

Pediatric Diabetes Research Updates

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DIABETES & ENDOCRINE



Affiliated with



2024 Virtual Diabetes Management Conference for School Nurses

Provided by Texas Children's Hospital

NURSING CONTINUING PROFESSIONAL DEVELOPMENT

Texas Children's Hospital is approved with distinction as a provider of nursing continuing professional development (NCPD) by the Texas Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation.

REQUIREMENTS FOR SUCCESSFUL COMPLETION

To receive contact hours for this nursing continuing professional development activity, the participant must:

- Register for the continuing professional development activity
- Attend at least one session of the professional development activity
- Complete the pre-conference survey
- Complete the post-conference survey online

Print your contact hour "Certificate of Successful Completion" once you have completed the post-conference survey online .

LEARNING OUTCOME

As a result of this professional development activity, 90 % of attendees will be able to name one concept learned on the post conference survey as it relates to care of the child with diabetes as well as attendees will demonstrate increased knowledge as evidenced by an increase in scores on the post conference survey when compared to the pre-conference survey.

RELEVANT FINANCIAL RELATIONSHIPS

Explanation: a relevant financial relationships occurs when an individual has an opportunity to affect or impact educational content with which he or she may have a relationship with an ineligible company or a potentially biasing relationship of a financial nature. All planners and presenters/authors/content reviewers must disclose the presence or absence of a relevant financial relationship relative to this activity. All potential relationships are mitigated prior to the planning, implementation, or evaluation of the continuing education activity. All activity planning committee members and presenters/authors/content reviewers have had their relevant financial relationships assessed, identified and mitigated by Activity Director & the nurse planner.

The activity's Nurse Planner has determined that no one who has the ability to control the content of this nursing continuing professional development activity – planning committee members and presenters/authors/content reviewers – has a relevant financial relationship.

DISCLOSURES

- I have no relevant financial relationships with any ineligible company to disclose.
- I will discuss interventional clinical trials using medications that are not currently approved for diabetes treatment.

OUTLINE

- Type 1 diabetes prediction and prevention
- Diabetes technology
- Type 2 diabetes in children
- Atypical diabetes

FIRST PATIENT TO HAVE RECEIVED INSULIN INJECTION FOR T1D - 1922



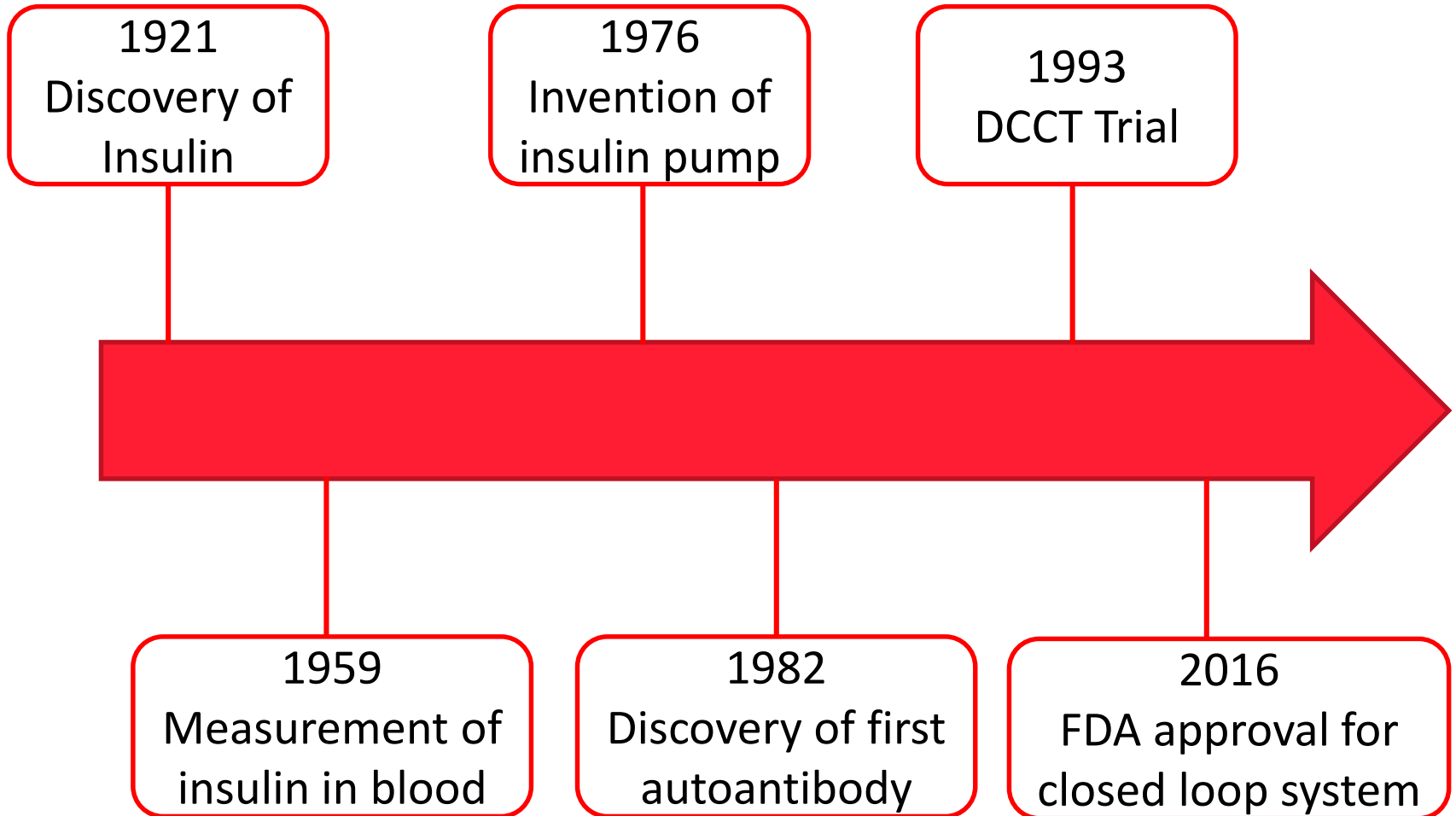
Before insulin

2 months after
insulin

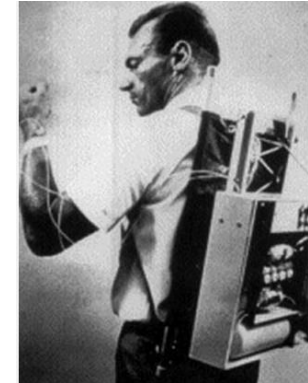
diapedia.org

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WE HAVE COME A LONG WAY...

