From Awareness to Action: Driving Multidisciplinary Application of Screening and Disease Modifying Therapies in Early Stage T1D

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Disclosures

- **Dr Antoinette Moran, MD,** discloses that she has received fees for non-CME/CE services received directly from Novo Nordisk DSMB, consulting fees from Abata, and provided contracted research for Abbott Diabetes, Medtronic, and Prevention Bio.

During this lecture, the faculty may mention the use of medications for both US Food and Drug Administration (FDA)-approved and non-FDA-approved indications.

All relevant financial relationships have been mitigated.

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Learning Objectives

- Identify criteria for T1D screening, focusing on high-risk patients to facilitate timely referral and monitoring
- Interpret T1D screening results and effectively communicate next steps to support patient education and inform treatment decisions
- Identify appropriate patients who would benefit from treatment with disease-modifying therapies for delaying T1D progression based on clinical evidence

Polling Question

In your current practice, do you screen for T1D with islet autoantibodies in persons without symptoms?

a) Yes

b) No

Type 1 Diabetes: Prevalence and Risk

US Prevalence and Incidence of T1D

1.7 million Americans have T1D, including **~300,000** children and adolescents

Diagnosis

- T1D is the most common form of diabetes in childhood, but it can occur at any age
- 64,000 people are diagnosed each year (27,000 children and 37,000 adults)
- With the availability of autoantibody testing, many adults who might have previously been diagnosed with T2D simply because of their age are now recognized as having T1D

Centers for Disease Control and Prevention (CDC). National diabetes statistics report. Updated 5/4/2024 (https://www.cdc.gov/diabetes/php/data-research/index.html). Accessed 2/13/25. Rogers MAM, et al. *BMC Med*. 2017;15:199. Dabelea D, et al. *JAMA*. 2014;311:1778-1786. Phillip M, et al. *Diabetes Care*. 2024;47:1276-1298.

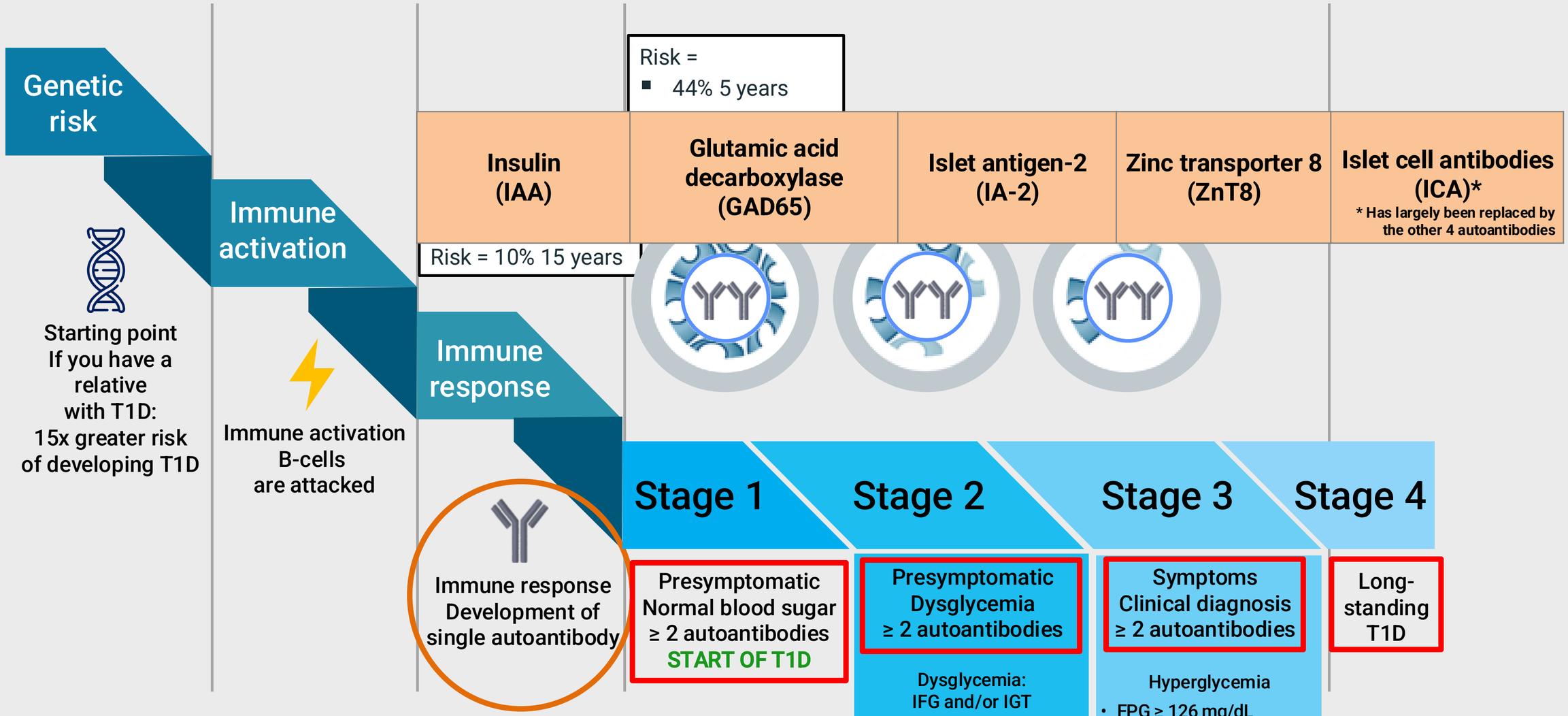
Genetic Susceptibility Is Important, But Not All of Those Who Are Susceptible Develop T1D

T1D risk in individuals who have an affected relative

	Risk of T1D	
General population	**0.4%**	**1/250**
Father with T1D	4%–7%	1/25–1/14
Mother with T1D	1.5%–3%	1/67–1/33
Sibling with T1D	5%–7%	1/17–1/14
Identical twin with T1D	30%–70%	1/3–1/1.4

DiMeglio LA, et al. *Lancet*. 2018;391:2449-2462. Parkkola A, et al. *Diabetes Care*. 2013;36:348-354.

T1D Develops in Predictable Stages Related to Risk



FPG = fasting plasma glucose; HbA_{1c} = glycosylated hemoglobin; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; PG = plasma glucose; RPG = random plasma glucose.

