New Criteria for Diagnosis of Diabetes and Obesity

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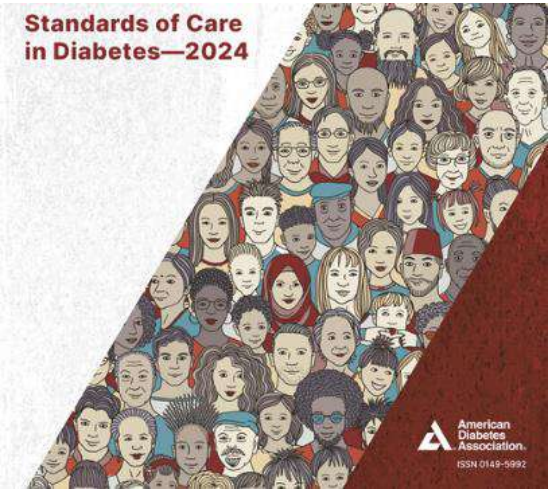


DISCLOSURES

Guillermo E. Umpierrez, MD, CDCES, FACE, MACP

Research support to Emory University: Dexcom, Bayer, Abbott, Corcept

Advisory Panel/Consultant: Glycare, Sanofi

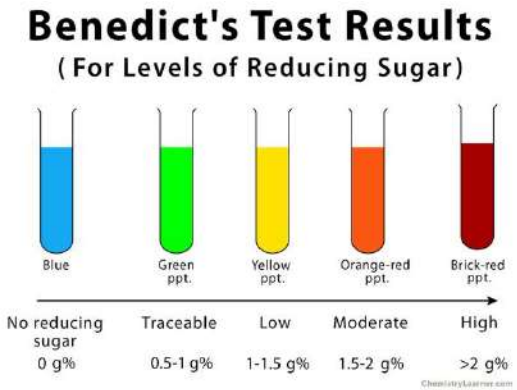
The history of diabetes diagnosis

1500 BC (Egyptian Era)
Excessive urination

500 BC (India)
Honey urine

5th–19th Century
Urine tasting

1908, Cornell University
Stanley R Benedict



Blood Glucose Measurement

1885: Claude Bernard, liver glycogen
Blood glucose estimation

1913: Somogyi improved the accuracy of glucose measurement

1930-1950: Blood Glucose Measurement

1950
oral glucose tolerance tests (OGTT)

Hemoglobin A1c

1958: Hemoglobin A1c identified by Huisman and Meyering

1968: Samuel Rahbar – High HbA1c in patients with diabetes.

1970s: HbA1c, a reliable indicator of long-term glycemic control.

1986: DCCT – relationship between diabetes control and Complications

History of Glucose Levels to Diagnose Diabetes?

1920s-1940s

• Measurement of glucose directly in the blood. No clear criteria for diagnosis.

1950s-1970s

•**OGTT** became a standard diagnostic tool (50, 75, 100 g), but the criteria were not defined.

- Fasting plasma glucose (FPG) < 120 mg/dl was considered normal
- BG at 30, 60, 120, and 180 min with values < 200 considered normal.

1979

•The **National Diabetes Data Group (NDDG)** in the United States established specific blood glucose thresholds for diagnosing diabetes:

- Fasting plasma glucose (FPG) ≥ 140 mg/dL
- OGTT (2-hour plasma glucose) ≥ 200 mg/dL

1997

•The **American Diabetes Association (ADA)** revised the FPG criteria to **≥ 126 mg/dL**, linking glucose levels to long-term complications like retinopathy.

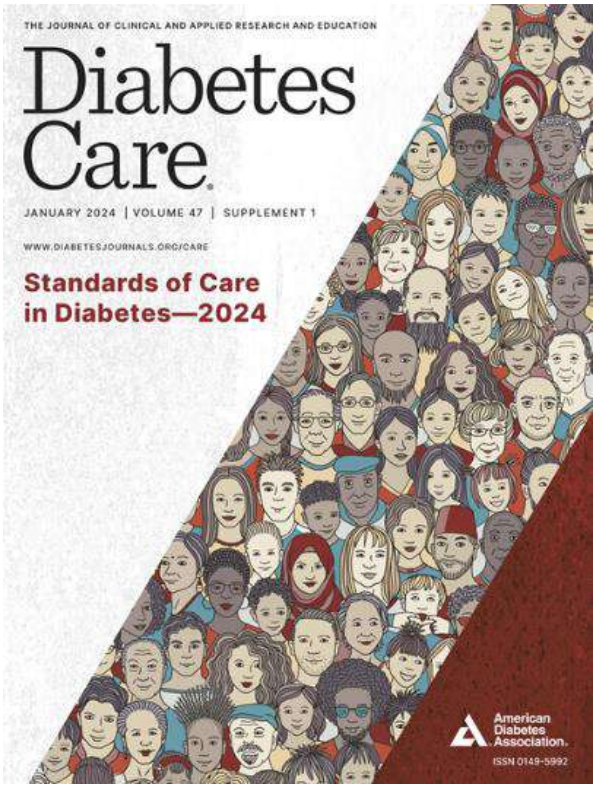
•The 2-hour OGTT threshold of ≥ 200 mg/dL remained unchanged.

2009-2010

•HbA1c ≥ 6.5% was added as a diagnostic criterion.

Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2024

ADA Standards of Care in Diabetes – 2024



Diagnostic Tests for Diabetes

Recommendations

- Diagnosis based on A1C or plasma glucose criteria, either the fasting (FPG), 2-h plasma glucose (2-h PG) during a 75-g OGTT, or random glucose value accompanied by classic hyperglycemic symptoms. A
- FPG, 2-h PG during 75-g OGTT, and A1C are appropriate for diagnostic screening.
- Diagnosis requires confirmatory testing in the absence of unequivocal hyperglycemia (e.g., hyperglycemic crises). A

Diagnosis and Classification of Diabetes: HbA1c

Table 2—*Crite diabetes*

ADA, SOC 2010

A1C ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

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

OR

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

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.

Table 2.2—Criteria for the diagnosis of diabetes

ADA, SOC 2018

FPG ≥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 the WHO, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.*

OR

A1C ≥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).

*In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.

