Managing Diabetes in an Endo Desert

Debbie Hinnen APN, BC-ADM, CDCES, FAAN
Advanced Practice Nurse and
Certified Diabetes Care and Education Specialist
dh@sugar3rn.com

The Mirage: Sometimes it isn't what we think…..

Debbie Hinnen APN, BC-ADM, CDCES, FAAN
Advanced Practice Nurse and
Certified Diabetes Care and Education Specialist
dh@sugar3rn.com

Meet Mr G, 56 year old Hispanic Male

Key health data	
Height, in	63
Weight, lb	224
BMI, kg/m^2	38.4
Waist circumference, in	37.3
Blood pressure, mm Hg	150/72
A1C, %	6.3
FPG, mg/dL	119
Liver function	WNL
Renal function	WNL[a]; no microalbuminuria

Current medications

Losartan/HCTZ: 100/25 mg daily

Atorvastatin: 40 mg daily

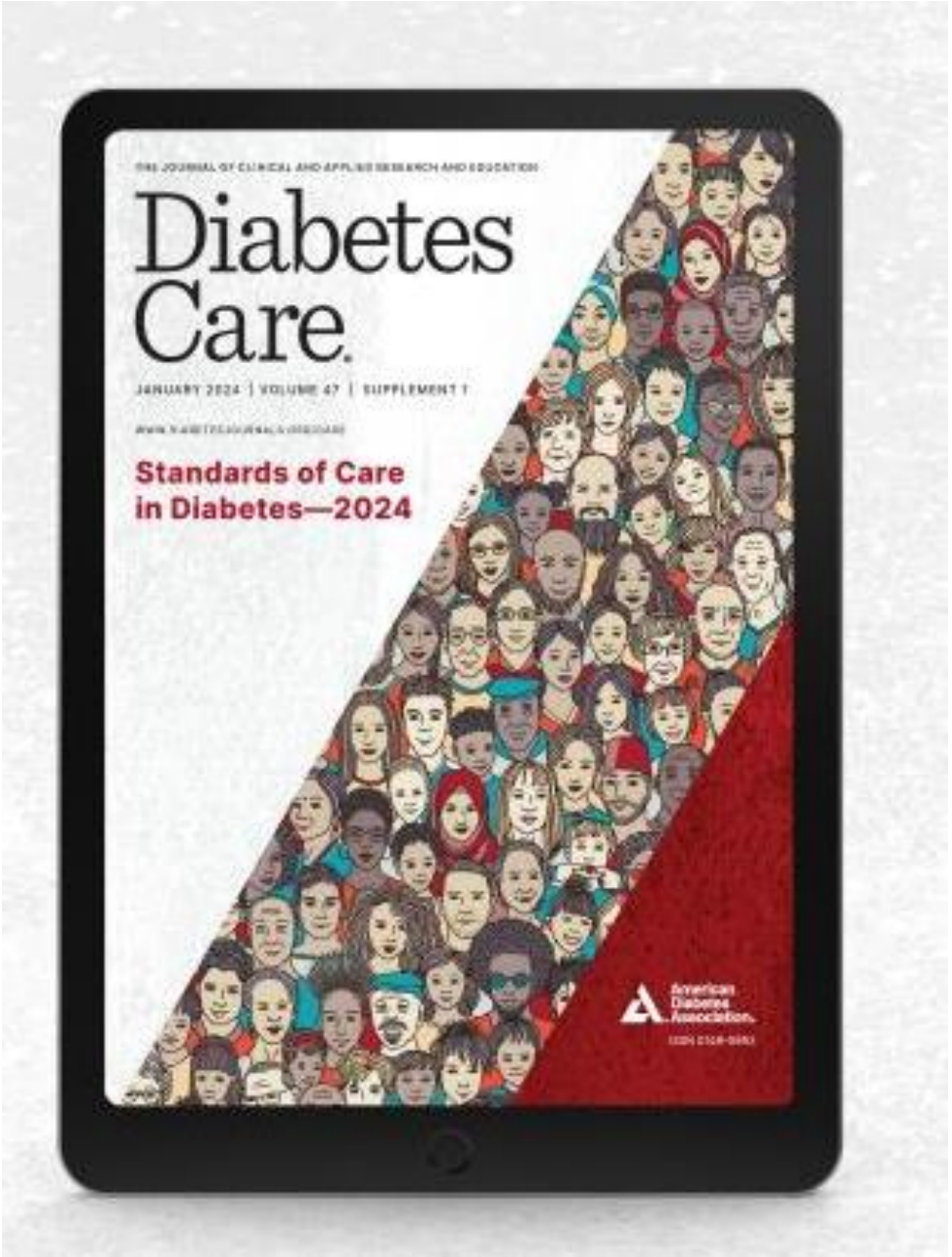
Aspirin: 81 mg daily

Bisoprolol: 15 mg daily

Does he have Diabetes?

Let's look at the Guidelines….

The American Diabetes Association Standards of Care 2024.



DIAGNOSIS AND CLASSIFICATION OF DIABETES

Table 2.1—Criteria for the diagnosis of diabetes in nonpregnant individuals

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
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
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.

DCCT, Diabetes Control and Complications Trial; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; NGSP, National Glycohemoglobin Standardization Program; WHO, World Health Organization; 2-h PG, 2-h plasma glucose. *In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results obtained at the same time (e.g., A1C and FPG) or at two different time points.

Diagnosis and Classification of Diabetes:
Standards of Care in Diabetes - 2024. Diabetes Care 2024;47(Suppl. 1):S20-S42

NO.

What is his diagnosis then?