American Diabetes Association (ADA) Professional Practice Committee. *Diabetes Care*. 2025;48(suppl 1):S27-S49. Haller MJ, et al. *Horm Res Paediatr*. 2024:1-17. Insel RA, et al. *Diabetes Care*. 2015;38:1964-1974. Sims EK, et al. *Diabetes*. 2022;71:610-623. Phillip M, et al. *Diabetologia*. 2024;67:1731-1759.

Screening and Early Detection of T1D

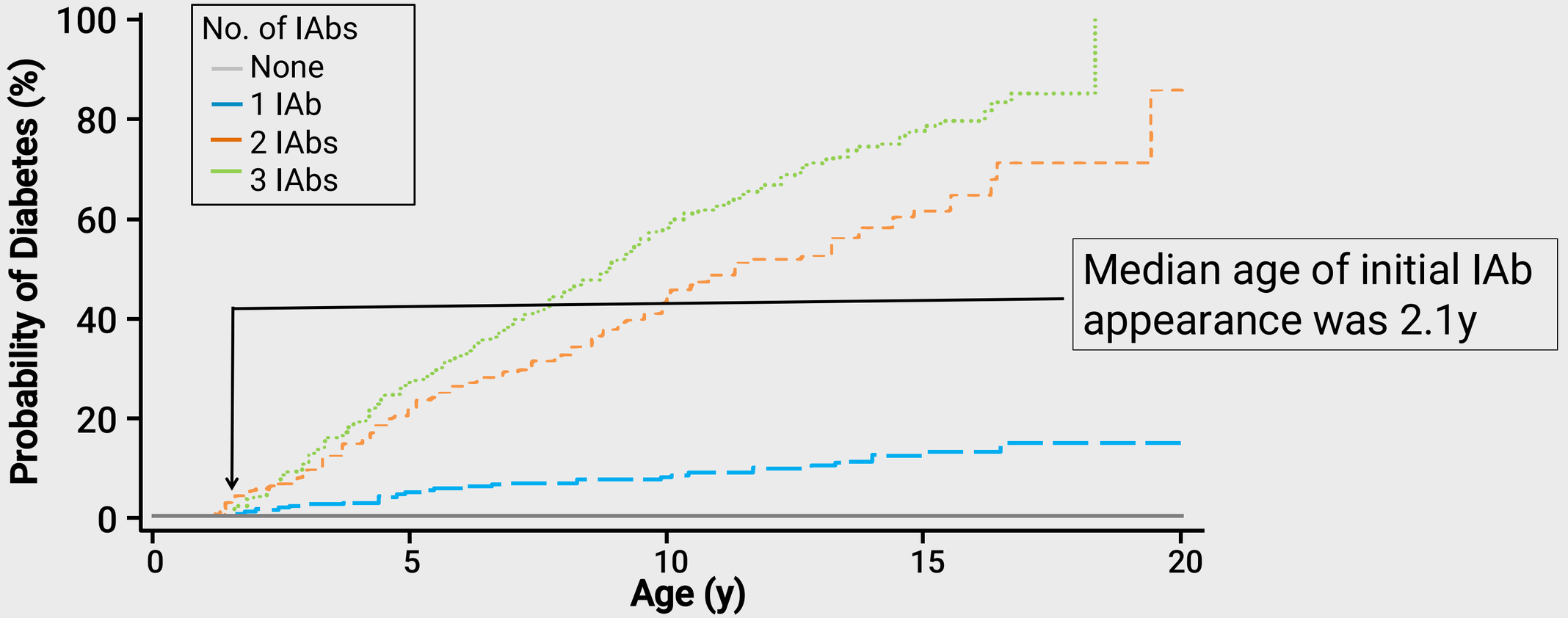
Polling Question

What are your biggest barriers in screening for T1D?
Select all that apply

a) Lack of knowledge/evidence about screening
b) Uncertainty about how to identify whom to screen
c) Lack of knowledge on when to screen
d) Lack of knowledge about how to screen
e) Difficulty with interpreting screening results and next steps
f) Addressing patient/caregiver anxiety about screening in the absence of symptoms

We Can Identify Asymptomatic T1D With Autoantibody Screening

Screening of birth cohorts from the US, Germany, and Finland showed development of IAbs long before progression to clinical stage 3 T1D

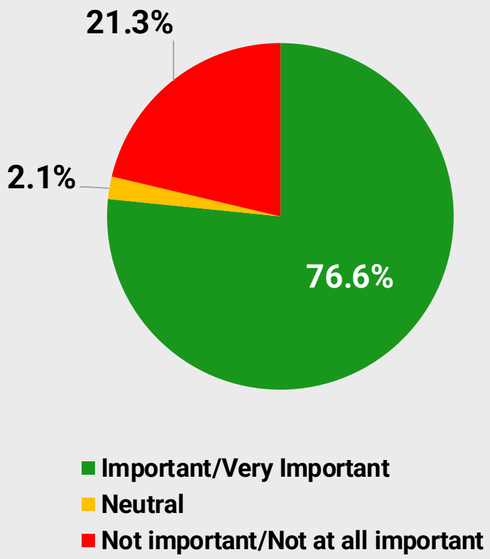


No. at risk IAbs, No.					
3 IAbs	358	250	112	20	0
2 IAbs	227	168	82	19	1
1 IAb	474	430	272	118	9
None	12318	8875	5253	1161	44

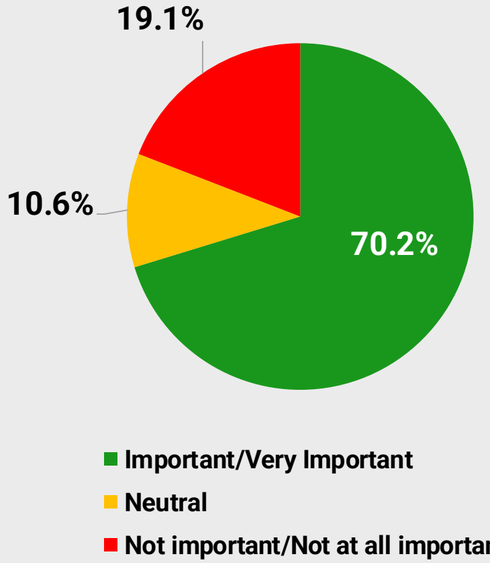
Zeigler AG, et al. *JAMA*. 2013;309:2473-2479.

