2018 ANNUAL REPORT

SOLUTIONS FROM THE
REAL WORLD

T1D Exchange

CONTENTS

FROM THE CEO

Dear Members, Partners, Colleagues, and Friends,

Nine years ago, T1D Exchange launched with our mission to accelerate therapies and improve care for people living with type 1 diabetes. That mission emerged from the heartfelt desire to support a community that has struggled for decades to achieve better outcomes.

As we worked toward defining clinical practice and access to care, we built a firm foundation of research and innovation. T1D Exchange's leaders understood that without input from patients, fresh ideas would not translate to improved outcomes or a better quality of life.

From that foundation, T1D Exchange is now building a robust type 1 diabetes platform and using it to drive meaningful, patient-centered research and innovation toward prevention, cure, and improved care.

I am thrilled to now steer the organization this year as it unveils that platform in the form of new portals and analytic capabilities to support novel research, quality data collection, and insightful analysis.

At the same time, researchers are citing our data from our Clinic Registry; providers are praising our Quality Improvement model to redefine best practices at their clinics; partners have awarded our public health efforts; and entrepreneurs have joined our Diabetes Innovation Challenge in record numbers to advance their discoveries.

Most of all, our patient and caregiver community (founded in Glu and our newly launched T1D Exchange Registry) is growing. Members are continually learning from our news, engaging with our posts, adding data for research, gratefully sharing stories, and telling us again and again how much they need us as a trusted voice of authority in making sense of all the new data, devices, and directives entering their world.

I am happy to share with you our progress in 2018 and thank you wholeheartedly for your continued support.

Dara Schuster, MD, CEO T1D Exchange

EXECUTIVE SUMMARY

We have the opportunity to join forces and transform the future of diabetes. At T1D Exchange, the effort starts with a new model of research and care improvement. It involves a combination of direct-to-patient and in-clinic platforms. These provide the means to generate real-world evidence (that obtained from outside formal clinical trials) to gain new insights and decipher what individuals with type 1 truly want and need.

As we highlight our efforts from this past year, we invite you to continue in partnership with us, harnessing our platforms and resources to improve outcomes, access…and ultimately lives.

ENGAGING PATIENTS IN RESEARCH

To achieve our mission, we must first look at—and then beyond—the profusion of evidence we have already amassed. This year, our T1D Exchange Clinic Registry presented a wealth of findings in 14 published manuscripts and 24 abstracts at various scientific meetings. This data, as well as the insights collected over the five years of Registry duration, informed us about the unmet needs of people with type 1 diabetes and the direction we need to take to support our community.

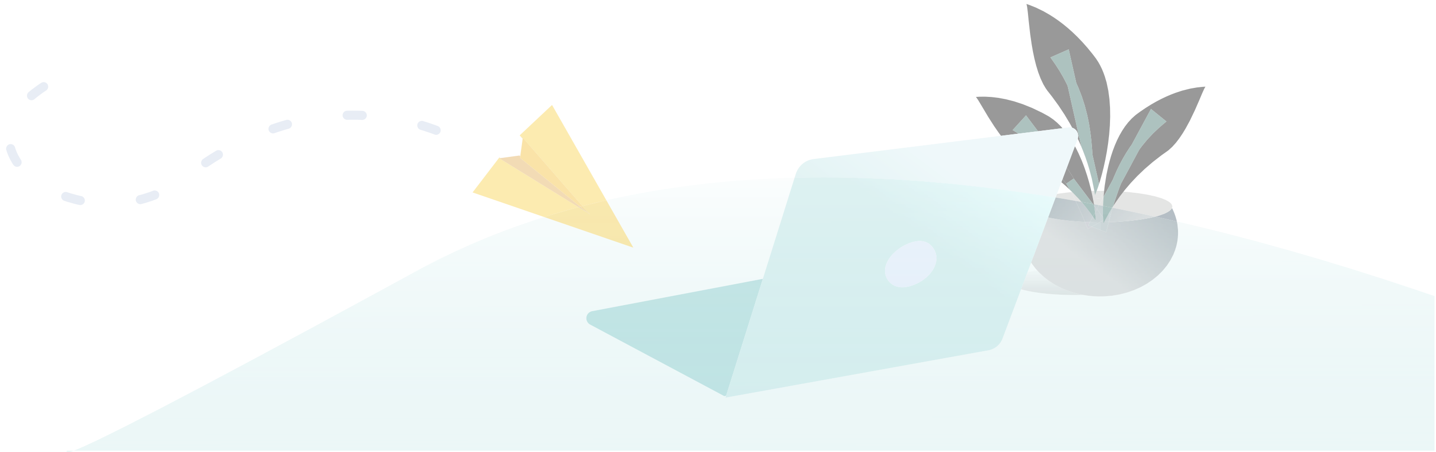
The Clinic Registry will continue to disseminate findings through 2019. Last March, however, we began transitioning patients to our new T1D Exchange Registry. We did this to create a novel model in which recruitment, registration, and consent proceed online—rather than through a particular clinic site(s). The new Registry opened in December for early enrollment. The formal launch date is set for June 2019.

The new T1D Exchange Registry aims to build a diverse cohort of individuals with type 1 diabetes in the U.S. for longitudinal studies. By unlocking recruitment from clinic geography, we reach a broader mix of individuals. By engaging individuals over time, we can track the progression of disease, study the impact of aging, and gain insights not possible through traditional cross-sectional studies.

In addition, we recently announced a new partnership with Tidepool, which will link participants' health data with uploads from their continuous glucose monitoring (CGM) devices. In November, we teed up this effort by beginning recruitment for a pilot study with Tidepool to track the effects of mild-to-moderate variations in blood glucose levels on overall health.

We learned that for these efforts to work, we must redouble our efforts to reach our patient community. Thus, last November we launched a brand new T1D Exchange website linked to an equally revamped T1D Exchange Glu community portal. The goal is to foster cutting-edge connectivity and offer our patient community news, advice, and the means to directly participate in research.

THE NEW T1D EXCHANGE REGISTRY AIMS TO BUILD A DIVERSE COHORT OF INDIVIDUALS WITH TYPE 1 DIABETES IN THE U.S. FOR LONGITUDINAL STUDIES.



Biobank Portal

We also built new campaigns to better engage our community. For example, during diabetes month in November we posted a graphic Instagram series, drawn from information people with diabetes gave us via our daily Questions-of-the-Day. #YouToldGlu: 30 Facts, 30 Days was a resounding success, giving the community useful tips to share and significantly growing our social media channels. We are excited for more initiatives in the pipeline.

ENHANCING AND PERSONALIZING CARE

As we continue on our ambitious patient engagement effort, we realize that the data our community generates must lead to solutions, each tailored to a person's unique combination of medical, psychosocial, and behavioral needs.

This is the basis for precision medicine, and T1D Exchange initially invested in the concept to build our Biobank, a collection of biological samples from 2,200 patients, gathered from eight different clinical studies related to type 1 diabetes. Over the last two years, we have coupled those samples to individual patient health data. In September, we crowned those efforts with the launch of a new user-friendly portal that allows scientists to obtain both samples and data from different studies simultaneously. Searching is as easy as online shopping, and we have marketed the resource to help researchers discover the genetic underpinnings of disease, or biomarkers to facilitate diagnosis and treatment.

> IN SEPTEMBER, WE LAUNCHED OUR BIOBANK, A USER-FRIENDLY PORTAL THAT ALLOWS SCIENTISTS TO OBTAIN BOTH SAMPLES AND DATA FROM DIFFERENT STUDIES SIMULTANEOUSLY.

T1D EXCHANGE UNVEILED ITS QUALITY IMPROVEMENT PLATFORM, EXTRACTING DATA FROM THE RECORDS OF UP TO 24,000 PATIENTS.

