T1D Exchange

Data Governance Committee Meeting

April 15, 2024

Data Governance Committee Meeting Agenda

1. Welcome
2. Data Governance Committee charter updates and co-chair update
3. Sponsored project preliminary results – total daily insulin analysis
4. Sponsored project update – T1D screening and monitoring QI and implementation
5. T2DX-QI industry partnership discussion

Data Governance Committee

Purpose of the T1DX-QI/T2DX-QI Data Governance Committee

Expand research and QI focus through academic and industry support for projects and support collaborative viability by:

- Reviewing new EMR data-based industry/sponsored project proposals
- Monitoring ongoing sponsored projects
- Brainstorming/proposing new industry partnerships with T1DX-QI/T2DX-QI

DGC Charter Update – Summary of Changes

- Updated DGC Purpose (prior slide)

- Update roles and responsibilities (Table 1) and description of co-chair nomination process

Committee Co-Chairs	Committee Members	T1DX Members
• Contribute to the long-term vision of Committee goals and deliverables • Facilitate conversations with Committee members on data proposals, ongoing project updates, and exploring potential partnership opportunities • Develop meeting agendas	• Attend quarterly meetings • Create and refine procedure for data sharing • Provide feedback on data use requests and current projects • Approve relevant data use requests • Review IRB and data use protocols • Support the research and QI focus of the collaborative by promoting opportunities for potential sponsored partnerships	• Support with meeting scheduling, logistics, minutes, and recordings • Maintain the Data Governance Committee website with up-to-date information and documentation

- Addition of DGC Data Review Process
  - Existed previously but not included in the Charter.

- Removal of Committee member names
  - To support Charter longevity as members/terms change.

Total Daily Insulin preliminary results

Saketh Rompicherla

T1D Exchange

Cell therapies and treatment for T1D

Vertex working on investigational approach is to replace the insulin-producing cells that have been destroyed in people with T1D with healthy beta cells created from stem cells

One approach, known as VX-880, involves delivery of the insulin-producing cells via infusion into the hepatic (liver) portal vein, and requires ongoing immunosuppression to ensure immune cells don't attack transplanted cells.

The second approach, known as VX-264, encapsulates these same cells in a device to be surgically implanted in the body. These devices are designed to shield the cells from the body's immune system.

Daily Insulin Dose in Children and Adolescents With Type 1 Diabetes

Study aim was to estimate total daily insulin dose in children and adolescents with T1D

Total daily insulin dose (TDD) to manage type 1 diabetes (T1D) is expected to change with age, puberty, and growth, but there is limited current literature with respect to those variables, especially among those using advanced technologies for the treatment and management of T1D (i.e., continuous glucose monitoring (CGM) and insulin pumps, including automated insulin delivery systems [AIDS]).

TDD was assessed in U/kg and U at each age from 2 to 25 years. Median TDD was reported for the overall sample and stratified by sex, BMI category, and insulin delivery method (multiple daily injections [MDI], pump excluding AIDS and AIDS alone.

Feasibility study

- Background
- Clinical
- T1D
- Insulin dose

Full scale study

- Insulin dose tables by various categories
- Boxplots in insulin dose in IU and IU/kg

Additional analysis

- Sensitivity analysis
- Inulin dose by BMI value categories

T1D Exchange

Methods

TDD was assessed at each age from 2 to 25 years where an individual could contribute data from multiple ages to this analysis if available (e.g., TDD at age 5, age 6, etc.). A total of 46,451 units of analysis for TDD were included in the analysis from 14,358 individuals. Basal and bolus daily dose was also assessed at each age as well.

Inclusion Criteria

Confirmed diagnosis of T1D.

Age between 2 and 25 years at most recent encounter.

Record of total daily insulin received at least once between 2 and 25 years of age.

Duration of T1D for at least 2 years.

Exclusion Criteria

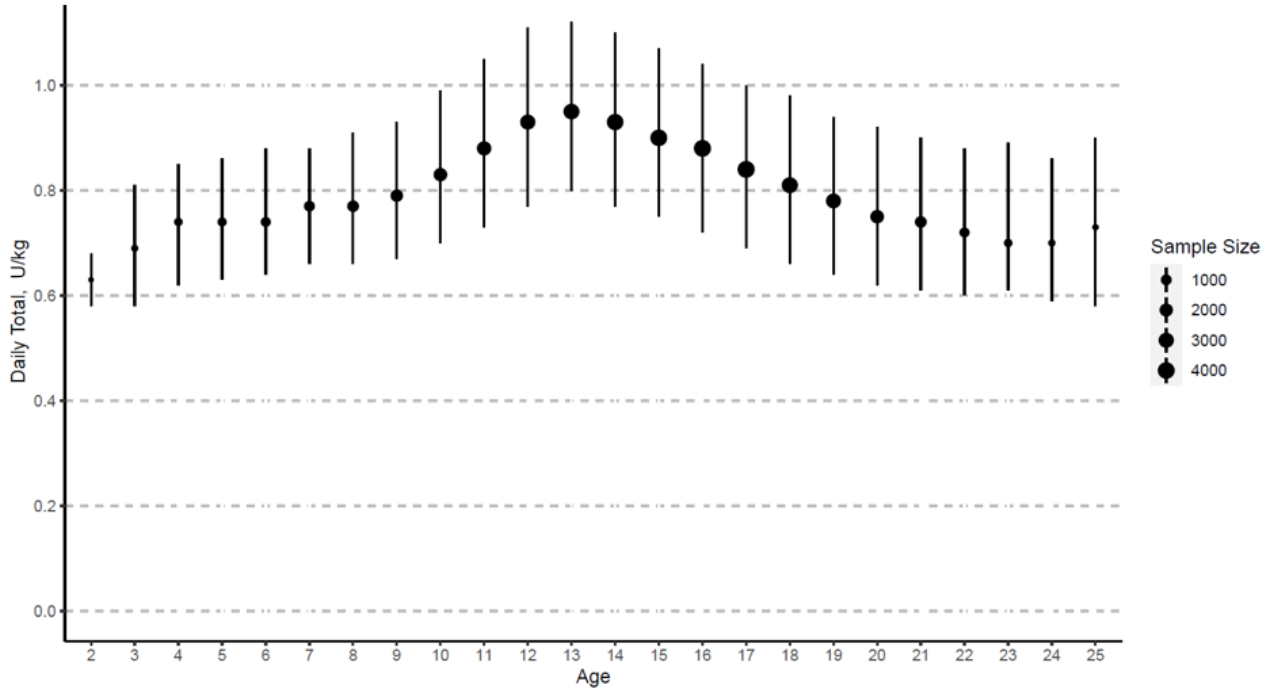
Pregnancy (exclude year of pregnancy, year before, and year after).

