diaTribe®

research and product news for people with diabetes

in this issue

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from the editor

As we begin 2014, it seems appropriate to step back for a moment and reflect on the past year in diabetes. I like to use a game called "Rose, Bud, Thorn" to think of one big trend that was positive (the rose), one that has potential (the bud), and one that remains a problem (the thorn).

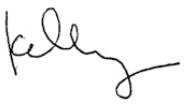
Let's start with my rose. No advance was more exciting this year than the progress made on SGLT-2 inhibitors for type 2 diabetes. That includes Janssen's Invokana, which received FDA approval this past March, and BMS/AZ's Farxiga, which was approved in Europe in November 2012 and was just approved in the US on January 8. This past year's round of regulatory meetings have offered several opportunities to see new data on the efficacy and potential side effects of SGLT-2s, and the results have been encouraging. Invokana and Farxiga are once-daily oral drugs with, for most patients, manageable side effects, a low risk of hypoglycemia, and slight weight loss that make them appealing for patients. In the near future, we could see exciting growth for the drug class as well as possible fixed-dose combinations.

Moving onto the bud, I'm not sure I've seen anything in my decade of writing about diabetes research that has more potential than the artificial pancreas. This year, we published my test drive on Dr. Ed Damiano's system and "The Bionic Kids put the Artificial Pancreas Through the Rigors of Summer Camp", which are already among *diaTribe*'s most widely read articles!

Let's spare a moment to consider the thorn. Frankly, it's hard not to be pessimistic about the current state of diabetes care in the big picture, due to giant challenges in reimbursement and access. The problem with this pricing pressure is that it leaves little room to encourage innovation. The higher cost of drugs helps fund research and development and brings greater investment into the field. There's no room left for innovation, and big companies may well start pulling out of R&D altogether if they can no longer justify the costs.

Let me finish my reflections on 2013 with a call to action for 2014. The current state of reimbursement is a problem that we have to solve, and when I say "we," I really do mean the entire diabetes community. Advocates need to create effective arguments to be heard, and we need to present a unified front. This is the time for ambitious resolutions, after all. Every patient needs to be a patient advocate, because if we're not going to stand up for ourselves, then who is? If we can all start living by that credo, then 2014 and beyond can be a time of limitless potential for us all.

Very Best,



quotable quotes

"We're treating diabetes; we're not treating A1c levels. Diabetes is a complex disorder… we should be treating diabetes with a combination approach tied to pathogenesis [how diabetes develops] rather than tied to a reduction in A1c levels."

– Dr. Merlin Thomas (Baker IDI, Melbourne, Australia) on using fixed-dose combinations for diabetes at the World Diabetes Congress in Melbourne, Australia on December 2-6.

"Social media is only one tool in a toolbox, but an increasingly important one."

– Kelly Close (Editor in Chief, diaTribe) to a standing-room only audience at her workshop on patient empowerment through social media at World Diabetes Congress.

"I do not cope with diabetes; diabetes copes with me."

– A character with type 2 diabetes in Novo Nordisk's play "Getting Straight to The Point" about the misconceptions surrounding injections. The play had its world premier at the World Diabetes Congress.

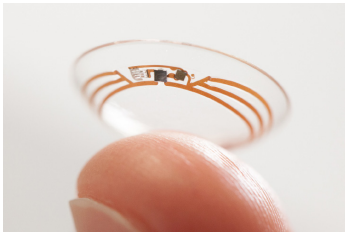
fingersticks

ILLUSTRATION: JOSEPH SHIVERS

"Meditation seems to make my glucose 'spikes' smaller… especially when I meditate on grilled chicken instead of spaghetti!"

new now next

T1/2 Glucose Sensing Contact Lenses – Google[x]'s Ambitious Venture into Diabetes



Today, Google announced that it is working to develop a contact lens that could non-invasively monitor glucose levels from tears. The smart contact lens team at Google has put together the existing electrochemical technology of a continuous glucose monitor (CGM), a soft contact lens, a chip (about the size of a piece of glitter), and an antenna. Google is now testing prototypes that can generate a reading once per second and would, as planned, not need calibration. Though the device is in its early days and not close to coming to market, some clinical trials have been done, and the team has recently spoken with the FDA. The smart contact lens project clearly falls alongside other hugely ambitious projects that the company's top-secret research arm, Google[x], is working on: a self-driving car, balloon-powered Internet, Google Glass, and affordable wind power. The smart contact lens is the fifth Google[x] project ever – with the x indicating that Google believes the technology could be ten times better than what is currently available, as we understand it. Wow! What a statement. Even if they may not get there, it is a giant statementt hat Google is taking on diabetes.

Monitoring glucose non-invasively is obviously not new in diabetes. A number of companies over the years have tried similar projects – C8 MediSensors, FoviOptics, SpectRX – though none has succeeded. We know Google[x] can learn from others in the field as well - academics, researchers, executives, and patients alike. Looking back, FoviOptics was run by two particularly smart and well-respected leaders, but after Mr. Lortz and Mr. Liamos exited the field, there has been little hope that a non-invasive monitor could be developed or commercialized. Historically, isolating glucose molecules with sensors has been impossible to do in either a practical or affordable way.

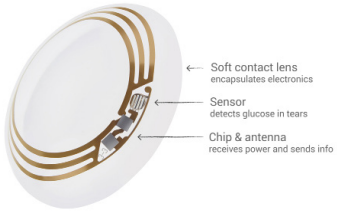
Other leaders in the diabetes arena have also been working on initiatives to make blood glucose monitoring easier, less invasive, and more intuitive.

Dr. Brian Otis, the project co-leader at Google[x] (along with Babak Parviz), explained some of the specific barriers to monitoring glucose in tears. First, glucose levels in tears are five to ten times lower than concentrations found in blood, making detection difficult. Second, methods that involve collecting tears often contain artifacts from using capillaries. There are also concerns that contact lenses could be uncomfortable or difficult to wear. Historically, continuous glucose sensor development has had to balance many other factors: the size of electronics, power/battery constraints, the need for an antenna to send the information to a receiver, on-body comfort, and more.

Other leaders in the diabetes arena have also been working on initiatives to make blood glucose monitoring easier, less invasive, and more intuitive. Dexcom has a long-term goal of eliminating fingersticks through a more accurate, factory-calibrated CGM sensors. In the short-term, Dexcom is hard at work on Share (a remote monitoring system currently under FDA review) and its Gen 5 mobile platform (CGM data straight to the smartphone!). Meanwhile, Abbott Diabetes Care is developing the Flash Glucose Monitoring System, which will involve use of a glucose sensor worn under the skin (like current CGM) for up to 14 days and a wireless touchscreen reader device. A patch worn over the sensor will be silver dollar-sized and about a finger-width thick. Users will scan the touchscreen reader over the sensor patch to get their real-time sensor glucose value, a glucose trend arrow, and a trend graph showing the last eight hours. The system will be calibrated at the factory, meaning users will not need to enter any fingerstick values for calibration. Exciting times ahead in glucose monitoring!

On an inspiring note, given Google's resources to move the field of diabetes forward, the Google[x] team made it clear it is by no means planning to do this project alone. The company is looking to partner with other companies and people who have experience bringing medical technologies to the market. The hope is for others to use the smart contact lens technology and develop apps that would make measurements available to patients (e.g., on a smartphone or a receiver) and to their health care providers (e.g., in an electronic health record). One major question is how to produce this device at a reasonable cost, since the lenses would not last forever; we do think Google could subsidize continued R&D in a significant way should companies decide they would like to pursue this.

To be sure, the talent at Google is renowned - Dr. Otis has a killer bio (for example, he used to run a chip design research lab and has worked at Intel Corp. and Agilent Technologies) and we found him at once humble as well as inspiring in our interview with him. As we understand it, Google has also been quietly building its internal team with smart hires, with "not just process engineers, but research chemists" who can really bring understanding of how to move this project forward.



For those worried about where the data would go, Joseph Lorezo Hall, chief technologist at the Center for Democracy and Technology was briefed on the project before it went public. In a Washington Post article, he said he was assured that the data would never hit Google's servers. We're glad to hear that Google is treating this sensitively, although aggregated data could actually be a a positive way to measure the diabetes status of the public using the device. No doubt, eduation on what to do with all the numbers patients see will be something that Google[x] will work on in partnership.

Big picture, a non-invasive method of measuring glucose has the potential to improve the ease and frequency of monitoring, avoid the use of needles, and harness technology to improve the lives of people with diabetes. Although the Google[x] device is still very much a prototype in its early stages, we feel confident that Google could drive forward very valuable thinking in diabetes. With the company's massive reach, we are very excited about the ability it has to bolster what the diabetes ecosystem can achieve for patients. The smart contact lenses have already attracted some major attention, with great coverage from the BBC (that includes a video of the lenses), NPR, and the Telegraph.

