Type 1 Diabetes: It's not just for juveniles

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Breakthrough T1D™
Formerly JDRF

Disclosures
Full time staff member, JDRF International (Non Profit)
Founder and Board Chair, Diabetes Toolkit (A Florida-based 501c3 Corporation)
Any unlabeled/unapproved uses of drugs or products referenced will be disclosed

Learning Objectives

- Describe T1D early detection and the benefits of screening for autoantibodies
- Discuss clinical trials aimed at the delay and prevention of type 1 diabetes
- List process for monitoring individuals in early stage T1D

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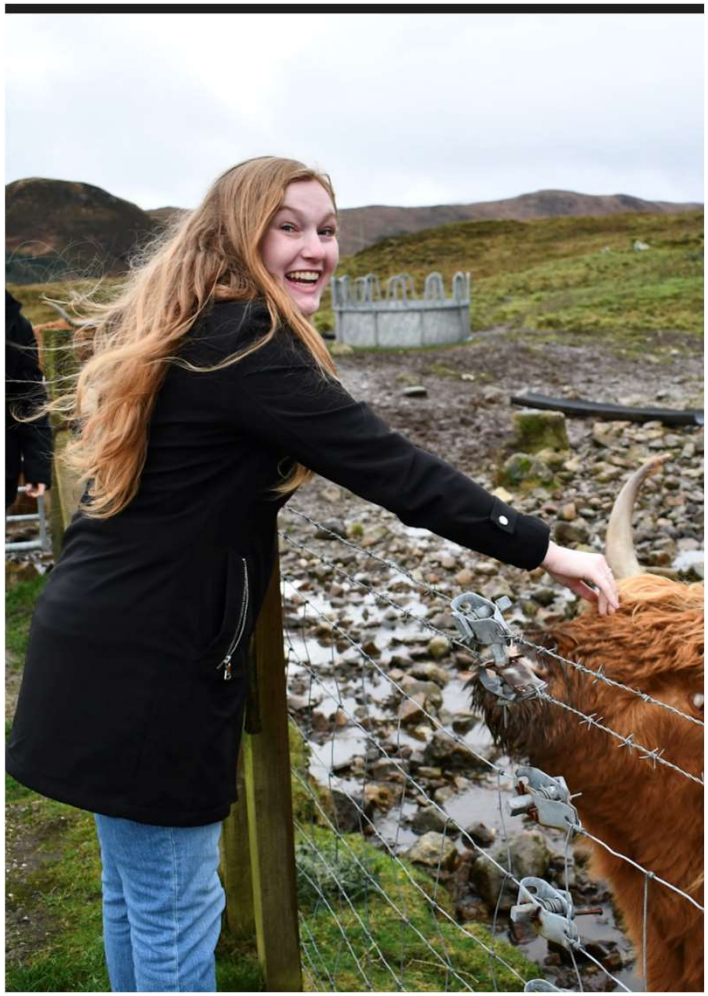
Past: circa 2002

The Prescribed "Technology"



Present: 2024

The standard of care in technology

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What do these advances have in common? Clinical Trials!

A New Paradigm in Type 1 Diabetes Care

3. Prevention or Delay of Type 2 Diabetes and Associated Comorbidities: *Standards of Care in Diabetes—2023*

Diabetes Care 2023;46(Suppl. 1):S41–S48 | https://doi.org/10.2337/dc23-S003

3. Prevention or Delay of Diabetes and Associated Comorbidities: *Standards of Care in Diabetes—2024*

Diabetes Care 2024;47(Suppl. 1):S43–S51 | https://doi.org/10.2337/dc24-S003

Removing just two simple words from the title of this updated clinical guideline signifies momentous progress.

For the first time in history, we can delay the onset of type 1 diabetes.

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"3.14 Teplizumab-mzwv infusion to delay the onset of symptomatic type 1 diabetes 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"

There has been an associated increase in clinical complexity

1989
4 Pages
10
Citations

POSITION STATEMENT

Standards of Medical Care for Patients With Diabetes Mellitus

Diabetes is a chronic illness that requires continuing medical care and education to prevent acute complications and to reduce the risk of long-term complications. People with diabetes should receive their treatment and care from physicians with expertise and a special interest in diabetes. The following standards define basic medical care for people with diabetes. These standards are not intended to preclude more extensive evaluation and management of the patient.

INITIAL VISIT

Medical history. The comprehensive medical history can uncover symptoms that will help establish the diagnosis in the patient with previously unrecognized diabetes. If the diagnosis of diabetes has already been made, the history should confirm the diagnosis, review the previous treatment, help evaluate the present degree of glycemic control, determine the presence or absence of the chronic complications of diabetes, assist in formulating a management plan, and provide a basis for continuing care. Elements of the medical history of *particular* concern in patients with diabetes include:

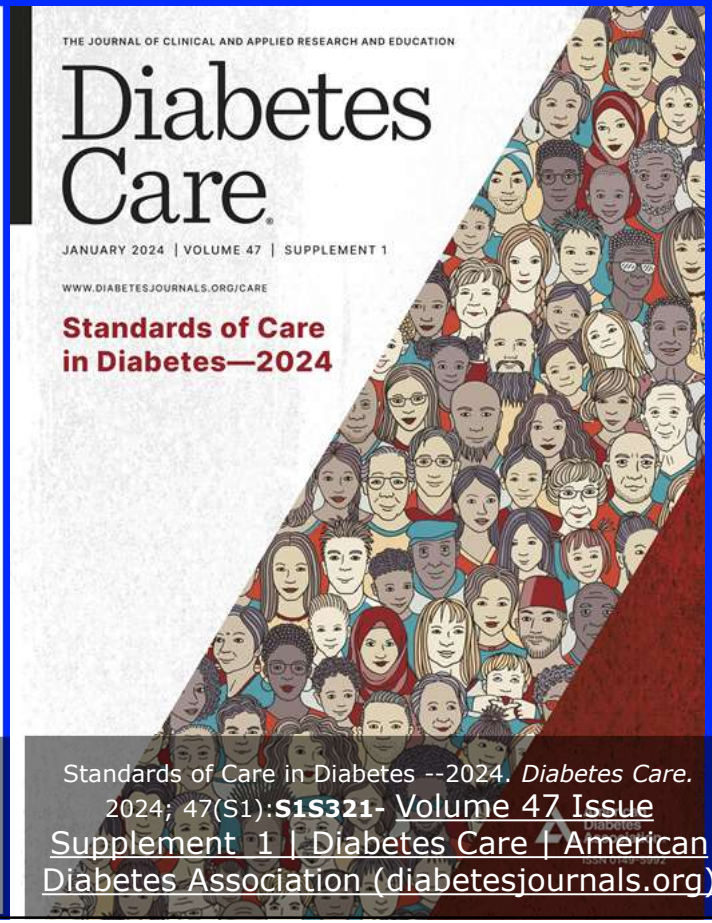
- Symptoms and laboratory test results related to the diagnosis of diabetes
- Dietary habits, nutritional status, and weight history;
- Frequency, severity, and cause of acute complications such as ketoacidosis and hypoglycemia
- Prior or current infections, particularly skin, foot, dental, and genitourinary
- Symptoms and treatment of chronic complications associated with diabetes: eye, heart, kidney, nerve, sexual function, peripheral vascular, and cerebral vascular
- Other medications that may affect blood glucose concentration
- Risk factors for atherosclerosis: smoking, hypertension, obesity, hyperlipidemia, and family history
- Psychosocial and economic factors that might influence the management of diabetes
- Family history of diabetes and other endocrine disorders
- Gestational history: hyperglycemia, delivery of an infant weighing >9 lb, toxemia, stillbirth, polyhydramnios, or other complications of pregnancy

Physical examination. A complete physical examination should be performed during the initial evaluation. Individuals with diabetes are at high risk of developing eye, kidney, nerve, cardiac, and vascular complications. Patients with type I (insulin-dependent) diabetes also have an increased frequency of thyroid disease, and all individuals with diabetes are at increased risk of infections. Children may have delayed growth and maturation. Therefore, certain aspects of the physical examination require special attention. These include:

- Height and weight in children
- Diabetes education
- Foot, and results of glucose monitoring
- Blood pressure determination with orthostatic pulse

DIABETES CARE, VOL. 12, NO. 5, MAY 1989 365

•Standards of Medical Care for Patients With Diabetes Mellitus. *Diabetes Care* 1 May 1989;12(5):**365-368**. https://doi.org/10.2337/diacare.12.5.365



THE JOURNAL OF CLINICAL AND APPLIED RESEARCH AND EDUCATION

Diabetes Care

JANUARY 2024 | VOLUME 47 | SUPPLEMENT 1

WWW.DIABETESJOURNALS.ORG/CARE

Standards of Care in Diabetes—2024

Standards of Care in Diabetes --2024. *Diabetes Care.* 2024; 47(S1):**S1S321-** Volume 47 Issue Supplement 1 | Diabetes Care | American Diabetes Association (diabetesjournals.org)

2024
321 Pages
3000+
Citations

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T1D Screening and Early Detection