Reasons to Get Screened for T1D: Responses from a Patient Survey

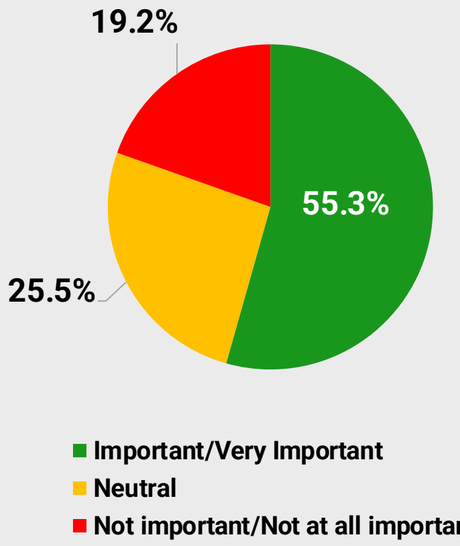
Percent of Respondents



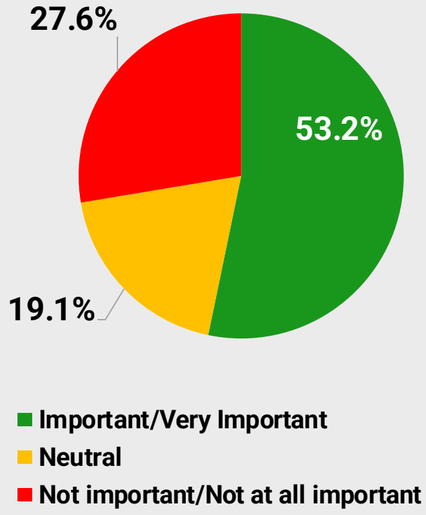
I wanted a chance to have more time before I (or my child) gets T1D



I (or the child I care for) wanted to know whether I/they would be at risk to have T1D myself/themselves



I wanted to contribute to the advancement of T1D research



I was worried about diabetic ketoacidosis (DKA)

Responses were: Not at all important, Not important, Neutral, Important, and Very Important

O'Donnell HK, et al. *Diabetes Obes Metab*. 2025;27:2495-2506.

Who, and When, and How to Screen for T1D

IAb Testing: In Whom?

To ***screen*** for T1D in

- Relatives of a person with T1D
- Person with history of other autoimmune disease(s)
- Relatives of a person with other autoimmune disease(s)
- Elevated genetic risk score (if tested)
- Population screening in organized programs

To ***clarify diagnosis*** of T1D

- History of hyperglycemia (misdiagnosis is possible)
  - Illness, stress, or steroid-induced hyperglycemia
  - Gestational diabetes
- Persons with new-onset diabetes to evaluate for T1D versus other forms of diabetes

In all IAb+ patients, a full venous IAb panel should be done within 3 months of the first test to confirm.

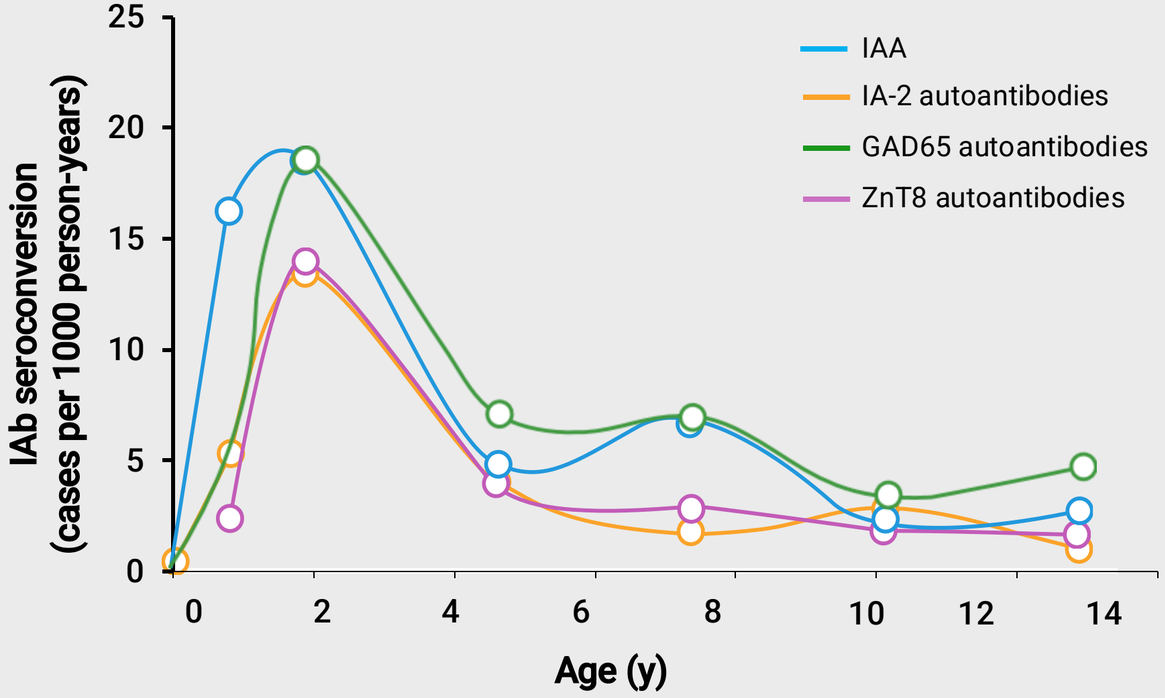
Education, especially for a patient with abnormal or high glucose levels, should not be delayed while waiting for confirmation.

ADA Professional Practice Committee. *Diabetes Care*. 2025;48(suppl 1):S27-S49. Phillip M, et al. *Diabetologia*. 2024;67:1731-1759

Screening for Islet Autoimmunity Should Occur at Multiple Times During Childhood

- In genetically at-risk individuals, T1D autoantibody seroconversion peaks **between 9 months and 2 years of age**
- Insulin autoantibodies may develop **earlier than GAD65, IA-2, or ZnT8 autoantibodies** in young children
- **Screening at ages 2 and 6 years** may optimize sensitivity and positive predictive value for predicting T1D during childhood, while an additional testing at age 10 years may aid in predicting T1D during adolescence

Incidence of specific T1D autoantibodies by age



Ziegler A-G, et al. *Diabetologia*. 2012;55:1937-1943. Ghalwash M, et al. *Lancet Diabetes Endocrinol*. 2022;10:589-596. Ghalwash M, et al. *Lancet Child Adolesc Health*. 2023;7:261-268.

