

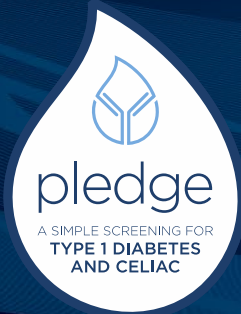
The Sanford PLEDGE Study

T1D and Celiac Screening Integrated into Routine Pediatric Care Across a Health System

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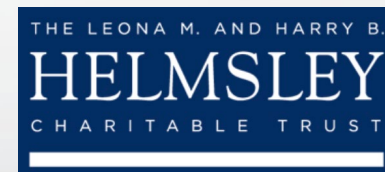
Research Director
Sanford Research
Sioux Falls, SD



7th Childhood Diabetes Prevention Symposium
Barbara Davis Center
14 November 2024



Benaroya
Research Institute



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RESEARCH

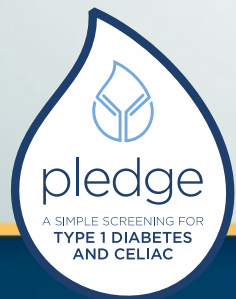
Disclosures

Clinical Trial Funding Paid to Institutions:

- Sanford Health (Todd and Linda Broin Chair; PLEDGE)
- Leona M. and Harry B. Helmsley Charitable Trust (PLEDGE)
- Diabetes TrialNet (TN-01, TN-22, TN-25, TN-28, TN-31)
- Immune Tolerance Network (DESIGNATE, T1DES)
- Sanofi (PROTECT, PROTECT Extension)

Advisory Boards

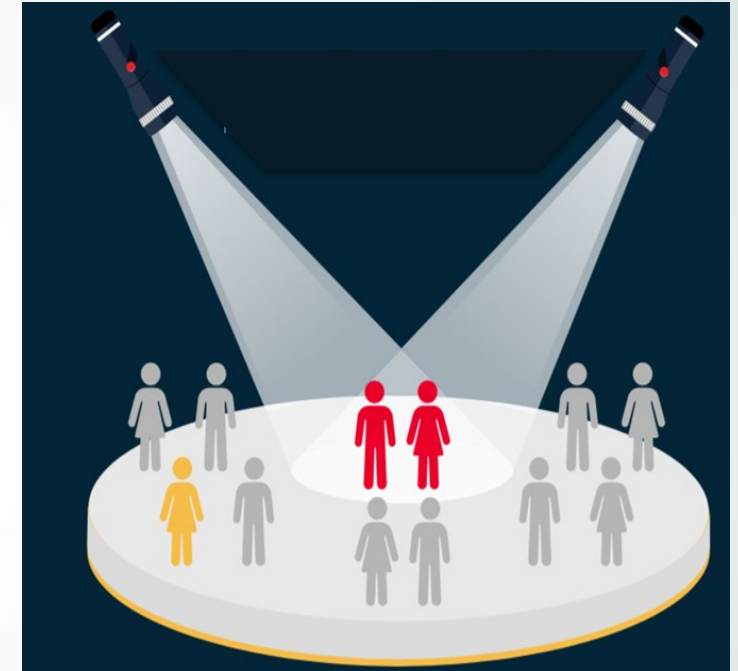
- North Carolina Early Check
- CanScreen T1D



Integrating General Population Screening Into Routine Pediatric Care

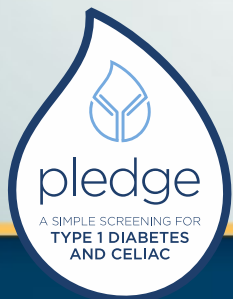
Need a Novel, Pragmatic Design:

- Minimize burden on:
 - Providers & Staff
 - Families
 - Research Coordinators
- Integrated into routine clinic visits
- Leverage existing Epic electronic record system and
- MyChart patient messaging for enrollment & questionnaires
- Economic analyses and modeling
- No cost to families



Goals of PLEDGE Screening

- Prevent initial diabetic ketoacidosis
- Identify patients for possible intervention:
 - Teplizumab when appropriate and available
 - Offer enrollment in intervention trials to delay progression
- Generate evidence to support including T1D screening
 - Demonstrate feasibility of *integration into routine pediatric care*
 - Prospective validation of GRS and assessment of utility to focus screening
 - Assess cost effectiveness of general population screening



PLEDGE Overview of Procedures

Entry before 6th birthday
OR once 9 -16 y.

