Digital Diabetes Congress 2019

May 14-15, 2019; San Francisco, CA; Day #2 Highlights - Draft

Executive Highlights

- **Day #2 started with an FDA keynote (Dr. Marisa Cruz), followed by a panel discussion that spanned the digital health Precertification program (Pre-Cert), interoperability, AI and machine learning (ML), real-world evidence, and cybersecurity.** Notably, Pre-Cert's v1.0 test continues, and the Agency seeks additional test cases; Ms. Yarmela Pavlovic outlined a number of the initiative's question marks during the panel, and Dr. Cruz underscored that the program is still in its learning phase. Both panelists were also somewhat skeptical about the possibility of users one day being given the ability to piece together "build-your-own" medical devices, suggesting that the scope of interoperability will have to be prespecified and limited. Dr. Cruz also presented an overview of FDA's new proposed AI/ML regulation framework.
- **We were fascinated to hear representatives from Uber Health and Samsung discuss their company's endeavors in the healthcare space during a panel on the future of digital health.** Uber has already created a platform through which providers can order rides on behalf of patients, and the company hopes to eventually incorporate Uber Eats for meal delivery and add on prescription delivery as well. While Uber remains laser-focused on finding new applications for its established offerings, Samsung is considering several areas for investment, including non-invasive glucose monitoring, home health, and virtual reality.
- **Stanford's Dr. Korey Hood detailed the DiabetesWise online resource that helps patients identify the optimal device combination for themselves.** And we learned that the opt-in rate for Dexcom's Clarity mobile app weekly glucose summary notifications is in the high 80%s! (This isn't too surprising - patients just get it sent to them and it would be some work to get out of these emails, which are very compelling when first received. Kelly personally is pretty riveted to receive them each week.)

Greetings from San Francisco, where a very successful third annual Digital Diabetes Congress has come to an end. Cheers to the Doctor Davids - Klonoff and Kerr - for another highly successful meeting. See our Day #1 coverage for a fantastic keynote from IDEO's Mr. Dennis Boyle on thinking like a designer and the results from the inaugural Diabetes App Contest (kudos to Welldoc as well as all the participants), and read on for our top five highlights from the final day.

Table of Contents

4. Stanford's Dr. Korey Hood Presents Diabetes Wise, a Free, Well-Designed Resource to Help Patients Pick Optimal Diabetes Tech Combinations for Themselves
5. We Must Do Better on HCP Engagement with Diabetes Technology for Patient Adoption to Grow; Dexcom Clarity App Weekly Notification Opt-In Rate in the High 80%s

Top Five Highlights

1. Regulatory Panel with FDA's Dr. Cruz: Pre-Cert v1.0 Test Ongoing, Skepticism Over "Build-Your-Own" Medical Devices w/ iController, SPS ACP AI Regulation Framework, RWE, & Cybersecurity

A panel on digital health regulation, featuring FDA's Dr. Marisa Cruz, featured updates and commentary on a number of hot-button issues: the digital health Precertification program (Pre-Cert), data and device interoperability, artificial intelligence and machine learning regulation, the role of real-world evidence (RWE), and cybersecurity. Attendees were urged to write to FDA with input on all things digital health regulation at Digitalhealth@fda.hhs.gov because, as Hogan Lovells' Ms. Yarmela Pavlovic put it, "This is the world you will live in. Don't just let this happen to you. Provide your input."

