AUTOMATED BOLUS CALCULATOR...

HELPS GLYCAEMIC CONTROL
Advanced carbohydrate counting can support people with diabetes in a more flexible insulin regimen that they can tailor to their lifestyles. A new study shows that the benefits of this approach are enhanced when it is supported by the use of an automated bolus calculator.

People with diabetes on insulin therapy generally have two regimen options. In fixed dosing, the individual adapts their food intake and activity level to their insulin. Flexible dosing, on the other hand, allows people to adapt their insulin dosing to their lifestyle. There are several flexible insulin therapy strategies, one of which involves advanced carbohydrate counting.

This systematic method for calculating an insulin bolus combines estimating the carbohydrate content of food intake, blood glucose measurement and evaluation of the factors that might influence insulin sensitivity, such as exercise, stress or illness. Advanced carbohydrate counting focuses on the impact of carbohydrate on post-prandial blood glucose with protein and fat assumed to be covered by basal insulin.

Estimating the carbohydrate content of a composite meal and subsequent calculation of the insulin bolus required to cover it require good arithmetical skills. Unfortunately, low levels of numeracy are common and, in people with Type 1 diabetes, there is a link between numeracy and glycaemic control.

**Automated bolus calculators**

To relieve people with diabetes of the stress associated with bolus calculation, and to prevent mistakes, a number of bolus calculators have been developed. The most advanced are automated and take into account the amount of insulin remaining in the body from previous boluses. While these advanced bolus calculators (ABCs) have been available to pump users for many years, they have only recently been introduced for those on multiple daily injections (MDIs).

The first study of the impact of ABCs on people with diabetes on insulin therapy was a four-month, randomised, parallel group open label trial. The participants had Type 1 diabetes for more than one year and were on MDI therapy. HbA1c was between 64 and 100 mmol/mol. Groups of up to 10 participants were assigned, after randomisation, to a 3.5h training course in advanced carbohydrate counting from a diettian and diabetes nurse. Those in the ABC group had additional training in the device set-up and use. After that, there was follow-up at two weeks and then at three, six, nine and 12 months.

Weight and HbA1c were measured at baseline and at the three, six, nine and 12 month visits. At these visits, participants were asked about occurrence of hypoglycaemia and results from their blood glucose meters and ABCs were downloaded. At the end of the study, the participants reported their use of advanced carbohydrate counting at breakfast, lunch, dinner and snack times over the study period using a visual analogue scale. Participants wore a continuous glucose monitoring (CGM) device at the beginning and end of the study for six days. The CGM readings were divided into three categories: below, within or above target range. A lower threshold of 3.9 mmol/l was used for the target range, but two different upper thresholds – 7.8 mmol/l and 10 mmol/l – were used for the upper thresholds.

The ABC used in this study was a palm-sized blood glucose meter with built-in bolus calculator function (ACCU-CHEK Aviva Expert; Roche Diabetes Care). It provides bolus advice based upon the blood glucose value, target blood glucose, insulin correction factor (insulin sensitivity factor), insulin to carbohydrate ratio, active insulin in the body, time of day, amount of carbohydrate to be consumed, health status, stress and exercise level. The device has memory function and various graphic display options.

The primary endpoint of the study was HbA1c change from baseline to study end. Secondary endpoints were change in distribution of CGM values, frequency and variability of blood glucose measurements and frequency of severe hypos.

The StenoABC study's aim was to test the hypothesis that long-term advanced carbohydrate counting with ABC results in greater improvements in HbA1c than advanced carbohydrate counting alone. Participants were people with suboptimal metabolic control and no previous experience of advanced carbohydrate counting.

**The StenoABC study**

The study was conducted at the Steno Diabetes Centre, Denmark, and was a 12-month randomised, parallel group label trial. The participants had Type 1 diabetes for more than one year and were on MDI therapy. HbA1c was between 64 and 100 mmol/mol. Groups of six to 10 participants were assigned, after randomisation, to a 3.5h training course in advanced carbohydrate counting from a dietitian and diabetes nurse. Those in the ABC group had additional training in the device set-up and use. After that, there was follow-up at two weeks and then at three, six, nine and 12 months.

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Results
Sixty six people completed the ABC arm of the study and 64 completed the control arm (no ABC). Overall, HbA1c was significantly reduced in both groups by the end of the study. In the ABC group, the reduction was -5.0mmol/mol (95% CI -6 to -3.5) and in the control group it was -2.2mmol/mol (95% CI -4 to -1). The median baseline HbA1c in the study population was 73mmol/mol. Participants with higher HbA1c at the start lowered their HbA1c by 4mmol/mol more than those with a lower starting HbA1c. Seven of those in the ABC group lowered their HbA1c by more than 6mmol/mol, compared with eight in the control group. At the end of the study, no participant had an HbA1c less than 53mmol/mol.

