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How It Started, How It Is Going: The Future of Artificial Pancreas Systems (Automated Insulin Delivery Systems)

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Abstract

Originally, the future of automated insulin delivery (AID) systems, or artificial pancreas systems (APS), was having them at all, in any form. We've learned in the last half dozen years that the future of all artificial pancreas systems holds higher time in range, less work required to manage automated insulin delivery systems to improve quality of life, and the ability to input critical information back into the system itself. The data and user experience stories make it clear: APS works. APS are an improvement over other diabetes therapy methods when they are made available, accessible, and affordable. Understanding the unmet expectations of current users of first generation APS technology may also aid in the development of improved technology and user experiences for the future of APS.

Keywords

artificial pancreas, APS, closed loop, automated insulin delivery, AID, hybrid closed loop

Introduction

In the early 2010s, the future of artificial pancreas systems or automated insulin delivery systems was simply having them at all. I know this well, as I was one of the first people to build my own hybrid closed loop system in December 2014.[1] In subsequent years, the first hybrid closed loop commercial systems have become available in some countries around the world, although more work is needed to be done to make them universally available[2] (and affordable and accessible). And, over those same years, the system I first used and made open source became used by thousands of individuals[3] around the world. What we've learned in the open source community among those who have chosen to "do it yourself" (or "DIY") is what the future of all artificial pancreas systems holds: higher time in range, less work required to manage automated insulin delivery systems to improve quality of life, and the ability to input critical information back into the system itself.

"How it Started" for Artificial Pancreas Systems

The early results for all artificial pancreas systems, also known as hybrid closed loops or automated insulin delivery systems, is fairly similar. Time in range (TIR) typically starts low for manual diabetes treatment methods, even in "highly motivated" populations, and increases once people use this technology. This is true for the earliest studies of open source systems, where the first self-reported study showed TIR increase from 58 to 81%[4] and later analyses of larger populations also showed similar increased TIR.[5-8] These open source closed loop systems reduce hyperglycemia without increasing hypoglycemia[9] and improve quality of life.[10] They have been studied not only in retrospective and observational studies[11,12] but also in silico[13] as well as ongoing, randomized control trials.[14]

Similarly, commercial closed loop systems[15] have shown the ability to increase time in range for people living with diabetes. Compared with manual control (where the person with diabetes is doing all decision making), commercial automated insulin delivery systems also typically increase time in range. In some cases, TIR increases upwards of 21 percentage points.[16] More recent systematic reviews and meta-analyses with data as recent as 2018 also show significant improvement up to 9.6 percentage points.[17]

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The data and user experience stories make it clear: artificial pancreas systems work, when they are made available, accessible, and affordable, and are an improvement over other diabetes therapy methods.[18] However, expectations[19] of the individual using the automated insulin delivery system are key. Understanding the unmet expectations of current users[20,21] of current APS technology may also aid in the development of improved technology and user experiences for the future of APS.

"How it's Going" for the Most Advanced Artificial Pancreas Systems

It's possible to get more than 10 percentage point improvements in TIR out of insulin-only artificial pancreas systems. And it's possible to achieve these TIR gains with minimal burden on the end user of the system.

For example, the open source community initially focused on using temporary basal adjustments for automating insulin delivery. This was done for safety reasons,[22] so that if the insulin pump lost connectivity with the system, the temporary basal rate would expire and the pump would resume standalone pump therapy. Later, however, it was determined that it would be possible to add boluses to the algorithm's ability to adjust insulin delivery. The method was named "supermicroboluses" (known as SMB),[23] because it was a miniature version of the "superbolus" approach to "front-shift" insulin activity. It was not a synonym for a no-bolus, fully closed loop automated insulin delivery system; however, combined with other features such as the "unannounced meal" (UAM) feature, it became possible for some individuals to achieve a fully closed loop, that did not require user input for meals, while achieving the same TIR as before.

Some makers of commercial systems are working on a full closed loop system as well.[24] Some are experimenting with "no carbohydrate counting"—which does not mean zero meal announcement, but may include a meal announcement that requires roughly categorizing meal size. Others are experimenting with no announcement at all. Depending on the speed of insulin that is used in the system, as well as the algorithm, users may get different results in terms of meal outcomes and TIR with a "fully closed loop system." With future faster insulins, it will be easier for a full closed loop system to respond to unexpected increases in blood glucose levels, regardless of the cause, and with a shorter insulin tail, further minimize the risk of hypoglycemia as well.

