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Improving HbA1c levels with advanced hybrid closed-loop therapy

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Commentary on 'Advanced Hybrid Closed-loop Study in An Adult Population with Type 1 Diabetes

(ADAPT): A Randomised Controlled Study'

Closed-loop insulin delivery systems improve glucose outcomes for people living with type 1 diabetes, although the improvement in HbA1c has been modest. In a study by Brown and colleagues from 2021, a multicentre trial of Insulet's Ominpod 5 showed a reduction in HbA1c of -0.38 in adults, most of whom were previously on open loop pump therapy.¹ Other studies of commercial closedloop systems have similarly found modest reductions in HbA1c in the range of -0.2 to -0.5% .^{2,3} A possibility for such modest reductions in HbA1c could be because the participants in these studies—many of whom were on sensor-augmented pump therapy—already had well controlled glucose before using the closed-loop system. Choudhary and colleagues⁴ report results on a prospective, multicentre, randomised controlled trial across 14 European countries to determine whether an advanced hybrid closed-loop (AHCL) automated insulin delivery system built by Medtronic (MiniMed 670G with the MiniMed 780G algorithm system) performs better than standard multiple daily injection therapy combined with intermittently scanned continuous glucose monitoring (isCGM) in a population of people

living with type 1 diabetes who are not meeting glucose control targets. Choudhary and colleagues found that for these participants who had a baseline HbA1c of 9.04% , use of the AHCL system can lead to a substantial reduction in HbA1c of -1.42% . The large reduction in HbA1c in this study compared with other studies is at least partly due to the population tested; the inclusion criteria required participants to have an HbA1c greater than or equal to 8.0% . As a comparison, the baseline HbA1c for the participants

in the closed-loop trial by Brown and colleagues³ was 7.4%; participants on closed-loop had a -0.7% reduction in HbA1c compared with those on sensor-augmented pump therapy showing a -0.5% reduction. In addition to investigating a population of people with poor glucose control, the study by Choudhary and colleagues is also unique in comparing AHCL with a control group of people using isCGM and multiple daily injections, rather than a sensor-augmented pump as has been done previously. Most people around the world with type 1 diabetes continue to use multiple daily injection therapy, and CGM plus multiple daily injection therapy represents the standard care in the western European countries where the current study was done. Use of isCGM combined with multiple daily injections have been shown by Fokkert and colleagues⁵ to reduce HbA1c in people with type 1 diabetes from 7.8% to 7.4% over 6 months compared with self-management of blood glucose. Similar to Choudhary and colleagues, Fokkert and colleagues also found that the benefit of isCGM was substantially larger for people with type 1 or type 2 diabetes with elevated HbA1c of greater than 8.6% at baseline with a reduction of -0.8% shown in this group. The reduction in HbA1c for people using AHCL compared with isCGM plus multiple daily injections as shown in study by Choudhary and colleagues was substantially larger than the reduction in HbA1c in the study by Fokkert and colleagues comparing isCGM plus multiple daily injections with multiple daily injections plus self-management of blood glucose. This finding further supports that people with poorly controlled glucose using isCGM plus multiple daily injections could have substantial benefit by switching to closed-loop therapy.

Although the results by Choudhary and colleagues are significant, most participants using AHCL were still unable to achieve the consensus guideline target goal of an HbA1c of less than 7.0%,⁶ with only 27.8% achieving this goal in the AHCL group. Importantly, 0% of the participants in the control group using isCGM and multiple daily injections achieved this goal, which again shows the benefit of AHCL. Nonetheless, this low percentage of people achieving the target HbA1c

highlights shortcomings of closed-loop technologies and the need for improvements. Choudhary and

colleagues also theorise that a possible reason for this could be that a population with higher HbA1c might have a higher likelihood of missed or late boluses, more errors with carbohydrate counting, and a greater fear of hypoglycemia leading to increased intake of unnecessary carbohydrates. Future advances could include fully closed-loop systems that do not require entry of carbohydrates, integration of additional hormones including co-formulation of insulin with pramlintide [7], and more personalised and adaptive systems that can respond automatically to exercise and other life events [8].

There are many factors that contribute to peoples' choice of a glucose control therapy; cost, form factor including the size and number of devices that must be worn, insurance reimbursement, and improved glucose control are all important factors. The results in the study by Choudhary and colleagues indicate that an improvement in glucose control can be achieved using closed-loop therapy for people for whom multiple daily injections plus isCGM was not working. They also report patient-reported outcomes, which provide more information about whether people on isCGM plus multiple daily injection therapy would appreciate switching to closed-loop therapy. Quality of life scores improved for both the AHCL and the control group, but the improvement was larger for the AHCL group, although the difference was not significant. This finding is relevant because AHCL requires the person to wear both a sensor and a pump, thereby increasing patient burden compared with multiple daily injections plus CGM. The quality-of-life score improvements suggest that this is not a major impediment to adoption of AHCL. Reimbursement from insurance companies is essential to enable use of closed-loop technologies more broadly in the USA, Europe, and other countries around the world. More work is needed to assess the economic burden of closed-loop therapies compared with isCGM plus multiple daily injections. Improvements in HbA1c observed in the study by Choudhary and colleagues indicate the importance of comparing these cost differences to make closed-loop therapy more broadly reimbursable to people currently on isCGM and multiple daily injections with poorly controlled glucose.

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