‹ CLOSER LOOK

MEMORANDUM

The State of T1D Outcomes published in DT&T: only 21% of adults meet A1c <7%, despite 4x rise in CGM use; young adult outcomes worsen - January 23, 2019

Executive Highlights

- **In an extremely concerning [publication](#), the T1D Exchange has published updated Registry data in *DT&T*, comparing outcomes in 2016-2018 (n=22,697) vs. 2010-2012 (n=25,529).** This gives an updated snapshot on the state of type 1 diabetes management and outcomes at 81 of the top US centers - including A1c, use of devices, and prevalence of severe hypoglycemia and DKA across a wide age range (1-93 years old).

- **The headline is distressing: only 17% of youth and 21% of adults are meeting A1c goals (<7.5% for youth, <7% for adults).** Mean A1c has also *risen* to 8.4% in the T1D Exchange in this new dataset, up from 7.8% in 2010-2012! This meaningful increase was predominately seen in adolescents and young adults, as shown in the first picture below. "There is no indication," note the authors, "that A1c levels in the registry as a whole have improved over this 5-year period despite an increase in the use of insulin pumps and CGM." We include a few questions on this front below.

- **The data's biggest bright spot is CGM use is now up to ~30% of the T1D Exchange in 2016-2018, a four-fold rise from 7% in 2010-2012.** CGM has risen more than ten-fold in children <12 years old - from 4% to 51%! (CGM has the lowest penetration in 18-25 year olds, at just 22%.) Dexcom dominates in the Exchange, with 77% penetration. Caveat: this data was collected across a wide timespan - January 1, 2016-March 31, 2018 - meaning it is underreporting FreeStyle Libre, MiniMed 670G, Guardian Connect, Dexcom G6 and the Senseonics Eversense. The rise is encouraging and expected (given the [category's strong sales](#)), albeit against a depressing backdrop of poorer A1c outcomes in young adults and no change in adults. We wonder how much worse the A1c averages would look with no CGM.

- **Of participants ≥50 years old, 10% (!) reported a seizure/loss of consciousness due to hypoglycemia in the three months before questionnaire completion** - a reminder of how urgently CGM and automation need to move into this population, as well as possibly better education (e.g., interpreting data optimally).

On Tuesday, the T1D Exchange Clinic Network published a must-read seven-page paper, "[State of Type 1 Diabetes Management and Outcomes from the T1D Exchange in 2016-2018](#)" in *Diabetes Technology & Therapeutics* (Foster, Beck, et al.,) - including a treasure trove of supplemental data. Like the previous data (*[Diabetes Care 2015](#)*, *[JCEM 2012](#)*), these updated T1D Exchange Registry outcomes are concerning, showing no improvement in A1c outcomes in the past five years, including a worsening in young adults. Moreover, these remain a best-case scenario for the US, since they occur at the best US centers and most people (74%) have private health insurance; real-world, average outcomes in the US are likely worse than these already-grim data, though the "best" centers may also see tougher, more complicated patients.

This paper serves as a major reminder for the field: far more work is needed to move population-level outcomes in type 1 diabetes in the US. CGM use is rising nicely, but remains used by a minority of people with type 1 overall - even at the top clinics. Leveling the playing field on outcomes still demands breakthrough innovation coupled with strong access - to drugs, to devices, to automation and decision support, to engaging education, to insightful data, to healthy food, and to meaningful familial and other support.


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- ▪ **Registry data was collected between January 1, 2016-March 31, 2018 (n=22,697),** comparing diabetes management/outcomes to similar data collected in 2010-2012 (n=25,529). In 2016-2018, participants spanned from 1-93 years, with 74% on private health insurance and 49% (n=10,249) classified as overweight or obese - a reminder that weight loss also remains a critical need in the type 1 population.

A1c - No Change in Adults, Worsening in Young Adults

- ▪ **In the latest T1D Exchange data, only 21% of type 1 adults met an A1c goal of <7%; only 17% of youth met an A1c goal of <7.5%.** Overall, the adjusted mean A1c was 7.8% in 2010-2012 and *rose* to 8.4% in 2016-2018 (p<0.001) - this was mostly driven by worse outcomes in adolescents/young adults. The chart below compares mean A1c levels by age, with orange representing previous 2010-2012 data and blue representing 2016-2018 data. The hump is a big concern - mean A1c during childhood was ~8.1% at 5 years of age, peaks at ~9.3% between ages 15-18, and decreases down to 8.0% by age 28. Beyond age 30, mean A1c remained fairly steady around 7.5%-7.9%. The paper's conclusion is clear: "there is no indication from these data that HbA1c levels in the registry as a whole have improved over this 5-year period despite an increase in the use of insulin pumps and CGM." Unfortunately, these concerning data are probably a best-case scenario - these are the best US centers! In the general population - especially those getting care in primary care - outcomes may be even worse than these registry data. Racial and socioeconomic differences also continue to exist in A1c levels, as shown in Supplementary Table S5.