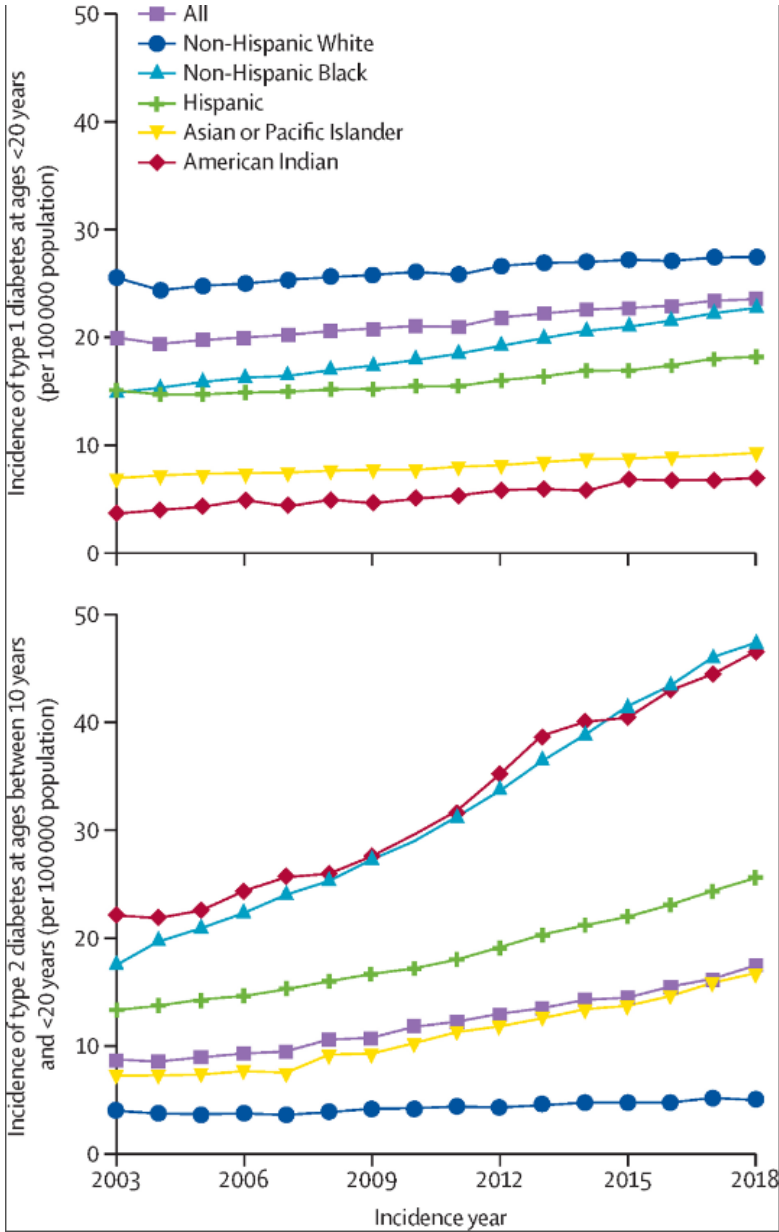


WE HAVE COME A LONG WAY



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INCREASING INCIDENCE OF TYPE 1 AND TYPE 2 DIABETES IN CHILDREN IN THE US



Trends in incidence of youth-onset type 1 and type 2 diabetes in the USA, 2002–18: results from the population-based SEARCH for Diabetes in Youth study

Prof Lynne E Wagenknecht, DrPH [✉] • Jean M Lawrence, ScD ^{*} • Scott Isom, MS • Elizabeth T Jensen, PhD • Prof Dana Dabelea, MD PhD • Prof Angela D Liese, PhD • et al. [Show all authors](#) • [Show footnotes](#)

Published: February 28, 2023 • DOI: [https://doi.org/10.1016/S2213-8587\(23\)00025-6](https://doi.org/10.1016/S2213-8587(23)00025-6) • [Check for updates](#)

ULTIMATE GOAL

~~Diabetes~~

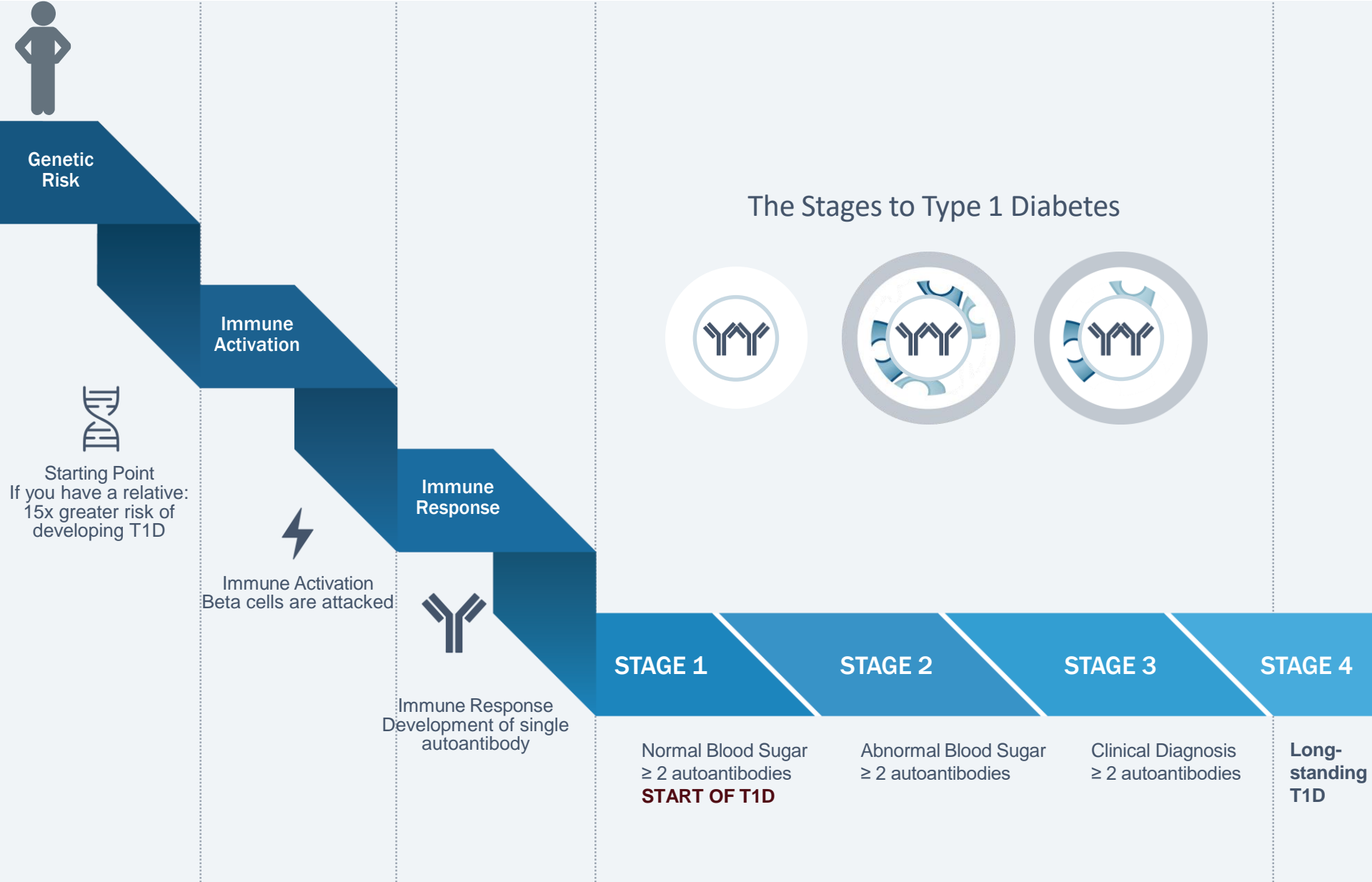


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TYPE 1 DIABETES PREDICTION AND PREVENTION

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TYPE 1 DIABETES DISEASE PROGRESSION

