



Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

6th Childhood Diabetes Prevention Symposium General Population Screening for T1D

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Guidelines for Monitoring and Education in Pre-Symptomatic T1D: Monitoring of Children

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Case

Mom of Kennedy, a 9-year-old female, recently watched an ad campaign suggesting that she screen herself and her family for T1D. There is autoimmune disease in the family, so mom ordered a T1D antibody test. Kennedy came back positive for two antibodies. Mom called the PCP, and PCP referred Kennedy to a pediatric endocrinologist. The endocrinology office gave Kennedy an appointment in 4 months. Mom is anxious and doesn't want to wait 4 months. She did a web-dive and called EXPERTS for help determining next steps.



Evidence Based Monitoring Guidance

- There is a lack of published guidance on monitoring patients in early stages of T1D.

Historical Insights and Current Perspectives on the Diagnosis and Management of Presymptomatic Type 1 Diabetes

Kimber M.W. Simmons, MD, MS, Brigitte I. Frohnert, MD, PhD, Holly K. O'Donnell, PhD, Kimberly Bautista, MPH, Cristy Geno Rasmussen, MPH, PhD, Andrea Gerard Gonzalez, MD, Andrea K. Steck, MD, and Marian J. Rewers, MD, PhD

Diabetes Technol Ther. 2023 Sep 11. PMID: 37695674



Children & Adolescent Group Leaders:

Rachel Besser & Kurt Griffin

Subgroup Leaders:

Jennifer Couper, Maria Craig, Kimber Simmons & Riitta Veijola



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1
Screen

2
Confirm
↑

+
Rule
Out
Clinical
T1D

What are the steps
we need to take to
identify and care
for individuals with
Early Stages of
T1D?

- Especially important in cases where only 1 antibody is positive
- Should not limit initiation of monitoring
- May be waived if testing in CLIA certified, high quality (IASP participant) lab with low false positives



Rule Out Clinical T1D



Assess Symptoms



#TestOneDrop

Check blood or urine glucose.



Check HbA1c when possible.



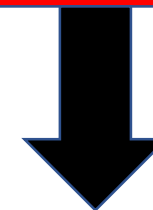
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Confirms + AND Hyperglycemia: Stage 3

Random blood glucose
<140 mg/dl
and
HbA1c <5.7%

Random blood glucose
140-199 mg/dl
and/or
HbA1c 5.7-6.4%

Random blood glucose
≥200 mg/dl
and/or
HbA1c >6.5%



- Evaluate for symptoms of hyperglycemia and diabetic ketoacidosis
- Referral to pediatric endocrinologist (if managed by PCP to this point)



Confirms + AND Absence of Hyperglycemia

Random blood glucose
<140 mg/dl
and
HbA1c <5.7%

Random blood glucose
140-199 mg/dl
and/or
HbA1c 5.7-6.4%

Now what?



1
Screen

2
Confirm

3
Monitor

What are the steps
we need to take to
identify and care
for individuals with
Early Stages of
T1D?



Monitoring



for progression of T1D (dysglycemia or hyperglycemia)



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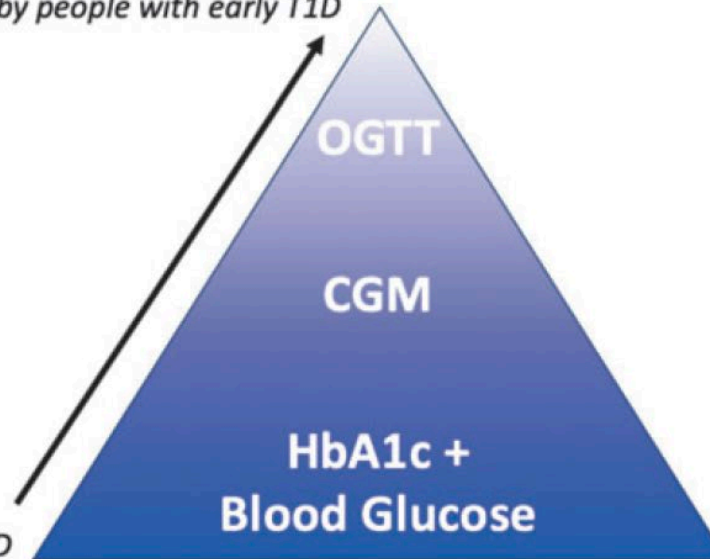
Goals of Follow-Up with IA Positive Patients