**Average A1c by year of age: 2016-2018 (blue) vs. 2010-2012 (orange)**
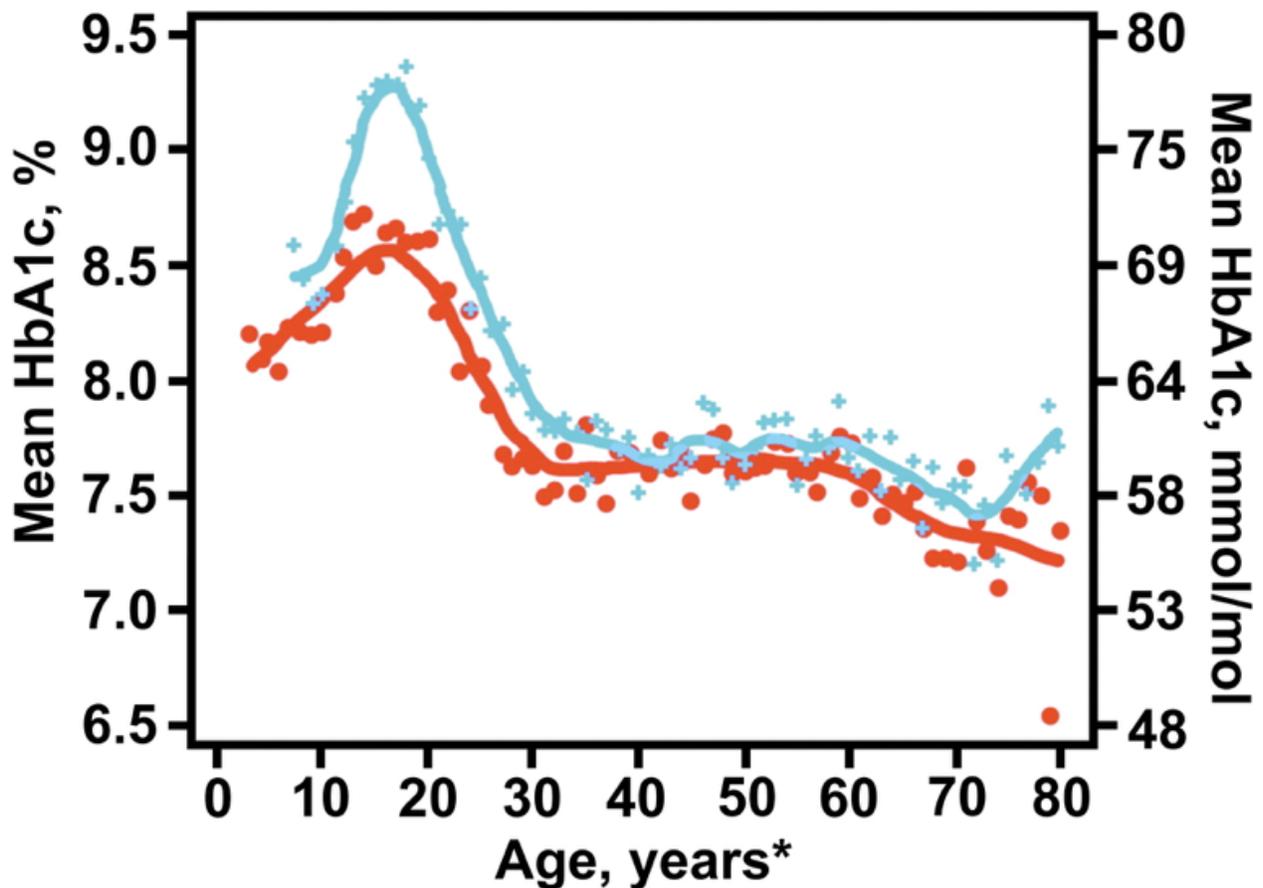
- **CGM users have lower A1c levels, with fairly minimal differences between pump+CGM vs. MDI+CGM. The chart below plots mean A1c by technology use in the new 2016-2018 data set** - MDI+fingersticks (solid black), pump+fingersticks (horizontal stripes), MDI+CGM (solid white), and pump+CGM (diagonal stripes). The one advantage for CGM users on pumps was in adolescents - note the middle bars below, where mean A1c was ~0.5% lower in CGM/pump users vs. CGM/MDI users. Dexcom has shared these data at numerous conferences, emphasizing that CGM confers clear, consistent A1c benefits regardless of insulin delivery method. This offers a clear opportunity for both sides of the field - smart pens/decision support should add further value to current MDI+CGM, and pumps+CGM with automation will add further value over what non-automated systems offer now.
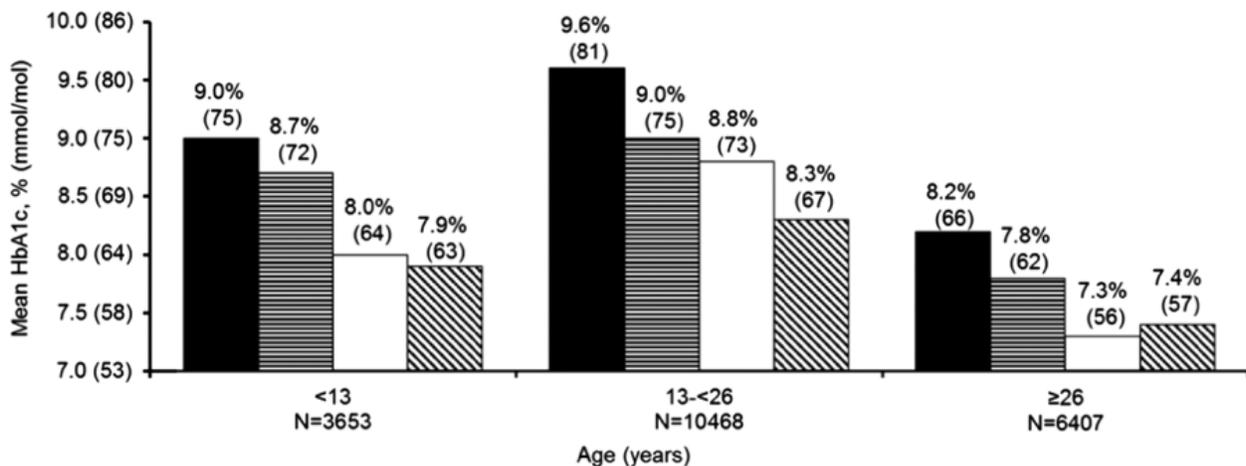
CGM Use - Quadruples to 30% of Participants, >10X Pediatric Gain