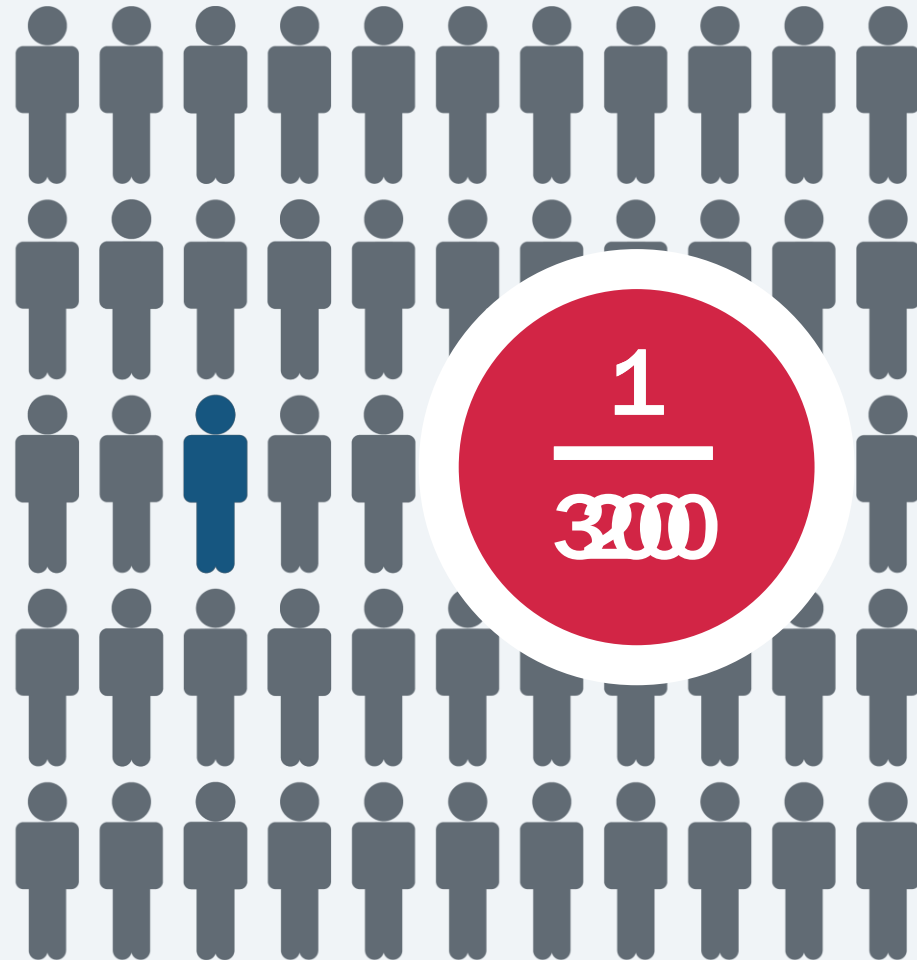


T1D DISEASE PROGRESSION

Starting Point Genetic Risk

The path to T1D starts here

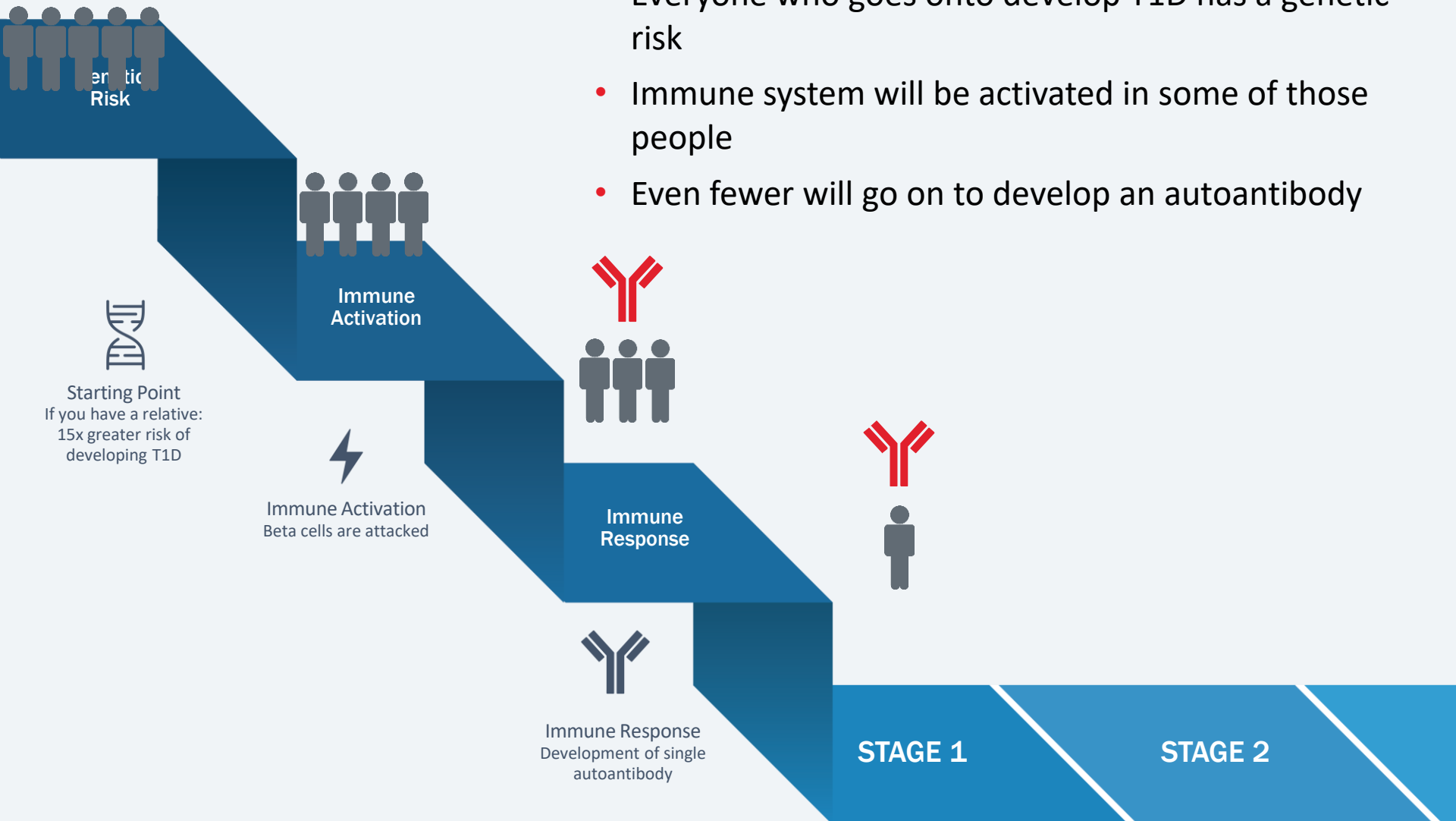
- Everyone who is diagnosed with T1D has the gene(s) associated with T1D
 - General population risk is 1 in 300
- Family members are at 15x greater risk to develop T1D
 - Relative risk is 1 in 20