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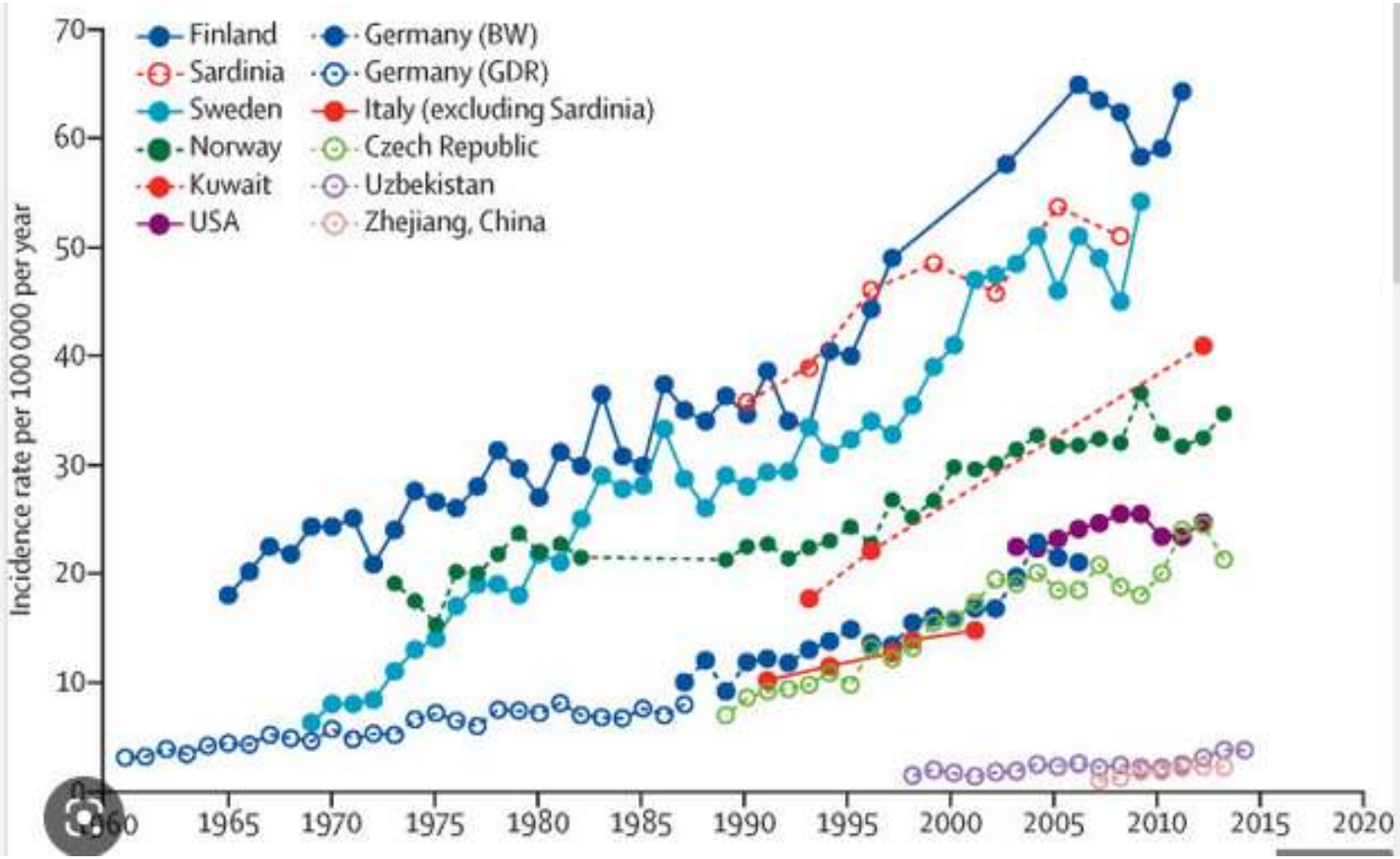
The Rising Global Incidence of Type 1 Diabetes



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Family history is not typical in Type 1 Diabetes

Approximately 85% of people have no family history of type 1 diabetes at diagnosis.

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McQueen et al. Diabetes Care. 2020;43(7):1496-1503; Besser et al. BMJ. 2021.

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Breakthrough T1D Research Investments in General Population Screening

Breakthrough T1D provided catalytic funding to the DIPP, Fr1DA, and ASK programs at a time when only familial screening was being performed in the research setting

DIPP/Fr1da – Europe
- Newborn
- GRS + IA

ASK – Colorado
- Children and adults
- IA
- Cost effectiveness analysis

ELSA - UK
- Children
- IA
- IA test improvement

ADIR – Israel
- Children
- IA

GPS – Australia
- Children
- GRS + IA
- Test preference and Implementation

RTI – US
- Newborn
- GRS + IA

AL-DIAR – Qatar
- Children
- GRS + IA

EDENT1FI – Europe
- Children
- IA

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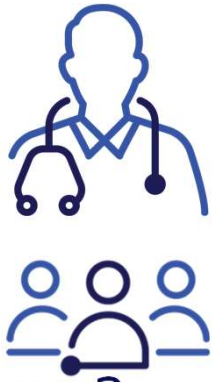
IA: Islet Autoantibody test GRS: Genetic Risk Score

What have we learned?

PAST

- Benefits of screening unclear
- Unable to predict which individuals would progress to insulin dependent T1D
- No approved therapy to delay onset



TODAY

- Ability to predict individuals likely to progress to stage 3 (insulin requiring)
- Staging criteria developed (Stages 1, 2 and 3)
- Benefits of screening well describe
  - Prevention of DKA at Diagnosis, Time to plan and prepare
- First FDA approved therapy to delay disease onset
- Multiple clinical trials underway to delay and prevent T1D

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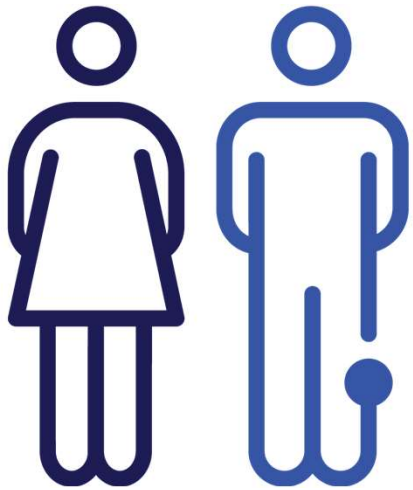
Family History Is a Strong Predictor of T1D

Risk for First Degree Family Members is up to 15 times higher



First Degree Relative with T1D

~1 in 20

No Family History of T1D

~1 in 300

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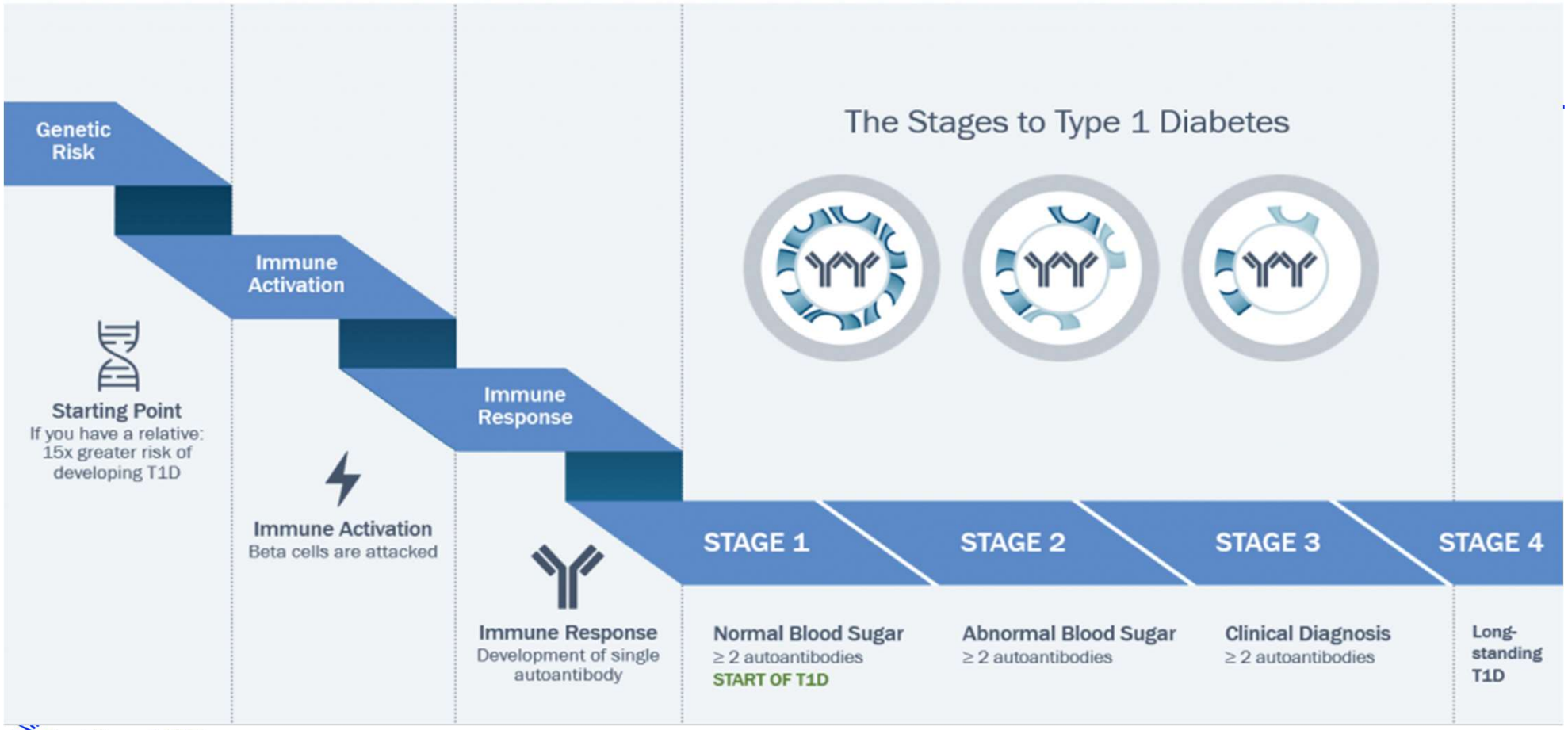
T1D Disease Progression

Type 1 Diabetes TrialNet



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Source: https://www.trialnet.org

Stages of Type 1 Diabetes and Risk for Progression

No Diabetes
No islet autoantibodies

Stage 1
Two or more persistent autoantibodies and normoglycemia

Stage 2
Two or more autoantibodies and dysglycemia

Stage 3
Diagnosed type 1 diabetes

Stage 4
Established Type 1 Diabetes

Progression to a Stage 3 Type 1 Diabetes Diagnosis:

~70%
10 YEARS

~84%
15 YEARS

"It is clear from prospective studies that the persistent presence of two or more islet autoantibodies is a near-certain predictor of clinical diabetes"

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American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Suppl 1):S20-S42. doi: 10.2337/dc24-S002. PMID: 38078589; PMCID: PMC10725812.. 4. American Diabetes Association. *Diabetes Care*.