Google's move into healthcare is a major statement by the technology giant; notably, diabetes is its first healthcare focus with this fifth moonshot!

Google's move into healthcare is a major statement by the technology giant; notably, diabetes is its first healthcare focus with this fifth moonshot! We cannot wait to watch more and learn. In the meantime, we hope the diabetes field will look to share its brainpower with Google… sometimes one plus one is not only not two – it could be ten! As Google[x]'s Dr. Otis says "We're actively looking for partners to help us out…" *-NL/KC/AB*

Our questions (email us to add to the list!)
What will be the accuracy of the smart contact lenses?
Where will the data emerge (phone, website, app)? Will it be open source?
Can patients put their data from these contact lenses in an anonymous registry?
How long will the contacts last?
How will the technology be priced?
What is the FDA's impression?
Will the contact lenses be released in the US or internationally first?

Bristol-Myers Squibb
AstraZeneca

T2 FDA Approves the SGLT-2 inhibitor Farxiga (dapagliflozin) for Type 2 Diabetes

On January 8, the FDA approved Farxiga (dapaglifozin) for the treatment of type 2 diabetes. The drug is called Forxiga in Europe, where it has been approved since November 2012. Farxiga is an SGLT-2 inhibitor like J&J/Janssen Cilag's Invokana (canagliflozin), which works to lower blood sugar by excreting excess glucose through urine. Patients using Farxiga typically reduce their A1c by an average of 0.8% to 1% in trials lasting a year (this is from a starting A1c of 8.5% before the trial began – so that's pretty good!). Urination of excess glucose also means losing some excess calories each day, and indeed, participants in clinical trials lost a few pounds on average and saw a small drop in blood pressure. As a note, Kelly took the SGLT-2 Invokana "off-label" for some time and lost ten pounds. Farxiga's most common side effect is urinary and genital tract infections, which many experts believe are fairly easy to manage should they occur.

In order to understand the long-term effects of Farxiga better, the FDA is requiring six long-term studies for the drug after it is put on the market.

In order to understand the long-term effects of Farxiga better, the FDA is requiring six long-term studies for the drug after it is put on the market, which includes a cardiovascular outcomes trial (CVOT), two bladder cancer risk studies, a pediatric study, and a program that will monitor other side effects. Until the long-term effects of Farxiga are well established, Farxiga is not recommended for patients with active bladder cancer or with moderate to severe kidney impairment. Although it will be very interesting to see if any of the newer medications are "cardio-protective," we continue to wonder about the value of CVOTs since they are so expensive to design and execute and the safety data is still not clear. In this case, the CVOT is required after approval, which is a big positive – other drugs in development are often delayed because they require a CVOT pre-approval.

After BMS/AZ's initial regulatory submission of Farxiga in January 2012 the FDA called for more data to address concerns related to bladder cancer, cardiovascular issues, and liver safety. In December 2013, the Advisory Committee (a panel of experts that provides recommendations to the FDA on the safety and effectiveness of new therapies) reviewed the data and decided that these concerns did not appear to be serious enough to keep the drug from reaching the American public, and voted an overwhelming 13-1 in favor of approving Farxiga. Notably, the vote was a closer 10-4 on whether the drug met the FDA's cardiovascular safety guidelines, which suggests that some panelists don't see the guidance as necessary for having a drug approved. Having more options in diabetes treatment is essential – especially since only around half of patients are at their A1c goal – and the approval of Farxiga is positive news for the future of SGLT-2 inhibitors and other drugs in development. *–NL/JD/KC*

T2 Invokana is Approved in Europe – An Exciting Year for SGLT-2s

On November 22, J&J/Janssen Cilags' SGLT-2 inhibitor Invokana (canagliflozin) was approved in Europe. This makes Invokana the second SGLT-2 inhibitor approved in Europe, following BMS/AZ's Forxiga (dapagliflozin), which received approval in November 2012. Farxiga (the US name for Forxiga) was just approved in the US on January 8, 2014. Invokana and Farxiga are oral drugs that lower blood glucose by excreting excess glucose through urine. Invokana has been approved in the US since March 2013. This has been an exciting year for the brand new SGLT-2 inhibitor drug class, given the launch of Invokana in the US this past spring, the launch of Forxiga in Europe in December 2012, and the approval of Farxiga this January in the US. For more on Invokana, see our article on the US approval and our accompanying learning curve. *–TW/AB*

T1 The Helmsley Charitable Trust's $30 Million Program to Fund Automated Insulin Delivery

On December 2, the influential Helmsley Charitable Trust (HCT), one of the world's largest funders of type 1 diabetes research – and the 12th largest private foundation in the US – announced a $30 million program to fund the development of new automated insulin delivery technologies for patients with type 1 diabetes over the next three years. Four broad areas of interest exist for this funding opportunity, reflecting HCT's desire to work on many different aspects of automated insulin delivery:

1. Fully External Systems (i.e., currently available pumps and CGM sensors)
2. Fully Implanted Systems;
3. Mixed External and Implanted Systems (i.e., an implanted CGM and an external pump);
4. Handheld Controller, Software, & Connectivity.

HCT is a very patient focused organization, and their diabetes side is no exception.

HCT is a very patient focused organization, and their diabetes side (about 20% of its funding) is no exception – for instance, to qualify for funding related to external systems, HCT requires that proposed systems should not be larger, more cumbersome, or more complicated than current devices on the market. Major kudos to HCT for putting together a large grant program with so much potential to help bring automated insulin delivery technology to the market faster. We cannot wait to learn who applies to this program and what projects are ultimately funded, as the scope is so broad. The HCT has been particularly influential in funding automated insulin delivery and moving next generation technologies forward through industry partnerships with BD (a new type of CGM and advanced insulin infusion sets), Dexcom (the highly accurate Gen 6 sensor), and Medtronic (a new type of redundant CGM), as well as academic partnerships with Boston University (Dr. Ed Damiano) and Stanford (Dr. Bruce Buckingham). So much to look forward to in the coming years! To learn more about the HCT's work, we recommend watching the very inspirational video about the bionic pancreas called "Until There Is A Cure." *–TW/AB/KC*

[Editor's Note: Since 2012, diaTribe *has been supported in part by a grant from the Helmsley Charitable Trust.]*

T1 UVA Receives $3.4 million NIH Grant for Artificial Pancreas Trial with 250 Participants in Network Closed-Loop System

On November 18, the University of Virginia (UVA) announced that it received a $3.4 million NIH grant for three artificial pancreas studies to be conducted at UVA and Stanford. Notably, the three studies will occur in patients' homes, and a very large population of 250 adults and children in total will participate in the three trials combined. The first study will be one month long, aiming to reverse hypoglycemia unawareness. As currently planned, a follow-up study will be even longer, lasting an impressive three months and aiming for long-term improvement in glucose control (A1c). The goal is to begin the trials in April/May 2014 depending on FDA approval, with the first results expected in mid-2015. The large size, long-term, and more real-world nature of these trials is very notable, especially considering that results from the first artificial pancreas studies to occur outside of the hospital were first reported not so very long ago in February 2012. See this issue for Kelly's recent experience on this system – she had an incredible time testing it and sees it as a landmark product.

The University of Virginia's artificial pancreas system, called the Diabetes Assistant, runs a control algorithm on an Android smartphone that communicates with an insulin pump (Roche or Tandem) and a Dexcom CGM. The insulin-only system uses "treat-to-range" control during the day, meaning patients will still bolus for meals, but the system will aim to keep glucose in a designated range by increasing/decreasing insulin infusion as needed. Overnight, the system will "treat-to-target," with the goal of stabilizing glucose and giving patients a fresh start at 110-120 mg/dl every morning – yes! These trials will also use a new network approach to artificial pancreas design, which is intended to make the system safer by distributing the system's computing between local services and the cloud.–*TW/AB*

T2 **FDA Removes Restrictions on Avandia, But is it Too Little Too Late?**

On November 25, the FDA announced the removal of the major restrictions on the prescription and use of GlaxoSmithKline's Avandia (rosiglitazone) for type 2 diabetes. Based on re-examined and updated evidence, the FDA decided that use of Avandia does not show an increased risk of cardiovascular disease (disease in the heart and blood vessels). This means that Avandia, which used to carry a severe warning for risk of heart failure, will now have its restrictions lessened and can now be available to the general type 2 diabetes population. However, given the bad press the drug has received and the low level of current sales, it's not clear if many doctors will prescribe it or patients will take the drug in the future. Avandia is now off-patent, which means that generic rosiglitazone drugs are more affordable for patients.

The Avandia saga underscores the importance of calm decision-making and proper data interpretation.

