

Developing diabetes therapies for real-world patients: why the next generation of automated insulin delivery requires a new generation of ultra-concentrated, ultra-rapid insulin

By Sarah Howell PhD, Chief Executive Officer and Executive Director, Arecor Therapeutics plc



Dr Sarah Howell PhD
Arecor Therapeutics

Dr Sarah Howell PhD, CEO of Arecor since 2015, has led its growth into a clinical-stage biotech dedicated to reducing the treatment burden for people with diabetes, obesity, and cardiometabolic diseases. She brings extensive experience in pharmaceutical development, manufacturing, supply, and licensing, having served as Vice President of CMC (Chemistry, Manufacturing and Controls) at BTG plc and Director at UCB-Celltech. She holds a BSc in Chemistry from Birmingham and a PhD in Physical Organic Chemistry from St Andrews.

Abstract

Despite extraordinary advances in diabetes technology, fully automating insulin therapy remains one of medicine's most complex engineering and biological challenges. Modern AID systems use sophisticated algorithms to continuously analyse glucose data and determine how much insulin should be delivered. But unlike many automated systems, they cannot simply react to current conditions.

This is the primary challenge in delivering safe and effective insulin to patients. This paper looks at the problem and modern solutions and the drawbacks.

No chronic illness requires patients to make more daily treatment decisions than type 1 diabetes. A person with hypertension takes a pill. A person with asthma uses an inhaler. Unlike a number of chronic conditions managed through scheduled medications and periodic doctor visits, type 1 diabetes and insulin-dependent type 2 diabetes demand continuous attention.

Without the ability to regulate blood glucose automatically, people living with diabetes must constantly perform calculations that a healthy pancreas makes invisibly. Every day involves analysing glucose trends, predicting the impact of meals and exercise, reacting to illness and stress, managing infusion sites and sensor function, and making treatment choices to balance the risks of hyperglycaemia

against the immediate danger of hypoglycaemia. People living with diabetes serve as their own algorithm (Erik Verhoef), and as a result, bear a significant cognitive and emotional burden that impacts their quality of life and long-term health. (Gonzalez et al, 2025)

Reducing that burden, along with improving glycaemic control, has been a defining goal of diabetes innovation. The progress over the past decade has been impressive and increasingly driven by advanced technology devices and is bringing that goal closer to reality. Continuous glucose monitors (CGMs) now provide near-real-time glucose readings and are the standard of care for most people on insulin therapy, replacing fingerstick testing with continuous streams of glucose data.

Automated insulin delivery (AID) systems integrate insulin pumps with sophisticated algorithms that can continuously adjust insulin delivery. In a major policy shift, the American Diabetes Association (ADA) announced its 2026 Standard of Care guidelines recommending CGM be used beginning at diagnosis for people using insulin and recognising automated insulin delivery (AID) systems as the preferred insulin delivery approach for individuals with type 1 diabetes American Diabetes Association Professional Practice Committee for Diabetes) because of their demonstrated ability to improve glycaemic outcomes while reducing treatment burden over multiple daily injections. (American Diabetes Association Professional Practice Committee for Diabetes2)

The promise of AID goes beyond better devices and algorithms and is about creating closed-loop systems that can manage and take over more of the tasks people with diabetes perform every day, allowing them to sleep, exercise more easily, travel confidently, or eat meals without constant management. However, despite advances in sensors, algorithms, software, and devices, fully achieving this promise is more challenging than many anticipated. Building an automated system that can safely replace the decisions patients make every day requires solving complex biological and engineering challenges.