In the end, it comes down to a user and what they prefer, and allowing them to choose between their tradeoffs:

- No need to bolus
- No need to count carbs and/or announce meals
- The ability to consume medium to higher carbohydrate meals
- 80%+ time in range
- No hypoglycemia.

We believe, and have demonstrated in the open source community, that it's possible to choose any combination of 4 of the 5—and with the latest, fastest insulins, even all 5 are possible.[25]

This is what we should be striving for with the future of artificial pancreas systems. Settling for only 1 or 2 of these items (such as 70%-80% TIR and no or limited hypoglycemia) is the current status quo.

What's in a Name? Microbolus, Correction Bolus, and More—It Doesn't Matter

It ultimately doesn't matter what you call various components and features of the closed loop systems, but it does matter that we work to make it clear to end users—people living with diabetes—what the capabilities of the systems are, and what they can or cannot do.

For example, much attention is given to whether a "correction bolus" can be issued by a closed loop system. That is perceived to be different than "microbolus(es)."

What matters, ultimately, though, is how much insulin is allowed to be delivered by the system; when and how often; and what the target is. That information determines how "aggressive" a system can be for correcting or preventing hyperglycemia.

What's Going Away: A Perception of a Fixed "Correct" Basal to Bolus Ratio

Similarly, an artifact of past diabetes treatment methodologies has been a perception of the "correct" ratio of basal to bolus insulin, as a proxy of determining whether someone's settings in their pump are "correct." In an automated insulin delivery system, where the algorithm determines whether to issue a "basal" adjustment or a "bolus correction" (or microbolus, or correction bolus, etc.), the "choices" of type of insulin delivery is no longer a reflection on the user. Additionally, there are new tools such as Autotune[26] that can be used (and should be further studied and adapted by commercial companies, to better improve use of their closed loop systems) to adjust a person's baseline basal rates, ISF, and carb ratio, whether that's used by the closed loop system or whether that information is only used when a user "falls back" to manual mode.

What Needs to be Added to The Future of APS: Flexible User Inputs

One of the benefits—and detriments—of open source automated insulin delivery systems is the plethora of customization and input options. On the other end of the scale, with very few user input options beyond carbohydrate counting, are current first-generation commercial closed loop systems. The future of APS is somewhere in between these two.

While a typical person with diabetes doesn't need all of the customization options available in DIY, there is pent up frustration in the diabetes community with the first generation of commercial APS technology. Because of the timing of insulin, and a person's knowledge of their own behavior, it is important to be able to interact with a closed loop system and give it information that it can't possibly predict, such as whether someone is about to eat or exercise. But beyond carbohydrate entries and slight target adjustments, the future of APS needs to involve and develop a few more, carefully designed user inputs.

For example, a person with diabetes needs the ability to tell the system that it has learned something "wrong," such as when it detects a pattern that no longer exists.[27] Similarly, a person may have taken action to adjust for thing that the system has learned. For example, if the system is increasing insulin because it perceives the user to be more resistant, and the reason for resistance is resolved by a pump site change, the user needs to be able to inform the system to revert back to neutral or to otherwise stop applying whatever the system has "learned."

These user inputs don't need to be things that users input all the time, but they need to be available for the once a week or once a month occurrences that can otherwise often derail diabetes management, and leave users frustrated if the system can't adapt quickly enough because it doesn't know about the situation, or because it's too slow to learn the situation has reverted back to normal.

Conclusion

At the end of the day, the future of artificial pancreas systems is already here: it is just not distributed widely enough yet. We know it is possible to achieve 80%-90%+ time in range without regular meal announcement or precise carbohydrate counting by end users, while still preventing hypoglycemia, reducing burden and improving quality of life for individuals living with diabetes who want to use these systems.

Abbreviations

AID, automated insulin delivery; APS, artificial pancreas/artificial pancreas system; CGM, continuous glucose monitor; DIY, do-it-yourself; TIR, time in range.

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