

diaTribe®

research and product news for people with diabetes

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from the editor



The end of June means we’re halfway through the year and we’ve just completed another ADA meeting. We’re lucky to attend each year, since there’s no finer barometer of just where we stand in the search for better therapies, better devices, and better outcomes – not to mention better lives. I wrote last month how special it was that the ADA was holding this year’s meeting in diaTribe’s hometown of San Francisco, and in this issue I’m proud to present our latest edition of conference pearls, which examines the biggest takeaways from this ADA: major progress on the artificial pancreas, a new and exciting position statement for type 1 diabetes, updates on novel drug combination therapies, and much more! Please read more about advances in type 1 diabetes and type 2 diabetes, as well as about the recent FDA approval of MannKind’s Afrezza for both type 1 and type 2 – an exciting month indeed!

My favorite phrase to describe the ADA is – “a meeting of the minds.” So much brainpower was assembled this past month in San Francisco’s Moscone Center, and all of it geared toward diabetes. For the eighth year, The diaTribe Foundation and Taking Care Of Your Diabetes (TCOYD) hosted the annual Diabetes Forum, in which TCOYD founder Dr. Steven Edelman and I were joined by five renowned experts in the field. When you add up the years that the seven people on stage have been working on, thinking about, or in some cases living with diabetes, it totals more than a century of experience.

The ADA gave us plenty of reasons to feel optimistic, but one of the most notable developments was the greater acknowledgment of the patient voice. I must admit I’m probably a little biased here, as ADA was kind enough to let me run an entire panel during its sessions on the patient perspective. I tried to capture all the difficult realities that can make diabetes so hard to live with: the challenges of finding good food and time to exercise in a modern society that leaves little time for either; the fact that there are no vacations from this 24/7/365 disease; the fact that diabetes is “invisible” – one that other people won’t necessarily know we have unless we tell them – but it also carries a social stigma when we do tell people; and the many difficulties that come with taking care of children with diabetes. That’s why I hope my calls for big strides in diabetes research and care will be heeded. That includes better access to care for all patients, improved care in schools, a more patient-centered regulatory process, and technology that is both easy to use and provides peace of mind. If all of this year’s ADA attendees can go forward with a greater understanding of people with diabetes, then the conference will have been a success.

very best,

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quotable quotes

“Artificial pancreas systems will be the most revolutionary advance in diabetes care since the discovery of insulin.”

– Dr. Aaron Kowalski (JDRF) on the promise of artificial pancreas technologies in a JAMA article entitled, “Fully Automated Artificial Pancreas Finally Within Reach.”

“We need to look in a mirror and realize the struggles our patients are having with their diabetes are like the struggles we have ourselves.”

– Dr. William Polonsky on understanding patient obstacles at the American Diabetes Association (ADA) 74th Annual Scientific Sessions on June 13-17, 2014 in San Francisco, CA.

“We are not the enemy. Diabetes is the enemy. Together we will learn how to live well.”

– Dr. Parresh Dandona (University of Buffalo, NY) on the difficulty of interpreting clinical trials at AACE 2014

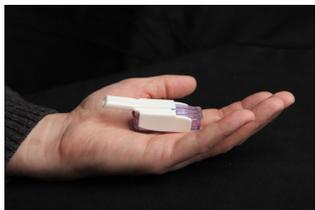
fingersticks



ILLUSTRATION: JOSEPH SHIVERS

“Yes, it still hurts every time...but since you came along, I’ve got a million more reasons why it’s worth it.”

new now next



The convenience of an inhaled, needle free insulin should be attractive to many patients.

We believe patients and health care providers played a role in this approval and we applaud it as it means more treatment options for patients.

T1/2 **FDA Approves MannKind's Rapid-Acting Inhaled Insulin, Afrezza, for type 1 and type 2 diabetes**

On June 27, the FDA approved MannKind's Afrezza for type 1 and type 2 diabetes, a new rapid-acting inhaled insulin. This marks a major win for another mealtime insulin option. There is no firm launch timeline yet, though the company expected to launch Afrezza within six months of FDA approval. MannKind has also previously stated that Afrezza would be priced roughly comparably to current rapid-acting insulins (Humalog, Novolog, and Apidra); if this is the case, we are optimistic about reimbursement for type 2 patients in particular. We think most type 1s would prefer to use Afrezza as a "supplement" to their current mealtime insulin rather than as a substitute so we imagine reimbursement may be more challenging initially for type 1s.

Afrezza will come packaged as a powder that is administered with a small inhaler – based on videos and pictures we've seen, the device fits in the palm of the hand and is fairly unobtrusive and easy to use. Based on studies, we understand that Afrezza is a very fast insulin that peaks in the blood stream within 12 to 15 minutes, much faster than currently available rapid-acting insulins that take around 50 minutes to peak.

The inhaled insulin has been approved in two dosing options – a cartridge equivalent to four units of injected rapid-acting insulin, and another equivalent to eight units. This means that patients will only be able to take Afrezza in multiples of four units, which could make it challenging for type 1s and those who are very insulin sensitive. Patients with type 1 diabetes saw significant benefits to taking Afrezza such as less hypoglycemia (moderate and severe) and less weight gain compared to Novolog (insulin aspart). In type 2 diabetes, there is much less concern over the dosing, and the convenience of an inhaled, needle free insulin could be attractive to many patients.

Four additional clinical trials, post-approval, are required for Afrezza, including a long-term study to determine its cardiovascular and lung safety. People with type 1 diabetes must use Afrezza with long-acting insulin, and the FDA does not recommend Afrezza for people who smoke or who have prior lung conditions.

