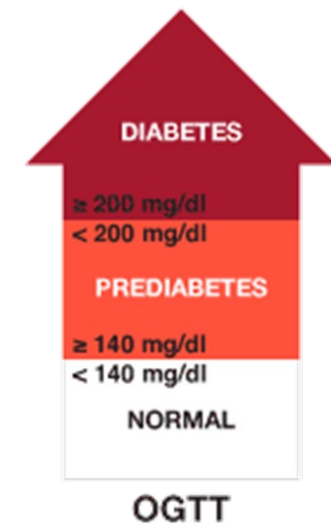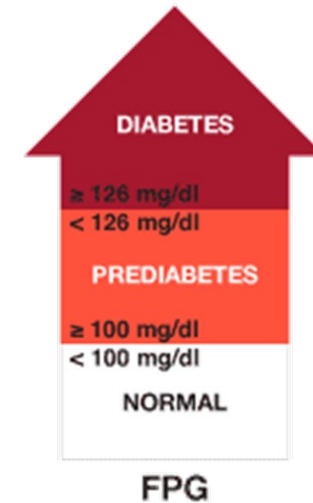
Confirming the Diagnosis of Diabetes

- Diagnosis requires two abnormal screening test results*, measured either at the same time or at two different time points.
  - If using samples at two different time points:
    - The second test should be performed promptly (immediately)
    - May be either a repeat of the initial test or a different test
      - For example, if the A1C is 7.0% and a repeat result is 6.8%, the diagnosis of diabetes is confirmed.

  - If using two different tests (such as A1C and FPG) collected at the same time or at two different time points:
    - Diagnosis is confirmed if both tests have results above the diagnostic threshold.
    - If one test is above threshold and the other is not, repeat the test that is above threshold
      - E.g., FPG 119 and A1c 6.9% - repeat the A1c/ if A1c is 6.2% but FPG is 129, repeat the FPG
      - *Careful consideration of factors that may affect measured A1C or glucose levels*
    - Diagnosis is made based on the confirmed test
      - E.g., , if an individual meets the diabetes criterion of FPG (126 mg/dL or more) on two tests but A1c is <6.5% , that person should nevertheless be considered to have diabetes

*Unless there is a clear clinical diagnosis (e.g., individual with classic symptoms of hyperglycemia or hyperglycemic crisis and random plasma glucose ≥200 mg/dL),

Confirmation Confusion

- Due to pre-analytic and analytic variability of all the tests, it is also possible that when *a test whose result was above the diagnostic threshold is repeated*, the *second value will be below the diagnostic cut point*. This is
  - least likely for A1C
  - somewhat more likely for FPG
  - most likely for the 2-h PG

- Unless there is a laboratory error, such patients are likely to have test results *near the margins of the threshold for a diagnosis*
  - If individuals have test results near the margins of the diagnostic threshold, the HCP should educate the individual about the onset of possible hyperglycemic symptoms and **repeat the test in 3–6 months**.

- Consistent and substantial *discordance between glucose and A1C* test results should prompt additional follow-up to *determine the underlying reason for the discrepancy* and whether it has clinical implications for the individual.

The Diagnosis of Diabetes

A. Must be confirmed by a 2-hour oral glucose tolerance test (OGTT)

B. Can be made based on a fingerstick blood glucose

C. Can be made in a person with classic hyperglycemic symptoms and a venous blood glucose level =/>200 mg/dl

D. Can be established based on CGM (Continuous Glucose Monitoring) results

References & Resources

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