Table 2.2—Criteria defining prediabetes in nonpregnant individuals

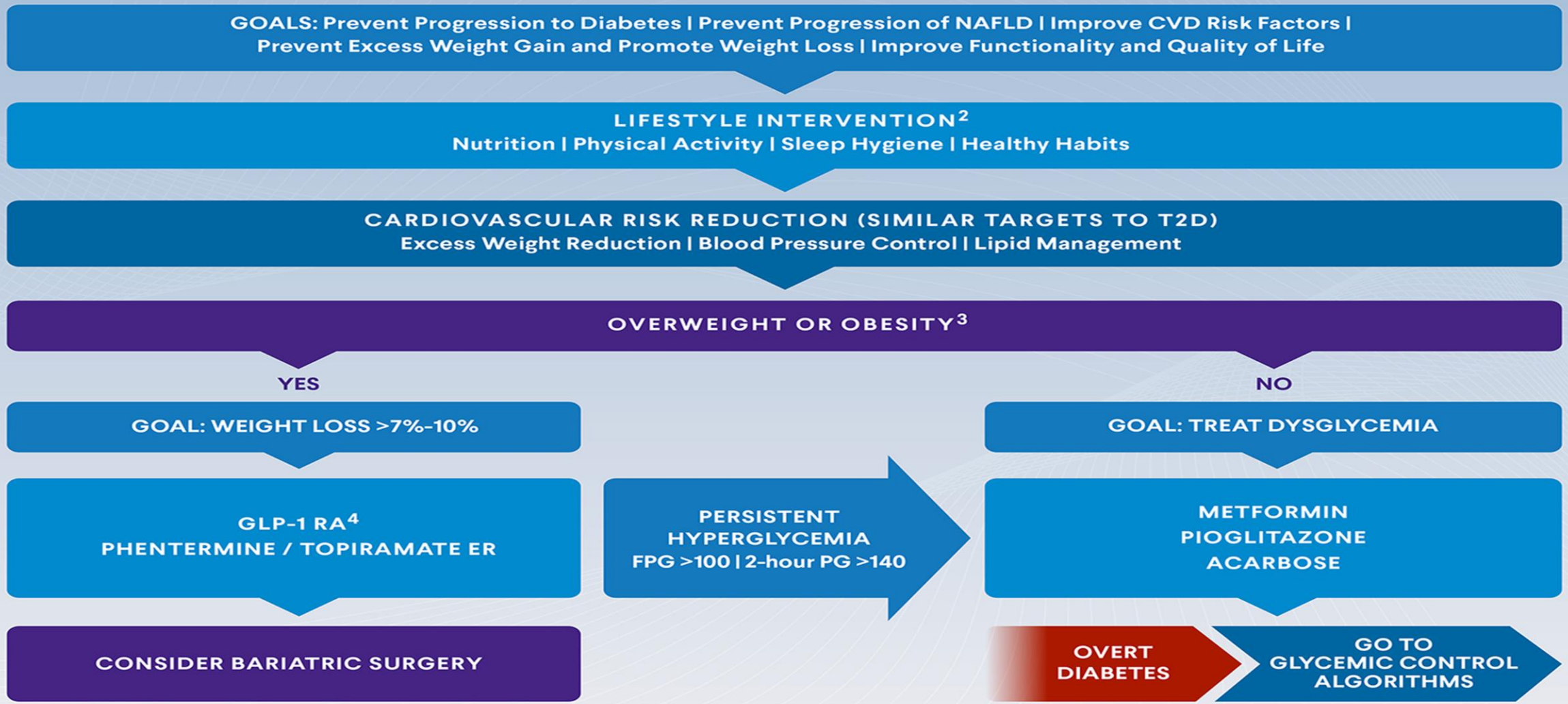
A1C 5.7–6.4% (39–47 mmol/mol)
OR
FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG)
OR
2-h PG during 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT)

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

Diagnosis and Classification of Diabetes:
Standards of Care in Diabetes - 2024. Diabetes Care 2024;47(Suppl. 1):S20-S42

PREDIABETES ALGORITHM

IFG (100-125 mg/dL) | IGT (140-199 mg/dL) | A1C (5.7%-6.4%) | METABOLIC SYNDROME[1]



[1]NCEP ATP III Criteria. [2]See COMPLICATIONS-CENTRIC MODEL FOR THE CARE OF PERSONS WITH OVERWEIGHT/OBESITY. [3]If no overweight or obesity, consider T1D antibody testing for LADA. [4]Indications for weight-loss medications are obesity or overweight BMI >27 kg/m^2 with ABCD complication(s) including prediabetes. Choose GLP-1 RA for approved for weight loss. Also consider other approved weight-loss medications (phentermine [short term], orlistat, naltrexone-ER/bupropion-ER). See also PROFILES OF WEIGHT-LOSS MEDICATIONS table.

Algorithm Figure 3-Prediabetes

Endocrine Practice 2023 29305-340DOI: (10.1016/j.eprac.2023.02.001)

DIAGNOSIS AND CLASSIFICATION OF DIABETES

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/m^2 or ≥23 kg/m^2 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 prediabetes (A1C ≥5.7% [≥39 mmol/mol], 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

GDM, gestational diabetes mellitus; IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

Diagnosis and Classification of Diabetes:
Standards of Care in Diabetes - 2024. Diabetes Care 2024;47(Suppl. 1):S20-S42

Mr G, 57 year old Hispanic Male, a year later…

Key health data	
Height, in	63
Weight, lb	218
BMI, kg/m^2	38.6
Waist circumference, in	37.5
Blood pressure, mm Hg	141/72
A1C, %	7.1
FPG, mg/dL	164
Liver function	WNL
Renal function	WNL[a]; no microalbuminuria

Current medications

Losartan/HCTZ: 100/25 mg daily

Atorvastatin: 40 mg daily

Aspirin: 81 mg daily

Bisoprolol: 15 mg daily

Does Mr R have diabetes now?

Yes
What Classification?

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 non-autoimmune progressive loss of adequate β-cell insulin secretion, frequently on the background of insulin resistance and metabolic syndrome)
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, 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 or other types of diabetes occurring throughout pregnancy, such as type 1 diabetes).

Another patient: Matthew

32-year-old man
at new patient appointment with you, his primary care provider

- Matthew has started a new job and is here for a new patient appointment after several cancellations

- He and his wife just had a baby and between that and his job he has found it difficult to make it in for an appointment

- His past medical history reveals GERD (takes omeprazole), seasonal allergies, and mild hypertension (takes low dose amlodipine)

– Family history: His father was diagnosed with T1D at 45 years of age which is managed with insulin and mother has hypercholesterolemia

–• His vitals today are normal
- BMI: 24.4 kg/m_2; BP, 122/80 mmHg; SpO_2, 98%

What do you do?

- You order a complete blood count, fasting lipid, and metabolic panel to establish a baseline

Matthew's Test Results

Glucose 110 mg/dL 70-100
BUN 13 mg/dL 6-20
Creatinine 0.98 mg/dL 0.57-1.00
eGFR If Non-African Am 76 mL/min/1.73 m_2 >59
BUN/Creatinine Ratio 13 9-23
Sodium 144 mmol/L 134-144
Other electrolyte parameters were normal

Triglycerides 145 mg/dL 9-150
Cholesterol, Total 163 mg/dL <200
HDL Cholesterol 38 **Low** mg/dL ≥40.0
LDL Cholesterol, Direct 96 mg/dL ≤100

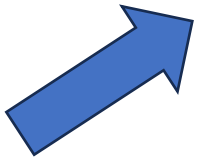
How would you interpret Matthew's results?

- What are your next steps?

How would you interpret Matthew's results?

- What are your next steps?
- Should Matthew receive screening for islet autoantibodies?
- He has never had a test for T1D

Type 1 Diabetes



2.6 Screening for presymptomatic 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**

2.7 Having multiple confirmed islet autoantibodies is a risk factor for clinical diabetes. Testing for dysglycemia may be used to further forecast near-term risk. When multiple islet autoantibodies are identified, referral to a specialized center for further evaluation and/or consideration of a clinical trial or approved therapy to potentially delay development of clinical diabetes should be considered. **B**

2.8 Standardized islet autoantibody tests are recommended for classification of diabetes in adults who have phenotypic risk factors that overlap with those for type 1 diabetes (e.g., younger age at diagnosis, unintentional weight loss, ketoacidosis, or short time to insulin treatment). **E**

