T1D Exchange in Action

Patient-centered research, insights and data

July, 2015 – December, 2016

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"Be proud of your diabetes. **It's part of you** and it makes you who you are"

– Maddie B

T1D Exchange®

Dear Member,

I am proud to deliver **T1D Exchange in Action**, a comprehensive report outlining our findings and accomplishments over the past 18 months.

The past year and half have provided tremendous momentum for T1D Exchange (see key achievements, next page). In addition to these milestones, we've also:

- partnered with The Leona M. and Harry B. Helmsley Charitable Trust and JDRF on a **Health Policy Initiative** to improve health outcomes and access to therapies and technologies

- completed our first **Diabetes Innovation Challenge**, where 6 innovators received cash and in-kind awards to help advance their novel diabetes solutions

- announced a multi-million dollar **automated insulin delivery (AID) investment initiative**, designed to advance the category of AID

Most of all, our momentum is a result of the partnerships we've formed – with you, our members; with other leading non-profits and family foundations; with clinics and clinicians; and most of all, with the community of people touched by type 1 diabetes.

Today, we directly engage 50,000 people affected by T1D in research; through our Clinic Network we more broadly reach another 100,000 people and our social sphere of influence exponentially expands our circle.

Our goal is to continually grow our "research-ready" cohort of people affected by T1D and amplify their personal experiences to direct how we invest our resources to advance better treatments, devices and solutions they really need and want.

That's a win for the entire T1D eco-system because it:
- leads to more informed studies from the very start
- supports product development by increasing understanding of patient needs and gaps
- accelerates delivery of novel therapies and devices that meet our community's needs, lessen the burden of management and improve outcomes.

Thank you for your continued support.

Sincerely,

Dana A Ball

Dana Ball
Executive Director and Co-Founder, T1D Exchange
CEO, Unitio

IN THE PAST 18 MONTHS, WE HAVE:

Published **18** manuscripts and presented **60** times at scientific conferences

Started/or Implemented **35** member-driven research projects using T1D Exchange resources and services

Enabled **8** new studies with Biobank samples and data

Launched the T1D Quality Improvement initiative in **10** strategic clinical sites to improve T1D care in the clinic

Added **5,000** more research-ready participants on Glu, growing our online research community to ~20,000 overall participants touched by T1D

Patient Centered Program
~20,000 participants on Glu (myglu.org)

T1D EXCHANGE RESOURCES
a single resource
for real-world research

Clinical Program
81 Clinic Sites following
100,000 T1D patients
33,232 enrolled
clinic registry participants

Science Program
Biosamples from 2,276
unique T1D participants

"I think only a fellow type 1 truly gets the complexities, frustrations, and **daily triumphs** of living well with type 1."

– Jessica

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Executive Summary

Since 2010, we have been building an innovative model that puts the community of people touched by type 1 diabetes at the core of research that will meaningfully impact their lives. The last 18 months have been transformative ones for T1D Exchange.

OUR IMPACT

- Our findings have significantly grown the knowledge base about life with type 1 diabetes and at times even challenged conventional schools of thought; resulting in more informed research, more meaningful studies on unmet needs, and improved care.
- Our model offers collaborators across academia and industry access to research participants who have taken part in a variety of clinical studies, including several large-scale intervention studies and clinical studies that have helped accelerate a potentially game-changing treatment of severe hypoglycemia.
- Our participants from the Clinic Registry, our online community Glu and Biobank represent an actively engaged community of people touched by T1D who are ready to share their health experiences to drive research forward and learn practical tips and information that can help them address daily challenges.

Over the past year and a half, we've continued to leverage our model in new ways with the goal of increasing the breadth and depth of impact we can have in the T1D landscape.
Here are some of the highlights of our work.

DEVICE USE AND DEVELOPMENT

We have conducted multiple studies about device use in real-world T1D populations. We seek to get a holistic view of device use in the T1D community so that we can:

- understand who is using both current and potentially available devices and why some people discontinue device use
- inform those developing devices about human factor design needs and other considerations from the user perspective
- seed the way for the new innovations that can enable the next generation of device development (learn about our Diabetes Innovation Challenge (page 34) and about our automated insulin delivery initiative, (page 37)
- understand the barriers to device adoption across clinical and patient audiences (see health policy initiative, page 39)

Additionally, our work in validating outcomes other than A1c will hopefully lead to new regulatory pathways to get devices approved and commercially available. Holistically, our work demonstrates our comprehensive approach to prepare a community of people who are ready to adopt devices, clinicians who will prescribe them, and insurance plans that will make them accessible.

UNIQUE SUBPOPULATIONS

T1D Exchange has produced a great deal of insights around life with T1D, including insights about vulnerable populations. In the past 18 months we've conducted important studies in unique populations of people with type 1 diabetes including T1D in African American populations, older populations, people living with T1D and other autoimmune disease(s) and children under six years old (see Racial Differences spotlight, page 15). We've also participated in international studies to understand how the the Clinic Registry participants compare and contrast with T1D populations in other countries.

NEW CAPABILITIES

While T1D Exchange is a relatively young non-profit organization, we are continually seeking to build new capabilities that will help us amplify our impact. Our Quality Improvement initiative (page 39) is a significant preliminary step towards trying to improve clinical care for people with T1D. We are currently building an innovative technology infrastructure that will enable improving care and outcomes as well as support open access to data that may help researchers all over the world better study T1D.

In our online community Glu, we've expanded our capabilities to power more robust real-world research studies. In 2016, we launched two different studies that asked participants to not only answer multiple questionnaires, but also upload corresponding data from activity trackers and diabetes devices. A study design of this type allows us to correlate perceptions with biological events to generate a robust understanding of a participant's experiences.

In an effort to marry qualitative and quantitative data, we have implemented a multiphase approach to our research study designs. By using a combination of online and in person focus groups with survey data, we are able to create an informative data set that takes advantage of the richness of personal interactions with the robustness and diversity of study data.

2016 represents the first time that T1D Exchange performed research studies across both the Clinic Registry and Glu populations at the same time. This offers us the ability to reach a wider, more diverse total cohort (see DKA page 26).

Additionally, in the past 18 months, T1D Exchange has developed new initiatives that provide education back to the type 1 community on topics they care deeply about. These infographics and articles give the community access to the findings of recent research and actionable items to help improve their daily lives.

Project CGM is a four-part series that tackles challenges such as eating pizza, drinking alcohol and getting good sleep in type 1 diabetes. These popular educational pieces have been shared on Glu and in social media, and have been disseminated in printed form to patients in endocrinology clinics, camps and events for people with T1D across the country.

In 2017, Glu seeks to expand on the learning series into areas such as Project CGM to tackle more challenges and bring more education to the patient community. We welcome the opportunity to work with our member constituents to develop these educational pieces. For more information,
contact Liz Bevilacqua (ebevilacqua@t1dexchange.org).

"Every needle has its **own story.** What you ate, where you were, all the situations and the feelings."

– Andres

WHAT'S NEXT

Despite today's medicines, technologies, and standards of care—type 1 diabetes remains a signficant quality of life and financial burden. At T1D Exchange, we remain committed to expanding and developing initiatives aimed at improving outcomes for this community.

We recognize this community needs better solutions faster. How can we deliver?

- We work better when we keep the community of people touched by type 1 diabetes at the center of research to ensure that it remains focused on those solutions and outcomes that will meaningfully impact their lives.
- We work faster when the entire eco-system (non-profits, industry, advocacy, academia, and the community) collaborate together to accelerate treatments and care.

At T1D Exchange, we won't stop until living with type 1 diabetes is worry-free – where the daily management burden has been relieved, quality care will be accessible and good outcomes can be readily achieved for all. We invite you to be a key partner on the journey with us.

Clinic Network and Registry
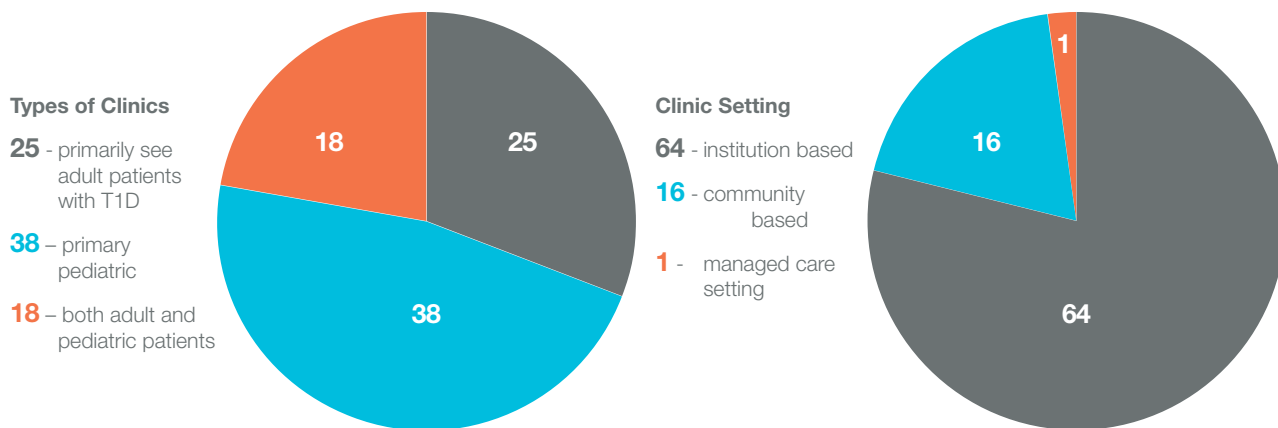
HEALTH EXPERIENCES IN THE LAST 18 MONTHS

OVERVIEW

Since its establishment in 2010, the T1D Exchange Clinic Network and Registry support and accelerate clinical, translational and epidemiological research by helping researchers:

- characterize individuals living with T1D
- conduct exploratory or hypothesis-generating analyses
- identify and recruit participants for clinical studies
- conduct multi-site studies that advance translational research and drive meaningful health outcomes for people with type 1 diabetes

CLINIC NETWORK UPDATE

Since July 2015, the Clinic Network has added 7 new sites to support expansion of the patients in the Clinic Registry. Today, the Clinic Network includes 81 sites in 35 states, including North Dakota, South Dakota, Montana and Idaho. These states are notable because typically, their patients are not- or under-represented in clinical studies. The Clinic Network sites collectively follow more than 100,000 patients with T1D.