As we continue to provide these tools for precision medicine, we also aim to personalize care. For that, we need data from population health studies. These provide the basis for assessing where any given patient falls on a larger spectrum, and a benchmark for what he or she might need going forward.

A growing body of evidence backs up the notion that traditional clinical trial data which supports population health can be enhanced by data collected from the "real-world," sources that include de-identified electronic medical records. In fact, the Food and Drug Administration recently recognized the utility of such data to generate so-called real-world evidence, defined as "clinical evidence about the usage and potential benefits or risks of a medical product that emerges from a robust analysis of real-world data."

In that vein, T1D Exchange this year unveiled its Quality Improvement (QI) platform, designed in partnership with 10 clinics in our QI Collaborative. I am happy to report that the platform is now extracting data from the records of up to 24,000 patients with type 1 diabetes who are visiting these clinics. We mapped data from four of the 10 QI sites and compared these results to more traditional clinical and laboratory study data. Preliminary results suggest that the overall clinic population is faring differently than those participating in formal clinic trials.

As we enter 2019, we are adding data from more sites to the pool, streamlining collection, and deepening analysis to obtain actionable real-world evidence. This will answer fundamental questions about type 1 diabetes population health. It will also launch our effort to establish a framework for using clinic-derived patient data to conduct pragmatic trials and traditional clinical research.

ACHIEVING THE HIGHEST STANDARDS OF CARE AND ACCESS

As we continue to add clinic-derived data to our QI pool, we aim to create a body of real-world evidence to drive medical decision-making. This evidence can also set more realistic standards for best practices in the clinic, influence policy, and possibly improve affordability of care.

Toward this end, we fashioned our 10-clinic Quality Improvement Collaborative into a unique model for effectively improving care for people with type 1 diabetes.

The Collaborative, a close-knit group of providers, set up metrics to track the results of small changes that they make in their daily practices, sharing their learnings at biannual sessions.

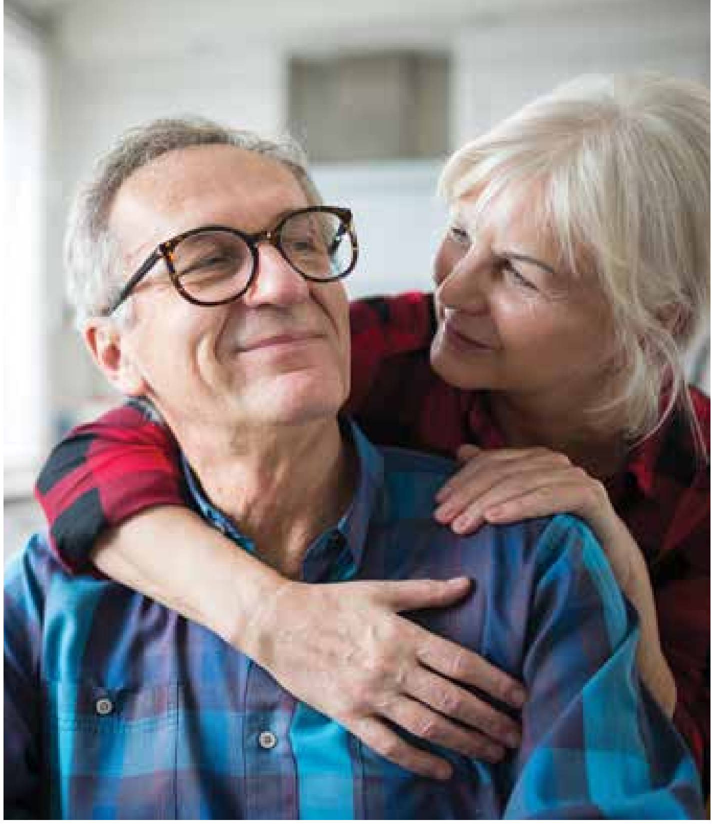
This year, the major targets of the Collaborative have been addressing patients' mental health and reaching high-risk populations. I am excited to report the impact of these efforts, including:

- more vigilant depression screening
- better-than-expected increases in the use of continuous glucose monitoring
- attempts to overcome barriers that patients cite as hampering them from seeking/getting care.

We are also buoyed by the success of this year's two QI Collaborative learning sessions, during which participants met in Cincinnati, Ohio in May and Kansas City, Missouri in November. Members experienced powerful presentations about insulin affordability, taking home resources to share with patients that can help them find ways to pay for insulin, for example.

The Collaborative took a lesson in quality improvement from nephrologist David K. Hooper, MD, MS, Medical Director of Kidney Transplantation at Cincinnati Children's Hospital Medical Center in

THE OBJECTIVE IS TO BRING TOGETHER ENTREPRENEURS, INVESTORS, INDUSTRY REPRESENTATIVES, AND GOVERNMENT OFFICIALS WORKING IN THE TYPE 1 DIABETES SPACE TO FIND, FOSTER, AND FUEL INNOVATION.



Ohio. He spoke to the group about his assessment that identifies barriers to compliance. Inspired, the QI Collaborative created its own barriers assessment to understand why type 1 diabetes patients struggle to regularly check their blood glucose. Collaborative members are now testing the assessment and planning novel interventions in their home clinics.

In addition, T1D Exchange made an impact on patient access by helping a team of leading diabetes care and research organizations to provide critical diabetes supplies to regions impacted by Hurricanes Harvey, Irma, and Maria. We are thrilled to note that our efforts—as part of the Diabetes Emergency Relief Coalition—won the American Society of Association Executives 2018 Summit 'Power of A' Award, the organization's highest recognition for exemplary commitments to solving problems and creating a stronger world.

DIRECTING INNOVATION TOWARD NEED

Because innovation is so pivotal to advancing therapies that do more than just promise to improve outcomes and care, we hosted our second T1D Exchange Diabetes Innovation Challenge this May.

I am pleased to report that the Challenge garnered 60 proposals from 17 countries around the world, drawing innovators from Canada, Brazil, the United Kingdom, France, Germany, Israel, China and India, among others. Not only did the prizes and accolades help jump-start the careers of budding research entrepreneurs, but the event itself simulated activity within—and so strengthened—the T1D Exchange ecosystem of industry, entrepreneurs, and investors throughout the diabetes community.

Testifying to the long-term impact of the event, our 2016 Challenge alumni are still reporting continued success. For example, Admetsys—a Boston-based company that developed an algorithm linked to a device for blood glucose regulation in hospitals—has currently completed three successful clinical trials and aims to receive FDA approval for the technology within the year.

As we look forward to the next Challenge in 2020, we aim to expand it into a more robust partnering and networking opportunity. The objective is to bring together entrepreneurs, investors, industry representatives, and government officials working in the type 1 diabetes space to find, foster, and fuel innovation.

We will also work to connect Challenge participants to our T1D Exchange Glu community and other sources of data. This will create a direct and unprecedented exchange of ideas and information between innovators and people with diabetes, and results will ultimately improve outcomes. Product development will better match patient needs and individuals with diabetes will feel the hope and reassurance that researchers are working diligently on solutions that matter.

CONCLUSION

T1D Exchange has successfully moved through its transformation into a research organization, producing real-world data in-house. It has now built the means to not only capture patient data (both directly and indirectly) but also to harness its power to answer the questions that are most relevant to the type 1 diabetes community. We will drive innovation toward the medications, devices, and procedures that will make a difference in people's lives.

With your support, we can seize the opportunity that this era of big data provides and use it to form a body of real-world evidence that will impact our community. It is only by joining forces that we can ultimately make a difference in the lives of individuals with type 1 diabetes and the organizations working hard to find better solutions for that community.