We believe patients and health care providers played a role in this approval and we applaud it as it could help improve adherence and increase patient acceptance of insulin. With nearly 45% of patients not at their glycemic targets in the US alone and only 29% on insulin of any kind, we believe more patients considering insulin would be a benefit. We salute with special gusto the legendary entrepreneur and CEO of MannKind, 89-year-old Mr. Al Mann, who advocated for years for Afrezza's approval (its first two attempts at FDA approval were rejected) finally got to see his hard work pay off. We look forward to hearing real-world patient use of the product – we'll certainly be testing it out in *diaTribe*. -AJW/AB/KC

T1/2 **Medtronic's New Pump and CGM Products – predictive low glucose suspend and a combined insulin infusion and CGM sensor**

Medtronic provided updates on several upcoming CGM and insulin delivery products at an early June analyst meeting. Though these meetings are really meant for investors, there is typically lots of valuable learning between and in the lines! Nearest term is the MiniMed 640G system, which we learned is actually



already approved in the EU (!); this device uses a CGM reading to actually predict hypoglycemia before it occurs and thus suspend insulin delivery to avoid it. It then resumes insulin delivery once sensor glucose levels recover. The device is the next step forward from the MiniMed 530G/Enlite CGM, and it sounds like it has proven itself significantly more effective both in reducing time spent in hypoglycemia and avoiding hypoglycemia entirely. The MiniMed 640G system is expected to launch in Europe by April 2015, and a US trial of the device is starting very soon. You can see a sneak peak of the MiniMed 640G in the photo above, which is waterproof, will have a color screen, and feature a completely redesigned, simpler user interface. The system is expected to launch in Europe with a second-generation Enlite CGM sensor, while the US version will test a third-generation version with improved accuracy and comfort.

The Analyst Day also announced that the MiniMed 670G, a “hybrid closed-loop system,” is in development – no details were offered, but this system will automate even more insulin delivery beyond the MiniMed 640G (e.g., automatically controlling background basal insulin delivery 24 hours a day, with patients bolusing for meals on their own). A MiniMed Flex “hybrid” pump is in the works as well; this pump will have a smaller footprint and give patients the flexibility to wear their pump “on” or “off” the body (e.g., attached to the abdomen or in a pocket).

Medtronic announced the initial European launch of the MiniMed Duo, a three-day wear combined insulin infusion and CGM sensor set.

Last, Medtronic announced the initial European launch of the MiniMed Duo, a three-day wear combined insulin infusion and CGM sensor set. This combo device locates both the CGM sensor and the insulin catheter under a single adhesive patch, known as a “snake bite.” The MiniMed Duo will launch first in the United Kingdom and in other European countries over the next few months. On accuracy, the three-day-wear device has a MARD of 15.5% vs. paired blood glucose meter readers, while the Enlite’s labeled accuracy is 13.6% compared to YSI readings. The Duo may be a good option for very young patients who have less space on their body for separate CGM and insulin delivery sites. There is not yet a timeline to bring the MiniMed Duo to the US and we’re not sure about how reimbursement would work ~ overall, we don’t anticipate a huge uptake for this product, but we’re impressed it is out.

A postscript – at the ADA itself, though not at this meeting, what looks to be a compelling partnership between Medtronic Diabetes and Sanofi was announced. It should be a win/win – Medtronic will help Sanofi with insulin delivery outside a syringe and pen, as well as professional CGM, while Sanofi will help Medtronic think in a simpler way from a product introduction perspective. We’ll continue to watch the launch...– *AJW/AB*



T1

Xeris Doses First Patient in Phase 2 Study of Mini-dose Glucagon for mild-moderate hypoglycemia in T1D patients

On June 5, Xeris Pharmaceuticals announced that the first patient had been dosed in its phase 2 clinical trial, which is testing “mini-dose” glucagon for the treatment of mild to moderate hypoglycemia (e.g., a glucose of 60 mg/dl). The 18-patient study is expected to wrap up by the end of the summer/early fall, which would pave the way for Xeris to conduct a larger study. For those unfamiliar, the concept of a “glucagon mini-dose” allows patients to precisely administer small amounts of glucagon to correct low blood sugars without needing to eat

This could help avoid the rollercoaster pattern of overtreating hypoglycemia.

or drink excess carbs. This could help avoid the rollercoaster pattern of overtreating hypoglycemia with too much food and perhaps even prevent some of the weight gain associated with taking insulin. Xeris plans to make a portable pen for its mini-dose glucagon, much like how current insulin pens work. Based on the most recent timeline, Xeris' mini-dose glucagon could be on the US market as soon as 2016. We think many patients would like this. While some, clearly, have a candy bar (or other favorite food) to treat low blood sugar, many of us know the feeling of having had enough sugar but not being able to stop eating! This would be an excellent alternative though of course it won't be appropriate for all.

Currently, of course, glucagon is only approved in the form of one-time use "emergency kits" for severe hypoglycemia (i.e., when a patient is unconscious or not responding) – these kits from Novo Nordisk and Lilly require mixing dry powder with water, a process known as reconstitution. Xeris has figured out a way to stabilize the glucagon molecule, allowing it be packaged in a ready-to-inject liquid form. Several other companies, including Bidel, Locemia, Latitude, and Zealand, are also in the process of developing and testing improved glucagon therapies. Locemia is the furthest along, as the company is currently testing its intranasal glucagon for severe hypoglycemia in phase 3 trials in children and adults. –AJW/AB



T1/2 **iHealth Lab launches Align Smartphone Meter with Cloud Connectivity and Test Strip Savings Program**

On June 12, iHealth Lab announced the launch of the Align blood glucose meter, a very small device that plugs directly into the headphone jack of an Apple iOS- or Android-compatible smartphone. The meter does not have a screen but instead displays and stores the blood glucose results directly within a free app, iHealth Gluco-Smart. The app itself has a colorful four-screen user interface that makes it easy to see recent results, tag them (e.g., before/after meal, exercise, etc.), and view statistics and charts. All the information can also be emailed straight from the app, which should help many patients share recent results with healthcare providers. We felt the design could use some improvement (e.g., takes a bit of time to load, some of the settings and tagging is not particularly intuitive), but it is fairly user friendly overall.