SAFETY

symptom awareness
home blood glucose testing

MONITORING FOR PROGRESSION

least accepted by people with early T1D



most accepted by people with early T1D



Complete when
healthy, without illness

- Pay attention to growth
- Appropriate weight gain
 - Healthy diet

Simmons et al., *DTT*, 2023



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1
Screen

2
Confirm

3
Engage



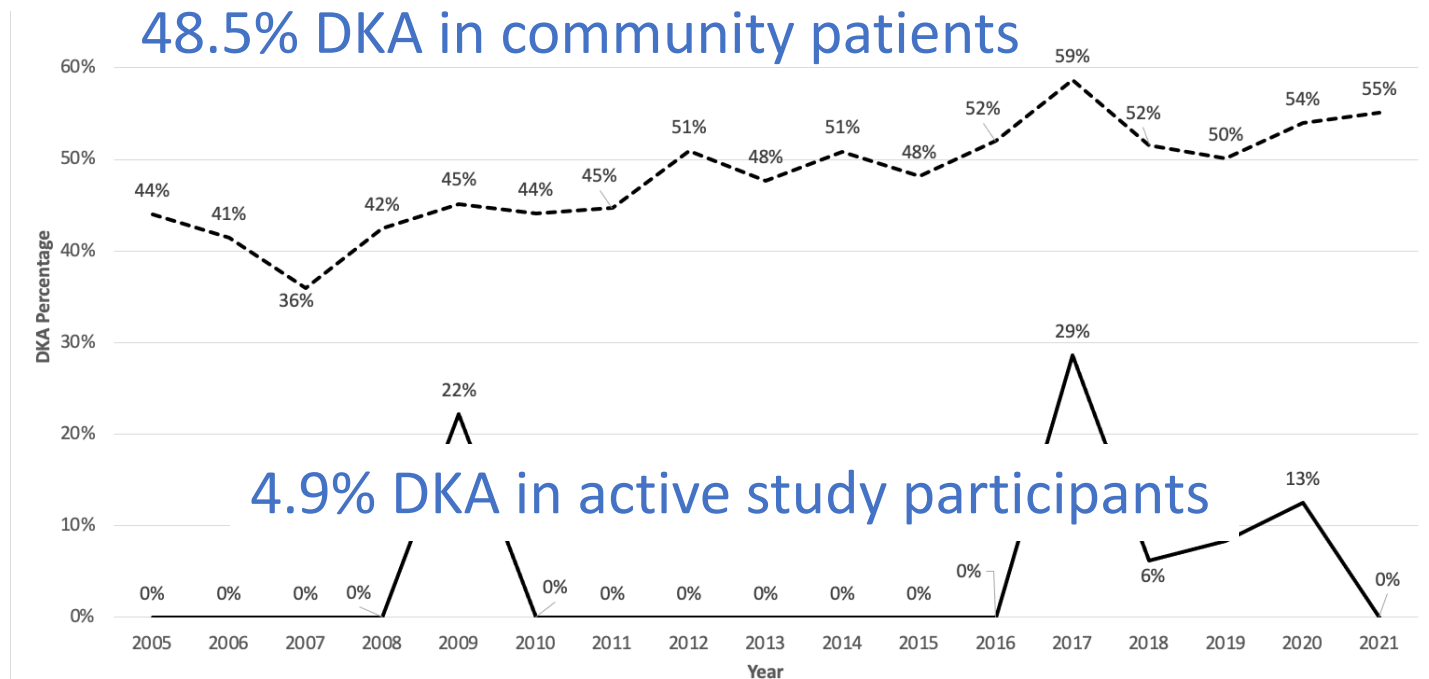
Clinical Visit

- Educate
- Stage (Monitor) for Dysglycemia/Hyperglycemia
- Provide Psychosocial Support
- Discuss Early Treatment Options



Engagement is Important for Medical Safety

- DKA Prevention
- Facilitate smooth transition to clinical T1D
 - Initiation of insulin
 - Psychological needs addressed
 - Social needs addressed

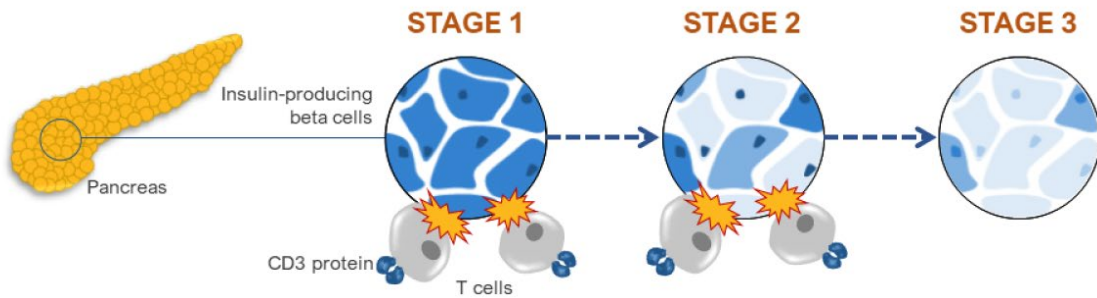


DKA occurrence at onset in study participants undergoing routine metabolic monitoring is 10X lower than in community patients.