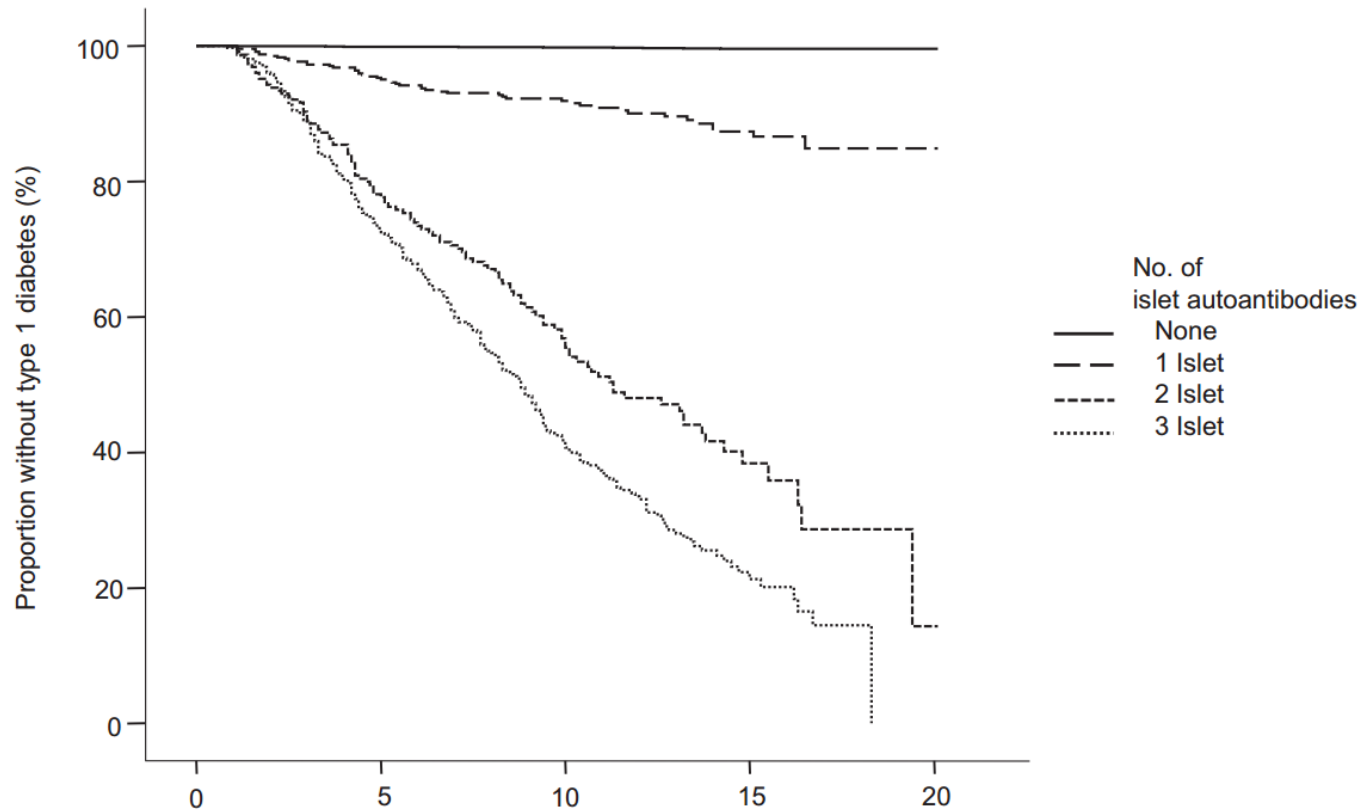
T1D DISEASE PROGRESSION

Progression by Population:

- Everyone who goes onto develop T1D has a genetic risk
- Immune system will be activated in some of those people
- Even fewer will go on to develop an autoantibody












Probability of progression to symptomatic T1D stratified for number of islet autoantibodies



No. of events	Age (years)				
Islet autoantibodies, No.	0	5	10	15	20
3 Islet	358	250	112	20	
2 Islet	227	168	82	19	1
1 Islet	474	430	272	118	9
None	12318	8875	5253	1161	44

T1D DISEASE PROGRESSION

The impact of AGE on disease progression & beta cell decline

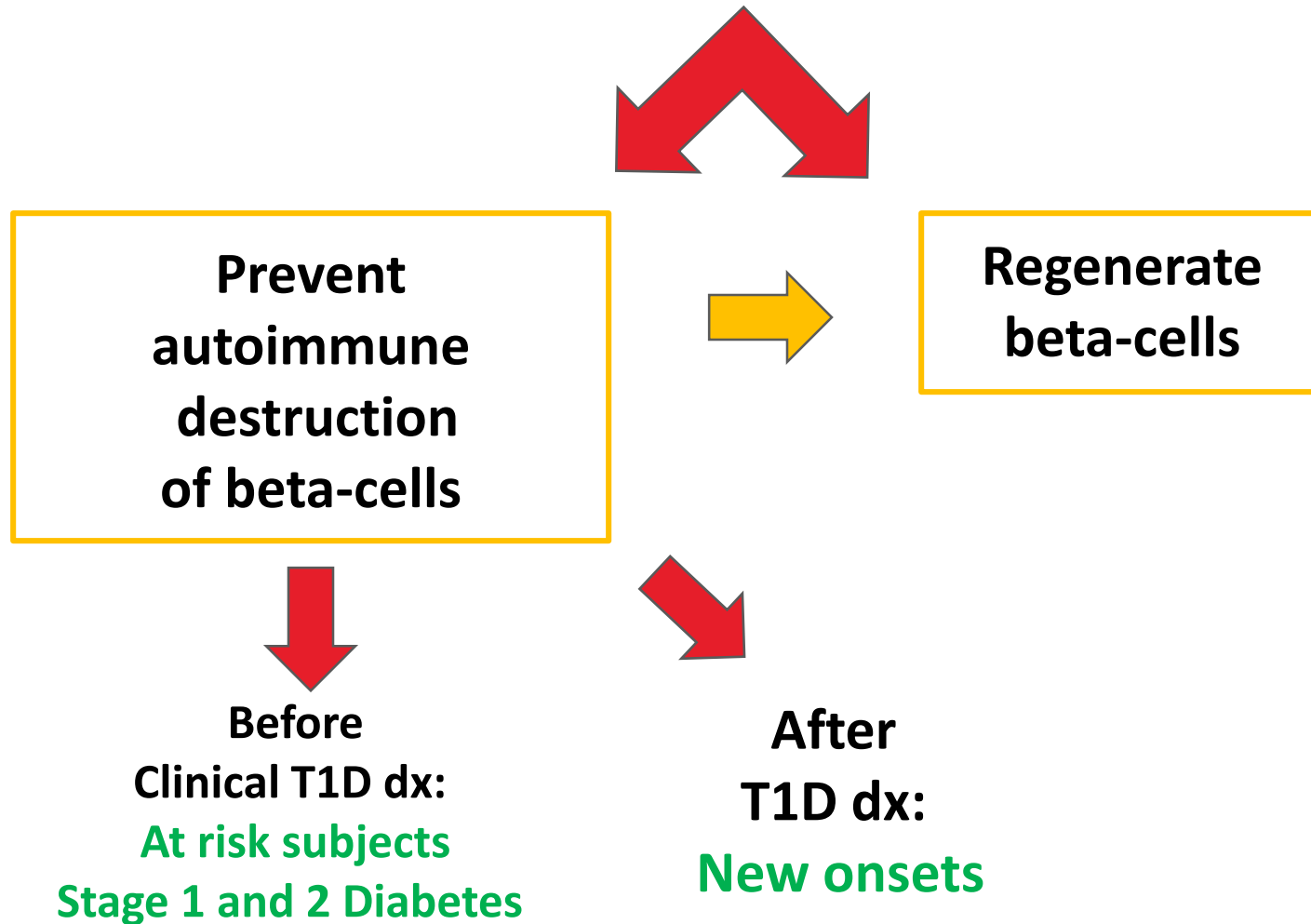
				
	STAGE 1 (Start of T1D) ≥ 2 autoantibodies	STAGE 2 ≥ 2 autoantibodies	STAGE 3 (Clinical Dx) ≥ 2 autoantibodies	STAGE 4 Long-standing T1D
Age <5 				
Age 5-9 				
Age 10-14 				
Age 15-19 				
Age ≥ 20 				

