

diaTribe®

research and product news for people with diabetes

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from the editor



Next week, our entire *diaTribe* team and its sister company Close Concerns will be heading to Chicago for the 73rd Scientific Sessions of the American Diabetes Association (ADA). Every year we go to ADA, and every year we learn so much about all aspects of diabetes, obesity, and their complications. If you're going to be in Chicago during the week of ADA, I hope to see you around!

While ADA always dominates our schedule this time of year, I'd also like to draw your attention to a pair of key meetings. On June 5-6, a 26-person panel met to discuss the future of GlaxoSmithKline's thiazolidinedione (TZD) Avandia.

Though the meeting was about the drug, I had hoped that there would be a greater discussion on the FDA's proceedings for drug approval. There were times when the debate seemed to highlight larger questions related to clinical trial design, the truth of the data, and the FDA's past regulatory proceedings. However, since most of the meeting focused on the drug, the more important issue of improving how the FDA evaluates safety concerns was left unresolved.

The second meeting is the Workshop on Pancreatitis-Diabetes-Pancreatic Cancer held by the National Institute of Diabetes and Digestive and Kidney Diseases and National Cancer Institute. At this meeting, researchers discussed how incretins' relate to pancreatitis, and pancreatic cancer. Our *diaTribe* team covered the workshop, and the consensus is that we simply do not know enough about the matter. This is consistent with the ADA and the American Association of Clinical Endocrinologists' statement, which expressed that we need to wait for results from additional large randomized controlled trials before we can fully understand how incretins affect the pancreas.

Now, I'd like to talk about my transformative experience with the bionic pancreas. I go into more detail about how the bionic pancreas works and my reactions in this issue's test drive, but I want to reflect on just what those days meant to me.

During the trial, the bionic pancreas's algorithm automatically recalculated my insulin and glucagon needs every five minutes! I didn't have to worry about the little things I've spent the last 27 years worrying about. I found myself in a world where my day was no longer dominated by the constant micro-adjustments needed to manage my diabetes, and that is a fundamentally different experience.

Like some of you, while I like to think I do as good a job as I can with these daily challenges, the reality is that I'm still slightly out of control most of the time. We're all chasing the best control possible, but that's a long way from perfect, and an even longer way from "normal." But that's what I got with the bionic pancreas – a week of not having to worry about diabetes, of not feeling hyperglycemic or hypoglycemic. I didn't have to monitor or worry or think about my diabetes. It's about the most incredible thing that has happened to me in the nearly 30 years that I've been managing this disease.

And what was amazing to me? For that week, I was a nicer person – even, a cooler person. I only understood all the myriad subtle, subconscious ways in which diabetes shapes who I am when they were removed. I really liked the person that emerged when all the challenges of diabetes were removed, and I hope to meet her again. If nothing else comes of this, I'll still always have that week, and, believe me, it was worth it. With any luck, many more weeks like that lie ahead for all of us.

Very best,

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quotable quotes

“I don’t know how to treat diabetes without a download. I just don’t know how.”

– Dr. Irl Hirsch (University of Washington School of Medicine, Seattle, WA) calling on endocrinologists to download data at the Annual Congress of the American Association of Clinical Endocrinologists, Phoenix, AZ, May 1-5, 2013.

“My bias is that prediabetes is diabetes... we have an arbitrary cut point.”

– Dr. Ralph DeFronzo (The University of Texas Health Science Center at San Antonio, San Antonio, TX) stressed that diabetes is a spectrum and that in the VAGES study beta cell function is not normal even in those who are considered as having normal glucose tolerance. He presented his talk during the Annual Congress of the American Association of Clinical Endocrinologists, Phoenix, AZ, May 1-5, 2013.

“Although a hammer is required, the carpenter builds the building. SMBG [self monitoring blood glucose], CSII [continuous subcutaneous insulin infusion], and CGM [continuous glucose monitoring] are all just tools. Insulin pumps deliver insulin and glucose monitors generate numbers. Glucose improvement is dependent on how those tools are used by patients.”

– Dr. David Price (Executive Director, Clinical Affairs, Dexcom, San Diego, CA) when he presented about the pros of using CGM at the Annual Congress of the American Association of Clinical Endocrinologists Phoenix, AZ, May 1-5, 2013.

fingersticks

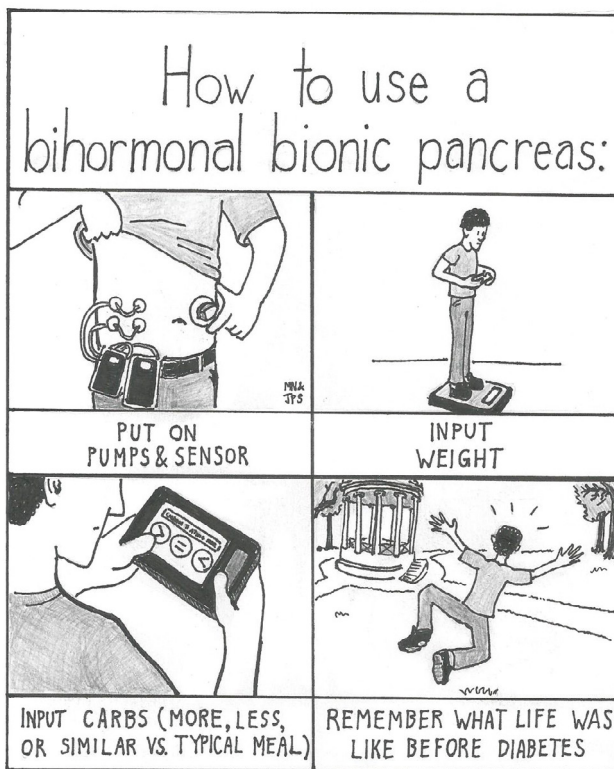


ILLUSTRATION: JOSEPH SHIVERS

The real impact of a bionic pancreas...

new now next

The consensus from most speakers at the workshop was that, while this possible link requires further investigation, the available evidence does not suggest any need for current or prospective users to stop taking GLP-1 or DPP-4 medications.

These various safety trials and epidemiological studies will likely begin reporting data in a few years, although it will take much time for the data to be analyzed and fully understood.

T2 **Most at NIDDK and NCI Workshop on Incretin Therapies and Pancreatitis Do Not Find Significant Cause for Concern**

On June 13, the National Institutes of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Cancer Institute (NCI) concluded a two-day workshop on diabetes, pancreatitis, and pancreatic cancer. The workshop was prompted by studies suggesting a possible link between the use of incretin therapies, such as GLP-1 agonists or DPP-4 inhibitors, and an increased risk of pancreatitis and pancreatic cancer. GLP-1 agonists include Amylin's Byetta and Bydureon and Novo Nordisk's Victoza, while available DPP-4 inhibitors include Bristol-Myers Squibb and AstraZeneca's Onglyza, Merck's Januvia, Takeda's Nesina, and Boehringer Ingelheim and Eli Lilly's Tradjenta. The consensus from most speakers was that while this possible link requires further investigation, the available evidence doesn't suggest a need for users to stop taking incretins. An increased risk of pancreatitis or pancreatic cancer has been a known possible side effect since the early development of these drugs, and the FDA label already cautions people at risk for these diseases against incretins. This workshop is not a major change in experts' thinking about either GLP-1 agonists or DPP-4 inhibitors.