- **Dr. Cruz provided an overview of the Pre-Cert program, and verified that the Agency is testing version 1.0 throughout 2019 to ensure that the firm-based excellence appraisal process results in the same assurance of safety and effectiveness as the traditional evaluation process.** Dr. Cruz echoed sentiments shared in the February user session, that FDA is looking for opportunities to work with companies outside of the nine pilot participants as additional test cases. Ms. Pavlovic, who works with a number of the Pre-Cert participants and is expert in this domain, is supportive of the Pre-Cert initiative, but called attention to a handful of uncertainties in the road ahead. For one, she pushed back against the general sense in the industry that Pre-Cert will result in products getting to market faster. She's hoping for "net neutral" impact on regulatory timeline, but expressed concern about the case in which a new company brings a product to market. "If you're talking about a first-to-market company, you need to go through the excellence appraisal fist, then submit the streamlined application, and there's a time cost associated with that. When the pilot is complete, it'll be interesting to see the analysis of total time to market and how the Agency is thinking about cost, especially for startups and small companies where time-to-market can be a significant piece of the puzzle when it comes to milestone payments from investors and demonstrating to the market that you are capable." While she didn't want to speak for Mr. Bradley Thompson (who couldn't make the meeting), Ms. Pavlovic believes he is more cautiously pessimistic in that he is less certain that the burden will come out net neutral. She also expressed concerns over the operational cost of precertification (e.g., the burden of gathering, analyzing, and sharing real-world data in the postmarket setting), user fees (which are quite lofty in the De Novo pathway, through which Pre-Cert is at least initially operating), and how a shift to third-party excellence appraisers would fare. Ms. Cruz responded that this is a "learning year" for the Agency, different parts of the framework will mature faster than others, and people have opportunities to weigh in. She maintained that the goal of Pre-Cert is still to reduce the time of a review cycle, and importantly, allows for modifications and iterations without new 510(k) submissions. There's no question that something has to be done with digital health regulation given the deluge of submissions, and we're glad that Mr. Bakul Patel, Dr. Cruz are taking such a tactical, iterative, and collaborative approach to the development of Pre-Cert.
- **Even if a lower-risk, interoperable iController does make it onto the scene (to work with iCGMs and ACE pumps), Dr. Cruz isn't sure that we will ever get to the point where patients can "build-your-own" medical devices.** Ms. Pavlovic similarly cautioned that the field must tread that water carefully." Dr. Cruz posited that iController developers would likely have to be specific about the range of devices the device is interoperable with, not just a general purpose iController to be interoperable with everything: "Be very specific, give due consideration to:

'Do devices sample at the same frequencies? Are the data interpretable? What's the intended use? How much flexibility does the patient have to do this ad hoc assembly vs. having a limited range of options knowing how they will interface and have a predictable outcome. There's a lot of challenges..." The field certainly seems to be heading in the direction of plug-and-play systems - that's the whole point of the special controls for iCGMs and ACE pumps - and we suspect that these obstacles are surmountable via standardization and transparency. Those two words are certainly easier said than accomplished, but as Dr. Barry Ginsberg pointed out yesterday, a bigger pie awaits the ecosystem that successfully interoperates.

- **FDA recently published a discussion paper - open for comment until June 3 - on artificial intelligence (AI) and machine learning (ML).** The group is grappling with tough questions, such as: (i) How do you enable continuous learning while assuring safety and effectiveness?; (ii) How do you guarantee availability of large and robust training data sets with representative clinical variability to avoid codifying existing biases?; (iii) How do you allow for continuous algorithm updates?; and (iv) How do we get to interoperability and explainability of the "basis of the recommendation"? The current proposal is abbreviated as the SPS ACP model: (i) SPS (SaMD Pre-Specification) - the manufacturer outlines anticipated modifications to the performance, inputs, or intended use of an AI/ML-based SaMD ("draws a virtual region of potential changes"); (ii) ACP (Algorithm Change Protocol) - the manufacturer explains the specific steps it has in place to achieve the SPS. Dr. Cruz underscored the importance of HCPs understanding the basis for recommendations and implied that FDA is unsure of how to handle the question of how much a device can be modified before it effectively becomes a different device. "Are there ways to bound that - you need safeguards while not denying the ability of the device to improve over time... The SPS ACP framework was one idea about how you might set boundaries around what kind of modifications would be appropriate whether or not you can specify exactly how the algorithm will learn over time.
- **Stanford's Dr. Perrine Janiaud gave a most clear overview of FDA's current use of RWE (e.g., historical control groups, granting additional indications after initial approval), and an important caveat regarding pragmatic trials.** Meeting co-host Dr. David Kerr made an interesting point in Q&A, noting that in the digital health world, companies know little about their users, so real-world data often lacks demographic information as basic as age, gender, and ethnicity. Dr. Cruz said FDA would absolutely be interested in trying to persuade the industry to capture more evidence about its users, though privacy issues arise when collecting real-world data in an ongoing manner due. It's not as simple as in a structured clinical trial, where there is clear informed consent. However, she noted that the Pre-Cert program requires developers provide information on the demographics of the installed base.
- **Dr. Cruz emphasized that cybersecurity is a shared responsibility, not falling solely on manufacturers.** Manufacturers of course have to build in cybersecurity, requiring ongoing vigilance and reporting, but there must also be solid communication throughout all stakeholder communities, and providers and healthcare institutions have to make patches in a timely manner when a vulnerability is identified. To this point, Ms. Christine Sublett (Sublett Consulting) noted that a lot of hospitals today are running devices that are not appropriately patched, and they probably don't even know they have the vulnerability!

