

# diaTribe®

research and product news for people with diabetes

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## from the editor



We gathered recently in Vienna for the European Association for the Study of Diabetes (EASD) Conference to learn the latest in science and technology in the field. That included the official European launch of Abbott's Freestyle Libre, its new glucose monitoring product, the FDA approval of Lilly's once-weekly GLP-1 agonist Trulicity, and the European approval of Novo Nordisk's sure-to-be transformative combination basal insulin/GLP-1 analogue Xultophy. At diaTribe, we also wanted to take a broader look at the most urgent issues in diabetes

and to muse on what steps experts think can be taken to address them. So we held what we ultimately perceived as a most valuable (and honestly, quite daunting) discussion with two esteemed panelists, Professor Philip Home, a Professor of Diabetes Medicine at Newcastle University in the UK, and Professor Jens Sandahl Christiansen, a clinical professor in the Department of Endocrinology and Diabetes at Aarhus University in Denmark.

Our focus was on solvable problems in diabetes, which is important to me both personally and professionally. And really – solvable?! That's a big word – maybe addressable is a little easier way to look at this, given all the valuable work already being done. The discussion focused on several key issues, including the challenges of government regulation and reimbursement policy in the US and in Europe, how to best use the therapies we already have, and how Professor Home and Professor Christiansen would spend \$10 billion in diabetes. Notably, Professor Home would spend the money on education on diet/exercise for the prevention of type 2 diabetes, while Professor Christiansen noted that A1c reductions for both type 1 and type 2 are eminently possible with investment in better therapies. Patient engagement was a key focus, as we discussed both hypoglycemia and weight gain as barriers to adherence and how to better use insulin so that it does not cause hypoglycemia. As Professor Home said, "Insulin does not cause hypoglycemia. It's the way we give insulin that causes hypoglycemia. We need technology to give insulin only when it's needed. That will revolutionize the field."

It's heartening to know that as a patient community, we have been able to work on some of the big problems in the field – addressing the lack of insulin access in developing countries with campaigns like #SpareARose (which raised more than \$26,000 this year), encouraging innovation in diabetes by working with the FDA to discuss patient perspectives on November 3, and increasing options for the unmet need in obesity medications with our recent testimony at the liraglutide Advisory Committee. We've always been delighted by the uplifting response from the community in taking action and look forward to seeing what many more meaningful steps we can accomplish together in the future.

very best,

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## quotable quotes

**“We have not put enough resources into prevention...I would put more resources into helping those individuals lead healthier lifestyles, which will make them happier and could also give them several additional years of diabetes-free life, and for some, prevent it altogether. That would be huge.”**

– Dr. Naveed Sattar, MD, PhD (University of Glasgow, Glasgow, UK) at the European Society of Cardiology 2014 Congress in Barcelona, Spain.

**“Providers are also human. Families and patients should see physicians as humans who also sometimes need to mature.”**

– Dr. Tadej Battelino (University Children’s Hospital, Ljubljana, Slovenia) at the Keystone 2014 Conference.

**“Family support and a tight-knit community are huge. We have grandparents who log everything when we’re away... Diabetes is really a whole group effort.”**

– Parent panelist at a panel discussion on managing pediatric diabetes at the Keystone 2014 Conference.

## fingersticks

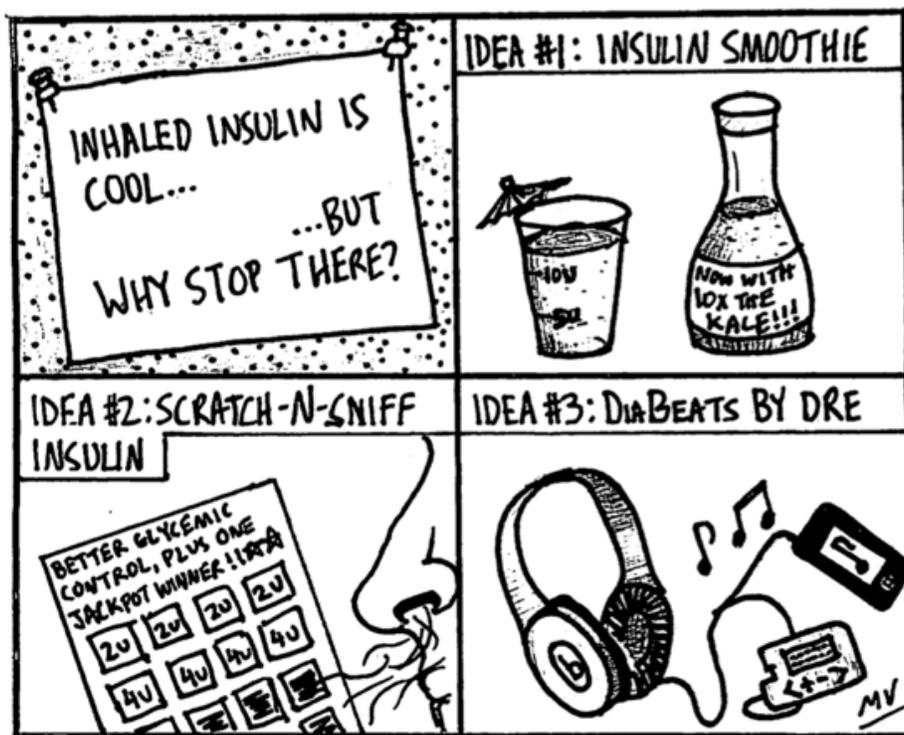


Illustration by Manu Venkat

## new now next



## T1/2 Abbott Receives European Approval to Launch the Freestyle Libre System – Glucose Monitoring Without Fingersticks

*Twitter Summary: Abbott receives EU Approval to launch Freestyle Libre – updates from EASD on payment, device accuracy, design, and user experience*

On September 3, Abbott announced that it received a CE mark (the European stamp of approval to market and distribute a product) for its Freestyle Libre Flash Glucose Monitoring System. In the upcoming weeks, the product will become available in France, Germany, Italy, the Netherlands, Spain, Sweden, and the UK. Abbott intends to bring Freestyle Libre to the US in the future, and a major trial is expected to start before the end of the year. Abbott first introduced this Flash Glucose Monitoring technology a year ago at the EASD 2013 Conference – this system brings an entirely novel technology to the diabetes landscape, eliminating fingersticks to obtain real-time glucose and trend information. The product is intended to be a replacement for traditional blood glucose meters but is also designed to overcome some of the limitations of CGM (cost, device on the body, need for fingersticks).

The Abbott system includes a tiny glucose sensor (0.2 inches in length, about the thickness of a hair) worn under the skin connected to a water resistant on-body patch the size of a one-dollar coin. The sensor remains inserted for 14 days and does not require fingerstick calibrations (“factory calibrated”); after putting it on the upper arm and waiting one hour, it begins reading glucose and trend information.



To use the system, users take a touchscreen reader device, hold it up to 1.5 inches above the sensor patch, and in less than a second can see their real-time glucose value (e.g., 102 mg/dl), a glucose trend arrow, and a trend graph showing the last eight hours of data. The sensor can be scanned through clothing. The reader device also has a number of nice reports, including a graph that shows time-in-target right on screen. FreeStyle Libre downloads to PC and Mac compatible software, which includes a traffic light approach to identify problematic times of the day. The system is approved for people with both type 1 and type 2 diabetes.

FreeStyle Libre is approved for dosing insulin except in three cases: when hypoglycemic, when glucose is changing rapidly, or when symptoms don't match the system's readings. In these cases, Abbott recommends confirming the value with a fingerstick. One important difference from current CGM devices (Dexcom G4 Platinum, Medtronic Enlite) is that FreeStyle Libre does not have alarms or alerts, since the sensor data is not sent continuously to the reader device.