Perhaps the most notable feature of the iHealth Align is its affordability.

Perhaps the most notable feature of the iHealth Align is its affordability: the meter with lancing device (which is cool and hip) costs just \$16.95, and 50 strips are just \$12.50. iHealth's goal was to make the strips inexpensive enough that users can pay for them out of pocket, especially since insurance reimbursement is not currently available. Both the Align device and its test strips are available for sale on the company's website and eventually on Walgreens.com. iHealth also offers a wireless smart glucose monitoring system that works with Bluetooth.

Since the meter must have a smartphone to work, all data is automatically stored on the phone and sent to an online account, an improvement over most other meters that typically rely on a cable and computer software for downloading. The one downside to this approach is that the meter will not work without a smartphone, so it's only a good option for those who always have their smartphone around while testing. The small size and low price could make the Align particularly attractive for those desiring a few low-cost backup meters, or perhaps for use during exercise when carrying capacity is limited. – AJW/AB



T2 **BI/Lilly's SGLT-2 Inhibitor Jardiance (empagliflozin) resubmitted to the FDA**

On June 17, Boehringer Ingelheim (BI) and Lilly announced the resubmission to the FDA of the SGLT-2 inhibitor Jardiance (empagliflozin) for the treatment of type 2 diabetes. In this particular case, the FDA review process is expected to take about two months. Most expect the drug to be approved, as the FDA has not requested an advisory committee, and two other drugs – Janssen's Invokana and AstraZeneca's Farxiga – of the same class have already been approved by the Agency. When BI/Lilly first submitted Jardiance to the FDA in 2013, the FDA found no problems with the drug's efficacy or safety, but submission had been denied because of an issue with the drug's manufacturing plant. The FDA cleared the plant on June 3 of this year.

SGLT-2 inhibitors are a relatively new class of diabetes drugs that work by allowing glucose to be excreted through the urine. Interest in this drug class has grown dramatically since last year, and the future looks encouraging, as companies are working on combining these drugs with other type 2 therapies (e.g., metformin, DPP-4 inhibitors), and many are investigating the potential of SGLT-2s in type 1 diabetes. –AJW

The goal is to educate users about their own diabetes and improve awareness of hypoglycemia.

T1/2 **Joslin and Glooko Launch HypoMap software to Identify and Improve Hypoglycemia Unawareness**

On June 11, Glooko and the Joslin Diabetes Center announced the release of their HypoMap software, a cool product that really should be able to identify and help improve hypoglycemia unawareness. The software relies on a patient survey within the existing Glooko mobile app; after patients upload glucose data, HypoMap will flag episodes of low blood glucose that have occurred within the past two weeks. Patients will then be prompted to enter more information about the hypoglycemia episodes: the symptoms they experienced, such as sweating or feeling nervous; what they think caused the low, like too much insulin or overexertion during exercise; and how they treated it, such as drinking juice. The software then maps the symptoms onto an awareness grid, allowing providers to identify patients that cannot feel symptoms of hypoglycemia until very low glucose levels. The goal is to educate users about their own diabetes and improve their awareness of their own hypoglycemia, and part of that process is helping providers identify which users are at the highest risk of severe hypoglycemia episodes. HypoMap will also direct patient-provider conversations to patients' most pressing hypoglycemia issues. Currently, the software is only available to Joslin patients, though Glooko expects to make it available to more providers and health systems soon, and we look forward to learning more details about privacy and different ways the data can be used.



The Glooko system consists of a universal MeterSync cable that can download glucose data from 27+ glucose meters (Accu-Chek, Bayer, FreeStyle, OneTouch, and Nipro) to an Apple/Android smartphone app. We've found the download process pretty hassle-free and the app's charts and graphs highly useful (particularly the time in range graphs by time of day). The data is also viewable by patients and providers on a web dashboard. The MeterSync cable is \$39.95 on Amazon – right now only the Android version of the cable is available, as a Bluetooth version is coming soon for both Apple and Android. –AJW/AB



T1/2 **Diabetes Technology Society Announces Launch of Surveillance Program for Blood Glucose Monitors**

On May 20, the Diabetes Technology Society (DTS) announced the launch of a post-market blood glucose monitoring surveillance program, which will aim to assess and monitor the accuracy of meters and strips after they are approved. As we outlined last year, test strips and monitors are currently only tested for accuracy prior to FDA approval, and companies can self-report their own data. The DTS surveillance program plans to setup independent, third-party centers to routinely test the accuracy of meters and strips after they are out on the market. With initial funding from Abbott, a Steering Committee will meet next month in Washington DC to begin hammering out the program's details. The committee consists of world-class experts in blood glucose monitoring, diabetes, and laboratory methods from academia, medical practice, government, industry, and medical organizations.

We were encouraged to hear that patient advocacy group(s) will be represented in a future Advisory Board.

We were encouraged to hear that patient advocacy group(s) will be represented in a future Advisory Board that will be established soon. Ultimately, DTS hopes to publish the accuracy data to inform patients, payers, and regulators like the FDA about which products meet or fail accuracy standards. Hopefully, this effort will increase transparency, raise the level of conversation around test strip accuracy, and drive inaccurate products off the market. Particularly now that competitive bidding can prioritize affordability over accuracy in blood glucose monitoring, it is imperative that DTS and other advocates are pushing to create a safer, more accountable system for determining the accuracy of meters and strips. —AJW

T1/2 **CDC Releases 2014 National Diabetes Statistics Report with New Outlook**

The Centers for Disease Control (CDC) has released its new data on the state of diabetes in the United States, providing an update on its 2011 National Diabetes Fact Sheet. Using data from 2012, this new report finds that 29.1 million people, or 9.3% of the entire American population, have diabetes, of which roughly 8 million of those cases are currently undiagnosed. There was a slight decline in the number of newly diagnosed cases per year from 1.9 million to 1.7 million people, but this shouldn't be taken as much of a cause for optimism, particularly when the number of people with prediabetes increased from 79 million in the 2011 Fact Sheet to 86 million.