2. Uber Health Focuses on Addressing "Real Problems," Samsung's Interest in Non-Invasive Glucose Monitoring, Home Health, and Virtual Reality; Envisioning Diabetes Care in The Next Five Years

Sansum Diabetes Research Institute's Dr. David Kerr moderated an eclectic panel spanning industry members, clinicians, and non-traditional healthcare players on the future of digital health - we applaud the broad ecosystem. Accordingly, when Dr. Kerr asked the panelists to describe "an episode of care" for a patient with diabetes in the next five years, we were treated to a diverse array of responses. UC Berkeley's Dr. Harry Green foresees a patient with diabetes receiving a retinal image at a

pharmacy, getting the image read by an automated algorithm, and then immediately and automatically having an appointment scheduled with a provider if necessary. The catch? Dr. Green estimates about a 3%-4% chance of this scenario actually being realized. Dr. Patricia Salber, Founder of The Doctor Weighs In, hopes to see care consumed "at a distance" and would like to "re-look at HIPAA" so that we can employ easy-to-use technology such as Zoom to facilitate virtual visits. Uber Health's Ms. Kristina Lee envisions "more real-time monitoring of the way patients can take care of themselves," enabling more continuous adjustment by physicians and immediate care in emergencies - does it need to be physicians or could it be from those that physicians train? With residency programs not filling up in endocrinology ("I'll take oncology …") we think creativity on this front will be critical. Lastly, Samsung's Dr. Divya Shah is focused on improving prevention and non-invasive monitoring. With all the exciting tools being discussed throughout this meeting, we appreciated Dr. Kerr's question probing the potential for digital health advances to enhance "the clinical divide and worsen the impact of chronic diseases like diabetes" in underserved populations. While the panelists did not provide concrete responses to this critical question, it serves as an important reminder to consider accessibility along with innovation.

- **We've been intrigued by the increasingly bold entry of non-traditional players into the healthcare space and were eager to hear representatives from Uber Health and Samsung describe their company's endeavors.**
    - **Ms. Lee explained that Uber Health aims to address "as many social determinants of health as we can," by creating a HIPAA-compliant platform through which providers can order rides on behalf of patients.** While the company is currently focused solely on transportation, Ms. Lee pointed to interest in leveraging Uber Eats for meal delivery and eventually incorporating prescription delivery as well. All of these applications have obvious implications for diabetes - anything to facilitate continuity of care, a healthy diet, and medication management could be meaningful (we may have heard "will be monumental" but we've got to see more first!) in reducing patient burden. We liked her emphasis on identifying "tangible, real problems that we can address in the moment." She explained that the current system used for patient transportation lacks transparency and involves paper vouchers that "magically max out at $50." To mitigate some of these issues, Uber provides specific metrics to its clients including drop-off/pickup locations and trip duration in miles and minutes. We appreciated her acknowledgement that Uber is not likely to manipulate the data it collects. As she put it, "there are so many different avenues, so we really want to focus on doing well and not stray too far." It makes perfect sense for a company like Uber to expand the applications of its existing network, while not attempting to add on entirely different offerings.
    - **Dr. Shah shared that Samsung "wants to go deep into sensor technology," particular regarding non-invasive glucose monitoring** She admitted that the field is "not there yet," but finds it an "interesting" space warranting investment. While there are an array of non-invasive or minimally invasive CGMs in development (Nemaura Medical's 24-hour SugarBEAT disposable skin patch is farthest along), we are fairly skeptical on the potential for a non-invasive CGM to ever reach the high accuracy requirements for insulin dosing. That said, one could certainly be useful for other things like weight loss. Dr. Shah also pointed to appliances in the home as an exciting area in digital health. She explained that "what is happening outside the clinic is very interesting to us." We can certainly see implications for diabetes here - monitoring patients' diet, medication adherence, and sleep from the home could add incredible richness to data from traditional wearables. Lastly, Dr. Shah sees promise in virtual reality, noting that Samsung has already invested in a few projects, mostly for pain management. We were excited by Time Inc.'s virtual reality digital solution demoed at CES 2018 - the experience, called LUMEN 2.0 is designed to relax the user in a matter of minutes. There was also a feature that allows patients to learn from virtual peers who have gone through a particular surgery