Recent studies appear to question the safety of these drugs, although it is important to understand where their data comes from. The Institute for Safe Medication Practices used the FDA's adverse events database to track reports of pancreatitis and pancreatic cancer and found that they were significantly higher among uses of GLP-1 agonist medications. However, the adverse events database is generally considered useful only to suggest the possibility of risk, not to confirm it. (One reason is that the database relies on voluntary submissions from healthcare providers whose standards for reporting may vary.)

At the workshop, Dr. Solomon Iyasu, the FDA's Director of Pharmacovigilance and Epidemiology, said that the agency has reviewed individual cases of people with pancreatic cancer, and they have not shown "any unique cancer signal or potential risk factor that stands out." As for pancreatitis, the FDA required drug companies to analyze the potential for risk using insurance claims databases. Dr. Iyasu explained that this sort of observational study is imperfect by nature, but most of the published studies so far have not indicated an increased risk of pancreatitis.

This meeting is unlikely lead to regulatory changes in the near term, in part because several large studies are already looking at incretin safety. These various safety trials and epidemiological studies will likely begin reporting data in a few years, although it will take much time for the data to be fully analyzed and understood.

In the meantime, the NIH workshop offers a good guide to the current thinking: GLP-1 agonists and DPP-4 inhibitors are certainly effective glucose-lowering drugs, and patients and their healthcare providers must weigh the benefits and risks of these drugs against those of other therapies in order to select the right treatments.—AW

T2 **FDA Advisory Panel Votes to Loosen Restrictions on GlaxoSmithKline's Avandia**

On June 5 and 6, an FDA advisory panel voted in favor of modifying the current Risk Evaluation and Modification Strategy (REMS), for GlaxoSmithKline's (GSK) Avandia (rosiglitazone), a thiazolidinedione (TZD). The advisory panel met to reevaluate the REMS, or the rules for who can take a drug, and give a recommendation on if they should



The FDA held an Advisory Committee Meeting to discuss the safety of Avandia; however, panelists also brought up issues with the FDA's drug approval process.

be relaxed. The 26-member panel discussed the Duke Clinical Research Institute's (DCRI) analysis of the data from GSK's Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycemia in Diabetes (RECORD) trial, a study that looked at the risk of heart disease related to taking Avandia. Their final vote reflected the huge diversity of opinions surrounding this topic. Half of the panel voted to loosen the existing REMS, seven voted to remove the REMS entirely, five voted to keep the REMS as currently written, and one person voted to withdraw Avandia from the market completely. The FDA will now make the final decision on how Avandia usage should be regulated moving forward.

As a reminder, Avandia was an extremely popular medication for type 2 diabetes until 2007, when a provocative study linked the drug with a 40% increased risk of heart attack. In 2009, GSK held the RECORD trial, which studied Avandia's link to cardiovascular risk. The results showed that Avandia does not increase the risk. However, the FDA did not believe the results were completely reliable and recommended that GSK choose an independent body to reevaluate RECORD's data. While the DCRI investigated the RECORD trial's data, the FDA applied a REMS for Avandia, restricting who could be prescribed the drug.

It's not entirely clear why this meeting was held now, as GSK's patent on Avandia expired in 2011 and only about 3,000 people still use the drug. Possibly, the reason was to justify the FDA's previous actions. There will likely be few practical changes for Avandia as a result of this meeting, but it does reaffirm that Avandia can still be useful to a small subset of people with type 2 diabetes.

Since the drug's future isn't in question, the panelists had a rare opportunity to discuss past mistakes in clinical trial design and the FDA's overarching approach to cardiovascular safety issues. Indeed, the RECORD trial's unclear results prompted the FDA to create its 2008 cardiovascular safety guidelines for diabetes drugs, requiring companies to show in a large, expensive separate trial that antihyperglycemic drugs are safe for the heart. Since most panelists now believe that Avandia is safer than previously thought, the question is if the FDA should reassess those guidelines.

These are major issues that require expert discussion but most of the meeting was squarely on Avandia's safety profile, so this discussion is very much in its infancy. We are optimistic that this advisory panel meeting will eventually spark the debate that these cardiovascular safety issues deserve.—AW/MN/JD



T2

Merck and Pfizer Enter an Agreement to Develop an SGLT-2 Inhibitor, Ertugliflozin

On April 29, Merck and Pfizer announced that they are entering a partnership to develop ertugliflozin for type 2 diabetes. Ertugliflozin is a sodium-glucose linked transporter-2 (SGLT-2) inhibitor that comes in a once-daily pill. Originally, Pfizer was developing and testing ertugliflozin as a drug to be taken alone. However, this partnership will allow the companies to also develop ertugliflozin combination pills: ertugliflozin plus Merck's DPP-4 inhibitor Januvia (sitagliptin) and ertugliflozin plus Januvia and metformin. These combinations should make taking medication much easier, since they will reduce the number of pills from two or three to one.

Currently, ertugliflozin has finished its phase 2 trials and is ready to begin phase 3 trials. In phase 2, ertugliflozin reduced A1c by an average of 0.8%, weight by 5.5 pounds, and blood pressure by about 4 mmHg. As we've noted in previous articles on SGLT-2 inhibitors, the drugs also work in a glycaemic-dependent fashion, meaning there is a very low risk of hypoglycemia. Since ertugliflozin is still in development, safety data is still pending

from larger phase 3 studies. We'll be especially interested to see the risk of genital infections, a common side effect of other drugs in this class. Please see our learning curve on SGLT-2 inhibitors to learn more.

As a reminder, the FDA approved Janssen's Invokana (canagliflozin) at the end of March. Invokana is the first drug in the SGLT-2 inhibitor class, though others, such as ertugliflozin and Lilly and Boehringer Ingelheim's empagliflozin, which was recently submitted to the FDA, may soon join Invokana. Forxiga is available in the EU, and Bristol-Meyers Squibb and AstraZeneca plan to reapply for FDA approval in mid-2013. Additionally, Lexicon is developing an SGLT-1/SGLT-2 inhibitor for type 1 diabetes, LX4211.—MN



T1 Lexicon Releases Initial Results on SGLT-1/SGLT-2 Inhibitor for Type 1 Diabetes

In May, Lexicon announced its results of LX4211, an SGLT-1/SGLT-2 inhibitor. The phase 2 trial finished its open-label, pioneer section, which showed a decrease in hypoglycemia and A1c. These positive results came from a very small group (three people were enrolled in the trial) and are mostly suggestive of potential effects; however, they allow researchers to expand the trial. Unlike many other antihyperglycemic drugs in development, Lexicon is exploring FDA approval for LX4211 for type 1 diabetes first.

LX4211 is a different sodium glucose linked transporter (SGLT) inhibitor than other drugs that are available or being developed. The drug inhibits both SGLT-1 and SGLT-2, while most other SGLT-inhibitors only inhibit SGLT-2. SGLT-1 is located mostly in the gastrointestinal tract and SGLT-2 is mostly in the kidney. Both transporters bring glucose back to bloodstream from the GI tract and kidneys, respectively (to read more on SGLT-2 inhibitors, see our learning curve from *diaTribe* #51). LX4211 lowers blood sugar by preventing both of these proteins from working.

Inhibiting SGLT-1 could lower after meal blood glucose rises, similar to a GLP-1 agonist (such as Bydureon, Byetta, or Victoza). Since LX4211 can blunt the post-meal spike, there is potential for the drug to replace bolusing before meals, though the drug needs to be studied in a larger population before this becomes clear. Additionally, an SGLT-1 inhibitor could eliminate more glucose through the GI tract and less through the kidneys, which would allow patients with kidney impairment to take the drug too. We are very interested in LX4211 and will continue to follow its development.—MN

Unlike many other antihyperglycemic drugs in development, Lexicon is exploring FDA approval for LX4211 for type 1 diabetes first.