At this year's EASD Conference in September, Abbott held a major symposium on the Freestyle Libre System. Our team attended and learned some more about the device – our key takeaways are summarized below, including a few updates from their recent press release.

### Payment/Reimbursement Updates:

- The touchscreen reader will cost €59.90 (~\$77 US). Each 14-day sensor will cost the same.
- Payment for the system will be out-of-pocket initially, though Abbott is currently enrolling participants for two clinical trials that should help support European reimbursement.



- People do not need a prescription to purchase the device at online European web sites, which are expected to begin selling the system in the next month.

### Freestyle Libre's Accuracy Updates:

- Freestyle Libre's accuracy vs. fingersticks is 11% (e.g., if blood glucose is 100 mg/dl on average, the system would be off by about 11 mg/dl, on average). This accuracy is roughly comparable to the Freestyle Navigator II (12%) and slightly better than the G4 Platinum (14%) and the Enlite (14%).

### Device Design Updates:

- The patch is only approved for wear on the upper arm.
- The touchscreen reader has a color screen and a built-in FreeStyle blood glucose meter.
- The reader's display has three icons: check glucose, history, and settings.
- User can add notes to each reading and customize the notes.
- The reader has a micro-USB port to recharge the device, which can connect to a Mac or a PC. Charging the reader for three hours should last up to a week.
- The sensor patch can store up to eight hours of data. Each scan of the sensor downloads the data to the reader device, which can store up to 90 days of data.
- Each sensor comes with a simple applicator to apply it to the upper arm. In a demo of the device, this seemed much easier than the insertion process of current CGM products.

### User Experience Updates:

According to a user experience study of the Freestyle Libre system, Abbott reported:

- 93% of people agreed that Freestyle Libre is comfortable to wear.
- 91% of people agreed that it is easier to check glucose with this system than with other glucose monitoring systems.
- 83% agreed it was painless to apply the sensor (100% agreed it was either painless or almost painless).
- 96% agreed that Freestyle Libre provides an easy and discreet way to check blood glucose.
- After seeing a live demonstration of the system, we can attest that it is simple and takes less than five seconds to obtain a glucose reading.

From what we have seen, the Freestyle Libre system is easy to use and patient friendly, and its relatively affordable price should make it an attractive option, particularly if reimbursement is approved.

Abbott is currently enrolling participants for two trials of the Freestyle Libre system in Europe. For any EU resident interested in enrolling, please see the clinical trial pages for both the REPLACE trial in type 2 diabetes and the IMPACT trial in type 1. A pivotal study for the Freestyle Libre system is set to begin in the US by the end of 2014. -AJW/AB



## T1/2 **Contrave Weight-Management Drug Receives FDA Approval**

*Twitter Summary: FDA approves Contrave weight management drug, with potential future use in #T2D*

This approval makes Contrave the third weight management drug approved in the US after a 13-year period of no obesity drug approvals.

On September 10, the FDA announced the approval of Orexigen's weight management drug Contrave (naltrexone/bupropion combination). Orexigen had initially submitted Contrave to the FDA in 2011, and the FDA had delayed its approval until further heart safety information was known about the drug. After undertaking an extensive cardiovascular (CV) outcomes trial beginning in June 2012, Contrave was resubmitted in December of 2013. This recent approval makes Contrave the third weight management drug approved in the US after a 13-year period of no FDA approvals for obesity drugs, following Arena/Eisai's Belviq (launched in the US in June 2013) and Vivus' Qsymia (launched in September 2013). Orexigen's partner Takeda expects to launch the drug this fall – we're excited to see this plan, as there hasn't been a company with extensive marketing experience like Takeda's that has taken on the responsibility of getting an obesity drug to patients.

Contrave is approved for use in adults with a body mass index (BMI) of 30 or greater or adults with a BMI of 27 or greater who have at least one weight-related condition such as high blood pressure, type 2 diabetes, or high cholesterol. In clinical trials, Contrave averaged about 5% greater weight loss over one year than those using a placebo, and 42% of people on Contrave lost at least 5% of their body weight compared to 17% of those on placebo. That said, some "super-responders" had better results, and it is this "sub-population" that is most interesting to us – who, in other words, are the people that will respond best to the drug. Like other weight loss medications, Contrave's weight loss effects for people with type 2 diabetes may be less prominent (those with diabetes tend to have a harder time losing weight than those without diabetes) – a year-long trial in type 2 patients found that those on Contrave only lost 2% more weight on average compared to those on placebo. But there is some hope for weight-loss drugs benefiting diabetes for those who don't fall in the "super-responder" bucket: another weight loss drug, Vivus' Qsymia, has been shown to reduce the progression of type 2 diabetes in high-risk individuals, and recent weight-loss medications have also demonstrated some A1c benefits.

The FDA is requiring at least seven additional clinical trials for Contrave, including another CV outcomes trial.

From what we have learned from key researchers, Contrave can increase the risk of high blood pressure and heart rate and is thus not recommended for anyone with uncontrollably high blood pressure or a history of cardiovascular complications. The FDA is requiring at least seven additional clinical trials for Contrave, including another CV outcomes trial, pediatric trials, a trial testing Contrave in people with kidney or liver impairment, and a trial examining the interactions between Contrave and other drugs.

We don't yet know about pricing or reimbursement for Contrave, though Belviq and Qsymia have made some notable strides in easing the reimbursement process for obesity drugs. Still, access is a major issue for many. Yet, as the most recent Center for Disease Control and Prevention data indicates that nearly 35% of Americans are obese (BMI greater than 30), the need for more tools to address this growing and complex epidemic has never been greater. In the future, Orexigen has expressed interest in pursuing a diabetes indication for Contrave,

potentially combining the drug with the DPP-4 inhibitor class of diabetes medications (Januvia, Onglyza, Tradjenta, Nesina, Galvus). This work is still in the early discussion phases, but a weight loss drug combined with a diabetes medication would certainly be a huge win for patients. –AJW



## T2 Lilly's Patient-Friendly Ready-to-Use once weekly GLP-1 agonist Trulicity approved in the US

*Twitter summary: FDA approves Trulicity for #T2D, 1st ready-to-use once-weekly GLP-1 agonist in the US, with an amazingly patient-friendly "auto-injector" – launch for later this year*

On September 18, the FDA approved Eli Lilly's Trulicity (dulaglutide) for type 2 diabetes, making it the third once-weekly injectable GLP-1 agonist approved in the US after GlaxoSmithKline's Tanzeum (albiglutide) and AstraZeneca's Bydureon (exenatide). Eli Lilly plans to launch Trulicity later this year, available in both .75 mg and 1.5 mg doses. It is not recommended for anyone with a history of pancreatitis or severe GI problems (e.g., gastroparesis). For more information on Trulicity's side effects, please see its approved drug label. There is no word yet on reimbursement or pricing information for Trulicity.

Trulicity is truly a leap forward in terms of user convenience. It is available in a new type of injection device called a single-use pen or an "auto-injector" that allows users to never have to see a needle.

Trulicity is truly a leap forward in terms of user convenience. The once-weekly GLP-1 agonists that are currently available require multiple steps and 15-30 minutes (mostly wait time) to prepare the injection. Trulicity is ready-to-use out of the box in the same way that once-daily GLP-1 agonists already are. Additionally, Trulicity is available in a new type of injection device called a single-use pen or an "auto-injector" that allows users to never have to see a needle. Taking Trulicity is as simple as uncap, unlock, and inject: users take the cap off of the pen, twist one end to unlock, and then place the flat end of the pen to their skin. With the push of a single button, the pen inserts a previously hidden needle into the skin, administers the injection in a couple of seconds, and then withdraws the needle back into the device. This process strikes us as an enormous plus given the stress that "needle phobia" can cause. Although Lilly is the first company to receive approval for an auto-injector for its once-weekly GLP-1 agonist, other companies (including AstraZeneca) are working on their own auto-injectors as well.