The complexities of automated systems

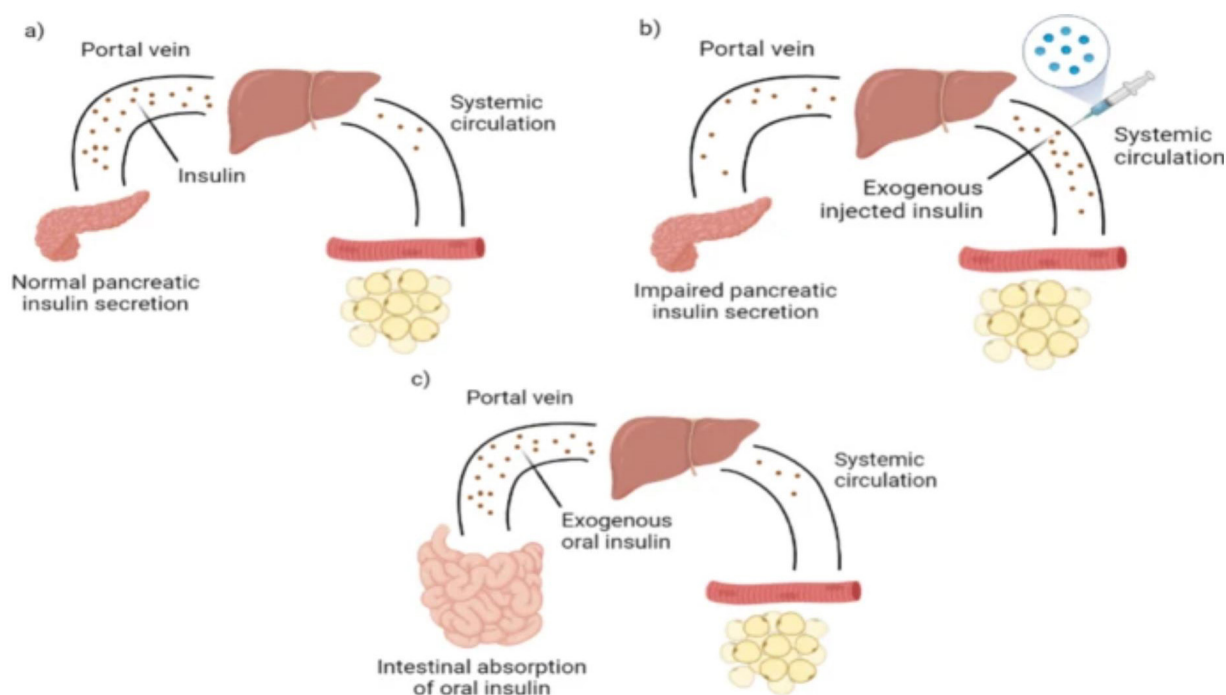
Despite extraordinary advances in diabetes technology, fully automating insulin therapy remains one of medicine's most complex engineering and biological challenges.

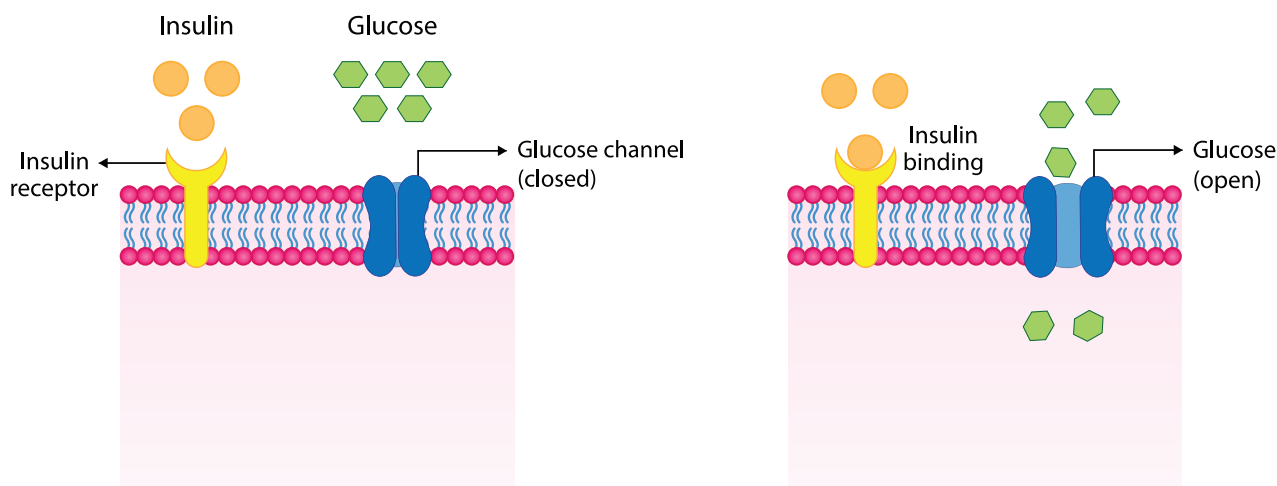
Modern AID systems use sophisticated algorithms to continuously analyse glucose data and determine how much insulin should be delivered. But unlike many automated systems, they cannot simply react to current conditions. Instead, they must predict where glucose levels are heading over the coming hours and deliver insulin before those changes occur. Even today's most advanced algorithms face one fundamental biological limitation.