- **CGM use has increased from 7% in 2010-2012 to 30% in the 2016-2018 dataset, including a >10x rise in children <12 years old - from 4% to 51% use in <6 years and 3% to 37% in 6-12 years!** Since the full 2016-2018 data was collected over a wide time span (depending on when the questionnaire was filled out), there is a separate plot with the subgroup of data collected in each year - as of 2018, CGM stood at 38% penetration in the Exchange, up from 31% in 2017 and 24% in 2016. This impressive uptick (especially from a higher base) parallels the rise in sales in the field. In line with prior exchange updates, Dexcom has a dominant share of the Exchange, with 77% penetration in 2016-2018. We expect growth to continue or possibly even accelerate further given product innovation and an expanded field.

- **Overall, the clear message is that CGM still has enormous runway in the US - it is still not at a majority of users at the best US centers.** Paired with the A1c data, there is clearly huge room to drive better *outcomes* with CGM - obviously, real-time glucose data is a tool, not a therapy, and we look forward to decision support/automation helping to safely reduce hyperglycemia.

Figure (A) CGM use over time and (B) CGM use in 2010-2012 (white) vs. 2016-2018 (black).
CGM was used in 7% of people overall in 2010-2012 vs. 30% in 2016-2018.
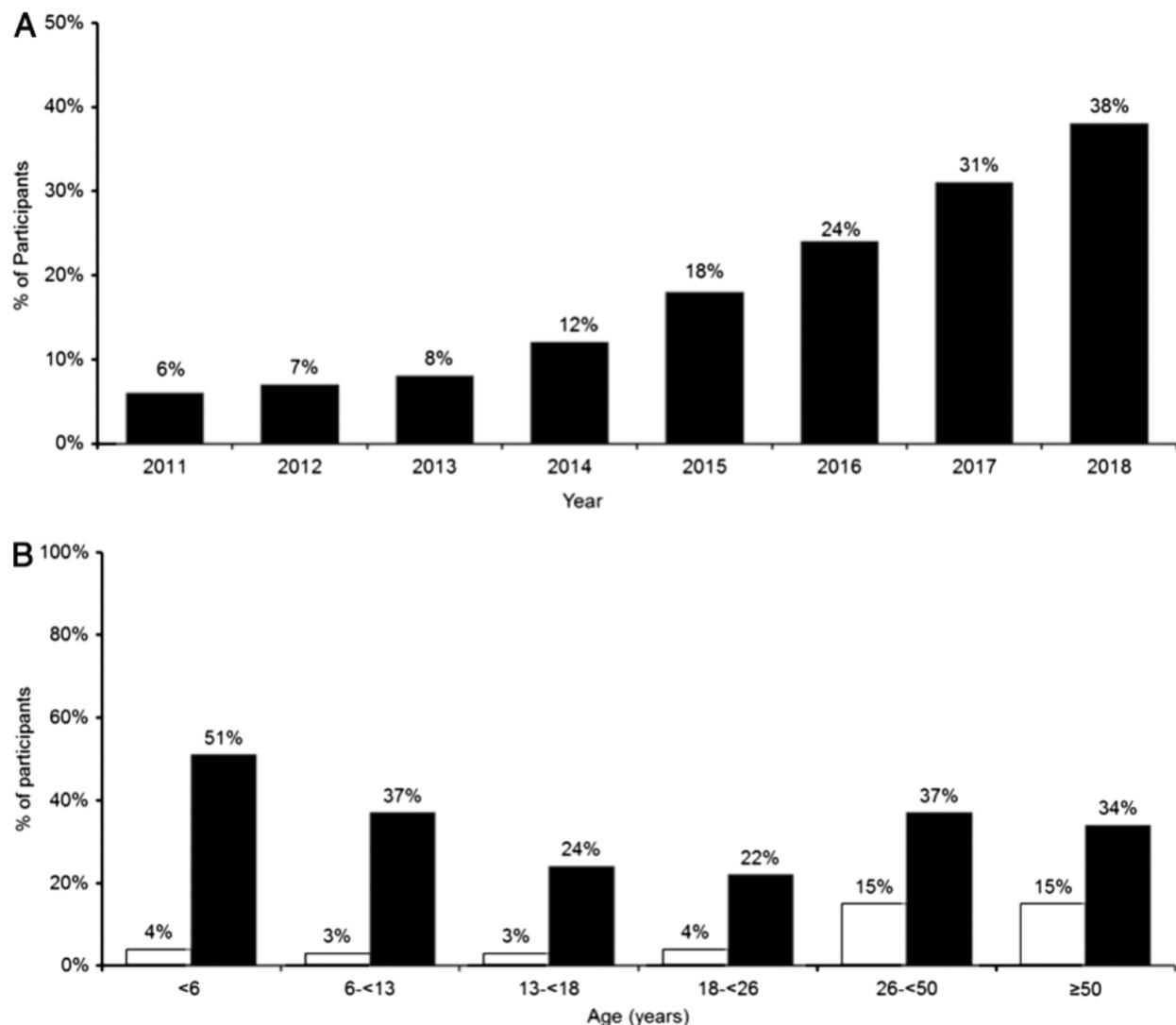
SMBG Use

- **Mean fingersticks per day were 4.1 in 2016-2018 (down from 4.7 in 2010-2012), with a sizeable 41% reporting 0-3 fingersticks/day**. **Even if we assume 0-3 fingersticks/day is the case for every CGM user in the Exchange** (30%), that means a full one in nine type 1's (11%) at the best US centers are checking their blood sugar 0-3 times per day! We'd love to see more granularity on the 0-3 - how many are taking one fingerstick per day or none? How many are on CGM? We cannot imagine anyone being anywhere close to standard of care if they are not on CGM and using zero or one strip a day. If those with zero checking could become a greater focus, likely those patients who are generating the most spending may see improved outcomes - this would be a big deal in such a high-risk population.