Trulicity has the potential to transform the conversation that people with type 2 diabetes have with their providers when oral therapies are no longer enough to control their blood glucose. Currently, when reaching that point, many people choose to begin basal insulin. Lilly studied Trulicity in comparison with the basal insulin Lantus (insulin glargine), and found that Trulicity 1.5 mg provided greater reductions in A1c, weight loss benefits, and less hypoglycemia. Trulicity is also the first GLP-1 agonist to show similar efficacy to that of the once daily GLP-1 agonist Victoza (Novo Nordisk's liraglutide). With such compelling clinical data and its remarkable ease of use, we can't help but wonder if Trulicity could be used even earlier in the course of type 2 diabetes than GLP-1 agonists have been used until now. GLP-1 agonists provide important benefits to patients – strong glucose lowering with less hypoglycemia and weight gain – and we are glad that Trulicity will make this class easier for people to take. –MV/AJW

## T2 Novo Nordisk's Much-Awaited GLP-1 Agonist/Basal Insulin Combination Xultophy Approved in Europe

*Twitter Summary: After huge anticipation for this innovative drug combination, Novo Nordisk's Xultophy received approval in Europe for #T2D, 1st ever basal insulin/GLP-1 analogue combo approved – launch for early 2015*

The news marks a major moment for type 2 diabetes: Xultophy is now the first ever basal insulin / GLP-1 analogue combination to gain regulatory clearance - for years we have heard nothing but enthusiasm for combining these two classes.

On September 18, Novo Nordisk announced that it received European approval in all 28 European Union member states for Xultophy (previously known as IDegLira), a combination of the ultra-long-acting basal insulin Tresiba (insulin degludec) and the GLP-1 agonist Victoza (liraglutide). Xultophy was also recently approved in Switzerland on Sept 12, 2014. After receiving a positive recommendation from a body within the European Medicines Agency in July, the Xultophy approval came as no surprise. The news does, however, mark a major moment for type 2 diabetes: Xultophy is now the first ever basal insulin/GLP-1 analogue combination to gain regulatory clearance – for years we have heard nothing but enthusiasm about combining these two classes. The product is expected to be launched commercially in Europe in early 2015. Pricing and reimbursement discussions are still ongoing and can be quite complex in Europe.

As described in diaTribe #67, Xultophy is a once-daily injection taken independently of mealtimes. Bringing GLP-1 agonists and basal insulin together is a very impressive match: Xultophy builds on the already impressive glucose-lowering efficacy of its components (Tresiba and Victoza) while also ameliorating the side effects associated with each therapy. For example, Victoza's beneficial effects on weight and hypoglycemia help counteract the weight gain and increased hypoglycemia typically seen with insulin. Recent clinical trial results demonstrated that people with type 2 diabetes adding Xultophy onto oral therapy achieved a striking average A1c reduction of 1.8% after one year vs. 1.4% for those who added Tresiba and 1.2% for those who added Victoza. Additionally, people treated with Xultophy had a mean weight loss of 0.4 kg (~1 lb) compared to weight gain of 2.3 kg (~5 lbs) with Tresiba, as well as 37% less hypoglycemia than with Tresiba. Nausea is sometimes a major issue for people beginning Victoza or other GLP-1 agonists, but an added bonus with Xultophy is a much lower rate of nausea and other gastrointestinal side effects. The clinical data on Xultophy is some of the most promising we've seen for a new type 2 diabetes drug – Dr. John Buse, a highly renowned researcher in diabetes, notably said, “to me, IDegLira [Xultophy] is sort of like insulin on steroids.” The take home message is stronger efficacy with fewer side effects (and also fewer injections) – a real winning recipe.

Xultophy cannot be submitted to the FDA in the US until its basal insulin component (Tresiba) receives FDA approval.

As exciting as Xultophy is, those in the US will have to wait quite a while before being able to use it. Xultophy cannot be submitted to the FDA in the US until its basal insulin component (Tresiba) receives FDA approval. As a reminder, the FDA did not approve Tresiba in 2013, citing concerns over cardiovascular risk. Novo Nordisk is currently conducting a massive cardiovascular outcomes trial in around 7,500 participants to evaluate the drug's safety; the plan is resubmit Tresiba to the FDA sometime in mid-2015, and the company has not shared how much later it might submit Xultophy. –MV/AJW



## T2 BI/Lilly Launch Jardiance for type 2 diabetes – Now the Third Commercially Available SGLT-inhibitor in the US

*Twitter summary: BI/Lilly launch Jardiance in the US, making it the 3rd SGLT-2 inhibitor on the market; savings program for one-year free supply*

After its recent FDA approval on August 1, Jardiance (empagliflozin) is now commercially available in the US by prescription at major pharmacies for people with type 2 diabetes. The launch makes Boehringer Ingelheim (BI)/ Eli Lilly's Jardiance the third SGLT-2 inhibitor available in the US after Janssen's Invokana and AstraZeneca's Farxiga. After receiving European approval back in May 2014, Jardiance has already begun a European launch – available in both the UK and Germany.

The SGLT-2 inhibitor Jardiance comes as an oral, once-daily tablet, to be taken in addition to diet and exercise for adults with type 2 diabetes.

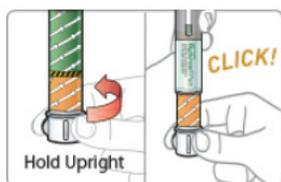
The SGLT-2 inhibitor Jardiance comes as an oral, once-daily tablet, to be taken in addition to diet and exercise for adults with type 2 diabetes. This class of drugs causes the kidneys to excrete excess glucose through the urine, which lowers A1c and can even cause weight loss and improvements in blood pressure. As with other SGLT-2 inhibitors, Jardiance's main side effects include genital tract infections (6% of people with type 2 diabetes on Jardiance developed a genital infection, compared to 2% of those on placebo), though they are manageable in most cases. While Jardiance is only approved for type 2 diabetes, some health care providers already use SGLT-2 inhibitors off-label for type 1 diabetes, and some trials are looking more closely at its effects in type 1. In some data we've seen, SGLT-2 inhibitors have allowed people with type 1 to spend more time in an ideal glucose range (less hypoglycemia and hyperglycemia) while taking less insulin.

BI/Lilly are offering a Jardiance Simple Savings program that offers eligible patients with insurance one year of free access to Jardiance – this program is similar to those for both Invokana and Farxiga, which also have year-long savings programs. Without insurance, out-of-pocket costs for 30 pills (a one month supply) of the 10 mg or 25 mg doses of Jardiance are \$359.99 and \$361.99 (respectively) at a local Walgreens.

Compared to Invokana and Farxiga, Jardiance may be the most accessible people with impaired kidney function.

Compared to Invokana and Farxiga, Jardiance may be the most accessible for people with impaired kidney function. People with eGFRs (a measure of kidney function, with lower numbers indicating worse function) down to 45 ml/min/1.73 m<sup>2</sup> can use both doses of Jardiance (10 mg or 25 mg). In contrast, people with moderate kidney damage (eGFR between 45 and 60 ml/min/1.73 m<sup>2</sup>) are required to take the lower dose of Invokana, and Farxiga is not recommended at any dose.