Genetic Risk Score
GRS2 Once at study entry
(blood spot; can be with Newborn Screening)

Anxiety Survey
Entry & Annually

T1D AutoAb

Celiac Testing



Birth

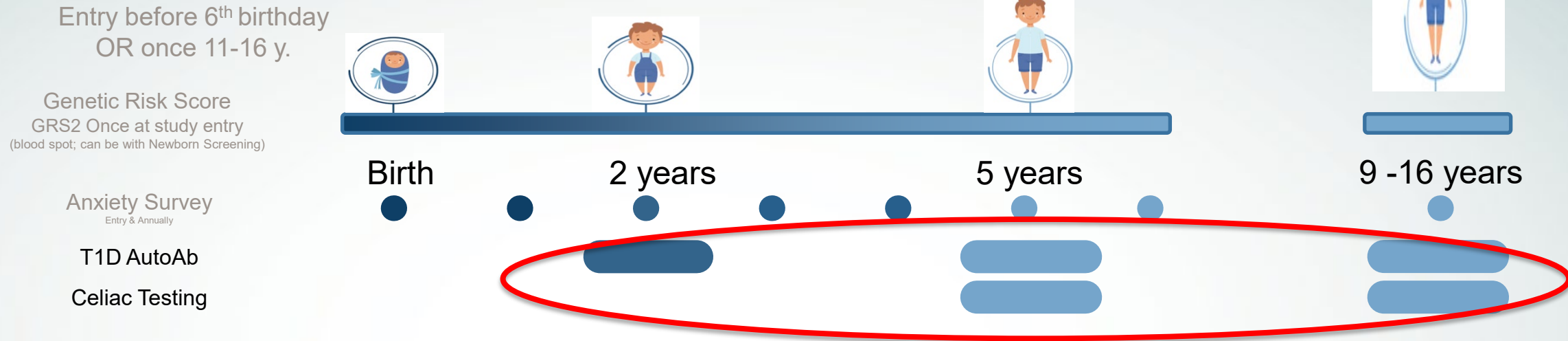
2 years

5 years

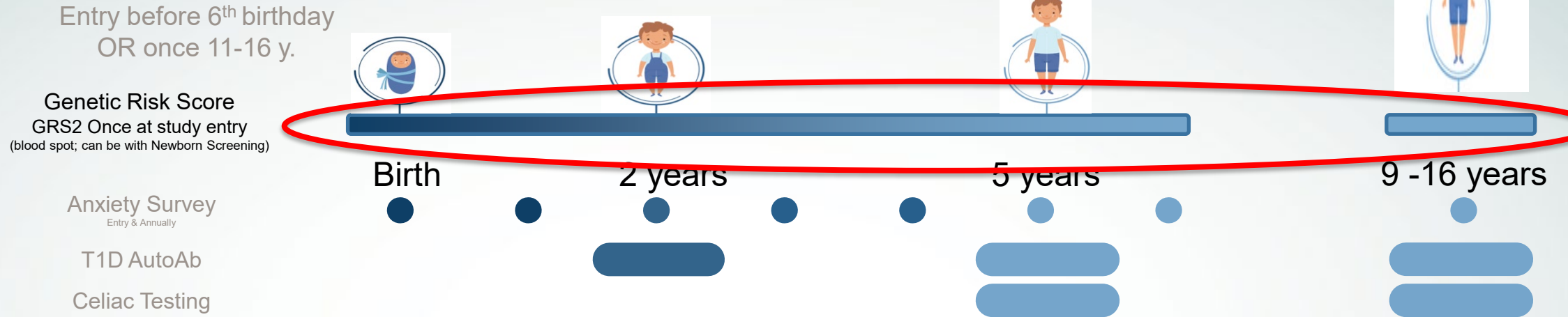
9 -16 years



PLEDGE Overview of Procedures



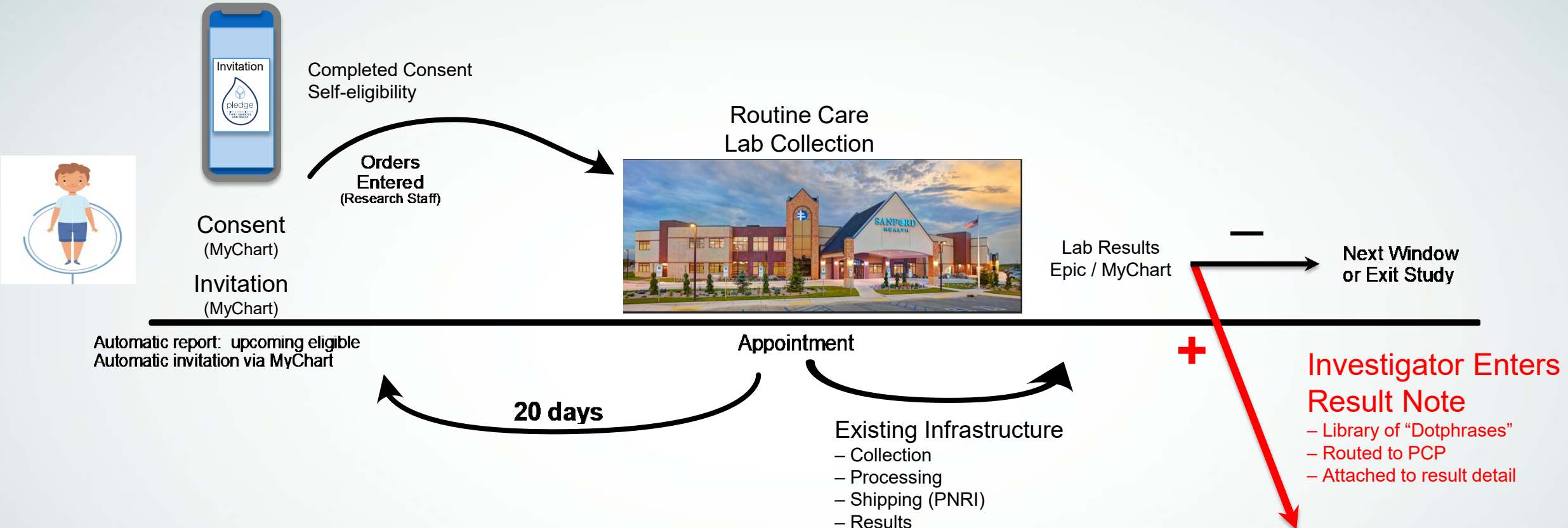
PLEDGE Overview of Procedures



GRS2 at study entry

- SNP-based risk score for T1D and Celiac autoimmunity
- Can enroll before birth and collect with newborn screens

Innovation and Infrastructure



Automatic report: upcoming eligible
Automatic invitation via MyChart

Consent (MyChart)
Invitation (MyChart)

Completed Consent
Self-eligibility

Orders Entered (Research Staff)

Routine Care
Lab Collection

Lab Results
Epic / MyChart

Next Window
or Exit Study

20 days

Appointment

- Existing Infrastructure
- Collection
 - Processing
 - Shipping (PNRI)
 - Results