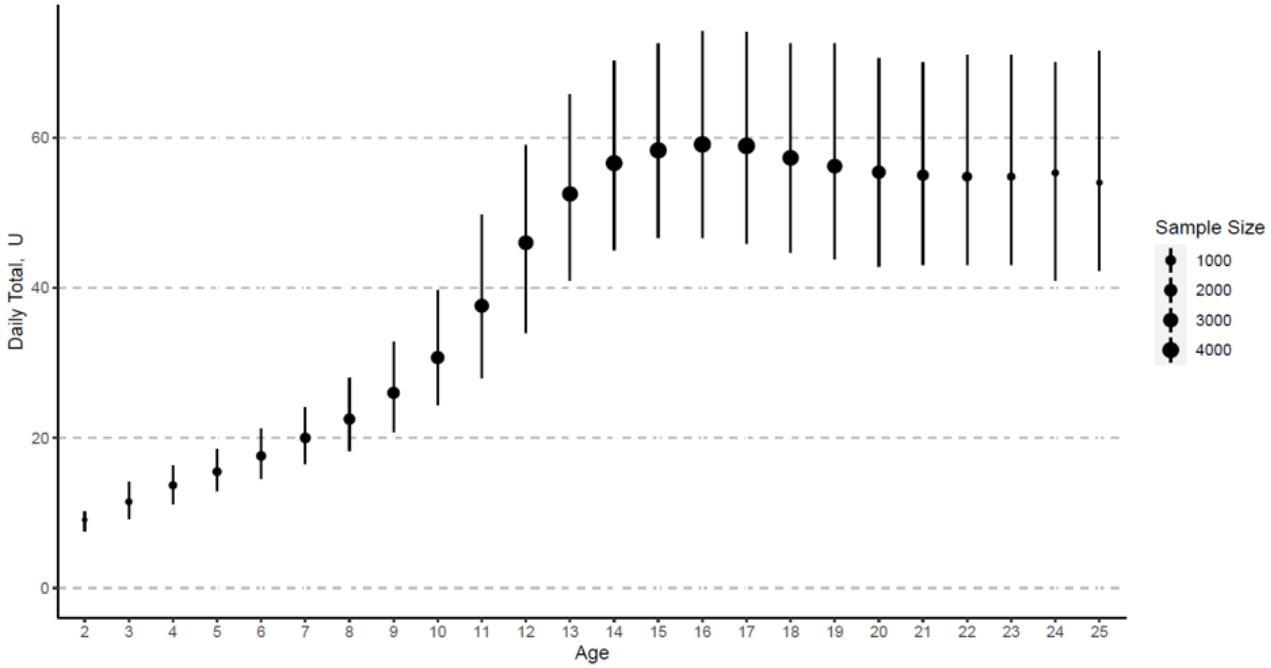
Antihyperglycemic medication use other than insulin (exclude year of use).

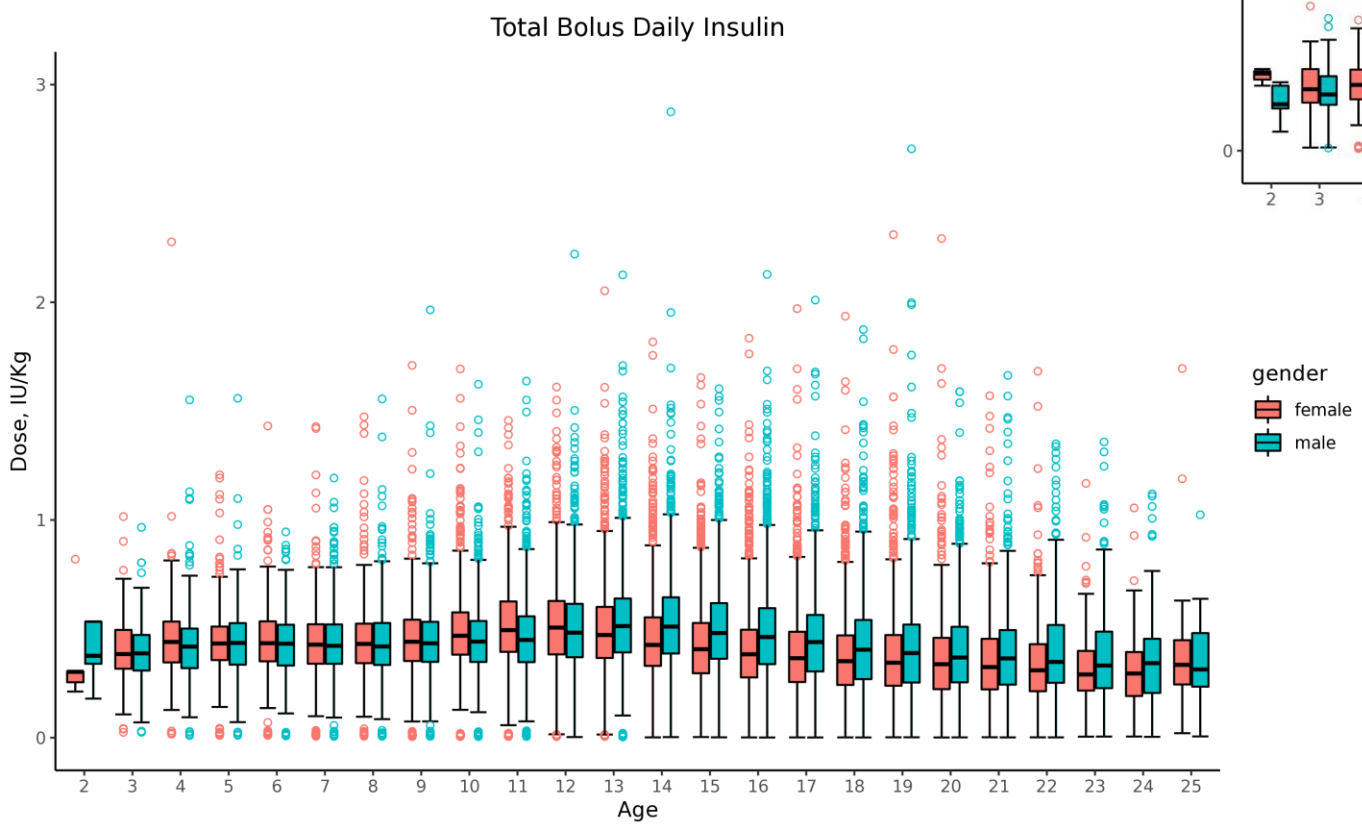
Use of calcium channel blockers.