ENGAGING PATIENTS IN RESEARCH

FROM THE T1D EXCHANGE CLINIC REGISTRY

As always, T1D Exchange has positioned patients at the heart of our research efforts. In 2018, we continued that focus with a wealth of insightful information from our T1D Exchange Clinic Registry and Patient-Centered Research. One point of emphasis this year was glucagon, addressed in two different studies that yielded provocative results.

A HIGH FOR GLUCAGON

It appears that mini-dose glucagon (MDG) can prevent exercise-induced hypoglycemia in people with type 1 diabetes. In fact, results from the T1D Exchange Clinic Network, collected by the Jaeb Center of Health Research, show that glucagon intervention may result in less subsequent hyperglycemia, as compared to ingestion of carbohydrates, which has traditionally been used to counter the blood sugar effects of aerobic exercise.

The news brings a welcome alternative to the type 1 diabetes community, for whom exercise presents unique challenges due to the risk of exercise-induced hypoglycemia and the complexity of managing that condition. Still, regular physical activity and structured exercise are associated with lower HbA1c levels and reduced prevalence of diabetes complications, such as retinopathy—not to mention the sense of wellness from building fitness!

For the study, 15 physically active adult individuals with type 1 diabetes—all on continuous

THE STUDY CONCLUDED THAT GLUCAGON IS A GOOD ALTERNATIVE TO THE INGESTION OF CARBOHYDRATES TO PREVENT EXERCISE INDUCED HYPOGLYCEMIA

subcutaneous insulin infusion or "pump" therapy—engaged in four 45-minute morning exercise sessions, each with a different intervention. After fasting, participants completed all of the following, one per session: walking briskly on a treadmill after having had their basal insulin reduced by half, ingesting 40 g oral glucose tablets, receiving 150µg subcutaneous MDG (G-Pen Mini, provided by Xeris Pharmaceuticals), or no intervention.

Results showed that during exercise and its early recovery, participants' plasma glucose increased slightly with MDG. Blood sugar increased more with glucose tablets and decreased with control or insulin reduction.

Whereas six of the participants experienced hypoglycemia during control sessions, none did so after receiving glucose tablets or MDG. On the other end of the spectrum, five of the participants experienced hyperglycemia with glucose tablets and only one did so with MDG.

Overall, the T1D Exchange Mini-Dose Glucagon Exercise Study Group concluded that glucagon is a good alternative to the ingestion of carbohydrates to prevent exercise induced hypoglycemia, in part because MDG produced less episodes of subsequent hyperglycemia, post intervention. Glucagon also won favor because it can be administered at the time of exercise and avoids additional caloric intake at odds with body weight goals.

A LOW FOR GLUCAGON

Despite the promise of these glucagon therapies, T1D Exchange researchers showed in October that many individuals with type 1 diabetes are not making use of the blood sugar raising hormone, which by many is viewed as useful only for emergencies. After analyzing 322 online surveys completed by people with type 1 diabetes or their caregivers, our patient-centered research team found that more than a third of respondents did NOT have a current glucagon prescription. More troubling, only 18 percent of the 90 adults who had received glucagon reported that it was administered problem-free.

Three more key findings from the study

- Just 85 percent of adults with type 1 diabetes said they had been prescribed glucagon by a healthcare provider, compared to 100% of the surveyed caregivers who said their child had been prescribed glucagon.
- Only 71 percent of adults with type 1 diabetes said they had been educated about how to use glucagon in an emergency situation.
- Just over half of adults (51%) with type 1 diabetes reported treating severe hypoglycemia with something instead of glucagon.

While such findings suggest the need for better standardization of glucagon prescribing practices and education on glucagon use, they also suggest that improved rescue kit design might increase the use of glucagon in critical situations.

The study, conducted in collaboration with Baylor College of Medicine, was funded by Zealand Pharma and published in Clinical Diabetes.

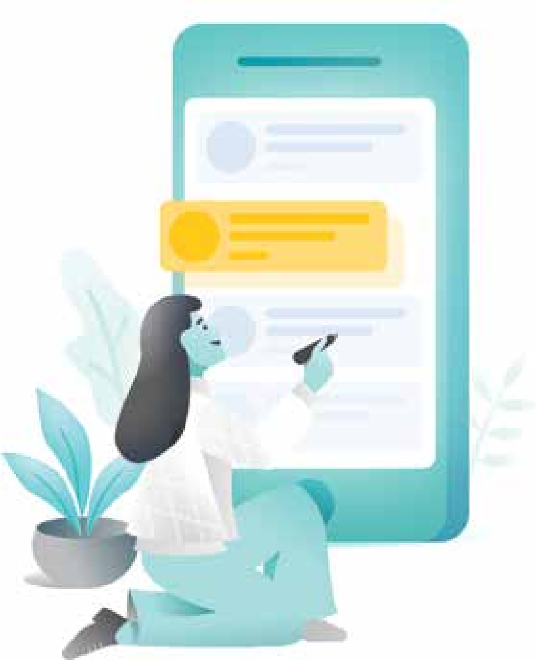
NEW T1D EXCHANGE REGISTRY LAUNCHES

We are pleased to report that in December, T1D Exchange opened its novel T1D Exchange Registry for early enrollment. The effort stems from the need for a web-based platform to engage people with type 1 diabetes more directly in research and connect their efforts to discovery and innovation that may affect their daily lives.

The T1D Exchange Registry is a longitudinal, significant, and accessible data set for type 1 diabetes. Researchers will collect data annually and enable studies that are otherwise difficult to conduct. The new Registry will also become a powerful and valuable tool aimed at accelerating discovery and drug development, one that can be used by industry partners, academic partners, and internal research teams.

Some details: In March, we officially closed the T1D Exchange Clinic Registry—run in collaboration with the Jaeb Center for Health Research—and began transitioning participants into our new web-based model. This will allow previous Clinic Registry participants to bring their data from the last five years of participation to our new T1D Exchange Registry.

As we move into 2019, we are expanding recruitment for the T1D Exchange Registry, as well as transitioning in those who were part of the original Clinic Registry.



MORE FROM THE T1D EXCHANGE CLINIC REGISTRY

CGM USE IS RISING, BUT SO ARE HBA1C LEVELS

THE STUDY

Researchers described patterns in HbA1c levels and use of diabetes technology over five years.

THE TAKEAWAY

CGM use quadrupled over the five-year period, yet HbA1c levels did not drop and, in fact, increased over that time, especially in adolescents and young adults.

YES, PEOPLE WITH TYPE 1 DIABETES DO DRINK

THE STUDY

936 adults with type 1 diabetes provided information about their drug and alcohol use.

THE TAKEAWAY

Nearly two thirds of respondents said they drank alcohol in the last month, and the rate of drug and alcohol use among adults with type 1 diabetes was the same or higher than that of the general population.

OBESITY IN KIDS WITH TYPE 1 DIABETES

THE STUDY

Researchers analyzed data from 11,513 children with type 1 diabetes from Australia, Austria, Germany, and the U.S. to see how their Body Mass Index (BMI) scores changed over time.

THE TAKEAWAY

Most of the children maintained a steady BMI, but obese children with type 1 diabetes in Australia actually lowered their BMI. Ethnic minority and high HbA1c levels were related to higher BMI scores over time.

DOES A CHANGE IN HBA1C GUIDELINES ACTUALLY RESULT IN LOWER HBA1C LEVELS?

THE STUDY

After the American Diabetes Association lowered its recommended HbA1c target level for children with type 1 diabetes, researchers examined HbA1c levels before versus after the switch.

THE TAKEAWAY

In children 6-17 years old, HbA1c levels were higher in the post-change group, as compared to pre-switch. Children using a CGM were more likely to meet HbA1c targets than those not using a CGM; children using both a CGM and insulin pump were most likely to meet HbA1c targets.