ADA, SOC 2024

A1C ≥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

FPG ≥126 mg/dL (≥7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

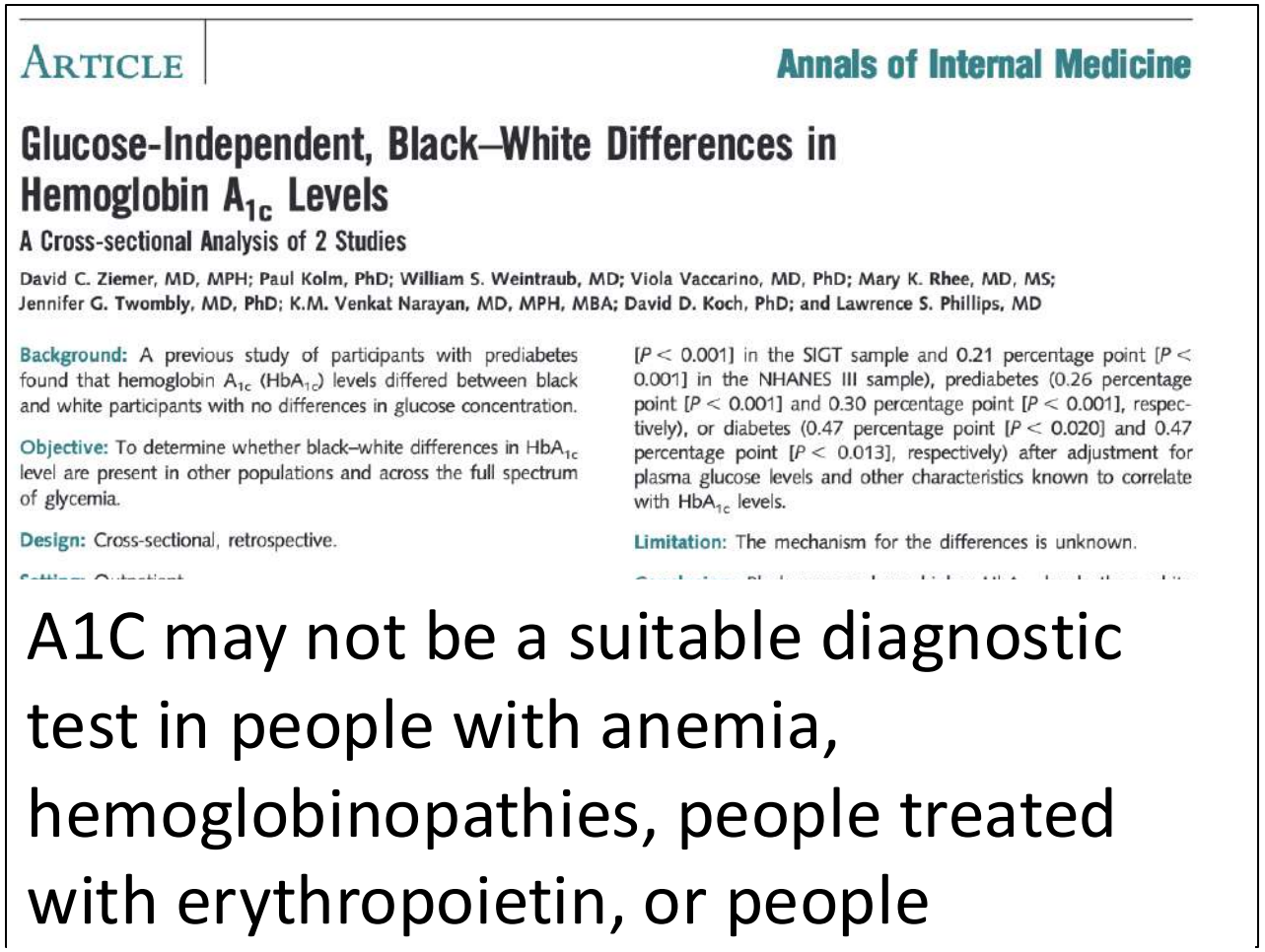
A1C has moved to the top of the testing hierarchy to recognize real-world practice in diagnosing diabetes.

OR

In an individual with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (≥11.1 mmol/L). Random is any time of the day without regard to time since previous meal.

Confirming the Diagnosis of Diabetes

- Two different tests (A1C and FPG) when collected at the same time or at two different time points confirm the diagnosis.
- When discordant results from two different tests, the test result that is above the diagnostic cut point should be repeated, with careful consideration of factors that may affect measured A1C or glucose levels.



ARTICLE | Annals of Internal Medicine

Glucose-Independent, Black–White Differences in Hemoglobin A_{1c} Levels

A Cross-sectional Analysis of 2 Studies

David C. Ziemer, MD, MPH; Paul Kolm, PhD; William S. Weintraub, MD; Viola Vaccarino, MD, PhD; Mary K. Rhee, MD, MS; Jennifer G. Twombly, MD, PhD; K.M. Venkat Narayan, MD, MPH, MBA; David D. Koch, PhD; and Lawrence S. Phillips, MD

Background: A previous study of participants with prediabetes found that hemoglobin A_{1c} (HbA_{1c}) levels differed between black and white participants with no differences in glucose concentration.

Objective: To determine whether black–white differences in HbA_{1c} level are present in other populations and across the full spectrum of glycemia.

Design: Cross-sectional, retrospective.

[$P < 0.001$] in the SIGT sample and 0.21 percentage point [$P < 0.001$] in the NHANES III sample), prediabetes (0.26 percentage point [$P < 0.001$] and 0.30 percentage point [$P < 0.001$], respectively), or diabetes (0.47 percentage point [$P < 0.020$] and 0.47 percentage point [$P < 0.013$], respectively) after adjustment for plasma glucose levels and other characteristics known to correlate with HbA_{1c} levels.

Limitation: The mechanism for the differences is unknown.

A1C may not be a suitable diagnostic test in people with anemia, hemoglobinopathies, people treated with erythropoietin, or people undergoing hemodialysis or HIV treatment.