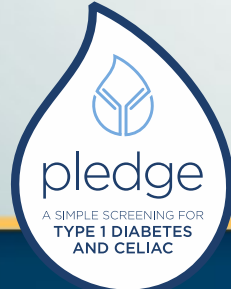
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Investigator Enters Result Note

- Library of "Dotphrases"
- Routed to PCP
- Attached to result detail

Research Staff will:

- Contact Family & Explain
- Retest
- If persistent:
 - Monitoring Protocol for T1D
 - Clinical referral to peds GI for celiac



Integration into routine care
Leverage existing processes and infrastructure
Automation of invitation, enrollment, and messaging

Epic Notifications

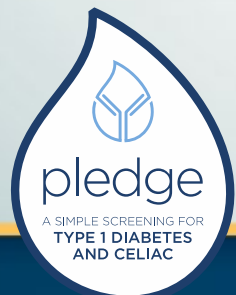
“BPA” [light] in Storyboard

A screenshot of the Epic Storyboard interface for a patient named Callie K. Bear. The interface shows various tabs like 'Chart Review', 'Results', 'Rooming', etc. A red arrow points to a notification in the 'Patient' section: 'May qualify for SH-PLEDGE Study'. Other notifications include 'TDAP vaccination due' and 'Consider HIV screening today'.