The Benefits of Screening and Early Detection of T1D

- Reduce risk for diabetic ketoacidosis (DKA) at diagnosis
- Identify people who may benefit from early-intervention clinical trials
- Give individuals and families time to prepare
- Provide option to intervene early with FDA-approved therapy to delay a clinical diagnosis of T1D and the need for insulin

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Benefit 1: Screening and Monitoring Reduce DKA at Diagnosis

Study	Setting	DKA (Hospitalization) Rate
ASK	**General Population** (Colorado, U.S.)	**3%**
Frida	**General Population** (Bavaria, Germany)	**Less than 3%**
20th Anniversary DAISY	**Genetic Risk+AAb Screening (Relatives)** (Colorado, U.S.)	**3%**
TEDDY	**Genetic Risk+Aab Screening (Relatives and General Population)** (Sweden, Finland, Germany, U.S.)	**6% (1%, 8%)**

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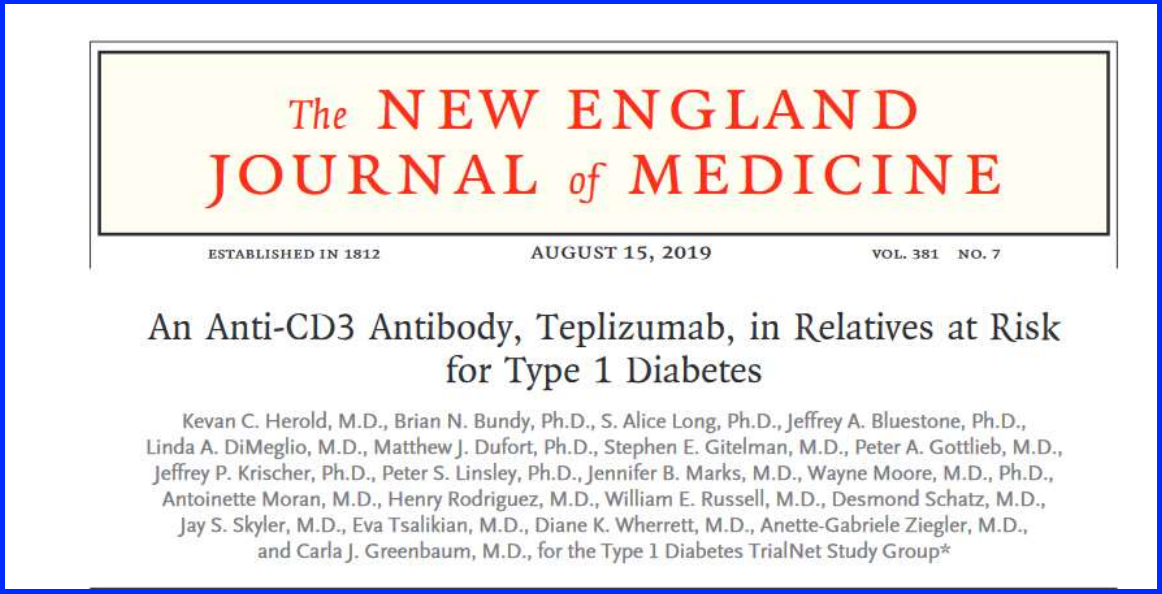
Rewers M, et al. Presented at: European Association for the Study of Diabetes 2019 Annual Meeting; Poster 279. Ziegler AG, et al. *JAMA*. 2020;323(4):339-351. Barker JM, et al. *Diabetes Care*. 2004;27(6):1399-1404. 4. Larsson HE, et al. *Diabetes Care*. 2011;34(11):2347-2352. Jacobsen et al., Diabetes Care, 2022;45(3):624-633. Note: Hospitalization rate, which was mainly driven by DKA in the control patients, was reported rather than DKA in DAISY

Benefit 2: Consider an FDA Approved Therapy to Delay the Onset of Stage 3 T1D



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 15, 2019 VOL. 381 NO. 7

An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes

Kevan C. Herold, M.D., Brian N. Bundy, Ph.D., S. Alice Long, Ph.D., Jeffrey A. Bluestone, Ph.D., Linda A. DiMeglio, M.D., Matthew J. Dufort, Ph.D., Stephen E. Gitelman, M.D., Peter A. Gottlieb, M.D., Jeffrey P. Krischer, Ph.D., Peter S. Linsley, Ph.D., Jennifer B. Marks, M.D., Wayne Moore, M.D., Ph.D., Antoinette Moran, M.D., Henry Rodriguez, M.D., William E. Russell, M.D., Desmond Schatz, M.D., Jay S. Skyler, M.D., Eva Tsalikian, M.D., Diane K. Wherrett, M.D., Anette-Gabriele Ziegler, M.D., and Carla J. Greenbaum, M.D., for the Type 1 Diabetes TrialNet Study Group*

- Individuals 8 years and older
- Stage 2 type 1 diabetes

You must identify candidates before Stage 3 Type 1 Diabetes

American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Suppl 1):S20-S42. doi: 10.2337/dc24-S002. PMID: 38078589; PMCID: PMC10725812. American Diabetes Association Professional Practice Committee. 3. Prevention or Delay of Diabetes and Associated Comorbidities: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Suppl 1):S43-S51. doi: 10.2337/dc24-S003. PMID: 38078581; PMCID: PMC10725807.

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Patient Selection Per FDA-approved Prescribing Information

- Adult patients and pediatric patients 8 years of age and older who have a diagnosis of stage 2 type 1 diabetes
- At least two positive pancreatic islet cell autoantibodies
- Dysglycemia without overt hyperglycemia using an oral glucose tolerance tests (if an oral glucose tolerance tests is not available, an alternative method for diagnosing dysglycemia without overt hyperglycemia may be appropriate)
- Ensure the clinical history of the patients does not suggest type 2 diabetes

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Benefit 3: Consider Participating in a Stage 2 or 3 Clinical Trial

PETITE-T1D
Tepluzimab in Pediatrics
- 1-7 Years of Age
- Stage 2 T1D
- 14 Day Infusion

STOP-T1D
TrialNet ATG Prevention Study
- 12-35 Years of Age
- High-Risk Stage 2 T1D
- 2-day infusion

www.breakthrought1d.org/clinical-trials/

JAKPOT T1D
TrialNet JAK Inhibitors Study
- 12-35 Years of Age
- New Onset T1D (3 months)
- Oral Pill

GLADIATOR
Ladarixin Study
- 14-45 Years of Age
- New Onset T1D (6 months)
- Oral Pill

DESIGNATE
Siplizumab Study
- 18-45 Years of Age
- New Onset T1D (18 months)
- Weekly Injection

T1D RELAY
Rituximab/Abatacept Study
- 8-45 Years of Age
- New Onset T1D (3 months)
- Oral Pill

DIAGNODE-3
DIAMYD Study
- 12-29 Years of Age
- New Onset T1D (6 months)
- 3 Lymph Node Injections

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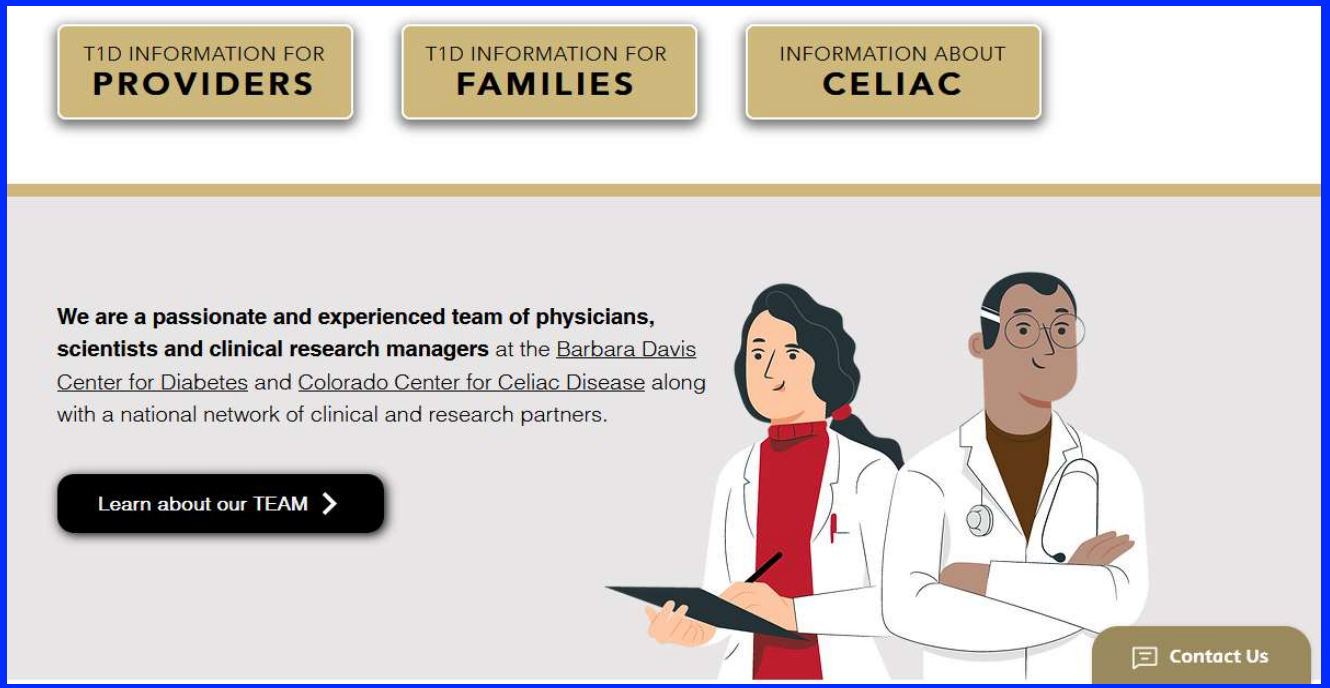
Where can I find support?

Ask the Experts is a resource for individuals, families and healthcare providers to guide screening and monitoring.



