Closer Look

Diabetes Mine 2015 D-Data Exchange

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Executive Highlights

Greetings from Stanford University and Diabetes Mine's Fall 2015 D-Data Exchange. Today's intimate gathering brought together ~100 patient, industry, academic, and government attendees to discuss the state of diabetes data, patient-led do-it-yourself (DIY) innovation, interoperability, and new diabetes apps and devices. This is the kind of meeting where jokes about non-standardized date/time data formats are greeted with rousing laughter and characterized as "Death by a thousand paper cuts."

To sum it up in one phrase? "Things are moving really quickly," shared Tidepool CEO Howard Look with us during the concluding reception. Indeed, it has been a transformative year for diabetes data and connectivity, with major product launches from Dexcom (G5), Medtronic (MiniMed Connect), and Abbott (LibreLink), just to name a few. But what today made clear was the rapid pace of progress in the patient-led DIY community (OpenAPS, Nightscout), the continued serious demand for interoperability (see our own Adam's Brown slides from today here), the focus on better user experiences (iLet), and strong industry interest in partnering externally. See our top six highlights below.

1. Dr. Joyce Lee shared compelling evidence that Nightscout's crowdsourced movement has achieved an impressive trifecta - increasing CGM adoption, improving quality of life, AND reducing self-reported A1c (~0.7%-1.2%). While CGM adoption is still far lower than many believed it would be, it is certainly moving in the right direction.

2. Type 1 patient Chris Hannemann shared data from 83 days of his own OpenAPS artificial pancreas experience. Notably, 15 people around the world are now using the open source closed-loop system spearheaded by Dana Lewis (former Close Concerns summer associate - she's a powerhouse!) and Scott Leibrand.

3. Patient champion Dr. Stayce Beck gave a highly optimistic talk on the FDA's approach to regulating "Do-It-Yourself" (DIY) devices, underscoring the Agency's desire to promote innovation and speed the safe development of new diabetes management tools.

4. In a panel on interoperability, Dexcom's CTO Jorge Valdes thanked Nightscout developers for pushing Dexcom and the entire field faster on connectivity and remote monitoring.

5. Tidepool designer Sara Krugman shared the fascinating design process behind the iLet bionic pancreas' user interface, reframing her design school's motto, "Build, test, repeat," with "Feel, understand, make."

6. Companion Medical's CEO Sean Saint shared a few new design details and screenshots of the company's Bluetooth-enabled reusable insulin pen and bolus calculator app.

Top Six Highlights

1. Dr. Joyce Lee shared compelling evidence that Nightscout's crowdsourced movement has achieved an impressive trifecta - increasing CGM adoption, improving quality of life, AND reducing self-reported A1c (~0.7%-1.2%). The findings came from a recent University of Michigan-led survey of members of the CGM in the Cloud Facebook group (n=1,276), aiming to understand how this patient-driven movement has impacted real-world diabetes care. Dr. Lee's data on CGM adoption was especially fascinating: ~20% of CGM in the Cloud members started on CGM as a result of Nightscout and ~9% restarted CGM as a result of Nightscout. This provided some evidence that mobile technology can drive the adoption of CGM, and yet another reason for companies to embrace connectivity. Indeed, a further 6% of respondents actually switched to Dexcom CGM from another system just because of Nightscout. Practical

benefits that patients experienced were also discussed. A majority of patients (>85%) found the technology "extremely empowering," while across all age groups patients reported taking fewer blood sugar checks per day on Nightscout (though the latter may be confounded by new CGM users). Self-reported A1c also indicated that glycemic control improved meaningfully (0.7%-1.2%) pre- vs. post-Nightscout - -0.7% in 0-5 year olds (baseline 7.6%), -0.8% in 6-12 year olds (baseline: 7.5%), -1.1% in 13-17 year-olds (baseline: 8.1%), and a remarkable -1.2% in those 18+ years (baseline: 7.4%). Granted, the self-reported results are coming from a self-selected community, though this technology is clearly helping many parents and patients (see quotes below). More information is coming on hypoglycemia rates - that's the promise, of course, of automating insulin delivery - lower A1cs as well as less hypoglcyemia and less variability overall. Said Dr. Lee: "This movement has REALLY found life."