The CDC's reports can be crucial indicators of how people think about disease.

The CDC's reports can also be crucial indicators of how people think about disease. In particular, this report places a much greater emphasis on the risks of hypoglycemia than its 2011 counterpart, which remarkably didn't even mention hypoglycemia in its larger discussion of diabetes. The report also combined the old sections "Treating Diabetes" and "Preventing Complications" into a single section, "Managing Diabetes," which indicates that public officials are now much more aware of the complex, interconnected nature of this disease; the very acts of monitoring and managing glucose levels are the cornerstones of preventing complications. Perhaps most impressively, the CDC highlights the need for individualized care and patient-specific glucose targets. Even as the data in the CDC's report suggest we still have a long way to go in dealing with the diabetes epidemic, it suggests that public health officials are listening to the ideas of both experts and patients, and that can only be a good thing moving forward. —ARW

The Latino population is a critical one to study, as Latinos have a two-fold greater risk of type 2 diabetes.

T2 Can Texting Interventions Help Type 2 Diabetes Management?

At the 2014 American Diabetes Association conference, Maria Isabel Garcia, NP presented preliminary data from Project Dulce’s text-messaging based intervention, “Dulce Digital” in San Diego, CA. The study looked at a group of Latinos with poorly controlled type 2 diabetes, low income, and low health literacy. The intervention had two arms: a control group, in which patients continued with their normal clinical care, and the Dulce Digital intervention, in which patients received around two to three text messages per day containing motivational or educational diabetes content. Patients could respond to these texts indicating the message had been received and read. According to the preliminary results, patients in the Dulce Digital arm who responded to texts concerning the topic of blood glucose saw an average 1% drop in A1c from a baseline of 9.5% maintained over a six-month period. As one would expect, the number of text responses correlated with better outcomes; too few texts back was associated with a weaker A1c reduction.

The Latino population is a critical one to study, as Latinos have a two-fold greater risk of type 2 diabetes, suffer more complications and hospitalizations, and have an increased mortality rate compared to non-Latino whites. Though the results of this study are preliminary, given that 91% of the US population owns a cell phone, interventions such as Dulce Digital could offer promising potential for improving diabetes care, particularly (but not limited to those) in those who do not have access to healthcare providers or diabetes medications. –AJW



T1/2 New Documentary Fed Up Takes Audiences Inside the Obesity Epidemic

The provocative documentary Fed Up, which offers an unflinching look at the real causes and challenges of America’s obesity epidemic, is currently playing in select cities; a list of theaters is available here. Directed by Stephanie Soechtig and executive produced by Katie Couric – who also narrates – and An Inconvenient Truth’s Laurie David, Fed Up has received almost uniformly positive acclaim from critics. The film offers a no-holds-barred look at the failings of both the food industry and the general food culture. Arguing that “Everything we’ve been told about food and exercise for the last 30 years is dead wrong,” the film mixes expert commentary, journalistic investigation, and real-world case studies to offer a compelling, persuasive picture of the public health dangers of processed food, sugary soda, inadequate school lunches, and much more. As part of its attempt to educate audiences about the perils of sugar, the filmmakers have launched the Fed Up Challenge, which asks all participants to go sugar free for 10 days. To find out more about the film and the challenge, please visit the movie’s official website at fedupmovie.com. –ARW

conference pearls



T1 The American Diabetes Association 74th Scientific Sessions - New Insights for Type 1 Diabetes

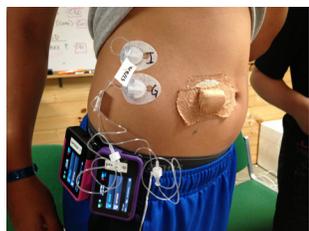
by Alexander J. Wolf, Nancy Liu, Adam Brown, and Kelly Close

Twitter summary: Lots of updates in #t1d at #2014ADA – an evolving artificial pancreas, more efforts at finding a cure, & the first position statement ever.

Short summary: This month, we attended the 74th annual Scientific Sessions of the American Diabetes Association, the largest diabetes conferences of the year. Lucky for us, it was held in our hometown of San Francisco. The conference featured updates on major progress with the artificial pancreas, a new and exciting (and a bit daunting) position statement for type 1 diabetes, and progress in type 1 diabetes cure research. *twitter summary:* How can we build healthier cities? Novo Nordisk tackles the challenge with an innovative new program. Plus, a reader poll!

Major Progress on the Artificial Pancreas

At the ADA 2012 conference, the artificial pancreas (pump + CGM + control algorithm to automatically control blood glucose) seemed like a dream for the distant future. Just a year later at ADA 2013, the device took center stage as the most exciting and a not-so-distant development in diabetes. At this year's ADA, we saw some of the largest, longest and most ambitious real-world trials testing automated insulin delivery.



Dr. Steven Russell (Massachusetts General Hospital, Boston) presented exciting results from the Beacon Hill and Summer Camp Studies, which compared five days of 24-hour wear with the bionic pancreas (automated insulin and glucagon delivery) to five days of usual care. Wearing the team's device improved mean blood glucose in both studies. Adults improved from 159 mg/dl to 133 mg/dl, while adolescents went from 157 mg/dl to 138 mg/dl. This improvement was achieved with a reduction in hypoglycemia. That's a very rare occurrence with diabetes interventions, as usually any attempt to improve mean glucose will translate to increased hypoglycemia. After wearing the bionic pancreas for just a few days, all patients achieved an average blood glucose that, when projected, came in under the ADA goals of 7% A1c for adults and 7.5% A1c for adolescents. The studies were jointly published in the *New England Journal of Medicine* and received significant attention in the media. The team has already started a larger multi-center study and hopes to conduct a pivotal study in 2015-2016 to support approval. The goal is still to have the bionic pancreas (Drs. Damiano and Russell's system) on the market in 2017.