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THE LEONA M. AND HARRY B. HELMSLEY CHARITABLE TRUST

https://www.askhealth.org/experts

Call to Action: Share Screening Pathways

Type 1 Diabetes TrialNet

Autoimmunity Screening for Kids ask A SIMPLE TEST TO DETECT Type 1 Diabetes (T1D) + Celiac

First degree relative ages 2 -45 years
Second degree relatives ages 2 to 20 years

Visit a research center
Order a kit in the mail

Any child ages 1-17 years in the United States (also screen for celiac disease)

Order a kit in the mail

Anyone (however, insurance more likely to cover family members)

Blood collected at your doctor's office or at a lab

www.breakthrought1d.org/early-detection/

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Which labs will be ordered by my doctor?
Insulin Antibody (IAA)
GAD autoantibody
IA2 autoantibody
Zinc Transporter 8 Autoantibody (ZNT8)

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Early Detection of Type 1 Diabetes (T1D)

Type 1 diabetes has three stages, and through autoantibody screening (a simple blood test) it can be detected before an individual requires insulin. Early detection has many proven benefits, including a reduced risk of diabetic ketoacidosis (DKA) at diagnosis, providing time to plan and prepare, and opening doors to research opportunities or available treatments.[1,2]

Screening Options for Patients

Option 1: Screen Through a Research Study

TrialNet
- For people 2 to 45 years old who have a parent, brother/sister, or child with T1D, or
- For people 2 to 20 years old who have an aunt/uncle, cousin, grandparent, niece/nephew, or half-brother/sister with T1D
- Lab or at-home tests available

ASK
- For all children ages 1-17
- No family history of type 1 diabetes is required
- At-home tests available
- Also screens for Celiac Disease

Option 2: Screen Through Your Doctor's Office

Your doctor (or your child's doctor) can order labs to detect type 1 diabetes autoantibodies and the cost may be covered by your insurance. Consider contacting your insurance company regarding coverage prior to testing.

Positive Result?
- Confirmatory testing must be performed, either through TrialNet (free for ages 2-45 years) or your doctor's office
- Ask the Experts can provide individualized support for you in partnership with your doctor (visit www.asktheexperts.org or scan QR code)

Information for Healthcare Providers

Clinical guidelines support autoantibody screening for early detection of type 1 diabetes. Confirmatory testing is indicated for individuals with positive results.[1]

Labs to order (4)

- Insulin Autoantibody (IAA)-CPT 86337
- Glutamic Acid Decarboxylase (GAD) Autoantibody-CPT 86341
- Islet Antigen 2 (IA-2) Autoantibody-CPT 86341
- Zinc Transporter 8 (ZnT8) Autoantibody-CPT 86341

Related diagnosis codes

- Z83.3 - Family history of diabetes
- R73.9 - Hyperglycemia, unspecified
- Z13.1 - Screening for diabetes mellitus

Expert support at no cost for clinical management available at asktheexperts.org

Negative Result?

Consider additional testing in future if at risk for developing T1D.

Positive Result?
- Order confirmatory testing for persistent autoantibody status
- Consider referral to TrialNet for free confirmatory testing and possible referral to research studies
- Additional testing: HbA1c, random blood glucose
- Provide patient education including T1D symptoms
- If multiple autoantibodies present or dysglycemia, refer to Endocrinology

With your support, we are creating a movement to improve and change life with T1D, advancing breakthroughs on the way to cures.

To find out more about resources and support, visit **BreakthroughT1D.org/early-detection/.**

May 2024

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Frequently Asked Questions

What is type 1 diabetes?

Type 1 diabetes is an autoimmune disease in which insulin-producing beta cells in the pancreas are mistakenly destroyed by the body's immune system. It occurs in children and adults of all ages. Its causes are not fully known, and there is currently no cure. People with T1D are dependent on injected or pumped insulin to regulate blood sugar. Type 1 diabetes can now be detected in its early stages, before glucose is elevated and insulin is required.

What is type 1 diabetes risk screening?

Type 1 diabetes develops in stages over time. A blood test can identify people in early stage type 1 diabetes by identifying proteins in the blood called autoantibodies. These autoantibodies signal that the body's immune system is attacking the insulin-producing cells in the pancreas. If a person has two or more autoantibodies, they have a high likelihood for progression to stage 3 type 1 diabetes.[1,2]

Stages of Type 1 Diabetes

STAGE 1	STAGE 2	STAGE 3
2 or more autoantibodies Blood glucose normal **No symptoms**	2 or more autoantibodies Blood glucose abnormal (dysglycemia) **No symptoms**	Autoantibodies present Blood glucose elevated (hyperglycemia) **Usually symptomatic**

Why screen for type 1 diabetes?

Screening for type 1 diabetes has shown the potential to:
- Reduce the risk of diabetic ketoacidosis (DKA) at diagnosis of stage 3 type 1 diabetes.
- Introduce autoantibody-positive individuals to research or clinical trials aimed at delaying/preventing the onset of stage 3 T1D
- Refer autoantibody positive individuals to specialists for follow up and consideration of FDA-approved therapies to delay onset of stage 3 T1D
- Give families time to plan and prepare

Who should screen for T1D?

Individuals who have a first-degree relative with type 1 diabetes are at an increased risk (up to 15x) for developing the condition. However, 85% percent of T1D diagnoses occur in people with no known family history, which is why Breakthrough T1D has a long-term goal of global universal screening. Clinical guidelines support screening for type 1 diabetes autoantibodies[1]. Everyone should know the signs and symptoms of T1D–**Early detection and awareness are key!**

What are the signs and symptoms of T1D?

**Breakthrough T1D content is for informational purposes only and is not a substitute for professional medical advice. Please contact your doctor or other qualified health provider with any questions you may have regarding type 1 diabetes or any medical condition.

1. American Diabetes Association Professional Practice Committee; 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2024. Diabetes Care 1 January 2024; 47 (Supplement_1): S20–S42. https://doi.org/10.2337/dc24-S002

2. Besser REJ, Bell KJ, Couper JJ, Ziegler AG, Wherrett DK, Knip M, Speake C, Casteels K, Driscoll KA, Jacobsen L, Craig ME, Haller MJ; ISPAD Clinical Practice Consensus Guidelines 2022: Stages of type 1 diabetes in children and adolescents. Pediatr Diabetes. 2022 Dec;23(8):1175-1187. doi: 10.1111/pedi.13410. Epub 2022 Sep 30.

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International Consensus Monitoring Guidance

"Consensus guidance for monitoring persons with islet autoantibody-positive pre-Stage 3 type 1 diabetes"

73 International Experts

4 Continents

8 Partner Organizations

ADCES · ads Australian Diabetes Society · EASD European Association for the Study of Diabetes · Endocrine Society · AACE American Association of Clinical Endocrinology · ISPAD International Society for Pediatric and Adolescent Diabetes · ATTD Advanced Technologies & Treatments for Diabetes · American Diabetes Association · Breakthrough T1D Formerly JDRF

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New ICD 10 Diagnosis Codes for Early Stage T1D

CMS released its Medicare hospital rule to include CDC's new ICD-10 diagnosis codes to capture early-stage, presymptomatic type 1 diabetes.

These ICD-10 diagnosis codes will become effective October 1, 2024 in the US:

- E10.A0 – Type 1 diabetes mellitus, presymptomatic, unspecified
- E10.A1 – Type 1 diabetes mellitus, presymptomatic, Stage 1
- E10.A2 – Type 1 diabetes mellitus, presymptomatic, Stage 2

They can be found at : FY 2025 IPPS Proposed Rule Home Page | CMS - they are in a zip file under "Table 6A"

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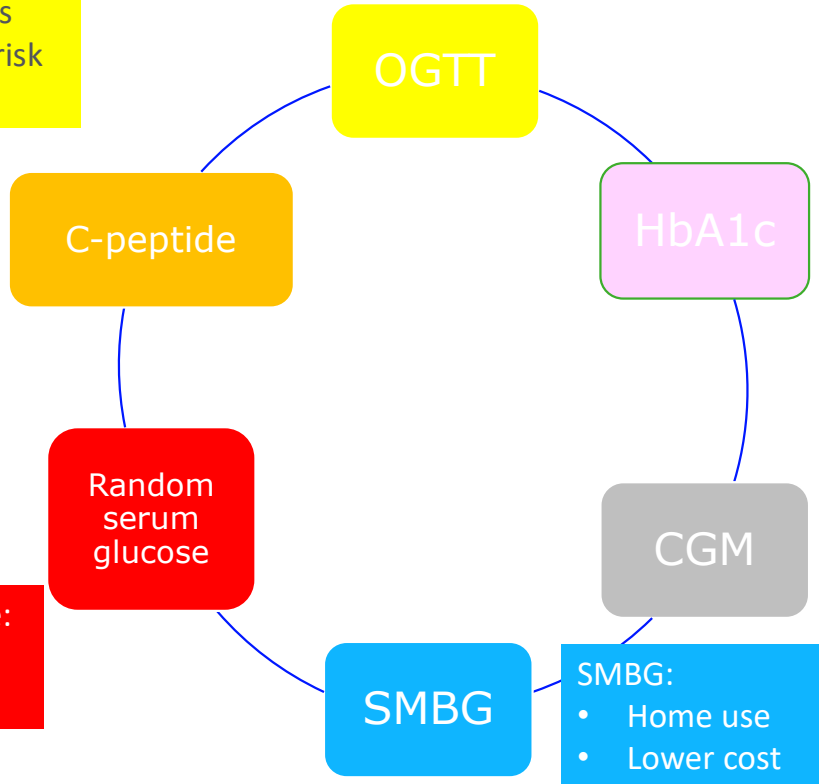
Background: Seven Monitoring Methods

Antibody Monitoring

Metabolic Monitoring

OGTT:
- Gold standard in research setting
- 2-5 blood draws over 2 hours
- Useful for glycemic staging, risk scores



HbA1c:
- Highly specific but can be normal with recent onset hyperglycemia
- *longitudinal 10% rise
- False values (anemia, renal disease)

C-peptide:
- many adults presenting with T1D have C-pep ≥ 0.2 nmol/L,
- C-pep can be falsely low in hypoglycemia, fasted state, or in DKA

CGM:
- Home use
- Lots of information
- Can be masked
- Requires education
- +Cost