Down the road, companies are looking at combining SGLT-2 inhibitors with other type 2 diabetes medications in a single pill. The fixed-dose combination (FDC) of Jardiance and Tradjenta (linagliptin, a DPP-4 inhibitor) is currently under FDA review, with a decision expected as early as February 2015. BI/Lilly's Jardiance/ Tradjenta FDC is the first in its class to be reviewed by the FDA, and if approved, would represent the first SGLT-2/DPP-4 inhibitor available to patients in the US.  
-AJW



## T2 AstraZeneca Launches the New Bydureon Pen in the US

*Twitter summary: New Bydureon pen launched in US – user-friendly “twist, tap, twist” procedure simplifies the injection process*

AstraZeneca recently launched its Bydureon dual-chambered pen (once-weekly exenatide) for type 2 patients in the US. The FDA approved the pen on March 3, and the pen has been recommended for European approval (meaning approval is likely to occur in the upcoming months). For full safety and side effect information for Bydureon, please see AstraZeneca’s website. The new Bydureon device is a pre-filled, single-use pen injector, which eliminates the need for patients to manually mix the drug before injection (“reconstitution”) and reduces some of the “hassle factor” of taking Bydureon. Before, users of Bydureon had to go through a more involved process to prepare and inject the drug.

The device involves a “twist, tap, twist” preparation process, an improvement from the previous vial-syringe injection process. The user attaches the needle, twists the base of the pen (stopping at the sound of a “click”), taps the pen firmly against the palm of his/her hand until the medicine is mixed (up to 80 times or more), twists the base of the pen once more until the injection button is released, and then finally removes the needle cover and injects. For a full how-to video on using the Bydureon pen, please visit its website. While this new process is a significant upgrade from manual mixing, it is a step behind ready-to-use GLP-1 agonists such as Novo Nordisk’s Victoza (liraglutide), Sanofi’s Lyxumia (lixisenatide), or Eli Lilly’s Trulicity (dulaglutide) – these products do not require any preparation other than attaching the needle and injecting. AstraZeneca is working on a more automated form of delivery that will further increase Bydureon delivery convenience in the future. –NL/KC/AJW

## T1 BI/Lilly’s “Biosimilar” Insulin Glargine Receives European Approval

*Twitter Summary: BI/Lilly’s #insulin glargine receives EU approval – “Abrasia” set to launch in mid-2015 as 1st ever “biosimilar” insulin in Europe*

On September 10, Eli Lilly and Boehringer Ingelheim (BI) announced the European approval of their insulin glargine product, named Abrasia in Europe. Lilly/BI’s insulin glargine product is biologically similar to Sanofi’s Lantus (insulin glargine) and is the first insulin to be approved in Europe as a “biosimilar.” The “biosimilar” label reflects that Abrasia is created from the same protein sequence as Lantus and has a comparable glucose-lowering profile. Bi/Lilly’s insulin glargine received “tentative approval” from the FDA in August, but it will be branded under the name Basaglar in the US. The companies are working on a revised trade name for the product that can be either more similar or exactly the same across the globe. The FDA does not technically consider Basaglar to be a “biosimilar” insulin for regulatory reasons, though at *diaTribe* we like to think of it as a “non-biosimilar biosimilar.”

Abrasia will be available in Europe as a pre-filled pen (KwikPen) and in cartridges for a reusable pen. Abrasia cannot launch in Europe until Sanofi’s patent for insulin glargine expires, which will happen in mid-2015. In the US, the launch of

Lilly/BI’s insulins glargine product is biologically similar to Sanofi’s Lantus and is the first insulin to be approved in Europe as a “biosimilar”.

Basaglar is currently delayed until mid-2016 due to a lawsuit between Sanofi and BI/Lilly over Lantus patent infringement.

An advantage of biosimilars could well be potentially lower prices for patients, though we don't know anything about prices yet. As we discussed in our recent conference pearls, insulin prices have increased significantly in recent years. The introduction of Abrasia/Basaglar and other future biosimilar insulins (such as from Merck and Mylan/Biocon) to the market may potentially help make insulin more affordable over time. –AJW



### T1/2 **Apple Watch Revealed – Contains Fitness and Health Applications, No Glucose Monitoring**

*Twitter Summary: Apple unveils smart watch with several sleek fitness apps – available early 2015 starting at \$349*

On September 9, Apple unveiled its first-ever smart watch. There had been speculation that this watch would have glucose-monitoring capabilities, but unsurprisingly, this feature is not available in the first-generation of the watch. A last minute bug also prevented Apple from revealing any glucose applications for its new Health app or any integration with diabetes devices. However, we have heard that Apple does intend to work in diabetes for future iterations of its products – this would be very positive, as tech giants such as Apple can bring fresh ideas and designs to diabetes management (and perhaps, make it more fun). Google and Novartis, for instance, are working together on glucose-monitoring contact lenses.

The Apple Watch features several nifty health and fitness applications to help monitor day-to-day activity. The watch can track calories burned, time spent exercising, time spent standing versus sitting, and distance traveled by connecting to the user's iPhone GPS system. The watch requires an Apple iPhone to work. Apple's video of the watch's fitness aspects also provides a nice summary of its features. Hopefully, the watch will get people who aren't typically focused on fitness to take simple steps in improving their physical activity. The watches will become available in early 2015 at a starting retail price of \$349, an increase from simpler activity trackers like Fitbit (starting at \$59.95) or Jawbone (starting at \$79.99). –AJW/AB

### T1 **Lilly's Basal Insulin Peglispro Shows Superiority to Sanofi's Lantus in A1c Reduction**

*Twitter Summary: Lilly's new basal #insulin Peglispro superior to Sanofi's Lantus in A1c reduction, though some potential liver safety and hypo concerns*

On September 4, Eli Lilly announced results from its phase 3 IMAGINE trials comparing Lilly's basal insulin peglispro (BIL) to Sanofi's Lantus (insulin glargine) in type 1 diabetes. BIL insulin works primarily on the liver and less on peripheral tissue (like current insulins), more closely mimicking the way insulin works in someone without diabetes.

While Lilly has yet to release exact data from the trials comparing its new insulin (BIL) to Lantus, there were three positive high-level takeaways:

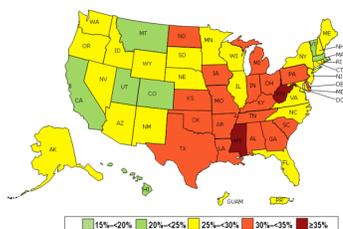
Basal insulin peglispro (BIL) works primarily on the liver and less on peripheral tissue like current insulins.

- Improved A1c – in both type 1 and type 2 diabetes.
- Less hypoglycemia at night – in both type 1 and 2 patients.
- Weight loss – Type 1 patients on Lilly’s new insulin lost weight on average (regardless of A1c reduction), while those on Lantus tended to gain weight. Type 2 patients on BIL tended to gain less weight than those on Lantus.

However, the IMAGINE results also indicated three concerns with Lilly’s new basal insulin:

- Increased daytime and overall hypoglycemia – in both type 1 and type 2.
- Increased severe hypoglycemia in type 1 diabetes (situations in which another person needed to help the patient because of low blood glucose)
- Increased liver and cardiovascular side effects – Lilly’s new insulin was associated with increases in certain liver enzymes, triglycerides, blood pressure, and LDL cholesterol, as well as reductions in HDL cholesterol.

Lilly plans to submit its new basal insulin to the FDA in the first quarter of 2015, meaning a decision could come by the end of 2015 or early 2016. –AJW



## T1/2 The CDC Releases State-by-State Obesity Data; Six States Show Significant Increases in Obesity Rates

*Twitter Summary: CDC releases state-by-state obesity data, several states see increases in adult obesity rates – childhood obesity rates level off*

The Center for Disease Control and Prevention recently released its newest state-by-state obesity (a body mass index, or BMI, 30 or above) data from 2013. The report highlights that the prevalence of adult obesity is still increasing in the US, with six states (Alaska, Delaware, Idaho, New Jersey, Tennessee, and Wyoming) showing significant increases. According to the data, Mississippi and West Virginia have the highest obesity rates – both at 35.1% of the adult population. Colorado, Hawaii, the District of Columbia, Massachusetts, California, Utah, Montana, and Vermont have the lowest obesity rates – all below 25%, with Colorado having the lowest rate at 21.3%. We continue to find obesity data quite alarming and a reminder of the challenges in helping people manage weight in a toxic food environment that promotes unhealthy choices. –AJW

Due to company misconduct by Andromeda, biotech company Hyperion terminates development of type 1 therapy.