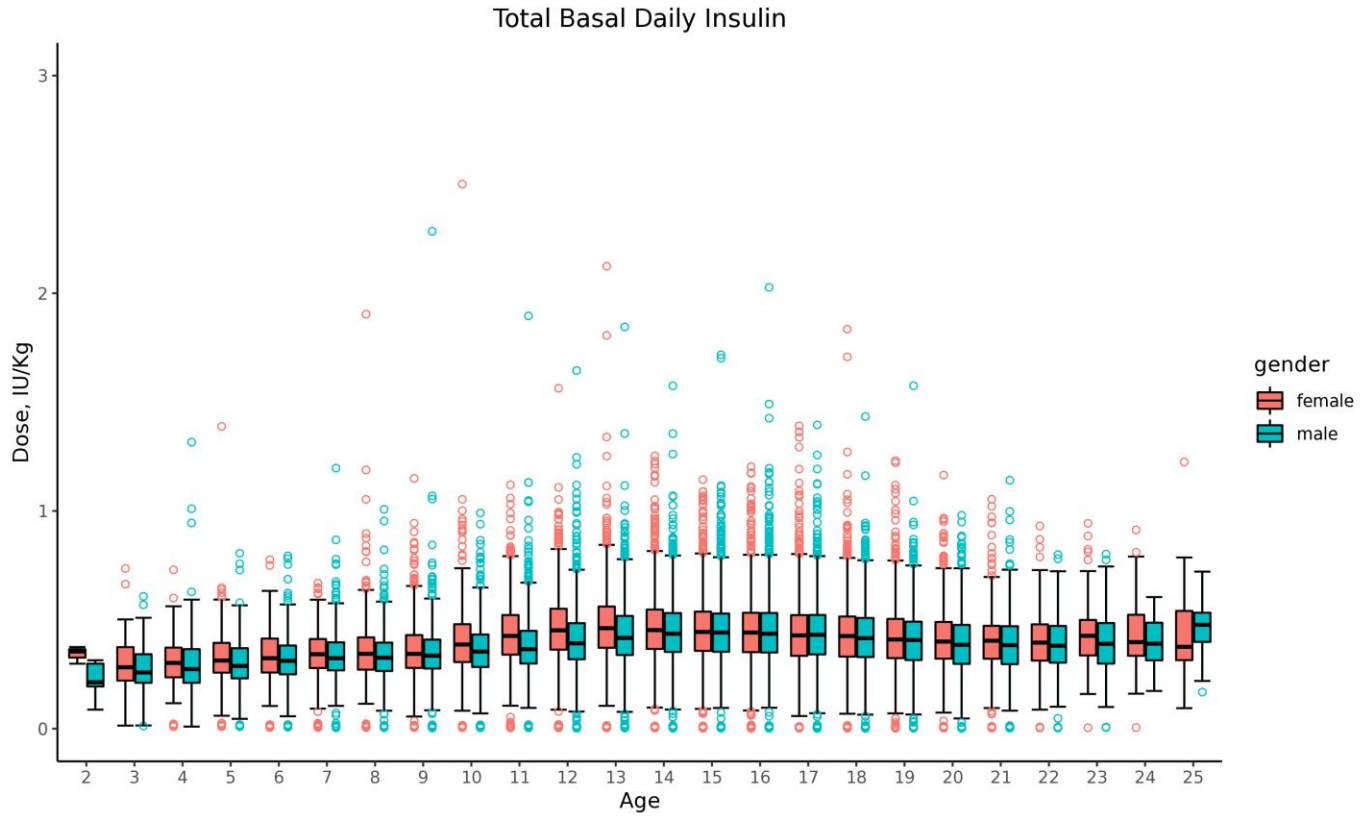
Results

- A total of 14,358 individuals were included (mean [SD] age: 16.2 [4.3] years; 48.0% female; 74.6% white; 58.3% private insurance).
- Study population had a Mean (SD) T1D duration of 7.8 (4.2) years, duration of follow-up of 4.9 (2.7) years and with 3.6 (2.9) endo visits per year
- Mean (SD) HbA1c (%) was 8.4 (2.0), majority used an insulin pump (69.5%), and even more used CGM (79.7%) and Mean (SD) time in range was 48.6% (20.3).
- TDD increased from age 2 (median 0.63 U/kg) to 13 (0.95 U/kg), and, when unadjusted by weight, similarly increased from age 2 (median 9.1 U) to 16 (59.1 U).
- Following these peaks, median TDD stabilized at around 0.70 U/kg and 55.0 U. For females, the peak TDD was at age 12 (0.98 U/kg) compared to age 14 (0.96 U/kg) for males.
- Higher TDD was observed among those with higher BMI; for example, at age 12, median TDD was 0.99, 0.98, 0.91, and 0.82 U/kg for obese, overweight, healthy weight, and underweight BMI, respectively.

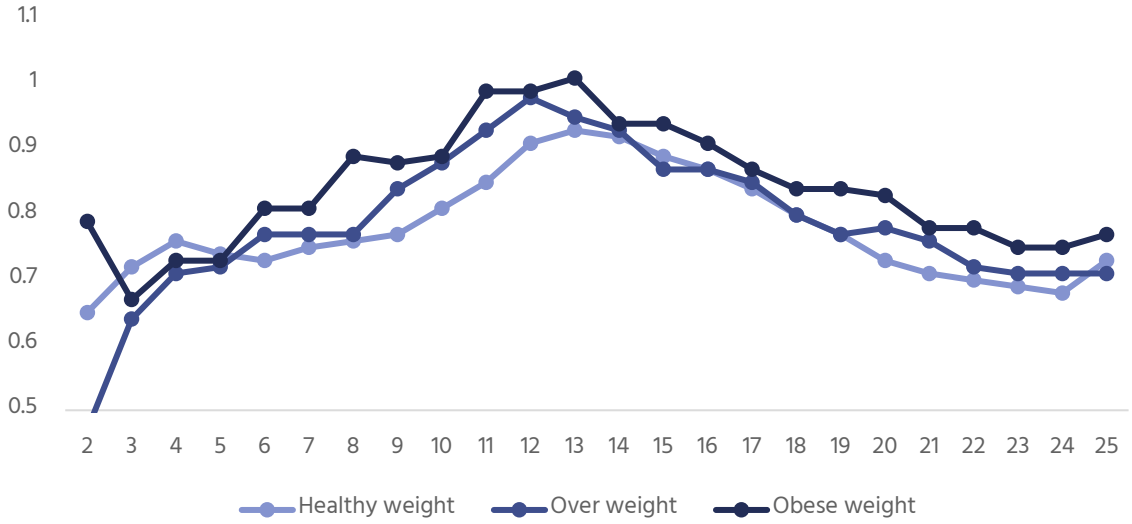

Daily Total, U/kg
1.0
0.8
0.6
0.4
0.2
0.0
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Age
Sample Size
1000
2000
3000
4000


Daily Total, U
60
40
20
0
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Age
Sample Size
1000
2000
3000
4000

