

ACHIEVING THE HOLY GRAIL OF T1DM TREATMENT

John McNamara

Whereas T2DM patients have a multitude of treatments (e.g., metformin, dipeptidyl peptidase-4 (DPP-IV) inhibitors, glucagon-like peptide (GLP)-1 agonists) available to them to assist in the management of their disease, those with T1DM are primarily reliant on insulin and insulin analogs to control their blood glucose levels. Though great strides have been made in developing short-, long-, and intermediate-acting insulins to optimize glucose control, T1DM patients have long been subject to hyperglycemia (post-meal) and hypoglycemia (overnight). These events can have numerous adverse effects on their health, which, in severe cases, can include diabetic neuropathy, blindness, and kidney disease. While the maintenance of optimal glucose levels (4-8 mmol/L (72 and 144 mg/dL) is largely predicated on the discipline of the patient, the emergence of patient-assisting devices have provided greater convenience and improved blood glucose control. These devices include continuous glucose monitors (CGMs), which alarm the patient if glucose levels become too high or too low, and insulin infusion pumps, which utilize complex algorithms to provide an appropriate dose of insulin to respond to vacillating glucose levels. Neither of these technologies is new (insulin pumps, for example, have existed for almost 30 years), but they have improved significantly over time with regard to clinical accuracy, patient convenience,

THE CLOSED-LOOP SYSTEM PROMISES BOTH CLINICAL AND LIFESTYLE BENEFITS, BUT IT IS FAR FROM BECOMING THE STANDARD OF CARE.

and aesthetic attractiveness. More importantly, using CGMs and insulin infusion pumps in concert creates an “artificial pancreas” of sorts, through which blood glucose is monitored in real-time and appropriate levels of insulin are delivered accordingly with minimal conscious effort required from the patient (especially following meals). These systems promise both clinical and lifestyle benefits over manual management methods, but they are far from becoming the standard of care for T1DM patients given their relative nascency in the market. Nevertheless, many clinicians and researchers agree that perfecting this closed-loop paradigm represents

the “holy grail” of T1DM disease management.

Hurdles to CGMs and insulin pumps adoption

Key obstacles to adoption of CGMs include the following:

- CGMs are not widely reimbursed across Europe, preventing widespread adoption as monthly costs for sensors can cost upwards of \$400; broadened incorporation into reimbursement schedules is occurring overseas, but it remains a significant hindrance to wider acceptance.
- Reported discrepancies between CGM readings and those obtained through traditional fingerstick testing have fueled cynicism from the endocrinologist community; as such, CGM use is only approved as an adjunctive use in the US and must be used in conjunction with traditional fingerstick testing.
- Patient compliance remains an issue with CGM systems, primarily with regard to the sensors. The

sensors for many CGM systems require a constant source of power, so the transmitter must be continuously attached; additionally, the adhesives sticking the sensor to the skin can cause irritation in some patients and/or may not hold up during certain activities including exercising or showering. Implantable sensors would circumvent some of these issues and could be easily masked. However, this much more invasive approach may not appeal to a number of patients.

Insulin infusion pumps also come with a similar set of limitations. These systems, which generally sit on a patient's hip, can be difficult to mask underneath clothing, and may be dislocated during physical activity. Furthermore, patients are concerned about the failure of programmed infusion or improper dosing, particularly older patients who have become very familiar with self-injected insulin management and are reluctant to switch to automated dosing through infusion pumps.

Technological advances and change in reimbursement offer hope for wider adoption

Despite these hurdles, significant technological advances have boosted adoption of these systems

in recent years. Medtronic, the global market leader in continuous glucose monitoring, offers the MiniMed Paradigm® REAL-Time REVEL™ system, which serves as their hallmark CGM + insulin pump product and is one of the most highly regarded products on the market. In an effort to provide a “closed-loop” solution to T1DM management, the CGM transmitter automatically submits a signal to the insulin

pump based on the glucose data collected to deliver the appropriate dose of insulin to the patient. The CGM component allows customizable alerts to warn the patient of oncoming highs and lows, and

provides trend data to help the patient better understand how their body responds to various activities (e.g., exercise, and eating) to further optimize control. The system remains the #1 prescribed insulin infusion pump in the United States and was the first to be approved with a built-in CGM component. The system, however, is not without its limitations. Patients have long complained about the tubing elements of the insulin pump, which are difficult to hide and can often become caught on stray clothing or other objects. To respond to this need, Insulet recently launched the OmniPod® patch pump, the world's first tube-free pump, which is becoming one of the fastest growing pumps on the market today. The pump is wireless and waterproof, allowing for significantly improved flexibility, and can communicate wirelessly with numerous CGM devices on the market, including the FreeStyle Navigator® (Abbott) or SEVENTM PLUS (Dexcom).

In addition to device improvements, the reimbursement landscape has improved as well, with many providers agreeing to cover CGMs and pumps as long as patients have demonstrated

proficiency in properly using the devices through the provider's specific training program.

So which hurdles remain? To date, insulin infusion pumps in combination with CGM devices cannot completely “close the loop” as current systems still possess inherent delays in glucose monitoring and subsequent insulin delivery, putting these devices at a disadvantage to self-monitoring using fingerstick methods and

self-injected insulin thereafter – hence the discrepancies in glucose readings between the two methods. Currently available pumps are sufficient for most situations, though self-induced injections

THOUGH THE CONCEPT OF A FULLY HANDS-OFF “ARTIFICIAL PANCREAS” HAS YET TO BE DEVELOPED AND NO CURE EXISTS FOR T1DM, THE MEDICAL DEVICES INDUSTRY HAS MADE ENORMOUS STRIDES IN RECENT YEARS.


may still be necessary for post-prandial dosing or for insulin delivery after strenuous exercise. Lastly, combination patch pumps with CGM systems remain a desired product for patients as it allows for an all-in-one solution that is light, easily masked, and flexible. Though the concept of a fully hands-off “artificial pancreas” has yet to be developed and no cure exists for T1DM, the industry has made enormous strides in recent years to make medical devices more attractive to diabetes patients and physicians alike.

The key moving forward is to focus on patient *convenience*, which inherently will lead to improved patient compliance and better clinical outcomes.

Consider, for example, the patch infusion pump, pioneered by Insulet, which has abandoned the tubing associated with earlier models in favor of a lightweight, all-contained pump that sits at the hip, resembling a pager attached to the body. Despite

Insulet’s relatively small share of the overall insulin pump market, leading providers like Medtronic are on the innovator’s toes. These players have recognized the potential of the OmniPod®’s emerging technology and are developing similar systems of their own. Furthermore, simplification of the pumps will be paramount to building

acceptance and ultimately patient/clinician adoption. Having too many parts and components that need to be replaced, moved, or recalibrated will not only confuse and inconvenience the patient, but have the potential to complicate reimbursement as well. At least in the near-term, the successful attempts at closed-loop systems will not only

offer improved outcomes for diabetics – it will make living with diabetes *easier*. 

THE KEY MOVING FORWARD IS TO FOCUS ON PATIENT CONVENIENCE, WHICH INHERENTLY WILL LEAD TO IMPROVED PATIENT COMPLIANCE AND BETTER CLINICAL OUTCOMES.

John McNamara is associate at Scientia Advisors.
jmcnamara@scientiaadv.com