- **Dr. Lee underscored that the presence of commercial solutions is "not necessarily going to squelch" Nightscout.** She shared results indicating that >80% of current CGM in the Cloud members planned to stay with Nightscout - vs. switching to Dexcom Share - at the time of the survey. The findings speak to the community that Nightscout has created, the wider device compatibility and more glanceable displays on smartwatches, and to the overall message that Nightscout brings to the diabetes community: an empowering solution to help patients and caregivers monitor glucose with increased safety and more peace of mind. We wonder how the commercialization of the more convenient Dexcom G5 might change perceptions, since the survey was conducted prior to G5 hitting the market.
- **Dr. Joyce concluded her talk with a number of patient perspectives on Nightscout**:
    - *"You guys rock!!!!!! Without you, life would suck.... Unable to thank you all enough for what you have done keep up the great work, you have changed the lives of many... thank you from the bottom of my heart"*
    - *You guys are great!! I owe you many hours of sleep. You are the most amazing people the world has ever been graced with. I am forever indebted for what you have done. You all are heroes in our home and hearts.*
    - *"You are freaking fabulous and have changed my life for the much much better."*

2. Type 1 patient Chris Hannemann shared data from 83 days of his own OpenAPS artificial pancreas experience. Notably, 15 people around the world are now using the open source closed-loop system spearheaded by Dana Lewis and Scott Leibrand. Mr. Hannemann has seen a solid 13%-point improvement in daily time in range (up to 83% - that's really good, equivalent to under a 6% A1c) and a 15 mg/dl decrease in daily mean glucose (to 129 mg/dl) since starting the system - while those don't sound like dramatic improvements, his starting baseline on pump+CGM was very strong, and it equates to a 0.5% improvement in A1c from a low baseline, fewer highs and lows, and significantly improved overnight control. Indeed, he said he wakes up pretty much every morning at approximately 100 mg/dl, and his Dexcom Clarity output showed an incredibly narrow spread of values in the early morning hours. The OpenAPS hardware is not for the faint of heart, consisting of a Medtronic insulin pump, Dexcom CGM receiver, a raspberry pi device for running Linux OS, a CareLink USB stick to enable communication to the pump, and a battery pack. But, it's all about experimentation and understanding what is possible! OpenAPS is built upon the earlier #DIYPS technology that enables communication between diabetes devices and in-depth data analysis. The http://openaps.org/ website has much more information on the approach.

- **According to Mr. Hanneman, 15 people are currently using the system, each with slightly different iterations in hardware and software.** They have adapted it for remote viewing on various smartphones, desktops, and wearables, and are using data to further improve the technology and better understand their glucose trends. The software includes codes for monitoring BG values, predicting future values, and controlling pump commands and other actions. There is a focus on simplicity and understanding what the system is actually doing, and the developers have put a lot of safeguards in place.

- **Mr. Hannemann shared his belief that medical devices are "tools" and not "therapies," and the responsibility of manufacturers is to provide these "tools" to patients.** This brings up the interesting dichotomy of whether automated insulin delivery is a "tool" or a "therapy" - some would argue it is the latter, since it can be a fundamentally different way of experiencing diabetes. But type A patients might disagree, and certainly, early artificial pancreas systems will require user input.

3. Regulatory leader (and patient champion) Dr. Stayce Beck gave a highly optimistic talk on the FDA's approach to regulating "Do-It-Yourself" (DIY) devices, underscoring the Agency's desire to promote innovation and speed the safe development of new diabetes management tools. She opened with a candid understanding of why the DIY community exists: type 1 diabetes is exhausting, patients are engaged, and they desire better tools *now*. Dr. Beck provided an overview of the requirements that DIY devices must fulfill (just like any other device): (i) a responsible party; (ii) design controls; (iii) transparency, adequate instructions, and human factors; (iv) safety mitigations; and (v) surveillance, recall, and corrective actions. [We heard a similar and more thorough discussion of these factors from Dr. Courtney Lias at DTM 2015.] Dr. Beck acknowledged that such standards appear daunting, though stressed that the safeguards are in place to ensure patient safety. It's hard to argue with that stance, though she noted that these policies have contributed to stereotypes that the Agency does not want to communicate with the diabetes DIY community - a sentiment, in her words, that could not be further from the truth. Dr. Beck characterized FDA pre-submission proposals as "awesome" and encouraged everyone in the room to use them - anyone can get free advice from the FDA early in the design process through pre-submissions. She emphasized that the Agency prefers discussion early on - something we've long heard from Dexcom - and the earlier companies seek feedback, the more flexibility there is to work through obstacles. We felt this was an extremely forward-thinking approach for such a thorny regulatory issue, and we applaud Dr. Beck for dispelling the Agency's aura of intimidation - indeed, she gave both her email and phone number to encourage innovators to reach out. There are many advantages to patient-led design and innovation - customizable design, rapid prototyping, real-world experience - and we're glad to see the Agency is not simply shutting organizations like Nightscout down. Of course, as the risk rises - for example, home-built artificial pancreas devices - it will be interesting to see if any actions are taken. Clearly things must be done safely, but it seems like hackers will have a safe sandbox to play in.