Major T1D Screening Programs in the United States

Research-based screening programs (no HCP order required)

Name and available locations	Age to participate
ASK (United States)	Children and adults aged 1–99 years (no family history of T1D required)
TrialNet (United States)	Aged 2–45 years with a parent, brother/sister, or child with T1D; or have tested positive for ≥ 1 T1D autoantibody outside of TrialNet *OR* Aged 2–20 years with aunt/uncle, cousin, grandparent, niece/nephew, or half-sibling with T1D

Clinical laboratory	
Quest Diagnostics, LabCorp, and Mayo Clinic Laboratories	All ages, HCP order required. CPT codes* ▪ 86341 (GAD65, IA-2, ZnT8 antibodies) ▪ 86337 (insulin antibody)

Relevant ICD10 Codes	
Z83.3	Family history of T1D
Z86.2	History of autoimmune disease
Z83.2	Family history of autoimmune disease
E10.A0	T1D, Presymptomatic, Unspecified
E10.A1	T1D, Presymptomatic, Stage 1
E10.A2	T1D, Presymptomatic, Stage 2

Not a comprehensive list of available screening programs; may be subject to change.
*CPT codes may be subject to change, and specific codes may differ between laboratories. Not all antibodies may be available under a specific laboratory or under a CPT code.

CPT = Current Procedural Terminology; HCP = healthcare provider.

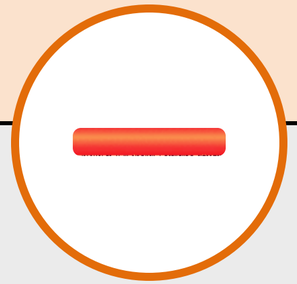
ASK (https://www.askhealth.org). TrialNet. Pathway to prevention (https://www.trialnet.org/our-research/risk-screening). Breakthrough T1D (formerly JDRF) (https://www.breakthrought1d.org/early-detection/). Ask the Experts (https://www.asktheexperts.org/for-providers). URLs accessed 2/12/2025.

Follow-up and Monitoring After T1D Screening

How to Interpret T1D Screening Results

0 autoantibodies

- Lower risk for developing T1D
- Rescreening may be considered in individuals with family history of T1D, especially if younger than age 12y.



1 autoantibody

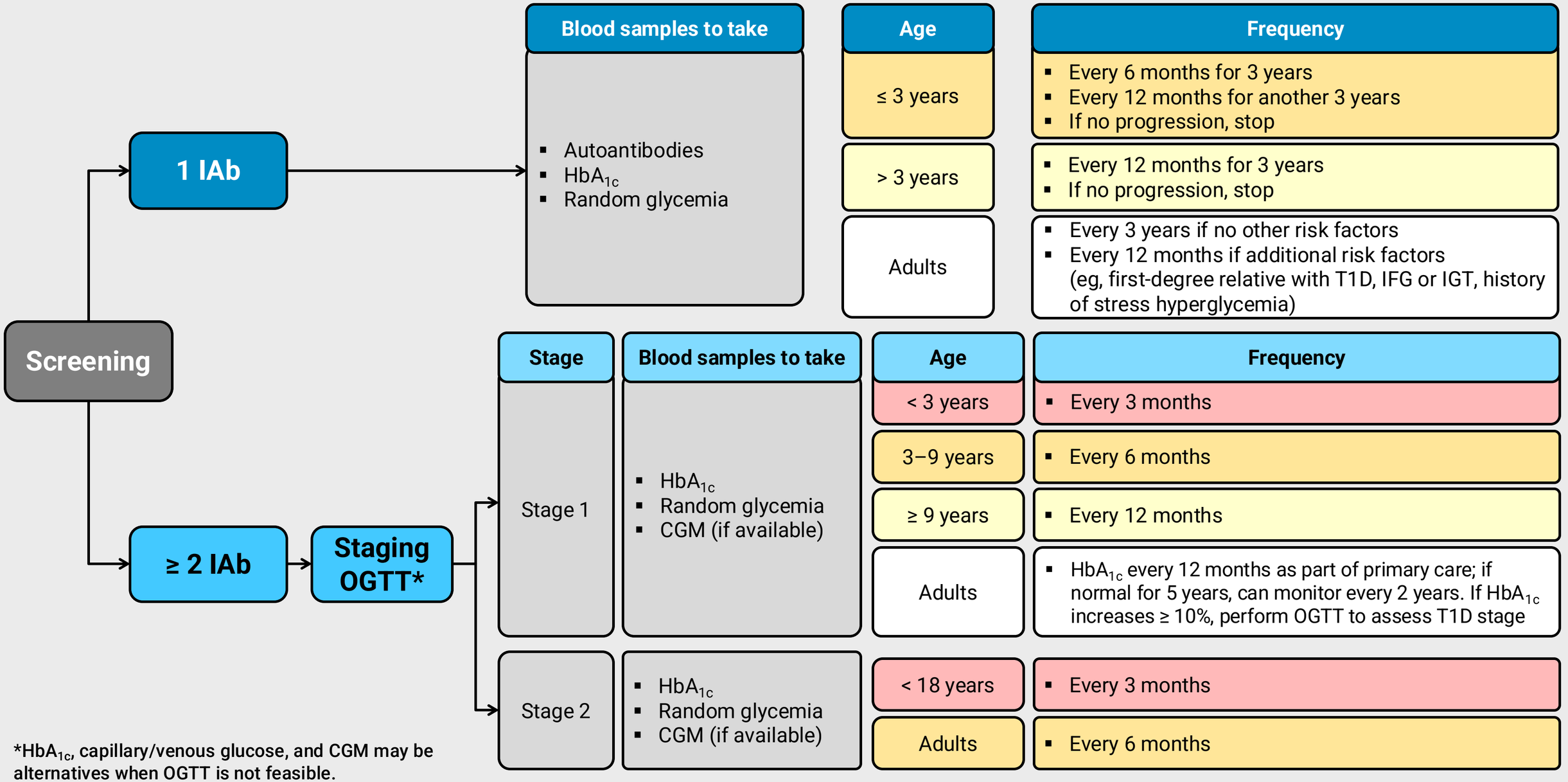
- Higher risk for developing T1D than those with no autoantibodies
- Autoantibody status should continue to be monitored, along with BG

≥ 2 autoantibodies

- Already in early stage T1D
- Metabolic staging and symptom evaluation
- If asymptomatic or no hyperglycemia, patient may be eligible for disease modifying therapy to delay progression to clinical T1D, or for clinical research prevention trials

ADA Professional Practice Committee. *Diabetes Care*. 2025;47(suppl 1):S27-S49. Simmons KMW, et al. *Diabetes Technol Ther*. 2023;25:790-799.