DIAGNOSIS AND CLASSIFICATION OF DIABETES

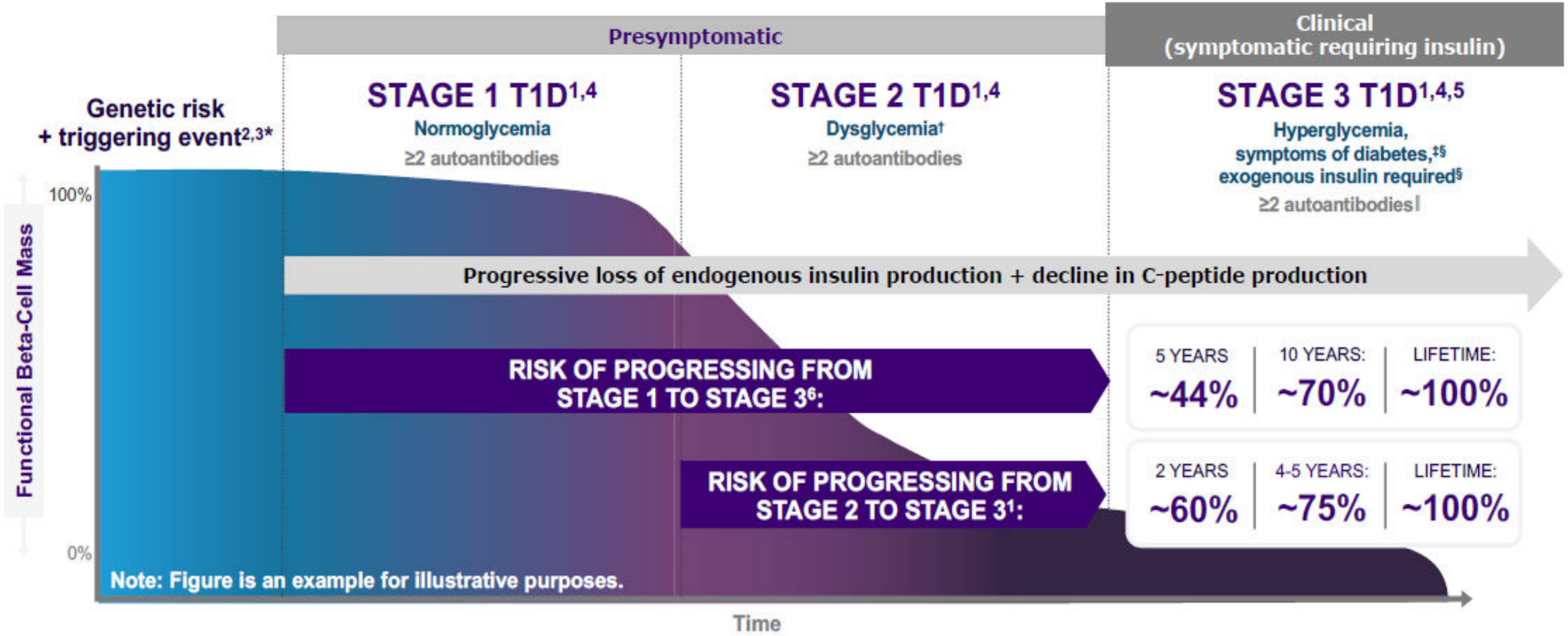
Table 2.3—Staging of type 1 diabetes

	Stage 1	Stage 2	Stage 3
Characteristics	• Autoimmunity • Normoglycemia • Presymptomatic	• Autoimmunity • Dysglycemia • Presymptomatic	• Autoimmunity • Overt hyperglycemia • Symptomatic
Diagnostic criteria	• Multiple islet autoantibodies • No IGT or IFG	• 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 ≥10% increase in A1C	• Autoantibodies may become absent • Diabetes by standard criteria

Adapted from Skyler et al. (40). FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; 2-h PG, 2-h plasma glucose. Alternative additional stage 2 diagnostic criteria of 30-, 60-, or 90-min plasma glucose on oral glucose tolerance test ≥200 mg/dL (≥11.1 mmol/L) and confirmatory testing in those aged ≥18 years have been used in clinical trials (79).

Diagnosis and Classification of Diabetes:
Standards of Care in Diabetes - 2024. *Diabetes Care* 2024;47(Suppl. 1):S20-S42

When ≥2 autoantibodies are present, the lifetime risk of developing clinical stage 3 T1D approaches 100%[1,2]



*Autoantibodies to ≤1 beta cell autoantigen (insulin, GAD65, IA-2, ZnT8, or ICA) are detected in patient serum.[1] †Fasting plasma glucose of 100 to 125 mg/dL, 2-hour plasma glucose during OGTT of 140 to 199 mg/dL, A1C 5.7% to 6.4% (39-47 mmol/mol), or ≥10% increase in A1C is observed.[4] ‡Common symptoms of T1D include polydipsia, polyuria, hunger, extreme fatigue, blurry vision, and weight loss.[1,7] §Early stage 3 may only have OGTT findings of hyperglycemia and may not be symptomatic or require exogenous insulin.[4] ‖In some patients, autoantibodies may become absent in stage 3 T1D.[4]

1. Insel RA, et al. *Diabetes Care*. 2015;38(10):1964-1974. **2.** van Belle TL, et al. *Physiol Rev*. 2011;91(1):79-118. **3.** Jacobsen LM, et al. *Front Endocrinol (Lausanne)*. 2018;9:70. **4.** American Diabetes Association. *Diabetes Care*. 2024;47(suppl 1):S20-S42. **5.** McCall AL, Farhy LS. *Minerva Endocrinol*. 2013;38(2):145-163. **6.** Ziegler AG, et al. *JAMA*. 2013;309(23):2473–2479. **7.** Mayo Clinic. June 3, 2021. Accessed October 20, 2023.

DKA is a Common but Potentially Avoidable Complication of T1D

DKA is the leading cause of mortality in youth with T1D[1-3]

1.5x-3x

less frequent among children or siblings of people with T1D[4-6]

30%-60%

of people with T1D in the US present with DKA at time of diagnosis[7-9]

~200,000

hospital discharges for DKA per year[2,10]

1. Gagnum V, et al. *Diabet Med*. 2017;34(1):56-63. 2. Ramphul K, Joynauth J. *Diabetes Care*. 2020;43(12):e196-e197. 3. Wasag DR, et al. *Arch Dis Child*. 2018;103(1):44-48.
4. Fredheim S, et al. *Diabetologia*. 2013;56(5):995-1003. 5. Duca LM, et al. *Diabetes Care*. 2017;40(9):1249-1255. 6. Bogale KT, et al. *Endocrinol Diab Metab*. 2021;4(2):e00186.
7. Muñoz C, et al. *Clin Diabetes*. 2019;37(3):276-281. 8. Cherubini V, et al. *Diabetologia*. 2020;63(8):1530-1541. 9. Alonso GT, et al. *Diabetes Care*. 2020;43(1):117-121.
10. Desai D, et al. *Diabetes Care*. 2018;41(8):1631-1638.

Multiple Studies Have Found Lower Rates of DKA Associated With T1D Screening[1-6]

Screening study	Setting	DKA rate	Expected DKA rate without screening
DAISY[1]	**Relatives with T1D/genetic risk** (Colorado, USA)	3.3% (1/30)	44% (44/101)*
TEDDY[2]	**Relatives/genetic risk** (USA, Sweden, Finland, Germany)	6.1% (23/379)	>30%†
Munich Family[3]	**Relatives with T1D** (Munich, Germany)	3.3% (N=65)‡	29%‡
DIPP[4]	**Genetic risk** (Oulu, Finland)	5.0% (N=159)§	23%‖
Fr1da[5]	**General population** (Bavaria, Germany)	3% (2/62¶)	17%-36%[3,†]
TRIGR[6]	**Relatives with T1D/genetic risk** (15 countries#)	4.6% (8/173)	19%-40%[7,8]

DAISY: Diabetes Auto Immunity Study in the Young; DIPP: Diabetes in Pregnancy Program; TRIGR: Trial to Reduce IDDM in the Genetically at Risk.
*Hospitalization rate, mainly driven by DKA in the control group, was reported rather than DKA. †The TEDDY study screened 424,788 children for T1D HLA risk at birth and enrolled 8676 children. ‡Mean adjusted for gender and age. §Based on 159 people with HLA-conferred risk of T1D with prospective follow-up. ‖Based on 229 people with no HLA screening at baseline. ¶There were 62 people who had Stage 3 T1D at screening (n=26) or who developed Stage 3 T1D during follow-up (n=36). #Australia, Canada, Czech Republic, Estonia, Finland, Germany, Hungary, Italy, Luxembourg, Netherlands, Poland, Spain, Sweden, Switzerland, and USA.