DIAGNOSIS AS A CHILD VERSUS AN ADULT

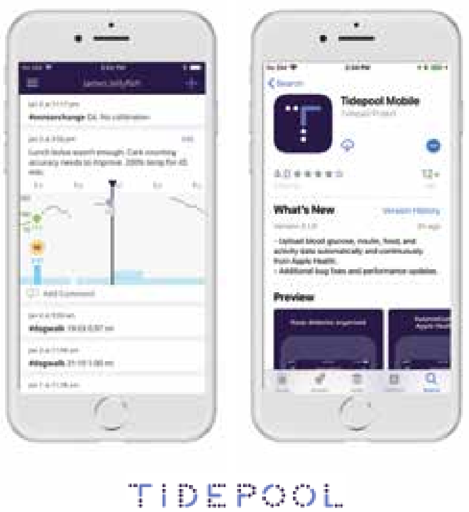
THE STUDY

Researchers compared diagnosis, treatment, and adverse medical outcomes of people with type 1 who were diagnosed as adults versus children.

THE TAKEAWAY

Researchers found those diagnosed as children were more likely to be in diabetic ketoacidosis (DKA) at the time of diagnosis. Those diagnosed as adults were more likely to be given oral drugs before diagnosis, likely because they were misdiagnosed with type 2 diabetes.

T1D EXCHANGE JOINS FORCES WITH TIDEPOOL

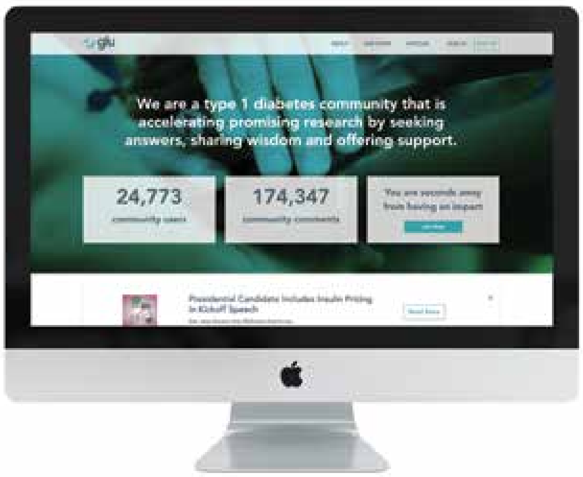


In November, T1D Exchange and Tidepool opened enrollment for the first-ever study of the impact of mild fluctuations in blood glucose—those that fall outside the normal range, resulting in either hypoglycemia or hyperglycemia. While every person with type 1 diabetes regularly experiences these moderate highs and lows in glucose levels, there has been very little research focused on how these fluctuations affect the patient's health, daily life, and long-term outcomes.

The study will leverage Tidepool's ability to capture data from nearly every glucose monitoring device on the market and T1D Exchange's capacity to reach the patient community and engage individuals directly in research.

AN EXTREME MAKEOVER

In November, T1D Exchange donned an entirely new look, showcased by a brand-new website, T1DExchange.org. Alongside a similarly revamped T1D Exchange Glu site, the two portals feature cutting-edge connectivity to better serve the type 1 diabetes community. In concert, the two sites act as a visually compelling hub to bring users in and allow them easy access to our rapidly advancing data-collection platform. The idea is to position patients at the forefront of our organization, while giving them, their providers, and research innovators the resources to succeed.



We are a type 1 diabetes community that is accelerating promising research by seeking answers, sharing wisdom and offering support.

MORE FROM THE T1D EXCHANGE PATIENT-CENTERED RESEARCH TEAM

THE UTILITY OF HALF-UNIT INSULIN PENS

THE STUDY

The PCR team surveyed people with type 1 diabetes about their use of half-unit insulin pens, which can deliver less than one-unit doses.

THE TAKEAWAY

Those who used half-unit pens reported less anxiety, as compared to full dose pens. Providers should consider different insulin delivery methods to help patients achieve narrower blood glucose target ranges.

PATIENTS ARE SATISFIED WITH TREATMENT EVEN WITH GLUCOSE VARIABILITY

THE STUDY

Researchers utilized the CGM data of T1D Exchange Glu members to test whether glucose variability impacted insulin treatment satisfaction or impaired work productivity and daily activity.

THE TAKEAWAY

People who used CGMs still experienced episodes of hypoglycemia when using their devices. Yet, these individuals recognized and tolerated the risk for hypoglycemia, likely because they more often met treatment goals.

MEDICARE FALLS SHORT ON INSULIN PUMPS

THE STUDY

The PCR team surveyed individuals on Medicare about insulin pump coverage.

THE TAKEAWAY

Approximately half of adults cited problems with Medicare coverage. The majority also cited the high costs of pumps and supplies as barriers to access. This study argues the need for easier access and better coverage of insulin pump therapy under the Medicare program.

PATIENTS AND PROVIDERS AT ODDS

THE STUDY

Patients and providers were both surveyed about the challenges associated with pump therapy.

THE TAKEAWAY

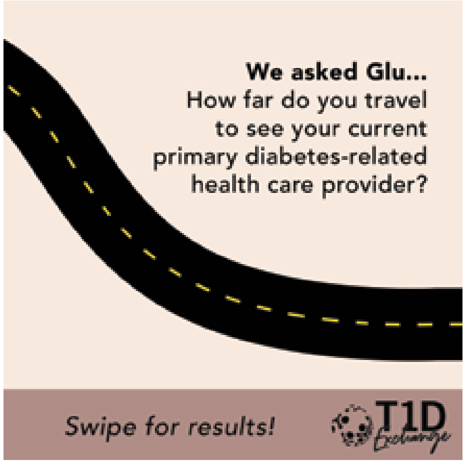
Patients said that they stopped using insulin pumps because they experienced elevated blood sugar levels. Providers attributed discontinuation of insulin pumps to high out-of-pocket cost and lack of insurance coverage. The study points to the need for better patient-provider communication and more individualized treatment.

REACHING A NEW COMMUNITY VIA PICTURES

In November, we celebrated Diabetes Awareness Month with our campaign #YouToldGlu: 30 Facts, 30 Days. We created Instagram graphics daily from our Glu community's responses to T1D Exchange Glu Questions of the Day. The team achieved success with a striking 14% rise in Instagram followers in one month, along with significant growth on our Twitter, LinkedIn, and Facebook channels. Finally, we coupled the campaign to November's Giving Month, scoring a record number of new donors to support our research and innovation efforts for people living with type 1 diabetes.

We asked Glu...
When are you most likely to forget to bolus?

We asked Glu...
What type of exercise do you find most difficult for blood glucose management?



We asked Glu...
How far do you travel to see your current primary diabetes-related health care provider?

We asked Glu...
People with type 1 diabetes, are you on medication(s) to treat a mental health diagnosis?

We asked Glu...
Have you ever contacted an insulin company about a prescription-assistance (cost-savings) program?

We asked Glu...
Does your healthcare provider ask about how you treat your lows (what you eat, when you start treating, etc.)?

OUR CAMPAIGN, #YOUTOLDGLU: 30 FACTS, 30 DAYS, ACHIEVED GREAT SUCCESS WITH A STRIKING 14% RISE IN INSTAGRAM FOLLOWERS IN A SINGLE MONTH.