Types of Clinics

25 - primarily see adult patients with T1D

38 – primary pediatric

18 – both adult and pediatric patients

Clinic Setting

64 - institution based

16 - community based

1 - managed care setting

CLINIC REGISTRY UPDATE

The Clinic Registry has completed enrollment for 33,232 participants. Registry enrollment is open to new clinic network sites.

Follow-up data for Clinic Registry participants:

at least one year	**at least two years**	**at least three years**	**at least four years**
24,877 participants	20,768 participants	17,082 participants	11,941 participants

Age Distribution – Current
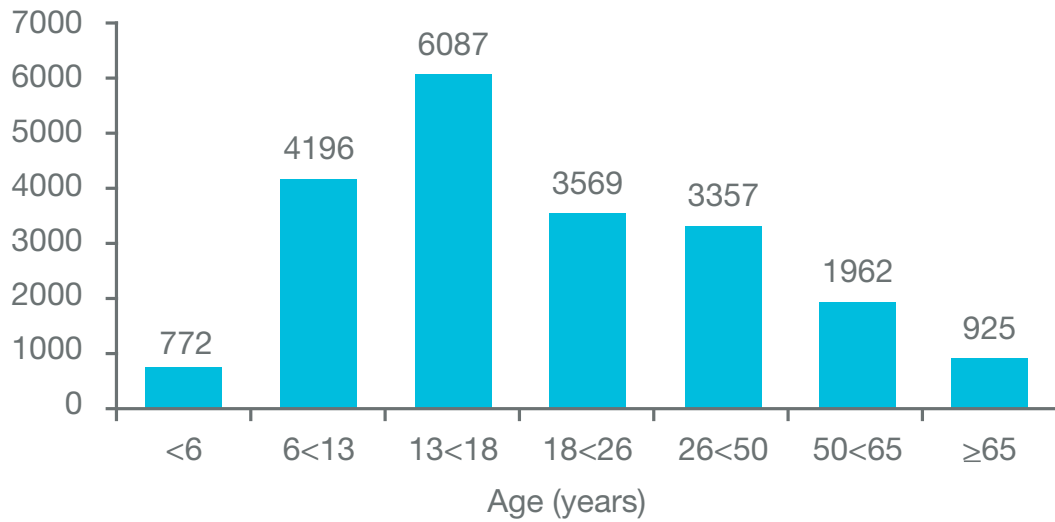
Duration of T1D – Current
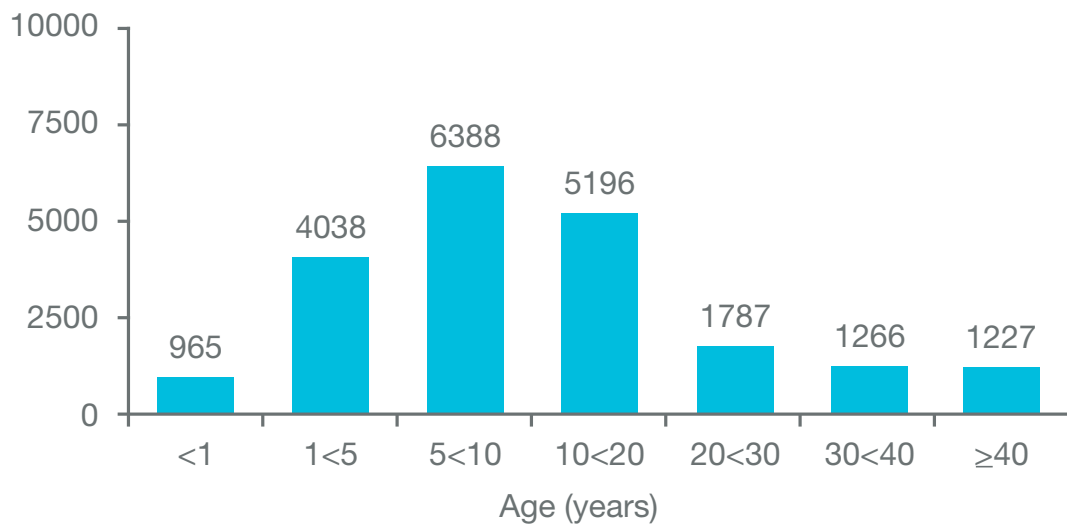
*Registry data current through August 1, 2016; N=20,868

GLYCEMIC CONTROL

In 2012, T1D Exchange first published its **Average Current HbA1c by Age** analysis from the Clinic Registry during its initial enrollment period of 2010 - 2012. The latest analysis of **Average Current A1c** reinforces the initial finding that there remains considerable room for improving treatment outcomes in type 1 diabetes across all age groups, especially for adolescents and young adults.

As the Clinic Registry matures, it provides us with the opportunity to track participant's A1c over time. What we've learned continues to demonstrate the challenge of achieving target A1c. Clinic Registry participants experienced a slight worsening of A1c over time, again most notably in adolescents and young adults.

While the Clinic Registry has provided a wide body of evidence illuminating gaps and unmet needs in type 1 diabetes, perhaps none is more meaningful to people with T1D and their clinicians than these findings on HbA1c. It's a validation that their A1c isn't a personal failing or "noncompliance." It's clear the tools simply do not yet exist that make good outcomes achievable for most people living with type 1 diabetes.

Average Current HbA1c by age
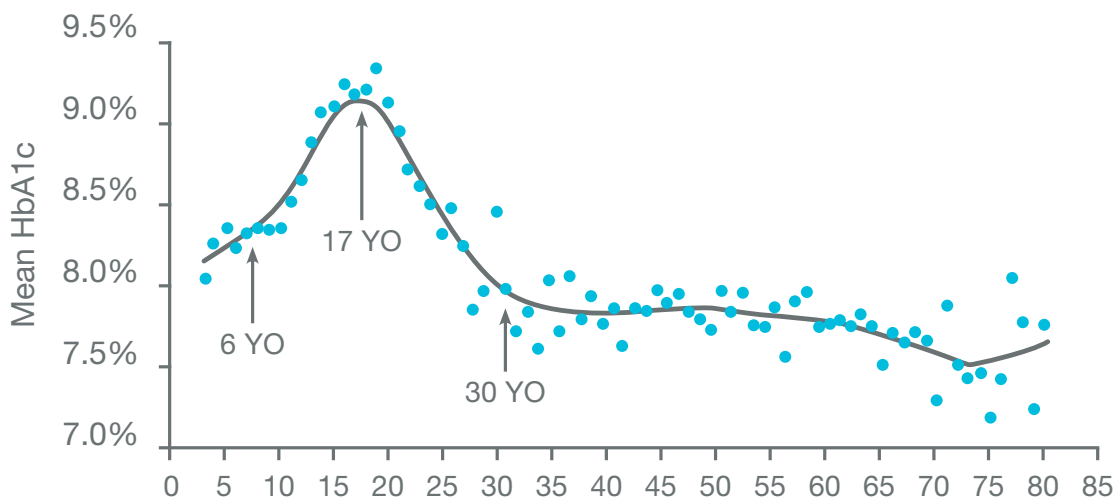
*≤2 years old and ≥80 years old are pooled

REVIEW THE T1D EXCHANGE FINDINGS

Hemoglobin A1c (HbA1c) changes over time among adolescent and young adult participants in the T1D Exchange clinic registry. doi: 10.1111/pedi.12295

*Registry data current through August 1, 2016; N=20,868

Currant HbA1c: Slightly worse in youth than at enrollment

Mean HbA1c

Legend:
- Enrolled 2010-2012 (orange)
- Current 2015-2016 (blue)

