How T1D Exchange is improving diabetes care through its collaborative approach to research

Henry Anhalt

Article points

1. T1D Exchange was established in the US in 2010 to help the clinical and research community work globally to improve the quality of care in type 1 diabetes.

2. An integrated model, which includes a clinic registry of 26 000 people with type 1 diabetes, has been developed to improve access to data and accelerate research and discovery.

3. T1D Exchange is collaborating with others in the global research community to work towards a common standard of care improvement.

Key words

- Patient registry
- Research and discovery
- Type 1 diabetes

Authors

Henry Anhalt is Chief Medical Officer, T1D Exchange, Boston, USA

Prior to 2010, there had been no large-scale registry in the US of people with type 1 diabetes. This presented challenges in executing projects, creating programmes and conducting studies. In response to this, the T1D Exchange was established. This article outlines components of the integrated model that it developed to accelerate the pace of research and discovery. Some of the T1D Exchange's successes, including those relating to the improved care of children and young people with type 1 diabetes will be discussed. The article also considers whether a collaborative approach could result in a global standard for quality improvement in clinical care.

Despite many advances in the treatment of type 1 diabetes, most patients struggle to meet HbA_{1c} goals, insulin replacement is still the only effective treatment and living with the condition remains a tremendous quality-of-life and financial burden. This invites some important questions to be posed:

- Have researchers struggled to provide meaningful discoveries and solutions because of the complexity of the condition or because they don't have access to the right resources and data at the right time?
- Has industry shied away from pursuing research due to the condition's complexity and the size of the population, or is the cost too high and the timelines too long to develop and commercialise new treatments?
- Have healthcare providers focused their patients on unattainable standards of care with today's treatment options?
- Is the job of approximating how a pancreas naturally produces insulin and responds to blood glucose simply too difficult for most people with type 1 diabetes to successfully manage?

With these questions in mind, can patient registries engage industry and the clinical research community to facilitate translational solutions that can improve the quality of care in people with type 1 diabetes globally? Proof of concept already exists in large-scale population and clinical centre-based patient registries, including the National Paediatric Diabetes Audit (NPDA; England/Wales), the DPV Scientific Initiative (Austria/Germany) and the Hvidøre Study Group (Denmark), that have benefited clinical, translational and epidemiological research.

In the US, no similar, large-scale registry of type 1 diabetes patients had been established before 2010. This resulted in inefficiencies in recruitment, and duplicative research competing for limited funding.

A new model

T1D Exchange was born out of the need to build a dynamic, multi-purpose, real-world patient data platform. While a patient registry was central to the approach, the vision went further. To help researchers overcome the many obstacles required to accelerate all aspects of drug and device development, the model offers easy access to aggregated clinical, biological, patient-reported outcomes and electronic health record data, all while fostering collaboration among patients,

physicians, researchers and industry.

The model includes the following components:

- **Clinic Registry** comprising more than 150 patient parameters, including both patient-reported and electronic health record data from over 26 000 well-characterised type 1 diabetes patients ranging in age, at the time of enrolment, from under 1 to 93 years. Participants span a wide range of demographic parameters, socio-economic statuses and care regimens. The Registry has become the most credible type 1 diabetes data set in the US.

- **Online patient and caregiver community Glu** (www.myglu.org) consists of over 13 000 patients and caregivers who find peer-to-peer support and educational material, and can access and participate in real-time research. The Glu cohort includes a collection of patient-reported outcomes and is made up of approximately 0.60% (7700) of the US population of type 1 diabetes patients. Glu is a key resource for real-world patient insight and research.

- A unified **clinic network** of more than 230 collaborating clinicians and coordinators from over 75 paediatric and adult sites in the US, which sees more than 150 000 unique type 1 diabetes patients.

- **Biorepository** with biosamples from over 1800 unique participants with clinical, demographic and study-derived information. A Living Biobank with over 1700 consented individuals supports research requests that can't be met through the existing biorepository collection.

As a resource, T1D Exchange combines well-characterised data, biosamples, expertise and patient perspectives into an effective, single-access programme (*Figure 1*).

Building upon success

T1D Exchange has demonstrated that this single-access model is, in fact, dramatically improving the speed and success of study development, patient recruitment and study execution. Since 2009, T1D Exchange has gone from a vision to a widely recognised resource in the type 1 diabetes medical and research community globally.

The Exchange has completed more than a dozen secondary observational manuscripts and several

intervention studies, with eight studies currently running and six in development. It also provides research support for an additional eight studies not directly run by the Exchange. These innovative studies include:

- **A novel glucagon rescue study.** In order to understand the unmet need with existing intramuscular glucagon therapy, a survey in 126 participants from the Glu community was completed over 4 days. This data was presented by an industry partner to the US Food and Drug Administration to demonstrate the need for an improved glucagon product. Preliminary clinical trial data from T1D Exchange has demonstrated that a new, user-friendly, needle-free nasal glucagon delivery system is as effective as the existing injected form of glucagon in adults. The product, known as Glucagon Nasal Powder and developed by Locemia Solutions, may represent a major step in advancing a treatment that has been largely unchanged for about 25 years (Rickels et al, 2015).