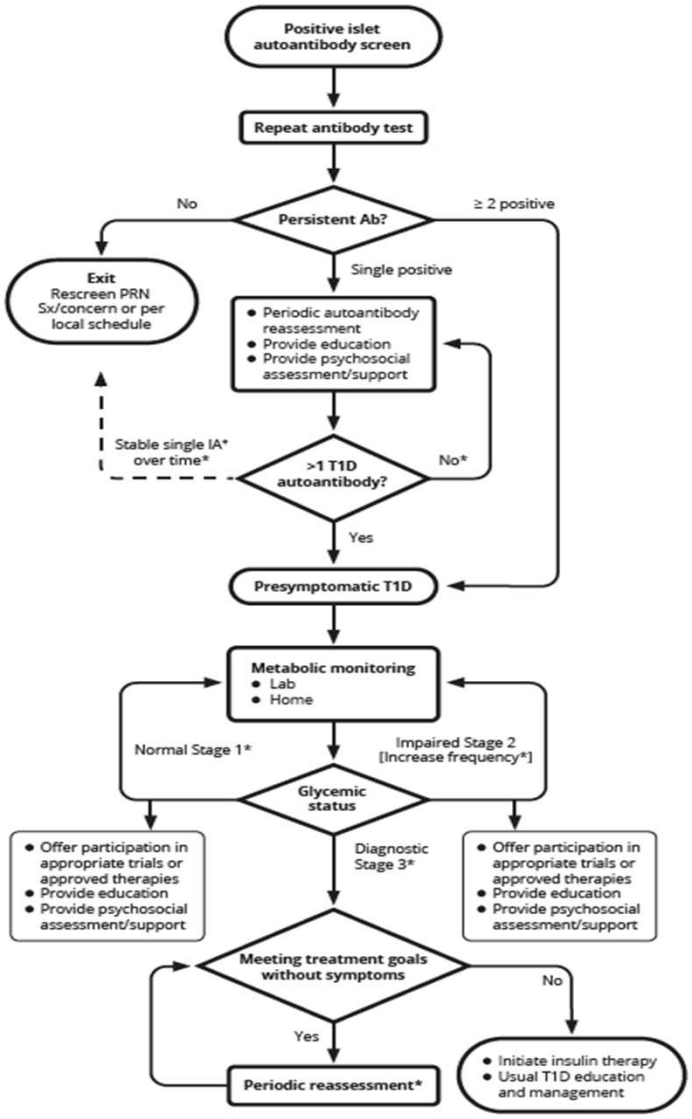
Random serum glucose:
- One-off sample
- Low cost

SMBG:
- Home use
- Lower cost
- Painful

Slide adapted from one created by R. Schulman-Rosenbaum

Vehik K et al. "Rising Hemoglobin A1c in the nondiabetic range predicts progression of type 1 diabetes as well as oral glucose tolerance tests." Diabetes Care 2022.
Iqbal S et al. "The predictive ability of C-peptide in distinguishing type 1 diabetes from type 2 diabetes: A systematic review and meta-analysis." Endocrine Practice 2023.

The suggest model



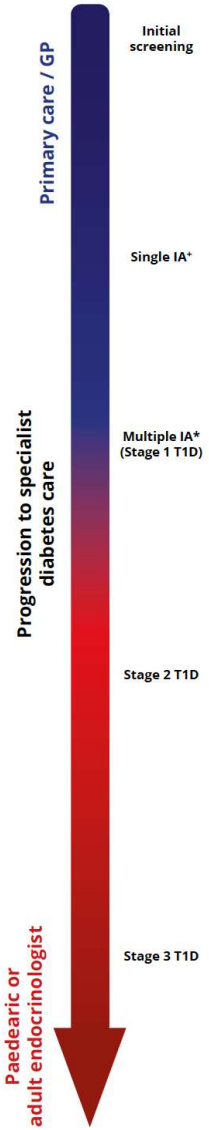


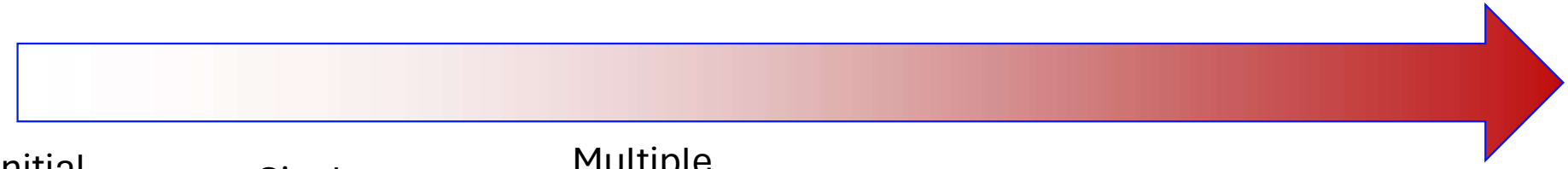
Figure conceptualized by Kurt Griffin

Audience for the Guidance Spans Care Continuum

Primary Care/ GP

Progression to specialist diabetes care

Pediatric or Adult Endocrinologist



Initial antibody screening

Single antibody+

Multiple antibody+ (Stage 1 T1D)

Stage 2 T1D

Stage 3 T1D

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Collaboration with Primary Care

Primary care HCPs should understand stages of T1D, methods of and suggested frequency for metabolic monitoring [E]

Some primary care HCPs with a specific interest can serve as a local referral sources [E]

The primary care provider, specialist provider, and the person who is Ab+ should determine who will have primary responsibility and what degree of collaboration is needed [E]

This may shift over time for the individual with Ab

Medical records must reflect the Ab status and the plan for monitoring and for urgent evaluation if needed [E]

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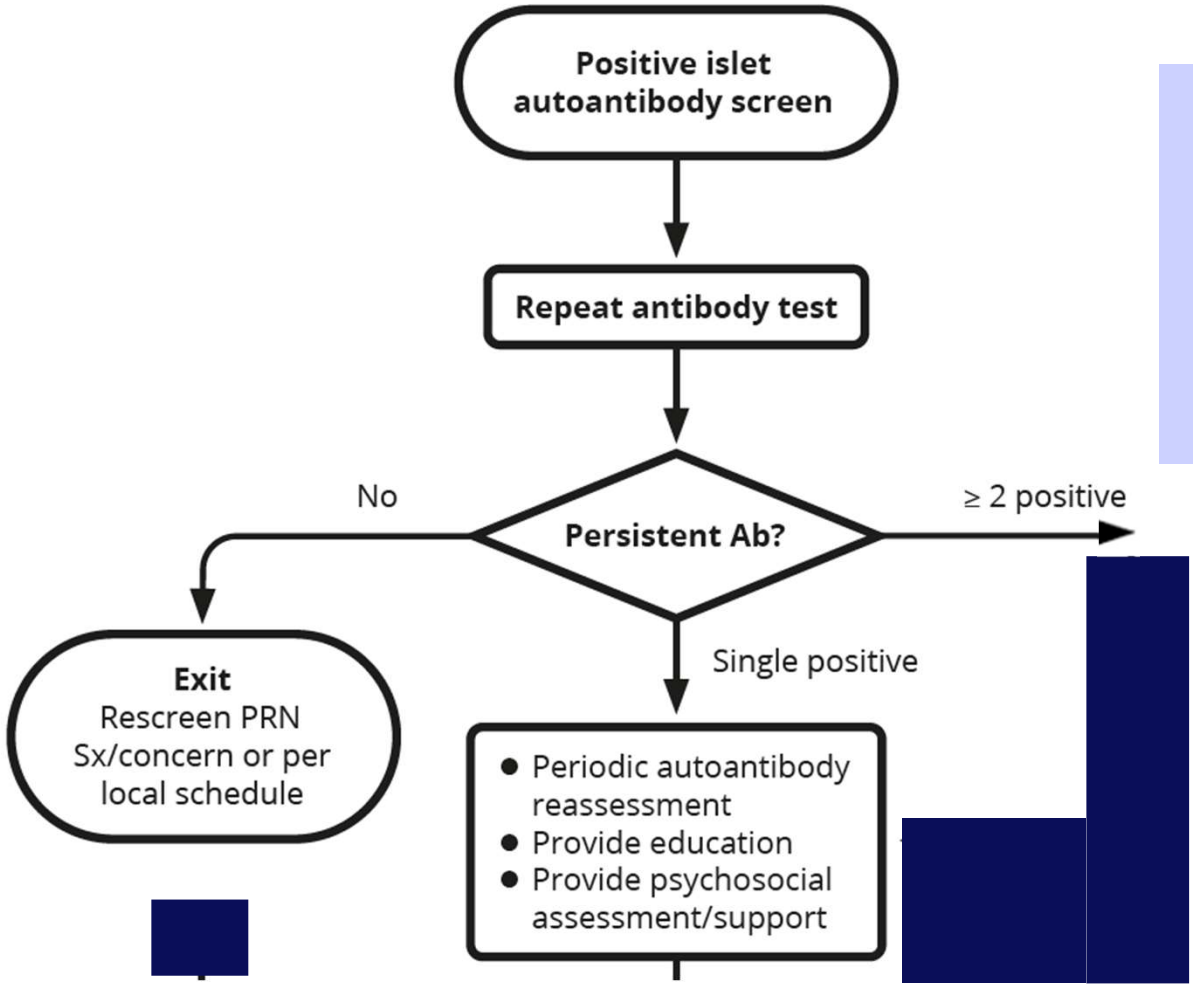
Primary Care



IMPORTANT
Always confirm initial positive Ab test with a second test in a certified lab [B]

Single Ab positive

Children

Educate on symptoms of T1D, DKA

Children ≤ 3 y monitor Ab status six monthly for 3 yrs then annually for 3 yrs, then stop [B]

Children >3 y monitor Ab status, annually x 3 years, then stop [C]

Perform metabolic monitoring (random BG and HbA1c) with Ab monitoring for 2 years after first positive test [B]