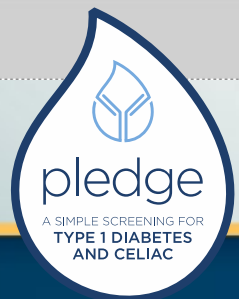
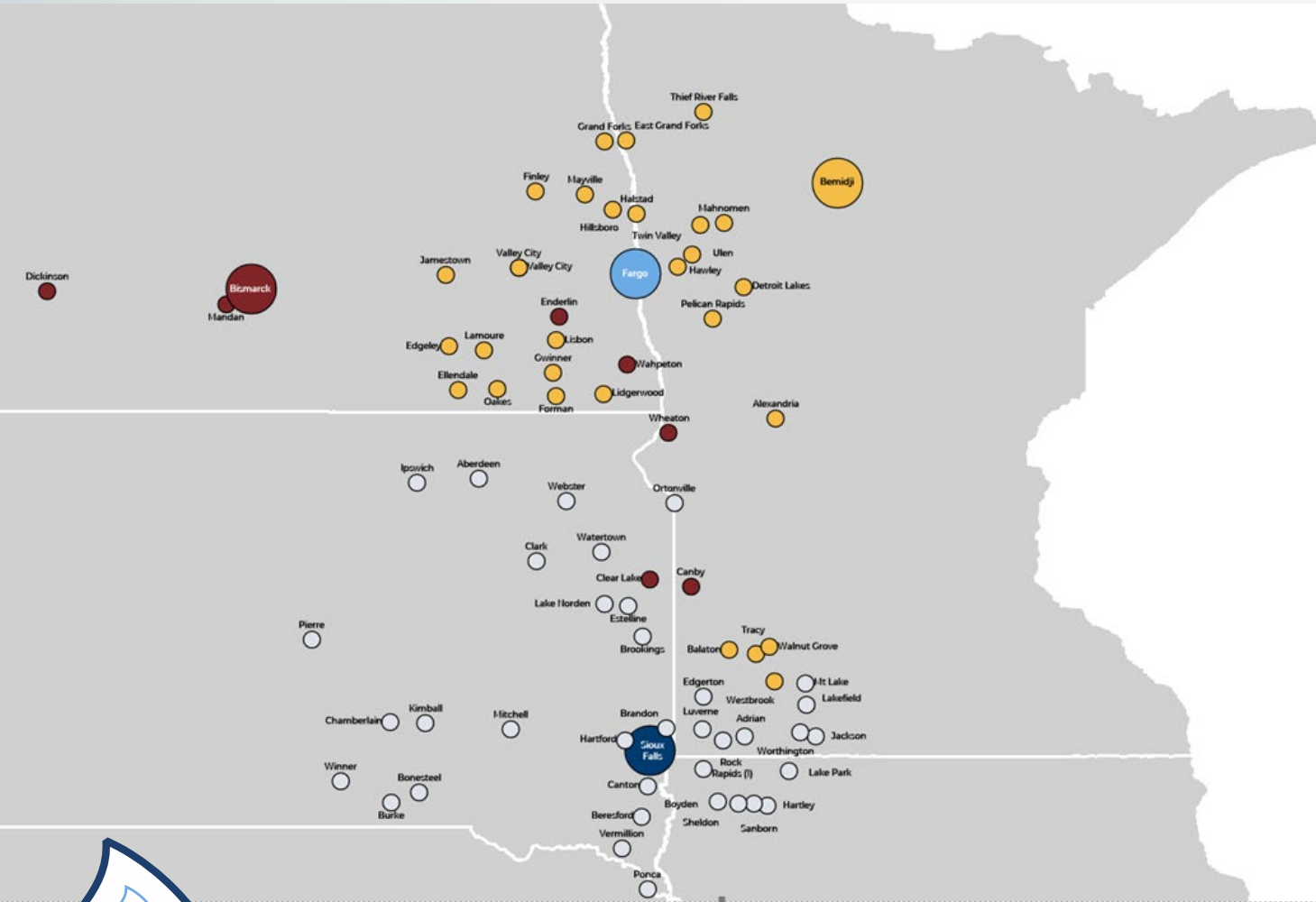
A screenshot of the Epic Patient Chart Advisories window for Claudia Raven. The window displays a warning: 'WARNING! Please see important patient care note in comments below: Special Patient Care Info'. The advisory text states: 'This patient has pre-symptomatic TYPE 1 DIABETES (Stage 1- multiple T1D auto-antibodies with normal glucose tolerance) NOT yet requiring insulin, and is a participant in the PLEDGE Monitoring study. PROVIDERS: If acutely ill or T1D symptoms present, consider screening for hyperglycemia & ketosis. Clinical Questions: Follow your clinic's policy for consultation with Pediatric Endocrinology. Non-Urgent Study Questions: Contact the Sanford diabetes research team: (605) 312- 3309, M-F 0800am-4:30pm.'