Glooko's updated system organizes diabetes management data and displays them with graphs and statistics.

T1/2 Glooko Releases Updated Glucose Management System and iPhone Application

On June 10, Glooko released an updated version of its smartphone-based diabetes management system. As a reminder, Glooko simplifies meter downloading through the use of a universal MeterSync Cable (\$39.95 on Amazon) – notably, the cable can upload data from 19 different blood glucose meters (ACCU-CHECK, Bayer, Freestyle, GLUCOCARD, i-SENS, OneTouch, and ReliOn) to an iPhone app. With this update, Glooko has notably added a web-based platform, allowing data from the mobile app to be viewed online. The app also has features such as graphs and statistics that makes it easier to observe when readings fall in and out of range and quickly compare current glucose averages to the prior week or month. Users can also input how much food they eat, how much exercise they do, and the medications they take. The data can be e-mailed or faxed as a PDF to healthcare providers (HCP) via a share button in the application, which we hope will facilitate better provider-patient communication and ideally help optimize therapy.

We are excited about Glooko's efforts to simplify data downloading, as it is a key area for improvement in glucose control. Ultimately, we hope to see companies go a bit farther and attempt to make glucose data more actionable for patients – for instance, through pattern recognition algorithms and smart analytics, an app could give treatment recommendations (e.g., “Your glucose is consistently high at 1:30 pm; you may want to take more insulin at lunch time”). Of course, once software goes down this road, the regulatory bar for approval rises significantly. Still, we are hopeful that the coming years will see an explosion in data management software. –AK/AB



ADA 2013 Preview: All the latest learning in CGM, insulin pumps, GLP-1, the cure for type 1, and more

The 73rd Scientific Sessions of the American Diabetes Association will be held from June 21-25 in Chicago. The five-day conference will feature hundreds of presentations, debates, discussions, and general sessions from the leading figures in diabetes research. The ADA Exhibit Hall will also welcome a whopping 175 companies to present their latest therapies and devices. Highlights of ADA this year include new data and discussion on continuous glucose monitoring, insulin pumps, bariatric surgery, type 1 diabetes cure efforts, and the results of University of Texas Health Science Center at San Antonio's Dr. Ralph DeFronzo's triple therapy study. The following is our preview of some of the major talks of the conference.

Dr. William Herman will discuss the cost-effectiveness of diabetes prevention – a major topic, considering diabetes cost the United States \$245 billion in 2012 alone and there's still no clear pathway to FDA approval for drugs targeting prediabetes.

An intriguing talk on Friday will come from the University of Michigan's Dr. William Herman, who will discuss the cost-effectiveness of diabetes prevention – a major topic, considering diabetes cost the United States \$245 billion in 2012 alone and there's still no clear pathway to FDA approval for drugs targeting prediabetes. Later that day, various research teams will present their latest work on the artificial pancreas – that includes Dr. Ed Damiano's bi-hormonal bionic pancreas, for which *diaTribe* Editor-in-Chief Kelly Close recently participated in a trial (see this month's test drive for more).

On Saturday, some of the most esteemed thinkers in the field of diabetes research will discuss the biggest topics in type 2 diabetes care. GLP-1 agonists will be a major topic as Dr. Ralph DeFronzo reveals the long-awaited result of his triple therapy study, which combines metformin, Amylin's once-weekly GLP-1 agonist Bydureon (exenatide), and Takeda's TZD Actos (pioglitazone).

On Sunday, a session will look at alternative insulin delivery mechanisms, including inhaled and oral insulin as well as patches and microneedles. Patch pumps – a big topic after the approval of Insulet's next-gen OmniPod and CeQur's PaQ – will also be discussed in a Tuesday session led by Dr. Howard Zisser of the Sansum Diabetes Research Institute.

In what promises to be one of the liveliest debates of ADA, a Monday session will see Tulane's Dr. Vivian Fonseca and Baylor's Dr. Alan Garber discuss whether insulins or GLP-1 agonists represent the next best therapy for people with type 2 diabetes who are not finding success with oral medications.

We at *diaTribe* are also pleased and honored to announce that Monday night will be the 7th Annual Close Concerns and Taking Control of Your Diabetes Soiree, in which *diaTribe* Editor-in-Chief Kelly Close will lead a discussion panel featuring six luminaries in diabetes research. Drs. John Buse, Bruce Buckingham, Jim Gavin, Bob Henry, Philip Home, and Virginia Valentine, CDE will all be one hand to offer their perspectives on ADA 2013 and all that lies ahead in the field. –AW



Only 33% of public schools have full-time nurses and 26% of schools do not have any licensed healthcare professional on staff.

T1/2

Safe At School: Who Can Administer Insulin in School?

On May 29, the American Diabetes Association (ADA) and the American Nurses Association (ANA) appeared before the California Supreme Court to argue whether designated unlicensed school personnel can administer insulin to students with diabetes. The ADA argued that unlicensed, but trained and designated school personnel can give insulin, while the ANA held that the law only allows licensed nurses to provide such care. The court's ruling on this matter will affect the 12,000-16,000 students in California public schools who have diabetes. Importantly, only 33% of public schools have full-time nurses and 26% of schools do not have any licensed healthcare professional on staff. When a nurse is unavailable and the student cannot self-administer insulin, parents or nurses from other schools must travel to the school and help the student. The court will decide the matter within 90 days after this hearing.

During oral arguments, the California Supreme Court Justices challenged Mr. Dennis Maio, who represented the ADA, by asking if an unlicensed person giving insulin intrudes on the responsibilities of a nurse. The ADA believes the Education Code permits unlicensed school staff to give insulin as long as three gatekeepers grant permission: the student's physician, parents, and the school district. The Justices also wondered if giving insulin required "substantial scientific knowledge and technical skill," the official language used to describe a nurse's duties. Mr. Maio countered that children self-administer insulin, and Justice Goodwin Liu brought up Supreme Court Justice Sonia Sotomayor, who gave herself injections when she was just a 7-year-old. Mr. Maio admitted that there are risks when a child takes insulin, but he also rightly pointed out there are risks when a child misses insulin if a nurse were unavailable.

Ms. Maureen Cones' presentation on behalf of the ANA argued that the case was about keeping students safe, and unlicensed individuals might cause harm. She asserted that administering medication is in the purview of a nurse and that the law does not allow anyone to engage in the practice of nursing without a license. The Justices questioned this interpretation and seemed to disagree with Ms. Cones. Most importantly, how can schools provide safe environments for students if 26% of them do not have a full- or part-time nurse? Ms. Cones held that federal law requires schools to provide for student health services, and budgetary issues cannot excuse using unlicensed staff to give medication.

For background, the ADA's Safe at School campaign advocates on behalf of students with diabetes for a medically safe environment and the same educational opportunities as other students. In 2005, the ADA filed a class action lawsuit against the California Department of Education for not providing appropriate diabetes care for students. That case was settled in 2007. As a result, the state issued an advisory that told school districts that school staff could be trained to give insulin if that was necessary to meet the needs of students under federal law and if nurses were unavailable. Four nursing organizations, including the ANA, challenged this advisory in a new lawsuit shortly after, and in 2008 the court sided with the nurses – the resulting decision meant only nurses were legally permitted to give insulin to students in schools. In 2010, the ADA appealed and lost, but a subsequent appeal has now brought the case to the California Supreme Court. –MN

T1

Online Sign-Up for TrialNet

TrialNet is bringing their services online, making it easier for people to be screened for type 1 diabetes. Family members of those with type 1 diabetes can answer an online survey at www.diabetestrialnet.org and, based on their responses, will

Family members of those with type 1 diabetes can answer an online survey at www.diabetestrialnet.org, and based on their responses they will receive a packet with testing materials.

receive a packet with testing materials. The family members can bring these testing materials to their local lab and have their blood drawn for the screening. If their results show antibodies that increase the risk for developing type 1 diabetes, the family members will be invited to participate in one of TrialNet's many prevention or cure studies. The online screen opens up access to people who have not been able to enroll in the past, either because they lived far from a screening center or because they could not attend a screening event.