Once insulin is delivered into the subcutaneous tissue, it requires time to be absorbed into the blood-stream before it begins lowering glucose. During that interval, blood glucose continues to change. As a result, researchers increasingly recognise that the future of diabetes automation depends not only on smarter algorithms and better sensors, but also on insulin formulations capable of responding as quickly as the technology directing them.

The focus on equipping patients with better tools and the significant advances in sensors, pumps, and predictive algorithms is bringing the field closer to fully closed-loop systems and the promise of an artificial pancreas. The goal now is to ensure these automated systems truly minimise patient intervention and improve how all components of the diabetes ecosystem work together to both reduce patient burden and improve outcomes. However, achieving this next major breakthrough with an integrated approach will require rethinking one of the oldest and most foundational elements of diabetes treatment – insulin.

The more advanced automated insulin delivery systems





become, the more the biology of insulin, rather than the sophistication of the algorithm, will be the limiting factor.

Developing insulin for the next generation of automated care

The future of automated diabetes management relies on developing ultra-concentrated and ultra-rapid insulin formulations tailored to increasingly miniaturised, autonomous delivery devices that can be worn for a week without requiring infusion line or cartridge replacements. This has the potential to truly lower treatment burden, support smaller, longer-lasting devices, and enable more precise blood glucose control. Advanced ultra-concentrated and ultra-rapid-acting insulin formulations could bridge the remaining gap between current hybrid systems and fully automated diabetes care.

Today's rapid-acting insulin analogues represent a major advance over earlier formulations and remain highly effective for conventional insulin therapy. But automated insulin delivery systems place fundamentally different demands on insulin than traditional injections ever did. As AID systems evolve toward becoming smaller, longer-wearing, and increasingly autonomous, edging closer to fully closed-loop technologies, they require insulin formulations designed not only for subcutaneous delivery but also for the unique needs of real-time glucose-responsive automation.

Currently, to achieve tight glucose control, AID systems remain hybrid. This means users need to announce meals, count and enter carbohydrates and make adjustments as needed throughout the day. The holy grail of a closed-

loop system would be for users to do nothing except fill their device with insulin once a week, or as infrequently as possible. Achieving this requires faster-acting insulins capable of supporting more precise and aggressive algorithms. This would help patients stay within target glucose ranges longer without increasing hypoglycaemia risk. To unlock the full potential of AID systems, insulin formulations need to be specifically designed for closed-loop automation rather than current insulin therapies. Combining manual inputs with automation is common because even the newest rapid-acting analogues cannot act quickly enough to fully match the body's fluctuating glucose levels throughout the day. No matter how advanced the algorithms become, insulin absorption will always involve some delay.

On the path toward a closed-loop system, every improvement that allows an AID system to assume more day-to-day decision-making reduces the cognitive burden on people living with diabetes. Faster, more predictable insulin action enables algorithms to respond more precisely to changing glucose levels. Higher insulin concentrations make it possible to deliver larger doses from smaller reservoirs, supporting compact devices that can be worn comfortably for longer periods with fewer interruptions.

Increasing insulin concentration has improved dosing efficiency by allowing more insulin to be delivered in a smaller volume. However, concentrated insulin formulations have traditionally shown slower absorption after subcutaneous administration, limiting their suitability for automated systems that depend on rapid pharmacologic

responses. As a result, developers have long faced an inherent trade-off: insulin could be highly concentrated or highly responsive, but achieving both simultaneously proved exceptionally difficult.