Age (years)	Enrolled 2010-2012	Current 2015-2016
<6	8.2%	8.2%
6<13	8.3%	8.5%
13<18	8.8%	9.1%
18<26	8.5%	8.8%
26<50	7.7%	7.8%
50<65	7.7%	7.7%
≥65	7.4%	7.5%
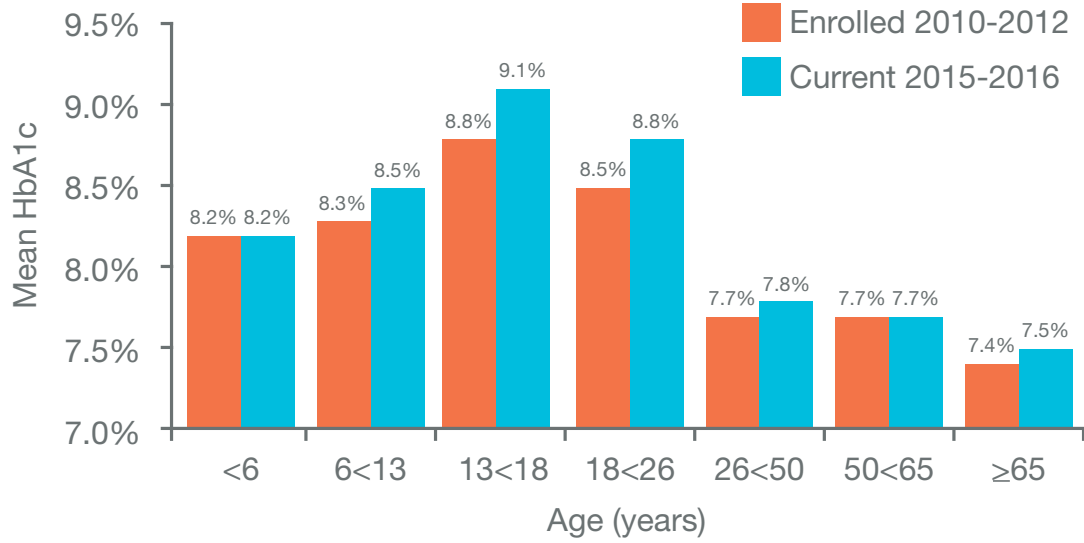
ADA HbA1c targets not met by most

A1c Goal = <7.5%   A1c Goal = <7.5%

Legend:
- Enrolled 2010-2012 (orange)
- Current 2015-2016 (blue)

Age (years)	Enrolled 2010-2012	Current 2015-2016
<6	24%	25%
6<13	24%	21%
13<18	22%	16%
18<26	17%	13%
26<50	31%	27%
50<65	28%	25%
≥65	36%	31%
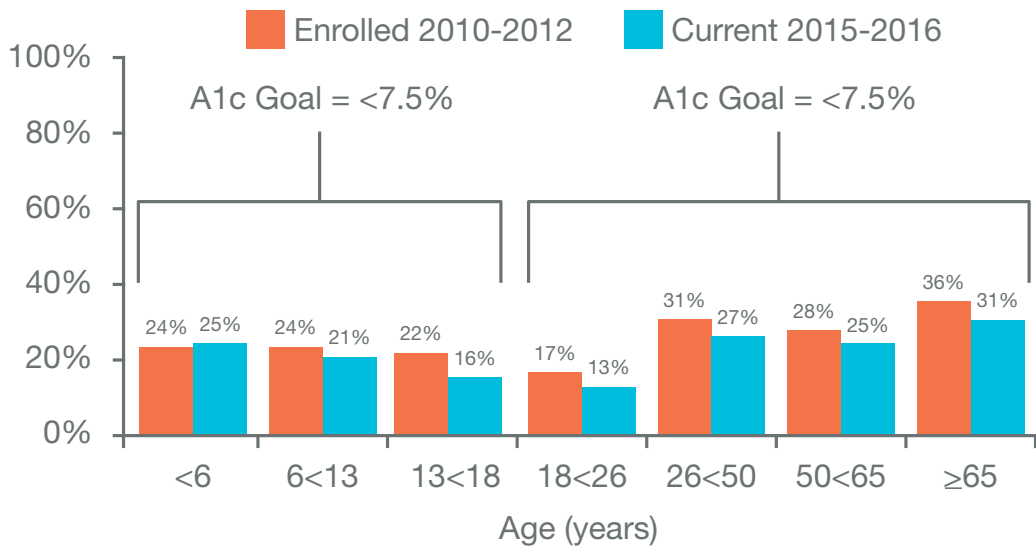
*Registry data current through August 1, 2016; N=20,868

WHAT WE'VE LEARNED

We know that target A1c remains a frustrating and at times out-of-reach measure for many people with type 1 diabetes. While it's a multi-faceted complex challenge, there is some good news.

- A1c is lower with the use of insulin pumps and/or continuous glucose monitors (CGMs).

- Additionally, the use of these devices is increasing across all age groups in the Clinic Registry. Notably, CGM use is increasing more rapidly for those who already use insulin pumps.

Lower HbA1c in CGM users regardless of insulin delivery method
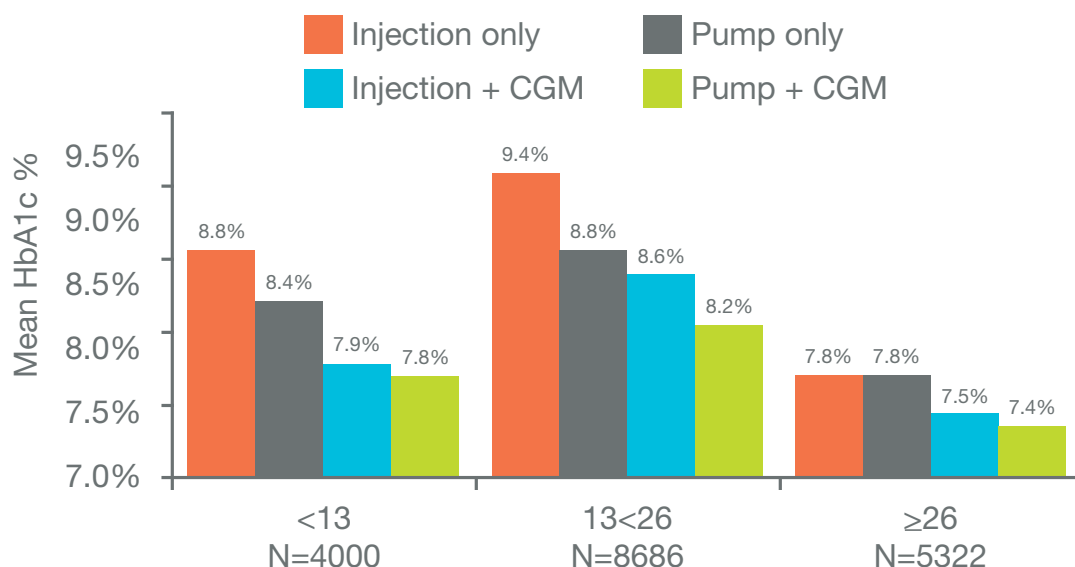
Lower HbA1c in CGM users
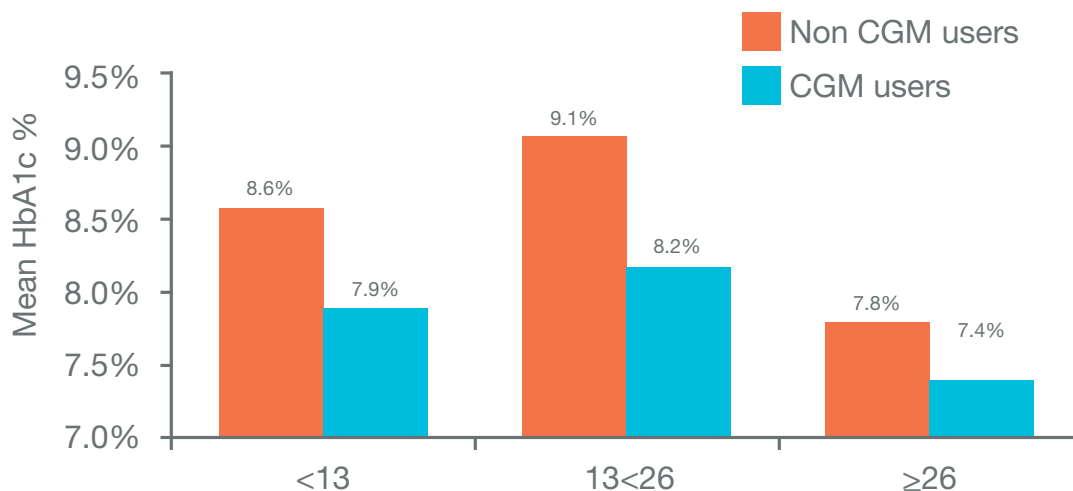
*Registry data current through August 1, 2016; N=20,868

Insulin pump is increasing

Legend:
- Enrolled 9/1/2010-8/1/2012
- Current 4/30/2015-7/31/2016

Age (years)	Enrolled	Current
Overall	57%	63%
<6	50%	63%
6<13	58%	66%
13<18	55%	62%
18<26	53%	59%
26<50	62%	64%
50<65	60%	63%
≥65	54%	61%

CGM use is increasing

Legend:
- Enrolled 2010-2012 (7% use CGM overall)
- Current 2015-2016 (21% use CGM overall)