Avandia is a thiazolidinediones (TZDs) that affects insulin resistance sensitizes the body to insulin. It launched in 1999 and was one of the best-selling diabetes drugs on the market despite a challenging side effect profile that included weight gain, edema, and an association with congestive heart failure. Still, Avandia remained popular because of its effectiveness in lowering A1c and because it had a long "duration" (meaning, it was effective for a longer period of time). In 2007, a controversial meta-analysis (a combined analysis of multiple studies) suggested that it could increase the risk of heart attacks. These results created widespread media attention, increased fear and uncertainty for patients, and led to the FDA's onerous cardiovascular requirements for diabetes drugs in development, which are still hotly debated (see the discussion on CVOTs for Farxiga in this issue). Re-examined results from the RECORD clinical trial did not confirm the increased risk of heart attack or death from use of Avandia. Ultimately, the Avandia saga underscores the importance of calm decision-making and proper data interpretation. To learn more about the history and controversy of Avandia, please read our learning curve. –*NL/KC*

T2 **Takeda Stops Development of Oral Drug for Type 2 Diabetes Due to Liver Safety Concerns**

On December 27, Takeda announced that it would stop development of TAK-875 (fasiglifam) due to liver safety concerns – this was one of the most unfortunate announcements we have heard in diabetes for a long time. The drug would have been the first in a new class of oral medications for type 2 diabetes called GPR40 agonists. The GPR40 agonist class has previously been billed as a "better sulfonylurea" because it improves glycemic control by stimulating insulin release, and without the higher risk of hypoglycemia. For our last update on TAK-875, please read our new now next in diaTribe #34.

TAK-875 has been in late-stage patient trials in the US, Europe, and Japan, including a very large cardiovascular outcomes trial. Takeda reported early results for TAK-875 in May 2013 that showed greater A1c reductions compared to placebo (-0.75% for the 25 mg

dose and -1.0% for the 50 mg dose) from an A1c baseline of around 7.8%. Little data have been shared about the liver safety issues and side effects of TAK-875, and it may be some time before the results are made public. We know that liver safety is extremely dangerous and the risk benefit ratio likely was not favorable enough for TAK-875 to move forward in the pipeline. This also comes at a time when an uncertain regulatory environment and increased competition in the field has raised the bar for advancing new therapies in diabetes. Nevertheless, it is very disappointing to hear that this new drug class will not be an option for patients anytime soon. *–NL/JD/KC*

T1/2 Orexigen Resubmits Weight Management Drug Contrave to the FDA

On December 11, Orexigen announced the resubmission of its weight management drug Contrave (naltrexone/bupropion) to the FDA. The company has previously stated that it expects the FDA to make a decision by June 2014. Overseas, Orexigen just submitted Contrave to the European Medicine Agency this past October.

If approved, Contrave would be the third obesity medication that would become available in the US, following a 13-year period of no FDA approvals of obesity drugs.

In previous trials, participants using Contrave averaged about 5% greater weight loss over one year than those using a placebo (a pill with no medication). People taking Contrave experienced slight increases in heart rate and blood pressure when compared to placebo. Concerns over these cardiovascular side effects led the FDA to delay approval for Contrave in 2011 while it awaited more data, which has now been shared. Orexigen is currently conducting a cardiovascular outcomes study with about 9,000 patients to assess whether there is any increased risk of cardiovascular events (e.g., stroke, heart attack, death from cardiovascular causes) associated with Contrave. To learn more about the study, please read our new now next.

If approved, Contrave would be the third obesity medication that would become available in the US, following a 13-year period of no FDA approvals of obesity drugs. Arena/Eisai's weight management drug Belviq launched in the US in June 2013 and Vivus' obesity drug Qsymia launched in September 2013. Aside from weight loss, Qsymia and Belviq have also demonstrated potential to help improve diabetes control, and in the case of Qsymia, to reduce the progression to type 2 diabetes in high-risk individuals. The obesity field has seen some real improvements on the reimbursement side, meaning patients will need to pay less out of pocket to use these drugs. Broadly speaking, 5% weight loss may not sound like much, but we know that there are some patients that are "super-responders" and have excellent results after taking the drug. *–NL/HD*

T1/2 Fight4MyFeet Campaign Fights to Increase Awareness of Diabetic Foot Ulcers

Last month, the Fight4MyFeet campaign launched to increase awareness of diabetic foot ulcers among people with diabetes, including a host of valuable tips on how to protect and care for your feet. Over time, high blood sugars can lead to impaired blood flow to the feet and nerve damage (neuropathy). These complications can lead to a loss of feeling in the feet, reduced ability to fight infection, and a reduced capacity to heal wounds. With such damage, patients might step on a sharp object and not feel it, or they might have a wound on their foot that is slow to heal or becomes infected. These kinds of sores are called diabetic foot ulcers. Fight4MyFeet provides an important resource to learn about foot care and this common complication of diabetes, since a stunning 15% of people with diabetes will experience a foot ulcer at some point in their lifetime. The risk of lower extremity amputation is actually 15 to 46 times higher in people with diabetes than people without diabetes, so anything that can improve these statistics would make an incredible difference in patients' lives.

We particularly appreciated the patient stories featured on the site, which provide testimonials from people with diabetes who have lived with diabetic foot ulcers and how DFUs can affect your daily life. The website contains easy-to-understand information and provides some actionable tips for people with diabetes to take care of their feet. Fight-4MyFeet is an educational program and its online resource includes websites dedicated to both patients and healthcare providers. You can learn more by visiting www.Fight4MyFeet.com. *-NL*

SANOFI

T1/2 **Calling All Innovators: The Partners in Patient Health Innovation Challenge Brings Patient Insights to Drug Development**

On December 9, Sanofi launched the second Partners in Patient Health (PIPH) Innovation Challenge on "Co-Creating for Breakthroughs: Moving toward a collaborative research and development ecosystem." The Collaborate | Innovate challenge invites non-profit patient, provider, and professional associations to partner with other non-profits and/or academic institutions to propose new approaches to bringing patient insights into improving the drug development process. The winning team will be awarded $100,000 to help patients play a role in drug research and development – and hopefully, to lead to improvements in the efficiency and effectiveness of developing new therapies.

This is an exciting opportunity for patient advocates working in any disease area, and organizations from a multitude of backgrounds can create partnerships and apply. Proposed ideas must focus on patient insights into drug development, include measurable goals with a view toward creating a pilot project, and all team members must be legally based in the United States. The submission period will remain open until February 23, 2014 and the final judging will take place in April of 2014. To learn more and enter, please visit www.collaborateinnovate.com. *-NL*

my diabetes HOME™

T1/2 **My Diabetes Home – A Tool for Diabetes Management**

My Diabetes Home is an online dashboard that allows patients to record, organize, and track personal diabetes information, including medications, daily blood sugars, A1c, blood pressure, weight, and more. Importantly, users can see automatic alerts on their blood glucose numbers if they are out of range.

One of the most actionable features is the Visit Optimizer tool, which takes all of the data gathered by My Diabetes Home and generates a comprehensive report to give to providers. It also lets you add specific health goals and questions to ask your provider – for more ideas about questions to ask your provider, you can view our patient guide at www.diaTribe.org/patientguide.

My Diabetes Home has announced the addition of new features in January 2014. These include adding the ability to schedule doctor appointments with custom reminders and coaching emails to help members get on the right track with their diabetes management. My Diabetes Home will also soon be launching a mobile version of their website, which will help its members record key information on-the-go and during their doctor visits. *-NL*

test drive

T1 UVA's Overnight Closed-Loop Makes For Great Dreams

by Kelly Close

Twitter summary: Details on the UVA overnight closed loop trial - an incredible opportunity for the field to move fast, reduce anxiety, + beat timelines

I knew that it was going to be difficult to beat the experience I had on the MGH/BU bionic pancreas, but there has been so much progress recently with automated insulin delivery technologies, and I am always excited to learn about new prospects and choices for patients. So, when I heard about the University of Virginia (UVA) study testing overnight closed-loop control, I jumped!

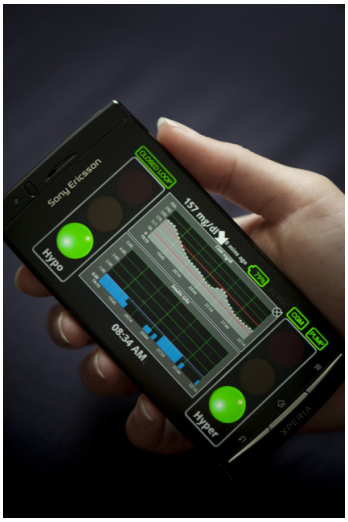
Over five days, I wore the study's DiAs (short for "diabetes assistant") system at night: a Roche Combo pump, two Dexcom CGMs [the second CGM is used as a backup at the FDA's request], and a control algorithm running on an android cell phone. A Dexcom Share is used to transfer the CGM data from the receiver to the DiAs system, although we expect this intermediate device won't be necessary when truly wireless sensors come out (there has been lots of progress coming on that front as we understand it).