T1D DISEASE PROGRESSION

IMPORTANCE OF STAGING

- 1. Accelerate the clinical development of therapies by providing a common framework for**
 - Regulators, funders, academia and industry
- 2. Identification of T1D in its' earliest stages can lead to a decreased risk of diagnosis in DKA**
- 3. Staging diabetes allows us to treat T1D early to delay progression and ultimately prevent stage 3 (symptomatic T1D)**
 - Treating high blood pressure, allows us to treat the disease early and ultimately prevent a heart attack or stroke

T1D RESEARCH STUDIES



HOW TO FIND STUDIES: CLINICALTRIALS.GOV



ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

Explore **432,718** research studies in all 50 states and in 221 countries.

See [listed clinical studies](#) related to the coronavirus disease (COVID-19)

ClinicalTrials.gov is a resource provided by the U.S. National Library of Medicine.

IMPORTANT: Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our [disclaimer](#) for details.

Before participating in a study, talk to your health care provider and learn about the [risks and potential benefits](#).

Find a study (all fields optional)

Status ⓘ

Recruiting and not yet recruiting studies

All studies

Condition or disease ⓘ (For example: breast cancer)

X

Other terms ⓘ (For example: NCT number, drug name, investigator name)

X

Country ⓘ

▼ X

[Search](#) [Advanced Search](#)

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TYPE 1 DIABETES TRIALNET

Who We Are & What We Do

TCH/BCM TrialNet Investigators:

Drs. Tosur (PI), Redondo, Patel, Uysal, Aguirre, Siller

TYPE 1 DIABETES TRIALNET

- NIH-funded, multicenter study to prevent or delay type 1 diabetes, since 2001
- Many clinical and affiliated centers in the US (TCH/BCM one of them), Europe and Australia
 - ❑ Observational, prospective arm, screens relatives of patients with T1D: Pathway to Prevention
 - ❑ Preventive studies enroll subjects at risk (positive Aab), no diabetes
 - ❑ Studies for new onsets diabetes patients



P2P Pathway to Prevention

Determine where you are on the path

- No cost
- 1st and 2nd degree relatives
- Screens for 5 autoantibodies
- Based on results:
 - Look to enroll in clinical trial to preserve beta cell function
 - Or monitor for disease progression
 - **Teplizumab treatment**



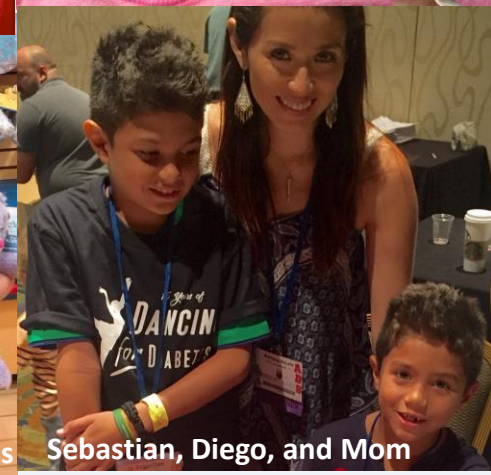
University of Florida at Friends
for Life



Keilyn
Pathway to Prevention



Brooke, Emily & Ava
Pathway to Prevention Participants

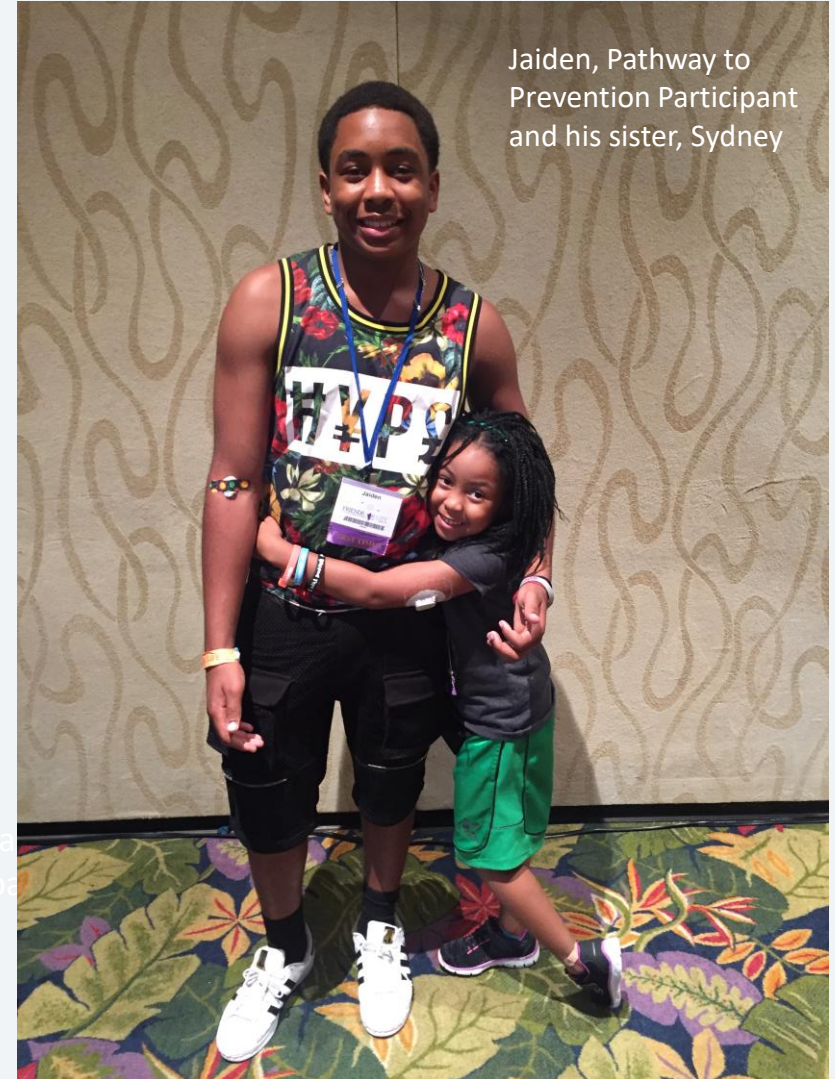


Sebastian, Diego, and Mom

P2P Pathway to Prevention

Eligibility Requirements

- Anyone between age 2.5 and 45 with a sibling, child or parent with type 1
- Anyone between age 2.5 and 20 with a sibling, child, parent, cousin, uncle, aunt, niece, nephew, grandparent or half-sibling with T1D



Jaiden, Pathway to
Prevention Participant
and his sister, Sydney

TRIALNET WEBSITE TO SIGN UP

trialnet.org

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Join the TrialNet #T1Dfamily
Detect future risk of T1D and advance important research!

