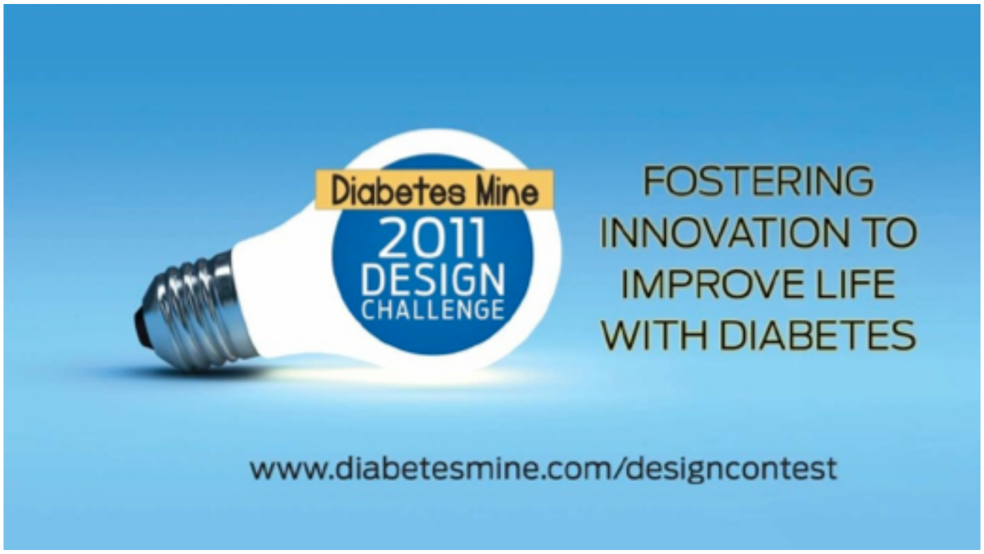

Insulin Wizard Smartphone App

Unlike other medical conditions, Type 1 Diabetes requires the patient to, in the words of one physician, "practice medicine without a license," since it is impractical for the patient's own physician to prescribe the exact times and amounts of insulin to administer during the day. While once physicians prescribed a fixed, exchange-based, meal size and insulin quantity, today the preferred regimen for "tight control" is Basal / Bolus therapy, which allows flexibility in meal size and timing, and can be implemented using multiple (3 or more per day) injections, or with an insulin pump.

Since Basal / Bolus began being used (in the late 1980s and early 1990s) many useful guidelines for determining the bolus dose have been developed: carbohydrate-to-insulin ratios for the contents of a given meal, glucose-to-insulin ratios to help adjust the bolus for abnormal pre-prandial glucose, and carbohydrate-to-glucose ratios to help estimate how much carbohydrate to eat when glucose is low.

The adoption of Basal / Bolus has been gradual, however, and slower in the US than in Europe. The extent to which these ratios are used, as well as the frequency and timing of glucose monitoring and injections, varies greatly. The basal insulin component of this regimen should be determined while fasting, but is not always. Basal insulin need fluctuates during the day, yet the 24-hour insulins detemir and glargine are often used for this despite their inability to handle both the dawn phenomenon and reduced afternoon need with the same dose. Apparently those using these insulins (alone, without combining them with other insulins at any rate) must not be determining, or validating, their basal dose empirically. The label "tight control" thus applies to a range of implementations, all of which remain tainted with the DCCT finding that "tight control" increases hypoglycemia by a factor of three.

Insulin pumps not only enable the Basal dose to be better tailored to fasting insulin need during the day than injections of NPH or Lente (never mind detemir and glargine), but also enable it to be adjusted on the fly should exercise or illness change that need unexpectedly. In the last half dozen years some pumps have added convenient use of the three ratios mentioned above into their operation, including an important but difficult-to-calculate factor: Insulin On Board (IOB). For example, Minimed calls theirs a Bolus Wizard®, Animas calls theirs ezCarb and ezBG (depending on whether it's for a meal or just post-prandial glucose correction), and OmniPod calls theirs a Suggested Bolus Calculator.

These calculations (built in to some, but not all, of these pumps) make it much easier to estimate the amount of insulin to take before a given meal. Significantly, one other pump feature can be used to further advantage: a 2-2½ hour post-bolus reminder to check post-prandial glucose. At this point in time (ideally when food, but not insulin, has been mostly absorbed), one can determine if the meal-time bolus was appropriate by subtracting target glucose from post-prandial glucose, calculating the insulin needed for this drop, and comparing that to the IOB. Curiously, none of the pumps does so in a manner that explicitly predicts impending hypoglycemia, much less how soon it will come, should the IOB be significantly larger than what is needed to bring post-prandial glucose down to normal.

Moreover, while pumps can be more effective than injections in covering the basal insulin profile, the User Guides for these pumps leave establishing that profile up to patients and their physicians. This is unfortunate because the basal insulin profile remains relatively unexplored by researchers, and few patients go to the trouble of establishing their basal profile empirically while fasting, and doing so over 18-20 hours or more (e.g. from bedtime to before dinner the next day) is almost unheard of.

Type 1 patients who do not use a pump with the carbohydrate / glucose / insulin calculation assistance mentioned above (in combination with IOB estimation) are stuck: either making do with food exchanges or doing as much calculation as they know how to do by hand or in their heads. Even pump users have no help establishing their true fasting basal insulin profile or in using glucose reminders to provide predictions of impending hypoglycemia. My design would help all Type 1 patients "practice medicine" better, be they pump or MDI users, by providing help and guidance using these three ratios, implementing a true basal insulin profile, and using my post-prandial hypoglycemia prediction strategy with a sophisticated smartphone App.