The control algorithm is called the USS Virginia, and it is designed to take control after dinner, maintain safe glucose levels overnight, and target a normal fasting morning glucose (e.g. 80-120 mg/dl) to "reset" for the new day. Using the Dexcom CGM readings, the algorithm directs the pump to give me the appropriate amount of insulin overnight to reach a target blood glucose of 120 mg/dl.

I lived in the groovy 1880s Victorian "research house" at UVA called Sunnyside that had four bedrooms, and lots of cozy places to work; the UVA team remotely monitored me from an adjacent room, though I was effectively on my own. I loved being in the house, as it had many researchers, scientists, inventors, and MDs roaming around. This was my idea of heaven!

Overnight closed-loop was powerful in a way I was not expecting. Every night, I settled down to bed at 11pm and turned on the system – how cool was it to push on my Android phone 'CLOSED-LOOP ON." And then as I drifted off to sleep, the best part of all happened – nothing. I didn't wake up in the middle of the night with a blood sugar of 54 mg/dl. I wasn't tired in the morning from a night spent at 180 mg/dl (where my Dexcom often hovers). Instead, for five straight days, I woke up at 7 am with a blood glucose of 120 mg/dl, having spent most of the last eight hours at that level. It felt incredible – and it felt different than just waking up at 120, which is possible when I hear my Dexcom alarms at night and adjust them appropriately. Here, it was all about the machine doing the work.

So often when I wake up, I'm *fixing* something or my husband Johnny is helping or fixing stuff for me. We hear my CGM beep, look at a meter reading, and immediately start troubleshooting – Why am I high? How much fat was really in that meal? Did I exercise more today than yesterday? Or, why am I low? I know I'm insulin sensitive in the morning, but it's anyone's guess when this sensitivity changes – most people with diabetes are more insulin resistant in the morning, so this has puzzled others looking at my numbers.



Yes, it's often playing a personal blame game, which can often become inordinately exhausting. This trial was really eye opening, as the algorithm gave me a totally different amount of insulin every night. Some nights I needed seven units, and others I needed four, which depended on how much I had eaten, what I had eaten, how much I had or hadn't exercised, whether I was feeling any anxiety – and the list goes on. The system was also able to vary the timing of the dosing differently across the night based on these factors. The power of this approach was not lost on me – the system took the guesswork out of setting a nighttime basal rate. It made micro-adjustments every five minutes, and there's no way I could beat it – I was sleeping the whole time. After one day of wearing the system, I was ready to take it home.

But I also started thinking, "What would it look like for the field of diabetes if we had this tomorrow?"

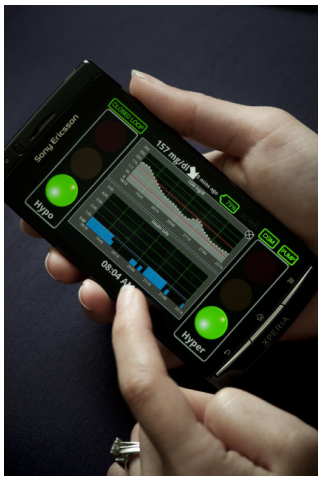
- "Dead-in-bed" could be gone, and severe hypoglycemia at night could effectively be eliminated;
- Since the nighttime period is one-third of the day, we would likely improve A1c levels in many people (and for those already in great control, keep A1c's the same and reduce hypoglycemia);
- "Time in Zone" could improve significantly – while I don't expect it would improve as much as with the bionic pancreas (since that would provide control in the day and night), it's clear to me now that control at night could possibly prompt better control in the day;
- We could help all people with diabetes sleep a lot better, have more energy the next morning, have better blood sugars throughout the next day, and best of all, be more productive sooner!
- We could make the lives of parents and partners A LOT easier

I dream of a day when I will put on a system and it will control my blood glucose automatically, without have to do anything.

I dream of a day when I will put on a system and it will control my blood glucose automatically, without having to do anything – no more carb counting, no more bolus calculating, no more treating lows. I cannot wait for that day, but we'll need some significant advances to get there: ultra-fast insulin; CGM that is as good as fingersticks; control algorithms that can deal with exercise, stress, and meals; and perhaps other hormones like glucagon and amylin.

Until that day arrives, I'm really excited about the potential of overnight closed-loop insulin delivery. This system has been undergoing work for a long time – the first meeting on "Obstacles and Opportunities on the Road to an Artificial Pancreas" started the project on December 19, 2005 at the NIH Lister Hill auditorium. Three months later, JDRF announced the first round of funding, and UVA was one of the six centers that first started the JDRF artificial pancreas consortium. The first closed-loop studies began at UVA, Italy, and France in 2008, and after years of in-hospital trials, the first portable DiAs systems were tested in pilot outpatient studies of closed-loop control in 2011.

Since then, the trials have become longer and the algorithms have improved. We've learned that the venerable Mayo Clinic and Mount Sinai will also be involved in these trials – this is incredibly exciting, as both of these institutions have the resources to push the research further. Although it's hard to predict regulatory approval, we believe that the system would need a pivotal trial that would shows the closed-loop system can significantly reduce hypoglycemia and is easy to use compared to a sensor-augmented pump.



The biggest hurdle will be establishing a solid wireless connection with the sensor and pump, and the UVA researchers are hoping to achieve appropriate connectivity in the next several months.

I think there's very little downside to approving this system once we're sure it can work reliably and accurately, especially when it's compared to the haphazard approach we currently use to give insulin at night. What's more, it would address one of my biggest problems about this field: unrealistic expectations. In my experience, overnight closed-loop really worked, and it was better than what I could ever hope to achieve on my own.

Incremental improvement is underrated, particularly in diabetes technology. All of us want the home run product, and we want it right now. But that's not how things work in the real world. Great products stand on the shoulders of first-gen products that came before – the Dexcom G4 Platinum is a remarkable advance in CGM, but it all started with the challenging-to-use Dexcom STS. The first-generation Insulet OmniPod was a landmark insulin pump, but it can now seem outdated compared to the much smaller second-generation version (and that's one of the best first-gen products we've ever seen). New products always have room for improvement, but they lay the foundation for future innovations. Importantly, the DiAs system has a "switch" that will be able to flip "on" and do post-meal corrections during the day, with no algorithm alterations necessary!

Overnight closed-loop is just the kind of victory we need in artificial pancreas development.

Overnight closed-loop is just the kind of victory we need in artificial pancreas development. Instead of shooting for the stars and expecting perfection, I'd like to see us move faster, but with smaller pieces, all with the same goal at the end – closing the loop just like we've been saying for the past year. I'm ALL for moving to a hybrid 24/7 closed loop and taking my brain out of the equation during the day. But until that's ready for primetime, I'll be happy to wake up at 120 mg/dl every morning!

The main question, of course, is when thi will be ready for patients. We'll be back with more news in the next issue, but as far as we're concerned - it couldn't come too soon! We want to advocate for this to move forward quickly at the FDA and hope you work with us on this front as that automated insulin delivery at night can become a reality for patients. If you are interested in participating in an artificial pancreas study at UVA, please email artificialpancreas@virginia.edu. You an also email to ask about other studies in different locations. Thank you so much to all of the fantastic researchers, scientists, and doctors at trial, especially Dr. Sue Brown and Dr. Boris Kovatchev, who took especially good care of me!

[Editor's Note: This study is supported by NIH grant RO1 DK 085623, at UVA and in Italy. The development of the DiAs system is supported by JDRF and Paul and Dianne Manning, Charlottesville, VA.]

If you are interested in participating in an artificial pancreas study at UVA, please email artificialpancreas@virginia.edu.

Kelly with the medical and technical team at the UVA trial.

Kelly with Kate Jenks at dinner.

thinking like a pancreas

T1 You Call That An Artificial Pancreas?

by Gary Scheiner MS, CDE

By now many of you have heard and commented on the latest product approved by the FDA: Medtronic's MiniMed 530G insulin pump with Enlite CGM. As a "threshold suspend" system, the MiniMed 530G technically falls under the FDA's new "Artificial Pancreas Device System" category. But before you go running around yelling "We're cured! We're cured!" and chucking your diabetes supplies into a recycling bin, there are a few things that everyone should know.

The 530G is NOT an artificial pancreas as many formally think of the term; it is a step toward the artificial pancreas. It doesn't deliver insulin automatically. It doesn't eliminate the need for fingerstick blood sugar measurements, though far fewer are required for many patients than in the old days! And it doesn't alleviate the ongoing decision-making required to manage diabetes on a daily basis. But it does represent an important first step toward the development of an artificial pancreas. Why? Because this is the first time the FDA has approved a device that makes a decision, any decision, about insulin delivery without the user's involvement. The 530G will temporarily suspend delivery of basal insulin for up to two hours any time the Enlite glucose sensor detects a blood sugar that is below a user's set low threshold (60-90 mg/dl). That's important progress – many don't realize it, but even traditional blood glucose monitors are not technically approved for insulin dosing decisions.