Imagine a future without type 1 diabetes

TrialNet is an international network of leading academic institutions, endocrinologists, physicians, scientists and healthcare teams at the forefront of type 1 diabetes (T1D) research. We offer risk screening for relatives of people with T1D and innovative clinical studies testing ways to slow down and prevent disease progression. Our goal: a future without T1D!

[Learn more](#)

GET STARTED

[Sign up to be screened!](#)

[Find a location near me](#)

[View upcoming events](#)



Get a home test kit

Select the home test kit option and receive a finger stick test kit in the mail. Collect your sample, then mail it back in a pre-paid envelope, at no cost to you.



Visit a Quest Diagnostics or LabCorp

US participants can receive a kit in the mail, then find a Quest Diagnostics or LabCorp near you and make an appointment for your blood draw.



Make an appointment

Schedule an appointment at a TrialNet location. Leading research centers in the US and worldwide provide free T1D risk screening.



Negative: Lower Risk NO AUTOANTIBODIES

No diabetes-related autoantibodies (AAB) detected.



One AAB Positive: Lower risk

ONE AUTOANTIBODY (AAB) DETECTED



2+ AAB Positive: Early Stage T1D

TWO OR MORE AAB

Two or more autoantibodies (AAB) detected.

TRIALNET DISEASE INTERVENTION AT EVERY STAGE

P2P Pathway to Prevention	TN20 Immune Effects of Oral Insulin	TN18 Abatacept	TN10 Teplizumab (Anti-CD3)	TN19 ATG/GCSF
RISK SCREENING	STAGE 1	STAGE 1	STAGE 2	STAGE 3
<p>This study screens relatives of people with T1D to study risk and learn about how the disease occurs.</p> <ul style="list-style-type: none"> • Screens for five autoantibodies • 1st and 2nd degree relatives • First step to identify eligibility for clinical trial participation <p>ACTIVE</p>	<p>Mechanistic study to learn how different doses and intervals of oral insulin affect immune response.</p> <ul style="list-style-type: none"> • 1st stage toward T1D • 2 or more autoantibodies <p>COMPLETED</p>	<p>This study test whether abatacept helps stop or slow beta-cell decline in people who are at high risk of developing T1D.</p> <ul style="list-style-type: none"> • 1st stage toward T1D • 2 or more autoantibodies • Approved and efficacious for treatment of RA/JIA <p>COMPLETED</p>	<p>This study tests whether teplizumab helps stop or slow down beta-cell decline in people who are at high risk of developing T1D.</p> <ul style="list-style-type: none"> • 2nd stage toward T1D • 2 or more autoantibodies with abnormal glucose tolerance <p>COMPLETED FDA APPROVED</p>	<p>This study tests whether ATG used alone or together with GCSF will help people continue to produce their own insulin.</p> <ul style="list-style-type: none"> • 3rd stage diagnosis of T1D • Combination therapy using two medications <p>COMPLETED</p>

TEPLIZUMAB (ANTI CD3 AB)

Recent Type 1
Diabetes Advances

FDA approved as of 11/17/22 for children 8 and older at stage 2 diabetes (2 ab+ with dysglycemia)

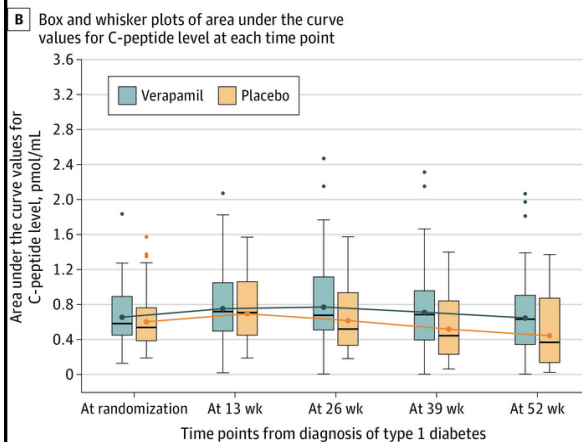
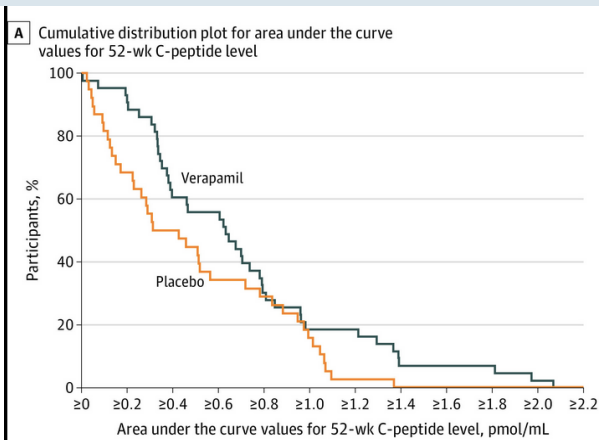
Landmark findings- the first drug to delay type 1 diabetes (T1D) for 2+ years in people at risk.

TCH is one of the a few sites in the US for Teplizumab infusion

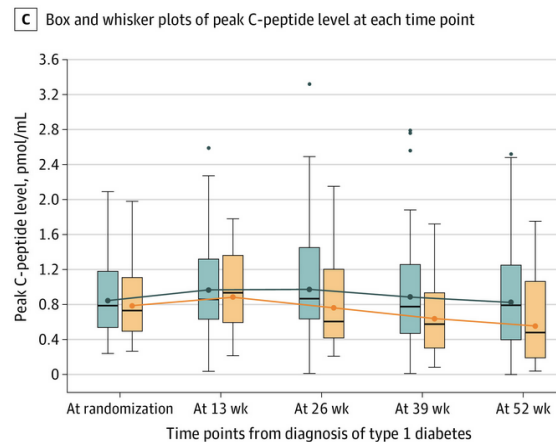
Another reason for antibody screening in relatives

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CALCIUM CHANNEL BLOCKER: A BLOOD PRESSURE MEDICINE



No. of participants	At randomization	At 13 wk	At 26 wk	At 39 wk	At 52 wk
Verapamil	46	46	45	43	43
Placebo	40	39	37	37	38



No. of participants	At randomization	At 13 wk	At 26 wk	At 39 wk	At 52 wk
Verapamil	46	46	45	43	43
Placebo	40	39	37	37	38

- Design: Double-blind, randomized clinical trial (ages 7 to 17 years with New onset T1D)
- Intervention: Once-daily oral verapamil (n = 47) or placebo
- C-peptide level after a mixed meal tolerance test at 52 weeks
- Result: 0.66 pmol/mL at baseline and 0.65 pmol/mL at 52 weeks compared with 0.60 pmol/mL at baseline and 0.44 pmol/mL at 52 weeks in the placebo group

ATG PREVENTION STUDY: STOP-T1D STUDY

- Testing low dose of the immunotherapy drug anti-thymocyte globulin (ATG) to see if it can delay or prevent T1D in people:
 - Ages 12 and up to 35
 - With 2 antibodies
 - Abnormal blood sugars (Stage 2)
 - 50% risk of clinical diagnosis (Stage 3) within 2 years (based on specific risk assessment)
- In the treatment phase you will get two doses of the study treatment (ATG or placebo) by intravenous (IV) infusion over 2 consecutive days. Each infusion will take between 6 and 10 hours, followed by 2 hours of monitoring. You may need to stay overnight at the treatment center for observation.
- Follow up is 24 months at least