I came up with the strategy outlined above in 1990 after my wife and I had both had it with 6 years of mild to randomly terrifying hypoglycemia. I patented some of this in 1996 and published it in 1997 — but not in a clinical journal, so it got little attention. I programmed an early version on a Palm Pilot, but couldn't get it into the ADA Scientific Sessions in 1999, though it was accepted as a poster in 2000. Their reviewers may not have liked putting power in patients' hands, or perhaps they couldn't believe my purported reduction of hypoglycemia by over an order of magnitude could be generalized.

The smartphone App would use many user interaction screens to ascertain how the patient has been managing glucose and what meter / pump / insulins they have available. Patients on Multiple Daily Injection will be guided through published basal dose establishment techniques, but with calculated feedback provided when they enter glucose both before and after injecting, suggesting modifications to each dose in turn until fasting glucose throughout the day is as close to normal as possible.

Pump users will be guided through the more detailed process of adjusting their basal dose rate for each hour of the day. The App can greatly help in this by calculating the insulin action from each prior hour's rate on the glucose value measured at a given time, enabling the App to suggest modifications to prior rates necessary to adjust the glucose at that time toward normal. Without this model-based assistance it is very difficult in practice to adapt the many basal rates during the day to achieve the almost perfectly steady fasting glucose (at normal) that pumps are capable of.

Once users have their basal insulin down, the App would guide them in an experiment to determine their insulin sensitivity and the time course of insulin action. This involves taking less insulin than is appropriate at breakfast, then a good four hours later, when glucose is well over 300 mg/dl and further glucose from breakfast can be ignored, a large enough insulin bolus is given to drop glucose to, or even below, normal. Then glucose is measured every quarter hour for an hour, then every half hour for two more hours, then every hour for a few more. If glucose falls too low, of course, the experiment can be aborted with food and tried again with the bolus dose adjusted.

Now the App knows both insulin sensitivity and the IOB action curve, and for those on MDI, how much their imperfect basal insulin has contributed to the results, so that it can be factored out. The next experiment is to eat several glucose tabs four hours or more after breakfast when glucose is normal. As with the previous experiment, glucose is measured every quarter hour, or even more frequently, as glucose rises, with the measurement rate stretching out as glucose levels off over time.

At this point setup is done, with the IOB duration empirically known, and the carbohydrate-to-glucose ratio and insulin-to-glucose ratio known as well, from which the carbohydrate-to-insulin ratio can be calculated. These are all the factors entered into pumps that help their users with insulin calculations, and the smartphone App can now do everything they do, but for MDI as well as pump users.

The key to avoiding hypoglycemia lies in my strategy of setting an alarm for 2-2½ hours after each bolus, when the food has been mostly absorbed but a quarter to a third of the bolus remains on board. The App reminds users to test glucose at this time, then uses that value, together with the timing and quantity of prior insulin bolus(es) and the IOB curve, to predict future glucose out to its ultimate value.

If much above normal, the insulin sensitivity is used to calculate an adjustment bolus, secure in the knowledge that the only uncertainty would be from the quantity of unabsorbed food, which would cause any error in the resulting ultimate glucose value to be on the high (fail-safe) side.

If close to normal, nothing need be done, though the App might congratulate the user on estimating the amount of carbohydrate in the meal so well.

Finally, if below normal, the IOB curve is used to calculate the ultimate glucose deficit, which is combined with the carbohydrate-to-glucose ratio to determine the size of snack to recommend. The current glucose and the IOB curve are further used to determine how long it will be before glucose falls below 50-60 mg/dl (which value can be configured). The user is advised to be sure to eat that snack well before this much time (including how long it will take for the snack to take effect) has elapsed.

In all of this MDI users would have the difference between the basal rate they were able to achieve and perfection used to adjust glucose predictions so as to make them more accurate, ideally as accurate as pump users, with near-perfect basal insulin profiles, can achieve using the App. Over time, the App's model-based glucose predictions can be compared with the corresponding glucose measurements, and the difference used to gently tweak the parameters that went into the prediction using the ADALINE algorithm. Over time, the App's parameter values will adapt to reality, even as they change.

Depending on the smartphone hardware, Bluetooth communication with meters and pumps may be possible, enabling the App to receive glucose information, and send bolus commands, to compatible meters and pumps, making the App's input and output that much easier to handle. Insulin, glucose and carbohydrate values, with their timing, can be logged as well and uploaded to a PC, where companion software can help analyze it, along with such external data as weight and exercise.

Since this App provides medical management in its insulin dosing advice it will need FDA approval. I've spoken to FDA representatives about this, and they indicate that this sort of App is capable of approval. Having used these algorithms for over 20 years I have no doubt that such an App can work. The question is for whom this is true. It is possible that adaptations will be needed for women during menses, for young children, athletes, or those who engage in extreme sports or exercise on occasion. A clinical trial with a suitably broad spectrum of Type 1 patients will help determine if and where adaptations are necessary, or might even preclude a subset of patients from its use.

Hypoglycemia is the bane of Type 1 diabetes, and it's a shame many think "tight control" increases the likelihood of it. The post-prandial glucose check this App facilitates, together with IOB glucose prediction, can reduce the incidence of hypoglycemia, even as patients lower their average glucose and HbA1c. It gives the most help patients using MDI can get. It just needs to be made available.

Further details, including the journal articles the strategy is based on, are available here.