So where do we go from here? Let's review the steps toward an artificial pancreas, examine the pros and cons of each stage, and see what we can do until it hits the market.

So where do we go from here? Let's review the steps toward an artificial pancreas, examine the pros and cons of each stage, and see what we can do until it hits the market.

STAGE 1: THRESHOLD SUSPEND (LOW GLUCOSE SUSPEND)

This is what the MiniMed 530G currently offers. Research has shown that the two-hour suspension of basal insulin does not tend to lead to undesirably high blood sugars or ketoacidosis. It simply takes a patient from a hypoglycemic state (who is not responding to alarms) and suspends basal insulin for two hours – over the next couple of hours blood sugar rises out of hypoglycemia (more details on the pivotal study are explained here). This can be a source of comfort for loved ones (particularly at night) and a potential life-saver for anyone who experiences hypoglycemia while unconscious or is unable to respond to the alert. But there are a few issues.

The MiniMed 530G with Enlite CGM relies on a sensor to measure glucose levels accurately in a relatively low blood sugar range. That's challenging for any sensor, since a 15% error is magnified at low blood glucose levels. Although Medtronic's new Enlite sensors are more accurate than their first-generation Sof-Sensors, they can still vary considerably from fingerstick and lab values (according to Enlite's product label, the sensor varies by about 14-15% from lab values, compared to about 20% with the Sof-Sensor). Despite the improvement in accuracy, there is still the chance that the Enlite will miss some low episodes and generate false alarms when the blood sugar isn't actually low. The threshold suspend feature is intended for use when someone is unresponsive (e.g., sleeping). Notably, eating (or drinking) rapid-acting carbs will raise the blood sugar MUCH faster and more predictably (5-15 minutes with carbs vs. at least 30 minutes with insulin suspension). It's good to see that Medtronic acknowledges this in the product's labeling, as the pump is not indicated for reducing hypoglycemia.

So what can we do today that mimics what the MiniMed 530G does?

So what can we do today that mimics what the MiniMed 530G does? Simple. Use a CGM with an alarm that alerts you to take action. If the CGM's standard alarms don't cause you to take notice or wake you while you're asleep, figure out a better system. Use the vibrate feature, put the receiver in an empty glass on a bedside table, place it near a baby monitor/speaker, keep it with a partner who is more likely to hear/feel it, or choose a CGM with a more robust set of alerts (in the US, the other option is the Dexcom G4 Platinum). Animal lovers can also look to obtain a Diabetes Alert Dog that lets its owner know when blood glucose levels are dropping. And of course, there is the old fingerstick fallback: More frequent blood glucose monitoring gives you a better chance of catching lows before they hinder your ability to self-treat them.

STAGE 2: PREDICTIVE LOW GLUCOSE SUSPEND

Products are already in the R&D pipeline that will slow or curtail a pump's basal insulin delivery when blood glucose levels are APPROACHING a low threshold (better than the aforementioned MiniMed 530G, which suspends insulin delivery when the low threshold is reached). The obvious benefit of predictive suspension is that it has the potential to greatly reduce the frequency, severity, and duration of hypoglycemic episodes. Of course, its success hinges on using a glucose sensor that is accurate and dependable, and an algorithm that knows when/how much to adjust basal insulin delivery when a low is approaching. Medtronic plans to launch a predictive low glucose suspend system outside the US in early 2014.

Responding to these alerts with food (when blood glucose is approaching hypoglycemia) is an effective way to prevent the low from happening in the first place.

Until that's available, there are several ways to prevent lows using currently available technology. All CGM systems feature a "Fall Rate" alert that lets the user know when the blood glucose is dropping quickly. Medtronic CGMs also feature a "Predictive" alert to let users know when a low is likely to occur soon. Responding to these alerts with food (when blood glucose is approaching hypoglycemia) is an effective way to prevent the low from happening in the first place.

Even those who don't have CGM can prevent most (if not all) low blood sugars through common-sense approaches: making sure basal and bolus insulin doses are set properly; accurate carb counting (so as not to over-bolus); adjusting food/insulin for physical activity; taking precautions when consuming alcohol; delaying mealtime insulin with slowly-digesting foods; and performing an adequate number of fingerstick blood sugar measurements throughout the day. It can also be extremely helpful to look at one's own data to determine the times and sources of lows so that preventive measures can be taken.

STAGE 3: NIGHTTIME AUTO-PILOT

A pump/CGM combination that will automatically keep blood sugars within an acceptable target range overnight is also in the research pipeline. This will be accomplished through the infusion of minute boluses when blood sugars are rising, and reductions in basal insulin when blood sugars are falling. For this type of system to function properly, the user must not eat or bolus for several hours leading up to bedtime, nor should they eat or bolus during the night. When working properly, auto-pilot has the potential to make nighttime highs and lows a thing of the past. (It's not clear if a treat-to-range system would come before or after nighttime auto-pilot, or if the two stages would be combined into a single product. The technology for both systems already exists and is in development and testing.)

For now, just about anyone with diabetes can keep their blood sugar reasonably steady through the night by making sure the doses of BASAL insulin (from a pump or injec-

tions) are set correctly. Basal insulin's job is to offset the glucose secreted by the liver, so it should keep blood sugar from rising or falling significantly while we sleep. Of course, there will be times when the standard basal insulin doses will need adjustment – we have to be prepared to make temporary changes to basal insulin levels after high-fat meals, extended exercise, alcohol consumption, use of steroid medications, and during illness.

STAGE 4: ALL-DAY AUTO-PILOT

The really BIG hurdle - automatically controlling blood sugar following meals, during exercise, with hormonal changes and other factors - is going to take a lot more time and work.

This is what I refer to as the "quantum leap." The first three stages are well within our grasp. Heck, even at the slow rate with which the FDA approves new products, we'll all probably see those first three stages within our lifetimes. But the really BIG hurdle – automatically controlling blood sugar following meals, during exercise, with hormonal changes and other factors such as stress and illness – is going to take a lot more time and work. In all likelihood, it will require the use of multiple hormones (perhaps adding glucagon and/or amylin to the mix), and a mechanism for making the insulin start/peak/dissipate much faster than it does now. The CGM sensors will have to be highly accurate and reliable, and the algorithm for interpreting the sensor data will have to work in an intelligent, proactive fashion.

But when it works, how sweet will that be? Blood sugars will approach those of the non-pancreatically-challenged, before and after meals. During and after exercise. Even during tax season. Not having to THINK about how every little thing affects our blood sugar will leave us enough extra RAM in our brains for more important things, like sports statistics, anniversary dates, and our kids' shoe sizes.

Until that happens, we owe it to ourselves to do the best job possible of being our own artificial pancreas. Someday the "real deal" will become reality. And when it does, we want to be in the best shape possible so that we can really enjoy it. And since we won't have to worry about bizarre middle-of-the-night lows, drinks are on me.

Gary Scheiner is Owner and Clinical Director of Integrated Diabetes Services, a private consulting practice for people with diabetes who utilize intensive insulin therapy. Gary is the 2014 AADE Diabetes Educator of the Year. He has written several books on diabetes self-management, including "Think Like A Pancreas" and "Until There's A Cure". Gary and his team offer consultations worldwide via phone and internet for those looking to gain better control of their diabetes and enhance their self-management skills. Gary has had type 1 diabetes for 28 years and has worn and trained on every make and model of continuous glucose monitor and insulin pump. He can be reached at gary@integrateddiabetes.com, or (610) 642-6055.

adam's corner

T1/2 Beating Challenging Meals and Winter Weather - Simple Tips for Better Blood Sugars, Eating, and Health

by Adam Brown

Twitter summary: Tips for better BGs this year: test more/use CGM, watch fat, sneak in exercise, change your food environment, + don't expect perfection!

If you're like me, you enjoy many aspects of special occasions: time with family and friends, delicious food, and a great opportunity to reflect on the year. However, holidays can also be stressful, particularly for people with diabetes: large buffet-style meals, "how-

many-carbs-are-in-that" side dishes, unpredictable schedules, and colder weather (just to name a few!). This article shares 15 simple tips that I hope will help you better manage your blood glucose during this time of the year. This reflects my personal experience and research, meaning the results may not translate to all patients in all cases. I've lived with diabetes for 12 years, but am not a healthcare professional. It's best to consult your healthcare provider before making any changes to your diet or medication regimen.

Test your blood sugar more often or wear CGM. This is particularly important during special occasions, when meals are abnormal and you may be off your normal routine. As we heard from our diaTribe advisory board on "What Every Person with Diabetes Should Know"– "Not knowing your blood sugar is like crossing a highway with your eyes closed" (Dr. Jane Seley) and "Real time knowledge of your glucose is the best teacher" (Dr. Nancy Bohannon).