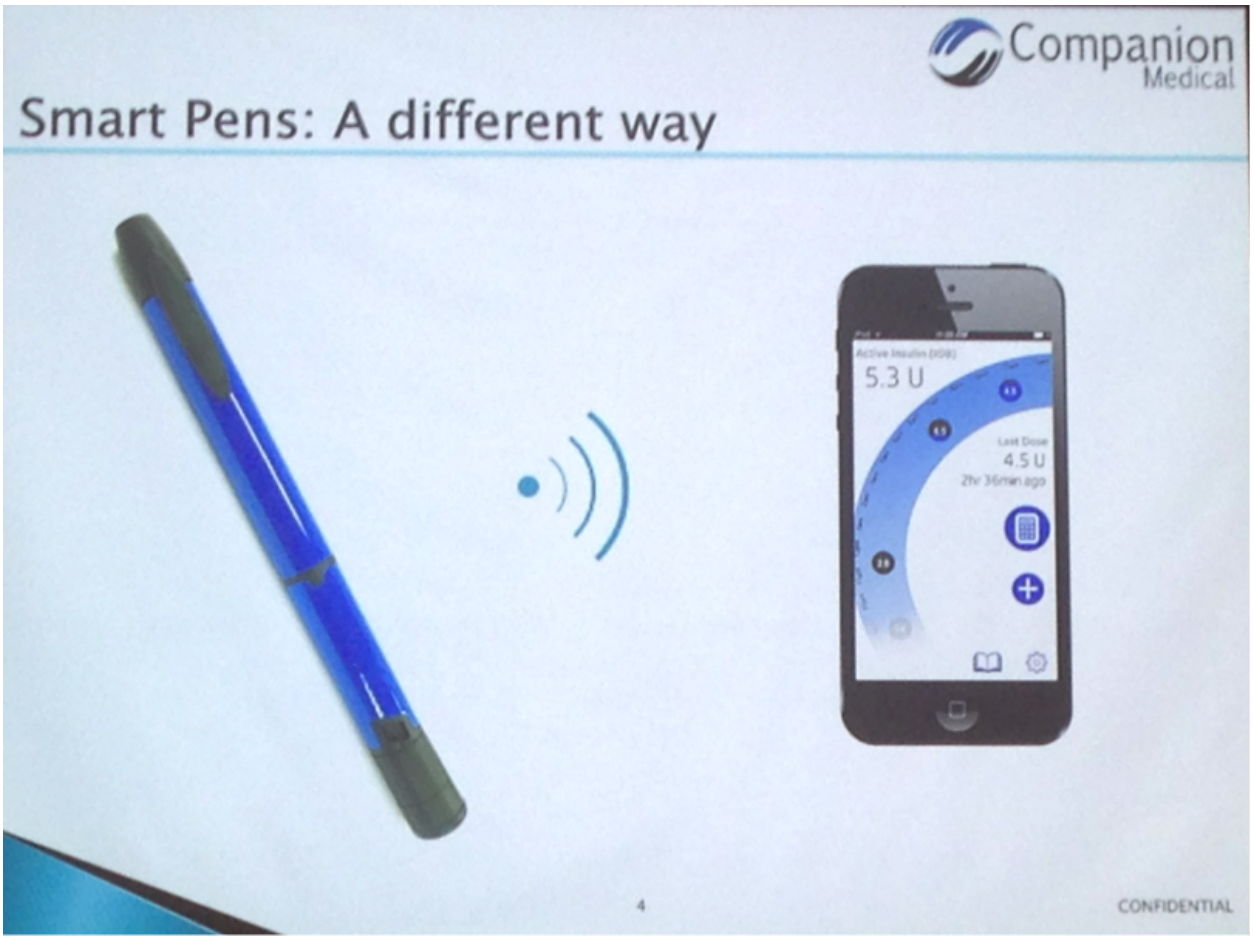
4. In a panel on interoperability, Dexcom's CTO Jorge Valdes thanked Nightscout developers for pushing Dexcom and the entire field faster on connectivity and remote monitoring. Mr. Valdes' immediate example of "interoperability that has meaningfully changed behavior" was Nightscout! It was an overt and fantastic gesture to witness, given the tenuous relationship, given the regulatory nuances (i.e., Nightscout is an open source, unapproved, unauthorized, community-led remote monitoring system that uses Dexcom CGM). Mr. Valdes disclosed that Dexcom has met with the Nightscout community - a major move - though there were still some points of tension in the Q&A. DIY hackers clearly want a lot from industry (e.g., "Access to the raw sensor signal!"), and understandably, companies are constrained by regulatory concerns and patient safety. Mr. Valdes suggested potential for a "user group" of developers to work directly with Dexcom as an authorized partner - we love the idea of stronger public-private innovation relationships and hope that is possible. Mr. Valdes also shared that Dexcom is trying to shorten the three-hour delay in posting CGM data to Apple Health, a regulatory compromise that we have long assumed would decline over time. Overall, Dexcom's commitment to opening its data came through loud and clear in Mr. Valdes' remarks, and applause from the hardcore audience broke out multiple times. Notably, Dexcom Executive VP of Regulatory Andy Balo was in today's audience, as was brand new Senior VP of Data Annika Jimenez - no other company had this many executive leaders in today's room. Dexcom has blazed the trail on sharing data with external partners, and we hope other diabetes device companies follow suit - it was certainly notable to see LifeScan announce Apple HealthKit compatibility last week, a major step for a Big 4 company.