ENHANCING AND PERSONALIZING CARE

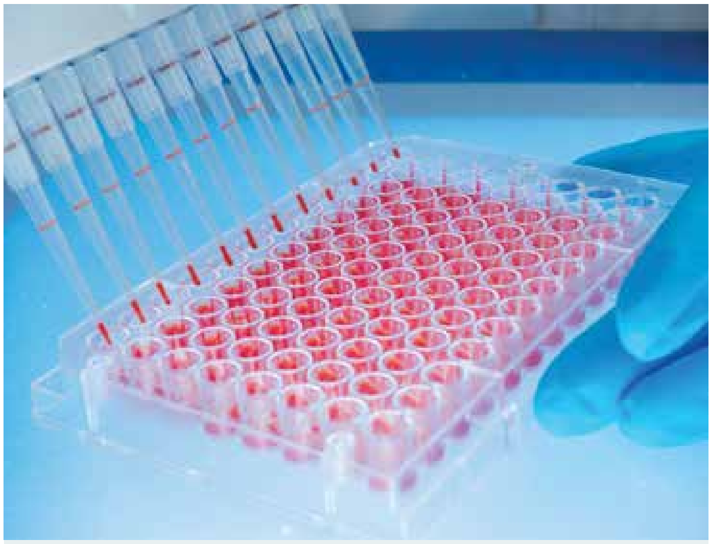
NEW BIOBANK PORTAL LAUNCHES

Advancing our goal to personalize diagnosis and expand understanding of type 1 diabetes, the T1D Exchange in December launched its Biobank's user-friendly portal.

The way in which researchers can now search, choose, and request samples is similar to shopping online. It's simple:

- Register for an account
- Browse the sample collection
- Add samples of interest into a shopping cart for request
- Submit an online Sample Request form for approval
- Receive your samples, shipped to your specifications

Researchers are already using our samples to advance our understanding of type 1 diabetes and search for new tools for diagnosis and monitoring of disease progression (see sidebars: "Uncovering a Molecular Story of Disease" and "Helping to Resolve a Longstanding Blood Sugar Question").



HELPING TO "RESOLVE" A LONGSTANDING BLOOD SUGAR QUESTION

For perhaps the first time ever, researchers are trying to standardize the definition of hypoglycemia and its aftereffects. Hypo-RESOLVE (Hypoglycaemia – Redefining SOLutions for better liVEs) is a 4-year, €26.8 million ($31.3 million USD), European-led research effort aimed at defining hypoglycemia.

The Hypo-RESOLVE team, led by Stephen Gough, PhD of Novo Nordisk A/S, determined that there were gaps in expertise on the project and reached out to other partners, including T1D Exchange. Our Biobank team has agreed to provide CGM hypoglycemia study datasets and biological samples/associated data from the Severe Hypoglycemia study.

"The Biobank was in fact created to support impactful projects such as this," says Biobank Director Wendy Wolf, PhD.

NEW T1D EXCHANGE QUALITY IMPROVEMENT (QI) PORTAL LAUNCHES

Controlled, randomized clinical trials, the hallmark of medical research, offer a great deal of information on drug and device safety and efficacy. However, the very constraints that position clinical studies as the gold standard of medical innovation also limit their utility in assessing the factors that exist in real-world situations.

Thus, we are excited to announce the launch of our new T1D Exchange Quality Improvement (QI) portal, created to bridge the gap between clinical study data and those collected by nontraditional means, such as electronic health records (EHR). In its first phase, four clinics in our QI Collaborative have uploaded EHR and other data from 10,000 patients who are visiting clinics. We are now mapping that data and feeding it into reports with filtering and customization features.

OUR REAL-WORLD, CLINIC-DERIVED RESULTS SHOW THAT CGM USE IS NOT IMPROVING HBA1C LEVELS, AND LESS SO THAN CLINICAL TRIAL DATA HAD PREVIOUSLY DEMONSTRATED.

Our portal is built to ensure standardization of data among clinics. This will allow us to compare clinic performance quickly and efficiently for benchmarking and quality improvement efforts. Our customized reports will also allow users to compare their own data against the Collaborative average.

Even more important, the anonymized data is streaming in from all patients who are visiting the clinic, not simply those who self-select to participate in a clinical trial. This approach, more in tune with real-world data collection, sidesteps much of the hypothetical bias that self-selection causes. Our early results bear this out.

Within our member clinics, we tracked the HbA1c levels of individuals either using or not using CGM. When we compared this data to that which emerged from the T1D Exchange Clinic Registry (a voluntary cohort that consented to participation), our real-world, clinic-derived results show that CGM use is not improving HbA1c levels, and less so than clinical trial data had previously demonstrated. In fact, in particular subpopulations, HbA1c levels are actually rising, even with increased CGM use.

As we refine the data collection and analysis and expand data collection into more clinics, we expect even greater insights to emerge.

UNCOVERING A MOLECULAR STORY OF DISEASE

In a study published in December, investigators at the Indiana University School of Medicine and the T1D Exchange Residual C-peptide Study Group reported that almost all participants with long-standing type 1 diabetes retained the ability to secrete proinsulin, an incompletely processed form of insulin. This included a surprising majority (89.9%) of individuals with low levels of C-peptide, a molecule that is produced when proinsulin is processed into insulin.

Investigators long believed that type 1 diabetes leads to the complete destruction of insulin-producing beta cells, and therefore the full loss of insulin production. However, a body of recent evidence has shown that the majority of people with type 1 diabetes actually maintain residual beta cells that do function, as measured by C-peptide production, for a very long time post-disease onset.

This study adds to that evidence. Results show that not only C-peptide but also proinsulin may function as testaments to that residual beta cell function. The results, generated in part from T1D Exchange Biobank data and samples, further suggest a hierarchy of beta cell function and a story (marked by C-peptide and proinsulin expression) of how type 1 diabetes might be progressing for some.

Model of a pancreas

POPULATION HEALTH: IT'S ABOUT THE DATA

A Q&A WITH SANJEEV MEHTA, MD, MPH

A pediatric endocrinologist by training and "IT guy" at heart, Dr. Sanjeev Mehta, Joslin Diabetes Center's Chief Medical Information Officer and Director of Quality, joined the T1D Exchange Quality Improvement Collaborative to help design and implement its novel IT platform. Here, he looks out at the landscape of big data in medicine and offers insights into how it might best be captured to enhance care for individuals living with type 1 diabetes.

QUESTION

OVER THE LAST DECADES, WHAT CHANGES HAVE YOU SEEN WHEN IT COMES TO HEALTH DATA?

ANSWER

We went from lack of readily available data in paper-based medical records, to a paucity of key clinical information in electronic health records (EHRs). For me at Joslin, the evolution has been about how I can get access to discrete, systematically captured data where you have extremely strict criteria for what can and cannot be entered. Basically, we are trying to get to the point where our EHR is viewed with that level of sophistication yet deployed in a manner that isn't burdensome for providers during their routine clinical encounters.

QUESTION

ARE WE NOW BETTER ABLE TO COLLECT STANDARDIZED DATA OUTSIDE OF A CONTROLLED LABORATORY OR CLINICAL TRIAL?

ANSWER

It depends. This whole movement to get people access to regulated EHRs has allowed us to conduct some high-level evaluations, such as diabetes prevalence, medication-based treatments, and general health outcomes. But to get to more nuanced questions, such as understanding what are the aspects of care that seem to work for the management of type 1 diabetes, we still have a long way to go.

QUESTION

WHAT NEEDS TO HAPPEN FOR US TO GET THERE?

ANSWER

Everyone is in support of standardization of diabetes-specific data, such as use of technologies and broader glycemic metrics. Our effort here in the T1D Exchange Quality Improvement Collaborative is to say, "Hey, how much standardization can we achieve at these 10 sites and use that experience to scale the solution to other sites?" And after that, the next step is creating clinical standards that can be used and supported by these organizations and institutions.

QUESTION

HOW WILL THE COLLABORATIVE HELP MAKE AN IMPACT ON THESE AND OTHER CHALLENGES IN TYPE 1 DIABETES CARE?