- *"Test – Don't guess!"* At some point, many of us have probably said, "I feel fine – I really don't need to test right now." However, a 2012 study found that most people are downright awful at accurately guessing their current blood sugar level. Better to pull out your meter and know for sure than to take a guess and fly blind.
- *If you are an insulin user, testing two hours after a meal* is a great way to ensure that you bolused appropriately.
- *Try real-time CGM*, which gives you a glucose reading every five minutes along with a trend arrow. It's been truly transformational for my diabetes control. See our most recent review of Dexcom's G4 Platinum. We'll also be updating our 2011 review of Medtronic's Enlite soon.

Try real-time CGM... it's been truly transformation for my diabetes control.

Keep in mind that high-fat meals can raise blood sugar and increase insulin requirements. In a fascinating 2013 study, *diaTribe* advisory board member Dr. Howard Wolpert and colleagues compared high-fat and low-fat dinners in seven people with type 1 diabetes. Patients underwent 18 hours of closed-loop, automated glucose control after each meal. The high-fat dinner required 40% more insulin vs. the low-fat dinner, and despite the higher dose, the high fat dinner also caused more hyperglycemia.

- *Watch your fat intake at large meals*. This is easier said than done, as large amounts of fat can hide in unsuspecting places like sauces and creams. When eating out, I always ask for sauces on the side and try to order things for which I can very predictably dose insulin.
- *Try some light exercise* after a high-fat meal to help counteract the insulin resistance.
- *If you wear an insulin pump and will be eating a high fat meal, you can try a dual-wave/combo/extended bolus*, which will deliver the insulin bolus over an extended period of time and help counteract the steady rise in blood glucose. I often find that these are hard to get right, so instead, I typically increase my basal rate (e.g., 130%) for a few hours after eating a high fat meal.

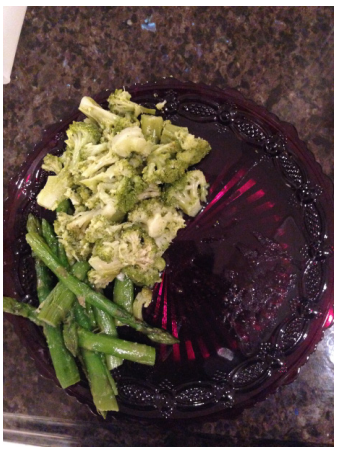
Even a few minutes of exercise is beneficial!

Even a few minutes of exercise is beneficial! When things are really busy or conditions aren't cooperating (e.g., two-feet of snow on the roads), it's easy to abandon your exercise routine altogether. Don't fall into that trap – I've found that even ten minutes or less of exercise can have a really positive impact on my mood, energy levels, and blood glucose.

In diaTribe #51, I discussed how walking really can improve your blood glucose control.

- *Go for a walk*. In *diaTribe* #51, I discussed how walking really can improve your blood glucose control.
- *Try the seven-minute workout,* which made a splash in the media earlier this year. The 12 exercises are each performed for 30 seconds, with 10 seconds of transition time between each. The circuit can be repeated two to three times. I have found the 7-minute workout app to be really useful (Apple and Android).
- *Use smartphone apps that guide you through simple indoor workouts that don't need any equipment*. I'm a fan of the free Sworkit (Apple and Android) and Power 20 (Apple and Android) apps, though there are many others out there.
- *Try the highly time efficient Tabata protocol* – 20 seconds on, 10 seconds resting, repeated eight times (four minutes total). Choose a single exercise or alternate between two exercises. Try jumping jacks, pushups, bodyweight squats, planks, lunges, or whatever you prefer (or buy a resistance band to expand your options). It's pretty hard to use a watch, so I recommend downloading a free Tabata timer app for your smartphone.

Change your food environment. Mindless Eating: Why We Eat More Than We Think is one of the best books I've ever read on food, behavior, and habits. Author Dr. Brian Wansink's compelling research shows that environmental and visual cues strongly influence food intake (e.g., how empty the bowl looks). In a series of fascinating studies, Dr. Wansink has identified several best practices for altering your food environment to eat less and choose better options. Below are just a few of my favorites, and here's a more complete list.



- *Use the ½ plate rule:* fill half your plate with veggies or salad. I love this one, since it's so actionable, easy to remember, and a definite health and diabetes win.
- *Don't eat directly out of the package*. I know that when I'm hungry (and especially when I'm hypoglycemic!), I often pour food directly into your hand. Despite the convenience, I consistently overeat when I fall prey to this approach. Research suggests it's better to pour from a package into a separate serving dish, and then eat.
- *Add some distance by leaving serving dishes in the kitchen at meal times*. The additional effort required to get more food adds a bit of a social and psychological barrier to getting seconds. I can definitely attest to this one – when I work from home at my kitchen table, I snack far more than if I work from the living room.
- *Use smaller plates (9.5 inches is optimal) and smaller bowls*. In a study published a month ago, Dr. Wansink and colleagues found that diners at a buffet with large plates served themselves 52% more, ate 45% more, and wasted 135% more food than those with smaller plates. Moreover, education did not appear effective in reducing such biases. Similarly, a 2012 study found that diners served 77% more pasta when given a large-sized bowl.
- *Make healthier food options more visible or accessible*. In a series of studies in school lunchrooms, Dr. Wansink and colleagues found that simply putting fruit in a nice bowl in a prime area of the lunch line increased fruit sales by a whopping 103%. Similarly, moving the salad bar to a more visible and accessible location – the center of the lunchroom – increased salad sales 200-300% in most schools. At home, that translates to having healthy options more visible (e.g., vegetables in the center of the kitchen table) and less healthy options more hidden (e.g., dessert in the cabinet).

Don't expect perfection and keep a positive attitude.

Don't expect perfection and keep a positive attitude. Even with all the knowledge and experience in the world, remember that you will still make mistakes – and that's okay! I'm consistently amazed at how often I make mistakes with my own diabetes, even after 12 years of experience and access to a pump, a CGM, and our incredible diaTribe advisory board. Instead of scolding myself and dwelling over the value on the meter, I find it's better to think of blood sugar values as merely information to help make a diabetes management decision – not judgments on my motivation or ability to control my diabetes. Stay positive this winter, and please let me know if there are any tips I left out!

[Editor's Note: Adam is a patient with diabetes and not a healthcare provider. Please consult with your doctor before making any changes to your diet, insulin, or medication regimen.]

Adam is the co-managing editor of diaTribe and Chief of Staff at Close Concerns. He is a graduate of the University of Pennsylvania and serves on the board of Insulindependence and the San Francisco branch of JDRF. He was diagnosed with type 1 diabetes at the age of 12 and has worn an insulin pump for the last 11 years and a CGM for the past three years. Most of Adam's writing for diaTribe focuses on diabetes technology, including blood glucose meters, CGMs, insulin pumps, and the artificial pancreas. Adam is passionate about exercise, nutrition, and wellness and spends his free time outdoors and staying active. He can be contacted at adam.brown@diatribe.org or @asbrown1 on twitter.

diaTribe dialogue

T1/2 *diaTribe*'s Testimonial Against Severe Limits on Test Strips in Oregon

by Nancy Liu

Twitter summary: Help Stop Oregon from Severely Restricting Test Strips for People with #Diabetes – 3,000+ signed and diaTribe speaks out for patients.

On December 5, *diaTribe* Managing Editor Nancy Liu traveled to Oregon to speak out on behalf of people with diabetes as part of the effort to stop a proposal aimed at severely restricting test strips. What follows is the full text of her speech. We also created a petition against the proposal that received 3,000+ signatures and 1,000+ comments over the course of a couple days - thank you for your help and advocacy! Please read more about the issue in Oregon in *diaTribe #59*.

Good afternoon. My name is Nancy Liu, and I'm here to represent The diaTribe Foundation, a nonprofit dedicated to improving the lives of people with diabetes and prediabetes and advocating for action. I am also the managing editor for *diaTribe*, which reaches thousands of readers across the United States and the world. We've written about Oregon's proposal to limit test strips for people with diabetes and created a petition against the proposal that now has more than 3,000 signatures and more than 1,000 testimonials of caregivers and people with diabetes.

Diabetes is not a one size fits all disease.

Diabetes is not a one size fits all disease, and this recommendation would unfairly limit glucose monitoring, which is critical in managing diabetes. We believe that studies that claim test strips do not benefit type 2 patients are fundamentally flawed. Test strips are not a therapy in and of themselves, but a tool used in conjunction with education to improve outcomes. An A1c result alone is an inadequate measure of management because

Patients need constant feedback, or information, to manage this disease.

it is only an average and does not reflect the daily volatility of blood sugars or the bleary feeling that accompanies those struggles. Patients need constant feedback, or information, to manage this disease. Only then can they adjust their medication, diet, or lifestyle. Without test strips, or by using only one a week, that is almost impossible.