Age (years)	Enrolled	Current
<6	4%	39%
6<13	4%	23%
13<18	3%	14%
18<26	4%	15%
26<50	15%	29%
50<65	16%	29%
≥65	10%	19%
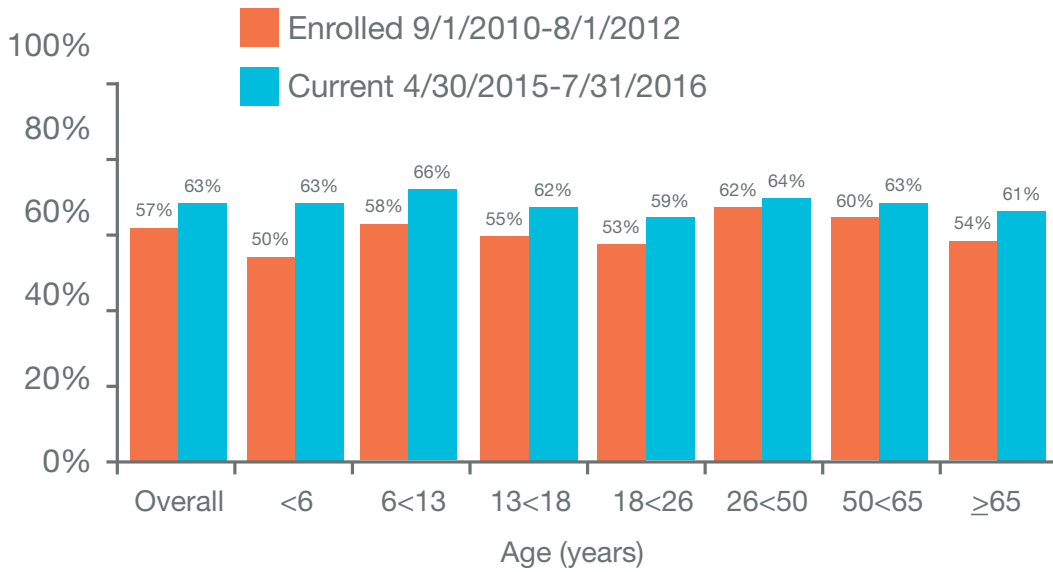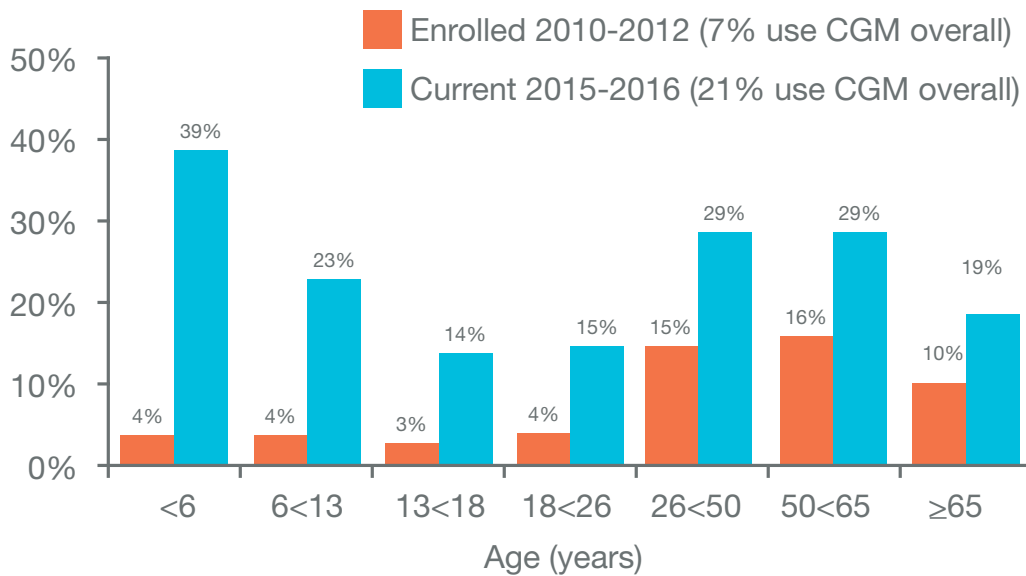
*Registry data current through August 1, 2016; N=20,868

RESEARCH SPOTLIGHT

Is there a Racial Difference in Glucose Control in Relation to the HbA1c?

T1D Exchange enrollment data
Racial differences in HbA1c

Clinic Registry analysis has shown that racial disparities exist in glucose control: Blacks have higher HbA1c levels than Hispanics or Whites in both pump and injection users. There has been much scientific speculation to whether this difference is due to worse glycemic control in Blacks or the consequence of racial differences in the glycation of hemoglobin.

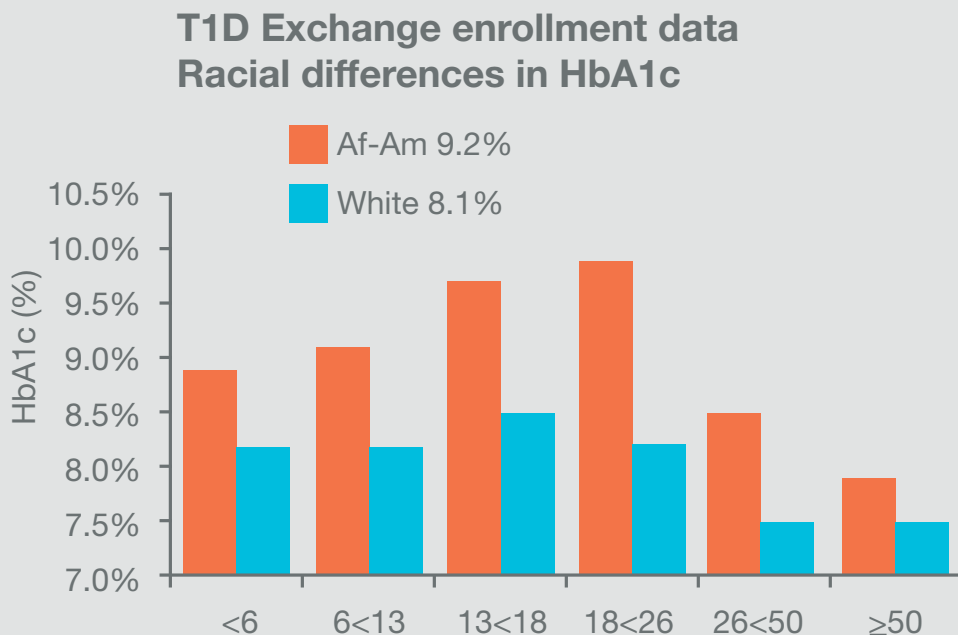In 2016, T1D Exchange completed a major 12-week study where mean glucose concentration was measured using continuous glucose monitoring and compared by race. Ten diabetes centers from the T1D Exchange Clinic Network in the US conducted the study with 104 Black and 104 White individuals (over 8 years old) participating. The participants had T1D for at least 2 years and HbA1c of 6.0% to 12.0%.

While study results are being prepared for publication at this time, T1D Exchange analysis reveals that HbA1c levels on average are higher in Blacks compared with Whites. As race only partially explains HbA1c differences between Blacks and Whites, we believe future research should focus on identifying and modifying barriers impeding improved glycemic control in Blacks with diabetes.

This study was funded by The Leona M. and Harry B. Helmsley Charitable Trust.

T1D INSIGHTS: GLOBAL PERSPECTIVES

T1D Exchange frequently seeks collaboration with others in the global T1D research community. Collaborative studies between diabetes registries provide a powerful platform for investigating different diabetes therapeutic approachs and methods of care that can lead to improved outcomes globally.

In the past 18 months, several collaborations have resulted in interesting data and insights.

Read on for highlights from two recent collaborations.

SEVERE HYPOGLYCEMIA RATES ARE NOT ASSOCIATED WITH HBA1C

The landmark Diabetes Control and Complications Trial (DCCT) reported that keeping blood glucose levels as close to normal as possible (median HbA1c 7%) slows the onset and progression of complications of T1D. However, a major adverse finding was a 3-fold increased risk of severe hypoglycemia (SH) events with those receiving intensive treatment.

T1D Exchange, the German/Austrian Diabetes Patienten Verlaufsdokumenation (DPV), and Western Australian Children Diabetes Database (WACDD) diabetes registries participated in a cross-sectional analysis to examine the association between glycated hemoglobin (HbA1c) and severe hypoglycemia rates in patients with type 1 diabetes receiving usual care.

The study involved participants with type 1 diabetes, aged <18 years and with a minimum duration of diabetes of 2 years. There were 7,102 participants from the T1D Exchange Registry (US), 18,887 from DPV, and 865 participants from WACDD. Participants in each registry were observed for a 12-month period between 2011 and 2012.

KEY FINDINGS

A key finding from this collaborative study of three independent contemporary cohorts of T1D youth reports the lack of an inverse relationship between rates of severe hypoglycemia (SH) and glycemic control as measured by HbA1c; observed in patients treated with both insulin pump and injection therapy.

However, frequency of SH differed across registries with higher rates in T1D Exchange and Australia. It was noted that participants in the US and to Australia registries with higher A1c levels also had a higher occurrence of SH; suggesting that higher HbA1c does not provide protection from SH.

Mean HbA1c was similar in those with and without an SH event in the past 12 months across all age groups.

REVIEW T1D EXCHANGE FINDINGS

This study was published in *Pediatric Diabetes* in October, 2016.
Severe hypoglycemia rates are not associated with HbA1c: a cross-sectional analysis of 3 contemporary pediatric diabetes registry databases, doi: 10.1111/pedi.12477
http://onlinelibrary.wiley.com/doi/10.1111/pedi.12477/abstract

TYPE 1 DIABETES IN OLDER ADULTS: COMPARING TREATMENTS AND CHRONIC COMPLICATIONS

Older adults with long-standing type 1 diabetes are a growing population globally; but the population is not well studied. Most research has concentrated on people with type 2 diabetes, many of whom do not require insulin therapy.