ANSWER

Members are all engaged in the Collaborative, not just because they are smart and believe in it but because they can drive meaningful quality improvement at their organizations. When people start to see the T1D Exchange Quality Improvement portal and realize how they can use the data more to work with populations in their clinics, the whole effort will be quite compelling.

ACHIEVING THE HIGHEST STANDARDS OF CARE AND ACCESS

The T1D Exchange Quality Improvement (QI) Learning Collaborative has long sought to redefine best practices in the clinic in order to improve the quality of care. The Collaborative is a network of 10 diabetes clinics represented by teams of dedicated providers from each location. The Collaborative uses a model in which providers make small changes incrementally in the clinic and then track and share success.

In June, the QI Collaborative presented the findings of their initial work with three poster presentations at the American Diabetes Association's 78th Annual Scientific Sessions, including a poster which described the T1D Exchange QI model itself.

Basically, clinic staff across various centers use patient input and data to identify potential gaps in care. They then collectively conceive of and test interventions that might fill those gaps. The group effort, spread across clinics with wildly different populations and constraints, requires strong relationships and open communication among the participants of the Collaborative.

That effective teamwork became clear as the Collaborative met twice in 2018 to share their learnings.

LESSONS FROM CINCINNATI

In May, the Quality Improvement Collaborative met at Cincinnati Children's Hospital Medical Center (CCHMC). The group gained practical insights from David Hooper, MD, a nephrologist at CCHMC, who spoke about his quality improvement work with the Improving Renal Outcomes Collaborative (IROC).

THE COLLABORATIVE RALLIED FOR THE TESTING OF NEW INTERVENTIONS AND PARTICIPATED IN A FRANK DISCUSSION OF INSULIN AFFORDABILITY.

Dr. Hooper's team had tried to understand why kidney transplant recipients were not taking their anti-rejection medications and emerged with a barriers assessment to highlight patient concerns.

Inspired, members of the T1D Exchange QI Collaborative later tailored this assessment for diabetes. Leading the charge, C.S. Mott Children's Hospital at the University of Michigan created their own evaluation to examine why patients struggled to monitor their blood sugar. Lucile Packard Children's Hospital at Stanford, Children's Mercy Hospital, and SUNY Upstate Medical University quickly followed suit.

Now, Collaborative clinics are testing these barriers assessments and gathering data to choose the most appropriate interventions, particularly to encourage patients who do not use continuous glucose monitors (CGMs) to check their blood sugar at least four times per day.

LESSONS FROM KANSAS CITY

In November, the Collaborative moved west to Kansas City, MO, to rally for the testing of new interventions and participate in a frank discussion about insulin affordability. Two representatives from the National Diabetes Volunteer Leadership Council, an advocacy organization for those living with diabetes, talked about the complexities of the issue, including how and why costs have increased and the impact of those costs on patient adherence.

The presenters—Stewart Perry and Erika Emerson—further provided short and long-term solutions, as well as a call-to-action for those interested in advocating for policy and insurance coverage changes. The Collaborative took away a more in-depth understanding of the complex topic and resources—including a stop-gap, what-to-do, one-pager—for providers to share with patients.

DEBUNKING A MYTH

To address concerns that adult diabetes clinics too often lacked support staff that might be more often found in pediatric clinics, the QI Collaborative took up the issue. It gathered data on the 10 clinics within its ranks, which collectively care for 23,000 people with type 1 diabetes.

The team found that staff diversity differed greatly between the two groups of clinics. Clinics that cared primarily for adults featured about half the diversity in staff roles as pediatric clinics, often lacking personnel such as psychologists and social workers. Armed with this data, officials from some of the adult clinics were able to make the case for diversifying staffing—and were able to actually hire for these roles based on the data.

“THERE’S THIS SENSE THAT KIDS ARE YOUNG; THEY NEED TO BE TAUGHT AND KEEP LEARNING,” SAYS NICOLE RIOLES, DIRECTOR OF THE QI COLLABORATIVE. “WHILE ADULTS DO NOT.”

The QI Collaborative data is debunking this myth.

“If you’re a person with a new disease, regardless of your age, you still need to be taught,” Rioles says. “And people with type 1 diabetes always benefit from support when getting on new devices and technology or managing major transitions in life.”

HELPING PATIENTS TAKE CARE OF THEMSELVES

What to do when you get sick is a question that has long frustrated the type 1 diabetes community. The answers so often conflict. As confused patients keep asking for a definitive tool that they could use to take charge of their own care, the T1D Exchange Quality Improvement Collaborative took up the charge. The process was a lesson in collaboration.

Providers in our QI network took first crack at drafting the resource. They assembled some fundamental medical recommendations. When patients and parents on the QI team saw the result, however, they later stepped in to transform the doctors' advice into something they could embrace as useful in the real world. The result: an effective one-page, how-to resource that parents, patients, or caregivers can post on a refrigerator or medicine cabinet door.

In February 2019, we launched a special campaign to spread the word and share the resource.

What are the symptoms of DKA?

- inability to drink fluids or urinate
- very dry mouth
- "fruity" smelling breath
- nausea, vomiting
- stomach cramps
- flu-like symptoms

T1D EXCHANGE RECOGNIZED FOR DISASTER EMERGENCY RELIEF

As part of the Diabetes Emergency Relief Coalition, T1D Exchange in June received the American Society of Association Executives (ASAE) 2018 Summit 'Power of A' Award for helping provide critical diabetes supplies to regions impacted by Hurricanes Harvey, Irma, and Maria. The award represents the highest recognition for associations that make exemplary commitments to solving problems and creating a stronger world.

BOOSTING DEPRESSION SCREENINGS

WITHIN 18 MONTHS OF IMPLEMENTING INTERVENTIONS, THE TEAM FOUND THAT 60 PERCENT OF ELIGIBLE PATIENTS WERE SCREENED FOR DEPRESSION. MOST RECENTLY, THAT NUMBER HAS RISEN TO 72 PERCENT.

As one of its first initiatives, the QI Collaborative took on depression. A growing body of evidence revealed that untreated depression is associated with poor blood glucose management for people with diabetes. Despite this, depression screening at clinics in general has been spotty.

Within a group of six Collaborative clinics, for example, some clinics were screening most patients for depression and others weren't doing depression screening at all. That meant that, on average, just 10 percent of the eligible patient population in the clinic network were being screened at the time when the Collaborative began to examine this issue.

These six clinics participated in three "learning sessions" and then designed and tested ways to incorporate depression screenings in a way that worked for both patients and clinics. The project boasts unequivocal success. Within 18 months of implementing interventions, the team found that 60 percent of eligible patients were screened for depression. Most recently, that number has risen to 72 percent.

"We're hoping we set that for our benchmark," says Nicole Rioles, Director of the T1D Exchange QI Collaborative "If we can do that for depression, we can do that for many other areas."

Endocrinologist Sarah Corathers, MD, from Cincinnati Children's Hospital at a recent meeting of the T1D Exchange Quality Improvement Collaborative.

DIRECTING INNOVATION TOWARD NEED

THE BUZZ ABOUT INNOVATION GETS LOUDER

In May, T1D Exchange hosted its second Diabetes Innovation Challenge, a world-wide competition to identify, nurture, and fast-track innovative scientific and clinical solutions for diabetes. A record 60 innovators from 17 countries applied for up to $250,000 of cash and in-kind prizes.

More than 150 people gathered for the event on a sunny day at the Royal Sonesta Hotel in Cambridge, MA. Ten finalists presented at a public Pitch Off, judged by an expert panel drawn from the diabetes stakeholder community.

- The winner was Protomer Technologies with its "smart" glucagon, which senses low blood sugar levels and automatically activates to prevent potentially life-threatening hypoglycemia (see sidebar: "Innovation takes on Hypoglycemia").
- Second place went to New York start-up Bonbouton, which designed a smart shoe insole to continuously monitor people with diabetes for foot ulcers that can lead to amputations.