Classification of Diabetes

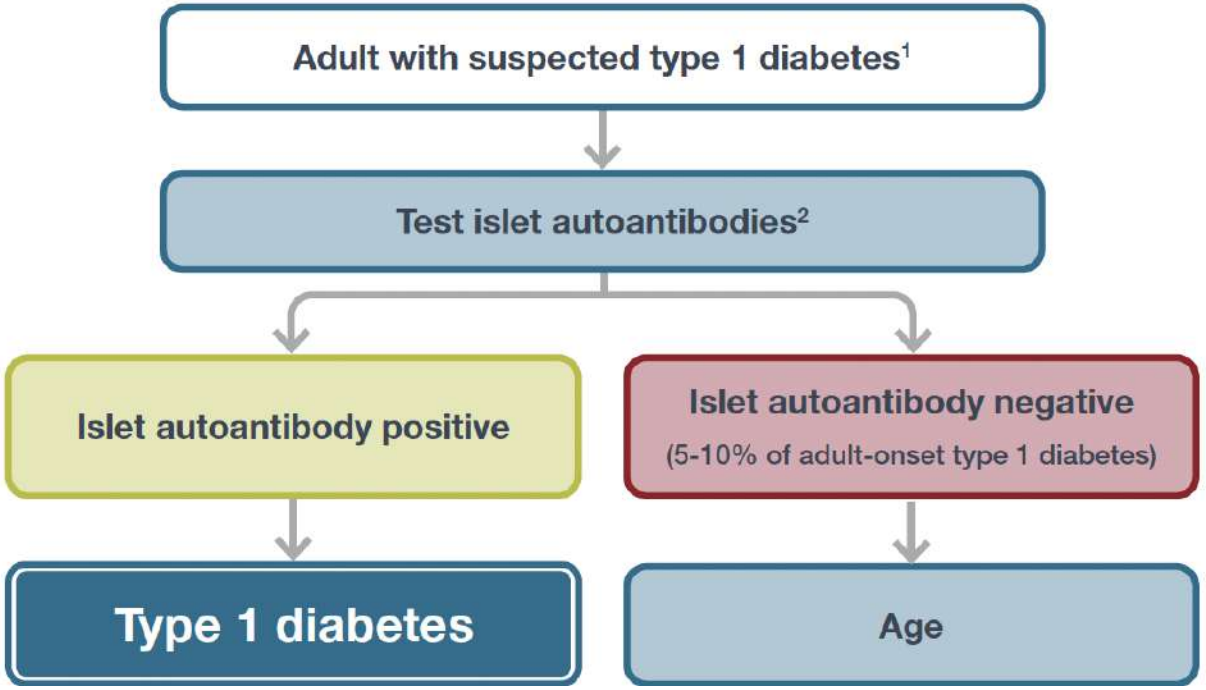
- Type 1 diabetes (due to autoimmune B-cell destruction)
- Type 2 diabetes (due to a non-autoimmune progressive loss of adequate B-cell insulin secretion)
- Specific types of diabetes: monogenic diabetes syndromes, diseases of the exocrine pancreas, and drug- or chemical-induced diabetes
- Gestational diabetes

FPG, 2-h PG during 75-g OGTT, and A1C are appropriate for diagnostic screening

A structured framework for the investigation of suspected type 1 diabetes in newly diagnosed adults

40% of adults with new type 1 diabetes (e.g., adults with type 1 diabetes) are misdiagnosed as having type 2 diabetes

Screening for pre-symptomatic type 1 diabetes may be done by detection of autoantibodies to insulin, glutamic acid decarboxylase (GAD), islet antigen 2 (IA-2), or zinc transporter 8 (ZnT8). B