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SOME CURRENT STUDIES IN NEW ONSET T1D

- Phase 3, multicenter, randomized controlled trial to assess efficacy and safety of Ladarixin in patients with new onset type 1 diabetes (TCH, PI Tosur)
- JAK Inhibitors Newly Diagnosed Study (JAKPOT T1D)
 - Abrocitinib and Ritlecitinib
 - 12-35 years old, diagnosis within 90 days
- Rituximab-pvvr / Abatacept Newly Diagnosed Study (T1D RELAY)
 - 8-45y, diagnosed 3 months ago
- Tolerance Using Plasmid (TOPPLE) Study: Phase 1 (ADULT)
 - TrialNet is testing the safety of a new treatment, NNC0361-0041, in adults diagnosed with type 1 diabetes (T1D) in the past 48 months.

TYPE 1 DIABETES PREDICTION AND PREVENTION: CONCLUSION

- Type 1 diabetes (T1D) results from immune-mediated destruction of insulin-producing beta cells.
- Efforts to prevent T1D have focused on modulating immune responses and supporting beta cell health; however, heterogeneity in disease progression and responses to therapies have made these efforts difficult to translate to clinical practice, highlighting the need for precision medicine approaches to T1D prevention.

DIABETES TECHNOLOGY

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SENSE STUDY: MULTIMODAL **SENSOR SYSTEMS** FOR PRECISION HEALTH ENABLED BY DATA HARNESSING, ARTIFICIAL INTELLIGENCE, AND LEARNING



- HypoMon—ECG and skin conductivity
 - 73% sen, 68% spec
- SenseWear Armband
 - 5 sensors :accelerometer, EKG, heat flux, skin temp and conductivity



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THE PEDIATRIC ARTIFICIAL PANCREAS AUTOMATED INITIALIZATION TRIAL (PEDAP-AI) (VIRGINIA)

- The goal of this clinical trial is to obtain safety data and exploratory glycemic control data from use of an at-home closed loop control (CLC) system (t:slim X2 with Control-IQ Technology) with periodic parameter adjustments driven by an AI-based Advisor system in young children with Type 1 Diabetes.
- The main endpoints this study aims to answer is the safety and efficacy of the use of the AI-driven pump parameters.
- Participants will use the study system (pump and Continuous Glucose Monitor) in closed-loop mode for eight weeks.

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TYPE 2 DIABETES IN CHILDREN

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AGE: PEDIATRIC VS ADULT-ONSET T2D

- Progresses to insulin deficiency faster, with early failure to non-insulin drugs
- Is associated with more frequent and severe complications
- Shortage of drugs for children complicates treatment and worsens outcomes

ONGOING RESEARCH IN PEDIATRIC T2D

- Understand what are the differences with adults and why
- Understand pediatric-specific causes and mechanisms of T2D
- Test drugs that are approved in adults
 - A Research Study to Compare a New Medicine Oral Semaglutide to a Dummy Medicine in Children and Teenagers With Type 2 Diabetes (PIONEER TEENS) (AL, CA, CT, FL)
 - A Study to Evaluate Tirzepatide (LY3298176) in Pediatric and Adolescent Participants With Type 2 Diabetes Mellitus Inadequately Controlled With Metformin or Basal Insulin or Both (SURPASS-PEDS)

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ATYPICAL DIABETES

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ATYPICAL DIABETES

- Diabetes of unclear or unknown cause and/or diabetes that follows an unusual pattern
 - Diabetes that is not type 1, type 2 or any of the known causes
- Problem: May receive incorrect treatment
- Examples:
 - Monogenic diabetes: Caused by a single gene. We know many forms but think that many other are still unknown
 - Ketosis-prone diabetes
 - Autoantibody-negative type 1 diabetes
 - Many other

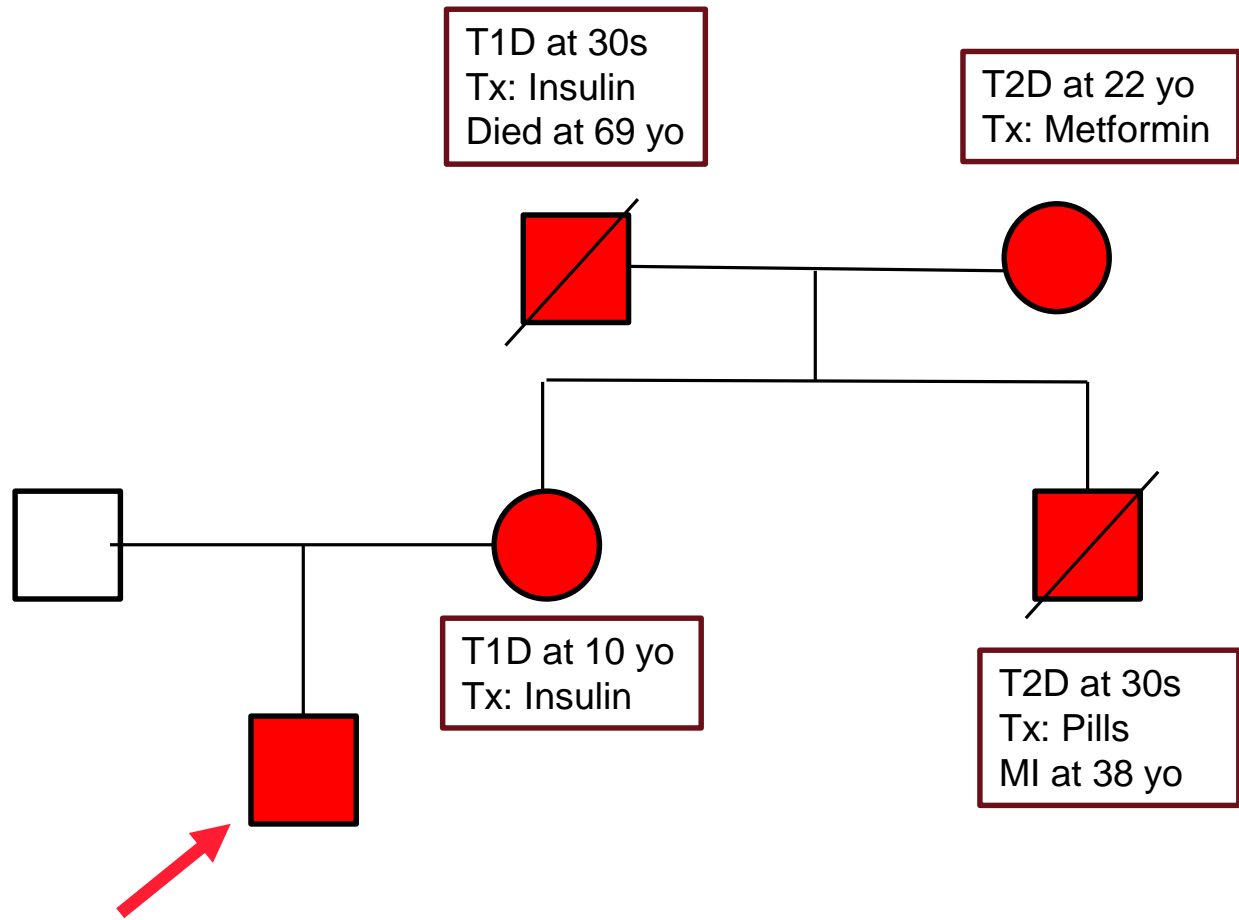
CASE PRESENTATION

- A 13-year-old male presents with excessive drinking, urination and some weight loss
- BMI 22.7 (87th percentile)
- No acanthosis nigricans on examination
- No diabetic ketoacidosis at diagnosis