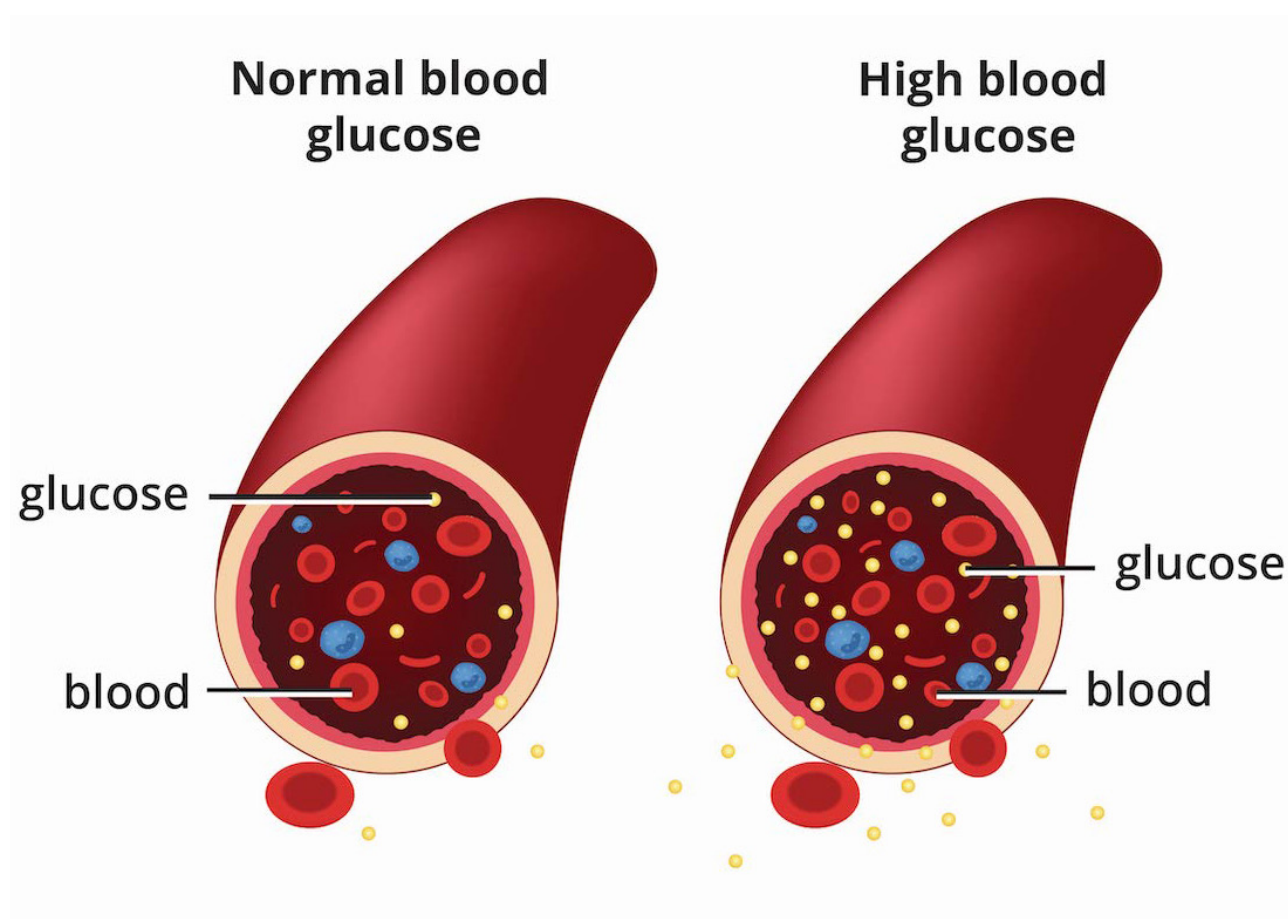
This challenge is becoming increasingly important as automated insulin delivery expands beyond people with type 1 diabetes to include the growing population of individuals with insulin-intensive type 2 diabetes. Many of these individuals require well over 100 units of insulin each day, meaning current pump reservoirs may be exhausted long before the intended wear period. A smaller device offers little practical benefit if it still requires frequent cartridge changes. Fully realising the promise of these miniaturised, extended-wear AID systems, particularly for individuals with higher insulin requirements, will require insulin formulations that deliver larger or more concentrated doses from smaller reservoirs without compromising rapid glucose-lowering activity. (American Diabetes Association Professional Practice Committee for Diabetes2)

Emerging formulation approaches suggest that it may be possible to combine high insulin concentration with rapid absorption, a combination that has, until now, not been achieved. One example of this approach is AT278, an investigational U500 (concentrated) insulin 'aspart' (a rapid-acting human insulin) formulation developed to

combine ultra-high insulin concentration with an ultra-rapid pharmacokinetic and pharmacodynamic profile. Rather than simply increasing insulin concentration, the formulation was designed to accelerate insulin absorption and early glucose-lowering activity while delivering five times the insulin concentration of standard U100 formulations. This reflects an innovative shift in insulin development toward engineering formulations that address the evolving needs of automated insulin delivery systems, including smaller reservoirs, longer wear durations, and enabling fully closed-loop automation. So, improving outcomes whilst significantly lowering the burden for people living with diabetes.