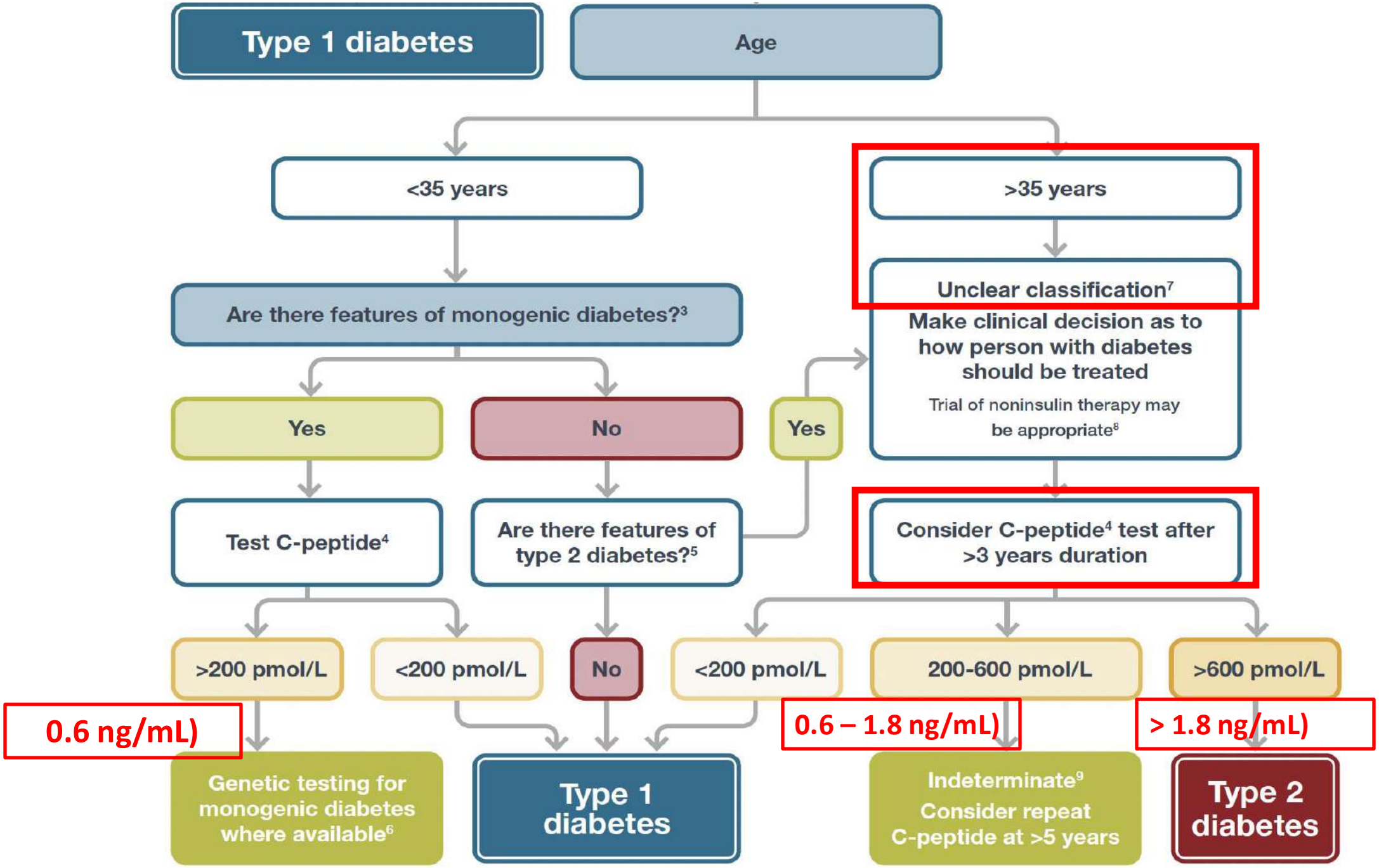


GAD should be the primary antibody measured. If negative, islet tyrosine phosphatase 2 (IA-2) and/or zinc transporter 8 (ZnT8) or insulin antibodies in insulin naïve

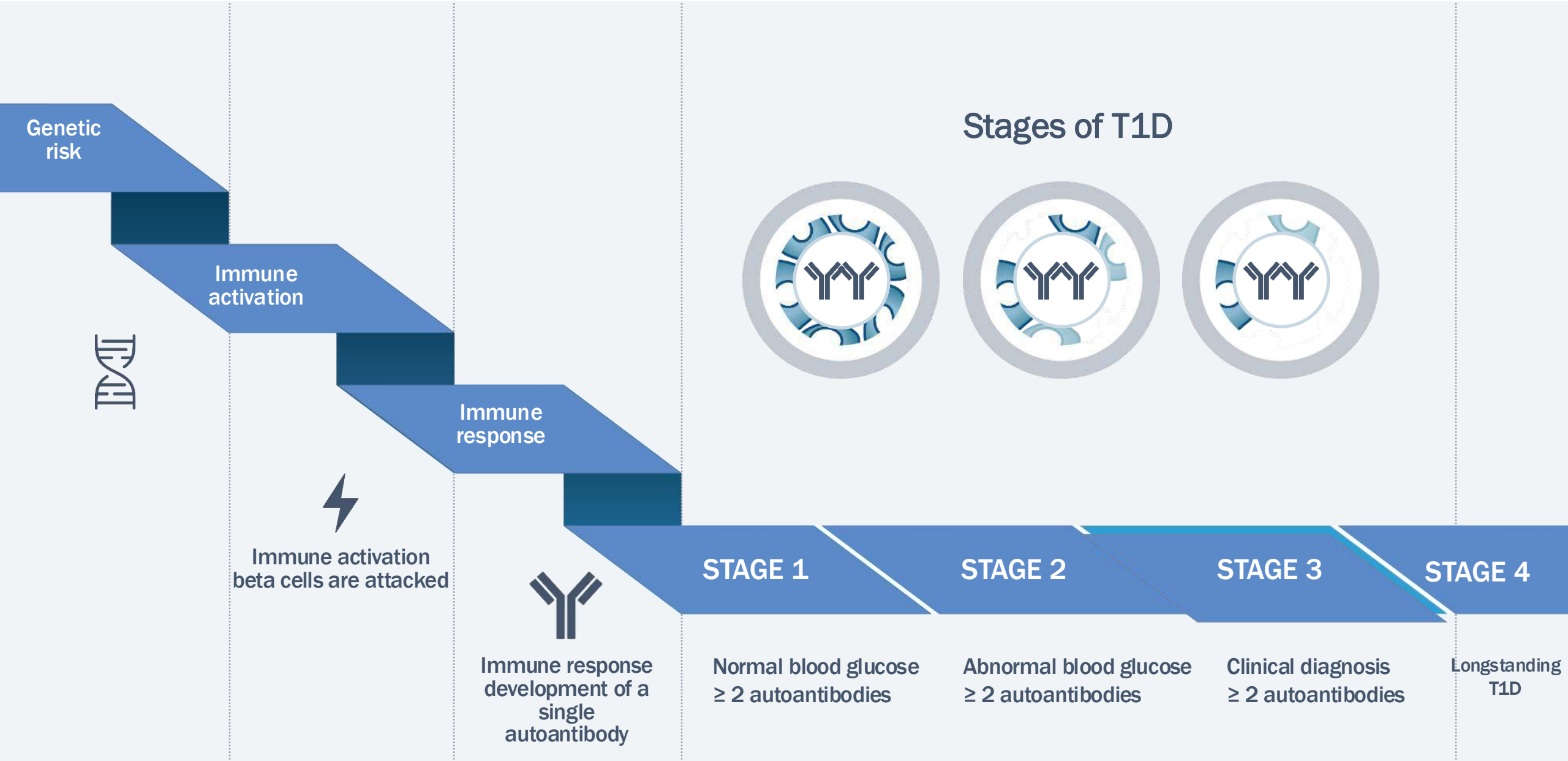
AABBCC approach:

- Age <35 years
- Autoimmunity (e.g., personal or family history of autoimmune disease or polyglandular autoimmune syn- dromes)
- Body habitus (BMI <25 kg/m_2)
- Background (family history of type 1 diabetes)
- Control (glucose control on noninsulin therapies)
- Co- morbidities (treatment with immune checkpoint inhibitors for cancer can cause acute autoimmune type 1 diabetes).