Exponential Growth of the Innovation Challenge from 2016-2018

Sponsors
$678,000
$330,000 (2016)

In-Kind Services
$307,000
15 PROVIDERS
$150,000 / 4 PROVIDERS (2016)

Registrants
196
74 REGISTRANTS (2016)

Countries
17
10 COUNTRIES (2016)

Brand Awareness
18 AWARENESS PARTNERS
17 AWARENESS PARTNERS (2016)

Total Impact

- 60 semifinalists
- $135,000 was distributed among the top three winners
- 2 live pitch-off events, 369 attendees
- 4,000 Online People's Choice votes 3 People's Choice winners
- 9 award recipients
- 7 press releases
- 8,200 Facebook views
- 4,500 Twitter views
- Ad in 6 media outlets generated 1.7M impressions

DATABASE GROWS MORE THAN **522%**, FROM 1,125 NEW CONTACTS TO **OVER 7,000 NEW CONTACTS**

IN JUST TWO SHORT YEARS WE HAVE SEEN THE DIABETES INNOVATION CHALLENGE GROW TO BECOME A SHOWCASE FOR NEW IDEAS AND AN INTERNATIONAL DRIVER OF PROGRESS.

- Metro Boston-based Cam Med took third for an ultra-thin, bandage-like patch pump that has the potential to greatly improve medication compliance and lower costs, especially for patients with challenging medication regimens that involve frequent injections.
- Two People's Choice Winners of online public voting were also named. Autonomous ID of Ottawa, Canada, is working to develop a self-contained biometric identification and monitoring technology called Smart Sole Salvation to support self-care management of diabetes. SciDogma Research of Bengaluru, Karnataka, India, is developing an E-pancreas with a closed loop delivery system.

"In just two short years we have seen the Diabetes Innovation Challenge grow to become a showcase for new ideas and an international driver of progress," said Jay Mohr, president and CEO of Dirigo Therapeutics and a member of the Board of T1D Exchange.

INNOVATION TAKES ON HYPOGLYCEMIA

As individuals with type 1 diabetes know, the pancreas normally releases a peptide hormone called glucagon in response to low sugars, which tells the liver to convert stored glycogen into glucose. However, individuals with type 1 diabetes mysteriously cannot release glucagon. Worse, those who have had type 1 for longer periods of time can lose their ability to sense episodes of low blood sugar. This hypoglycemic unawareness—added to the troubles of glucagon release—equals a very high risk of developing severe hypoglycemia, which can be a cause of sudden death.

Protomer CEO and chemical engineer Alborz Mahdavi set out to tackle the challenge. While working in the laboratory of David Tirrell (the current provost at Caltech) in the early 2010's, Mahdavi began toying with artificial amino acids—the 'Lego blocks' that join to make peptides and proteins. His student thesis won a prize and, more importantly, inspired the idea of engineering peptide hormones to turn on or off in response to glucose.

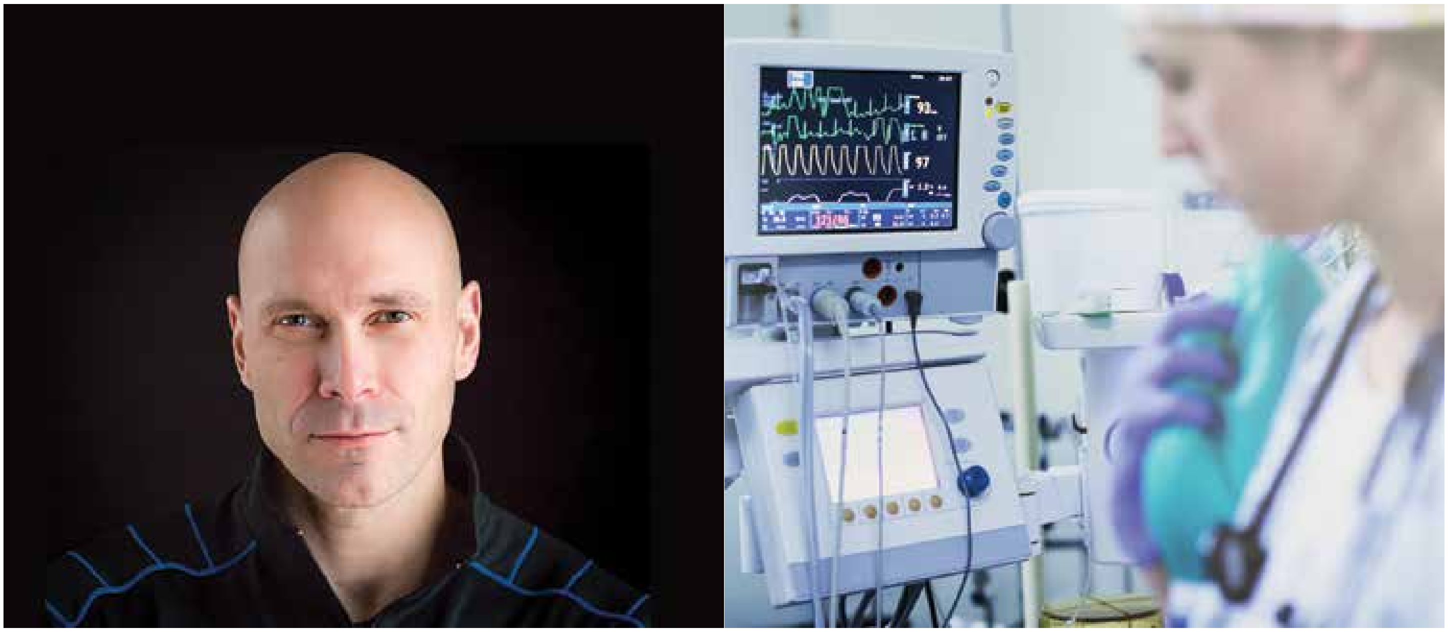
A glucose-responsive glucagon would "eliminate severe hypoglycemia and also allow individuals with type 1 diabetes to be a little bit more aggressive with their insulin injections," says Mahdavi. "We basically fell in the love with the concept."

While a graduate student at Caltech, Mahdavi began working on a "smart insulin." He engineered the insulin to activate only when blood glucose started to rise. Inject it once daily and let it circulate; the insulin could anticipate an episode of hyperglycemia. Once glucose levels returned to normal, the insulin would stop working, but still remain in the body, waiting for the next blood sugar high.

The idea won Mahdavi a Challenge contest in 2013, sponsored by JDRF. The prize money underwrote Protomer's launch. For two years, Mahdavi researched glucose-responsive insulin. In 2016, he scored a $1.5M grant, sponsored by JDRF and Sanofi, focused specifically on glucose-responsive insulins. That technology is now advancing toward pre-clinical development.

Meanwhile, Mahdavi and his team member Jack Hale, a stem cell scientist and Protomer's first employee, are focusing on glucagon. Through his contacts at JDRF, Mahdavi discovered T1D Exchange and decided to enter its 2018 Diabetes Innovation Challenge. His team won first place.

"Honestly, we were going into competition thinking already we won just because we were finalists," he says. "What T1D Exchange does very well is provide a platform for companies to be able to connect with important players in the field."



WHERE ARE THEY NOW?

After scoring second place at the 2016 Diabetes Innovation Challenge, Admetsys inches closer to the market with its artificial pancreas.

The critical care unit is one of the most high-tech locations in any hospital, filled with state-of-the-art medical equipment. Yet many clinicians still monitor patients' blood sugar levels the old-fashioned way—by manually analyzing blood samples and adjusting insulin infusion rates.