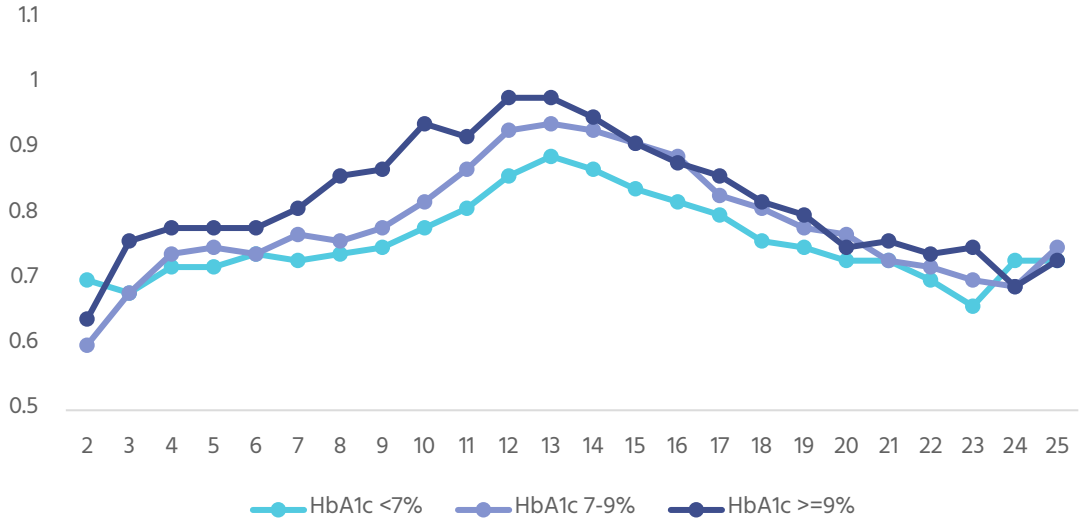

Total Bolus Daily Insulin
Dose, IU/Kg
Age
gender
female
male


Total Basal Daily Insulin
Dose, IU/Kg
Age
gender
female
male

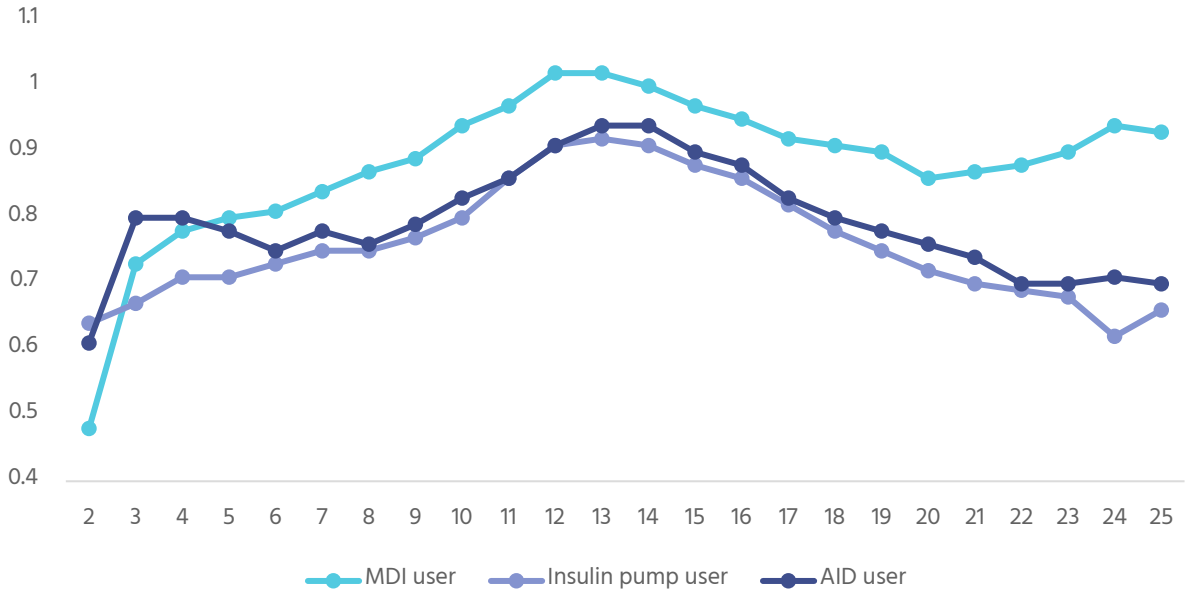
TDD by BMI catagories



TDD by HbA1c catagories



TDD by Device user



T1D Exchange

Conclusion

- TDD increased by age and reached a peak that coincided with expected pubertal timing, earlier for females vs. males.
- MDI users had higher TDD than pump users, which may reflect the impact of technology on dose.
- Only 16% of the study population meet glycemic goal of <7% and saw higher TDD among those with higher HbA1c; for e.g., at age 12 TDD was 0.86, 0.93 and 0.98 U/Kg for group with HbA1c <7%, HbA1c 7-9% and HbA1c>=9%.
- On average this study population did not meet HbA1c goals (<7%) or time in range goals (>70%), demonstrating potential for improvement in glycemic control, and subsequently potential impact on TDD.

T1D Screening and Monitoring project update

Ann Mungmode

Key findings

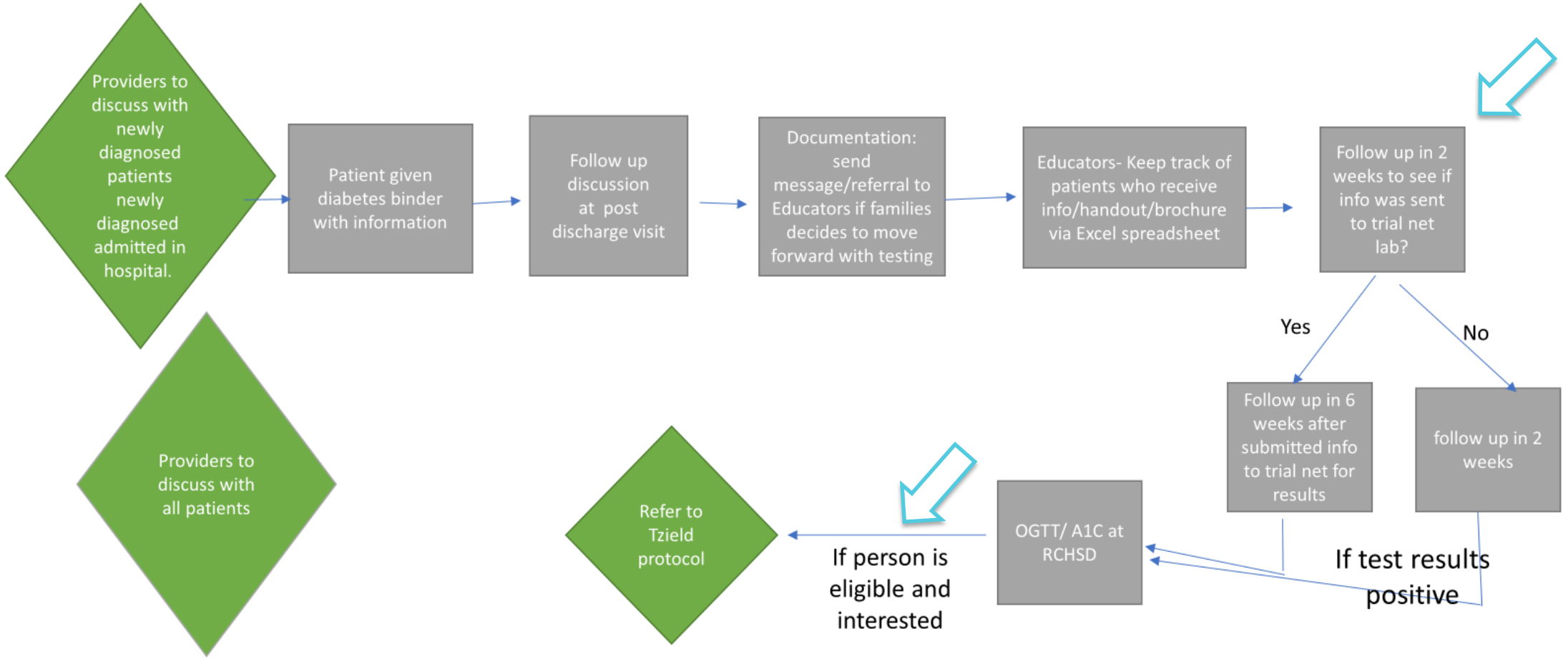
- Using a QI approach allows the teams to start on a small scale (i.e., one provider doing screenings, engaging 3-4 siblings of a child with T1D) to test a process before implementing widely

- Examination of the current process and barriers have clearly identified opportunities for improved efficiency
  - Communication of screening results
  - Follow-up monitoring across comprehensive teams

- Bigger picture questions to explore
  - Insurance coverage/billing
  - Ensuring equity (i.e., for patients who cannot afford Tzield, etc.)