unpublished data courtesy of Morgan Sooy, CDCES, RN, BSN



Engagement is Important for Monitoring T1D Progression

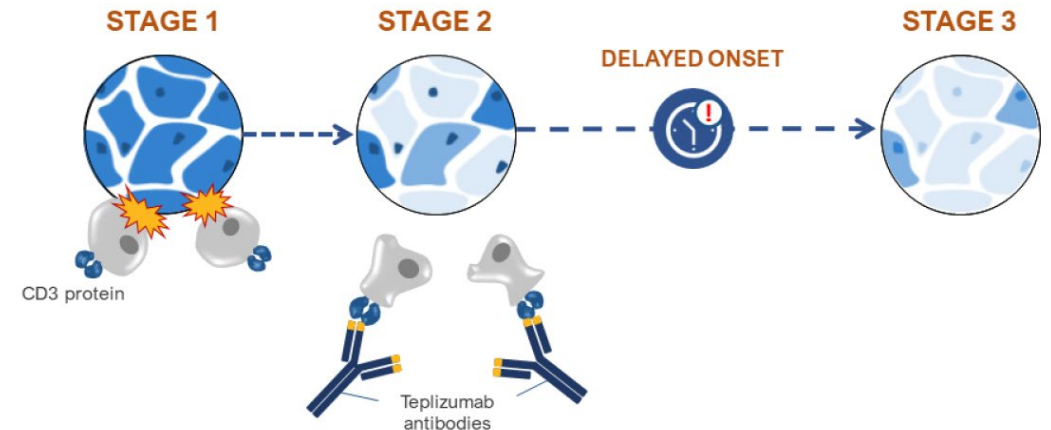


- Stage using ADA criteria
- Determine risk of progression (metabolic risk scores)

**Type 1
Diabetes
TrialNet**

ClinicalTrials.gov

Enroll in clinical
prevention trials



Offer approved early treatment options to delay clinical T1D (in US, Tzield® if \geq age 8)

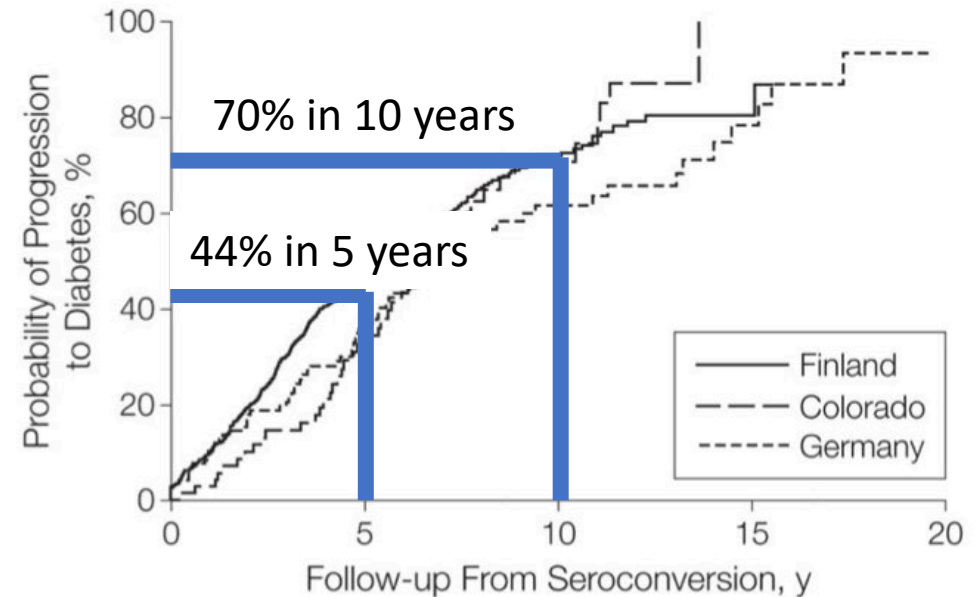
figures from <https://www.niaid.nih.gov>



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Islet Autoantibody (IA) Status Alone is Not Enough to Monitor for Progression

- Multiple IA+ more likely to progress to clinical T1D if younger, more T1D related IA, HLA DR3/DR4-DQ8 or IA-2A present.
- Single IA+ more likely to progress if 2nd IA develops sooner.