Proposals to limit the use of test strips are misdirected, and shortsighted – small savings now will only lead to increased complications, hospital visits, and operations, all of which will cost more money in the future. In 2010, the estimated direct medical and indirect societal cost for diabetes in Oregon was a whopping $2.82 billion. In 2012, the estimated costs in the US grew to $245 billion. Limiting management options will move us in the wrong direction in cost and quality of care.

We aim for policies that encourage active, smart diabetes management.

As patents and patient advocates, we acknowledge there is waste in the system. We are advocating arriving at a new policy that makes sense for patients, encourages active, smart, diabetes management, and eliminates waste. We MUST all work toward better policies for patients and HCPs that will be more effective in terms of cost and outcomes than continuing down the current path. Moving toward a policy of virtually eliminating strips for patients with a progressive disease won't serve any of us well and is emblematic of payers that are moving too fast and are not concerned enough about the impact to dangerous patient outcomes - hypoglycemia, cardiovascular disease, and everything in between. Patients and advocates would like to see a pause to the mad decision making in diabetes so that we can all work toward new policies that make sense for patients and for society in the short and long run. We aim for policies that encourage active, smart, diabetes management and far less waste and would like to work with policymakers on this front.

It is estimated that 12% of Oregon residents (that's 550,000 people) will have diabetes in 2025. This doesn't include the friends, family, and health care providers who will be affected by people with poor diabetes management and costly complications – which will occur if they are unable to monitor their blood sugars. Do you want to be part of a future where a third of your constituents suffer from the consequences of this proposal? We hope not.

conference pearls

T1/2 The DiabetesMine Innovation Summit: Delivering On The Promise of Diabetes Technology

by Nancy Liu, Adam Brown, and Kelly Close

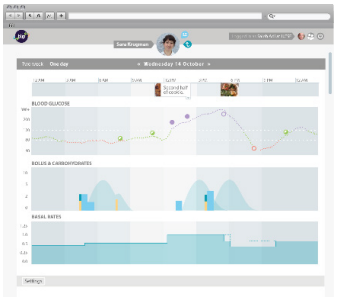
Twitter summary: Lots of learning from #dbminesummit on using tech to improve lives of people with #diabetes, great talk from FDA, +more!

This year's DiabetesMine Innovation Summit took place in November at the Stanford School of Medicine. The summit called on all attendees to focus on "Delivering on the Promise of Diabetes Technology," an area certainly ripe for discussion! Participants discussed the hefty challenges of creating "life-friendly" medical devices, understanding the impact of technology, and increasing access for patients.

New Apps to Deal with Diabetes Data

TIDEPOOL

On the theme of leveraging technology and data, we saw some very exciting new developments at Tidepool, a non-profit in the Bay Area. The organization's goal is to create open-source diabetes management apps, all built on the same underlying software platform. The hope is to use the information from open source development – think Wikipedia! – to build better technology for people with diabetes. Tidepool's CEO Howard Look (a parent of a child with type 1 and a very smart new leader in the field) discussed two apps in development: blip and Nutshell.



- **blip is a web-based program intended to be a "hub for diabetes data."** The application will take data from many devices (meters, CGMs, pumps, and even activity monitors) and aggregate in one dynamic, sleek online interface. The platform's integration goals are quite ambitious – "imagine seeing data from a Medtronic pump and a Dexcom CGM together, in one place." Historically, that has not been possible without a lot of extra work. Healthcare providers, family members, and anyone else will be able to use the blip to communicate and annotate logged events. Mr. Look showcased the app – while his daughter experienced a low blood sugar, he logged the event details on blip. His wife soon commented (she was out of the house), helping troubleshoot and uncovering the cause of the low (over-bolusing and taking the dog for a walk). His daughter's healthcare provider even checked in and asked if everything was okay. We were impressed with the interface and the seamless communication it enabled. blip is being tested at the University of California, San Francisco and Tidepool is in talks with the FDA. If you would like to learn more and sign up for a pilot study, please visit their website.

- **Meanwhile, Tidepool's Mr. Brandon Arbiter discussed Nutshell, spurred by the blousing challenges of tricky restaurant meals (and not getting it right much of the time).** Mr. Arbiter realized that he often goes to the same restaurants, typically ordering the same meals. With the Nutshell mobile app, patients/caregivers would "check in" to their favorite restaurants and log the meal they ate, insulin info, and blood glucose values. (Tidepool is working to make this as easy as possible.) Upon returning to the same venue, patients/caregivers would use the app to look back, assess their previous performance, and dose better for the same meal (what Tidepool calls "situational recall"). It's a simple use of data, but one that is very powerful and could help patients improve their mealtime dosing. Nutshell now exists in "proof of concept" form and Tidepool is gearing up to release a "minimum viable product."

Tidepool is an open-source and open-data platform, which can be used on different devices and is freely available.

Notably, both blip and Nutshell are built on Tidepool's open-source and open-data platform, which can be used on different devices and is freely available to patients, parents, doctors, and researchers. You can view screenshots of the apps as well as Mr. Look's full presentation at here.

What Patients Want

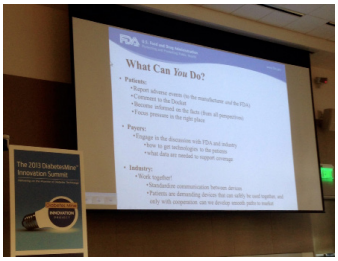
The summit also featured winners of DiabetesMine's Patient Voices contest, which called on patient advocates to create short videos about the current state of diabetes technology and what they consider to be the biggest unmet needs. Patients shared their views on how to create better human-centered design for diabetes technology, reduce the mental burden on device users, and access more shareable, integrated, and actionable data. The nine-minute 2013 Patient Voices Contest video is on YouTube (highly recommended) and you can learn more about the contest on the DiabetesMine website. If you have ideas, make sure to enter the 2014 Patient Voices contest!

Some of the most interesting winners included:

- Simon Carter: Creator of a new blood glucose prediction system called ManageBGL.com.
- Melissa Lee: Presented an idea for an "Insu-litmus" test to help gauge whether insulin is still effective.
- Kyle McClain: Creator of Gludi, a logging app designed to be "breathtakingly simple."
- Scott Strange: Discussed the need to emphasize the mental and emotional side of diabetes

We also saw the results of the Patient Voices Survey at the summit, where nearly 800 diabetes patients contributed their opinions on current and future diabetes technology. One of the most notable results we saw were how participants ranked the most important quality of life improvements as having fewer glucose highs and lows, feeling in control of their care, and reducing the daily hassle of devices. Hear hear!

An Update from the FDA



Dr. Courtney Lias, Director for the Division of Chemistry and Toxicology Devices at the FDA, delivered a great keynote address that gave us hope that the FDA will be more attuned to the needs of patients in the future – this was by far one of the best speeches we've ever heard from the FDA. Her talk clearly recognized the ongoing issues that people with diabetes face, including, "long term health risks due to glycemic variability" and "quality of life challenges." This was encouraging, since the agency has historically placed a major focus on A1c above all other measures.

Dr. Lias also acknowledged that patients are unhappy with the accuracy of blood glucose meters, which the FDA is unhappy about too. With this in mind, it was great to see the FDA recently published recommendations ("guidance") that will tighten blood glucose meter accuracy – look to our next issue for more details on the guidance. Though the requirements are still in draft form, the accuracy bar to get a meter approved will eventually get much higher, particularly in the hypoglycemia range (meter values will need to be within 15% of the true reference value).

Dr. Lias noted that the FDA device division receives more adverse events reports for blood glucose meters than for any other device.

Her discussion of blood glucose meters addressed post-approval safety as well – Dr. Lias noted that the FDA device division receives more adverse event reports for blood glucose meters than for any other device. Though surprising at first, this is due to the large number of people who use meters and the dangerous dosing errors related to insulin. That said, we were happy to hear her specifically mention the Diabetes Technology Society's new blood glucose meter surveillance program, which would monitor the quality and accuracy of strips/meters following FDA approval. Though this program is in the early stages, Dr. Lias seemed optimistic. For more information, please read our update from the Diabetes Technology Society's September 9 Meeting.

Her presentation followed with a great Q&A:

Q: CMS has started competitive bidding for glucose strips. How do you work with CMS to see if making this decision is a good idea? Won't it drive good players out of the marketplace?

A: We're starting to talk to CMS on that issue. Larger companies are concerned in the area of glucose test strips – that the policy will drive people to the off-brand meters. From their point-of-view, off-brand meters are not as high quality. One thing that spurred on the proposal for the surveillance program is that industry wants something that will prove that strips on the market are as safe as when they were cleared. What's happening a lot is

In our final artificial pancreas guidance, we emphasized flexibility... we are not tied to A1c being the only endpoint.

companies are sending data to get their meters cleared, but they're good lots. Then, they are modifying the manufacturing processes to cut corners. It's difficult for us to inspect factories in China. We have engaged CMS on this issue. At this point in time, CMS says that if a device is cleared by the FDA, it should be okay. That's still ongoing, and we'll see how that turns out. The surveillance program is another way to say these devices don't meet the standards. We'll have to talk more.