Holt et al. Diabetes Care 2021;44:2589–2625

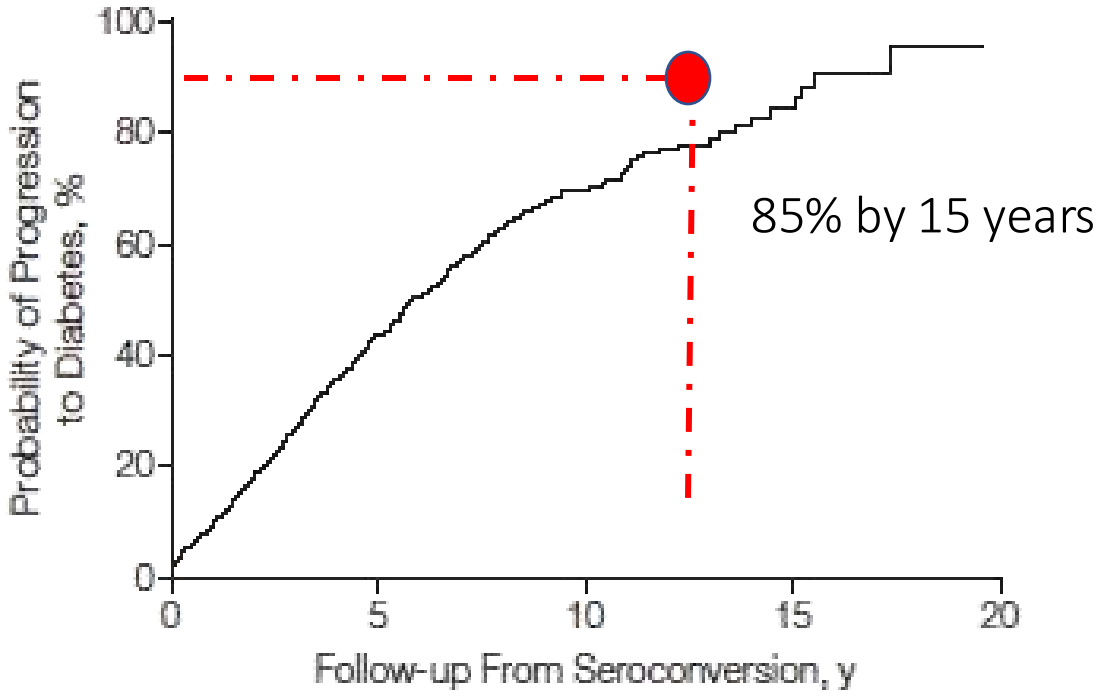

Type 1 diabetes
Age
<35 years
>35 years
Are there features of monogenic diabetes?[3]
Unclear classification[7]
Make clinical decision as to how person with diabetes should be treated
Trial of noninsulin therapy may be appropriate[8]
Yes
No
Yes
Test C-peptide[4]
Are there features of type 2 diabetes?[5]
Consider C-peptide[4] test after >3 years duration
>200 pmol/L
<200 pmol/L
No
<200 pmol/L
200-600 pmol/L
>600 pmol/L
0.6 ng/mL)
0.6 – 1.8 ng/mL)
> 1.8 ng/mL)
Genetic testing for monogenic diabetes where available[6]
Type 1 diabetes
Indeterminate[9]
Consider repeat C-peptide at >5 years
Type 2 diabetes

T1D disease progression



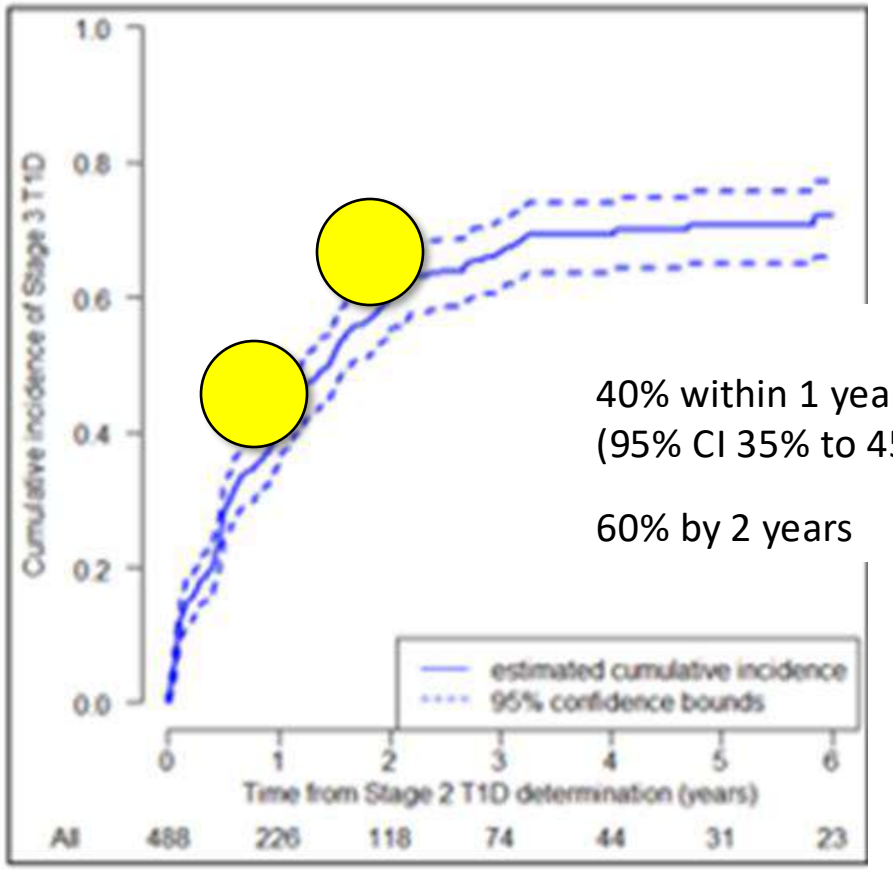
T1D disease progression

Progression from Stage 1 (multiple antibodies, normal glucose tolerance) to Stage 3 (clinical T1D)



No. of events				
No. at risk	585	257	70	8
Diabetes		236	95	20
Lost to follow-up		92	92	42