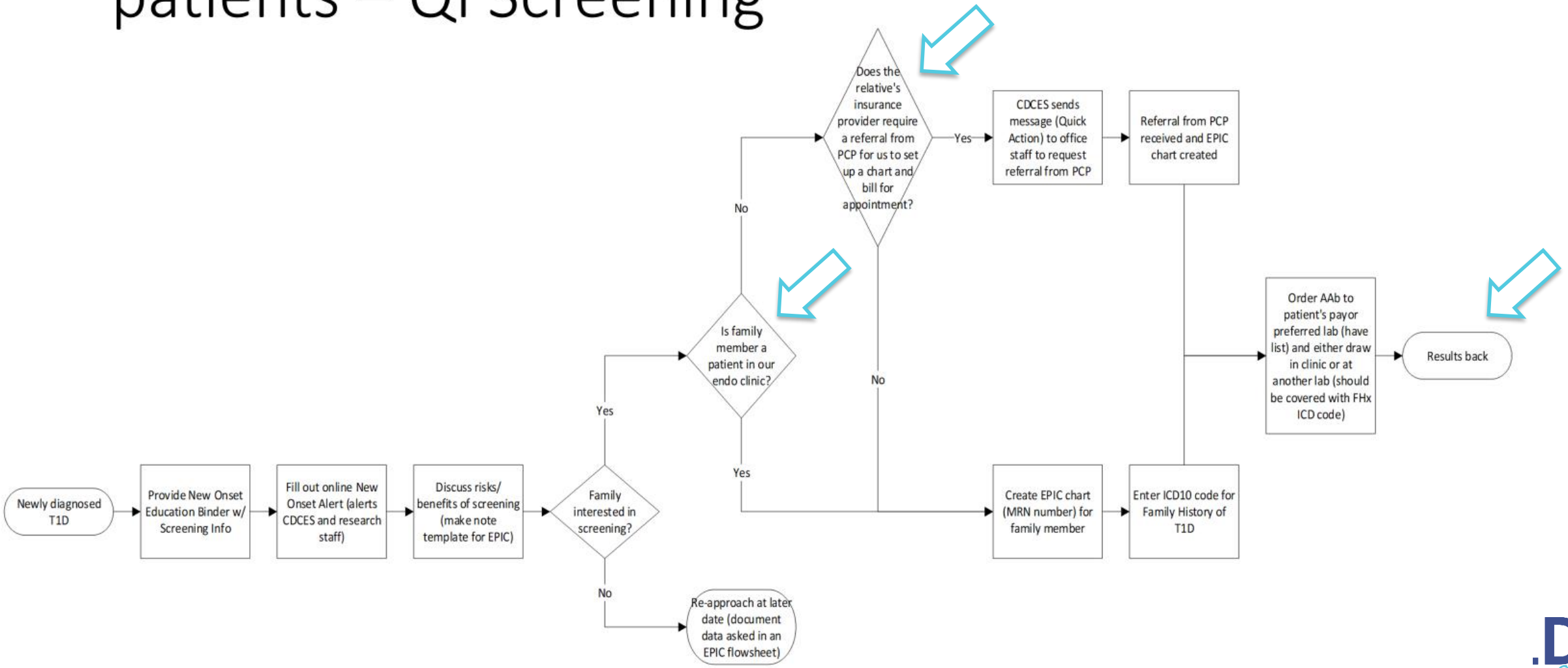
Map the existing process

RCHSD PROCESS MAP
T1D Screening and Monitoring QI and Qualitative Study

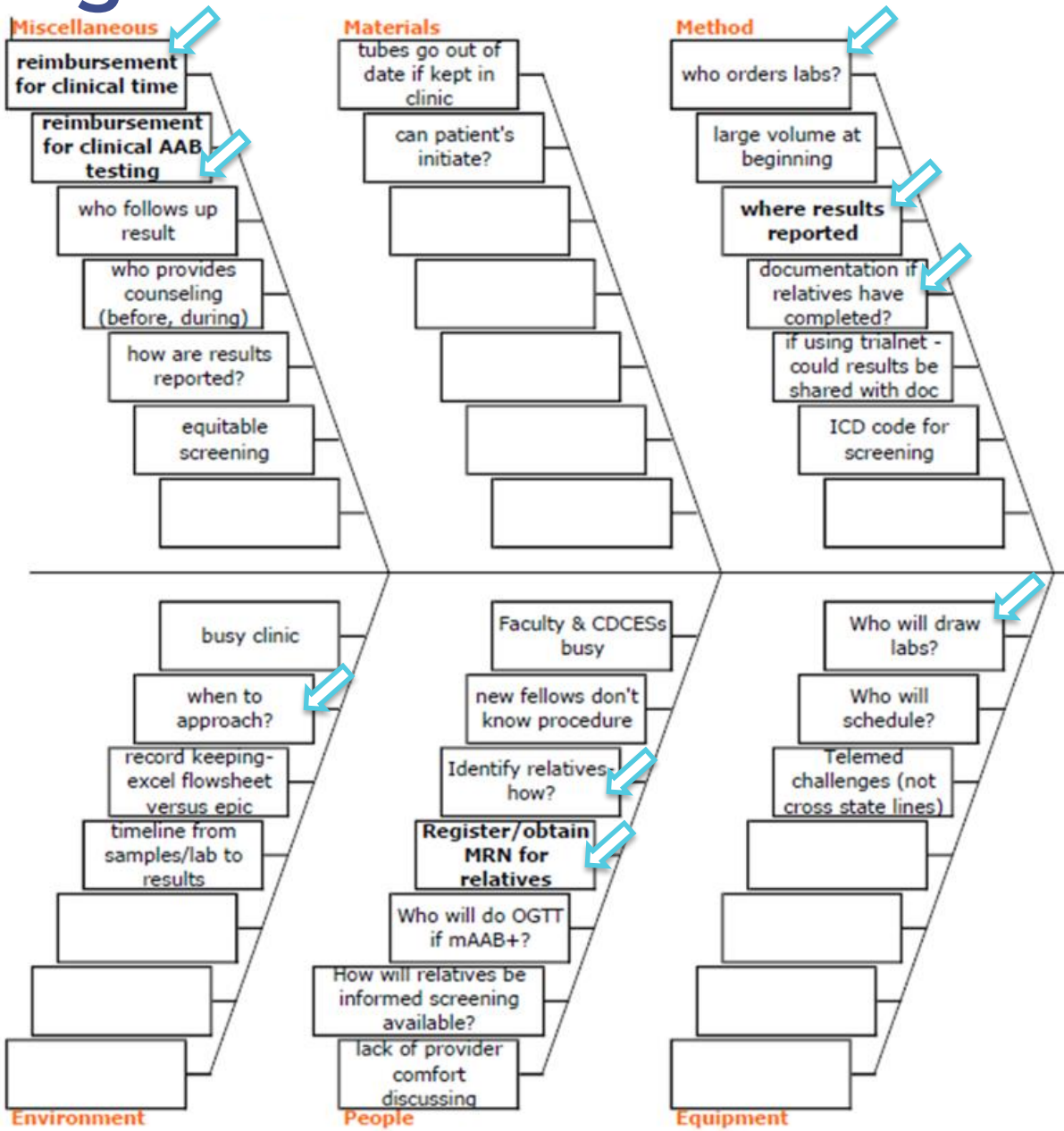


Map the existing process

University of Florida Relatives of T1D clinic patients – QI Screening



Examining root causes



Fixes:
e-Consent with QR code for research
who could get blood draw (consent) relatives in hospital since relatives often there?
screening- role for a clinic manager and CDCES? Slack?
online alert system ASK kits for non-relatives or TN kits for relatives if no chart available or concern for insurance not covering
ICD code for monitoring in process

Problem Statement

Lack of process/workflow for screening and monitor for T1D risk (clinically and via research)

Population:

Relatives with T1D

Later other endocrine patients

Even later gen pop/primary care patients

Project data collection

Piloting changes and tracking results

Parallel processes for meaningful data tracking

Qualtrics survey data collection

Allows for a nimble, reasonable data collection process while 2 JDRF centers are piloting small changes (2-5 patients per month)

Lessons learned in data tracking with strengthen T1DX-QI EMR reporting

T1DX-EMR Database and Smartsheet reporting

Formalizing data specification variables with T1DX-QI Data Science Committee

Piloting data collection in 2 JDRF project centers and beyond

Qualtrics Survey – Patient-level data collection

Center:

Name of person completing report:

Please answer the following questions for a positively screened individual with T1D Autoantibodies:

- Age of individual screened (years)
- Race of individual (dropdown selection: AI/AN, Asian, Black, NH/PI, Other, White, Unknown)
- Ethnicity of individual (dropdown selection: Hispanic, non-Hispanic, Unknown)
- Insurance type of individual (drop down selection: none/self-pay, private, Medicaid, Military, Medicare, Other, Unknown)
- Date of the test (mm/dd/yyyy)
- Are confirmed test results available? Y/N

Qualtrics Survey (continued)

Please answer the following questions for a positively screened individual with T1D Autoantibodies (continued):

- How many confirmed positive AA does the individual have? (single, multiple)
- If multiple AA are confirmed, what stage does the individual present with?
  - Stage 1 (normal blood glucose)
  - Stage 2 (abnormal glucose tolerance or HbA1c 5.7%-6.4%
  - Stage 3 (blood glucose above ADA diagnostic threshold or HbA1c >= 6.5%)
- Which AA is present?
  - GAD65
  - Anti-IA2
  - Tyrosine Phosphatases IA2 and IA-2B
  - ZnT8
  - ICA
  - Other (please list)

Qualtrics Survey (continued)

Please answer the following questions for a positively screened individual with T1D Autoantibodies (continued):

- Does this individual have a scheduled follow up with endocrinology in the next year/3 months? (depending on stage presented; Y/N)
- What is this individuals HbA1c?
- Has the individual had a documented DKA event in the last 12 months?
- Was the individual offered any of the following interventions? (select all that apply)
    - Teplizumab prescription
    - Monitoring
    - Research Trials

