10 YEARS:
10 STORIES OF IMPACT

CASE STUDY 5

Bringing automated glucose management to life

New technologies hold great promise for more automated management of type 1 diabetes (T1D). But progressing these systems from research to practice requires evidence gathered in clinical trials.

The Australian Type 1 Diabetes Clinical Research Network (T1DCRN) has funded trials testing the safety and efficacy of increasingly advanced systems of continuous glucose monitoring (CGM), paired with automated insulin delivery, with the assistance of sophisticated algorithms. As a result, Australians with T1D now have access to hybrid closed-loop technologies, making management safer, easier, and more effective every day.

Australian Type 1 Diabetes Clinical Research Network

JDRF IMPROVING LIVES. CURING TYPE 1 DIABETES.

WHAT PROBLEM DO WE NEED TO SOLVE?

The role of beta cells in the pancreas is to detect blood glucose levels and respond by precise adjustments in insulin production and secretion to keep those glucose levels within a tight range. In the absence of these cells, people with established T1D must take on this role themselves by testing blood glucose levels night and day, calculating how much exogenous insulin is required and administering it via injection or infusion.

Blood glucose levels are affected by several factors such as food, exercise, body mass index, stage of life and the presence of other conditions, making adjusting insulin a difficult task. This continuous need for balancing and calculation represents a significant medical challenge and mental burden for people in terms of time and mental load.

Through the T1DCRN, we have previously funded **Professor Elizabeth Davis** to investigate the impact on blood glucose levels of varying types of exercise and food consumption and to utilise this knowledge to develop guidelines and tools for clinical practice.

But what if the complex process of calculating and administering insulin could be automated through technologies that predict and adjust insulin requirements independently? Advancements in diabetes technologies are paving the way for systems that can accurately monitor blood glucose levels and automatically calculate and administer the precise dose of insulin needed.

Such solutions are commonly referred to as hybrid closed-loop systems (if material user input is necessary) or closed-loop systems/automated insulin delivery systems (if little or no user input is required).

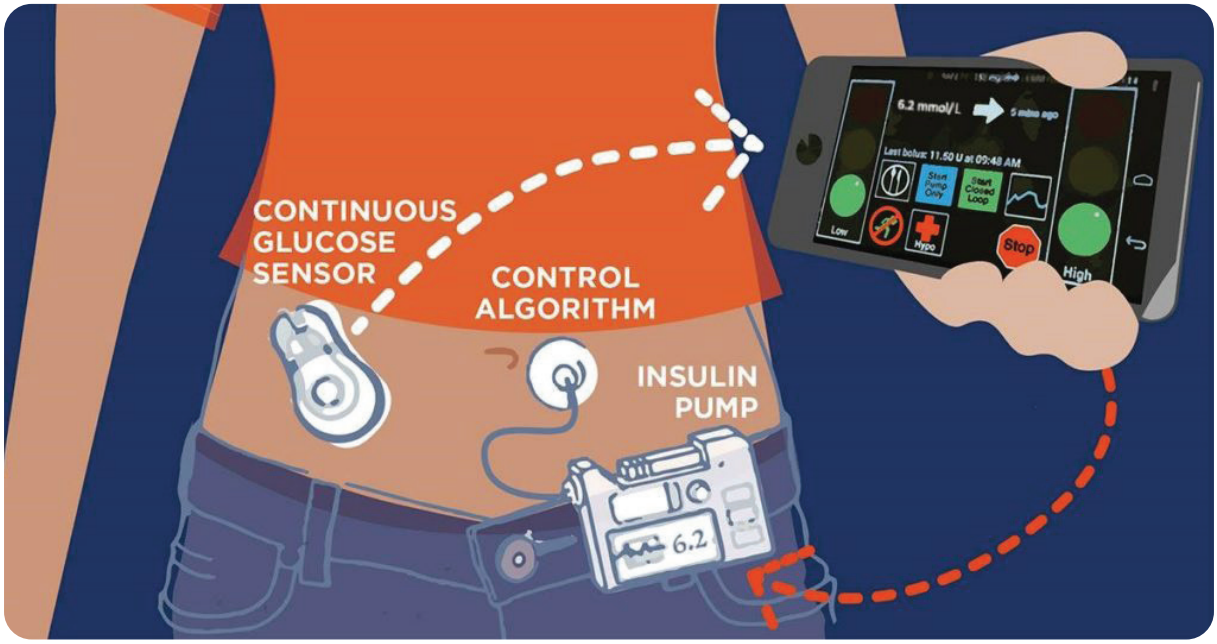

Figure 1: Closed and hybrid closed-loop systems contain a glucose sensor, an insulin pump and an algorithm that links the two. Hybrid closed-loop systems still require significant user input while closed-loop systems are fully automated (image courtesy of JDRF UK).

Closed loop and hybrid closed-loop systems include the following:

1 **a glucose sensor** on the skin that detects blood glucose levels 24/7, via a CGM

2 **a tubed or patch insulin pump** that delivers insulin into the body

3 **an algorithm** that links the two, telling the pump how much insulin to dispense, as well as providing increasingly sophisticated data about insulin use and blood glucose levels.

There are many steps required between the development of these systems and their adoption in real life. These steps include gathering sufficient information about the safety, efficacy and cost-to-benefit assessment of the new technology, eventually leading to regulatory approval, reimbursement, and availability through the health system.

WHAT WAS FUNDED BY THE T1DCRN, AND WHAT DID IT FIND?