Adults

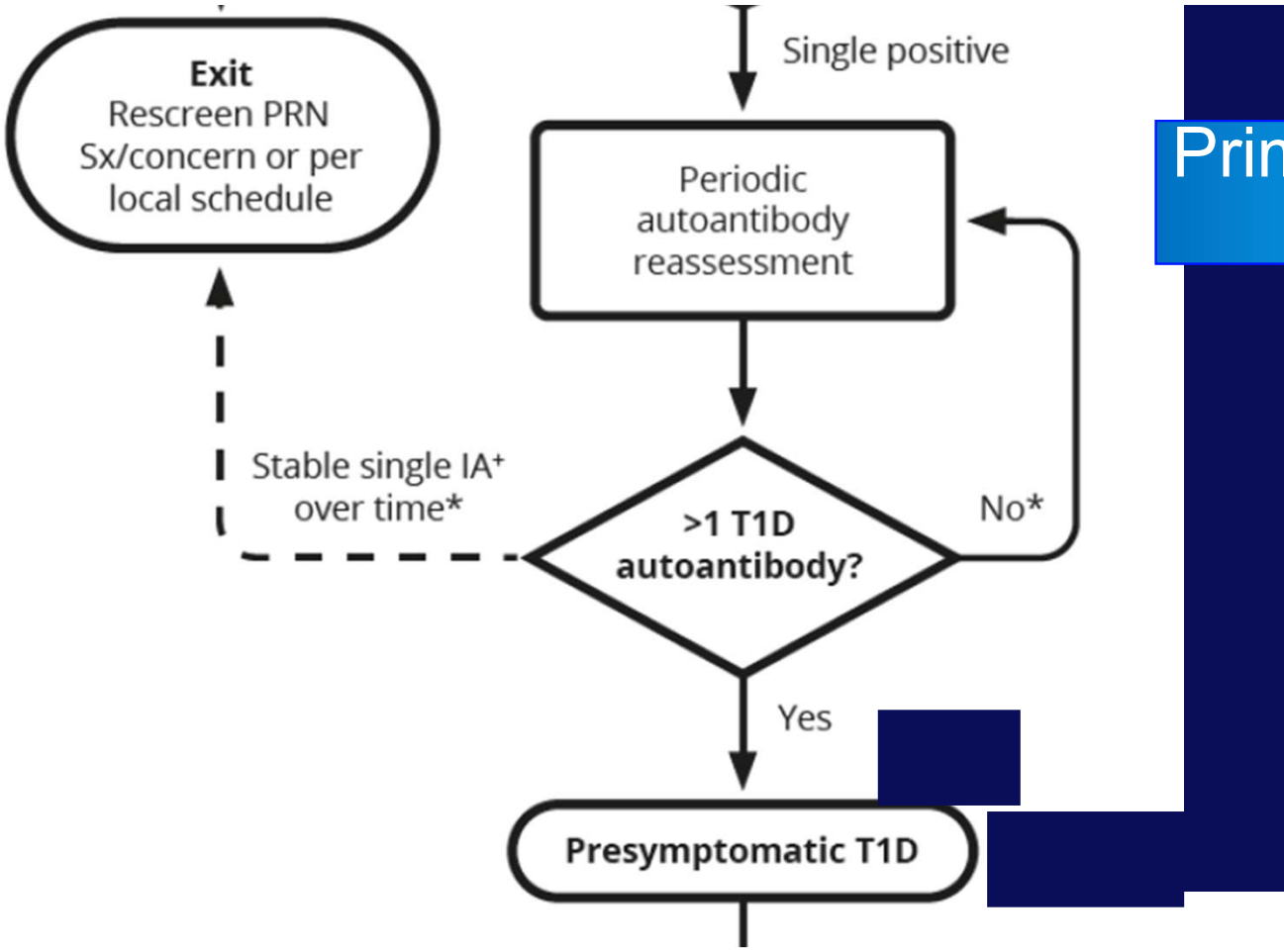
Consider annual metabolic monitoring if additional risk factors [E]:

First degree relative with T1D or elevated T1D genetic risk

Dysglycemia

History of stress hyperglycemia

Otherwise: perform q3 year repeat screening [E]



Primary Care =>
Subspecialty Care

Stage 1 Type 1 Diabetes

Children

Educate on need for monitoring, symptoms of DKA; provide written instructions, give SMBG meters/strips [E]

Check glucose with intercurrent illness [A]

If recent Ab+ can do SBMG q2 weeks and then q 1-3 months [E]

Repeated HbA1c with random BG [E]:

Children ≤ 3 y HbA1c every 3 months

Children 3-9 y every 6 months

Children >9 y at least every 12 months

Can consider using 10-14 d CGM rather than A1c [E]

Use OGTT to diagnose stage 2 or stage 3 diabetes [A], or a 2-h glucose after a carbohydrate rich meal [E]

Adults

Provide SMBG meters/strips to check glucose with illness or symptoms [E]

Repeat HbA1c every 12 months as part of primary care [E]:

Modify frequency based on individual risk assessment based on age, number/type of Ab, glycemic metrics

If A1c changes ≥ 10% perform OGTT to assess T1D stage

If normoglycemic x 5 years can monitor q 2 years

Stage 2 Type 1 Diabetes:

Referral to endocrinologist [E]

Children

Educate on need for monitoring, DKA; provide written instructions [E]

Give SMBG meters/strips [E]

Monitor metabolic status every 3 months [E]

Can consider using 10-14 d CGM rather than A1c [E]

Adults

Monitor metabolic status every 6 months [E]

Use A1c plus one of the following: blinded CGM, higher frequency SMBG (biweekly fasting or 2h post prandial) or OGTT

Longitudinal increase HbA1c ≥10% → disease progression, perform OGTT to stage

Consider c-peptide assessment when T1D vs T2D diagnosis unclear [B]

Monitoring in Adults: CAVEATS

- Misdiagnosis of T1D in adults is common, more likely with older age
- Can lead to **DKA** due to prescribing wrong therapy
- Many primary care providers lack awareness

No single clinical feature confirms T1D
- Not Age
- Not BMI
- Not DKA

T1D mistaken for:
- Type 2 Diabetes
- Ketosis prone T2D
- MODY
- Type 3C Diabetes
- Pancreatic cancer
- Checkpoint inhibitor associated DM

40% of persons developing T1D after age 30 are initially treated as T2D

Slide adapted from one created by R. Schulman-Rosenbaum

-Gregory GA et al. International Diabetes Federation Diabetes Atlas Type 1 Diabetes in Adults. Lancet Diabetes Endocrinol 2022.
-Holt RIG et al. The management of type 1 diabetes in adults. A consensus report by the ADA and EASD. Diabetologia, 2021.

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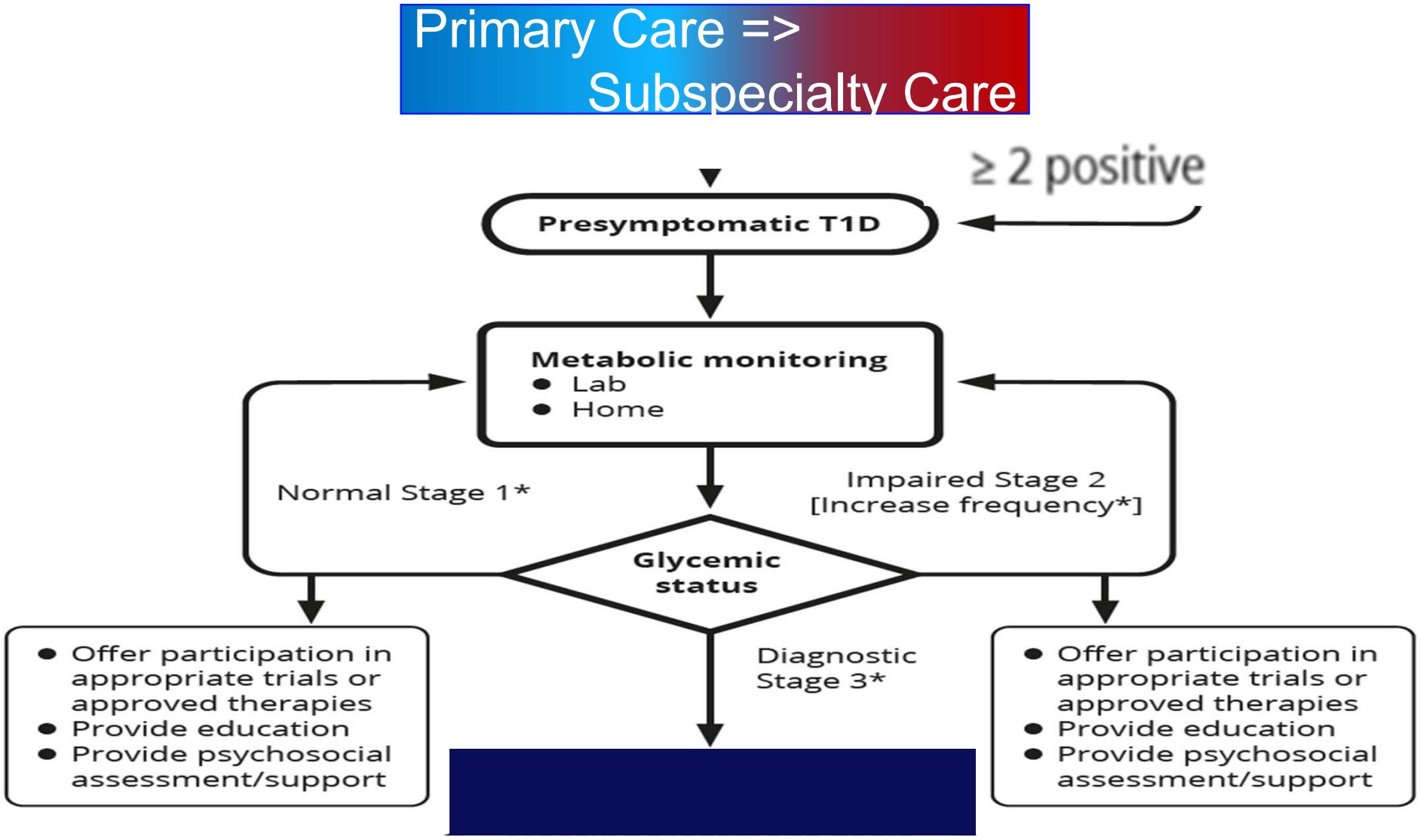
Primary Care =>
Subspecialty Care
≥ 2 positive
Presymptomatic T1D
Metabolic monitoring
Lab
Home
Normal Stage 1*
Impaired Stage 2
[Increase frequency*]
Glycemic status
Diagnostic Stage 3*
Offer participation in appropriate trials or approved therapies
Provide education
Provide psychosocial assessment/support
Offer participation in appropriate trials or approved therapies
Provide education
Provide psychosocial assessment/support

Reference: ADA Standards of Care 2024

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**

3.2 In people with preclinical type 1 diabetes, monitor for disease progression using A1C approximately every 6 months and 75-g oral glucose tolerance test (i.e., fasting and 2-h plasma glucose) annually; modify frequency of monitoring based on individual risk assessment based on age, number and type of autoantibodies, and glycemic metrics. **E**

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**

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– American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Suppl 1):S20-S42. doi: 10.2337/dc24-S002. PMID: 38078589; PMCID: PMC10725812. American Diabetes Association Professional Practice Committee. 3. Prevention or Delay of Diabetes and Associated Comorbidities: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Suppl 1):S43-S51. doi: 10.2337/dc24-S003. PMID: 38078581; PMCID: PMC10725807.