T1D Exchange and the Diabetes Patienten Verlaufsdokumenation (DPV) from Germany/Austria compared demographics, management approaches, cardiovascular risk factors, and diabetes related complications in older adults to help improve management strategies.

- T1D Exchange studied 1,283 participants from 32 adult centers with a mean age at Registry enrollment of 67 years and a mean diabetes duration of 32 years. 58% of participants were on pump.
- The DPV studied 2,014 participants from 111 specialized diabetes centers in Germany and Austria. Mean age at enrollment 71 years and mean diabetes duration was 29 years. 18% of participants were on pump.

The study analyzed the prevalence of micro/macroalbuminuria, glomerular filtration rate (chronic kidney disease/exocrine pancreatic insufficiency) and stroke and myocardial infarction.

Analysis showed that despite similar HbA1c concentrations, differences exist between the registries in blood pressure and lipid management, use of insulin pump therapy and reported microvascular and macrovascular diabetes complications, including:

- fewer myocardial infarctions and strokes in adults ages 60 years of age in the T1D Exchange clinic registry compared to the German/Austrian DPV, despite similar mean BMI and prevalence of obesity
- in the T1D Exchange clinic registry, there was also higher statin, antihypertensive, and aspirin use, lower blood pressures and LDL levels (even with stratifying for blood pressure and statin use), and less microalbuminuria and smoking.

These data support a potential benefit of increased attention to blood pressure treatment and statin use in older adults with T1D. Other findings include:

- microvascular complications were also lower in the T1D Exchange clinic registry compared to the DPV with similar HbA1c values.
- slightly more DPV participants had chronic kidney disease (based on eGFR calculations) than in the T1D Exchange. The lower percent of T1D Exchange participants with eGFR <30 ml/min/1.73m2 may be related to higher use of ACE-I and ARBs in the US and/or lower blood pressures
- Less retinopathy and neuropathy were also reported in the T1D Exchange.

Further studies are needed to better understand the observed differences and to determine if current management strategies should be modified to improve outcomes.

REVIEW T1D EXCHANGE FINDINGS

This study was published in *Diabetes Research and Clinical Practices* in October, 2016.
Type 1 diabetes in older adults: Comparing treatments and chronic complications in the United States T1D Exchange and the German/Austrian DPV registries. http://dx.doi.org/10.1016/j.diabres.2016.09.024
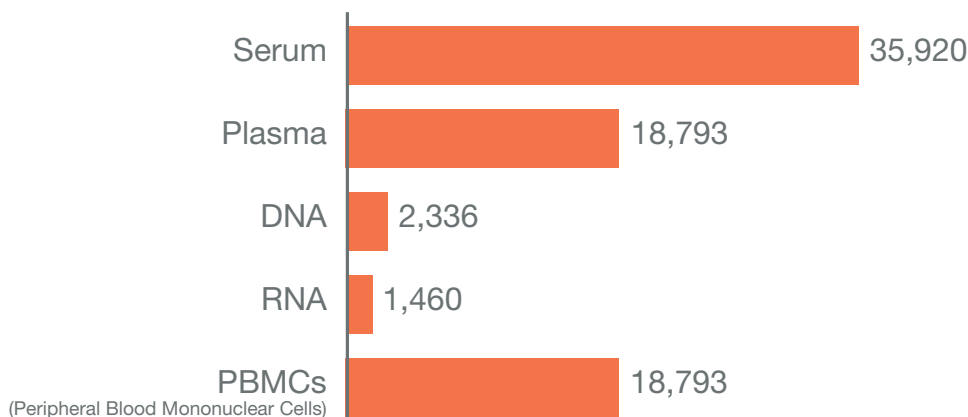
Collaborative Science

There are numerous challenges that exist in the T1D research space. Researchers often perform their studies in silos, limiting collaborations and information sharing that could accelerate progress. Many patient cohorts are developed within a single institution with relatively small numbers of participants. These cohorts often lack sufficient size or disease diversity to yield meaningful results. Studies requiring patient biosamples also require a significant time investment to secure the appropriate samples and patient data.

The T1D Exchange Collaborative Science program is built to accelerate all stages of medicine and science by bringing together multiple stakeholders performing research with our robust cohort representing a broad demographic of patients, biosamples and real-world data.

T1D EXCHANGE BIOBANK

At the heart of our Collaborative Science program is the T1D Exchange Biobank. Our program makes available biosamples and data to academic and industry researchers. We aim for this resource to support a cutting edge science program focused on understanding T1D, its heterogeneity, and complications to ultimately impact the outcomes of those with T1D.

The Biobank currently collects blood for the isolation and storage of:

Serum	35,920
Plasma	18,793
DNA	2,336
RNA	1,460
PBMCs (Peripheral Blood Mononuclear Cells)	18,793

IN THE PAST 18 MONTHS, WE HAVE:

Published **3** papers using T1D Exchange Biobank samples

Enabled **8** new studies with Biobank samples and data

Collected **hundreds** of biobank samples to support collaborative science research

A WELL-CHARACTERIZED COHORT OF BIOSAMPLES

Through its comprehensive resources, T1D Exchange has leveraged a unique opportunity to collect T1D specimens through its many clinical studies. This has helped us build a robust cohort representing a broad demographic of patients.

T1D EXCHANGE STUDY	#N	SPECIMEN TYPE	TIMEPOINTS
Residual C-Peptide in Patients with T1D	919	Serum, plasma, RNA, DNA, PBMC	All visits
Metformin Therapy for Overweight Adolescents with T1D	140	Serum, plasma, RNA, DNA, PBMC	Baseline and 6 months
Severe Hypoglycemia in Older Adults with Type 1 Diabetes	200	Serum, plasma, RNA, DNA, PBMC	Enrollment Visit
Assessment of Intranasal Glucagon in Children and Adolescents with T1D	48	RNA and DNA	Visit 1 and 2 (fasting and nadir)
Efficacy and Safety of Intranasal Glucagon for Treatment of Induced Hypoglycemia in Adults with Diabetes	75	RNA, DNA and serum	Visit 1 and 2 (fasting and nadir)
Racial Differences in Mean CGM Glucose in Relation to HbA1c	225	Serum, plasma, RNA, DNA, PBMC	Baseline visit
Randomized Trial Comparing CGM with and without Routine Blood Glucose Monitoring in Adults with T1D (REPLACE BG)	225	Serum, plasma, RNA, DNA, PBMC	Baseline visit
Beta Cell Function and Glucose Counter-regulation during the Progression of T1D	60	Serum, plasma, RNA, DNA, PBMC	Visits 1 and 3

PUTTING THE BIOBANK TO WORK

The T1D Exchange Biobank consists of thousands of biological samples from individuals with T1D. It's an important resource developed to advance the understanding of T1D and support a new generation of innovative research, collaboration the exchange of knowledge. We interviewed two leading scientists to learn more about their work using T1D Exchange biosamples.

COLLABORATIVE SCIENCE SPOTLIGHT: YUVAL DOR

Dr. Yuval Dor is a professor of biology at the Hebrew University of Jerusalem, Israel. A developmental biologist by training, Dr. Dor became interested in T1D research during post-doctoral training with Doug Melton at Harvard University (2001-2004). There, they found that the generation of new beta cells during adult life (in the mouse) is based on the replication on pre-existing beta cells, not on stem cells.

CURRENT STUDY

In his laboratory at Hebrew University, he and his team of 20 members (technicians, students, post-docs and research fellows) are collaborating with multiple groups, most closely with Prof. Ben Glaser, the head of Endocrinology at the Hadassah Medical Center. Together they are studying tissue dynamics in the pancreas, in particular beta cells, attempting to understand

- signals that control beta cell mass (mostly, what determines beta cell size and the decision of a beta cell to divide),
- how the function of beta cells changes in diabetes.

Recently, the teams have become interested in development of methods to detect beta cell death using DNA circulating in blood, opening up exciting opportunities for early detection of T1D and monitoring of disease progression and response to therapy.

THE VALUE OF T1D EXCHANGE BIOBANK SAMPLES

Dr. Dor's ongoing study of beta cell death using circulating DNA relies on plasma samples from healthy individuals, from people at risk to develop T1D, from recently diagnosed patients and from long time T1D patients who have, or don't have, measurable levels of c-peptide.

These studies are important because they can shed new light on the processes taking place in human T1D, which were not accessible so far for non-invasive interrogation.

READ THE RESEARCH

See the abstract "Identification of tissue-specific cell death using methylation patterns of circulating DNA" doi: 10.1073/pnas.1519286113.

COLLABORATIVE SCIENCE SPOTLIGHT:
MARIA J. REDONDO

Dr. Maria J. Redondo is Associate Professor of Pediatrics at the Section of Diabetes & Endocrinology, Texas Children's Hospital, Baylor College of Medicine.

She combines her passion for treating children with type 1 diabetes with her training, which led her to believe that it is possible to identify the causes of type 1 diabetes and stop its development. She hopes her research can help identify causes of type 1 diabetes to ultimately lead to prevention.

CURRENT STUDY

Dr. Redondo is researching the gene TCF7L2—a gene originally found to be a risk factor for type 2 diabetes. She and her team have learned that TCF7L2 may also play a role in the development of type 1 diabetes, particularly in those individuals who present fewer of its traditional markers, such as islet autoantibodies or certain HLA genes.