Recognising the significant clinical benefit of increasingly automated insulin delivery and blood glucose sensing to those with T1D, the T1DCRN has funded more than $6.8 million in research projects trialling the effectiveness of these technologies in adults and children.

The T1DCRN investment commenced with $1.6 million awarded in 2012 to University of Western Australia's **Professor Tim Jones** to undertake a small-scale, in-clinic trial to test if a hybrid closed-loop system had the ability to significantly lower rates of hypoglycaemia.

The positive results of this trial kick-started a larger, six-month trial involving 95 people with T1D.[25] This was the first study of the technology of its kind on such a scale.

Professor Jones was awarded a further $2.3 million from T1DCRN funds in 2016 to test the effectiveness of a hybrid closed-loop system with an algorithm that could predict patterns of blood glucose in children and adolescents with T1D.

> "My daughter Enahiya was diagnosed with T1D at 18 months old, and we were quickly introduced to the CGM and insulin pump which was a game changer for us and our lil' warrior. From two-hourly finger pricks and several insulin injections a day to no finger pricks and pumping, the mental and physical load is much less now!
>
> **Monica,** mum of **Enahiya,** who has T1D and has used a hybrid closed-loop system for several years

25. Ly TT, et al. Effect of Sensor-Augmented Insulin Pump Therapy and Automated Insulin Suspension vs Standard Insulin Pump Therapy on Hypoglycemia in s With Type 1 Diabetes: A Randomized Clinical Trial. JAMA. 2013;310(12):1240–1247. doi:10.1001/jama.2013.277818

Professor David O'Neal from the University of Melbourne, also received $2.9 million to assess the efficacy of the same hybrid closed-loop model in adults. The protocols of both trials were jointly developed to mirror one another.

The combined findings from these trials demonstrated that a hybrid closed-loop system resulted in better control of blood glucose levels, less hypoglycaemia and improved quality of life for adults and children with T1D compared with standard management through multiple daily injections.[26,27,28]

WHAT WAS THE IMPACT?

These Australian findings, combined with global efforts, demonstrated that these technologies were a safe and superior option for blood glucose management compared to standard treatments at the time. They provided the critical evidence to include technology in clinical care and to drive policy changes, including allowing thousands of Australians to access CGM technology.

In terms of clinical care, CGM has allowed 24-hour individualised glycaemia patterns to be established, leading to the development of a clinical tool called Time in Range (TiR).

TiR is the amount of time people spend in a safe, target blood glucose range. Because CGMs are relatively new, clinicians are still learning about the long-term effects of TiR. However, the data demonstrate that the higher the TiR, the less likely people are to develop complications.[29,30]

TiR is now increasingly used to support blood glucose management for those with T1D.

The research evidence, aided by a T1DCRN-funded health economic report[31], led to support from key diabetes stakeholders to advocate towards affordable access to new technologies for people with T1D.

In 2017, the Australian Government introduced a CGM subsidy for those under 21 years of age with T1D. This made CGM technology accessible for thousands of young Australians with T1D.

JDRF then provided T1DCRN funding in 2017 to the **Australasian Diabetes Data Network** and secured support from the Department of Health to undertake an evaluation of the effects of the CGM subsidy on clinical outcomes.

The evaluation found that the introduction of the subsidy markedly increased CGM use in under 21s from 5% to 79%, provided significant improvements in blood glucose measures for those using it, and lowered the incidence of DKA.[32] This analysis of real-life outcomes demonstrated a clear superiority of the CGM technology versus finger-prick glucose testing.

With this new evidence and community support, including JDRF's Access For All campaign, in 2022 bipartisan commitment was delivered for the extension of the CGM subsidy to all Australians with T1D, regardless of age. This now allows any Australian with T1D the chance to access this crucial technology.

26. Ly TT, et al. Effect of Sensor-Augmented Insulin Pump Therapy and Automated Insulin Suspension vs Standard Insulin Pump Therapy on Hypoglycemia in s With Type 1 Diabetes: A Randomized Clinical Trial. JAMA. 2013;310(12):1240–1247. doi:10.1001/jama.2013.277818

27. McAuley SA, et al. Six Months of Hybrid Closed-Loop Versus Manual Insulin Delivery With Fingerprick Blood Glucose Monitoring in Adults With Type 1 Diabetes: A Randomized, Controlled Trial. Diabetes Care. 1 December 2020; 43 (12): 3024–3033. doi.org/10.2337/dc20-1447

28. Abraham MB, et al. Effect of a Hybrid Closed-Loop System on Glycemic and Psychosocial Outcomes in Children and Adolescents With Type 1 Diabetes: A Randomized Clinical Trial. JAMA Pediatr. 2021;175(12):1227–1235. doi:10.1001/jamapediatrics.2021.3965

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30. El Malahi A, et al. Relationship Between Time in Range, Glycemic Variability, HbA1c, and Complications in Adults With Type 1 Diabetes Mellitus.J Clin Endocrinol Metab. Jan 18 2022;107(2):e570-e581. doi:10.1210/clinem/dgab688

31. Accenture and JDRF. Economic Costs of Type 1 Diabetes in Australia. April 2021

32. Johnson R, et al. Universal Subsidized Continuous Glucose Monitoring Funding for Young People With Type 1 Diabetes: Uptake and Outcomes Over 2 Years, a Population-Based Study. Diabetes Care 1 February 2022; 45 (2): 391–397. https://doi.org/10.2337/dc21-1666