Monitoring IAb+ Individuals (after confirmation with a second test)

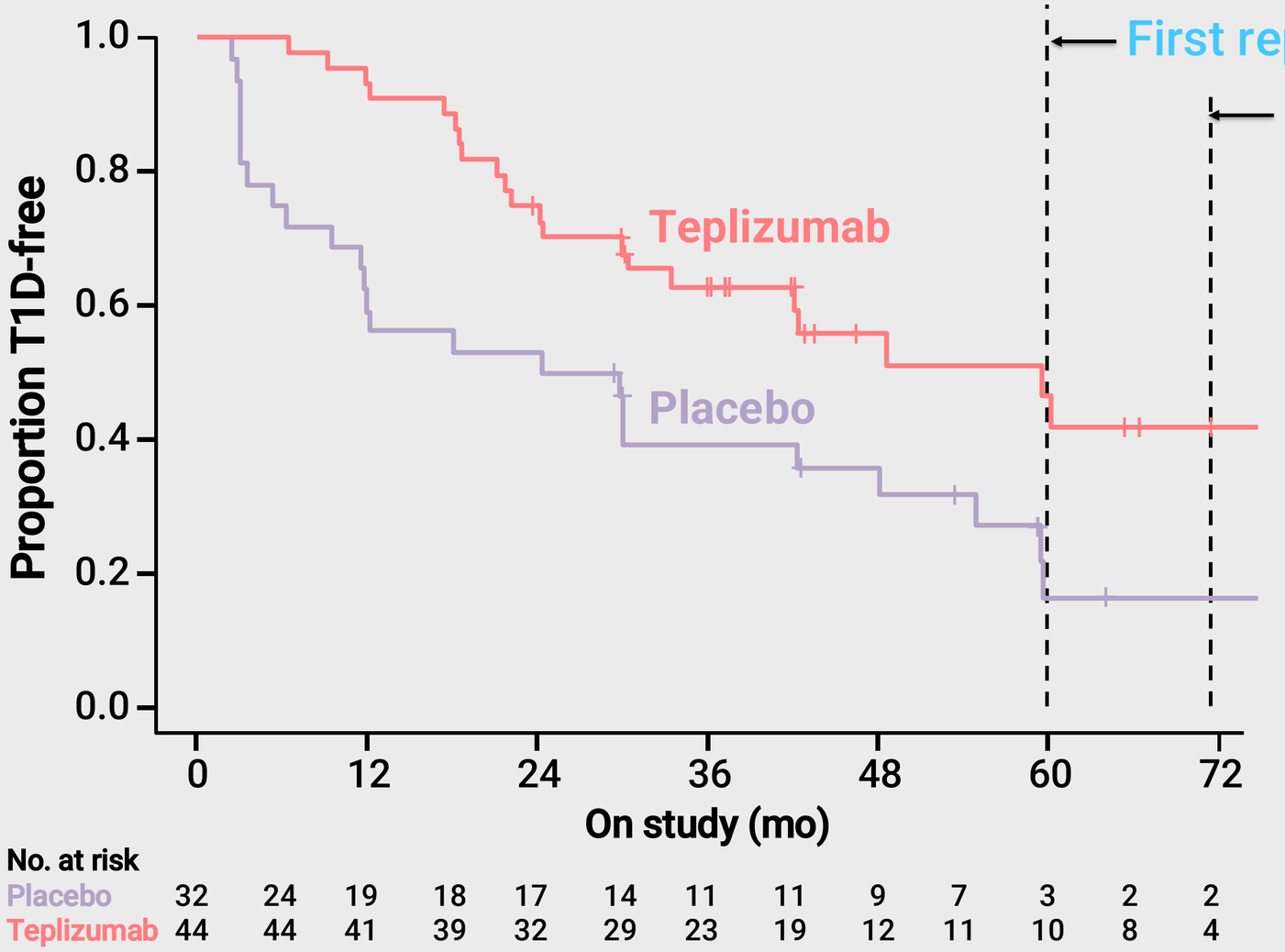


*HbA_{1c}, capillary/venous glucose, and CGM may be alternatives when OGTT is not feasible.

Modified from Phillip M, et al. *Diabetes Care*. 2024;47:1276-1298 and Haller MJ, et al. *Horm Res Paediatr*. 2024:1-17.

Advances in Delaying T1D Progression

TN10 Results: Effect of Teplizumab in Children and Adolescents With Stage 2 Diabetes

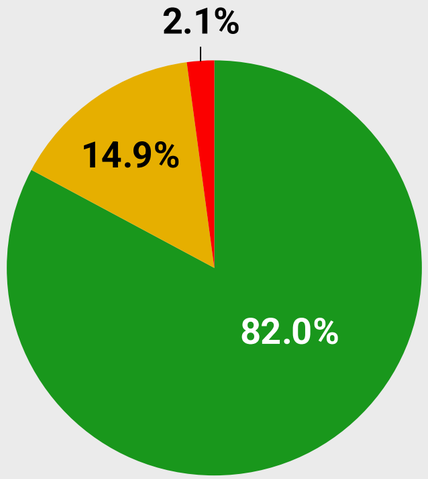


- In the first report (5 years), the time to stage 3 was delayed by 2 years with teplizumab
- 12 months later there was a 33-month delay
- By 6 years, 50% of teplizumab-treated subjects were diabetes-free compared with 22% of those in the placebo group

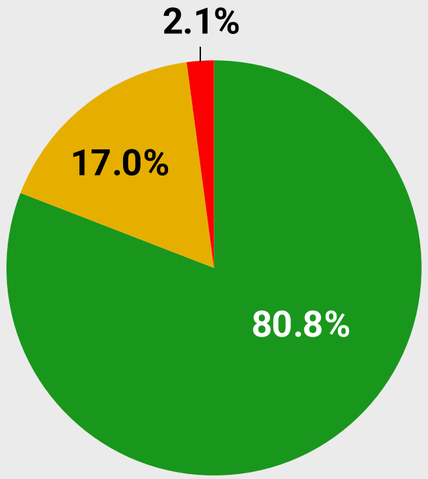
Herold KC, et al. *N Engl J Med.* 2019;381:603-613. Sims EK, et al. *Sci Transl Med.* 2021;13:eabc8980.