## THE VALUE OF T1D EXCHANGE BIOBANK SAMPLES

When her team made the TCF7L2 gene observation, it was in a relatively small, local group of patients. The results were intriguing—but needed confirmation.

T1D Exchange biosamples have allowed her team to validate their findings in a larger population from across the United States. And because these samples were well-characterized and openly available, it helped her conduct her study in a much shorter time than it is typically necessary.

Her team is now testing their hypothesis in individuals who are at risk of type 1 diabetes but have not developed it yet, which may provide definite evidence of the involvement of this gene in the disease.

READ THE RESEARCH

See the abstract from the published paper "Dissecting heterogeneity in paediatric Type 1 diabetes: association of TCF7L2 rs7903146 TT and low-risk human leukocyte antigen (HLA) genotypes."
doi: 10.1111/dme.13123
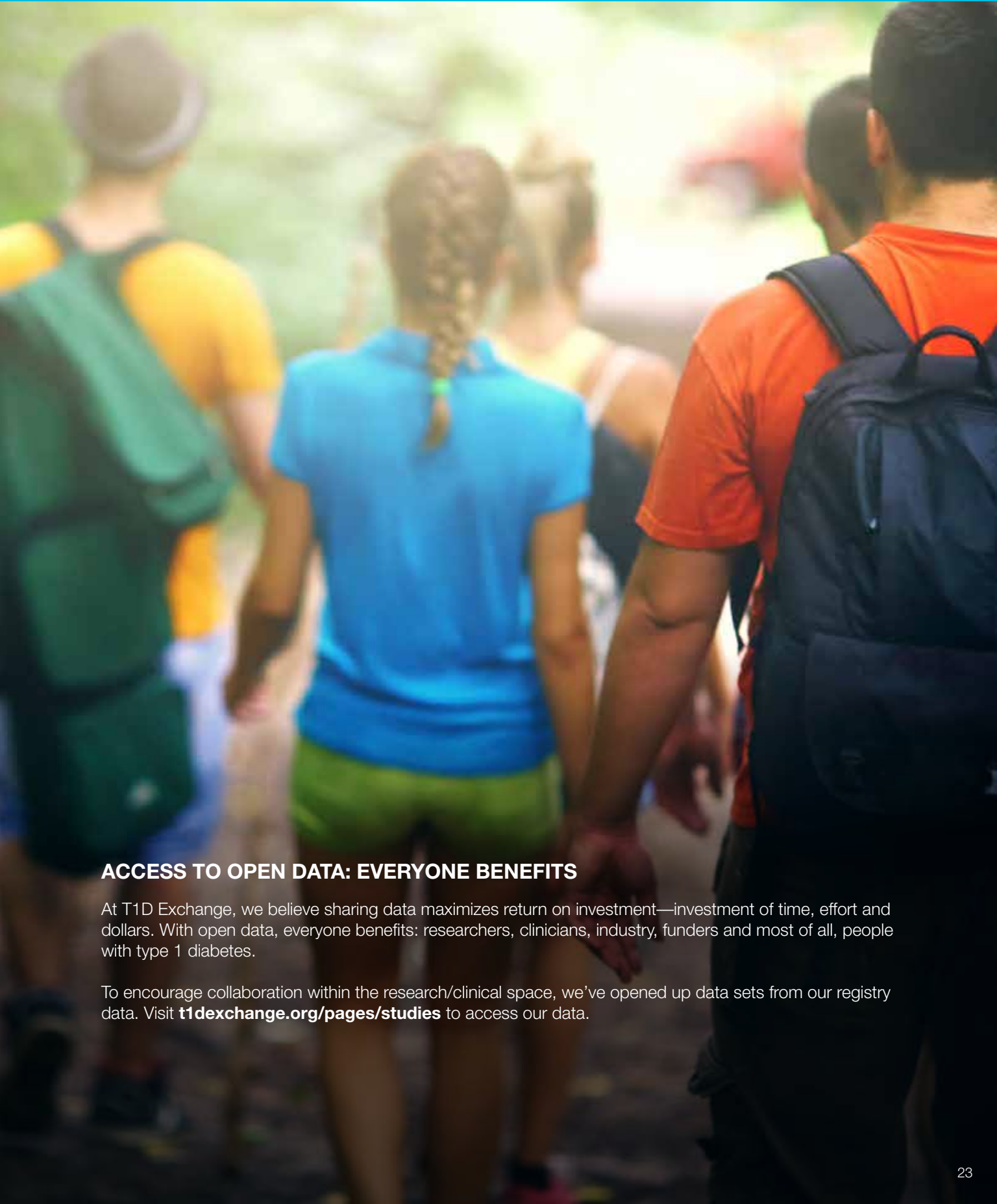
ACCESS TO OPEN DATA: EVERYONE BENEFITS

At T1D Exchange, we believe sharing data maximizes return on investment—investment of time, effort and dollars. With open data, everyone benefits: researchers, clinicians, industry, funders and most of all, people with type 1 diabetes.

To encourage collaboration within the research/clinical space, we've opened up data sets from our registry data. Visit **t1dexchange.org/pages/studies** to access our data.

Patient-Centered Research:
What We've Learned From the Community

At T1D Exchange, we believe the key to achieving better outcomes is when people touched by the disease are at the center of research. That's why we keep the patient and caregiver voice at the heart of all aspects of our scientific and clinical programs.

IN THE PAST 18 MONTHS, WE HAVE:

Conducted **25** patient-centered studies on Glu

Provided the patient perspective at more than **30** national events and conferences

Grown our Glu research community by more than **5,000** participants

Asked **544** Questions of the Day on Glu, which is the largest living library of T1D wisdom in the world

MISDIAGNOSIS AND DIABETIC KETOACIDOSIS IN TYPE 1 DIABETES

As a patient-centered organization, we hear about the terrible, sometimes fatal consequences of a delayed or completely missed diagnoses of type 1 diabetes. Yet, through a comprehensive literature review, our research revealed the scope of the problem is still largely unknown. We recognized an opportunity to learn directly from our community about misdiagnosis in type 1 diabetes.

In summer of 2016, T1D Exchange leveraged our patient-centered research networks to gain insights we hoped might help produce a sustainable decrease in the incidence of delayed and missed diagnoses.

With input from people with T1D, caregivers, clinicians, and statisticians, T1D Exchange designed a study to understand the prevalence, incidence, and the post-diagnosis impact on the relationship between patient and their T1D disease. Our goals are to understand the barriers and challenges around timely diagnosis, and hope seek to raise awareness raise awareness that will prevent any child or adult from dying or suffering medical or psychological consequences as a result of misdiagnosis.

We disseminated the study through both our Clinic Registry and Glu community participants. In just a few weeks, over 2,700 participants completed their survey about their (or their child's) diagnosis experience.

Preliminary data from our study shows that
*   41% of individuals* reported being in diabetic ketoacidosis (DKA) – the leading cause of mortality in children with type 1 diabetes – at the time of diagnosis.
*   20% reported being admitted to the ICU at the time of T1D diagnosis
*   Additionally, we learned that 35% of people were not diagnosed until more than one month after they noticed symptoms.
*   We also learned that those who were adults at the time of disease onset were more frequently misdiagnosed before being correctly diagnosed with T1D than those diagnosed in childhood and adolescence.

*These finding are preliminary results of our data analysis. At this time, T1D Exchange is preparing manuscripts and presentations based on the findings. Our goal is to reach and educate as many healthcare professionals and people who may be showing signs of type 1 diabetes as we can to help prevent DKA or worse and improve outcomes overall.

"So many stories of people being sent home by a provider, and told it was just a flu or a virus. With **more education**; missed type 1 diagnosis should almost be eradicated."

– Tom Karlya

## INFLUENCING T1D RESEARCH PRIORITIES FROM THE GROUND UP: THE ICELAND SUMMIT

The world of type 1 diabetes research is rapidly changing with transformational innovations taking place in the lab, and with diagnostics, therapeutics, medical devices and decision-support tools. While great strides are happening, are they in line with what people with T1D and their families need and want? The best way to answer this question is to simply ask.