Both studies showed that patients spent more time in the target range with these systems.

The research team from Cambridge also shared data from two automated insulin delivery studies. The first was a four-week overnight study, in which patients used a closed-loop system in their homes without any close monitoring. The second study highlighted results from a seven-day home study testing unsupervised 24-hour closed-loop control. Both studies showed that patients spent more time in the target range with these systems compared to usual care. Larger studies lasting two to three months are now getting off the ground.

JDRF's Dr. Aaron Kowalski summarized the artificial pancreas field as "right on the cusp"

JDRF's Dr. Aaron Kowalski summarized the artificial pancreas field as "right on the cusp," and the big question now is what commercial products will look like. Fortunately, most people in the field do not feel like the FDA is a barrier to these new products – the path forward seems clear, and what remains is collecting the data in larger trials and for industry to develop products that can be used in the real world.

First Ever Type 1 Position Statement Released

The ADA released its first ever position statement on type 1 diabetes during the conference. The statement pushed for both concrete changes for type 1 treatment and a cultural shift in the way we address type 1 diabetes. Arguably the most significant change was lowering the A1c target to less than 7.5% for all type 1 patients under the age of 18. The previous pediatric A1c recommendations were different based on age: less than 8.5% for patients five years old and under, less than 8.0% for those 6-12 years old, and less than 7.5% for those 13-18 years old. Those higher targets reflected concerns about the risk of hypoglycemia that came with intensive management for young patients; some experts also worried about the developmental consequences of severe hypoglycemia in very young patients. This move to a universal 7.5% goal for all young patients reflects that, with the better tools today available today – including insulin analogs, pumps, and CGM – patients can achieve better glycemic control with less hypoglycemia. However, more recent data from T1D Exchange have suggested that, regardless of one's A1c level, the risk for severe hypoglycemia remains the same. The move was also prompted about concerns about the potential complications of long-term hyperglycemia.

The statement highlighted the unique challenges people with type 1 diabetes face.

More broadly, the statement highlighted the unique challenges people with type 1 diabetes face and the need to start a conversation about the distinction between type 1 and type 2 diabetes. This will be a key factor in individualizing care, addressing issues of reimbursement, and increasing medical literature for type 1 diabetes. While it's too early to measure the impact of the position statement on the diabetes field, the statement could lead to greater focus on type 1 and perhaps improve care.

New Efforts in Finding a Cure for Type 1

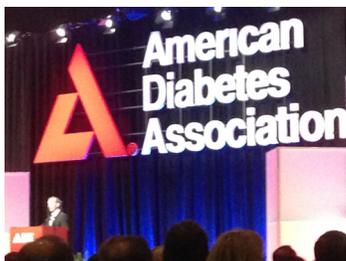
It was refreshing to see positive results again, after a bit of a drought, from research focusing on a type 1 cure. Dr. Michael Haller presented the results of a trial measuring the effects of a low-dose drug combination in patients recently diagnosed with type 1 diabetes. This drug combination, called the "Brazil Lite" cocktail, is a radical treatment for type 1 diabetes that essentially resets the immune system by replacing the body's T-cells to prevent attack on the beta cells. The results of the study showed that people taking the Brazil Lite cocktail retained their ability to secrete insulin ("C-peptide"), whereas those on a placebo saw a decline, and insulin independence was achieved in all 65 participants at least once during the trial. Unfortunately, the Brazil Lite cocktail did not result in a reduction in A1c. This treatment is notable as one of the first that addresses the fundamental cause of type 1 diabetes (autoimmune attack), instead of the symptoms. However, the positive results came with a major safety risk: 34 of the 65 patients in the treatment group experienced major side effects. Scientists are also working to make a safer version of the Brazil Cocktail as well as other new therapies in early-stage trials.



To read more about type 1 cures and treatments on the horizon, please read our book called "Targeting a Cure for Type 1 Diabetes".

To read more about type 1 cures and treatments on the horizon, please read our book on the topic called "Targeting a Cure for Type 1 Diabetes" at diatribe.org/cure.

conference pearls



T2 The American Diabetes Association 74th Scientific Sessions - Advances in Type 2 Diabetes

by Alexander J. Wolf, Nancy Liu, Adam Brown, and Kelly Close

Twitter summary: Lots of updates in #t2d at #2014ADA – will new exciting drug combinations make the gains of note that are needed? Also, new ways to make drug delivery easier.

Short summary: This month, one of the largest diabetes conferences of the year, the 74th annual Scientific Sessions of the American Diabetes Association, which was held in our home town of San Francisco. In the type 2 sphere, the conference highlighted exciting drug combinations including GLP-agonists with insulin, as well as SGLT-2 inhibitors with DPP-4 inhibitors. Also, we saw a focus on ways to make taking drugs easier to use and understand.

Combination Drug Therapies Show Promising Results:

A big focus at ADA was the study of drug combination therapies for the treatment of type 2 diabetes. Several big trial results were presented, including those for Novo Nordisk's IDegLira, Sanofi's LixiLan, and Lilly/BI's Jardiance/Trajenta therapies.