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Type 1 Diabetes Clinical Trials: Prevention Portfolio Focus

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Why a Breakthrough Priority?

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There are more T1D therapies and devices in clinical trials than ever before.

The Challenge:

Lack of clinical trial participants:

Leads to longer trials leading to delayed results

Requires more fundraising dollars to complete trials

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Why Clinical Trial Education Matters

Between

2-16%

of clinical trial participants are racial and ethnic minorities

97%

of participants in the TN10 Trial identified as Non Hispanic White

Approximately

0.2%

of people are **referred to research**

Original Research Manuscript | Published: 06 January 2020

US Physician and Nurse Proclivity to Refer Their Patients Into Clinical Trials

Kenneth A. Getz MBA

Therapeutic Innovation & Regulatory Science **54**, 404–410 (2020) | Cite this article

50 Accesses | **2** Citations | Metrics

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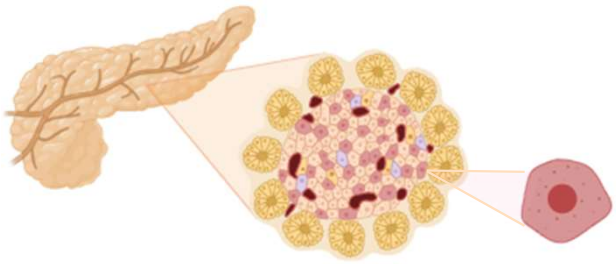
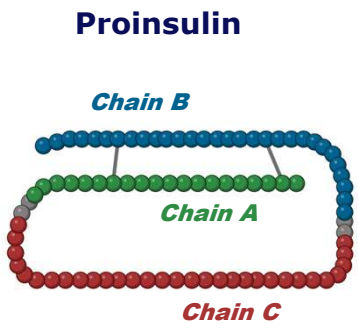
How do we measure success T1D Prevention Clinical Trials? C-peptide

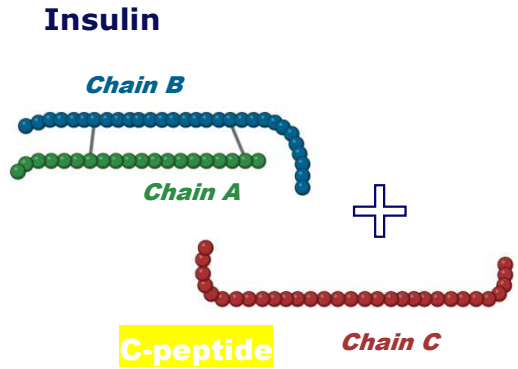
In beta cells, the process for making insulin starts with the precursor **proinsulin**, a protein composed of 3 different "chains"





Proinsulin breaks down into:

- **Insulin** (**A** and **B** chains)
- **C-peptide** (**C** chain 23 amino acid chain)



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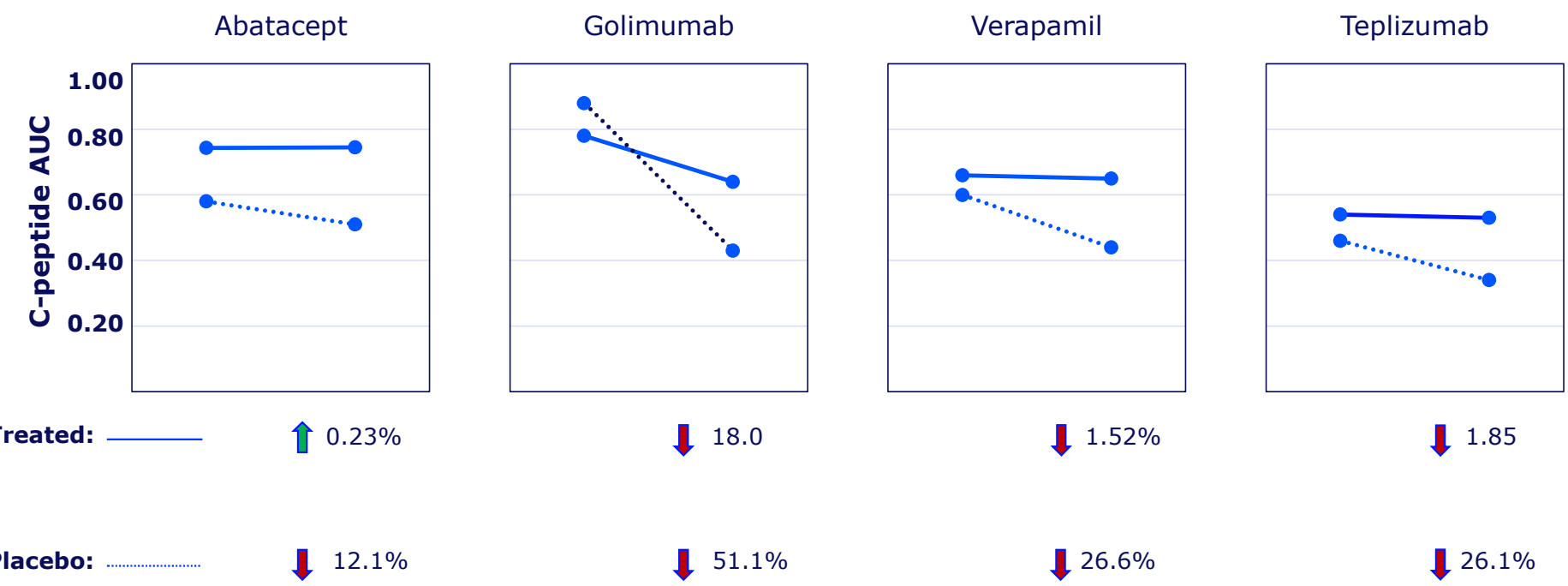
Clinical trials aimed at immune tolerance (preservation of c-peptide)



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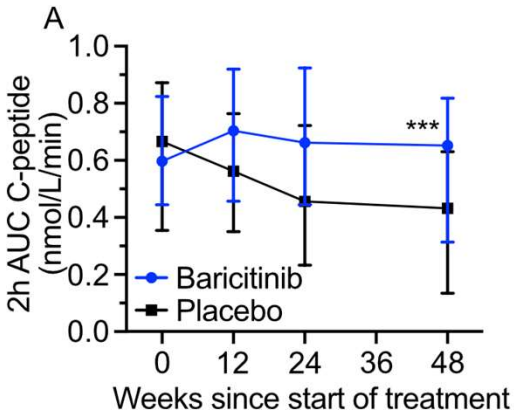
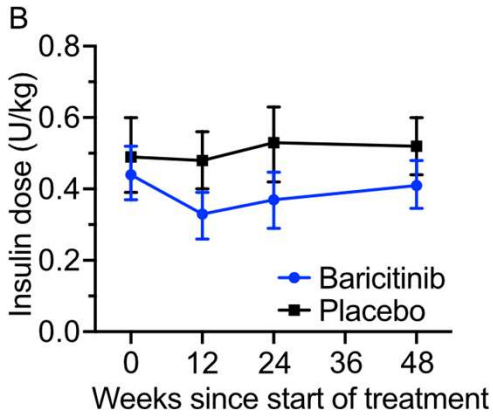
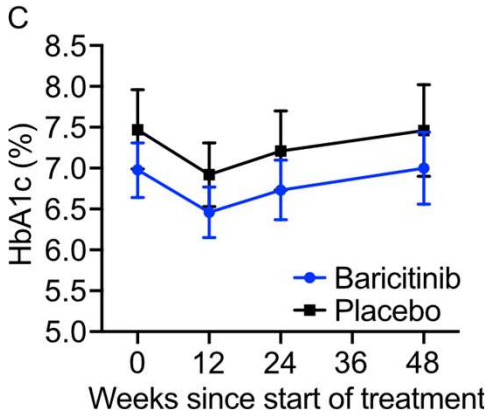
BANDIT Clinical Trial

- Baricitinib is a JAK inhibitor
- Currently used in rheumatoid arthritis, autoimmune hair loss (called alopecia)
- In 60 newly diagnosed children and young adults, it preserved the body's ability to produce insulin
- It is a pill







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Currently Recruiting Clinical Trials Stage 2 and 3

PETITE-T1D
Tepluzimab in Pediatrics
- 1-7 Years of Age
- Stage 2 T1D
- 14 Day Infusion

STOP-T1D
TrialNet ATG Prevention Study
- 12-35 Years of Age
- High-Risk Stage 2 T1D
- 2-day infusion

www.breakthrought1d.org/clinical-trials/

JAKPOT T1D
TrialNet JAK Inhibitors Study
- 12-35 Years of Age
- New Onset T1D (3 months)
- Oral Pill

GLADIATOR
Ladarixin Study
- 14-45 Years of Age
- New Onset T1D (6 months)
- Oral Pill

DESIGNATE
Siplizumab Study
- 18-45 Years of Age
- New Onset T1D (18 months)
- Weekly Injection

T1D RELAY
Rituximab/Abatacept Study
- 8-45 Years of Age
- New Onset T1D (3 months)
- Oral Pill