In late 2015, the Leona M. and Harry B. Helmsley Charitable Trust convened leading experts representing beta cell biologists, immunologists, clinical researchers, and clinicians in a global "Type 1 Diabetes Iceland Summit" to consider an integrated set of five-year priorities for the type 1 diabetes landscape. The summit took place in Iceland and included T1D Exchange Chief Medical Officer Henry Anhalt, DO.
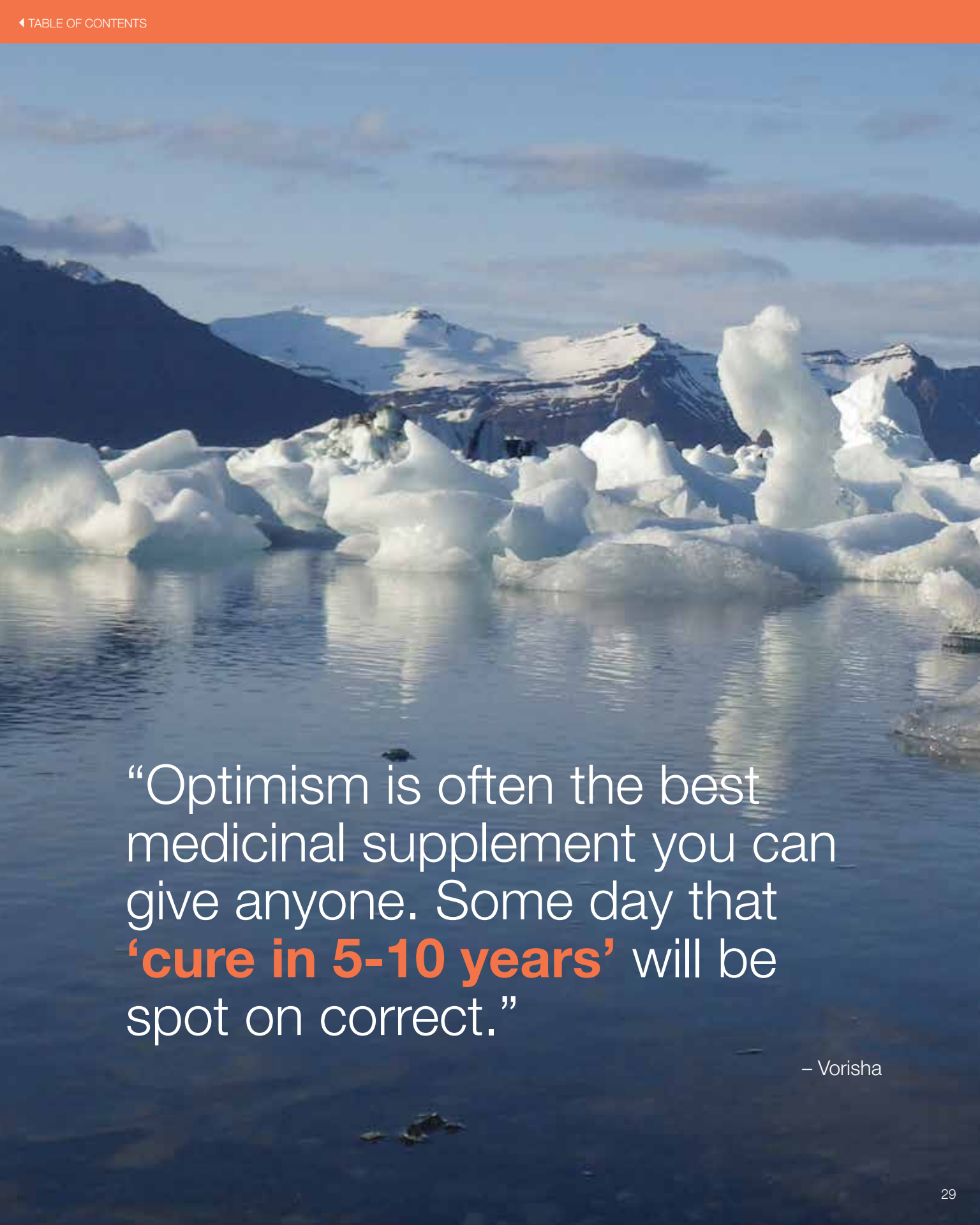
In addition to expert voices, T1D Exchange gathered and represented the community's voice to help shape discussions during the summit.

T1D Exchange reached out to its online Glu community with a daily "Question of the Day" poll to ask a series of questions about future directions in T1D research.

WOULD YOU PREFER TO SEE MORE RESOURCES INVESTED IN THE PREVENTION OR CURE OF T1D?

n = 530

CURE 85%
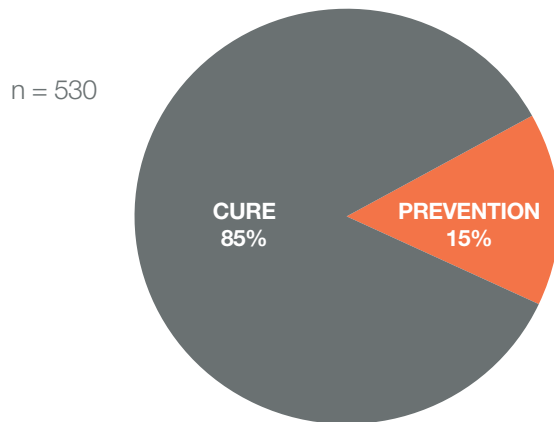
PREVENTION 15%

The community was relatively united in preferring to see more resources invested in cure versus prevention of T1D

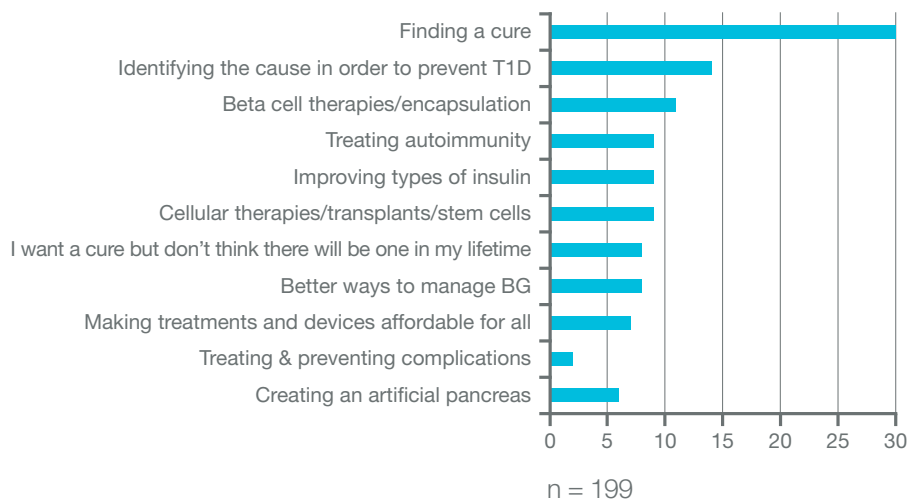"Optimism is often the best medicinal supplement you can give anyone. Some day that **'cure in 5-10 years'** will be spot on correct."

– Vorisha

What do you think should be the biggest research priority for scientists studying T1D?

Finding a cure
Identifying the cause in order to prevent T1D
Beta cell therapies/encapsulation
Treating autoimmunity
Improving types of insulin
Cellular therapies/transplants/stem cells
I want a cure but don't think there will be one in my lifetime
Better ways to manage BG
Making treatments and devices affordable for all
Treating & preventing complications
Creating an artificial pancreas

n = 199

When do you think there will be a biological cure for T1D

Not never, but not anytime soon
I want to be/am optimistic that a cure will come soon
There will never be a cure because companies/big Pharma...
Never
I've been lied to/told there would be a cure in 5 years for...
When research has more money and spends it more...
Technology will help, but a real cure is a long way away
In the next 10-15 years
I have no idea
More than 10 years but less than 50

# of times mentioned in comments

n = 268

For many who live with type 1 diabetes, they feel that there will never be a cure, or they have given up on a cure after being promised at diagnosis that it was right around the corner.

WHAT DOES IT MEAN?

When you look at the varying responses to questions about T1D research priorities from the Iceland Summit, one thing becomes clear. Like the disease itself, feedback from the community is complex and multi-faceted.

- Our community of responders indicated that the cure was the biggest research priority, yet were also pessimistic that there would ever be a cure.
- Artificial pancreas ranked last on the list of biggest research priorities; yet in a question posed in the community some six months later, responders to that question chose artificial pancreas as the most promising solution.

While these answer sets aren't corollary, they do help to tell a story of a community more than ready for change and new hope in type 1 diabetes. It's also a community of people who have raised their hands and volunteered to be part of the research process.

ICELAND DIABETES SUMMIT LEADS TO COHESIVE VIEWPOINT ON PRE-CLINICAL TYPE 1 DIABETES

The incidence of type 1 diabetes continues to rise at 2-5% per year worldwide and approximately 25% of those diagnosed are adults.[1] It's a difficult reminder of the urgent need to develop a means to prevent (and cure) type 1 diabetes.

An important part of the Iceland Diabetes Summit was a forum calling for staging definitions of pre-symptomatic type 1 diabetes. The goal is to increase awareness with clinicians and the general public that (via auto-antibody screening), pre-clinical type 1 diabetes is a diagnosable disease. Providing a diagnosis for pre-clinical diabetes will help accelerate industry, academic and public research activities leading to clinical trials that could reverse beta cell autoimmunity and halt progression to symptomatic insulin-requiring type 1 diabetes.

Chief Medical Officer Dr.Henry Anhalt represented T1D Exchange at this summit and was a contributing author to a recent viewpoint published in *Diabetologia* in September 2016.

Read the Viewpoint
http://link.springer.com/article/10.1007/s00125-016-4144-8

BETTER DIAGNOSTIC TESTING FOR T1D?

1. Maahs DM, West NA, Lawrence JM, Mayer-Davis EJ. Chapter 1: Epidemiology of Type 1 Diabetes. Endocrinology and metabolism clinics of North America. 2010;39(3):481-497. doi:10.1016/j.ecl.2010.05.011.

Accelerating Therapies, Improving Care

In the six years since our founding, T1D Exchange has built a comprehensive and innovative research model. In that time, we have gathered, analyzed and put to use: patient health data, health experiences, and biosamples to inform the development of therapies, solutions and clinical care.