“Patient Chart Advisory”

- Appears on opening chart
- Reminder to consider T1D
- Provides guidance
- Does not slow work
- Less intrusive than a “Best Practice Advisory”

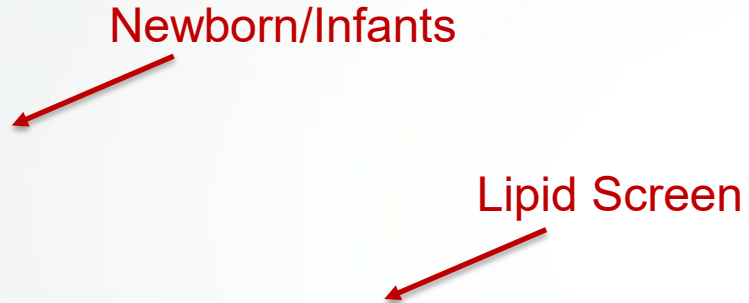


Expansion and Enrollment



Characteristics at Entry

Age at study entry with successful collection



Sex

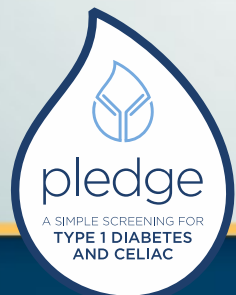
Male	5623
Female	5223

Race

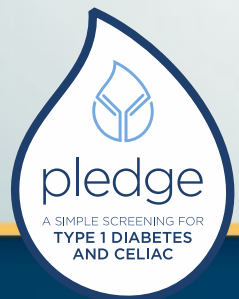
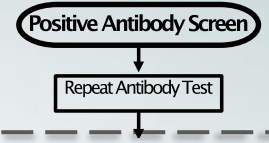
Caucasian	9,763
African American	370
Native American	389
Asian	186
HI/Pacific Island	24