GLP-1 Agonists and Insulin

Xultophy (also known as IDegLira) was one of the most exciting drugs discussed at ADA. It is an injectable mixture of Novo Nordisk's long-acting (basal) insulin Tresiba and its GLP-1 agonist Victoza. Xultophy was shown to significantly reduce A1c (from 8.3% at the start of the study to a final average of 6.4%), which was more than either drug could achieve alone. It also showed benefits on fasting glucose, hypoglycemia, and weight. Similarly, Sanofi's LixiLan, a GLP-1 agonist/ basal insulin fixed-ratio product reduced A1c from 8.1% at the start of the study to a final average of 6.3%. LixiLan demonstrated reductions in post-prandial glucose, no increase in hypoglycemia, and low incidence of nausea and vomiting as compared to GLP-1 agents, and it showed more weight loss than Lantus alone. Xultophy will only be available in Europe for the foreseeable future, since the FDA has required a major clinical trial of one of its components prior to approval. LixiLan is currently in phase 3 clinical trials (the last phase before approval), with FDA submission dates estimated for late 2015 or early 2016.

SGLT-2 and DPP-4 Inhibitors

SGLT-2/DPP-4 inhibitor combination therapies continue to be a promising option for type 2 diabetes, particularly since they will be available as a single pill. This combination should represent less of a burden to patients than managing multiple medications at once. What's particularly exciting about this combination is that these two drug classes work in entirely different ways. SGLT-2 inhibitors cause the body to excrete excess glucose in urine – an insulin-independent process – whereas DPP-4 inhibitors use the gut hormones to make the body produce more insulin in response to food. Studies on Lilly/BI's Jardiance/Trajenta combination therapy resulted in an

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SGLT-2/DPP-4 inhibitor combination therapies continue to look promising, and will be available as a single pill.

average A1c reduction of over 1%, as well as greater fasting glucose reductions compared to each drug by itself. This drug has been submitted to the FDA and is awaiting approval.

A focus on improving drug delivery

Although new drug options are essential, we were glad to see work being done to make taking drugs easier and faster. Eli Lilly presented a poster on its once-weekly GLP-1 agonist dulaglutide with a single-use pen, which found that participants had very little injection pain, thought the pen was easy to use, and had reduced fear of self-injecting. This news comes right on the heels of the launch of AstraZeneca's improved pen for the GLP-1 agonist Bydureon (once-weekly exenatide).



On a more experimental note, excitement surrounded Intarcia's ITCA-650, a small device for type 2 diabetes that continuously releases exenatide (a GLP-1 agonist). The device is implanted under the skin for three or six months and preliminary results (first shared earlier this year) look promising – after six months, A1c declined by an astounding 3.2% from a high 10.9% baseline. We had a chance to see the insertion and removal procedure, which were both simple – the insertion took a matter of minutes and removal a matter of seconds. The device is implanted through a tiny, 4 mm incision using a small insertion device. No stitches are even needed, and the incision is essentially covered with a Band-Aid. The device is currently in phase 3 trials.

Also in drug delivery, TransTech Pharma has been working on a GLP-1 agonist that could be taken as a pill instead of an injection, which would be a clear win for patients. This drug is still at an early stage, but it could make it much easier for patients to start and stay with a GLP-1 agonist.

diaTribe dialogue



David Panzirer (left) and Dana Ball (right) are the forces behind the influential HCT and T1D Exchange.

T1 Debates in Type 1 Diabetes – what is the future of diabetes technology and what is a “cure?” Our interview with David Panzirer and Dana Ball

by Adam Brown, Hannah Deming, Nancy Liu, and Kelly Close

twitter summary: *The biggest debates in diabetes – technology, debates and the “cure”. Find out more from the influential duo in our HCT interview.*

short summary: *We had a wide-ranging interview with two of the pioneers of the Helmsley Charitable Trust's (HCT) Type 1 Diabetes (T1D) program (which gives \$50 million a year to type 1 research, treatment, and services): HCT trustee David Panzirer, and patient advocate (and now T1D CEO) Dana Ball. In part three of our interview, David and Dana share insights on one of the biggest debates in type 1 diabetes – what is the future of diabetes technology, what is a “cure”, and more. Read on and please stay tuned for the last two installments in our five-part series:*

Part 1. How The Helmsley Charitable Trust became one of the most important players in diabetes, and the funding needs and challenges in type 1

Part 2. The Future of the Type 1 Diabetes Field – what challenges and promises lie ahead?

Part 3. Debates in Diabetes: Technology, Debates, and the “Cure”

Part 4. The T1D Exchange: A story of David and Dana’s drive to accelerate innovative type 1 diabetes research.

Part 5. What can diabetes advocates learn from successes of the HIV/AIDs movement?

DIABETES TECHNOLOGY

KELLY: The Helmsley Charitable Trust’s (HCT) T1D Program has a major focus on technology. How did that start?

“The most surprising thing was the family impact of having a child with type 1 diabetes. The devices should be smarter, and if they were, they could actually relieve some of the burden of families and people with type 1.”

DAVID: It became clear to us early on that the cure wasn’t around the corner and we needed to provide better care for people today. It was also obvious to us that technology was the way to do so.

DANA: David drove the technology interest and he helped me understand the importance of devices. Whenever I came to New York for work, I’d stay at his house, which provided a real understanding of what it means to have a child with type 1 diabetes. The most surprising thing to me was the family impact of having a child with type 1 diabetes; not the impact on his daughter. The devices should be smarter, and if they were, they could actually relieve some of burden for families and people with type 1 diabetes. This is the future.

ADAM: How can HCT help get more patients on diabetes technology? What are the biggest barriers?

DAVID: We need the help of the entire community and organizations like yours. We need a huge campaign that shows these new devices can actually ease the burden and make type 1 diabetes more manageable. The more people that use the devices, the more of an incentive there is for companies to innovate.

“Glycemic control is challenging and this is a 24/7 problem.”

DANA: Glycemic control is challenging and this is a 24/7 problem. I think we also need to work on awareness for clinicians, especially primary care providers who see adult type 1s. If physicians aren’t educated and supporting we won’t make progress.

DEBATES IN DIABETES

KELLY: Will an artificial pancreas be approved in the US?