Q: What are your thoughts on endpoints in trials such as "time in zone"? A1c is necessary but not sufficient...

A: In our final artificial pancreas guidance, we emphasized flexibility. We try to tie an endpoint for what makes sense to what's going on. A1c as a safety endpoint is easy to measure. But we are not tied to A1c being the only endpoint for effectiveness. If someone had a lot of glycemic variability, spent less time under 70, or had more time in range, we can all agree there is some benefit to that. We try to work with investigators and companies to make sure that the endpoint makes sense.

Heated Discussions between Payers and Patients

One of the main challenges that the summit identified was the conflicted technology agenda among patients, industry, and payers. We were pleased to see a diverse gathering of patient advocates, industry representatives, and an impressive payer panel that included representatives from Aetna, Capital Blue Cross, Kaiser Permanente, Humana, and the State of Arkansas to speak about innovation.

During a heated discussion, many patient advocates vented their frustrations with restrictive insurance coverage, puzzling reimbursement policies, and bureaucratic interactions with insurers. The conversation reached a climax when one patient expressed how "[payers] don't give a **** about me!" Patient advocate Kelly Close emphasized that companies operate in a competitive environment with extremely low profit margins. Unfortunately, it can be a challenge for payers to cover more expensive technologies that have a longer payback period, especially when patients can switch insurance every few years. We salute the DiabetesMine Summit for bringing payers into the room, since they are often absent from the discussion. We hope that the lines remain open so that patients and payers can work together to address gaps in diabetes care coverage.

learning curve

Behavioral Diabetes Institute

T1/2 The Behavioral Diabetes Institute: Six Lessons We've Learned Over the Past 10 Years

by Dr. Susan Guzman

Twitter summary: Our friends at Behavioral #Diabetes Institute (BDI) share the top 6 lessons they've learned from the past 10 years – congrats on their 10th year!

We were very disappointed to hear recently that BDI is changing due to lack of ongoing funding; we revel in the advice they have given and hope that many will be able to learn from Dr. Guzman's advice below.

BDI was founded in 2003 in an effort to help people with diabetes live healthier and happier lives by addressing the psychological aspects of diabetes. In the 10 years since the founding of BDI, we have had the opportunity to meet with thousands of people with dia-

betes. Hundreds of thousands of people in many different countries have read our print materials. Hundreds have participated in the research that we have conducted. We are grateful to all of these people who have reached out to us and been a part of BDI's legacy.

Over this decade in my work as a diabetes psychologist at BDI, we have learned some important lessons from the many people with diabetes we have had the opportunity to work with: about the challenges of life with diabetes, what seems to really be effective in making a difference in people's lives, and the enormity of the work we still have left to do.

Sometimes, people lose sight of their strengths and get lost in a sense of what is "wrong" with them.

1. **Help people see their strengths and find new ways to put them into action.** One of the most important lessons I have learned is to become a keen observer (and admirer) of the strengths that people have developed to get them through the challenges they face with diabetes. Sometimes, people lose sight of their strengths and get lost in a sense of what is "wrong" with them. One can end up feeling like a collection of frustrating numbers, body parts that don't work right, and losses from life with diabetes.
   Perseverance, a sense of humor, courage, wisdom, a proactive attitude, willingness to try new things, persistence, creativity, forgiveness, adaptability, assertiveness, and acceptance are some of the key strengths that I have seen people use to navigate life with diabetes. Those who are having a tough time often don't see their own strengths or how to use them. When things are going wrong, you still have value, so play to your strengths!
2. **"What has life with diabetes been like for you"?** I have learned that far too few have ever been asked this question. When trying to help someone, asking this question and really listening to the answer is the best way to understand not only what the person's challenges are, but also what the solutions are. There are good reasons why people struggle with diabetes. Listening to what obstacles get in the way can lead to targeted strategies to help people overcome these obstacles.

Care for yourself in your daily choices, respond with kindness in your self-talk, and remember you are worth all this hard work.

3. **The "care" in diabetes care is the most important component to helping someone achieve wellness.** Care is generated from a kind and knowledgeable healthcare professional, connections with others who have diabetes, support from family and friends, and most importantly YOU as the person with diabetes. Care for yourself in your daily choices, respond with kindness in your self-talk when you have a frustrating result or have made a mistake, and remember you are worth all of this hard work.
4. **I now understand the importance of acknowledging that we, as healthcare professionals, don't have all the answers.** We're still learning and have made some pretty big mistakes along the way. I have met many people with type 1 diabetes, now in their 50s and older, who were told (sometimes as children) that they would be dead by the age of 30. I hear the damage that statement caused in so many lives and I wonder about the people that I don't hear from, that never made it to their 50s because they didn't see any reason to bother with the hard work of diabetes care. Did you know that with modern technology and treatment, people with type 1 diabetes can live as long as people who don't have diabetes? That's a pretty big oops! And, I have heard from many people with type 2 diabetes that they were told they "failed" at their lifestyle changes when it was time to start insulin. And, as a result, they avoided starting insulin and for far too long. Who wants to feel like a failure? We now know that loss of insulin production is part of the natural course of type 2 diabetes over time. Needing insulin does not mean a person has failed; it simply means its time. The more we learn about diabetes, the more we realize what we don't know.
5. **There is so much more work to do.** Too many people still don't know the benefits of good care, feel doomed to suffer from complications, are unable to overcome obstacles to manage their diabetes, and suffer from depression. Too many healthcare professionals blame people for less-than-perfect control, are too quick to lecture with scary diabetes statistics, and don't understand how hard the work of diabetes care can

be. Too many loved ones feel helpless watching someone they care for struggle with diabetes, don't know how to be helpful and feel alone with their worry. And, there are way too few resources to help people who are facing these problems. Frankly, these are the kinds of things I lose sleep over.

Shame and blame are way too prevalent in our conversations about diabetes and can lead to some very unhealthy and unhelpful behaviors.

6. **A goal I have for the next decade of BDI is to promote a change in the way we talk about diabetes.** Shame and blame are way too prevalent in our conversations about diabetes and can lead to some very unhealthy and unhelpful behaviors. "What did you do wrong?" Asks the loved one, parent, doctor, or yourself. "You did this to yourself!" say many in response to people with type 2 diabetes or those who have developed complications. Ultimately, feeling shamed and blamed leads many people to hide, avoid taking action, feel guilty, discouraged, angry, and even hopeless. I feel confident we can make progress in promoting a community where all people with diabetes feel encouraged, supported, and cared for. It will lead to much better results than pointing a finger.

As an organization, BDI has learned a great deal about the psychological aspects of living with diabetes and has had the opportunity to help many people. Yet, we know our work is far from done. Because of funding challenges, BDI is in the process of refocusing its efforts. This year we are planning our first intensive trainings for diabetes healthcare professionals interested in improving their responsiveness to the emotional and behavioral challenges faced by people with diabetes in their own practices.

This article has been reprinted with permission from the Behavioral Diabetes Institute. The original article can be found at: http://behavioraldiabetesinstitute.org/six-lessons-weve-learned-over-the-past-10-years.

trial watch

How will a new once-weekly type 2 diabetes drug fare in trials?

T2

Study to Evaluate the Safety and Efficacy of the Addition of Omarigliptin Compared with the Addition of Sitagliptin in People with Type 2 Diabetes

ClinicalTrials.gov Identifier: NCT01841697
http://clinicaltrials.gov/show/NCT01841697

Merck's new drug, omarigliptin (MK-3102), is a once-weekly DPP-4 inhibitor intended to reduce blood glucose with a low risk of hypoglycemia and less frequent dosing than other drugs that must be dosed daily. This new study will compare omarigliptin to Januvia (sitagliptin) in participants with type 2 diabetes with inadequate glycemic control on metformin. The trial will examine the mean change in A1c after 24 weeks of treatment and will include 600 participants with type 2 diabetes. Patients must currently be on a stable dose of metformin for at least 12 weeks prior to the study and be willing to prevent pregnancy during the course of the study. Exclusion criteria include having a history of type 1 diabetes or ketoacidosis, taking any antihyperglycemic agent besides metformin within 12 weeks of the study, a hypersensitivity to DPP-4 inhibitors, and more that can be found on the Clinical Trials website. If interested in enrolling, please contact 1-888-577-8839. *-NL*

The diaTribe Foundation is a nonprofit organization that publishes diaTribe, *a free online newsletter about diabetes research and products. The information published in* diaTribe *is not a substitute for medical advice and should not be used to make decisions that change treatment. We urge readers to consult with professional healthcare providers for questions regarding their treatment and in all matters related to their health.*