CASE PRESENTATION – CONT'D

- HbA1c 8.4%, Glucose 232 mg/dL
- Suspected to have “type 1 diabetes” and started on multiple daily insulin injections
- Islet autoantibodies: Negative

FAMILY HISTORY OF DIABETES



GENETIC TEST RESULTS (5-MONTHS AFTER DX):

Athena Diagnostics – 5 gene panel:

A heterozygous, disease-causing genetic variant in *HNF1A*, consistent with MODY 3.

BLOOD SUGAR CONTROL ON ORAL MEDICATION ALONE (SU, 2.5 MG DAILY):

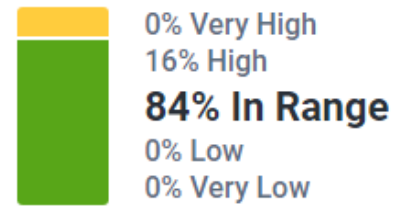
Average Glucose

148 mg/dL

Standard Deviation
32 mg/dL

GMI
N/A

Time in Range



Target Range:
70-180 mg/dL

HbA1c: 6.0%

RARE AND ATYPICAL DIABETES NETWORK (RADIANT) WEBSITE

TCH/BCM RADIANT Investigators:
Redondo (PI), Tosur, Sisley, Kubota-Misra, Siller



Our Research About Us Information for Researchers [Join RADIANT](#)
or Participant Portal Login [English](#) | [Español](#)



If you've been diagnosed by your doctor with diabetes, but do not fit the usual pattern of either type 1 or type 2 diabetes, you may be eligible to join RADIANT.

[Learn More](#)

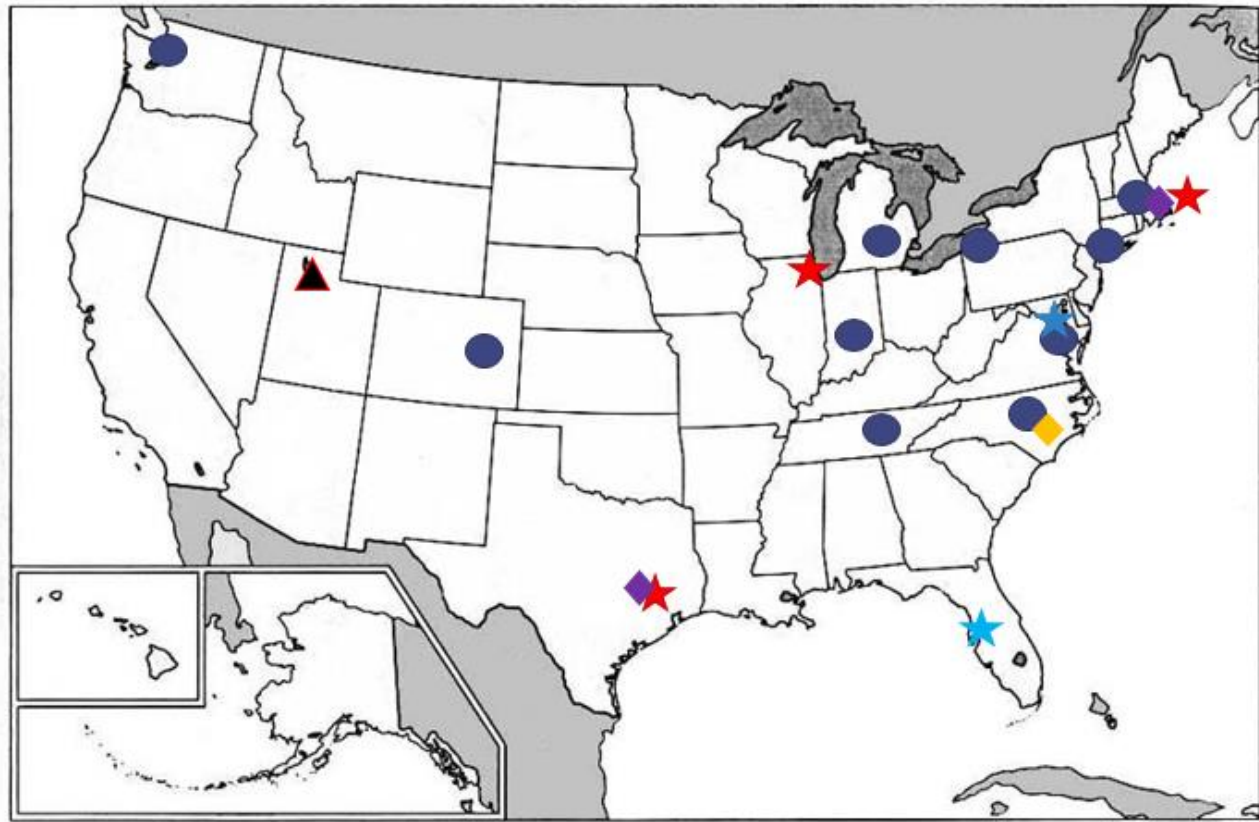
There is currently little information and resources for atypical diabetes.
RADIANT wants to change this.



RADIANT CENTERS AND CLINICAL SITES

Clinical Sites

- Baylor College of Medicine
- Columbia University Medical Center
- SUNY – Downstate
- Indiana University
- Massachusetts General Hospital
- Seattle Children’s
- University of Chicago
- University of Colorado
- University of Maryland
- University of Michigan
- University of North Carolina
- University of Washington
- Vanderbilt University
- Washington University in St. Louis



Genetic Cores

- Broad Institute
- Baylor College of Medicine

Metabolomics Core

- Duke University

RADIANT in nutshell:



You can help shape the future of diabetes care.

“ My doctor knew I didn't have the typical features for type 1 or type 2 diabetes. We didn't know what to do next. ”



RADIANT is a network of institutions across the U.S. who are studying atypical forms of diabetes. Our research staff identify people with atypical diabetes and learn more about their health.

Who can join?

Anyone between ages 0-80 with an atypical form of diabetes. Please reach out to our team to learn more.

Why should I join?

- You may learn more about your diabetes
- Help us better understand all types of diabetes

What will be expected of me?

- Questionnaires
- Genetic testing called whole genome sequencing
- Blood draws
- Other procedures as needed

Please visit www.atypicaldiabetesnetwork.org for more information

RADIANT is supported by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

Online application from anywhere in the U.S.

Whole genome sequencing and more for eligible subjects

Stage 1-2: no travel req'd

Stage 3: Travel to one of RADIANT sites required

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stay tuned...
More to Come!

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THANK YOU!



**Texas Children's
Hospital[®]**

COMMENTS/QUESTIONS?