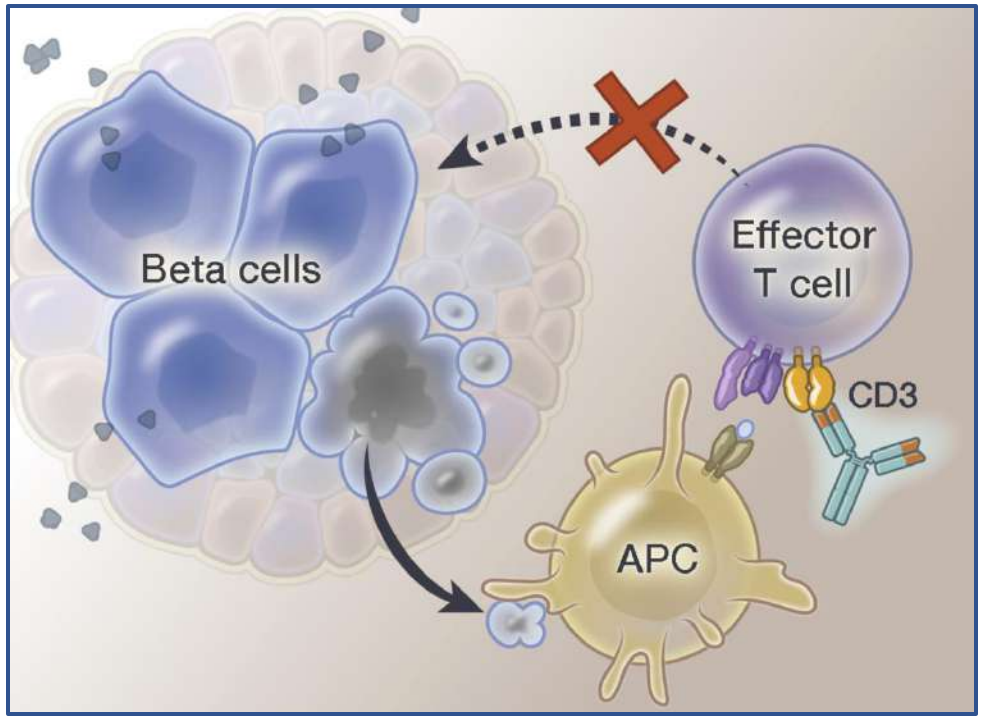
Development of T1D from Stage 2 (multiple Ab+, abnormal glucose tolerance)



Age 8 and above

Type 1 Diabetes Prevention

FDA Approves Teplizumab En Familiares De Personas A Riezgo Con Diabetes Tipo1



Anti-CD3 monoclonal antibodies, such as teplizumab; multiple patient studies reduce loss of beta cell function, even up to 7 years after diagnosis.

ADA Standards of Care. Diabetes Care Suppl 1, 2024

PHARMACOLOGIC INTERVENTIONS TO DELAY SYMPTOMATIC TYPE 1 DIABETES

Recommendation

3.15 Teplizumab-mzwv infusion to delay the onset of symptomatic type 1 diabetes (stage 3) should be considered in selected individuals aged ≥8 years with stage 2 type 1 diabetes. Management should be in a specialized setting with appropriately trained personnel. **B**

Prediabetes

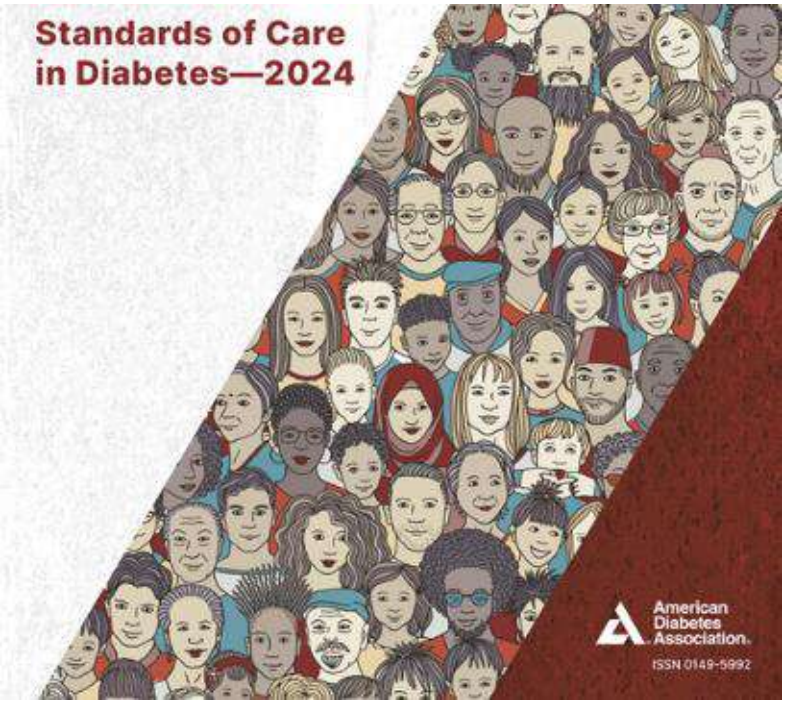
Criteria	American Diabetes Association (2023)	World Health Organization (2006)
Fasting plasma glucose, mg/dL	100-125	110-125
2-h Postload plasma glucose (75-g oral glucose tolerance test), mg/dL	140-199	140-199
Hemoglobin A_{1c}, %	5.7-6.4	NA

Recommendation change:

- Diabetes screening in adults with overweight or obesity (BMI ≥25 kg/m^2) and one or more risk factors **starting at 18 years**, and **screening in all asymptomatic adults from 35 years instead of 45 years.**

ADA Standards of Care. Diabetes Care Suppl 1, 2024

New Criteria for Diagnosis of Obesity



BMI Category

Obesity: Diagnostic criteria

The WHO adopted BMI for clinical classification of obesity in 1998

BMI Range (kg/m^2)	
Underweight	Less than 18.5
Healthy Weight	18.5 to less than 25
Overweight	25 to less than 30
Obesity	30 or greater
- Class 1 Obesity	30 to less than 35
- Class 2 Obesity	35 to less than 40
- Class 3 Obesity (severe obesity)	40 or greater

World Health Organ Tech Rep Ser. 2000;894:i–xii.

Strengths and Limitations of BMI in the Diagnosis of Obesity

BMI is only an indirect measure of adiposity, does not assess body composition, and is insufficient to indicate the degree to which increased adiposity affects health in individual patients.

Anthropometric assessment of adiposity.