under consideration by the patient. We see virtual reality playing a major role in diabetes - for example, patients could learn from others who use a pump before trying one themselves, or watch what happens to their body when blood sugar levels are high in order to try to prompt prevention the next time around.

- **It wouldn't be a digital health panel if artificial intelligence was omitted from the discussion.** Sure enough, we heard lots of commentary on the subject. Dr. Shah asserted that AI is "still a long way in terms of its promise," noting that quality, not quantity, of data is the current issue. She explained that, while consumer health companies like Samsung have vast quantities of data, they lack "continuity or depth of data." She called for the incorporation of clinical grade sensors to first establish a sufficiently granular dataset, followed by AI and machine learning application. She did, however, acknowledge there exist "deep pockets" in AI applications in imaging. To this end, Dr. Green pointed to AI already being "big news" for retinopathy screening, referencing the FDA approval of the IDx-DR system and Verily/Nikon's algorithm in pilots. The catch, Dr. Green emphasized, is ensuring modality - how can we make these technologies cheap enough and portable enough to ensure widespread access?

3. Proposed Rule to Improve the Interoperability for Health Information Receives "Aggressive" Physician Pushback; Dr. David Brailer Believes Rule will Mitigate Data Sharing Frustrations

Health Evolution's Dr. David Brailer asserted that the reason data ownership is so heavily disputed lies in the failure of health IT to deliver results. As he put it: "we debate ownership because we're frustrated that whoever is supposedly controlling us isn't getting the job done." To this end, Dr. Brailer outlined five use cases, in which there exist major data sharing failures: (i) Transitions to or from sites of care, particularly in hospitals; (ii) Unknown patients in the emergency room; (iii) Referrals to specialists or second opinions; (iv) Changes in hospital or health plans; and (v) Drug or device notices or recalls. The sharing failures are predominately due to lacking access to patient data, as well as the absence of requirements and standards. Action has been taken, Dr. Brailer explained, in the form of the Department of Health and Human Services' recently proposed rule to improve the interoperability of health information, which attempts to "lay out a framework" for mitigating these issues. The proposed rule, developed in collaboration with the Office of the National Coordinator for Health Information Technology (ONC), intends to implement key provisions of the 21st Century Cures Act. Dr. Brailer highlighted several of the proposed requirements including: (i) HL7 FHIR is the required API standard; (ii) Payers make protected health information (PHI) available through standardized open APIs; (iii) Payers exchange data as patients change health plans; (iv) Payers provide information about in-network providers; (v) Payers participate in trusted exchange networks; (vi) Medicare hospitals share electronic ADT notifications through the conditions of participation; and (vii) Information blocking rules and exceptions for providers are codified. Click here to submit comments on the proposed rule by June 3.

- **Dr. Brailer noted that the proposed rule has seen "aggressive pushback" from providers.** While he acknowledged that the "firestorm of criticism" has focused mainly on the potentially harmful implications for patients, he believes that "these are in play now and part of what we need to think about is: where do these end up?" According to Dr. Brailer, physicians are concerned that the requirements will be "too burdensome," ultimately impact quality of care. Still, Dr. Brailer is intent on "encouraging the government to stick to its guns" on the rule. We think providers are already encumbered by administrative work that restricts their time with patients - hopefully, the proposed requirements will not limit this precious time further. We felt very lucky that Dr. Brailer was present at the meeting and could discuss his views with attendees - he's extraordinarily highly regarded on the policy side and is seen as a bit of a muse for investors/private equity. He's very consumed with AI and the implications for various disease states.