1. Barker JM, et al. *Diabetes Care*. 2004;27(6):1399-1404. 2. Jacobsen LM, et al. *Diabetes Care*. 2022;45(3):624-633. 3. Winkler C, et al. *Pediatr Diabetes*. 2012;13(4):308-313. 4. Hekkala AM, et al. *Pediatr Diabetes*. 2018;19(2):314-319. 5. Ziegler AG, et al. *JAMA*. 2020;323(4):339-351. 6. Nakhla M, et al. *JAMA Pediatr*. 2021;175(5):518-520. 7. Nakhla M, et al. *CMAJ*. 2018;190(14):E416-E421. 8. Dabelea D, et al. *Pediatrics*. 2014;133(4):e938-e945.

Health-Related Quality of Life Can Be Reduced in Individuals with T1D[1*]

Work may be negatively affected by T1D

Adults with T1D reported higher rates of unemployment and use of sick leave compared with the general population[1,2,*]

T1D can impact sleep duration and quality

Children and adolescents with T1D sleep an average of 27 minutes less than controls[3†]

Adults with T1D reported significantly worse sleep quality than controls[3†]

Children with T1D may experience depression and anxiety

30% of children with T1D report depressive symptoms[4‡]32% of children with T1D report anxiety symptoms[4‡]

Diabetes distress can impair disease management[5,6]

Diabetes distress is associated with suboptimal self-management and A1C and impaired general emotional well-being

ISPAD has recognized that managing the psychosocial factors associated with T1D can improve glycemic control, regimen adherence, and quality of life[7]

*Data were from 2 Danish survey studies: The Steno Diabetes Center study of 2415 adults with T1D conducted in 2011 and the Capital Region survey of 48,511 members of the general population conducted in 2010 (control data). †Literature review up to 2015 and meta-analysis of 22 studies were conducted that compared sleep parameters in individuals with T1D and controls. ‡Literature review conducted/updated in 2014/2015 and meta-analysis of 14 selected studies assessing symptoms of depression and anxiety in pediatric patients with T1D were performed.

ISPAD: International Society for Pediatric and Adolescent Diabetes.

1. Nielsen HB, et al. *Diabetes Res Clin Pract.* 2016;121:62-68. 2. Cook AS, Zill A. *Front Psychol.* 2021;12:697833. 3. Reutrakul S, et al. *Sleep Med.* 2016;23:26-45. 4. Buchberger B, et al. *Psychoneuroendocrinology.* 2016;70:70-84. 5. Diabetes and Emotional Health. Chapter 3: Diabetes Distress. Accessed June 27, 2022. https://professional.diabetes.org/sites/professional.diabetes.org/files/media/ada_mental_health_workbook_chapter_3.pdf 6. Abdoli S, et al. *J Clin Transl Endocrinol.* 2021;23:100251. 7. Delamater AM, et al. *Pediatr Diabetes.* 2018;19(suppl 27):237-249.

Autoimmune Conditions May Co-Occur With T1D

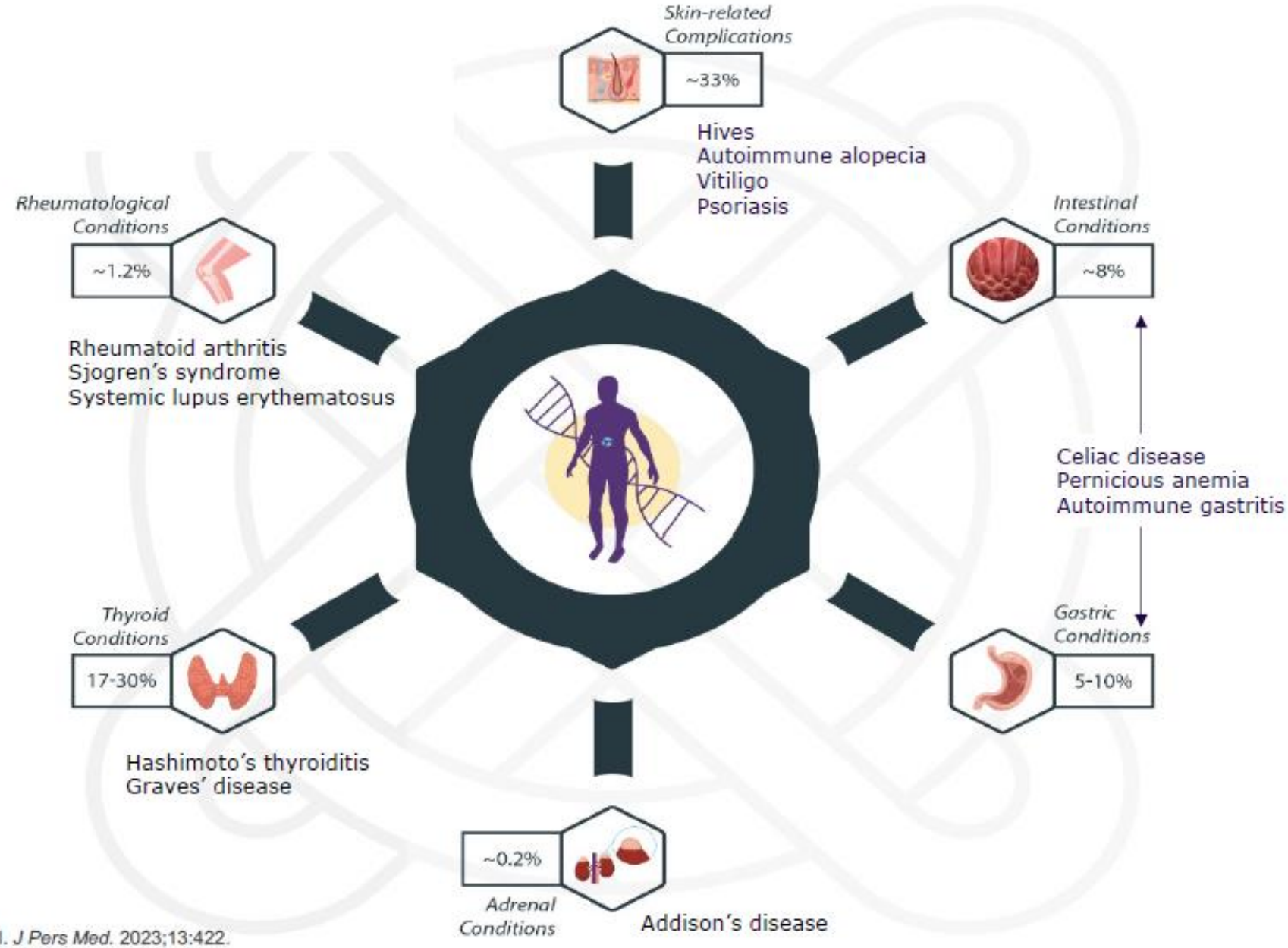


Figure adapted from: Popoviciu MS, et al. *J Pers Med.* 2023;13:422.

Patient Case: Further Test Results - Matthew

There are 3 autoantibodies detected in Matthew's blood sample. Additional metabolic parameters are normal.