If the test results show a risk of developing type 1 diabetes, TrialNet will monitor and continue to assess that risk. If positive for autoantibodies, research participants will be monitored annually (every 12 months) or semi-annually (every six months) depending on their risk level. TrialNet will follow changes in risk status by testing for autoantibodies, HbA1c, as well as performing oral glucose tolerance tests in those at higher risk having semi-annual visits.

For background, TrialNet is a large screening program that aims to connect researchers with participants at risk for or who have type 1 diabetes. There are 18 clinical research centers in the US, Canada, Finland, UK, Italy, Germany, Australia, and New Zealand. The researchers study methods to prevent, delay, and cure type 1 diabetes. Researchers from TrialNet are currently studying oral insulin to prevent type 1 diabetes and anti-CD3 medication to stop or slow the destruction of beta cells, among other potential cure therapies. For more on these therapies, please see our book, *Targeting a Cure for Type 1 Diabetes: How Long Will We Have to Wait?*—MN

T1/2

Samepage Health's VisitPrep Helps Organize Visits to Healthcare Providers

Samepage Health launched VisitPrep, a tool that helps patients organize their medical questions before going to their healthcare provider (HCP). The tool asks for the issues that patients want to discuss, what type of care they would like from the provider, and how they want to receive the information. After the information is filled in, the form can be printed out and brought to a visit. The tool quickly allows users to tell the HCP exactly how to tailor a visit to their needs, whether that's a diagnosis, methods to reduce stress, assistance with refilling a prescription, or something else.

Visits to an HCP can be stressful, and having goals for the visit can help ensure that questions are answered and that the visit is productive. We recommend downloading our *diaTribe* patient's guide to individualizing therapy (www.diaTribe.org/patientguide), which contains five key questions to ask your healthcare provider at a visit (you can also read about how lists have been helpful for Kerri in sum musings from *diaTribe* #52). As many would expect, previous studies have shown that lists can help keep appointments on point and reduce anxiety before and during the visit, and VisitPrep is one tool that can help.—MN

T1/2

Take 371 Million Steps for Diabetes

The International Diabetes Federation (IDF) is holding the Take a Step for Diabetes campaign to increase awareness for diabetes. This "step" can be a variety of actions, all of which are designed to help others learn about diabetes or improve physical fitness. IDF's goal is to reach 371 million steps by the World Diabetes Congress in Melbourne, Australia on December 2-6. Each of those steps represents one of the estimated 371 million people living with diabetes in the world.



The activities can be done individually or in groups, and the steps can be small (e.g., wearing blue for diabetes or committing to exercise more often) or grow into larger events (e.g., holding a flash mob in your community or lighting a building blue). Each step counts for a number of points, and you can track points when you register on the IDF's site. Remember to take a picture or record a video (we're really getting into Vine!) so that you can share your efforts with the global diabetes community. —MN/AB

test drive

T1 The Bionic Pancreas

by Kelly Close



Dr. Edward Damiano and Dr. Steven Russell's bionic pancreas using the iPhone.

I'm now exactly eleven days out of the five-day Boston University/Massachusetts General Hospital bionic pancreas' trial that I took part in. I can't quite talk about it too directly, without my eyes starting to fill up. So dramatic, I know! But I feel forever changed, having been part of this research study, and now knowing (albeit only for a week) what "normal" life was like before diabetes – not having to carb count, not experiencing *any* hypoglycemia, not feeling tired all the time, and not having diabetes on my mind every five minutes. In short, I felt like a whole new Kelly. You can see some of the pictures and videos I took on our *diaTribe* twitter at twitter.com/diaTribenews.

What is this study exactly? Well, Dr. Edward Damiano (the engineering genius from BU), Dr. Steven Russell (a star endocrinologist at MGH), and a slew of colleagues have built a system over the last decade to make life with type 1 diabetes much easier. The system uses an iPhone running a control algorithm, two Tandem t:slim insulin pumps (dosing insulin and glucagon), and a Dexcom G4 continuous glucose monitor (CGM). This bionic pancreas (also called an "artificial pancreas" or "closed loop") takes glucose data from the Dexcom CGM and runs it through a control algorithm on the iPhone. The algorithm then processes the data and automatically directs insulin and glucagon dosing – in a word, magical. This dosing happens every five minutes, so the system automatically makes very small adjustments to keep glucose in range. The bionic pancreas only needs your weight to start up, and the algorithm adapts and learns over time from its performance – in other words, if I become very insulin resistant for a few days (e.g., little sleep, stress, etc.), it will robustly adapt and increase the amount of insulin it gives. How cool is that!

What was also so impressive about Drs. Damiano and Russell's study was how very real-world it was. Unlike most past studies that confined bionic pancreas research participants to a hospital bed, I was able to roam around a three-square mile area of Boston. I could eat what I wanted, exercise as I wanted, and sleep by myself in a hotel room. Just in case anyone was ever close to danger, the study had three teams of nurses following me to ensure I stayed safe, even to the point where I wore an IV at night and they followed my minute-to-minute blood glucose readings on a screen next door. Big picture, it was fantastic to see what wearing a bionic pancreas would be like in a daily life setting. The study's goal is to assess the safety and effectiveness of the bionic pancreas, so its performance was compared to five days of my own "standard" care without the bionic pancreas.

I knew it would be cool to be part of the trial. I'm one of about 30 participants who get to take part in it, one of the first closed-loop trials in the world to take place outside the hospital setting. I love new technology, I love clinical trials, and I love the hope that accompanies early-stage research.

Unlike most past studies that confined bionic pancreas research participants to a hospital bed, I was able to roam around a three-square mile area of Boston.



On the back of the iPhone is the Dexcom G4 Platinum CGM, which helps track blood glucose levels. The numbers are fed into the system's algorithm and determine insulin and glucagon dosing.

What was very key was how the system brought me back down from these highs – super safely and far more quickly than I could regularly ever do.

So when they told me that I might be quite depressed when I had to give back the bionic pancreas (a little box that the research team kept calling “your pancreas,” as in “Oh, don’t forget your pancreas!”, “Don’t drop your pancreas...”, etc.) I felt “Oh right! Come on. This is so exciting being part of this trial. How could I ever be depressed!”

How, indeed.

So what was it like to have a machine making all these decisions for me? Well...

- I was never hypoglycemic
- I never felt hypoglycemic
- I was never worrying about hypoglycemia
- I was never recovering from hypoglycemia

That’s already enough of a game changer for me. But there was more...

- If I started veering low, my bionic pancreas figured it out and gave me the perfect amount of glucagon to make sure that hypoglycemia didn’t occur
- I always felt safe during the week – at no time did I feel threatened or scared
- My glucoses were being watched and stayed perfectly in range overnight, every night. Wow.
- I counted zero carbs
- I never “corrected”
- I never thought about insulin sensitivity and how I couldn’t figure that out
- I never thought about insulin to carb ratios
- I never bolused
- I was a nicer and kinder person the entire week with the bionic pancreas

Because the system uses both insulin and glucagon, I got to see mini doses of glucagon in action for the first time. There’s no question about it – glucagon is a cool hormone. It is ten times better than orange juice, glucose tabs, candy, gel, etc. It is SO precise and the power of having just the right amount was really cool. It was magic!

