CLOSER LOOK

MEMORANDUM

Diabetes Care publishes 12-week NIH-funded AID study led by Harvard's Drs. Frank Doyle and Eyal Dassau: 73% drop in overnight hypoglycemia, 0.3% A1c decline - October 30, 2017

Following initial results at ATTD 2017, a study recently published in Diabetes Care demonstrated favorable results from a 12-week, single-arm, multi-site automated insulin delivery (AID) trial (n=29 type 1s). Investigators used the Dexcom G4 Platinum with Share CGM, Roche Accu-Check pump, and a zone-based model-predictive control (MPC) algorithm with adaptation (adjusting carb ratios and weekly basal rates). After 12 weeks in closed loop, participants achieved a significant 0.3% A1c reduction from a well-controlled baseline of 7.0%. More importantly, time spent in hypoglycemia dropped from 5.0% to 1.9% during the day (a whopping 72 to 27 minutes) and 4.1% to 1.1% overnight (59 minutes to 16 minutes) - impressive 62% and 73% reductions, respectively. (And these were very low hypoglycemia numbers to start.) Said Dr. Doyle in an accompanying press release, "This is by far the longest duration trial we have conducted, and it is a testament to the robustness of the algorithm that our key performance indices were maintained from our earlier, shorter trials." As we noted at ATTD, this trial had an important adaptation component - three cycles of four-week parameter adjustment, with carb ratio changed once per cycle and basal insulin changed four times per cycle (weekly). We're glad to see academic AID trials moving into multi-month evaluations and adding adaptation, which could further improve closed loop system performance without needing new devices or drugs. We also wonder how industry and the academic community will together going forward - Where do commercial systems have the most upside for improvement? What research questions still need to be enhanced? Where do algorithms have the most upside to improve?

- **Led by Drs. Frank Doyle and Eyal Dassau from the Harvard John A. Paulson School of Engineering and Applied Sciences** and in collaboration with the William Sansum Diabetes Center (Dr. Jordan Pinsker), Mayo Clinic (Drs. Yogish Kudva and Ananda Basu), University of Virginia's Center for Diabetes Technology (Drs. Sue Brown, Stacey Anderson and Boris Kovatchev), and the University of Padova (Dr. Claudio Cobelli), this study was part of the five-year NIH DP3 grant-funded Ambulatory Control project (first shared at DTM 2012).
- **As a reminder, Dr. Doyle and colleagues developed the base MPC control algorithm back in 1996, expanding it to a zone-based version in 2010, which, as of *2012*, uses asymmetric cost function. The controller zone shifts from 80-140 mg/dl during the day to 90-140 mg/dl overnight to mitigate the risk of nocturnal hypoglycemia in this study. They also developed the first use of a run-to-run adaptive control algorithm for basal and carb ratio values back in 2001.** The algorithm was improved again in 2013, allowing for the ability to set a variable target zone and asymmetric cost functions for hyperglycemia and hypoglycemia. Additionally, an adaptive advisory system to adjust the basal and carb ratio values, developed for the researchers by the Universities of Virginia and Padova respectively, was implemented, receiving information from the sensor, CGM, pump, and patient diary to yield a patient-adapted baseline, as well as to estimate insulin sensitivity, used to optimize bolus delivery.

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