Autoantibody Tested	Result
IAA	Positive
GADA	Positive
ZnT8A	Negative
IA-2A	Positive

Laboratory Parameter	Result	Normal Range
Random glucose	135 mg/dL	<140 mg/dL
HbA1c	5.6%	<5.7%
C-Peptide (fasting)	0.54 nmol/L	0.3-0.7 nmol/L

Your Discussion with Matthew….

- You explain that the presence of more than 2 autoantibodies in the blood work predicts that he will progress to clinical T1D. With high fasting glucose, his risk is 75% in 5 years.
- Emphasize fasting glucose IS high, but other parameters are normal. He should be monitored frequently. (Annually)
- Review the sx of T1D: frequent urination, weight loss, blurry vision.
- Consider blood glucose monitoring (BGM) or Continuous glucose monitoring (CGM), especially at times of illness.
- He SHOULD be referred to an endocrinologist

Pharmacologic Interventions to Delay Symptomatic Type 1 Diabetes

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**

Teplizumab-mzww (Tzield) injection 2mg/2ml

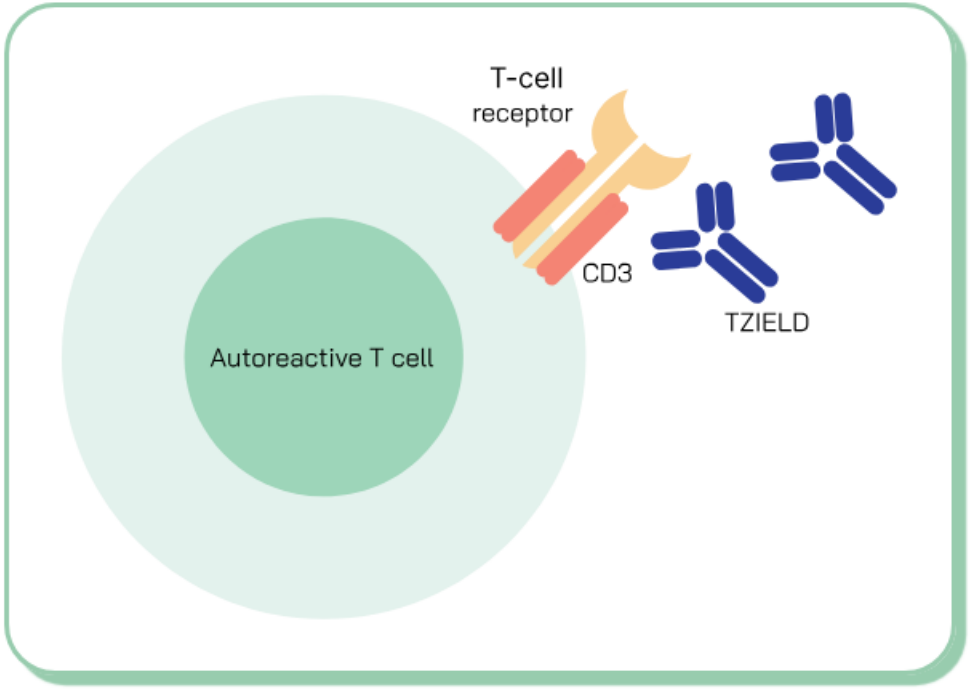
The first and only approved immunomodulator to delay the onset of Stage 3 T1D in patients 8 years and older with Stage 2 T1D[3,6]

•TZIELD is an anti-CD3 monoclonal antibody that binds to CD3 antigens on the surface of T cells

•The mechanism of action may involve the partial agonistic signaling and deactivation of autoreactive T cells that target pancreatic beta cell

•TZIELD leads to an increase in the proportion of regulatory T cells and of exhausted CD8+ T cells in peripheral blood

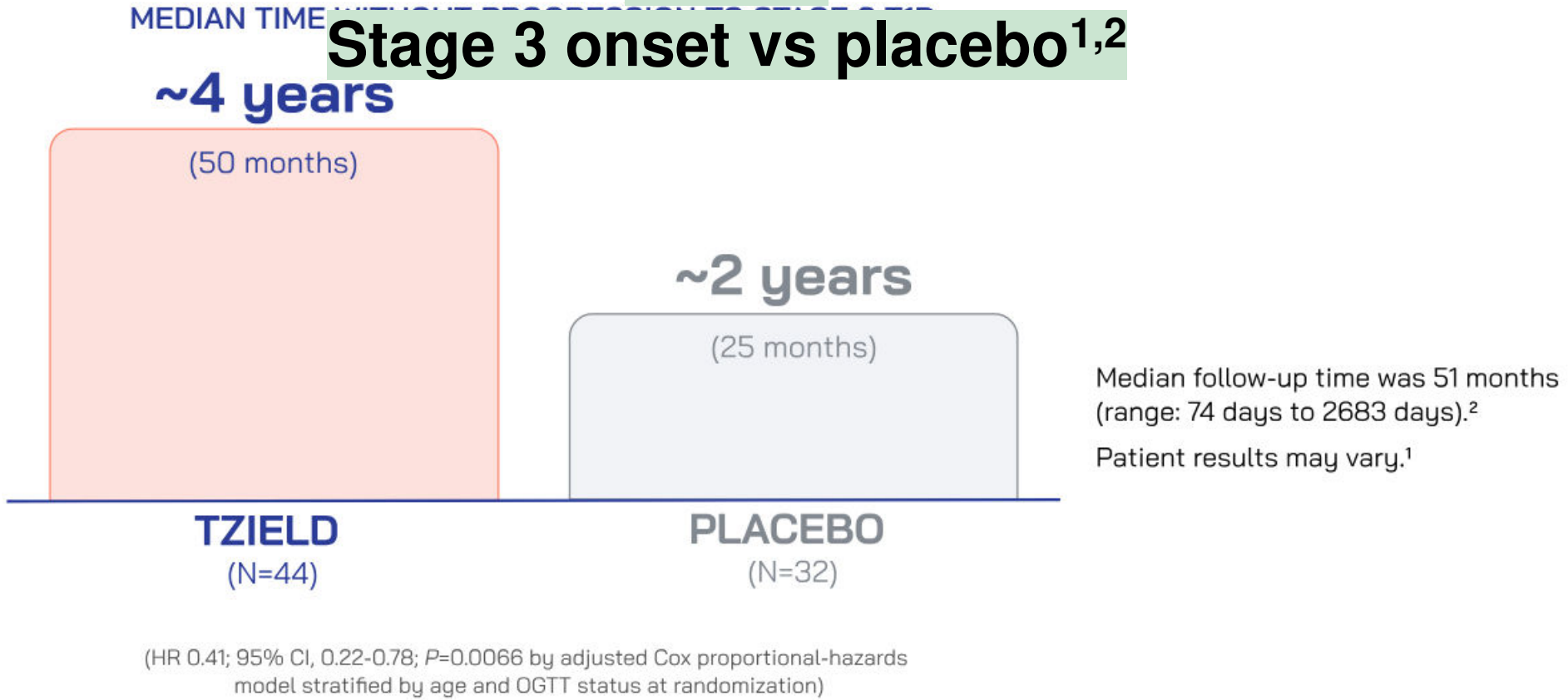
TZIELD was designed to target the underlying autoimmune process of T1D[6]



https://www.tzieldhcp.com/about-tzield for US hcps. Accessed 8-1-24

IN THE TN-10 STUDY WITH PATIENTS WITH STAGE 2 T1D

One 2-week course of TZIELD led to twice the median time to Stage 3 onset vs placebo[1,2]



1. TZIELD Prescribing Information. Provention Bio, Inc; 2023. 2. 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(7):603-613.