Pump Use - Slight Increase, Used by a Majority (63%) of Participants

- **Insulin pump use increased from 57% in 2010-2012 to 63% in 2016-2018, with the largest increases in children** (50% to 60% in children <6 years old and 58% to 68% in children 6-12 years old). Obviously this highly over-reports true pump penetration in type 1 in the US, which is still mostly assumed to be around 30%-35%. Without all companies reporting, however, this is an estimate.

- **In 2016-2018, 53% of pumpers were on a Medtronic pump, followed by 18% for Insulet, 18% on Animas, and 12% on Tandem.** Obviously those have probably changed quite a lot in the latter half of 2018, given Animas' exit, Medtronic's upgrade programs, and strong years for both Insulet and Tandem.
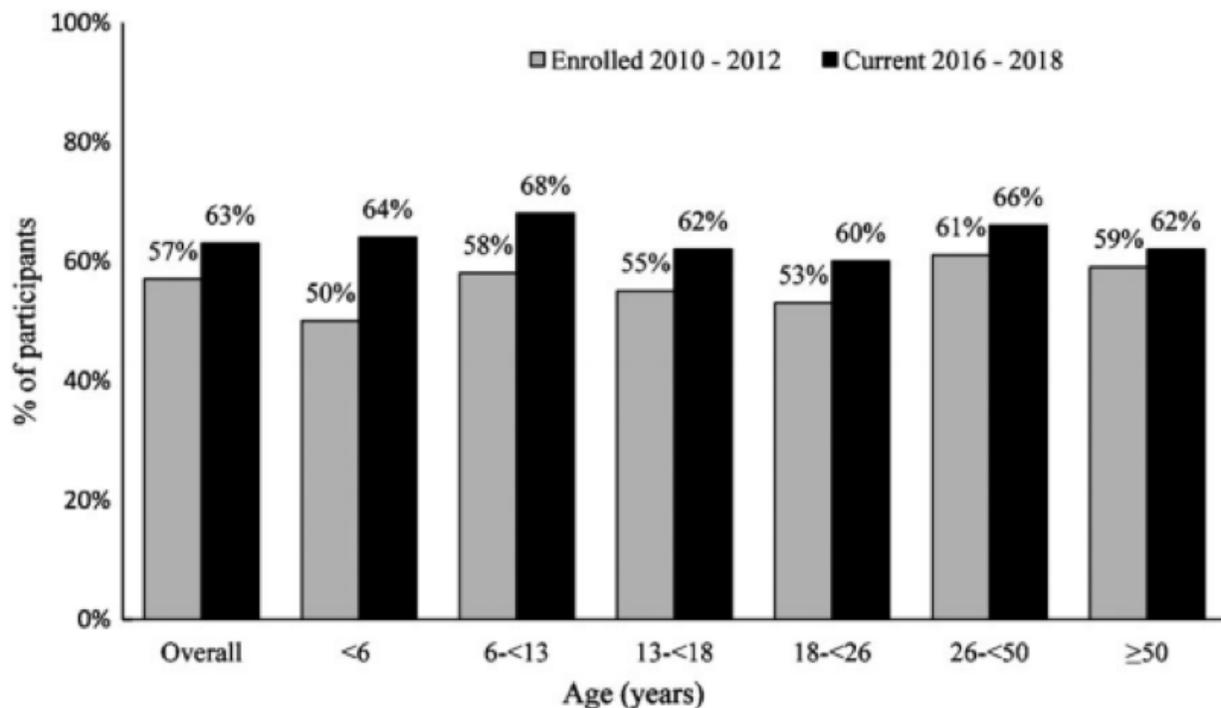
SUPPLEMENTARY FIG. S1. Pump use during 2010–2012 versus 2016–2018.

Severe Hypoglycemia - 1 in 10 in Older Adults Had An Episode in the Past Three Months

- **In 2016-2018, 6% of T1D Exchange participants reported a seizure or loss of consciousness due to hypoglycemia in the three months before questionnaire completion**; this ranged from 5% in participants <18 years to 10% in participants ≥50 years old. The latter is obviously very, very concerning - 1 in 10 is unacceptably high! So is the low end of the estimates, at 5%. Insulin pump use was associated with lower frequency of experiencing a severe hypoglycemia event (5% vs. 9%; p<0.001), and CGM use trended toward a lower severe hypoglycemia frequency (5% vs. 7%; p=0.06). Although CGM users would be expected to have a lower severe hypoglycemia frequency than non-users, the difference was "relatively small," potentially reflecting selection bias - i.e., CGM may have been prescribed or used because of frequent severe hypoglycemia in the first place.