## T1 Hyperion Terminates Development of Immune Intervention Therapy Due to Trial Misconduct

*Twitter Summary: Due to company misconduct by Andromeda, biotech co. Hyperion terminates development of immune intervention therapy for #T1D*

On September 8, Hyperion Therapeutics announced that it would stop development of DiaPep277, a phase 3 immune intervention therapy that would have targeted new onset type 1 diabetes. This past June, Hyperion had acquired the company Andromeda Biotech, which had already been developing DiaPep277. Previous trials had indicated that DiaPep277 may lead to reduced beta cell loss, improved A1c, and reduced rates of hypoglycemia in new type 1 patients. But Hyperion recently discovered that several Andromeda employees had falsified the

trial data. Employees had excluded 34 participants from the trial's data analysis; if those individuals had been included, the results would no longer have been statistically significant. While Hyperion plans to finish its current DiaPep277 trial, it does not plan to continue research or to bring the therapy to market – a disappointing outcome, by any measure. –AJW



## T1/2 Medtronic Recalls MiniMed Paradigm and 530G Systems Due to Hypoglycemia Concerns Resulting from Device Design Error

*Twitter Summary: Medtronic recalls MiniMed products due to minor design error leading to accidental hypo – new design in the works to fix the issue*

On August 22, the FDA posted a voluntary class II recall of Medtronic MiniMed Paradigm and 530G systems. There are three levels of FDA recalls (class I, II, and III), with a class II recall indicating an intermediate threat level, for those that can pose some health risks that are typically preventable and are not cause for major alarm. In this case, Medtronic mailed notices to customers earlier this year about the risk of an accidental overdose of insulin. Evidently, scrolling down past “zero” on the insulin dosing screen immediately scrolled to the maximum bolus dose of insulin, allowing users to accidentally give much more insulin than intended (e.g., hitting the down arrow once would scroll from 0.0 units to 10.0 units).

Reports of this serious error have fortunately been rare, with only one reported instance of severe hypoglycemia resulting in hospitalization. Medtronic already wrote its customers in March describing the issue and what safety precautions should be taken to minimize this hypoglycemia risk, and with this recall they plan to change the design such that the scrolling feature stops at zero. The FDA announcement said that 559,374 Paradigm and 530G systems had been recalled to date, impacting all Medtronic customers. Those who have Medtronic pumps do not need to return their pumps, but should read the safety information posted here. –AJW

## logbook



*Garrett with friends at camp.*

## T1/2 Celebrating an Anniversary: The Delicate Dance of a Diabetic Milestone

*by James S. Hirsch*

It begins, as these things do, with a simple complaint. “I’m thirsty,” my son tells me. Garrett is 3 years old. I’ve had type 1 since I was a teenager, so I know the symptoms. A couple weeks pass, and Garrett is still thirsty. Late one night, he complains that his stomach hurts. I finally test his blood sugar. “HI” it reads. I drive him through the dark streets of Boston, take him to the ER, and confirm the diagnosis.

On our first day back home, Garrett stands in the driveway, basketball in hand, and asks me, “How long will I have diabetes?”

Garrett is now 13, and on September 22, he observes his 10-year anniversary. I say “observe,” because I’m not really sure what we do with such an anniversary.

That was September of 2004. Garrett is now 13, and on September 22, he observes his 10-year anniversary. I say “observe,” because I’m not really sure what we do with such an anniversary.

Do we celebrate it?  
Recognize it?  
Or just ignore it completely?

I can’t speak for other chronic conditions, but diabetes has an interesting history regarding anniversaries. Insulin’s discovery in 1922 transformed the disease from a killer into something that could be managed; but given how crude the tools were – impure animal insulin, the inability to test blood sugars – and given how poorly understood diabetes was, insulin was a rickety crutch on which each patient stood. Survival was still the goal.

So it made sense for Elliot Joslin, who began treating diabetes patients in the 1890’s, to create a Victory Medal. Beginning in 1947, Joslin gave it to any patient who had diabetes for 25 years or longer and was found – after a thorough examination – to be in good health. The medal itself was pretty cool: Embossed on it was the word “VICTORY,” above a three-steed chariot, with the words inscribed at the bottom: “INSULIN EXERCISE DIET.” (Joslin was years ahead of his contemporaries in understanding the essentials of good care.)

Life with diabetes has and always will be like floating on an “uncharted sea,” each day trying to navigate the waters with imperfect tools, bracing the headwinds.

Over the years, other medals were created by clinics, health organizations, or companies. Some commemorated 50 years with diabetes; others, on a life well lived. My favorite was another Elliot Joslin medal, introduced in the 1950’s, that featured a boy with his dog in a small boat, the sun setting in the background, and the words: “EXPLORERS OF UNCHARTED SEAS.” Life with diabetes has been and always will be like floating on an “uncharted sea,” each day trying to navigate the waters with imperfect tools, bracing the headwinds. Joslin gave the medal to patients who outlived their “normal life expectancy,” whatever that meant; I’d like to think Joslin simply gave it to those who did their best.

Of course, when your 3-year-old is diagnosed, you’re not thinking about normal life expectancy. You’re just trying to make it through the night. Garrett doesn’t have any bad nighttime lows, but he does have one hypoglycemic experience, at age 7, that requires a call to 911 and an ambulance trip to the ER. It is his only diabetes-related emergency, post diagnosis, so we consider ourselves fortunate.

Garrett, in the beginning, doesn’t like taking shots and one time actively resists an injection in a restaurant bathroom. “I hate diabetes!” he tells us. He starts using the OmniPod system at age 6. It is not perfect – sometimes the pods fall off, other times they deactivate; after one day of several pod changes, he yells, “No more pods!” – but he soldiers on.

At age 5, a friend invites him to a birthday party – a baseball game in Rhode Island. Garrett looks at me with those big eyes to see if I can come also. He under-

His main goal in life is to be like all the other kids.

stands that there will be food at the game, and he is too young to give his insulin, and without insulin he may not make it home. Not many kindergarteners understand their own mortality. Garrett does.

His main goal in life is to be like all the other kids. At age 9, a documentary filmmaker asks him, “What is the worst part about having diabetes.”

Garrett recalls a birthday party in which he cannot eat the pizza and cake when everyone else can. I am late to give him his insulin, and the parents make him wait. So he sits at the end of the table while the other kids celebrate. The birthday party had occurred two years ago. Some wounds heal slowly.

At 7, he goes to Camp Joslin for kids with diabetes, but by 10, he wants to go to the same sleep-away camp that his big sister attends in New Hampshire. The camp is supportive, so off he goes – much to our fear, but if he wants to be like everyone else, it is time for him to learn. The first summer he goes for three weeks; the next three summers, seven weeks. He water skis, plays basketball, makes new friends, and loves every minute. He experiences some volatile blood sugars (three scones for breakfast will do that), but he carries his diabetes supplies in a red backpack, navigates the high-carb meals and non-stop schedule, and each year becomes more responsible, more resilient, more independent.

On his baseball team this fall, a teammate pulls out his black kit that is used for the OmniPod system. A kindred spirit!

Now in eighth grade, he no longer needs me to accompany him. He goes to the movies, hangs out with friends after school, has sleepovers. On his baseball team this fall, a teammate pulls out his black kit that is used for the OmniPod system. A kindred spirit! For the first time, Garrett is not the only kid on his team with type 1. I chat with the boy’s mother, who tells me about her son’s roller coaster numbers and high A1c’s. He was diagnosed at age 8. “He kind of lost his childhood,” she says.