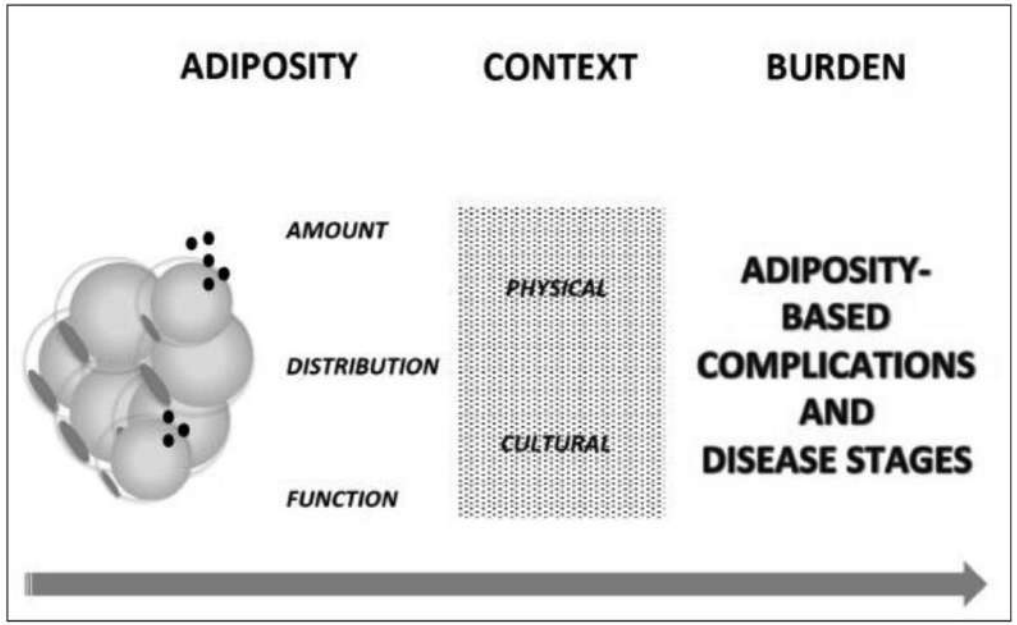
- BMI measures fat distribution (i.e., waist circumference, waist-to-height ratio, or WC divided by height 0.5.
- Bioelectric impedance (BIA) to estimate fat distribution.
- CT, MRI, and DXA

Clinical component assessing the presence and severity of weight-related complications.

BMI does not indicate the impact of excess adiposity on health in individual patients.

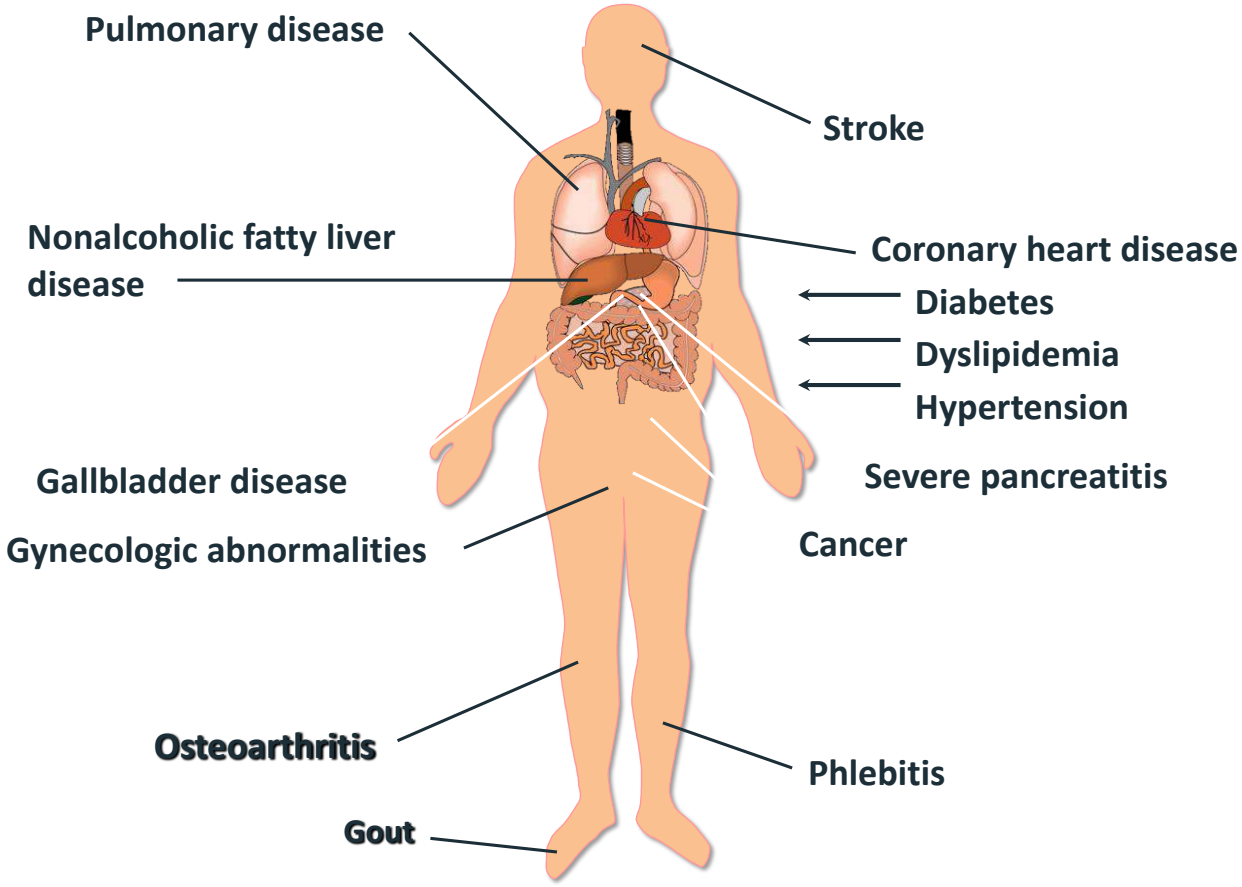
Adiposity-based chronic disease (ABCD) as a new diagnostic term: the AACE and ACE position statement

Translating adiposity and context into disease burden



Mechanic et al. Endocr Pract. 2017 Mar;23(3):372-378.

Obesity Is Associated With Many Comorbidities



Kinlen D, et al. *QJM*. 2018;111:437-443.