- **As data have continued to demonstrate, the frequency of severe hypoglycemia in the T1D Exchange was *not* associated with A1c level** - running with a high blood sugar all the time does not protect against severe lows.

DKA - Affected 4% of Participants <26 Years, Less Likely with Pump or CGM

- **At least one DKA event in the three months before the questionnaire was reported by 3% of participants, with the highest frequency (4%) in participants <26 years old**. Participants using an insulin pump were *less* likely to report experiencing a DKA event than participants using injections (2% vs. 4%; p=0.002). Similarly, participants using CGM had fewer DKA events than non-CGM users (1% vs. 3%; p=0.04). Participants with higher A1c were more likely to experience a DKA event than participants with lower A1c

  - **Only ~20% of registry members reported having a blood ketone meter**. This is not necessarily overly surprising, but concerning in light of potential for more widespread use of SGLT inhibits in type 1 diabetes. Read our detailed report on the FDA Ad Comm for Sanofi/Lexicon's sotagliflozin for more details. Presumably even fewer know how to interpret a ketone meter's results.

Additional Findings of Note

- **Racial and socioeconomic differences are pronounced, especially in use of devices.** For instance, at pretty much every age and every race, those with incomes ≥$75,000 have double the use of CGM vs. those with incomes <$50,000. The largest difference is in the Hispanic/Latino community, where there is a 3x difference in CGM use between high and low incomes - i.e., 16% CGM use in lower incomes vs. 51% use for higher incomes (adults ≥26 years). See all the data in Supplementary Table S3. Notably, the gaps are smaller for pumps, perhaps reflecting more established reimbursement or simply more awareness.

- **Across the board, use of non-insulin medications remains uncommon,** with metformin the highest at 6% use in adults (≥26 years). It is important to note that 49% of the participants in the 2016-2018 were overweight/affected by obesity, meaning there is huge potential for SGLTs and GLP-1s to help. SGLT-2s and GLP-1s were used by 1% of the panel each, translating to n=232 and n=500 users out of 22,297 participants. See the complete breakdown of non-insulin medication use in supplementary table S1. We've heard an estimate that 50,000 people with type 1 diabetes are on SGLT-2 inhibitors off-label, which sounds too high - on a base of 1.5 million type 1s that's 3% usage, and the Exchange presumably oversamples for early adopters.

- **Most participants reported *never* downloading blood glucose meters, CGM devices, or insulin pumps at home.** Other than using Dexcom Share (the most popular mobile app, by far), use of apps was also very uncommon. See the complete data in Supplementary table S4.

Close Concerns' Questions

Q: What will it take to drive population-level improvements in A1c in type 1 diabetes? How much value will automated insulin delivery add - both for pumps and injections?

Q: What is driving the adolescent/teen worsening in A1c levels? How much of a role is lack of sleep playing? (Stay tuned for Adam's upcoming diaTribe column on *Why We Sleep*, which specifically addresses this issue of sleep in teens.)

Q: How does type of insulin used impact average A1cs? What percentage use "next generation" insulins like Toujeo or Tresiba or Fiasp and how do their A1cs look? What about those using off-label "adjunctive" therapy (SGLTs, GLP-1) or those using old insulins like NPH and Regular?

Q: Where are PROs routinely collected and what do those show (measures of emotional well-being or other measures showing familial stability or lack thereof)?

Q: What can be learned from Bright Spots: the sub-group of patients with A1c <7% or <6.5% without severe hypoglycemia? What are they doing that could be replicated?

Q: How do A1c levels compare between different nutritional approaches to type 1 - e.g., low-carb vs. moderate carb vs. high-carb?

Q: How much variability is there between T1D Exchange clinics? What can be learned from Bright Spot clinics with a large percentage of type 1s at an A1c <7%?

Q: What is average time-in-range across CGM users in the T1D Exchange?

Q: How do T1D Exchange outcomes compare to the general type 1 population - i.e., how much is the registry data better-than-average?

Q: How much of CGM adoption is still gated by awareness vs. access vs. perceptions' of the technology? What will unlock the market? Could we see adoption cross 50%-60% in the next three years? How is education of CGM rated overall and how are HCPs scoring on this front?

--by Adam Brown and Kelly Close