- **A large, ground-breaking, longitudinal C-peptide study**, which collected a foundational set of more than 1000 unique samples, and generated findings that indicated 1 in every 3 people with type 1 diabetes produces insulin years post diagnosis, rendering significant clinical and health policy implications in the US (Davis et al, 2014).

- **A study of older adults (60 years and over) to shed light on severe hypoglycaemia**. Building from insights gained from the T1D Exchange Registry data, researchers noted that incidence of seizure and loss of consciousness due to severe

Figure 1. The four key components of T1D Exchange's single-access model.

1. To improve the quality of care for people with type 1 diabetes, T1D Exchange seeks to collaborate with others in the global research community.

2. Several collaborations, including with the Diabetes Patienten Verlaufsdokumentation in Germany and Austria and the National Paediatric Diabetes Audit in England and Wales, have resulted in interesting data and insights.

hypoglycaemia in older adults was significantly more frequent than previously understood. The researchers observed that older people who had experienced severe hypoglycaemia in the last year spent approximately an hour a day in the hypoglycaemic range and were largely unaware, despite more frequent testing of blood glucose levels (six times per day on average). In the US, older adults experience the most barriers to obtaining test strips and continuous glucose monitoring devices via Medicaid, the largest source of funding for medical and health-related services for people with low income. This study may lead to more evidence-based research with Medicare patients and consequently decrease the risk and incidence of hypoglycaemia.

A global view: Quality improvement toward a common standard

While T1D Exchange is leading a range of translational, observational and interventional studies, each study relates to one goal – to improve the quality of care for people with type 1 diabetes. To achieve this goal, T1D Exchange seeks collaboration with others in the global research community.

Can we create a common standard for quality improvement in clinical care?

It's a bold question that will require collaboration amongst the global research community. Several collaborations have already resulted in interesting data and insights.

Better clinical outcomes in older adults

A multinational study to compare patient characteristics and treatment-related factors associated with better clinical outcomes in older adults was conducted using T1D Exchange and German/Austrian Diabetes Patienten Verlaufsdokumentation (DPV) registries.

Data analysed from adults aged ≥60 years with type 1 diabetes highlighted differences in certain aspects of diabetes management and diabetes complications. Further assessments are needed to better understand the differences to determine if aspects of care can be modified to improve outcomes. Some of the data highlights follow (T1D Exchange compared with the DPV):

- Mean HbA_{1c} levels (60 vs 58 mmol/mol [7.6% vs

7.5%]) and percentage of participants with HbA_{1c} <58 mmol/mol (<7.5%; 55% vs 57%), but more participants had HbA_{1c} <8.5% (86% vs 81%; $P=0.006$).
- Self-monitoring of blood glucose (5.7 vs 4.3 times daily; $P<0.001$).
- Use of insulin pumps (58% vs 18%; $P<0.001$).
- Use of continuous glucose monitoring (15% vs 11%; $P=0.007$).
- Episodes of diabetic ketoacidosis (DKA; 2.0% vs 5.5%; $P<0.001$).

A limitation was the cross-sectional study design. Since data in the T1D Exchange were collected from diabetes centres in the US, they may not be representative of older adults with type 1 diabetes followed in other practice settings (e.g. primary care and nephrology; Weinstock et al, 2015).

Pump use

T1D Exchange has also been researching pump use in collaboration with the DPV and NPDA. The collaborations uncovered the following insights:
- Use of continuous subcutaneous insulin infusion (CSII) has increased over the past decade; however, there is considerable variability among countries in support for and use of CSII. In European countries young children were more likely to be on CSII in contrast to the US where it was more likely in older children. This illustrates the lack of agreement within the medical community on the optimal age and time after diagnosis to begin CSII therapy due, in part, to a lack of substantial empirical evidence (Maahs et al, 2014).
- While use of insulin pumps by children varies greatly between the United States, England/Wales and Austria/Germany, in all three regions, children from minority groups are less likely to use pumps to treat type 1 diabetes. Using data from the registries, a group of researchers analysed 54 767 children and adolescents under 18 years of age with type 1 diabetes to examine how many of these patients were currently using insulin pump therapy. In all three registries, "minority" children (defined by ethnicity in US and England/Wales, and country of birth in Austria/Germany) were less likely to use insulin pump therapy than their non-minority type 1 diabetes peers. Overall, 22.4% of minority children compared with

34.7% of non-minority children used a pump. Among each individual registry, similar results were found: in T1D Exchange, the difference was 29.3% minority vs 50.6% non-minority; in DPV it was 30.9% vs 41.9%; and in England/Wales it was 8.1% vs 14.8% (Rami-Merhar et al, 2014).