Ethnicity

Not Hispanic	10,087
Hispanic	623
Unknown	130



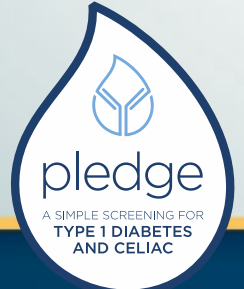
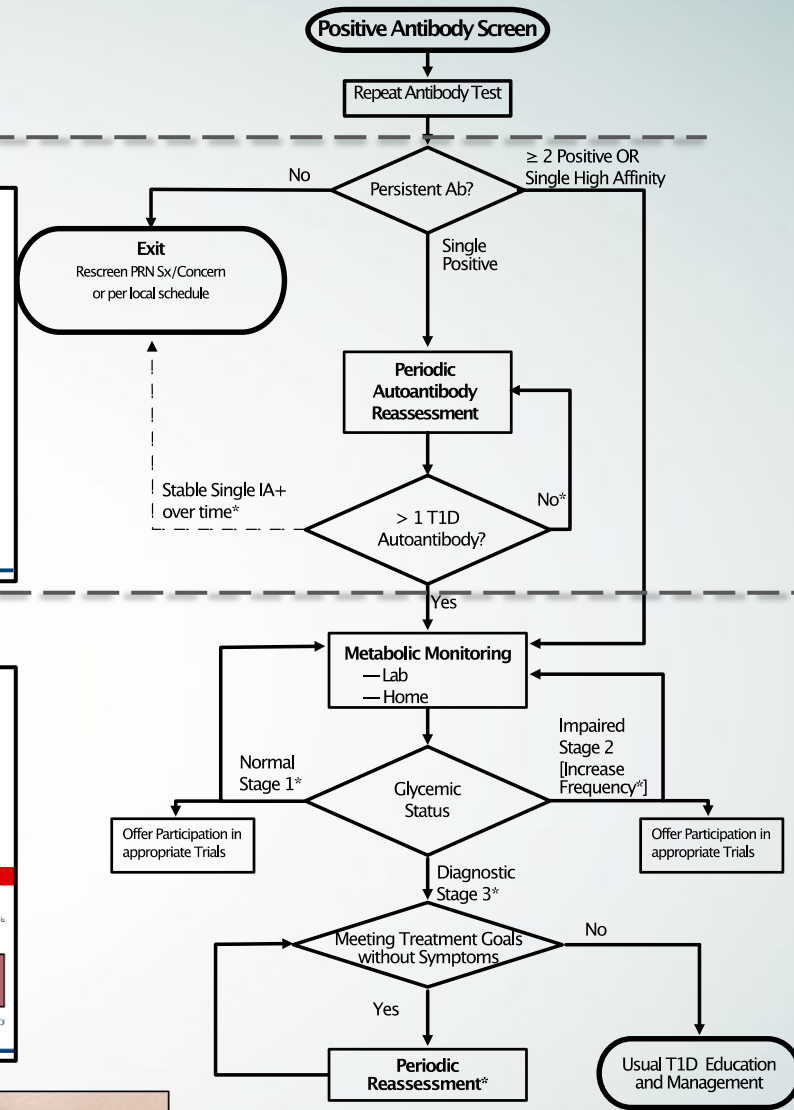
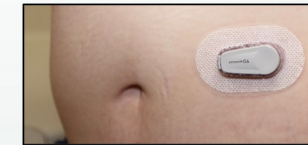
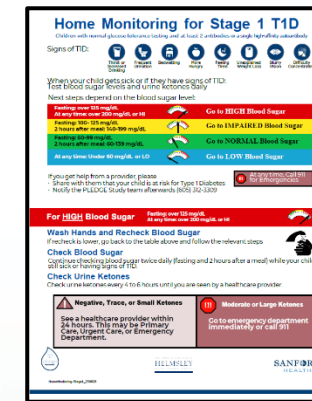
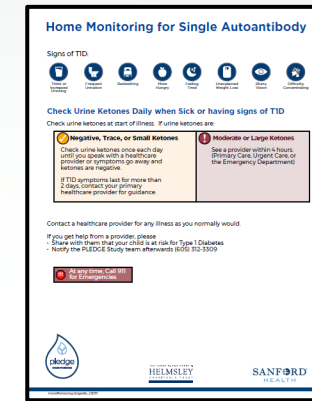
PLEDGE Screening



PLEDGE Screening

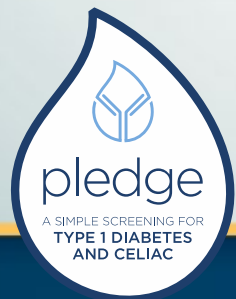
PLEDGE Monitoring

- Separate Protocol and Consent after confirmation of persistent antibody.
- Tailor extent and frequency to expected risk (Home and clinic)
- Results & Result Notes copied to Primary Care Provider
- Consensus guidance published 24 June 2024
 - *Diabetes Care* 2024;47(8):1–23 | <https://doi.org/10.2337/dci24-0042>
 - *Diabetologia* <https://doi.org/10.1007/s00125-024-06205-5>