Don’t get me wrong – the system still doesn’t match how great a pancreas is in someone without diabetes. The bionic pancreas must still deal with the 60-90 minute delays in rapid-acting insulin absorption. That means that my blood sugar did exceed 200 mg/dl after big meals. (An analogy to think about this is steering a car – if it took the car 60-90 minutes to respond to movements of the steering wheel, you would inevitably run off the road sometimes.) What was very key was how the system brought me back down from these highs – super safely and far more quickly than I could regularly ever do. I went from a high over 200 mg/dl to a safe, soft landing right in range. Usually when I stare at a number over 200 mg/dl, I take too much insulin (a “rage bolus” as Kerri Sparling would say), go low, eat too much, go high, and ride a roller coaster of highs and low all day.

During the trial, I also had a striking epiphany about living with diabetes: “Oh my gosh, I waste *so much time* having diabetes!” Being distracted because of a low, doing all these things to make sure I’m staying in range, and the super big time-leech, hyperglycemia.



The bionic pancreas gave small doses of insulin and glucagon throughout the day in order to keep the blood glucose level stable.

Getting rid of hypoglycemia and hyperglycemia for a week was one of the most powerful things I've ever experienced.

Whew! I felt like my whole world changed when I was constantly in a state of *normoglycemia*. And then I wondered how much I try to be “normal” and make it “seem” like diabetes is easy to manage – that mentality is also probably exhausting, even though I’m not even aware of it.

My bionic pancreas never failed me. I felt like the 17 year-old, completely carefree Kelly I used to know back before I was diagnosed. Getting rid of hypoglycemia and hyperglycemia for a week was one of the most powerful things I’ve ever experienced. I already like myself but with the bionic pancreas, I felt even better in my own two shoes. And in turn – this experience gave me renewed hope for what I used to say might be possible and what I know today absolutely is possible.

The fine print: There are a lot of things that have to go well in order for this to be commercially available by 2017. That is the year that Dr. Damiano’s son will go to college and the year that Dr. Damiano hopes to see a commercial system approved by the FDA. Here’s what has to happen:

- The rest of the current trial has to go well so that the researchers can move onto the next phase – testing the system at diabetes camps this summer (they will be followed by one nurse per four kids).
- After that, Drs. Damiano and Russell’s team will test the bionic pancreas in healthcare providers who have diabetes themselves. The two-week study will be more ambitious, as the participants will sleep in their own homes and go to work as they normally would. (This is pretty smart right – they still have healthcare providers around, to ensure safety, but they are themselves!)
- If all goes well, the research group plans to conduct pivotal studies, at least one of which will last six-months, that will test the final version of the system in 2015 and 2016.
- For these longer-term trials, a new pump will need to be built and approved that can carry both insulin and glucagon. Tandem Diabetes Care is currently working on developing such a pump (see our new now next on this news).
- A stabilized liquid glucagon must be developed that can last for a few days in a pump. In this study, the researchers used the current glucagon “kit,” which requires mixing glucagon powder with water. Unfortunately, it had to be replaced every day in the glucagon t:slim pump I was wearing. While this was acceptable in a research setting, it’s not a viable real-world solution because it is too expensive (it’s also a pain, though I would do it in a heartbeat). We believe that this is the biggest obstacle to overcome in the next few years. Fortunately, companies such as Xeris Pharmaceuticals, Bidel, and others are working hard on addressing this problem. The timeline will be tight to make the goal, though I’m optimistic.
- Before it can be sold, the FDA has to approve the bionic pancreas – certainly no easy task considering the ongoing three-plus-year delay in approving Medtronic’s MiniMed 530G. Known as the Veo outside the US, this is the most basic version of an automated insulin delivery system – it suspends insulin delivery for up to two hours when the CGM crosses a low threshold and the user does not respond to an alarm. We understand that Dr. Damiano and colleagues’ interactions with the FDA have been quite constructive, so we are hopeful here as well, though it

may be a complex journey. Indeed, given last year’s artificial pancreas guidance from the FDA, there does seem to be a clear approval path forward. (For more on that topic, see the learning curve in *diaTribe* #39.)

I had been warned that I wouldn’t want to give my bionic pancreas back to the researchers at the end of my five days with it. They said I might become depressed. I laughed – who could possibly become depressed after being so lucky to be chosen for this trial?

Well, they were right – I definitely *did not want* to give it back. And I certainly miss it.

(For more background on the artificial pancreas, please see the conference pearls in *diaTribe* #53 and *diaTribe* #54.)

¹ *The BU/MGH team believes the term “bionic pancreas” is more descriptive than “artificial pancreas” – 1) “bionic” literally means “Having anatomical structures or physiological processes that are replaced or enhanced by electronic or mechanical components,” which describes exactly what the system is trying to do; and 2) the term “artificial” lacks specificity, as it only describes what the system is NOT. Going into the trial, I wondered if this was semantics but coming out of it, I absolutely felt I had a bionic pancreas rather than an artificial one.*

thinking like a pancreas

INDIVIDUALIZATION is where it’s at: customizing whatever it is to best meet your particular needs.



Treating Hypos: One-Size Does NOT Fit All!

by Gary Scheiner MS, CDE



Imagine if there were only one car on the market. Or one type of breakfast cereal. Or (heaven forbid!) one type of insulin pump. Would you feel a little bit cheated? You should. INDIVIDUALIZATION is where it’s at: customizing whatever it is to best meet your particular needs.

In the diabetes field, healthcare providers and product marketers have been trying for years to stuff a one-size-fits-all approach down our throats when it comes to treating hypoglycemia, using 15 as the magic number. It doesn’t matter who you are, what you’re doing, or how low you are. Fifteen grams of carbohydrate is the magical elixir.

For those of us dealing with hypoglycemia on a regular basis, we understand that this is just plain wrong. Every person is unique, and every situation has its own unique characteristics. And we’re not talking about something superficial here like the body side moldings on a car. We’re talking about dealing with a true medical emergency. Undertreatment of hypoglycemia can result in a seizure, loss of consciousness, or much worse. Overtreatment can produce significantly high blood sugar levels for many hours.

In preparing to treat hypoglycemia (and this is something you should think about now, not when you’re low and can’t think too clearly), consider the following:

1. Body Size

The bigger you are, the more carbohydrates it takes to raise the blood sugar. This is because bigger people have more blood volume into which the glucose will dissolve. Every

Every person is unique, and every situation has its own unique characteristics.

gram of carbohydrate will raise a small child's blood sugar much more than that of a fully-grown adult. The chart below summarizes the amount that each gram of carbohydrate could be expected to raise a person's blood sugar based on their weight:

Weight in Pounds (kg)	One gram of carbohydrate raises blood glucose by...
<60 (>28)	6-10 mg/dl (.33-.55 mmol/l)
60-100 (29-47)	5 (.28)
101-160 (48-76)	4 (.22)
161-220 (77-105)	3 (.17)
>220 (>105)	1-2 (.05-.11)

2. How Low You Are

The lower your blood sugar, the more carbohydrates you will need to get back up to normal. The table below provides a guide based on body size with a goal of raising the blood sugar to approximately 120 mg/dl (6.6 mmol/l). Another way to determine the amount needed for you specifically is with this formula: (Target BG – Current BG) / BG rise per gram of carbohydrate.