I think Garrett kept his childhood. He has always had good friends who were understanding of his medical needs; he has traveled across the country for vacations and family gatherings; he loves ESPN and action films and science fiction books, and he is becoming increasingly particular about his clothes. (“You don’t have the right look,” he tells me more than once.) Blessed with compassionate doctors and nurses at the Joslin Clinic, he is in excellent health.

And what of his anniversary? We want to recognize his accomplishments, his hard work, his sacrifices, and we offer to buy a special gift of his choosing.

“What would you like?”

I assume he’s going to ask for a new pair of sneakers, or some clothes, or a video game. Instead, he shrugs.

“Nothing, really,” he says.

I’m surprised, but maybe his indifference is a good thing. Garrett has no memory

Garrett has no memory of life without diabetes, so maybe 10 years with diabetes is just what it is - it's life.

of life without diabetes, so maybe 10 years with diabetes is just what it is – it's life. And maybe Garrett has his eyes on a bigger prize.

My brother, Dr. Irl Hirsch, runs the diabetes clinic at the University of Washington in Seattle and is well-known in the field. He also has type 1, diagnosed as a young child, and in July, the Eli Lilly Company gave him his 50-year medal.

When I tell Garrett about his uncle's award, he does the calculation and says, "That means I'll be 103 and when I get my 100-year medal."

Something to celebrate.

## SUM musings



### CGM in the Cloud: The How, Why, and Why Not of Remote CGM Watching

by Kerri Sparling

**Twitter summary:** *Kerri Sparling talks about the pros and cons of CGM in the Cloud – a novel way to monitor CGM data that has some excited and others keeping away*

**Short summary:** *Kerri Sparling (Sixuntilme.com) discusses CGM in the Cloud, explaining what it is and how it works. Sparling writes about its benefits and drawbacks that are leading to a split in the diabetes community – some people are celebrating its attributes while others are keeping their distance.*

#### What is CGM in the Cloud?

The CGM in the Cloud group on Facebook was founded in April 2014, and currently has 6,204 members (talk about fast growth - there were fewer than 1,950 members in July 2014). Members join by the dozens every week, each seeking more information on how to send CGM data "into the cloud".

Wait, wait, wait ... what's "the cloud?" The cloud is the term for storing the data on a web-based server, instead of on specific devices. Sending CGM data into the cloud takes that data from the receiver and makes it possible for it to be distributed to multiple devices (e.g., smartphones, smart watches, tablets). Currently, Dexcom has its cloud-based Share application under FDA review, but does not have approval yet, and Medtronic does not have a cloud-based system as of yet. Dexcom also has plans to submit its Gen 5 system to the FDA by early next year; this would send CGM data straight from the transmitter to a smartphone app.



A new system called “Nightscout” uses CGM in the Cloud to take the data from the Dexcom G4 Platinum receiver and send it to an Android device by way of a custom-built application, which stores the data and sends it to an open-source device, like a Pebble watch, a computer screen, or perhaps even the coming-soon Apple Watch. The system requires an Android phone with data capability (either through a data plan or Wi-Fi access), two micro-USB cables, and a Dexcom G4 receiver. The system can be cumbersome to hook up – it takes anywhere from 30 minutes to several hours – but some members in the CGM in the Cloud group are willing to provide assistance. The Nightscout website provides all the information needed to set CGM in the Cloud up.

CGM in the Cloud is an inspiring example of grassroots action and patient advocacy.

Nightscout is the brainchild of people touched by diabetes who took matters into their own hands.

So why is sending data to the cloud important? It makes CGM data available not just to the person holding the CGM receiver, but to anyone linked up to the cloud. Blood sugars can be sent from a receiver in Rhode Island and viewed by a partner in Los Angeles, or from a receiver in middle school to a parent’s computer 20 miles away. The ability to remote monitor offers another safety net for those who want it.

Not only that, but CGM in the Cloud is an inspiring example of grassroots action and patient advocacy. Nightscout is the brainchild of people touched by diabetes who took matters into their own hands to improve management through better use of technology, and bypassing the sometimes slow bureaucracies present in government and industry that can delay innovation. Nightscout isn’t about money or profit - it’s about helping people with diabetes, and while the system has its drawbacks, the group’s mission is definitely worth applauding.

### Who Is Using It?

Initially, the system was created by parents of young children with diabetes, in efforts to keep track of CGM data by sending it to the cloud and then to devices like the Pebble watch, or a website-based platform.

“I am not waiting for an approved solution - in 2016 at the minimum - but using Nightscout to create a safer, less burdensome life for my eight year old daughter.”

“I am using [the Nightscout system] and started the [Facebook] group because I am not waiting for an approved solution - in 2016 at the minimum - but using Nightscout to create a safer, less burdensome life for my eight year old daughter,” said Jason Adams, who co-founded the CGM in the Cloud group. The other co-founder, John Costik, agreed. “For us and many like us, it enables freedoms that type 1 [diabetes] so desperately tries to take. From sleeping safely at home and on sleepovers to simplifying the task of self-monitoring at critical times, remote monitoring can bring these moments back to the realm of ‘normal.’ It brings a deeper understanding of type 1, an understanding that weakens its hold on our lives.”

Jacque Mullins, the parent of a type 1 child, cites the practical advantages. “I am using CGM in the Cloud to keep my child safe and to allow him to be a kid,” he

said. “For the first time, he has been able to go to a birthday party alone, with me popping in just to dose for food. I can keep an eye on him from wherever I am, and he can just be a kid.”

“...that small changes makes a huge difference in allowing diabetes to fit into my life instead of the other way around.”

Adults with diabetes are also using the system. Sara Nicaastro sends her CGM data to the cloud in order to make her data more accessible and to make viewing it more discrete, using the Pebble watch on her arm as her go-to viewing screen. “I was really skeptical,” said Sara. “I wasn’t sure if there was enough value in the system for me to make the investment of time and money, not to mention carrying around and troubleshooting the extra items. It seems like such a small difference to have my CGM data on my wrist as opposed to on a receiver in my purse, but that small change makes a huge difference in allowing diabetes to fit into my life instead of the other way around.”

Melissa Baland Lee, who’s had type 1 for over 20 years, sends her CGM data to the cloud as well. “My husband has woken me too many times for an overnight low. To have his phone alert him when I’m home alone with a 49-double-down [arrows on the Dexcom CGM that indicate a rapidly dropping blood sugar] that won’t budge gives us just a little peace of mind.” For adults with type 1, sending their CGM data to the cloud allows for parents, friends, and loved ones to remotely monitor their blood sugars. Melissa does acknowledge the hiccups in the hardware, though. “While the rig is a fragile beast, it’s a means to an eventually more elegant end – the end being that all of the hard work these folks spend coding this project will ultimately open up our data for us to own/review/manipulate in ways that make sense to us.”

### Who Is NOT Using It?

The set up process may be daunting for those who are not technologically savvy. For others, their CGM of choice may not be supported... and there is also the concern about the cost.

Of course, the first limiting factor for this category is that over 90% of people with type 1 diabetes aren’t using CGM, according to data from the T1D Exchange. For the ~10% that are, several hurdles have prevented some from using CGM in the Cloud. The set up process may be daunting for those who are not technologically savvy. For others, their CGM of choice may not be supported by Nightscout (currently, the system only works with the Dexcom G4 Platinum receiver). And there is also the concern about the cost of parts for the system (an Android phone with a data plan is required), and the potential for damaging the fragile USB port on a Dexcom receiver.

“We just got our first Dexcom, and I’ve heard the rig is hard on the charge port. I’m afraid of ruining [the USB port of] the receiver,” said Sherry Roberts, a parent of a child with diabetes.