Aggregate measure collection - Smartsheet

Screening
A) Number of individuals seen in reporting month who have been screened for T1D antibodies
Autoantibody Screening
1) Number of individuals in [A] that have been screened and confirmed positive for antibodies (GAD65, Anti-IA2, Tyrosine Phosphatases IA2 and IA-2B, ZnT8)
1a) Number of individuals in [A] that have been confirmed positive for multiple autoantibodies
1b) Number of individuals in [A] that have been confirmed positive for multiple autoantibodies

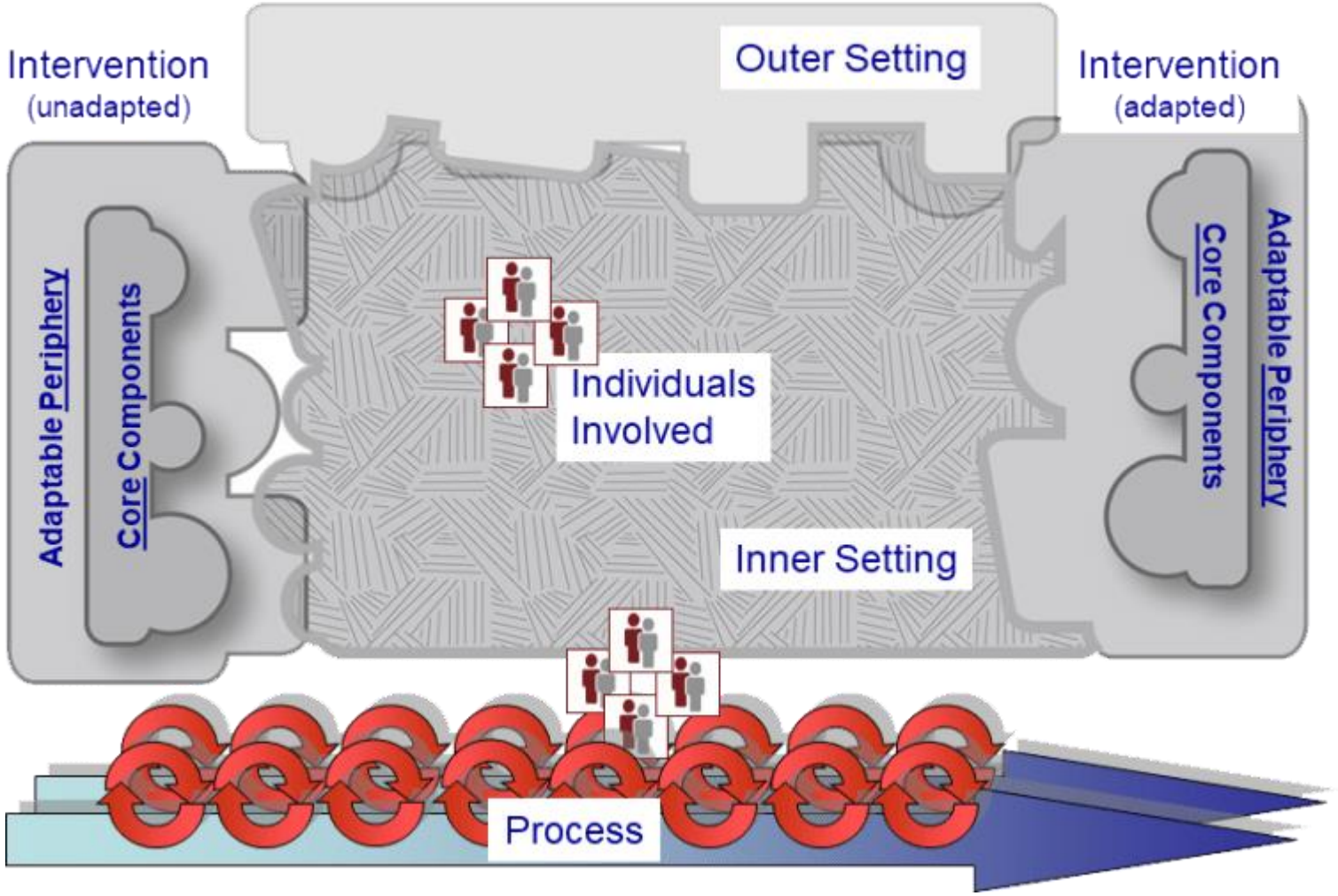
Smartsheet measures prepared (continued)

Stage 1
2) Number of individuals in [A] who have multiple islet autoantibodies, normal blood glucose
Stage 2 Diagnosis
3) Number of individuals in [A] who have multiple islet autoantibodies, abnormal glucose tolerance OR HbA1c 5.7%-6.4%
Stage 3 Diagnosis
4) Number of individuals in [A] who have blood glucose levels above ADA diagnostic thresholds OR HbA1c >= 6.5%

Smartsheet measures prepared (continued)

Monitoring
5) Number of individuals in [2] + [3] with a scheduled endocrinology visit per monitoring guidelines
DKA Events
6) Number of individuals monitored for T1D diagnosis in last 12 months who have a documented DKA event in reporting month
Intervention
7) Number of individuals in [4] offered Teplizumab prescription

CFIR Framework



Focus Groups

- Multiple touchpoints throughout the rest of the project
- Meet with entire care team
- Reviewing each of the main constructs from the framework during focus groups
  - Intervention characteristics
  - Outer Setting
  - Inner Setting
  - Characteristics of individuals
  - Process of implementation

Sanofi Expansion

Separate contracts and payments

Lessons learned will cross both projects to expand the impact

Centers identified to date:

- Texas Children's Hospital
- Children's National Hospital
- Indiana University
- Lurie Children's Hospital

Selecting centers on readiness in screening, monitoring, and data collection

	Number of newly diagnosed patients seen per year	Does your center currently screen and individuals at risk for developing T1D?	Does your center have a monitoring program for individuals that screen positive for T1D autoantibodies?	Does your center currently collect EMR data on screening and monitoring?	Is your center able to report EMR data on DKA Events and Autoantibody Screening?
Texas Children's Hospital	~500	Yes	Yes	Yes	Yes
Children's National Hospital	152-183	Yes	Yes	No	Yes
Indiana University	~150-200	Yes	Yes	Yes	Yes
Lurie Childrens	~150-200	Yes	No	Yes	Yes

T1D Exchange

T2DX-QI industry partners/sponsor brainstorming

Key T2DX-QI data elements

- Patient demographics (race, ethnicity, age, gender, language, insurance)
- Device use (CGM, insulin therapies)
- Medications (GLP-1, SGLT-2, etc.)
- BMI
- Comorbidities

Existing project: Type 2 Diabetes QI expansion

Sponsor: Abbott

Objectives:

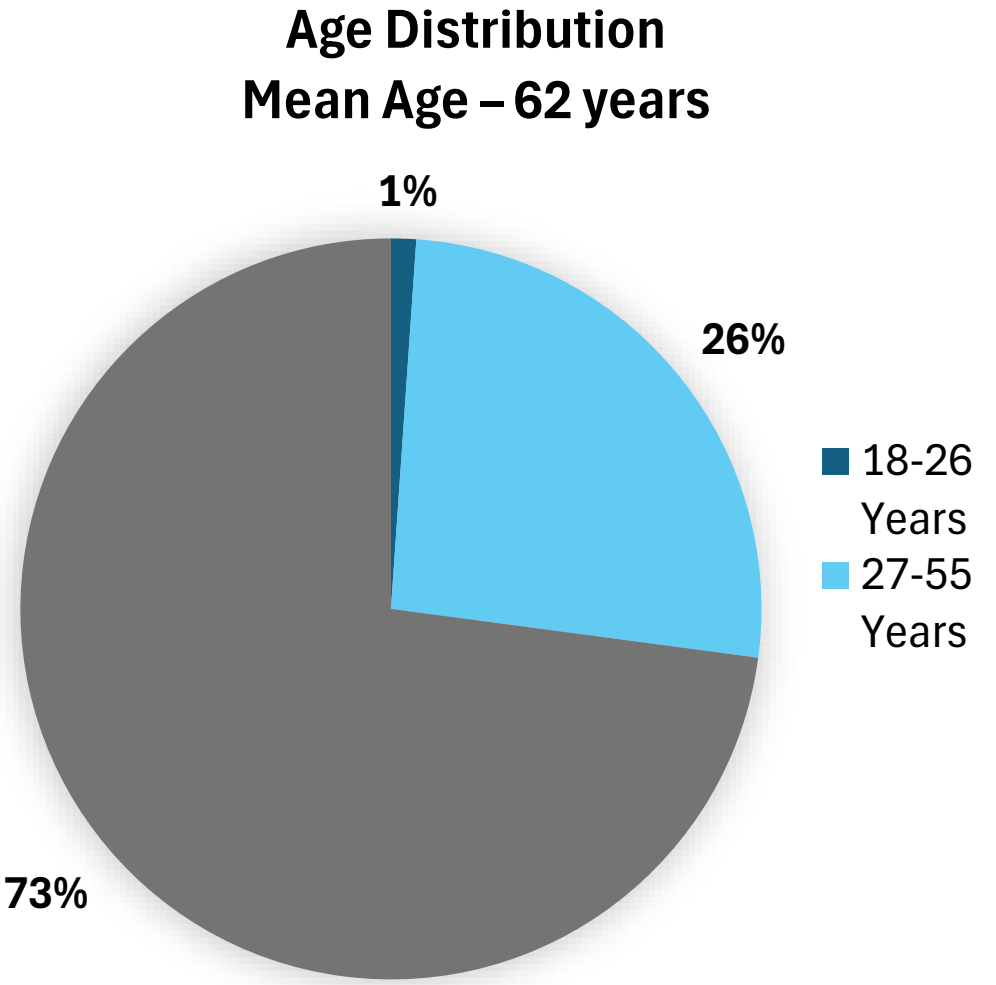
1. Establish a **large dataset for T2D patients**;
2. **Evaluate this T2D dataset for benchmarking and metrics** for the purposes of supporting quality improvement activities;
3. **Establish an independent data platform** to share and disseminate patient-level data for the T2D patient population

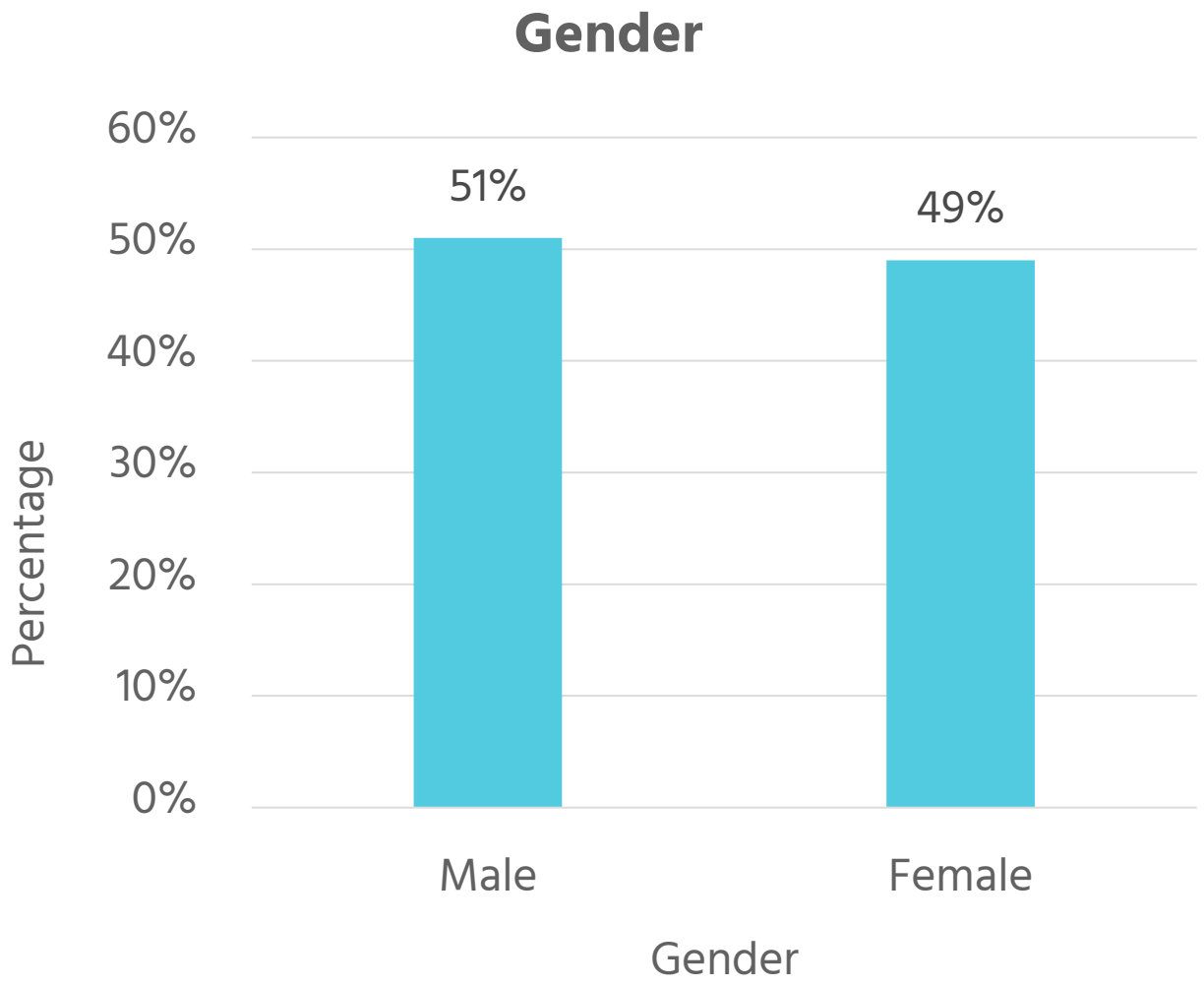
Participating Centers: BMC, Grady, UPMC; **3 total adult centers**

Project Status/Results: ✓On Track; all centers engaged in PDSA activities and initial T2D analyses initiated