For example, if your target is 100 mg/dl, your current BG is 60 mg/dl and each gram of carbohydrate raises you 4 mg/dl, then you need $(100-60)/4$, or 10g of carbohydrate.

Blood Sugar (mg/dl) (mmol/l)	60s (3.3-3.9)	50s (2.8-3.2)	40s (2.2-2.7)	30s (1.7-2.1)	20s (1.1-1.6)
Weight: <60 lbs (28 kg)	9 g	11 g	13 g	15 g	17 g
60-100 lbs (29-47 kg)	11 g	13 g	15 g	17 g	19 g
101-160 lbs (48-76 kg)	14 g	16 g	19 g	21 g	24 g
161-220 lbs (77-105 kg)	18 g	22 g	25 g	28 g	32 g
>220 lbs (>105 kg)	28 g	33 g	38 g	43 g	48 g

Editor's Note: These numbers should be used as a general guide, since the responses to hypoglycemia can vary based on many factors (e.g., amount of exercise, general level of carbohydrates in the diet, insulin resistance, etc). Unfortunately, it's difficult to study this in a very rigorous fashion and come up with evidence-based guidelines. As a result, we recommend that patients use a mix of these general principles and their own personal experience. If you have not ever done so, try a personal test of how many carbohydrates it takes to raise your blood sugar. Glucose tabs work well for this, since they are typically either four or five grams of carbohydrate each.

If your blood sugar is low and still dropping quickly, you will need more carbs than the “standard” amount. If your blood sugar is low and leveling off, the standard amount should work fine.

3. The Rate of Change

This is easily seen on a continuous glucose monitor. If your blood sugar is low and still dropping quickly, you will need more carbohydrates than the “standard” amount. If your blood sugar is low and leveling off, the standard amount should work fine.

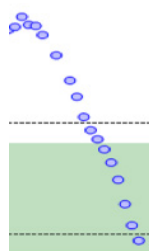


Figure 1. BG low and accelerating downward – consume extra carbohydrate

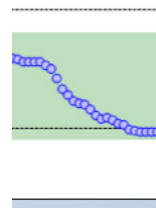


Figure 2. BG low but leveling off – consume “standard” amount of carbohydrate

4. The Sitchy-Ation

We all know that there are a million different variables when it comes to blood sugar management. As I often say, if it were simple, everyone would want it. A few other variables to consider when treating low blood sugar:

- **Insulin-On-Board (IOB)** – The more rapid-acting insulin you still have working in your body when a low occurs, the more carbohydrates it will take to treat the low. For lows that occur within a couple of hours of a mealtime bolus, extra carbohydrates will probably be needed. For lows that occur more than four hours after administering rapid-acting insulin, the standard treatment should work fine.
- **Muscle Activity** – If you plan to exercise soon after treating the low, or if you are coming off a bout of intense exercise, extra carbohydrates will be needed. Your muscles will be gobbling up glucose to replenish their energy (glycogen) stores, and that glucose will be drawn right out of the bloodstream.
- **Food-On-Board** – In the past couple of hours, if you had a meal or snack that consisted of mostly low-glycemic-index foods (such as legumes, dairy products, pasta, salad veggies, or had a great deal of fat along with the carbohydrates), there is a very good chance that some of the meal is still digesting. That doesn't mean that you should ignore the low blood sugar, but the treatment can be less aggressive than the usual amount.

So forget the “rule of 15”. Unless, of course, you weigh 180 lbs (86 kg), your blood sugar is 65 mg/dl (3.6 mmol/l), your target is 110 mg/dl (6.1 mmol/l), you aren't still dropping rapidly, you didn't just exercise, you have no insulin on board, and you haven't eaten for quite a while. Then it should work to a “T”.

Editor's note: Gary Scheiner MS, CDE is Owner and Clinical Director of Integrated Diabetes Services (www.integrateddiabetes.com), a consulting practice located near Philadelphia for people with diabetes who utilize intensive insulin therapy. He is the author of several books, including Think Like A Pancreas: A Practical Guide to Managing Diabetes With Insulin. He and his team of Certified Diabetes Educators work with children and adults throughout the world via phone and the internet. Gary has had Type-1 diabetes for 27 years and gone through a small mountain of DexTabs in that time. He can be reached at gary@integrateddiabetes.com.

sum musings

I'm prepared for the Big Three at all times: low blood sugar, high blood sugar, and pump failure.

To be blunt: guessing got me nowhere, and I needed the cold, hard numerical facts when calculating my insulin doses.

T1/2 Five Lessons from Diabetes

by Kerri Sparling



What I wanted to do most with this article was provide a list of tips for keeping diabetes well controlled and essentially boxed up, never causing a glitch of any kind. But I was at a loss, since the learning curve of diabetes is lifelong, and I'm still a long way from having anything "figured out." (Also, I couldn't find a box big enough.) I have found some "tricks of the trade" over the last twenty-six years with type 1 diabetes that are worth sharing, and they've played a part in keeping me healthy, happy, and moving forward. Maybe they'll help you? Or perhaps jump-start a little "Hey, this works for me!" list of your own?

Here's some of what I've learned:

Plan for the worst, hope for the best. Living with diabetes encourages a packrat mentality, in that your bag, glove compartment, or desk at work is crammed with "just in case" supplies of a wide variety. Life with a pancreas that decided to go rogue all of a sudden will do that to you, I suppose. Personally, I'm prepared for the Big Three at all times: low blood sugar, high blood sugar, and pump failure. My purse contains glucose tabs, an insulin pen, a spare infusion set, and a pump battery, with all of these items in my glove compartment. Some of my fellow PWDs (person with diabetes) think I'm over-doing it... until their pump battery needs to be replaced on the fly, or they need a quick glucose tab. Then I don't seem so crazy. Diabetes chaos can be a little scary, and I like to be best prepared for moments that jump out, even if it means packing heavy for short trips.

Always test before taking insulin. Having lived with type 1 diabetes for over 20 years, I've come to really appreciate and have a healthy fear of the power of insulin. I know how quickly it can make my blood sugar drop, and I've had my share of hypoglycemic episodes that left me feeling vulnerable and uneasy. One thing I've definitely learned is that I need to know what my blood sugar numbers are before dosing any insulin. For a while, I thought that I could guess my blood sugar by "how I felt," but I was quick to realize this was a crummy approach, and I needed more than just "a feeling" to help me make a dosing decision. (Because sometimes those "feelings" can be tied to entirely different issues, like exhaustion being mistaken for a high, or hunger as a low.) Knowing my numbers gives me more power to act precisely in response, or in projected anticipation, when it comes to making decisions about my insulin. To be blunt: guessing got me nowhere, and I needed the cold, hard numerical facts when calculating my insulin doses.

Seek support when you need it. You don't have to do this whole diabetes thing alone. You don't. Ask for help when you feel overwhelmed emotionally. An unsettled emotional state makes tending to the day-to-day needs of diabetes harder, and you deserve to give your health the best chance you can manage. If you feel depressed, or discouraged, ask your friends and family for help. If you need assistance making sense of blood sugar numbers or talking through the pros and cons of different management options, lean on your medical team. And seek out the information you need when you need it. And know that you aren't alone. Diabetes can feel isolating, and overwhelming at times, and the support of your local community, the online community, and your well-educated medical team can make a huge difference in how you handle your disease.

You know what works and your body best: empower yourself with that knowledge and follow the management path that earns you the best results. Take control!