Cathie Wallace, who has type 1 diabetes, shared concerns about cost. “I would love to use it but can’t afford it.” The cost of sending CGM data to the cloud varies depending on many variables – is the CGM system itself covered by insurance?

Does the household have an Android phone available, or does one have to be purchased? Does a data plan need to be purchased? And what about the cables and cords needed to set up the system? Costs for clouding CGM data vary widely, and can make or break someone's decision to move forward. According to Night-scout's website, the minimum cost for the initial set-up is about \$100, though it points out that it can cost much more than that in some cases.

CGM in the Cloud can lead to some parents micro-managing their child's life or being overly worried.

Then there's the issue of restricting access. Adults who use the system can give access, or revoke it, to whomever. For kids who have parents accessing the system, it can be a little more complicated, as CGM in the Cloud can lead to some parents micro-managing their child's life or being overly worried about every minute fluctuation in their child's blood glucose.

Tina Ghosn, who has three kids with type 1, is not using the system. "Could you imagine how quickly the remaining shreds of my sanity would unravel if I were to be watching the numbers of three kids 24/7?"

For Kimberly Robertshaw, she and her daughter (who has type 1) have mixed feelings about remote monitoring. "It's great for seeing trends, or for sleepovers, or if you are traveling. But it can make helicopter parents worse, and it's more to carry for a child. I firmly believe in letting [her daughter] be a kid and not make her whole life diabetes, so I worry this is a tad invasive. But we're giving it a shot."

Opening up CGM data offers patients and their loved ones access to a broader safety net of care.

Opening up CGM data offers patients and their loved ones access to a broader safety net of care. But too much information, in some circumstances, can also be damaging depending on the person's relationship with diabetes.

Scott Johnson, diagnosed with type 1 diabetes in 1980, has been using CGM in the Cloud for his personal use for several months – "I love being able to just glance at my wrist and see where I am and whether I'm moving, and if so, in what direction." But there's another side to his data upload that was only brought to light after sharing the streaming URL of his data with his father.

"My dad looked at it for a while, then said, 'I'm not ready to ride that rollercoaster with you.' All of this data was overwhelming to him...because his involvement in my diabetes is not anywhere near as active as it was when I was growing up. Now, information is a click away. Yet he doesn't know what he would do if he checked it and saw that I was 'in trouble.'" And what is "in trouble?" Way high? Way low is obvious, right? But then what? Call my wife? Wake the house up?... And imagine if the last thing on the screen was a sharp downward line?"

I was diagnosed in 1986 and only started using a CGM once I was living on my own, not under the care of my parents. My mother is both fascinated by the CGM

It's about personal preferences. In my life, I'm taking a preemptive bite out of fear by putting another safety net into place.

data and fearful of it, because seeing the constant shift in real time can be empowering but also scary.

It's about personal preferences. In my life, I'm taking a preemptive bite out of fear by putting another safety net into place. When I'm traveling for work, I will have my CGM data streaming to the cloud, and my husband and my mother (as needed) will have access to it. When I am alone in a hotel room, my family will have the peace of mind knowing that they can see my blood sugars while I sleep. Same for when my husband is traveling and I am alone with our daughter. I sometimes worry that my data will cause them undue stress, and I worry that I'm somehow sacrificing my privacy or independence by sharing this data, but in the long run, the feeling of safety is worth it for me.

"To cloud or not to cloud?" is a personal choice. Having diabetes is not a choice, but the tools we use to manage it can be, and for that, I'm grateful.

## diaTribe dialogue



T1

### How the Tidepool Data Integration Platform Can Ease Diabetes Management: Our Interview with Tidepool CEO Howard Look

by Adam Brown and Alex Wolf

**Twitter summary:** *Interview w/ Tidepool CEO Howard Look on how device data will ease T1D burden; @JDRF, Insulet, Dexcom, Asante already on board!*

**Short summary:** *The diaTribe team recently interviewed Tidepool CEO Howard Look. Tidepool is a diabetes non-profit organization that has developed an open-source data platform, allowing apps such as "Blip" to integrate data from multiple diabetes devices all into one place. Mr. Look – a parent of a child with T1D – discusses the need for data integration, what challenges exist for Tidepool, and its ambitions for the future.*

Earlier this year, we wrote a conference pearls piece about Tidepool, a non-profit organization that aims to use its open-source data platform to make diabetes management simpler and more accessible. One of Tidepool's applications, Blip, is a web-based program that integrates data from all kinds of diabetes devices (CGMs, meters, pumps, etc.) on a single, sleek interface. Tidepool is also developing an innovative "Universal T1D Device Uploader" tool to make the data import process easier, and today, announced a partnership with JDRF to accelerate development. Tidepool has already made official partnerships with Asante, Dexcom, and Insulet. The Blip program can currently integrate data from Medtronic



*Blip is a web-based program that integrates data from all kinds of diabetes devices on a single interface.*

“By liberating the data and making software that is much easier to use, we can make it easier for doctors to prescribe devices and easier of patients.”

and Animas devices as well (though these are not official partnerships). Tidepool plans to make all of its products available free of charge.

Data uploading has historically been unpopular in diabetes due to the hassle it can cause, but Blip allows patients to access data from multiple products and brands (e.g., an Asante insulin pump and a Dexcom CGM) all in one easy-to-use platform. UCSF is currently hosting a pilot trial of Blip, and Tidepool hopes to have a market-ready version of Blip, the Universal Device Uploader, and the Tidepool platform by the end of 2014. These products will need FDA approval, so they likely wouldn't be widely available until 2015 at the very earliest.

As a non-profit organization, Tidepool seeks to collaborate with industry, rather than compete with it. The organization gained full 501(c)(3) non-profit status this June and recently partnered with the JDRF. The diaTribe team recently sat down with Tidepool CEO Howard Look to learn more about Tidepool's mission, foreseeable challenges, and goals. Mr. Look is the parent of a child with type 1, and we admire his passion and commitment to improving diabetes care.

### **Q: What has been the biggest challenge in bringing Tidepool from just an idea to its current stage?**

**HOWARD:** Funding. Fundraising as a non-profit is much more challenging than I anticipated, and very different than my prior experience doing startup fundraising through the usual Silicon Valley, for-profit, venture capital channels.

But being a non-profit was, and is, the right decision for us. We could not have made the progress we've made as a for-profit entity. We would have been threatening to the industry, who would have thought “Wait, if there's value in liberating the data, then I want to keep it to myself!” That's how we got into this mess of closed, vertical and proprietary systems based on terrible software.

Only 6% of people in the T1D Exchange upload their data on a regular basis, and only 30% of people with type 1 diabetes use pumps or CGMs, despite clear evidence of better therapy and outcomes. By liberating the data and making software that is much easier to use, we can make it easier for doctors to prescribe devices and easier for patients, parents, and doctors to engage with data, make more effective therapy changes, and overall reduce the burden of managing type 1 diabetes.

By being a non-profit, we are able to credibly say to the industry, “This is better for everyone. This will help make your devices more valuable, and it will grow the overall market. And we are good at building software, so please let us for type 1 diabetes.” Being a non-profit allows us to truly deliver on our mission of helping everyone with T1D.

**Q: Thinking about what you have learned, what advice would you give to yourself if you were to start over again?**

**HOWARD:** Maintain laser-beam focus on delivering a “Minimal Viable Product” as soon as possible, getting feedback early and often, and iterating as quickly as possible. We did a pretty good job at this, but we can do even better.

**Q: As you look at your product roadmap, what is your biggest current challenge?**

**HOWARD:** From a product development standpoint, nothing we are doing is rocket science. This is all very straightforward software development. Silicon Valley delivers great software with a great user experience routinely; it just hasn’t had a focus on type 1 diabetes before.