We've listened and learned – from clinicians and key opinion leaders, from clinicians and key opinion leaders; from nonprofits, foundations and industry; from other disease groups who face similar challenges; and above all, from our T1D communities. We know that it's critical now more than ever to deliver on the promise of improved outcomes.

In the last 18 months, we've worked tirelessly to not only grow our program's reach and impact, but also kick-start new initiatives that we believe can have a significant and lasting impact over time – all with the goal to accelerate therapies and improve care.

ACCELERATING THERAPIES

Diabetes Innovation Challenge

In 2016, T1D Exchange held its inaugural Diabetes Innovation Challenge – an open competition created to support and accelerate the development of novel therapies, devices and solutions for all aspects of research, clinical care and patient quality of life.

The goal of the Challenge is to identify the most promising innovations in diabetes, and present them to our network of funders, investors, and partners from academia and industry. Our aim is to help find these innovative organizations, raise their visibility and allow them to make connections that can ultimately lead to them securing the necessary support to move them to the next stage of development. Ultimately, the vision for the Diabetes Innovation Challenge is to accelerate translation and delivery of discoveries to the patient community.

In our inaugural year, we partnered with M2D2 (a joint venture of the University of Massachusetts that incubates medical device start-ups) to host the Challenge, which consisted of tiered events, including semi-final events, a finals event and a winners showcase. The Challenge was generously supported by lead sponsors American Diabetes Association (ADA) and JDRF. Awards were presented totaling $150,000 cash or in-kind services to 6 innovative companies.

The events were well-attended by funders, investors, and partners from academia and industry. In addition to our Challenge awardees, 30 semi-finalist companies were able to present their promising innovations to this community for increased exposure and opportunity.

AWARD RECIPIENTS

From an impressive field of inspiring applicants, the winners of the 2016 Diabetes Innovation Challenge include:

EARLY-TO-PRECLINICAL STAGE PROJECTS

1st – Integrated Medical (Irvine, CA)
Fully-integrated, low cost, implantable, wireless, continuous glucose monitoring platform.

2nd – Glyscend (Baltimore, MD)
Orally-administered intestinal coating which mimics the therapeutic benefits of bariatric surgery on type 2 diabetes.

3rd – WindGap Medical (Somerville, MA)
Autoinjector that automates the rehydration and administration of lyophilized drugs,
such as glucagon.

LATE-STAGE PROJECTS (PRE-CLINICAL THROUGH TRANSLATIONAL)

1st – Enable Biosciences (San Francisco, CA)
Ultrasensitive non-radioactive autoantibody test that can be readily used for population screening.

2nd – Admetsys (Boston, MA)
Artificial pancreas system specifically for the needs of diabetics in-hospital.

3rd – Polyphotonix (Durham, UK)
Non-invasive, low cost diabetic retinopathy mask that can be used by the patient in their own home while asleep.

People's Choice – Sproutel (Providence, RI).
The teddy bear teaching tool.

THANK YOU!

In its inaugural year, the Challenge has far exceeded our expectations, from
- the breadth and quality of applicants
- the support from the many organizations who sponsored the event
- the participation of a varied and esteemed panel of judges and mentors who offered innovators a great opportunity to learn and develop their projects into products
- the enthusiasm of those who attended the event and connected with innovators to learn where there may be mutually-beneficial opportunities

As we begin planning for our next Diabetes Innovation Challenge, we are confident that it will be even better; yet we need resources to make that happen.

There are many opportunities to collaborate with us as we build another successful event, including sponsorship, mentoring, judging, and investment.

Contact Chief Advancement Officer Erin Gilbert to learn how to make an impact for yourself and innovation at egilbert@t1dexchange.org.

ACCELERATE THERAPIES

AUTOMATED INSULIN DELIVERY (AID)

The Diabetes Innovation Challenge is one new T1D Exchange initiative to help accelerate new and novel treatments. In 2016, we also announced an initiative aimed at advancing automating insulin delivery (AID).

In 2016, we used our Question of the Day poll on Glu to tell us what therapeutic solution currently being researched is the most promising. More than half of our respondents chose closed loop.

Which therapeutic solution, currently being researched for Type 1 do you feel is the most promising?
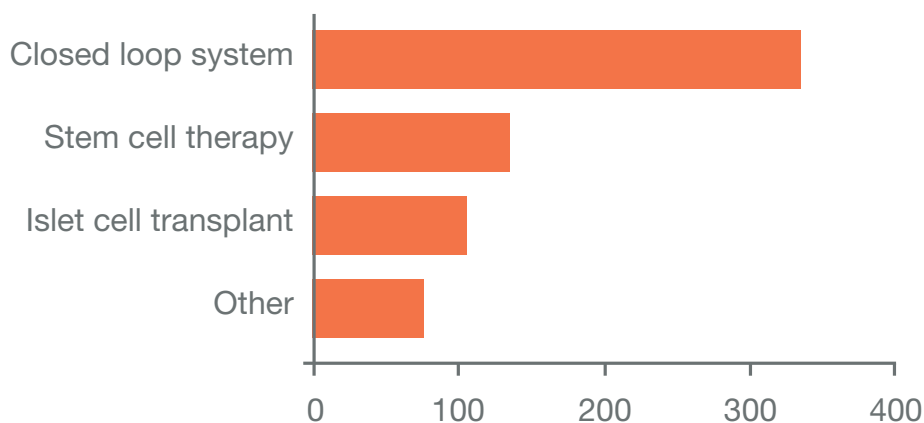
June, 2016. Responses from 653 Glu community members.

In September 2016, the entire community celebrated when Medtronic announced it won FDA approval for the first, hybrid closed loop system, which will be commercially available.

The T1D Exchange investment initiative is aimed at significantly advancing components of AID as well as accelerating differentiated system approaches.

SPOTLIGHT ON THE DIABETES INNOVATION CHALLENGE

The Diabetes Innovation Challenge attracted many innovators with next-generation products. One innovative company reminded us that sometimes, innovations don't need to be transformational to have a huge impact.

Dibatech LLC is a small Indian company hoping to solve a critical problem for those living in Southeast Asia, where nearly 80 million people live with diabetes, but only 10% of households have access to refrigeration or electricity. This small startup created a low-cost insulin storage device that protects insulin from extreme hot and cold temperatures.

Dibatech's solution meets a global need in the T1D community that often goes overlooked. At T1D Exchange, we were proud to offer companies like Dibatech a platform to showcase their product and make valuable business connections.

IMPROVE CARE

THE NEED FOR QUALITY CARE AND IMPROVED OUTCOMES

Today, despite uncertainties with the state of healthcare delivery, one thing is clear – for clinics and clinicians treating people with T1D, balancing quality care with financial sustainability is increasingly difficult.

T1D Exchange is leveraging its broad expertise and experience to take on this complex problem. Can we help clinics treating people with type 1 diabetes achieve better outcomes more efficiently?

In 2016, we launched the first phase of a Quality Improvement initiative whose goals are to create actionable measures that

- create an evidence-based understanding in the variability of outcomes across a varied type 1 diabetes population
- and test various care processes and interventions that can improve outcomes.

It's an ambitious initiative but we believe that improving the quality of care is some of the most important work we can do over the next few years.

BEYOND A1C: EVALUATING OTHER T1D OUTCOMES

There is consensus in the diabetes community that there needs to be clinically relevant outcomes other than A1c, such as hypoglycemia and time in range.

Working with JDRF and The Helmsley Charitable Trust, we seek to leverage our Quality Improvement initiative to gather input from individuals living with T1D, their caregivers, clinicians and research experts – all with the aim of expanding outcome measures that can be leveraged to improve clinical care and to evaluate and compare potential therapies in the research, regulatory, and healthcare settings.

UNDERSTANDING BARRIERS TO DEVICE ADOPTION

The evidence is compelling that outcomes improve with device use; yet there are still many in the community who do not use insulin pumps or CGMs. T1D Exchange seeks to better understand barriers to device adoption. We are conducting research with healthcare professionals to understand barriers to prescribing devices and with patients to understand why they are not using devices. For these studies, T1D Exchange will be recruiting both clinical and patient participants far beyond our existing clinic and online communities. Our goal is to generate an expansive and actionable data set that will help pave the path for adoption of today's and future technologies.

IT TAKES AN ARMY…
AND A VILLAGE

A goal of T1D Exchange is to create an army of research-ready participants who seek to influence and contribute to the landscape of T1D research. Our army is ready to and has been providing health data, biosamples and personal perspectives and insights to support critical research and development.

As we move forward, we seek to expand our army to find and include those people touched by type 1 diabetes who are outside of traditional research, advocacy and online circles.

As part of the Health Policy Initiative; T1D Exchange is currently engaged in an effort to reach out broadly to the T1D community as well as general practitioners, primary care physicians, nurse practitioners and physician assistants who may be treating type 1 patients. Reaching these clinicians and patients will be critically important to understanding a broad picture of clinical care and outcomes of type 1 diabetes in the United States.

HOW CAN YOU HELP?

The entire ecosystem works more efficiently and effectively when engaging with an army of research-ready participants in T1D. T1D Exchange frequently partners with industry, clinics, researchers and foundations/nonprofits to increasingly expand our reach and engage those with T1D who want to advance research.

We'd love to work collaboratively with you to continue to add members to our community who are ready to participate in research.

THANK YOU FOR YOUR CONTINUED SUPPORT

T1D Exchange®