4. Stanford's Dr. Korey Hood Presents Diabetes Wise, a Free, Well-Designed Resource to Help Patients Pick Optimal Diabetes Tech Combinations for Themselves

Stanford's Dr. Korey Hood presented an excellent, free patient resource that his group developed with the help of designers Ms. Sara Krugman and Mr. Brian Hoffer and funding of the Helmsley Charitable Trust: DiabetesWise.org. Based on previous work the Stanford group has done segmenting patients by their readiness to adopt various diabetes technologies (*JDST 2018*), the resource aims to help patients find the right diabetes devices for their lives. Visitors are met with a prominent "Check Up" button on the welcome screen, which directs them to a five-question survey asking about their current diabetes tech regimen, how they feel about their diabetes, top priorities for diabetes devices, etc. The Results screen then provides a recommended combination of diabetes technologies (e.g., switch from injections and SMBG to pump and SMBG) and why the individual should consider the new combo. The resource goes further, giving overviews of all of the technologies, advantages/disadvantages of specific products, and eventually, Dr. Hood hopes it will provide people with a Diabetes Device Choices report with actionable rankings of the best systems for them. Dropdown menus then allow users to hear from others who have similar technology preferences about the pros/cons of their choices, read about typical costs, and put together a plan for discussing the decision with a doctor. The whole mission of DiabetesWise is to create a digital space to promote uptake and optimal use of devices, because "If we don't move people down the path toward better uptake then I don't think we've done our job." Right on! This site promises to be a tremendous resource for patients, though maintaining it does not seem to be an easy feat - presumably, it would require continuous updating with new products and feedback from different types of patients who are using them. Still, it is a very well-designed experience and an awesome idea to empower patients and boost adoption of technology, and we hope to see it put into wide use!

- **Dr. Hood closed out his talk with a call for more attention paid to qualitative outcomes in diabetes.** Simply applying typical digital engagement metrics - number of clicks, downloads, subscribers, time on app/page, cost per click - does not necessarily capture the full experience or describe people's behavior. Health decisions are often not rational or objective, but based in emotion, so checking in on the emotional side of diabetes is critical. If we can zero in on someone's diabetes burden, then it is easier to know what medication dose to give them and at what pace - "everything we can deliver, it can be better understood by knowing if we're lowering burden."

5. We Must Do Better on HCP Engagement with Diabetes Technology for Patient Adoption to Grow; Dexcom Clarity App Weekly Notification Opt-In Rate in the High 80%s

Early into a panel on *patient* engagement, an astute attendee raised the issue of *healthcare provider* engagement with diabetes technology, which the panel agreed industry has done a poor job tackling writ large. Dexcom's Dr. John Welsh, Stanford's Dr. Korey Hood, and Vanderbilt's Dr. Shelagh Mulvaney noted that this is a tremendous unmet need, that HCP education about diabetes technology needs to improve in order for patient adoption to swell further, and that physicians may be at first harder to influence than other healthcare providers (e.g., CDEs, PAs, NPs). Dr. Mulvaney went so far as to suggest giving providers scripts, noting that "it'd be shocking to hear what is said to patients about technology, or what's not said." UCSF's Dr. Saleh Adi made the excellent point that the field has been plagued by early studies showing that pumps and CGM don't really help, and that information got engrained in many providers' heads, despite newer data supporting their benefit.

- **Dr. Welsh shared that the opt-in rate for weekly time-in-range/patterns notifications among Clarity mobile app users is "in the high 80%s." Wow!** This goes to show how willing - and even hungry - people with diabetes are to engage in retrospective data review, particularly when it is curated for them. The fact that this is an opt-in makes it all the more impressive! (Kelly does not remember "opting in" after downloading the new Clarity app but says there is no way she wouldn't want to receive it - the weekly numbers provide an awesome report card, though she wishes

AGP were more obvious. "Time in range" does appear each week, and she loves receiving it - see here for more on this report from Adam Brown.

-- by Brian Levine, Maeve Serino, and Kelly Close