DAVID: I do not believe a fully automated artificial pancreas is attainable. That being said, I do believe we can improve dramatically what is being done today. I don’t think you can ever completely remove the person with type 1 diabetes out of the equation. I believe the issues are more the companies than the FDA. We need the companies to step forward and commit resources towards insulin automation.

“Patients have to become aware that they will have a big role in the near future when challenges arise.”

DANA: When it’s ready to go, I think it will be approved. My new worry is what is the cost, will payers cover the device, and how high will the financial burden be on patients? I think our healthcare system is under financial pressure and payers have shared they are looking for superior solutions at no additional cost – they say, “no new money.” This is going to be tough as we prepare to bring new solutions forward and the community needs to work together to prepare accordingly. Patients have to become aware that they will have a big role in the near future when challenges arise.

ADAM: What do you think about a glucagon/insulin vs. an insulin-only artificial pancreas?

DAVID: I believe in the dual hormone approach because I have seen a lot of Dr. Ed Damiano’s work and results, and it more closely mimics the body’s natural functions. As I have heard some say, insulin alone is like driving a car without the brake pedal. *[Editor’s note: To learn more about Dr. Damiano’s work on a dual hormone approach in the bionic pancreas, please read our test drive on the Beacon Hill study and our learning curve on the Summer Camp study.]*

DANA: I love the combination, but it’s early and we don’t have an approved stable glucagon. This will continue to be an interesting debate over the next five years.

“If you told people with type 1 diabetes you could have a once-a-day injection that would normalize glucose and eliminate hypos, they would be all over it”

KELLY: Will glucose responsive insulin ever happen?

DAVID: I think if you told people with type 1 diabetes you could have a once-a-day injection that would normalize blood glucose and eliminate hypos, they would be all over it. That is the promise of glucose responsive insulin.

It is in very early stages and has very long time before it is a therapy in people, if at all. I am not sure if it will ever happen; give me a crystal ball and I will let you know. If we knew the steps to take to make this a reality, it would have happened a while ago; it is not that easy.

DANA: God I hope so! I agree with David, this would be an amazing breakthrough for patients with diabetes.

ADAM: Type 1 diabetes prevention vs. cure?

“Our major focus is giving people with type 1 diabetes better tools to manage their disease.”

DAVID: I am not a “cure” guy. Although we do and will continue to do cure-based research, we have started to put a focus on prevention. As a parent of a child with type 1 diabetes, I hope that I am wrong. If a cure happens, it isn’t even on the horizon now. Our major focus is giving people with type 1 diabetes better tools to manage their disease, so when there are cure therapies that come, they will be healthy enough to receive them.

DANA: With the right work over the next decade, we could see potential cures in decades to come, depending on your cure definition. It will be more than likely easier to ultimately prevent type 1 diabetes, but prevention is a tough conversation because

people live with the disease today. Type 1 diabetes is time consuming and a burden – patients need solutions now! I think we have new tools and resources to better characterize patients at risk and learn how the disease develops, why some people develop disease, and what protects those that don't get type 1 diabetes. My guess is there is a lot of work that has to happen first before we will be able to move forward more effectively.

LOOKING TO THE FUTURE

KELLY: Dana, as you think about the type 1 diabetes field over the next decade, what do you expect to see?

“Automating insulin delivery requires technology. How fortunate are we that we’re in the best era of technology development?”

DANA: I think it's going to be a very good decade for us. I wake up every day excited about the willingness of our community to work together – from the government, industry and the funding community, to families and individuals. Automating insulin delivery requires technology. How fortunate are we that we're in the best era of technology development? There's no doubt in my mind – we will be successful in type 1 diabetes. All the pieces are coming together. I think it's going to be a decade where we see less burden and less worry for people with type 1 diabetes. I think we're sitting on the cusp – we're armed with all the tools and it's like we've broken ground. We have the foundation of the house, and now we have to figure out what type of house we want and what's on the first floor. I'm hooked. All of the seeds I've planted for over a decade are finally moving. I think it's going to be an awesome decade.

KELLY: David, is there a finish line in your mind? What does it look like for you?

DAVID: The finish line for me would be to try and reverse or prevent type 1 diabetes and make it so that future generations don't have to worry about the disease at all. Recognizing that is a long way off, I would settle for getting tools to people with type 1 diabetes that significantly ease the burden of managing this disease. My immediate aspiration is to try to automate basal rates overnight, so that people can sleep through the night without fear and without running high to avoid severe hypos. I wholeheartedly believe that this is an attainable goal that would have an absolutely dramatic effect people's outcomes.

KELLY: What do you want the legacy of HCT to be?

“I want the legacy to be that we put our hearts and souls into easing the burden of managing this disease.”

DAVID: I want the legacy to be that we have put our hearts and souls into easing the burden of managing this disease. I want to be part of the solution that makes this disease easily treatable and keeps people healthy while we wait for that elusive cure.

DANA: I hope the HCT legacy becomes a place where passion meets strategic execution. In the very near future, I hope patients with diabetes will have a product in their hands that has been touched by HCT and co-created with the community.

[Disclosure: diaTribe is supported in part by a generous grant from the Helmsley Charitable Trust.]

learning curve



T1/2 Diabetes and Depression: Seven Things to Know and Resources to Help You Take Action

by Alexander J. Wolf

Twitter summary: #Diabetes and #depression – we go past A1c and examine the mental burden of diabetes + a list of resources 4 more information.

Short summary: Diabetes is far more than A1c, blood glucose values, and insulin doses – it's stress, mental burden, and worry. We were glad to see many talks dedicated to diabetes and mental health issues at ADA this year and have gathered our top seven takeaways – learn the stats and signs of distress or depression, talk to your healthcare provider, and take advantages of all the great resources out there.

Sometimes, diabetes can feel like a total numbers game. What's my A1c? How many carbs are in my meal? What's my blood glucose, and how fast is it rising or dropping? The mental burden of dealing with these questions day-in and day-out takes a toll. And the reality is that mental health issues, particularly diabetes distress and depression, are very real for many patients.