Exercise. Can I add an exclamation point to that? Exercise! I'm not an elite athlete, and I won't ever be known for my grace or athleticism, but I am not lazy. Even though I'm not the fastest runner or the swimmer with the best form, I make a point to move my body, and my health thanks me for it. (Even when my legs sometimes don't and would rather lounge on the couch.) Rough day of blood sugars? I'm revived by a workout. Plagued by a stubborn high blood sugar? A nice, long walk goes a long way in helping me even things out. And the weight that seems to pile on with more ease as I age? Exercise helps keep it controlled. It's good for my blood sugars. It's good for my muscles. It's good for my weight. It's good for me. Please – when you make a list of important diabetes tips of your own, add exercise to it.

Don't let yourself be bullied. Diabetes management varies from person to person, and from community to community. There is not a “set way” to best deal with diabetes, and you need to do what works for you as far as diet, medication, and all the other health-related bits that require juggling. But there are people – fellow PWDs, medical professionals, sometimes strangers you talk to on the subway – who want to weigh in on your management decisions. And everyone's results vary. If you are taking your insulin by pen or syringe, are satisfied with the results, and don't have any desire to use an insulin pump, then why should you switch? Are you content to prick the pads of your fingers instead of the outside edge? Keep doing what you're doing if that's what keeps you checking your blood sugar. Are you happy with your current diet, and is it yielding good results? Then don't let yourself be pressured to switch to a Paleo diet, or a gluten-free one, or a low-carb, or a high-protein, or a mostly-air-and-sometimes-a-peanut diet. Don't let a member of your medical team make you feel like you don't have the right to ask questions and get answers. Don't let a family member make you feel judged for the food on your plate.

And you know what? Make a point not to bully yourself – so long as you are doing your best, continuing to try, and constantly learning, you're making progress towards the best health possible. You know what works and your body best: empower yourself with that knowledge and follow the management path that earns you the best results. Take control!

Kerri Morrone Sparling has been living with type 1 diabetes for over 25 years. She writes a much-trafficked diabetes blog, Six Until Me (SUM), and is an active member of the diabetes community. She is known for her tagline, “Diabetes doesn't define me, but it helps explain me.” Dexcom is currently a sponsor of SUM, and through that relationship, the company provides her Dexcom sensors free of charge. For Kerri's full disclosure, please visit <http://sixuntilme.com/about/2010/03/disclosure.html>.

conference pearls



T1/2 The Annual Congress of the American Association for Clinical Endocrinologists (AACE) and the European Congress on Obesity 2013

by Margaret Nguyen

We attended many conferences in the past two months and have been blown away by the work researchers are doing to better understand and treat diabetes and obesity. Often, the talks centered on novel molecules or techniques to care for both conditions better, but there were also sessions on the practical day-to-day management of diabetes. The following are the lessons we've learned from the best thinkers in the field.

About 30-40% of endocrinologists and 80% of internists do not download pump data.

1. Downloading Data is a Key Part of Diabetes Care

During his talk at the Annual Congress of the American Association of Clinical Endocrinologists in sunny Phoenix, Arizona, Dr. Bruce Bode (Atlanta Diabetes Associates, Atlanta, GA) emphasized the critical importance of downloading insulin pump data. Unfortunately, he stated that about 30-40% of endocrinologists and 80% of internists do not download pump data (for patients, we have heard estimates that around 90% do not regularly download data). Dr. Irl Hirsch (University of Washington, Seattle, WA) also urged providers in the audience to download diabetes data. He credited the lack of insurance reimbursement and limited time as the reason why more providers do not work with the data from blood glucose monitors, pumps, and continuous glucose monitors (CGM). However, Dr. Hirsch also noted that he did not understand how it is possible to make treatment recommendations without data.

Once data is downloaded, Dr. Bode said there are two red flags that usually get his attention and cause him to change insulin doses. First, when a patient's blood glucose average minus the standard deviation (a calculation that measures the fluctuation between blood glucose measurements) is less than 75 mg/dl, it suggests that there is a lot of glycemic variability. Some researchers believe that large fluctuations in blood sugar can cause oxidative stress and contribute to long-term complications like blood vessel damage; however, this is still an ongoing debate in the academic community, and the effects of glycemic variability need to be further studied. Second, Dr. Bode often makes changes if bolus insulin accounts for less than 50% of the total daily insulin dose – in his view, these patients often have a higher likelihood of hypoglycemia.

To guide therapy adjustments, Dr. Hirsch recommends that the blood glucose standard deviation should ideally be no more than a third of the mean blood glucose, though less than half of the mean is still acceptable (e.g., for an average blood glucose of 100 mg/dl, a standard deviation less than 33 mg/dl is ideal, though less than 50 mg/dl is acceptable). Dr. Hirsch acknowledged a standard deviation less than one third of the mean is often very difficult for people with type 1 diabetes; those who are able to achieve this goal might be making some of their own insulin.

Dr. Hirsch also advised that patients do best when they override their bolus calculator 20-25% of the time.

Dr. Hirsch also advised that patients do best when they override their bolus calculator 20-25% of the time. Overriding the bolus calculator means that users are adjusting for things in real-time, such as blood glucose trends or anticipated exercise. In his view, adjusting over 30% of the calculations often means one of the bolus calculator's settings is incorrect.

Should a Meal's Fat Content Affect How Much Insulin to Dose?

During the European Congress on Obesity in Liverpool, UK, researchers discussed Dr. Howard Wolpert's paper on the impact of dietary fat on blood sugar (Wolpert et al., *Diabetes Care*, April 2013). The participants were put on a closed-loop system and monitored for 18 hours after eating. While on the closed-loop system, they ate two meals – both had the same carbohydrate and protein content, but had different amounts of fat. When the participants had more fat in their meals, they needed more insulin (as measured by the closed-loop system's insulin dosing) and had higher blood sugars.

The question is how much insulin should be taken? Dr. Hirsch said that there is often no way to know how to do this accurately every time, as the blood glucose change due to a meal's fat and carbohydrate content is different for every meal. Dr. Bode discussed one way he knew to take account of fat content for insulin dosing: with a high-fat meal, add

Dr. Bode and Dr. Hirsch asserted that a CGM is the best tool available to figure out if the right amount of insulin is taken.

20-30% more insulin and give the insulin dose as a dual wave bolus (a combination of a normal bolus and an extended bolus over several hours). Dr. Hirsch's rule of thumb was to add 10-20% more insulin for meals with a lot of protein or fat.

On the other hand, Dr. Hirsch commented that it is already difficult to calculate how much insulin is needed from carb counting alone – adding other layers of calculations might not be that helpful. In any case, both physicians asserted that a CGM is the best tool available to figure out if the right amount of insulin is taken. Additionally, Dr. Hirsch expressed optimism for upcoming technologies like Medtronic's MiniMed 530G (a low-glucose-suspend insulin pump currently under FDA review) and eventually, the artificial pancreas.

Continuous Glucose Monitoring and Healthcare Coverage

In a panel discussion, Drs. Bode and Hirsch also highlighted the benefits of using a CGM. Indeed, Dr. Bode stated that many patients who use both a pump and a CGM often give up the pump before they give up the sensor.