Common adverse reactions (ARs) in the TN-10 study[1†‡]

Adverse reactions	Placebo (N=32)	TZIELD (N=44)
Lymphopenia	6%	73%
Rash[§]	0%	36%
Leukopenia	0%	21%
Headache	6%	11%
Neutropenia	3%	5%
Increased alanine aminotransferase	3%	5%
Nausea	3%	5%
Diarrhea	0%	5%
Nasopharyngitis	0%	5%

Throughout the study, greater incidences of these ARs were reported in TZIELD-treated patients vs placebo-treated patients:

- cytokine release syndrome (2% vs 0%)
- serious infections[‖] (9% vs 0%)
- hypersensitivity reactions and serum sickness (2% vs 0%)
- lymphopenia (73% vs 6%)
- neutropenia (7% vs 3%)

Lymphocyte count began to recover after Day 5 and returned to baseline by Week 6 in most patients.

CYTOKINE RELEASE SYNDROME (CRS)
Of the 76 patients in the TN-10 study, CRS occurred in a single TZIELD-treated patient[1]
CRS can be mitigated by premedicating with antipyretics, antihistamines, and/or antiemetics, or by pausing dosing.

1. TZIELD Prescribing Information. Provention Bio, Inc; 2023. 2. 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(7):603-613.

T1D vs Latent Autoimmune Diabetes in *Adults* (LADA)

- Both have positive Autoantibodies
  - LADA Positive autoantibodies to islet β cells
- LADA typically is thought of as slow onset T1 in adults
  - Slower autoantibody destruction
- Age greater than 30 years
- Insulin independence (initiated in the initial 6 months after diagnosis (Immunology for Diabetes Society)….(Clinically debatable)
- *Off label treatment*: GLP-1RAs plus insulin.

Sally is 34 and 12 weeks pregnant

- Her mother has T2D
- Sally's BMI is 28
- She is otherwise healthy with normal labs

- What should your clinical concerns be?
- When should you screen for Gestational Diabetes (GDM)?

DIAGNOSIS AND CLASSIFICATION OF DIABETES

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/m^2 or ≥23 kg/m^2 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 prediabetes (A1C ≥5.7% [≥39 mmol/mol], 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

GDM, gestational diabetes mellitus; IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

Diagnosis and Classification of Diabetes:
Standards of Care in Diabetes - 2024. Diabetes Care 2024;47(Suppl. 1):S20-S42

Gestational Diabetes Mellitus

2.25 In individuals who are planning pregnancy, screen those with risk factors **(Table 2.4)** **B** and consider testing all individuals of childbearing potential for undiagnosed prediabetes or diabetes. **E**

2.26a Before 15 weeks of gestation, test individuals with risk factors **(Table 2.4)** **B** and consider testing all individuals **E** for undiagnosed diabetes at the first prenatal visit using standard diagnostic criteria if not screened preconception.

2.26b Before 15 weeks of gestation, screen for abnormal glucose metabolism to identify individuals who are at higher risk of adverse pregnancy and neonatal outcomes, are more likely to need insulin, and are at high risk of a later gestational diabetes mellitus (GDM) diagnosis. **B** Early treatment for individuals with abnormal glucose metabolism may provide some benefit.

E

Gestational Diabetes Mellitus (continued)

2.26c Screen for early abnormal glucose metabolism with dysglycemia using FPG of 110–125 mg/dL (6.1–6.9 mmol/L) or A1C 5.9–6.4% (41–47 mmol/mol). **B**

2.27 Screen for GDM at 24–28 weeks of gestation in pregnant individuals not previously found to have diabetes or high-risk abnormal glucose metabolism detected earlier in the current pregnancy. **A**

2.28 Screen individuals with GDM for prediabetes or diabetes at 4–12 weeks postpartum, using the 75-g OGTT and clinically appropriate nonpregnancy diagnostic criteria. **A**

2.29 Individuals with a history of GDM should have lifelong screening for the development of prediabetes or diabetes at least every 3 years. **B**

After delivery it is more appropriate to say diabetes is in "remission", not "gone" dh

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-Coustan’s interpretation of the older O’Sullivan and Mahan criteria.

Pancreatic Diabetes or Diabetes in the Context of the Exocrine Pancreas

2.17 Screen people for diabetes within 3–6 months following an episode of acute pancreatitis and annually thereafter. Screening for diabetes is recommended annually for people with chronic pancreatitis. **E**

Cystic Fibrosis-Related Diabetes

2.18 Annual screening for cystic fibrosis-related diabetes (CFRD) with an OGTT should begin by age 10 years in all people with cystic fibrosis not previously diagnosed with CFRD. **B**

2.19 A1C is not recommended as a screening test for CFRD due to low sensitivity. However, a value of ≥ 6.5% (≥48 mmol/mol) is consistent with a diagnosis of CFRD. **B**

2.20 Beginning 5 years after the diagnosis of CFRD, annual monitoring for complications of diabetes is recommended. **E**

Posttransplantation Diabetes Mellitus

2.21 After organ transplantation, screening for hyperglycemia should be done. A formal diagnosis of posttransplantation diabetes mellitus (PTDM) is best made once the individual is stable on an immunosuppressive plan and in the absence of an acute infection. **B**

2.22 The OGTT is the preferred test to make a diagnosis of PTDM. **B**

2.23 Immunosuppressive plans shown to provide the best outcomes for individuals and graft survival should be used, irrespective of PTDM risk. **E**

Monogenic Diabetes Syndromes

2.24a 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**

2.24b 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 (MODY). **A**

2.24c 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**

DIAGNOSIS AND CLASSIFICATION OF DIABETES

Table 2.6—Most common causes of monogenic diabetes

	Gene	Inheritance	Clinical features
MODY	*HNF1A*	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
	HNF4A	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
	HNF1B	AD	HNF1B-MODY: developmental renal disease (typically cystic); genitourinary abnormalities; atrophy of the pancreas; hyperuricemia; gout
	GCK	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])
Neonatal diabetes	*KCNJ11*	AD	Permanent or transient: IUGR; possible developmental delay and seizures; responsive to sulfonylureas
	INS	AD	Permanent: IUGR; insulin requiring
	ABCC8	AD	Permanent or transient: IUGR; rarely developmental delay; responsive to sulfonylureas
	6q24 (*PLAGL1*, *HYMA1*)	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
	GATA6	AD	Permanent: pancreatic hypoplasia; cardiac malformations; pancreatic exocrine insufficiency; insulin requiring
	EIF2AK3	AR	Permanent: Wolcott-Rallison syndrome: epiphyseal dysplasia; pancreatic exocrine insufficiency; insulin requiring
	EIF2B1	AD	Permanent diabetes: can be associated with fluctuating liver function (157)
	FOXP3	X-linked	Permanent: immunodysregulation, polyendocrinopathy, enteropathy X-linked (IPEX) syndrome: autoimmune diabetes, autoimmune thyroid disease, exfoliative dermatitis; insulin requiring

Adapted from Carmody et al. (156). 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.

Diagnosis and Classification of Diabetes:
Standards of Care in Diabetes - 2024. Diabetes Care 2024;47(Suppl. 1):S20-S42

Patient Tips….

Helping your patients “Get Started”

Once the diagnosis of diabetes is made…..