Clinical trials

In phase 1 clinical trials evaluating AT278 in people with type 1 diabetes, researchers observed earlier insulin appearance, faster onset of glucose-lowering activity, and significantly greater early insulin exposure and glucose-lowering effect compared to standard U100 insulin aspart. (Svehlikova et al, 2023) These findings demonstrate that novel formulation science can overcome the challenge of increasing insulin concentration, compromising the rapid pharmacologic response needed for automated insulin delivery, a challenge that has existed for decades. (Wilson and Castle, 2020)



“ The next era will be defined by complete, integrated technologies that allow people to spend less time managing their disease, reducing the disease burden and ultimately improving health ”

Although further studies are necessary to see how these pharmacologic benefits translate into everyday use with automated insulin systems, this research demonstrates how advances in formulation science could remove a key barrier to more autonomous diabetes management.

For AID systems, these pharmacokinetic characteristics will become increasingly important as developers continue to meet patient needs by creating smaller, longer-wear devices that respond more quickly to dynamic changes in glucose levels. Although additional clinical studies are needed, advances in formulation science suggest that ultra-concentrated and ultra-rapid insulin will enable the development of next-generation AID systems and ultimately the fully closed-loop system.

Realising this will require an integrated approach among formulation scientists, device engineers and digital health developers, reflecting the growing recognition that no single innovation will lead to a fully autonomous diabetes management system – creating advanced, ultra-concentrated and ultra-rapid insulin is essential to the system. Together, this strategy could turn the fully automated artificial pancreas into a reality.

While innovation in diabetes care has given people better tools to manage their disease, the next era will be defined by complete, integrated technologies that allow people to spend less time managing their disease, reducing the disease burden and ultimately improving health. ●

References

- American Diabetes Association Professional Practice Committee for Diabetes (2026) Introduction and Methodology: Standards of Care in Diabetes. *Diabetes Care* 1 January 2026; 49 (Supplement_1): S1–S5. <https://doi.org/10.2337/dc26-SINT>
- American Diabetes Association Professional Practice Committee for Diabetes2 (2026) 7. Diabetes Technology: Standards

of Care in Diabetes. *Diabetes Care* 1 January 2026; 49 (Supplement_1): S150–S165. <https://doi.org/10.2337/dc26-S007>

Erik Verhoef. The Convergence Trap: Shared Insight Does Not Differentiate a Market: It Synchronizes It (n.p: Independently Published), 53

Gonzalez JS, Hoogendoorn CJ, Hernandez R, Schneider S, Mustafiz F, Siddhanta M, Pyatak EA (2025) Diabetes-Related Distress and Glycemic Dysregulation in Everyday Life With Type 1 Diabetes: Which Comes First? *Diabetes Care* Aug 1; **48**(8):1453–1460. doi: 10.2337/dc25-0559. PMID: 40554543; PMCID: PMC12279033

Svehlikova E, Ashcroft NL, Gatschelhofer C, Gerring D, Höller V, Jezek J, Lackner B, Lawrence F, Pillai V, Ratzer M, Urschitz M, Wolf M, Pieber TR (2023) Pharmacokinetics and Pharmacodynamics of a Novel U500 Insulin Aspart Formulation: A Randomized, Double-Blind, Crossover Study in People With Type 1 Diabetes. *Diabetes Care* **46** (4): 757–764 <https://doi.org/10.2337/dc22-1054>

Wilson LM, Castle JR (2020) Recent Advances in Insulin Therapy. *Diabetes Technol Ther* Dec; **22**(12):929–936 doi: 10.1089/dia.2020.0065. Epub 2020 May 12. PMID: 32310681; PMCID: PMC7864088

KEY TAKEAWAYS

- Reducing patient burden, not just improving glycaemic control, is the next major goal of diabetes innovation.
- The future of automated insulin delivery depends as much on advances in insulin formulation as on algorithms and devices.
- Ultra-concentrated, ultra-rapid insulin will enable smaller, longer-wear, fully closed-loop systems that require less patient intervention and improved outcomes.
- The next milestone in diabetes management will come from integrating advances in insulin, sensors, algorithms, and device technology to create truly autonomous systems.