Really, our biggest challenge in delivering great software is funding, again. Nearly everyone working at Tidepool took a significant pay cut to work at a non-profit. We have no stock options. No one is in this for the money. We’re doing this because we believe that this is the right thing to help people with diabetes, and it needs to be done. In addition, we will need to hire a few more folks to pull off everything we want to pull off, as well as enlisting help from an FDA consultant.

Six Tidepool employees have type 1 diabetes. Two of us have family members with type 1 diabetes. Three of our four board members have family members with type 1 diabetes. We like to say, “We have pancreas in the game.” We’re doing this for ourselves, and we’re doing this to help the entire type 1 diabetes community.

**Q: For which of the following groups do you imagine Tidepool will be the biggest gamechanger: patients, clinicians, payers, researchers, others?**

**HOWARD:** First and foremost, for patients, we think that what we are doing is a game-changer because it will help make engaging with data and devices much easier, which in turn will make it much easier to achieve effective therapy and reduce the overall burden of managing type 1 diabetes. We hope that apps like Blip and Nutshell [an app that helps you “remember what you ate, how you bolused for it, and how your body reacted to it.”] will simply make life living with type 1 diabetes easier. Also over time, we believe that an ecosystem of apps will emerge, such as an app for athletes with type 1 diabetes, or an app for pregnant moms living with type 1 diabetes.

For clinicians, our software makes it much easier to get data from devices, and much easier to engage with patients about their therapy. Early anecdotal feedback from doctors at UCSF is that using Blip makes in-clinic visits much more productive.

“Six Tidepool employees have type 1 diabetes. Two of us have family members with type 1 diabetes. Three of our four board members have family members with type 1 diabetes.”

“Early anecdotal feedback from doctors at UCSF is that using Blip makes in-clinic visits much more productive.”

We have not yet spent a lot of time focusing on the needs of payers, though we do believe that over time the data will show that better software will lead to better outcomes and therefore lower costs from both the acute and long-term complications of type 1 diabetes.

And finally, we're not there yet, but we hope that the Tidepool platform will enable a whole new class of research studies based on "ground truth" data acquired directly from devices. We're excited about the possibilities that this will enable.

"Really, there's no place to go but up - T1DExchange data shows that only 3% of pumpers upload their data more than once per week, and 60% never upload."

**Q: If the whole suite of Tidepool products was out tomorrow, what fraction of patients do you estimate would ultimately download their devices? Is your dream to automate everything, so that patients and providers don't ever need to even look at their data – they just get actionable recommendations? Or is this fairly unrealistic given regulatory challenges?**

**HOWARD:** Really, there's no place to go but up – T1DExchange data shows that only 3% of pumpers upload their data more than once per week, and 60% never upload. And that's from a self-selected group of patients at highly-engaged member clinics.

We think that's just a crime, but it's not a surprise when you actually try to do it. For example, getting up and running with CareLink is an endless barrage of Java security warnings, OS incompatibilities, USB incompatibilities and more. And even if you are able to get it up and running, the user experience is complicated and inaccessible to most. I'm a smart guy and do software and user experience for a living, and I can barely get it working. Medtronic could solve this by simply making their data protocol available so that others, like Tidepool, can write software to access the data.

If we can cut that 60% number of pumpers who have never downloaded in half, I will consider it a huge win. But I think we can do even better. I do think that automated recommendations will come, but as you said that has a much higher bar from a regulatory, safety and efficacy standpoint. We may get there, but for now our goal is to simply make it easier to engage with existing data.

"Today, much of the burden of data analysis is on the person with diabetes, their parents, and their provider."

**Q: Do you imagine that automated insulin delivery will reduce the need to analyze diabetes data?**

**HOWARD:** Automated insulin delivery will increase the need to analyze diabetes data. But the way we analyze the data will evolve. Today, much of the burden of data analysis is on the person with diabetes, their parents, and their healthcare provider. Together, they use data to refine insulin-to-carb ratios, insulin sensitivity factors, and basal rates to optimize insulin therapy.

As insulin delivery is automated, the burden of analysis will be shared with the researchers who create the delivery algorithms. These researchers will need to understand how their algorithms are performing on real people so they can continue to improve them. For example, does the system effectively detect intense exercise in time to prevent hypoglycemia? Or, under what conditions are bad sensor readings causing undesirable insulin delivery? These are just some of the questions that may be analyzed.

The data generated by the system can be augmented with data from accelerometers, activity trackers, and other sources and be used to answer these questions. For researchers, automated insulin delivery will be a forcing function for more sophisticated data analysis.

“This is a new kind of analysis for people living with diabetes that will require elegant, intuitive, real-time data displays that they don’t have today.”

From the perspective of a person using an insulin delivery system or their parents, automation will reduce the number of times they have to intervene with the therapy, but it will increase their need for visibility into what their devices are doing and why. Trust drives adoption of new technologies, especially when lives are on the line. Transparency through remote monitoring and telemetry will create trust in the automated insulin delivery system. This is a new kind of analysis for people living with diabetes that will require elegant, intuitive, real-time data displays that they don’t have today.

**Q: What would be a home run for Tidepool in 2014? In 2015? In 2020?**

**HOWARD:** Home run in 2014: We deliver Blip, the Universal Device Uploader, and the Tidepool Platform to multiple clinics for IRB-approved pilot studies or clinical trials. Two-run home run: Blip is available for broad deployment with all necessary regulatory filings in place. Three-run home run: We get funded to complete Nutshell development and deploy it to at least one clinic for a pilot study. Grand slam: All of the above, plus we generate revenue from at least one device maker.

Home run in 2015: Everything we didn’t get done in 2014, plus we become a self-sustaining non-profit by the end of the year. Two-run home run: We deliver a research query interface that enables free access to our donated, anonymized research database. Three-run home run: We deliver a robust platform for custom-designed research studies. Grand slam: All of the above, plus multiple FDA-approved third-party applications are delivered using the Tidepool platform.

“Home run by 2020: Multiple closed loop systems are deployed and in wide use...”

Home run by 2020: Multiple closed loop systems are deployed and in wide use. Their data is automatically uploaded to the Tidepool Platform, enabling further research and validating post-market safety and efficacy. Tidepool software is in wide use around the world, and data clearly shows that we’ve made it easier for doctors to prescribe and maintain devices, that patients find it easier to engage with their data, and that outcomes have improved while lowering costs.

## trial watch

How will a new drug combination for type 2 diabetes fare?

### T2 Ertugliflozin and Sitagliptin Study in People with Type 2 Diabetes

ClinicalTrials.gov Identifier: NCT02099110  
<http://clinicaltrials.gov/ct2/show/record/NCT02099110>

In this clinical trial, Merck, in collaboration with Pfizer, is testing whether people taking ertugliflozin (Merck's in-development once-daily SGLT-2 inhibitor pill) plus sitagliptin (Merck's once-daily DPP-4 inhibitor pill, Januvia) will improve their A1c more than people taking sitagliptin alone. The trial will measure the A1c reduction from baseline, the number of participants who experience adverse events, and the number of participants who drop out of the trial due to adverse events. The hope is that the combination therapy (ertugliflozin + sitagliptin, an SGLT-2/DPP-4 inhibitor combo) will have additive benefit over sitagliptin alone, a possibility because SGLT-2 inhibitors and DPP-4 inhibitors work through different mechanisms to lower blood glucose.

To participate in the study, volunteers must have type 2 diabetes, be 18 or older, and have a BMI greater than 18. Exclusion criteria include using other weight loss medications, having a history of intolerance with SGLT-2/DPP-4 inhibitors, and having bariatric surgery 12 months prior to study start, among other criteria. There are 44 trial locations, including centers in CA, CO, FL, GA, IN, ME, MD, NY, ND, OH, OK, OR, PA, and TX. For more information, please call 1-888-577-8839 or visit the ClinicalTrials.Gov site. -AJW



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