Real-World Experience With Teplizumab: *Survey Results of Individuals Treated With Teplizumab for Stage 2 T1D*

Views and Expectations Associated with Teplizumab

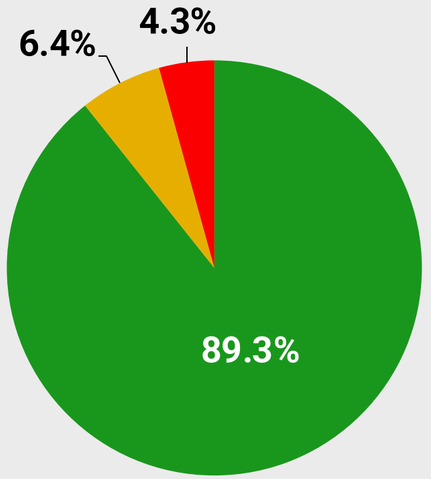


I am glad I (or my child) did the teplizumab infusion



I would recommend teplizumab to others in my situation

Outlook After Teplizumab Treatment



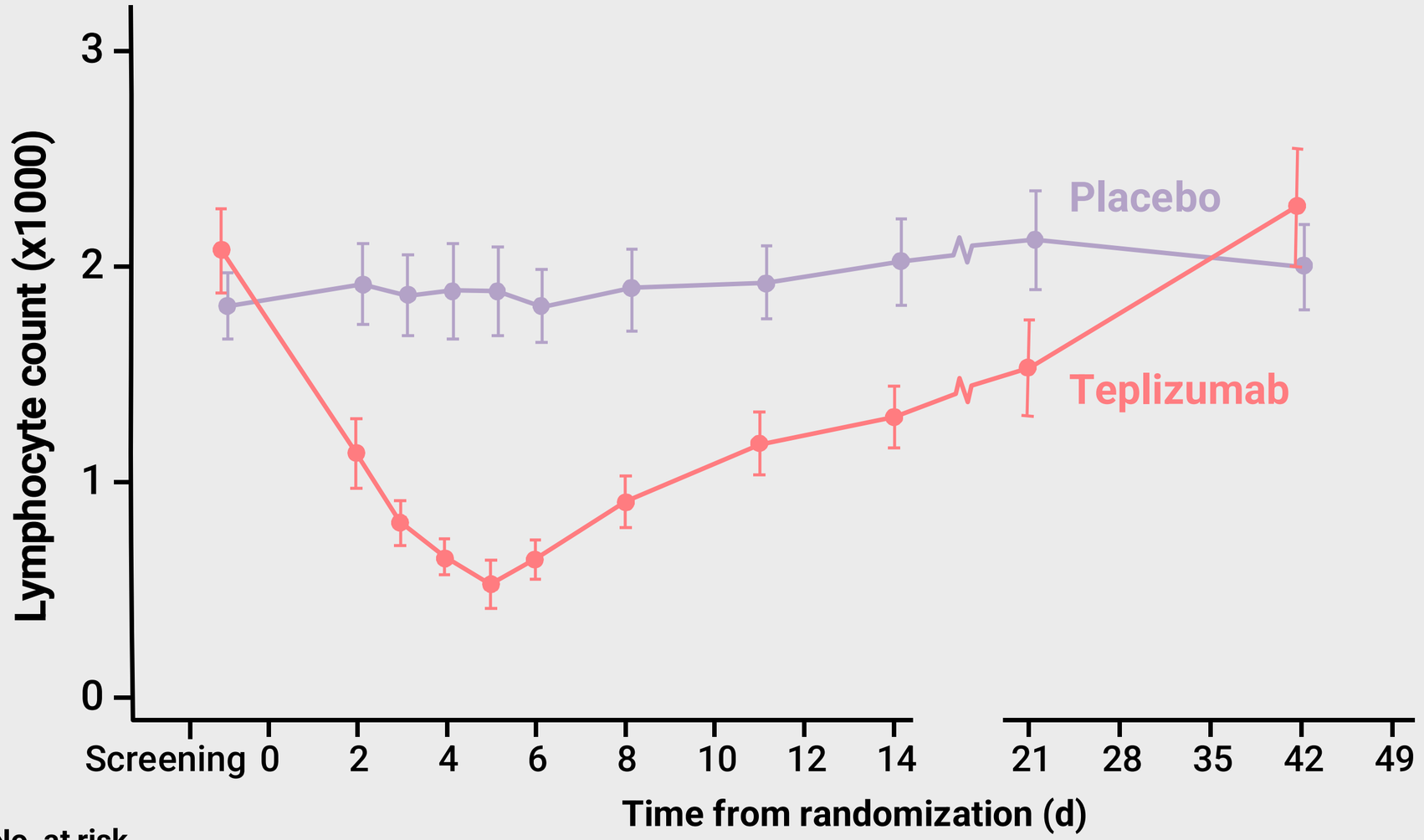
I would make the same decision in the future about teplizumab if another family member needed it

Responses were: Strongly disagree, Disagree, Neutral, Agree, Strongly Agree

O'Donnell HK, et al. *Diabetes Obes Metab*. 2025;27:2495-2506.

Teplizumab Therapy General Considerations

TN10 Results: Lymphocytes Are Transiently Suppressed



Herold KC, et al. *N Engl J Med*. 2019;381:603-613.