- Make a referral for diabetes self management education and support (DSMES)
  - Education referrals should be made: at diagnosis, annually, if glycemic goals not met, when major changes happen, ie, need for insulin, death of a spouse
- Initial Survival skills include:
  - Setting A1C/glycemic goals
  - Teaching glucose monitoring, recording data, observation of patterns
  - Providing basic eating guidelines and exercise/activity guidelines
  - Discussion of meds and side effects, ie, hypoglycemia.
  - Setting initial goals; ie, I will walk 30 minutes 5 days/week

In a Nut Shell…..

Life Style Recommendations The PWD Job:	-**Healthy Eating**: 5 Minute Nutrition Consult : -After your assessment, be sure you have worked these tips into the discussion: -Don't drink sugar. *Juice is sugar.* Sweeteners are ok. Try Stevia. Coke and Pepsi have it. - Be consistent and modest with Carb intake. 100% of carbohydrate turns into sugar. – Generally the RD's recommend 2-3 carb servings/meal - Have solid protein with all meals. It improves satiety. -It's ok to have a piece of B-Day cake. On *YOUR* birthday -**Activity**: 30-60 minutes activity/day. *Starting is the hardest part.* -**Weight loss** goal: 5-10% body weight, *But every pound counts*
Treatment: Your Job:	- Start: +/-Metformin XR 500mg. 1 tab/in pm, increase 1x/week til 1000mg bid - Add GLP1-RA or SGLT2. Then the other one ASAP - Continue Mod/high intensity statin, HTN mgt - Self Monitoring of Blood Glucose (SMBG);finger stick or CGM - Foot Exam - Annual: Standards of Care: Eye/Retinal Exam, UACR, eGFR, immunizations
Referral: Your Job:	- Diabetes Self Management Training/Support!! *As important as eRX* - *1. At Dx, 2.Annually, 3.When changes, ie, complications, insulin start, 4. Life changes* -

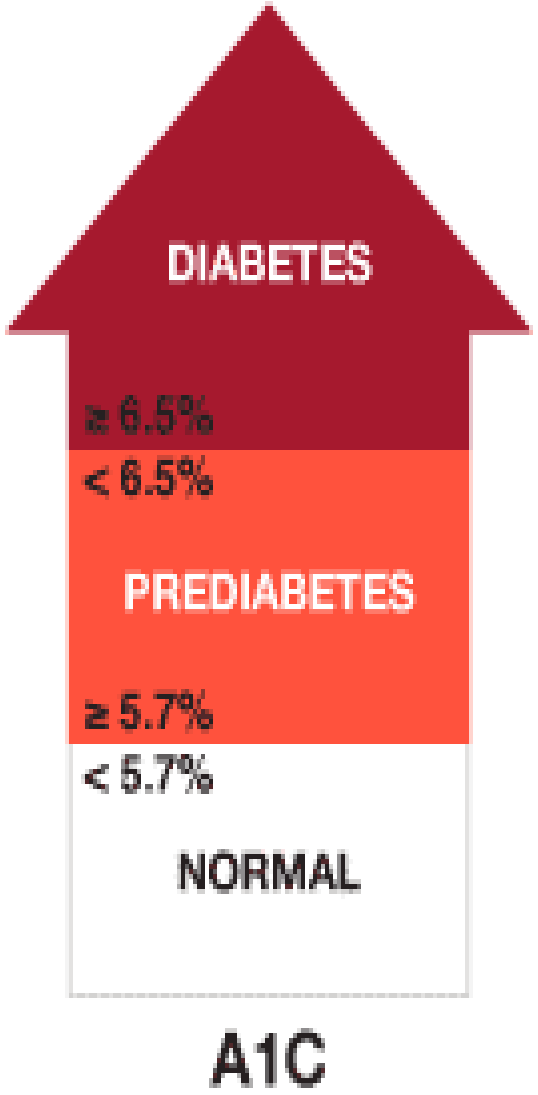
Diabetes Glucose Goals

Glycemic Goals for T2DM

	ADA	IDF	AACE/ACE
HbA_{1c} (%)	<7.0	<6.5	<6.5
FPG (mg/dl)	<130	<110	<110
2 Hr PG (mg/dl)	<180	<140	<140

ADA = American Diabetes Association
IDF = International Diabetes Federation
AACE= American Assoc of Clinical Endocrinologists

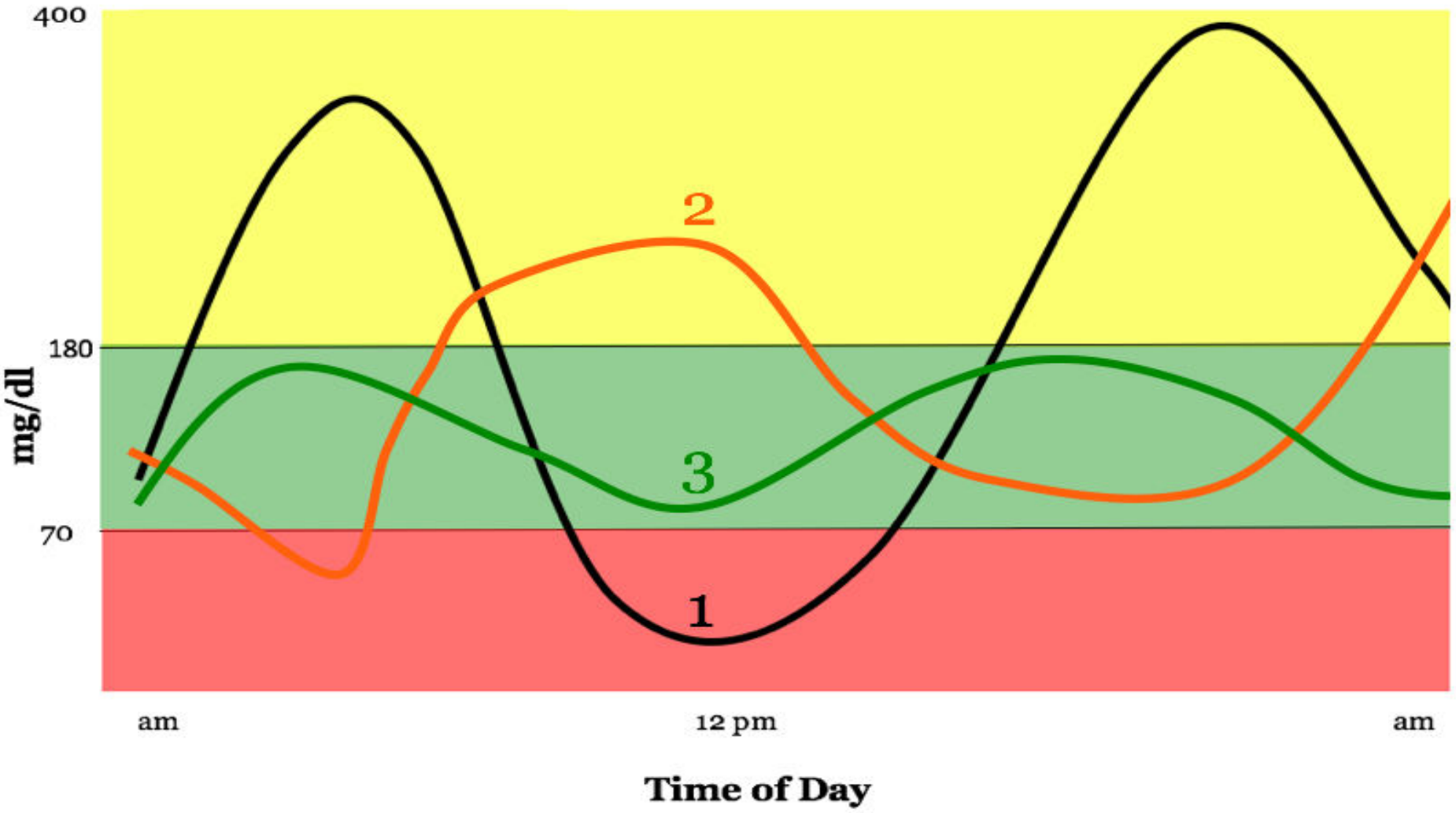
Hemoglobin A1c vs Glucose



A1C%	eAG mg/dl
5	97
5.5	111
6	126
6.5	140
7	154
7.5	169
8	183
8.5	197
9	212
9.5	226
10	240
10.5	255
11	269
11.5	283
12	298