- **Our own Adam Brown moderated today's panel; his introductory slides are posted here.** Adam argued that the bar for interoperability is not just sharing data between two platforms; it is doing something actionable and meaningful with that data. His slides summarized two examples of Fitbit integrations - one with the exercise app Strava which simply shows the data, and

one with the LoseIt! food tracking app which uses the data for a meaningful purpose. Let us know what you think about this topic. What are the big interoperability challenges industry faces? How can the patient community help overcome them?

5. Tidepool designer Sara Krugman shared the fascinating design process behind the iLet bionic pancreas' (Boston University/MGH) user interface, reframing her design school's motto, "Build, test, repeat," with "Feel, understand, make." When designing the iLet interface, her team talked to a group of bionic pancreas users to understand their experience with the device, how they used it, and how they felt at the time - this heavily informed the design process and allowed separation of the device's *end goals* (functionality) from the *experience* goals (What does safety mean when someone is using the device? How should it feel? How do we build trust in the device?). Those two goals are often very different, and that dichotomy led to Sara's biggest takeaway from the process: "Go talk to the people you are going to build for. Understand the difference between empathy and sympathy. Understand what they know and how they know it." Continuous prototyping and testing was also critical to the process. The team used a Yota phone to test both eInk and OLED displays simultaneously, and a web app allowed for rapid modifications to the user interface (e.g., enlarging icons). She emphasized how technical constraints dramatically influence design - the iLet is ultimately going with an eInk display (e.g., like an Amazon kindle), which is thinner, uses one quarter of the battery power, meets the end goals of the device, and achieves the desired user experience. We found her example quite valuable of why fonts matter too- a slide showed DONE, Done, and done, illustrating how capitalization impacts the way a device communicates with a user (YELLING, Telling, collaborating). Everything in the iLet's user interface is lower case for this reason. Another part of interface centers on taking quick action: alerts that pop up stimulate an immediate action on the spot ("No glucagon - replace") instead of requiring someone to clear the alert and go into several menus. Said Sara, "The device is more of a partner in care. You don't have to wrangle it." Her goal with the user interface was to build a more integrated, holistic device experience: "This device is part of my body. I spend more time with it than my partner. It better feel more like me and respect my decision making." As a reminder, Dr. Damiano first unveiled the iLet user interface and integrated dual-chamber device at Friends for Life 2015, and Sara followed with a series of blog posts recounting the design process in July. We look forward to seeing it tested in a bridging study, potentially in 4Q16.

6. Companion Medical's CEO Sean Saint shared a few new design details and screenshots of the company's Bluetooth-enabled reusable insulin pen and bolus calculator app: one-year battery life without recharging; one-year data storage; automatic dose transfer if the pen and phone are separated and then come back in range; and temperature alarms if the insulin gets too hot or cold. We saw the latest version of the mobile app, which includes prominent insulin-on-board displayed on the home screen, a timeline of recent doses, and a bolus calculator. The app will also provide dose reminders and therapy reporting for healthcare providers. Mr. Saint noted that insulin dose data is missing for most people with diabetes (~70% of type 1s not on pumps and nearly all type 2s), and Companion plans to open its data to any interested partners - great to see this commitment from the get-go. There were no new details on regulatory submission or launch - per our May coverage (Series B financing led by Lilly), an FDA 510(k) submission was expected in the "near future," with potential launch in two years or less. We completely agree with Mr. Saint that data from injection users is a critical missing piece of the diabetes data ecosystem - the big question is how expensive a reusable pen will be, and whether patients will tradeoff of the lower price and higher convenience of disposable. Lilly's early investment and Companion's experienced team does give us optimism.



--by Adam Brown, Varun Iyengar, Ava Runge, and Kelly Close