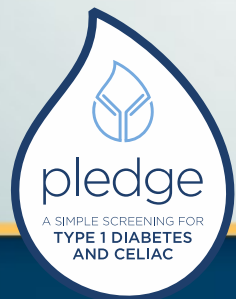
Enrollment

7 % over 95th percentile in UK Biobank
12 % over 90th percentile in UK Biobank
23 % over 80th percentile in UK Biobank

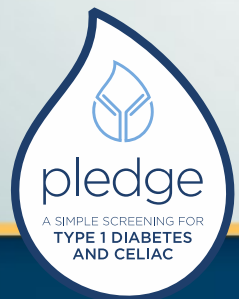


Celiac Disease Screening and Confirmation

Feedback from families and
GI providers has been very positive



T1D Screening and Confirmation

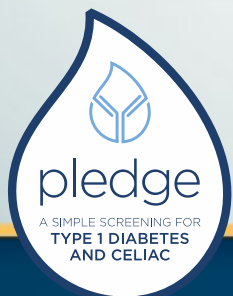


Monitoring those with T1D Antibodies

X = off study

Current Status of PLEDGE Participants in Monitoring (N=63)

Negative Ab	7 <i>(one now off study after 3 y)</i>
Single Low-Affinity Ab	10
Single Hi-Affinity Ab with Normal OGTT	16
Early Stage T1D:	
Staging Pending	1
Stage 1	18
Stage 2 (3 single high affinity)	7
Transition to Clinical Care: (Off study)	
Stage 2* (<i>off-study</i>)	1
Stage 3 (<i>off-study</i>)	3



Presentations at Transition to Clinical Care

	Age	Time from positive screen	Time since last study visit	Most Recent Stage	Symptoms	Stage 3 Diagnosis Criteria	A1C	Fasting Glucose	2-hr OGTT Glucose	Insulin Initiation
A	3 y	1.2 y	< 3 months	Stage 2	None	Clinical provider based on home testing	5.7	Not Assessed	Not Assessed	At diagnosis
B*	5 y	2.3 y	3-6 months	Stage 2	None	Outside Study Labs • A1C • 2-hour glucose	6.6	101	346	Within 3-6 months of diagnosis
C	14 y	NA	Initial Visit	NA	Fatigue	PLEDGE Monitoring Study Labs • 2-hour glucose	5.4	90	252	Within 3-6 months of diagnosis
D	4 y	0.7 y	6-12 months	Stage 1	Increased urination	PLEDGE Monitoring Study Labs • 2-hour glucose	5.7	89	286	Within 1-3 months of diagnosis
E*	3 y	NA	Initial Visit	NA	None	PLEDGE Monitoring Study Labs • 2-hour glucose	4.9	90	168	N/A

None had DKA or required inpatient admission.



Looking to the Future

How can we transition screening from research to clinical care?

Demonstrate clinical impact

Measure economic costs and benefits

Sanford leadership looking at how to make this transition in within that health system

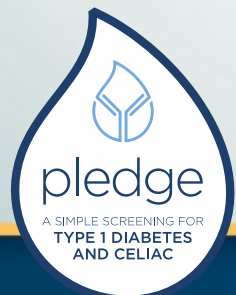
Eventual adoption will require incorporation into standards of care, e.g.:

- ADA & ISPAD
- AAP Bright Futures
- USPSTF

Programa DeteKtA: Detectando diabetes tipo 1 y previniendo Ketoacidosis Diabética (DKA)

Sanford World Clinics & Hospital Metropolitano,
San José, Costa Rica

Launching February 2025



Thank you

All the families who participate

The Sanford Project Team

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Lana Baerenwald
Connie Hoffman

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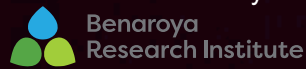
**Providers and staff across
all Sanford clinics and Labs**

**Benaroya Research Institute
Center for Interventional Immunology**



We are looking for Outstanding immunologists using experimental or computational approaches to study immune-mediated diseases

More information at www.benaroyaresearch.org/careers



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