Risk of progression from time of seroconversion, in high-risk individuals with antibodies done at gold standard laboratories

Ziegler et al., 2013



Home Blood Glucose Testing

Home Glucose Testing Reminders

- A HIGH blood glucose (BG) on home testing is not sufficient to diagnose diabetes; it should be confirmed by a health care provider.
- If your child has a HIGH BG level, wash the child's hands with soap and water again and retest.
- If the BG is still HIGH, follow the instructions in this chart (see reverse).

Remember to Monitor for Symptoms of T1D

Most common symptoms include:

- **Excessive thirst**
- **Frequent urination** or getting up at night to urinate
- **Wetting the bed** in a child who was previously dry
- **Unexplained weight loss** or poor weight gain
- **Change in appetite**

+ **Additional symptoms people experience include:** low energy, blurred vision, yeast infections, mood changes, behavior changes

+ **Symptoms that require urgent attention include:** heavy breathing, vomiting and confusion


SMBG meters and strips should be provided to all IA⁺ children and their families to be used during illness or when symptoms may be present.



Home Blood Glucose Testing

HOME GLUCOSE TESTING

Test 1 time per week and every day during illnesses




Ask the Experts
FOR EARLY T1D ANSWERS AND GUIDANCE

TIME blood glucose (BG) was tested	NORMAL BG	ELEVATED BG	HIGH BG
FASTING No food or drinks with any sugar for at least 8 hours	Below 100	100 – 124	125 or higher
PREFERRED METHOD 2 HOURS after meals	Below 140	140 – 199	200 or higher

Contact Name: _____

Contact Phone: _____



If the meter displays “**HI**” (no number displayed) your blood sugar reading is **over 300 mg/dL. This is a life-threatening situation and a medical emergency. Contact your nearest urgent care or emergency department.**

Repeat test and contact your healthcare provider

Test blood glucose once biweekly and with any illness or T1D symptoms.



Frequency of Metabolic Monitoring Depends on Age and Stage

<4 years

Q3 months

Q3 months

4-5 years

Q3-6 months

Q3 months

≥6 years

Q6 months

Q3 months

Stage 1 T1D

- **Islet autoantibodies**
- **Normal glucose** (FPG <100mg/dL; 2h-PG <140 mg/dL; HbA1c <5.7%)
- **No symptoms**

Stage 2 T1D

- **Islet autoantibodies**
- **Abnormal glucose** (FPG 100-125mg/dL; 2h-PG 140-199mg/dL; HbA1c 5.7-6.4%)
- **No symptoms**



Consider Stage of T1D When Deciding Tool(s) for Metabolic Monitoring

CGM

- Blinded to the individual wearing it.
- Applied and interpreted by trained HCP, with education for the user and their family.

OGTT
HbA1c
CGM



FPG = fasting plasma glucose / 2h-PG = 2-hour plasma glucose / RPG = random plasma glucose

* ADA Standards of Medical Care in Diabetes: In absence of unequivocal hyperglycemia, diagnosis requires 2 abnormal test results from same or separate samples



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HbA1c

Classify
Stage of
T1D

<5.7%



- Highly specific for T1D
- Can use capillary finger poke sample
- POC testing widely available

5.7-6.4% *or*
≥10% increase



- Not sensitive for T1D
- Late indicator, often normal or mildly dysglycemia in patients with early stage 3 by another glycemic indicator

≥6.5%



Oral Glucose Tolerance Test

Classify
Stage of
T1D

2-hour BG
<140 mg/dl



2-hour BG
140-199 mg/dl

2-hour BG
≥200 mg/dl



- Gold standard
- Calculate metabolic risk scores (DPTRS, DPTRS60, Index60, M60, M120), which can help estimate the risk of progression to clinical diagnosis of T1D
- Identify people eligible for early treatment options through clinic or research

- Requires glucose load, which isn't always well tolerated
- Preceding diet and activity can impact results
- Risk scores not used clinically and time points needed for BG and c-peptide vary among scores (60, 90, 120 minutes)



Continuous Glucose Monitor (CGM)