Despite its value, it was somewhat discouraging to hear that reimbursement for CGM is still insufficient, or even unavailable, for many patients. For example, Medicare does not cover personal use of CGM, which makes this potentially life-saving technology (i.e., detecting and preventing hypoglycemia) quite expensive for older individuals with diabetes. To emphasize the important role CGM can play in this population, Dr. Hirsch cited T1D Exchange data: 12% of those who have had diabetes for over 40 years and are older than 50 years have experienced having a seizure or being in a coma from hypoglycemia. There are some cases of Medicare covering a CGM, but both Drs. Bode and Hirsch said that it took dedicated patients who wrote letters, called, and demanded that they get coverage for a CGM. Certainly, there are no guarantees, but persistence might currently be the only option. Dr. Hirsch advocated for a CGM trial with Medicare patients to demonstrate the technology's benefits on hypoglycemia. Encouragingly, the American Diabetes Association and Lilly announced a partnership on June 4 to better understand diabetes care in older adults. We hope some of the research efforts include studies on CGM in this population.

12% of those who have had diabetes for over 40 years and are older than 50 years have experienced having a seizure or being in a coma from hypoglycemia.

European Congress on Obesity 2013 – The Mediterranean Diet

At the European Congress on Obesity in Liverpool, UK, we appreciated hearing Dr. Miguel Ángel Martínez-González (University of Navarra, Pamplona, Spain) speak on his landmark study about the Mediterranean diet, PREDIMED (PREvención con DIeta MEDiterránea). The investigation, in which he was the senior author, was recently published in the prestigious *New England Journal of Medicine* (Estruch et al., NEJM, April 2013).

The study found that a Mediterranean diet reduced the risk of heart disease by 30% in people with a high risk for the disease. This type of diet consists of mainly plant-based foods (e.g., fruits, vegetables, whole grains, legumes, and nuts), healthy fats (e.g., virgin olive oil, nuts, and seeds), fish and poultry. The PREDIMED study had nearly 7,500 participants ranging from 55 to 80 years old. They had either type 2 diabetes or three or more metabolic syndrome risk factors (e.g. hypertension, elevated LDL cholesterol, low HDL cholesterol, etc.), but did not have heart disease. Dietitians counseled everyone in the study on what to eat through group sessions and educational materials like lists of appropriate foods to eat and weekly menus. The control group was advised to simply reduce their dietary fat, while two other groups ate a Mediterranean diet supplemented with either nuts or virgin olive oil. Different participants stayed in the trial for different years, but after an average of 4.8 years, those who were in either of the two Mediterranean diet groups fared better than those in the control group.

PREDIMED is the first randomized controlled trial in nutrition aimed to prevent cardiovascular disease. Oftentimes, lifestyle modifications, such as changing what people eat or how much exercise they do, are very difficult to sustain over long periods of time. However, participants in the study were able to maintain the Mediterranean diet for nearly five years! We hope that there will be more nutritional studies that investigate interventions with the potential to work well after the trials end.

trial watch

Can a new medication speed insulin absorption?

T1 **CONSISTENT 1: Metabolic and Safety Outcomes of Hylenex Recombinant (Hyaluronidase Human Injection) Preadministered at CSII Infusion Site in Subjects With Type 1 Diabetes (T1DM)**

ClinicalTrials.gov Identifier: NCT01848990

<http://clinicaltrials.gov/ct2/show/NCT01848990>

Halozyme's Hylenex is an enzyme that breaks down hyaluronan (a component in the skin and subcutaneous tissue), allowing injected medications to be absorbed more rapidly. This trial is testing the efficacy and safety of Hylenex when used with insulin pumps; patients will give Hylenex through their infusion set immediately after each new set is inserted (every 2-3 days). The expectation is that Hylenex will speed insulin absorption and make its absorption more consistent over the life of an infusion set (some data suggests insulin absorption is slower early on in an infusion set's life). There are four different trial arms, and participants are randomly placed into one of these groups. The trial lasts two years and will follow participants' changes in A1c, rates of hypoglycemia, average blood sugar, and other outcomes. We very much look forward to seeing the outcome of this study, as Hylenex could be one of the first new ultra-fast-acting insulin approaches that could come to market. (MannKind's Afrezza, an inhaled insulin, would be next to market if it is approved by the FDA. If all goes well, this could happen as soon as mid-2014.)

To enroll in the study, participants must be at least 18 years old and have had type 1 diabetes for at least 12 months. They must also have an A1c between 6.5 and 9.5%, and they need to be using an insulin pump and an infusion set with tubing that works with Hylenex, or be willing to switch to a compatible infusion set and tubing. Individuals with type 2 diabetes, with known or suspected allergy to any part of the drugs in the study, or those with a history of certain heart problems cannot enroll. The trial is taking place across 32 centers in CA, FL, GA, ID, IA, KS, KT, MD, MN, MT, NV, NC, OH, TN, TX, WA, and WI. To learn more about the trial please visit the ClinicalTrials.gov site. To enroll, please call (858) 794-8889. –MN

Will a new non-surgical procedure help better manage type 2 diabetes?

T2 **Safety and Efficacy of EndoBarrier in Subjects With Type 2 Diabetes Who Are Obese (ENDO)**

ClinicalTrials.gov Identifier: NCT01728116

<http://clinicaltrials.gov/ct2/show/study/NCT01728116>

EndoBarrier is a device being tested for reducing blood sugar and weight to treat type 2 diabetes that is not adequately controlled with medication. The device is a tube-shaped liner placed inside the small intestine (right after the stomach) through a non-surgical procedure. When the EndoBarrier is in place, it prevents the beginning section of the small intestine (the duodenum and the proximal jejunum) from absorbing nutrients. In this study, researchers will randomize subjects, with half receiving the EndoBarrier and

the other half a “sham” procedure (i.e., the same non-surgical procedure, but no device placed). Researchers will then follow participants’ changes in A1c, weight, and heart disease risk factors over the course of a year.

Participants in the study must be between the ages of 21 and 65, have type 2 diabetes with an A1c between 8% and 10%, and a BMI between 30 and 50 kg/m². They cannot have a diagnosis of type 1 diabetes, have a history of ketoacidosis, or have had previous gastrointestinal surgery. Please see ClinicalTrials.gov for the trial’s full criteria. The trial is currently taking place in AL, CO, GA, LA, MD, MT, NY, NC, and TX. If you are interested in learning more about the EndoBarrier or in enrolling in the study, please visit www.endobarriertrial.com or call 1-888-978-8399.—MN

How will a closed-loop system work in the hospital?

T1/2

Inpatient Closed-Loop Glucose Control

ClinicalTrials.gov Identifier: NCT01819844

<http://clinicaltrials.gov/ct2/show/NCT01819844>

A closed-loop system would potentially allow many people to manage their diabetes without having to constantly worry about hypoglycemia or hyperglycemia. Many trials are now investigating automated closed-loop control outside the hospital setting, though such an approach would also be helpful for patients in the hospital. Dr. Steven Russell (Massachusetts General Hospital, Boston, MA) and colleagues are testing that hypothesis with an Abbott FreeStyle Navigator CGM, the Symbiq insulin-dextrose infusion system, and a control algorithm that takes input from the CGM and doses insulin and dextrose automatically. Participants will wear the system for 12 hours and have their blood glucose levels recorded during that time period.

Dr. Russell and his research group are looking for participants with type 1 or type 2 diabetes. For those with type 1 diabetes, they are searching for those who take less than 1 unit of insulin per kilogram (kg) of body weight each day. For those with type 2 diabetes, participants should be taking a relatively high insulin daily dose (greater than 0.75 units of insulin per kg of body weight each day) in order to enroll. Participants must also be between 21-80 years old. The exclusion criteria are pregnancy, kidney insufficiency, cancer, and others listed on the ClinicalTrials.gov site. The study will take place at MGH in Boston. If you are interested, please contact Kerry Grennan, NP at kgrennan@partners.org.—MN

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