DIAGNODE-3
DIAMYD Study
- 12-29 Years of Age
- New Onset T1D (6 months)
- 3 Lymph Node Injections

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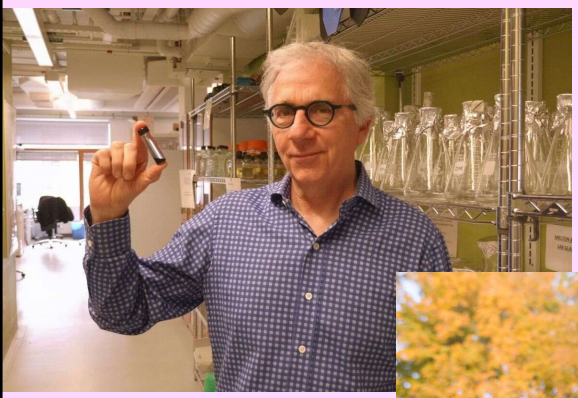
Cell Therapy for Type 1 Diabetes



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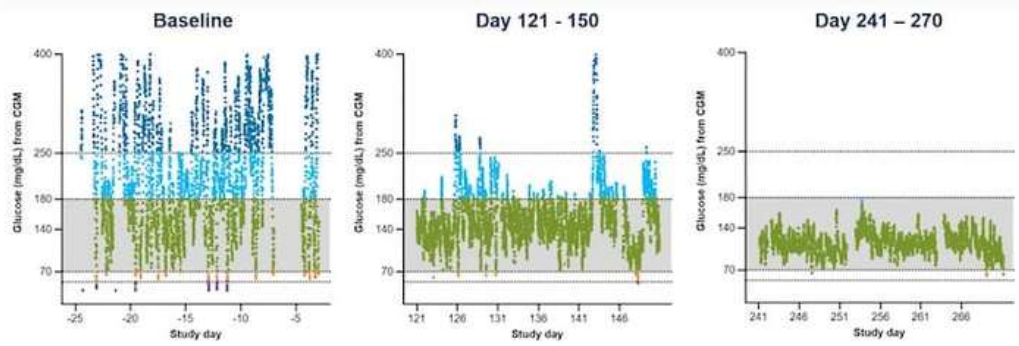
VX 880 Study
Phase 1 / 2 **SAFETY** Study – Early Results

Participant 1

Study day	Day 0 (baseline)	Day 121-150	Day 241-270
Daily Insulin dose	34 units	2.6 units	0 units
Time in Range	40.1%	81.4%	99.9%
A1C	8.6%	6.7%	5.2%



Glucose data generated by a continuous glucose monitor (CGM) worn by participant 1.

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Currently Recruiting Clinical Trials

wwwbreakthrought1d.org/ clinical-trials/ .

Established T1D Cell Therapy

VERTEX - 880
Cell Therapy Study – Phase I Trial
- 18-65 Years of Age
- T1D > 5 Years
- Cells Infused Via Hepatic Portal Vein

Established T1D Prevention

COVALENT-112
Menin Inhibitor Study (Prevention)
- 18-60 Years of Age
- T1D < 3 Years
- Oral Pill

VERTEX - 264
Cell Therapy Study – Phase I Trial
- 18-65 Years of Age
- T1D > 5 Years
- Devices Containing Cells Implanted

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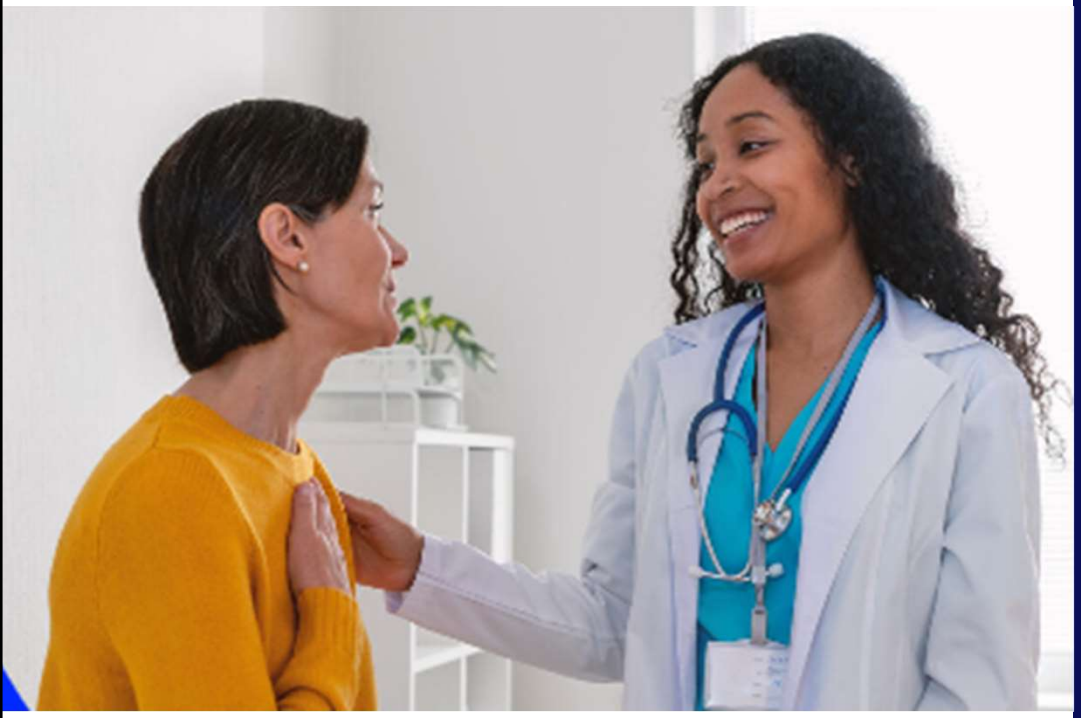
Call to Action: Share the Benefits of Clinical Trial Participation



wwwbreakthrought1d.org/clinical-trials/

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Contribute to science to help others in the future

Participation may lead to a more active role in your health

Researchers are often leaders in their discipline and experts in their field

More participation = more progress

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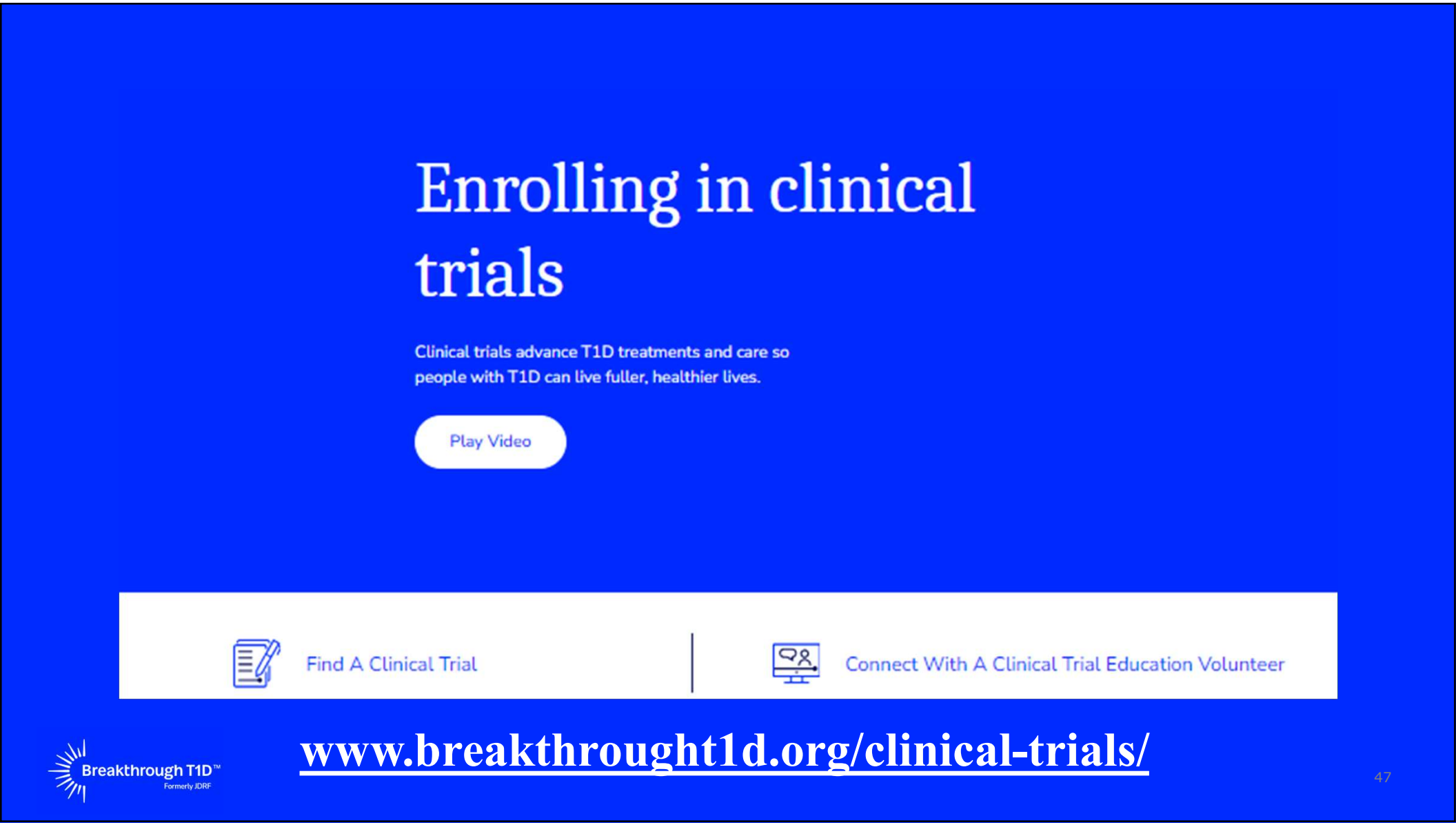
Enrolling in clinical trials
Clinical trials advance T1D treatments and care so people with T1D can live fuller, healthier lives.
Play Video
Find A Clinical Trial
Connect With A Clinical Trial Education Volunteer
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Thank you!

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