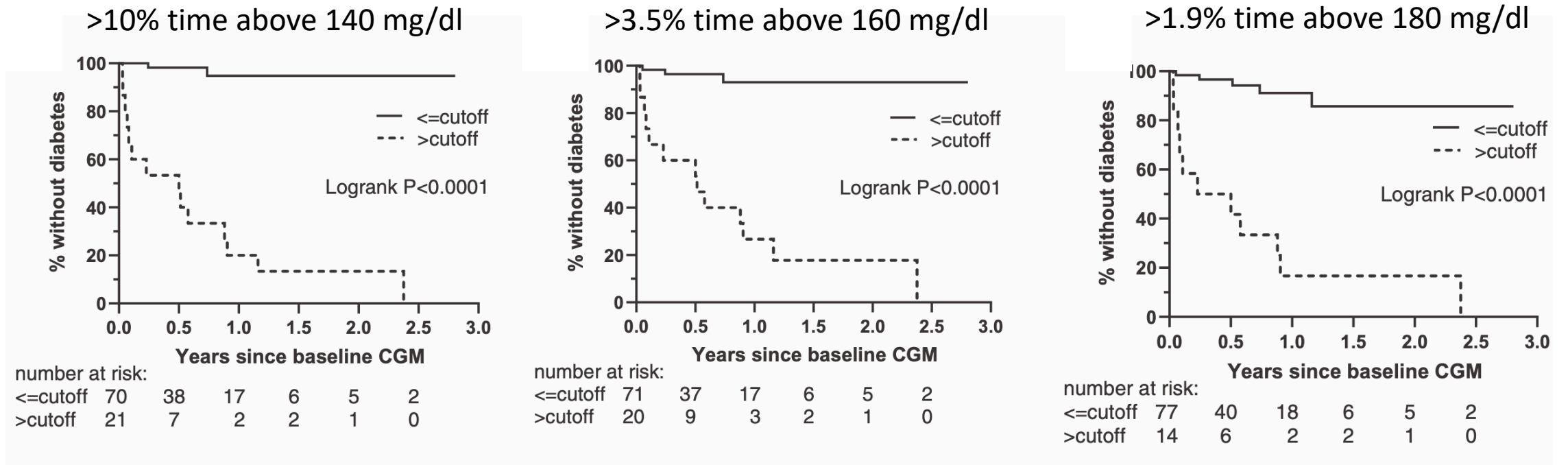


- Collects glucose every 5 minutes at home
- Collects glucose data during normal daily activities
- Finger pokes limited to confirming abnormal glucose levels
- Helpful in detecting glucose impairments earlier than HbA1c and random blood glucose
- Wearing of device may increase burden
- If unblinded, numbers may increase psychological distress/anxiety
- Low glucose alarms common
- Requires HCP expertise to interpret results for a person without diabetes diagnosis
- Payor coverage unpredictable (R73.03)

*If placing a CGM on a person without diabetes, the recommendation is for it to be worn blinded. If an unblinded CGM is preferred, then adequate provider support should be made available to the individual.



CGM Interpretation



The risk of progression to T1D in 1 year was 80% in those with time above 140 mg/dl >10%.

Steck et al., 2022



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Learning Opportunities



Do recommendations
for frequency of
antibody and metabolic
testing apply to general
population individuals?



What biomarkers can be
developed to monitor
disease progression?



How do we engage
patients in active follow-
up to derive benefits
associated with
screening?



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Case

Kennedy confirmed to be positive for multiple antibodies (GADA and ZnT8A). A random blood glucose was 103 mg/dl. HbA1c was 5.4%.

What stage of T1D does Kennedy have?

Kennedy is seen in clinic every 6 months. She refuses to do an OGTT and is followed with HbA1c and CGM wear. At her most recent visit, HbA1c was 5.9%, fasting blood glucose was 112 mg/dl and the percentage of CGM glucoses >140 mg/dl was 35%.

What stage of T1D does Kennedy have?

MONITOR

CLINICAL RESEARCH

TZIELD TREATMENT (US)



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Key Messages

- After a positive screen, confirm antibody status and rule out clinical type 1 diabetes with a random blood glucose and HbA1c.
- Engagement of antibody positive individuals results in reduced DKA at onset.
- Metabolic monitoring is important for staging of type 1 diabetes and determining available treatment options.
- HbA1c, OGTT and CGM can be used to monitor for disease progression.
- Monitoring should occur every 3-6 months in children and adolescents depending on age and stage of type 1 diabetes.





Evidence Based Guidance
Will be Updated as
Available on
www.AsktheEXPERTS.org.



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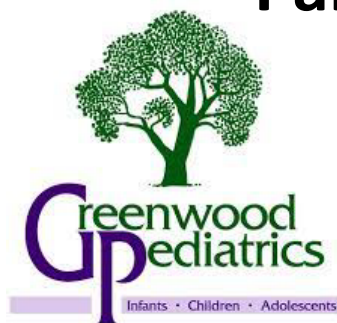
**Our ASK
participants,
their families,
and ASK
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Partners



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Ask the Experts