Practical Tips for Teplizumab Therapy Based on TrialNet Protocol and Experience

Locale for drug administration—ideally, an infusion center with an onsite provider comfortable with cytokine release syndrome/drug reactions (eg, chemotherapy/rheumatology centers); emergency medications on hand in case of hypersensitivity reaction

- Particularly important during the 5 days—while the prescribing information states infusions can be given at clinic or in the home via home health, during the first 5 days the patient is likely to experience some degree of cytokine release syndrome and an acute care setting is the safest way to provide the availability of rapid and experienced emergency care
- For additional information, including pre-infusion vaccine recommendations, pre-medications and drug withholding criteria, refer to the 2024 PES guidance statement on teplizumab treatment
- ICD10 codes specific to early stage T1D:
  - E10.A0 = T1D, presymptomatic, unspecified
  - E10.A1 = T1D, presymptomatic, stage 1
  - E10.A2 = T1D, presymptomatic, stage 2

ICD10 = *International Classification of Diseases, Tenth Revision*; PES = Pediatric Endocrine Society.
Adapted from Mehta S, et al. *Horm Res Paediatr.* 2024:1-12.

On the Horizon: Diabetes Modifying Therapies in New Onset (Stage 3) T1D

Current Directions for New-Onset Stage 3 T1D

- Various agents in new onset and prevention trials temporarily slow β-cell loss in some subjects, but it appears less and less likely that a single course of a single agent will completely prevent clinical diabetes or will be effective in all people
- Multiple agents are in trials or under consideration, especially in combination, often targeting different things (eg, T-cells, B-cells, inflammation, β-cell health, insulin resistance, viruses, microbiome)
- Some investigators are considering “induction” with an agent to temporarily alter the T-/B-cell milieu (eg, teplizumab, ATG, abatacept, rituximab), followed by maintenance with agents that are safer and more practical for chronic use (antigens, verapamil, anti-inflammatory agents, etc)
- Breakthrough T1D (formerly JDRF) and TrialNet are good resources to discuss study availability

ATG-anti-thymocyte globulin; JDRF = Juvenile Diabetes Research Foundation.

Conclusions

- There are practical benefits to diagnosing preclinical T1D
- Autoantibody screening identifies individuals at high risk for progression to clinical stage 3 T1D. This can be done locally or through established programs such as TrialNet
- If ≥ 2 IAbs are present, the next step is an OGTT for staging, and close follow-up
- Stage 1 or 2 T1D: May be eligible for therapy (teplizumab in stage 2, other drugs as they become available) or may be eligible to participate in a prevention study
- Patients with new-onset T1D may be eligible for a study but this usually needs to be initiated within the first couple months of diagnosis
- Information can be found through TrialNet or Breakthrough T1D

Q&A

Cases

Case: Ava and Her Siblings

- Ava is 10 years old and was diagnosed with new onset T1D after presenting to ER with mild DKA 2 weeks ago
  - Previously healthy; PMH unremarkable, physical exam normal
  - Paternal great aunt with hypothyroidism
  - Regained weight previously lost
  - Insulin needs have decreased since last week
- Ava has 4 siblings: Asher and Ezra (16-year-old twins), Leo (14 years old), and Charlotte (11 years old)
- Research and screening of all family members are discussed during the delivery of diabetes education

Ava and Her Siblings: Question

Which stage of T1D does Ava have and what is the most appropriate treatment option for her?

a) Stage 2 T1D and teplizumab
b) Stage 2 T1D and insulin
c) Stage 3 T1D and teplizumab
d) Stage 3 T1D and insulin + consider a clinical trial

Ava and Her Siblings: Question

What are the risks of Ava’s siblings developing T1D?

a) ~5% risk
b) ~33% risk
c) ~50% risk
d) I do not know/Unsure

Case: Ava and Her Siblings


Asher and Ezra

- Twins
- 16 years old
- 0 autoantibodies

Leo

- 14 years old
- + for 2 autoantibodies
  - Results are confirmed on repeat testing

Charlotte

- 11 years old
- + for 1 autoantibody (IA-2)
  - Results are confirmed on repeat testing

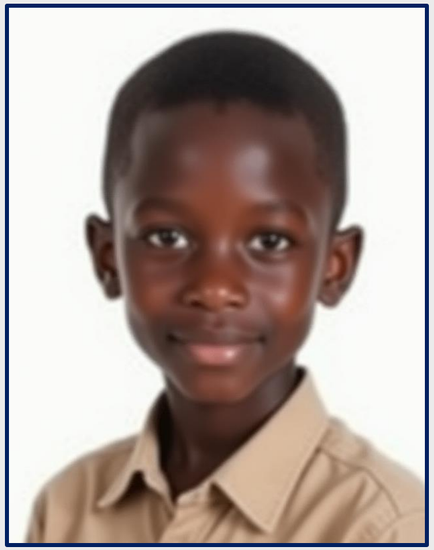
Ava and Her Siblings: Case Discussion

Click the “raise a hand” icon, which can be located on the participants’ icon on your zoom toolbar

- Based on the screening results, what are the next steps for:
  - Twins Asher and Ezra (age 16; negative)?
  - Charlotte (age 11; +1 antibody)?
  - Leo (age 14; +2 antibodies)?
- If one of the twins were to test positive for 2 autoantibodies, what would be the risk of the other twin also developing diabetes?

Case: Mohammed

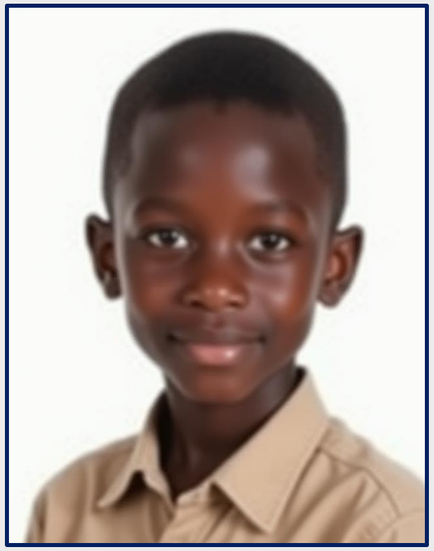
- 13-year-old Somali boy
- 3-year history of asthma, typically well controlled with chronic low-dose inhaled fluticasone
- Otherwise well: normal height (75th percentile) and weight (50th percentile), active, rarely sick
- Family history negative for T1D and other autoimmune diseases
- Brought to ER for an asthma exacerbation with a mild COVID-19 infection; given large dose of IV prednisone and started on a bronchodilator; admitted for 2 days for observation
- Glucose level is 240 mg/dL when he arrives on the ward; it drifts down over next 36 hours
- Glucose level is normal, and asthma symptoms have resolved by discharge; returned to baseline good health at 1-month follow-up with PCP; only on inhaled fluticasone, bid
- PCP orders IAbs, positive for GAD and IA-2
- HbA_{1c}: 5.6%