This challenge inspired father-and-son duo Tim and Jeff Valk, to launch Admetsys, a company focused on creating an artificial pancreas pump system designed specifically for hospital and surgical care. The Admetsys system is a dual-hormone automated pump system that would automatically adjust insulin and glucagon delivery based on glucose levels. According to Jeff Valk, who serves as CEO of Admetsys, the company's product fills a special niche among automated pump systems by being designed to be part of hospital infrastructure.

Their journey started over a decade ago when Tim Valk, a practicing endocrinologist in Orlando, FL, received a frustrated 3 a.m. phone call from one of his nurses; she lamented that too much staff time was being squandered on the tedious, easily automated task of patient blood sugar management.

"Why don't you fix this?" the nurse demanded, before abruptly hanging up.

Instead of feeling chastised, Dr. Valk felt inspired. He called his son Jeff, an engineer and self-described

"WE LITERALLY GIVE THE HOSPITALS A SOLUTION-IN-A-BOX FOR AUTOMATED GLUCOSE CONTROL," SAYS VALK.

computer "geek", and asked if an artificial pancreas at the bedside would even be possible.
Jeff believed it was. They teamed up with Glenn Robertelli, a medical device expert who previously worked at Johnson & Johnson. The trio soon launched Admetsys, a company with a central mission to bring the world's first critical-care artificial pancreas to the marketplace.

A decade later the company's artificial pancreas is well underway and generating promising results.

It was that promise, identified early on by T1D Exchange and its partners, which enabled Admetsys to win second place in the first Diabetes Innovation Challenge, hosted by T1D Exchange in 2016.

"The event hadn't been done before," says Jeff Valk, now CEO of Admetsys. "But the people who were there had a heck of a lot more commitment than you usually see in events like this."

Indeed, the event was the beginning of the company's relationship with T1D Exchange, which subsequently invested in the company.

The Admetsys system is designed to safeguard critically ill patients by complementing existing hospital infrastructure. In the company's "closed loop" glucose control system, a nurse never once has to visit the bedside to adjust medication. Moreover, Admetsys designed a user-interface so nurses can call up each patient's profile locally or remotely on any screen.

"We literally give the hospitals a solution-in-a-box for automated glucose control," says Valk.

Admetsys has already tested this device in three clinical research studies. The results are encouraging. Results for the third trial have been submitted as an abstract for an upcoming 79th American Diabetes Association Scientific Sessions. The company is currently planning a new, U.S.-based pivotal trial that will be used for FDA approval, and intends to launch another study in Denmark to support approval in Europe.

HOW IT WORKS

A tiny laboratory-on-a-chip is embedded within each diabetic patient's IV line. Every five minutes, that device measures blood glucose levels, sending the data to a bedside monitor. From there, an algorithm determines how much glucose or insulin a patient needs to maintain glycemic control, and the patient's medication levels are adjusted automatically.

MOVING FORWARD TOGETHER

We are thrilled to have shared with you another chapter in the T1D Exchange journey. There is more to come as the new infrastructure we have built and the platforms still in progress begin to yield a new crop of resources, results, and insights that are critical to achieving our mission.

As much as we are proud of our accomplishments in 2018, we know that we have to work harder than ever in 2019 to improve the quality of life for our patient community. The bar is higher—outcomes have not improved despite the deluge of advances in treatment and devices. For some individuals with type 1 diabetes, outcomes have actually worsened.

There remains a dire need for solutions that support better care and day-to-day management of the disease. And, with the average medical expenditures among people diagnosed with type 1 diabetes in the US being 2.3 times higher than for people without diabetes, it is critical to identify disruptive advances that not only improve diabetes management and quality of care but also ease the economic burden of the disease.

WE ARE STEADFAST AND COMMITTED TO MAKING THESE ADVANCES HAPPEN. WITH YOUR HELP, WE CAN.

We are steadfast and committed to making these advances happen. With your help we can.

Let us join together to face the many challenges of this complicated and chronic disease with a steady stream of new ideas, projects, and solutions. We look forward to our continued partnership and thank you for your leadership and continued support; it is only by working together that we can ultimately and meaningfully change lives.

Special thanks to the Leona M. and Harry B. Helmsley Charitable Trust for their steadfast support, enabling us to fulfill our mission to advance pivotal work for the diabetes community.

And thank you to our partners at the Jaeb Center for Health Research without which we would not be celebrating the success of the T1D Exchange Clinic Registry, proffering crucial data to advance academic research, industry, advocacy and policy efforts.

WE THANK OUR PARTNERS, MEMBERS, AND SPONSORS

Abbott Diabetes Care Inc.

Abvance Therapeutics

Admetsys

American Diabetes Association

Barbara Davis Center/UC Denver (pediatric and adult clinics)

Becton Dickinson and Company

Bigfoot Biomedical

Children's Mercy Hospital

Cincinnati Children's Hospital Medical Center

C.S. Mott Children's Hospital/ University of Michigan

Dexcom, Inc.

Diabetes Emergency Relief Coalition

Eli Lilly and Company

Insulet Corporation

JDRF

Lexicon Pharmaceuticals

Lucile Packard Children's/ Stanford University

Nationwide Children's Hospital

Sanofi S.A.

SUNY Upstate/Joslin Diabetes Center

Tandem Diabetes Care

Texas Children's Hospital

Tidepool

University of Pennsylvania

Xeris Pharmaceuticals

Zealand Pharma

And members of our QI Collaborative Patient/Parent Advisory Board and Data Governance Committee; our Biobank Scientific Advisory Committee; Our Clinical/ Research Advisory Committee and our Patient/Caregiver Advisory Committee for their insights and dedication to our mission.

Finally, thanks to Close Concerns, Diatribe, Beyond Type 1, and the College Diabetes Network for their partnership in reaching out to the type 1 diabetes community.

American Diabetes Association®

αβ ABVANCE THERAPEUTICS

admetsys ADVANCED METABOLIC SYSTEMS

Abbott Diabetes Care

BD

bigfoot BIOMEDICAL

dexcom

DDRC Diabetes Disaster Response Coalition

THE LEONA M. AND HARRY B. HELMSLEY CHARITABLE TRUST

Insulet Corporation

JCHR JAEB CENTER FOR HEALTH RESEARCH

JDRF IMPROVING LIVES. CURING TYPE 1 DIABETES.

Lexicon pharmaceuticals

Lilly

SANOFI

TANDEM® DIABETES CARE

TIDEPOOL

xeris PHARMACEUTICALS

ZEAL& ZEALAND PHARMA

OUR BOARD OF DIRECTORS

Dana Ball

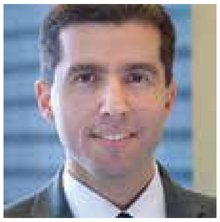
Co-Founder of T1D Exchange

Dominque Hurley

Vice President, Strategic Partnerships and Innovation, HealthVerity

Jack Collins

Sr. Vice President of Finance, P&B Intermodal



Haydon Keitner, JD

Partner, Nixon Peabody LLP

Cristina Csimma, PharmD, MHP

Board of Directors, Chair Nominating and Governance Committee, Neuralstem, Inc.

Jennifer McCabe, JD

Attorney, Outside General Counsel

Jay Mohr

President and CEO, Dirigo Therapeutics

Keith Ryan, Chairman

Founder and President, Geneous Biomedical Advisors, Inc.

Marijane Norris-Geary

President, Yozell Associates

Dara Schuster, MD

CEO, T1D Exchange, Inc.

Deborah Pine

Executive Director, Center for Women and Business, Bentley University

David Walton

CEO and Founder, Chronicare

11 Avenue de Lafayette
Boston, MA 02111
Phone: 617-892-6100
info@t1dexchange.org
t1dexchange.org