These findings underline the need to extract from these data best practices that will improve delivery of diabetes care to all patients with type 1 diabetes.

DKA in children

A multinational comparison of paediatric patients from England, Wales, United States, Austria and Germany included data from 59 191 patients living with type 1 diabetes under 18 years of age in the T1D Exchange (n=13 966), the National Paediatric Diabetes Audit (n=18 963) and the DPV Initiative (n=26 262). DKA was defined as having at least one hospitalisation for a venous pH <7.3 during the prior year.

Overall, researchers found that 5.3% of children had at least one DKA event in the past year with the following differences amongst countries: 6.2% US, 6.0% England, 4.5% Germany, 4.4% Wales, 3.3% Austria.

The risk of DKA was highest in adolescents (14–18 years, 5.8%) compared to younger children (6–10 years, 3.4%). Researchers found that the frequency of DKA increased with longer duration of diabetes, showing 3.5% for less than 2 years' duration, versus 5.9% for those patients living with type 1 diabetes for 2 years or more. Additionally, DKA was more common in girls compared with boys and more prevalent in patients from minority groups. Frequency of DKA was lower in patients on insulin pumps (Warner et al, 2014).

Conclusion: Much more left to do

In the US, T1D Exchange is demonstrating that a single-access model is dramatically improving the speed and success of study development, patient recruitment and study execution. As the organisation gains momentum, we continue to refine our focus on quality improvement and ask ourselves the following:
- Can we design an integrated clinical care and research system in type 1 diabetes where patients and providers work together to choose the best evidence-based care?
- Can we ensure that patients have access to appropriate care and can afford the best tools and therapies for managing their diabetes?
- Can we drive new discoveries as a natural outgrowth of patient care and ensure innovation, quality, safety and value for every type 1 patient?
- Quite simply, how can we improve the lives of people with type 1 diabetes?

While we don't know the answers, we do know that it starts with increased participation – engagement, interaction, collaboration and contribution – among all stakeholders (patient, caregiver, healthcare provider and investigator). Collaborating globally, we can start making the following improvements in real time:
- Patients achieving optimal HbA$_{1c}$ goals.
- Patients enjoying improved quality of life.
- Ease of patient self-management.
- Earlier and more frequent screenings for diabetes complications.
- More appropriate use of medications and monitoring of disease activity.
- Access to affordable care and treatment options.
- Clinician/patient interaction and value proposition.
- Generating new knowledge and discoveries.
- Transactional costs for research and increased planned experimentation.

The vision is bold; the mission is complex. We can only make real achievements for every person with type 1 diabetes when we collaborate, share and work together. We invite you to collaborate with us. ■

"We can only make real achievements for every person with type 1 diabetes when we collaborate, share and work together."

Davis AK, DuBose SN, Haller MJ et al, for the T1D Exchange Clinic Network (2014) Prevalence of detectable C-peptide according to age at diagnosis and duration of type 1 diabetes. *Diabetes Care* **38**: 476–81

Maahs DM, Hermann J, Foster N et al (2014) Insulin pump use in pediatric type 1 diabetes: Multinational comparison with 54,768 pediatric patients from the T1D Exchange (US), National Paediatric Diabetes Audit (England and Wales), and the DPV Initiative (Germany and Austria). Presented at: *40th Annual Conference of the International Society for Pediatric and Adolescent Diabetes (ISPAD)*. Toronto, Canada, 3–6 September

Rami-Merhar B, Maahs D, Warner J et al (2014) Pump use is less frequent in minority youth: transatlantic analysis in three large registries representing Austria, Germany, England, Wales and the United States. Presented at: *50th EASD Annual Meeting* (ePoster 939). Vienna, Austria, 15–19 September

Rickels MR, Ruedy K, Foster N et al (2015) Intranasal glucagon for treatment of insulin-induced hypoglycemia in adults with type 1 diabetes: a randomized, cross-over non-inferiority study. Presented at: *8th International Conference on Advanced Technologies & Treatments for Diabetes*. Paris, France, 18–21 February

Warner J, Hermann J, Kapellen T et al (2014) DKA in diabetes: a multinational comparison of 59,191 paediatric patients from England, Wales, United States, Austria and Germany. Presented at: *53rd Annual Meeting of the European Society of Paediatric Endocrinology* (Poster). Dublin, Ireland, 18–20 September. Available at: http://bit.ly/1Jvh6uM (accessed 08.05.15)

Weinstock R, Schütz-Fuhrmann I, Mubasher M et al (2015) Type 1 diabetes in older adults: Comparing treatments and complications in the United States T1D Exchange and the German/Austrian Dpv registries. Presented at: *97th Annual Meeting and Expo of the Endocrine Society* (poster FRI-658). San Diego, USA, 5–8 March. Available at: http://bit.ly/1GYLH15 (accessed 11.05.15)