Mohammed: Case Discussion

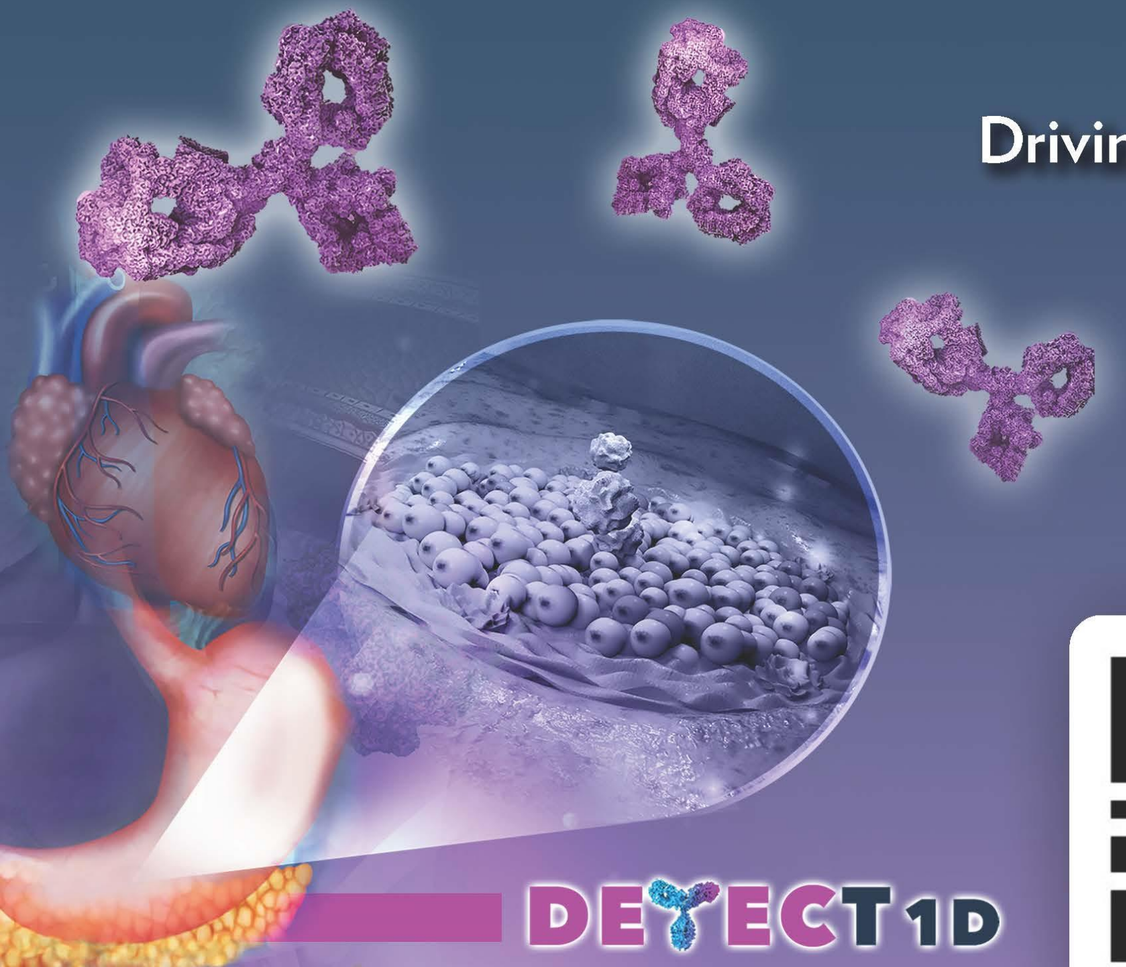
Click the “raise a hand” icon, which can be located on the participants’ icon on your zoom toolbar

- What is stress or steroid-induced hyperglycemia?
- What is the relation between COVID-19 and T1D?
- What is the next step for Mohammed? Is he eligible for treatment with teplizumab?



Q&A

Thank you!



DETECT 1D

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EARLY STAGE T1D

PROGRAM RESOURCES

https://detect-t1d.com/

- CREATE a complimentary personalized office poster & pocket card
- VIEW supplemental resources and animations
- REGISTER for a variety of CME activities

MED LEARNING GROUP

This activity is provided by Med Learning Group.
This activity is supported by an educational grant from Sanofi US.

Insights-to-action collaboration platforms

This is a secure, multi-disciplinary forum that brings together healthcare professionals, infusion specialists, patients, and expert faculty to improve the early screening and identification of type 1 diabetes (T1D), timely referral, and treatment of T1D to delay disease progression.

Organized into four interconnected boards, this initiative fosters cross-disciplinary collaboration, peer learning, and real-world problem-solving. Participants engage in moderated discussions, review curated content, and contribute to case-based conversations that address barriers to early screening, patient selection, and care along the continuum of T1D.

Infusion Hub:

A collaborative space for infusion specialists and other clinicians who treat patients with T1D to provide practical pearls for the application of disease-modifying therapies for T1D, including patient selection, appropriate infusion referrals, as well as standards and considerations for the safe administration of these therapies.

PCP/Endo - Regional:

Regionally focused forums that connect primary care clinicians and endocrinologists to discuss challenges and brainstorm solutions on screening protocols, streamline referrals, and ensure earlier access to care for disease-modifying therapies that delay T1D progression in eligible individuals.

Scientific Council/Ambassador Program:

A faculty-led forum uniting expert clinicians and ambassadors to address real-world challenges in T1D care - starting with early identification. Through structured discussions, members co-develop practical strategies to improve screening, strengthen referral pathways, and delay disease progression across the care continuum.

Patient Support Network:

A moderated, secure community where people with or at risk for T1D - and their caregivers - share lived experiences across the continuum of T1D, access curated resources, and offer critical input to ensure support remains patient-centered and timely.
[Intended for patients]