Basic Principles of the AACE (ABCD) Obesity Guidelines

Diagnosis: two components

- **Anthropometric**: BMI
- **Clinical**: Presence and Severity of Complications

Staging & Treatment

Complications	AACE Stage	Goal	Suggested therapy
No Complications	Stage 0	• Weight Loss or prevent further weight gain • Prevent complications	Lifestyle intervention
Mild-Moderate Complications	Stage 1	Weight loss sufficient to treat complications	• Lifestyle • Consider medication
Severe Complication	Stage 2		• Lifestyle • Medication • Consider surgery

Outcome Goal

Prevent or treat complications to target

Garvey WT et al. Endocrine Practice 22(Suppl 3):1-203, 2016

Endorsement of Adiposity-Based Chronic Disease (ABCD) as a Diagnostic Term for Obesity

AACE

Endocrine Practice
Volume 23, Issue 3, March 2017,
Pages 372-378

AACE/ACE Position Statement
Adiposity-Based Chronic Disease as a new Diagnostic Term

Jeffrey I. Mechanick, Daniel L. Hurley, W. Timothy Garvey

EASO

Obesity Facts
The European Journal of Obesity

2019

Obes Facts 2019;12:131–136
DOI: 10.1159/000497124
Received: October 25, 2018
Accepted: January 22, 2019
Published online: March 7, 2019

Guidelines

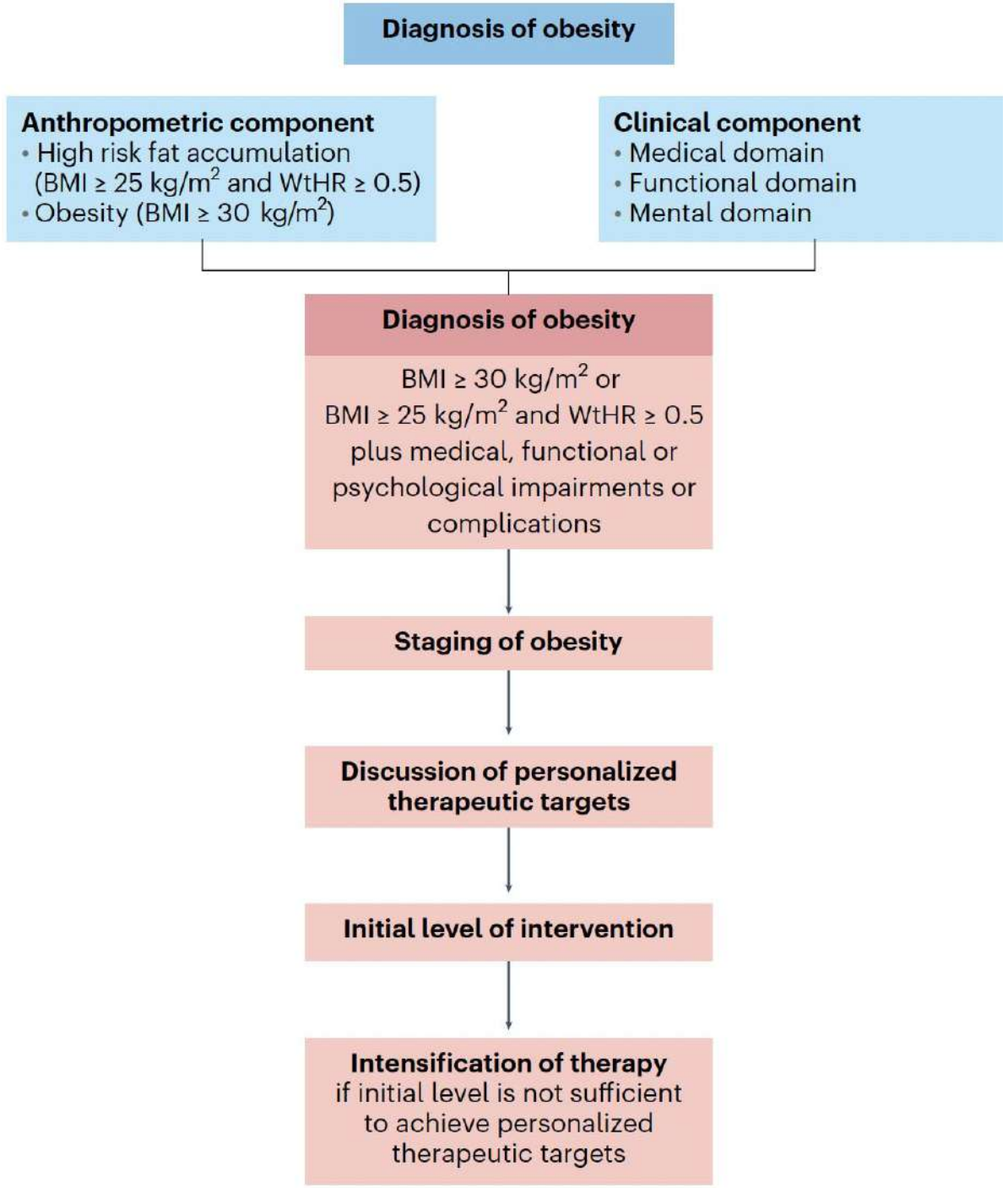
The ABCD of Obesity: An EASO Position Statement on a Diagnostic Term with Clinical and Scientific Implications

Gema Frühbeck[a, b] Luca Busetto[a, c] Dror Dicker[a, d] Volkan Yumuk[a, e]
Gijs H. Goossens[a, f] Johannes Hebebrand[a, g] Jason G.C. Halford[a, h]
Nathalie J. Farpour-Lambert[a, i] Ellen E. Blaak[a, f] Euan Woodward[a, j]
Hermann Toplak[a, k]

The European Association for the Study of Obesity: A new framework for the diagnosis, staging, and management of obesity in adults

- This framework better aligns with obesity role as an adiposity-based chronic disease
- BMI cut-off values do not reflect the role of adipose tissue distribution and functio in the severity of the disease

- The clinical component of the diagnosis should include a systematic evaluation of medical, functional, and psychological impairments (such as mental health and eating behavior pathology) in obese people.



Busetto et al. Nature Medicine, September 2024 | 2395–2399 | 2395

The European Association for the Study of Obesity: A new framework for the diagnosis, staging, and management of obesity in adults

Obesity management

- Behavioral modifications, including nutritional therapy, physical activity, stress reduction, and sleep improvement, are the main cornerstones of obesity management.
- Psychological treatment, obesity medications, and metabolic or bariatric (surgical and endoscopic) procedures may also be used.

- **The use of obesity medications should be considered in patients with BMI ≥ 25 kg/m2, a waist-to-height ratio > 0.5, and medical, functional, or psychological impairments or complications, independently of current BMI cut-off values.**

Busetto et al. Nature Medicine. Volume 30 | September 2024 | 2395–2399

Obesity Diagnosis: BMI vs ABCD

Body Mass Index (BMI)

Adiposity-Based Chronic Disease (ABCD)

Thank you!

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