We were pleased to see lots of discussion about these topics at the American Diabetes Association (ADA) conference earlier this month. Here are our top seven takeaways about diabetes and mental health:

1. **“Diabetes distress” is much more common than clinical depression and affects up to 39% of people with type 1 and 35% of people with type 2.** This term refers to the expected worries, concerns, or threats associated with diabetes. People should be aware that if they are struggling with depression or distress, these statistics make it clear that they are not alone.
2. **The conversation should start early.** Parents and health care providers are encouraged to educate adolescents with diabetes about the risks of developing mental health issues at an earlier age. As one presenter framed it, the first conversation a parent has with their child about diabetes and mental health should not be when they are in high school and already showing symptoms of depression or distress.
3. **Mental health screening should be a routine part of diabetes care.** According to Dr. Carolyn Thorpe, if physicians could screen their diabetes patients for only one thing, it should be depression. Unfortunately, many healthcare providers are not experienced or trained in mental health issues.
4. **False positives remain an issue when diagnosing depression.** When it comes to mental health screening, first impressions aren't enough. Any initial positive diagnosis for a mental health conditions must be followed up with an in-depth screening by a trained mental health professional. Particularly given that many first-stage screening processes only involve shortened surveys of mental health diagnostics, a more thorough follow-up is often necessary.
5. **Several therapies exist for coping with depression and diabetes distress;** people need to find the one that works for them: problem-solving thera-

People should be aware that if they are struggling with depression or distress, they are not alone.

Several therapies exist for coping with diabetes distress; people need to find the one that works for them.

While living with diabetes is 24/7, depression or diabetes distress are not. Just like diabetes, depression is not the same for everyone.

pies, cognitive behavioral therapy, exercise, mind-body therapy, medications, and more. A mental health professional will know what therapies make sense for a particular person, and finding one that understands life with type 1 or type 2 diabetes is key.

6. **Depression and diabetes distress change over time.** While living with diabetes is 24/7, depression or diabetes distress are not. Some patients may initially have these issues and then work to control them, whereas others may start out with no mental health complications and only over time develop them. Some days are worse than other days, some weeks worse than other weeks, and some months worse than other months. Just like diabetes, depression is not the same for everyone. For that reason, mental health screenings and awareness should not be a one-time check, but a routine part of diabetes check-ups.
7. **Depression has been linked to poor self-care, poor glycemic control, unemployment, decreased quality of life, and several other negative factors that only make it harder to live with diabetes.** In other words, treating depression is equally as important as treating diabetes. If diagnosed with depression or diabetes distress, people should take it seriously and take action immediately.

If you would like learn more about how to take steps towards managing your mental health as it pertains to your diabetes, here are some useful online resources:



For a valuable guide on depression and diabetes from the Behavioral Diabetes Institute (BDI), visit:

<http://behavioraldiabetesinstitute.org/print-preview/BDIDepressionBookletFINAL.pdf>

For BDI's guide to the emotional side of diabetes, visit:

<http://behavioraldiabetesinstitute.org/print-preview/BDIFinal2ndEdition.pdf>

Dr. William Polonsky's book, *Diabetes Burnout: What To Do When You Can't Take It Anymore*

For skills and strategies for healthy coping with diabetes, go to:

http://www.diabetesinitiative.org/build/hc_healthyCoping.html

If you're interested in using exercise to better your physical and mental health, check out:

<http://movemore.org/>

For an online assessment of your stress levels and tutorials on how to improve your quality of life, go to:

<http://www.williamslifeskills.com/>

To sign up for a free, online "Better Choices, Better Health" diabetes workshop, see this Stanford University resource:

<https://diabetes.selfmanage.org/bcbhds/SignUp>

trial watch

Can a type 2 diabetes drug improve kidney and heart health?

T2 Effects of Canagliflozin on Renal and Cardiovascular Outcomes (CREDESCENCE)

ClinicalTrials.gov Identifier: NCT02065791
<http://clinicaltrials.gov/ct2/show/record/NCT02065791>

Johnson & Johnson/Janssen is researching the effects of Invokana (canagliflozin) to determine its effects on kidney and heart health in patients with type 2 diabetes with stage two or three chronic kidney disease and macroalbuminuria (protein in the urine). Invokana is an SGLT-2 inhibitor, which works to lower blood glucose by excreting excess glucose through urine. Treatment is a once-daily pill taken over the course of up to 66 months. Participants should be over 29 years old and have type 2 diabetes with an A1c between 6.5% and 10.5%, among other criteria. The study will enroll around 3,600 subjects at hundreds of sites in the United States and Canada. Interested parties should visit the trial website to determine eligibility. More information can be located at ClinicalTrials.gov or by contacting JNJ.CT@sylogent.com.

– BH

Can a cancer drug benefit recently diagnosed type 1 diabetes?

T1 Imatinib Treatment on Recent Onset Type 1 Diabetes

ClinicalTrials.gov Identifier: NCT01781975
<http://clinicaltrials.gov/ct2/show/NCT01781975>

Type 1 diabetes stems from autoimmune destruction of beta cells, and many therapies are under investigation to stop or reverse this process. The cancer drug imatinib (Gleevec) is being tested by the University of California, San Francisco as a type 1 diabetes treatment. The belief is that Gleevec, a tyrosine kinase inhibitor, may be able to preserve beta cell function in patients recently diagnosed with diabetes. The study will assess insulin production, immune system function, and other health factors over a two-year course of treatment. Potential participants must be over 18, have had type 1 diabetes diagnosed in the past 100 days, and must agree to use birth control for the duration of the study, among other requirements. The study is located in the United States. To learn more, visit ClinicalTrial.gov or email sgitelma@pediatrics.ucsf.edu and jbluest@diabetes.ucsf.edu. -BH



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