A1c vs. Time In Range

Same A1C….very different glucose variability…



Monitoring Your Blood Sugar at Home: for most adults

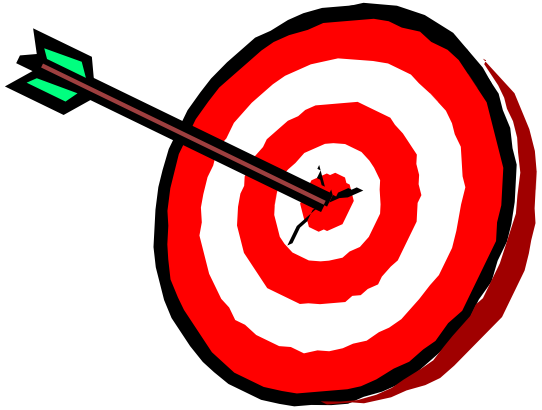
ADA Goal A1C less than 7.0%

Before meals: 80–130 mg/dL

2 hours (after meals):

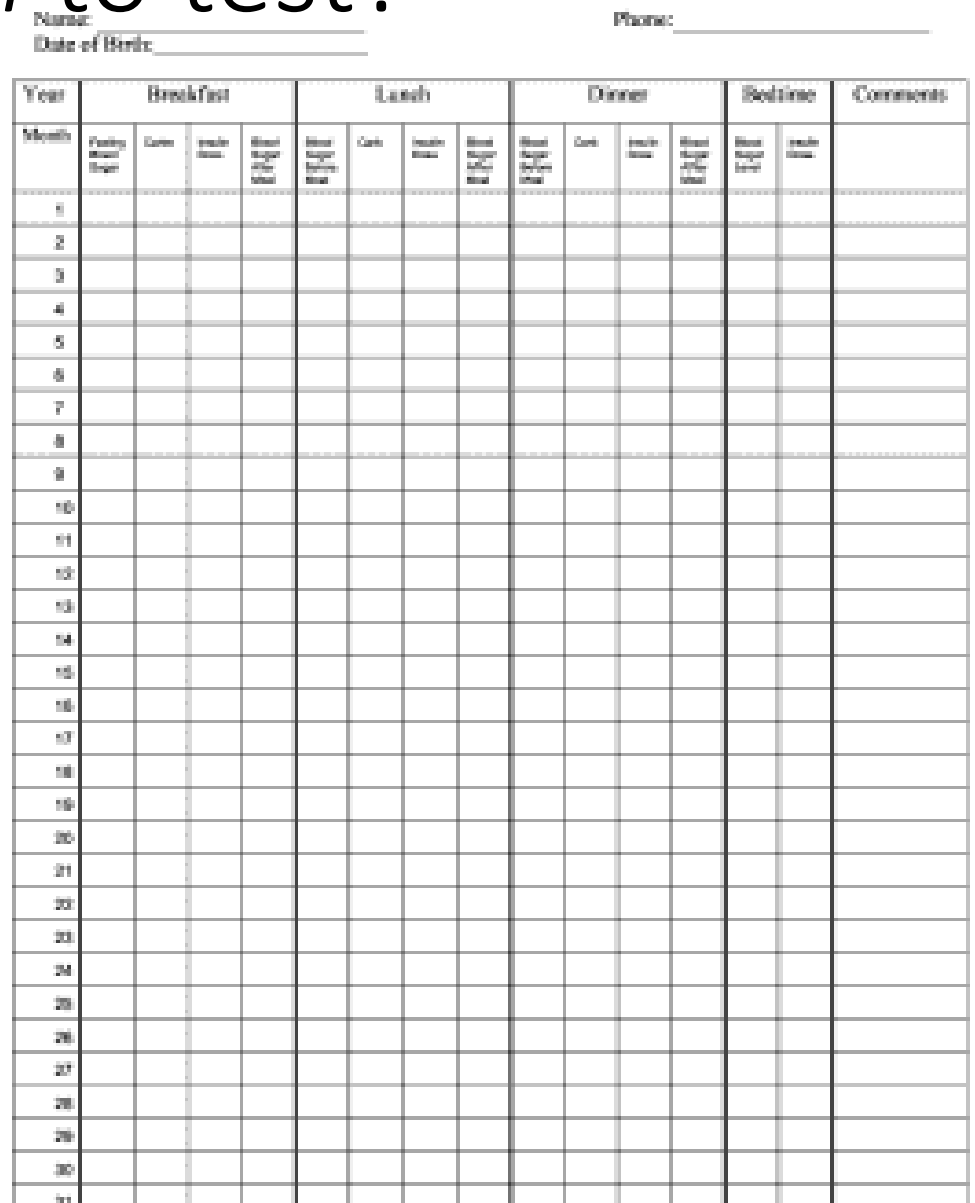
less than 180 mg/dL

uchealth



How *Often* and *When* to test?

- Testing Patterns
  - **Testing in pairs:**
  - Before Br & 2 hrs after
    - Skip a day
  - Before Lu & 2 hrs after
    - Skip a day
  - Before dinner & 2 hrs after


Name:_____ Phone:_____
Date of Birth:_____

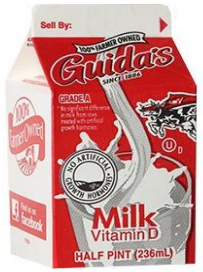
Year	Breakfast				Lunch				Dinner				Bedtime		Comments
Month															
1															
2															
3															
4															
5															
6															
7															
8															
9															
10															
11															
12															
13															
14															
15															
16															
17															
18															
19															
20															
21															
22															
23															
24															
25															
26															
27															
28															
29															
30															
31															

Lack of Exercise

Hypoglycemia Symptoms

Hypoglycemia Treatment

- A Sweet ***Bite***….



1 C milk

5-6 lifesavers

1/3-1/2 C. OJ

4 glucose tabs

-Eat a Sweet Bite
-Wait 15 minutes
-Re-check glucose (goal: >100mg)
-Re-Treat if needed
(try holding sweet in your mouth)
-Then have snack with solid protein
-Document it
-**Carry a sweet bite with you!**

6 steps for a accurate test

1 Wash your hands

2 Install the lancet

3 Insert the strip

4 Collect blood

5 Apply blood

6 Results in 7s

Summary

- Screening for and Diagnosing diabetes begins with the annual history and physical
- Consider screening and staging for T1D
  - Autoantibody testing for anyone with first degree relative with T1, other autoimmune diseases, rapid wt loss…
- There is no cure for diabetes, help your PWD understand and believe they can live a long and healthy life when they are diagnosed.
- Help your PWD “Get Started” with survival skills, then
- Make the referral for diabetes education