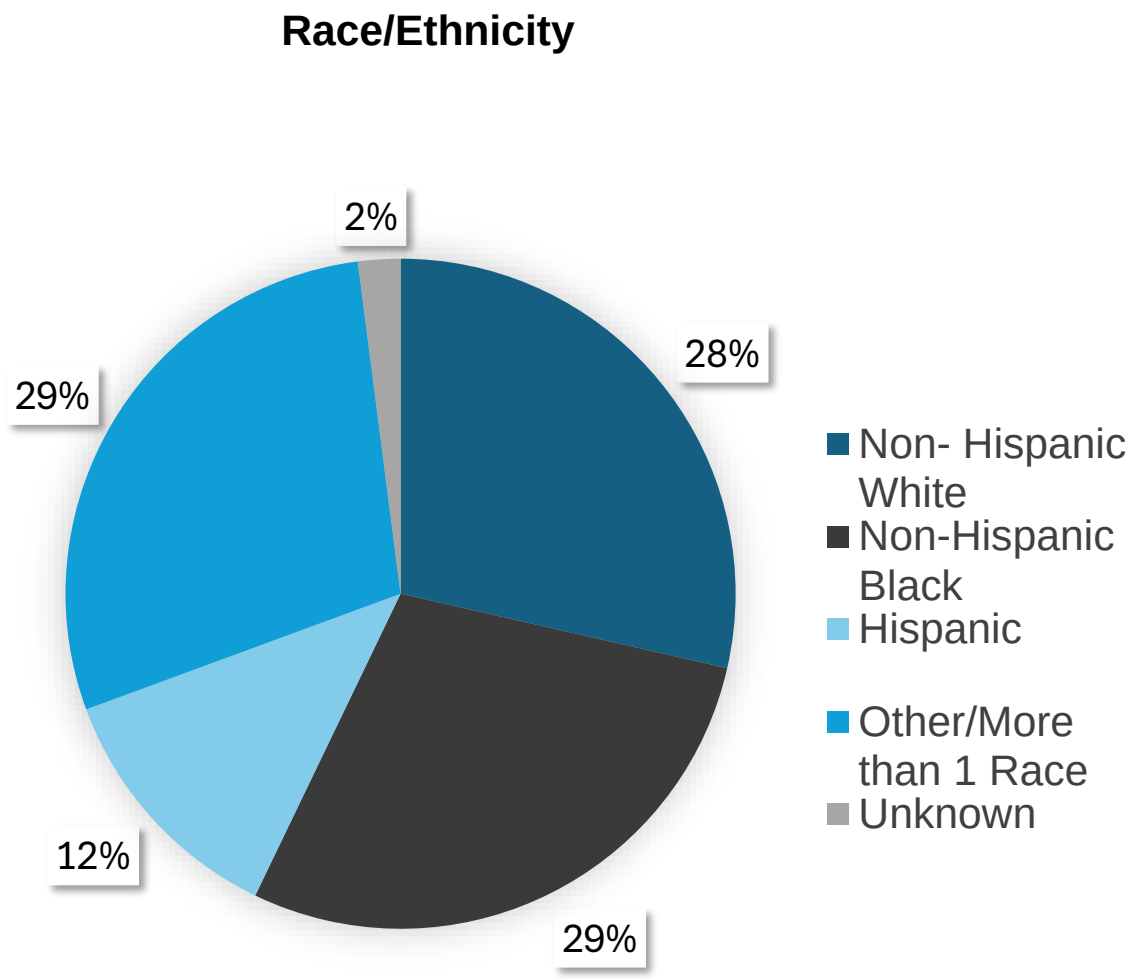
T1D Exchange

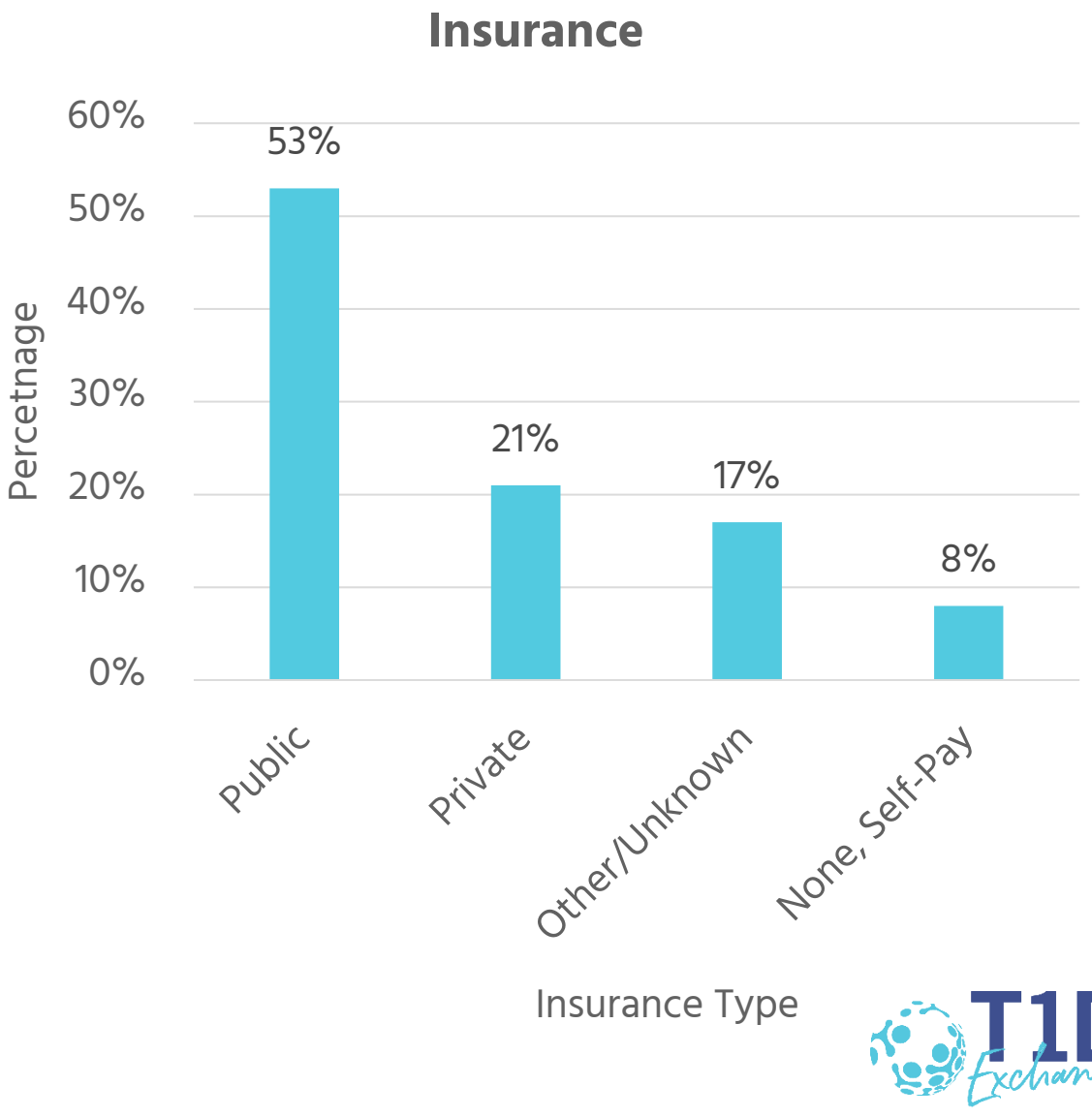
Age and Gender (Total EMR Mapped T2D N= 38,949)





Race/Ethnicity and Insurance (N= 38,949)





Novo Nordisk proposal Background

- The 2023 ADA Standards of Care recommends consideration of a GLP-1 RA and/or SGLT2 for individuals with type 2 diabetes given the improvements in cardiovascular and renal outcomes as well as weight loss and glucose, with GLP-1 RA given preference over initiating insulin in adults with T2D when possible.

- Despite limited research of non-insulin medications in T1D, use of GLP-1 RA off label is becoming increasingly popular, less so for SGLT2 use.

- Currently JDRF is funding two US-based trials assessing GLP-1 RA and/or SGLT2 in T1D with results expected in late 2024/2025

- Multi-center clinical trial evaluating once weekly semaglutide injection in overweight adults with type 1 diabetes (T1D), who are using FDA-approved hybrid closed-loop therapies but remain inadequately controlled (NCT05537233).

- Single center trial assessing whether the addition of dapagliflozin to semaglutide and insulin (triple therapy) improves glycemic control in patients with type 1 diabetes compared with semaglutide and insulin (dual therapy) and insulin only (standard) treatment (NCT03899402).

Study Aims

- To evaluate SGLT2 and GLP-1 RA use and compare characteristics (demographic and clinical) among users and non-users in the T1DX-QI EMR database.
- To evaluate SGLT2 and GLP-1 RA uptake over the past 3 years
- To assess changes in insulin dosing, weight, and glycemic outcomes following initiation of each drug class
- Exploratory assessment to examine outcomes among subgroups of patients including those using non-insulin med drug and automated insulin delivery technology.
  - Glycemic outcomes include HbA1c, DKA, and SH; Subset of pts with CGM summary statistics (~ 4,000)
- To evaluate lab values (cardiovascular and renal function) among those with available data

T1D Exchange

Brainstorm T2D sponsor/industry partners for projects

Potential partners brainstorm