Downloads of the blood glucose meter and the ABC showed that the mean number of daily blood glucose measurements per participant was 3.7 in the ABC group, compared with 3.4 in the control group. The distribution of glucose values determined by CGM did not differ between groups at the start (10.5mmol/l and 10.4mmol/l). At the end of the study, there was no difference between the groups in time spent with glucose values less than 3.9mmol/l (4.5 and 4.4 per cent). However, when it came to time spent in both predetermined target ranges (3.9–7.8mmol/l and 3.9–10.0mmol/l), those in the ABC group spent more time within target range (30.6 and 50.1 per cent of time) compared with the control group (22.8 and 40.9 per cent of time). They also spent less time above target (45.4 and 45.4 per cent of time) than controls (73.0 and 54.8 per cent of time). At the end of follow-up, mean glucose values for the ABC group were 10.2mmol/l compared with 11.1mmol/l. Although weight gain was noted in both groups, there was no significant difference in this between groups.

Discussion
From this study, it is clear that training adults with poorly controlled Type 1 diabetes in advanced carbohydrate counting results in significantly reduced HbA1c when the process is supported by use of an automated bolus calculator. Furthermore, ABC users spent more time in target glycaemic range compared with controls. These improvements were achieved without weight gain or increase in hypo frequency. These positive findings may arise from ABC encouraging participants to take a more systematic approach to their advanced carbohydrate counting. This is borne out by the fact that 83 per cent of those on ABC reported consistent use of this tool, compared with only 55 per cent of controls.

The authors note that in the present StenoABC study, the same training programme was used as in the earlier 16-week BolusCal pilot study. This new study confirms findings from BolusCal – that advanced carbohydrate counting does improve HbA1c. It also deepens our knowledge of automated bolus calculation, by showing significant improvements in metabolic control when ABC is used as a support.

However, the reduction in HbA1c was nearly twice as large in BolusCal as in StenoABC; at -9mmol/mol. This may have been because participants in BolusCal had more contact with healthcare professionals. Continuous glucose monitoring measurements in BolusCal showed a trend towards those using ABC spending more time in target glycaemic range and these findings have now been corroborated by the StenoABC findings.

The ABACUS study also looked at the use of ABC with advanced carbohydrate counting and found a small, but significant, difference in HbA1c reduction between those who did, and did not, use this tool. The difference was only 2mmol/mol. However, ABACUS participants differed in various respects from those in the current study – they had either Type 1 or Type 2 diabetes and had previous experience of advanced carbohydrate counting – so the two studies are not directly comparable.

Of course, the clinical relevance of a reduction of 5mmol/mol in HbA1c found in the StenoABC study might be questioned. However, the importance of such small reductions in HbA1c among people with poorly controlled Type 1 diabetes is highlighted in the Diabetes Control and Complications Trial. This showed that lowering HbA1c from 75mmol/mol to 69mmol/mol may reduce microvascular complications by 20 per cent. So any approach that can achieve this is clearly worthwhile. Also, complication rates are higher among those with HbA1c greater than 64mmol/mol than among those with lower HbA1c. Therefore, it is encouraging that those with the higher baseline HbA1c had the most to gain by advanced carbohydrate counting. Another positive finding is that ABC group members spend more time in target glycaemic range than controls. Recent evidence suggests that glucose value distribution may be a better measure of glucose control than HbA1c.

It is encouraging that these improvements were achieved without any increase in the frequency of severe hypoglycaemia or time spent in hypoglycaemia. However, it is possible that the findings are skewed by under-reporting of hypoglycaemia by the participants. A recent study suggests that under-reporting is not uncommon, because of more restrictive European Union driving licence regulations. It was perhaps a little surprising that there was no difference in hypoglycaemia between the ABC and control groups, given that the calculator has a feature that prevents insulin stacking (it subtracts active insulin from its bolus advice) which would be expected to help reduce hypoglycaemia. It may be that this feature rarely came into play in the context of this study, with ABC participants only measuring glucose and carrying out bolus calculations 3.7 times a day on average. Another explanation for the lack of hypoglycaemia could be that participants generally showed hypoglycaemia avoidance behaviour, which is indicated by the relatively high HbA1c levels pre- and post-study in both groups.

The authors further note that the 3.5h training programme in StenoABC and BolusCal is shorter than advanced carbohydrate counting programmes elsewhere, such as DAFNE training, which lasts five days. However, findings are similar which raises the prospect of training people in advanced carbohydrate counting in shorter courses. StenoABC
used short training partly because of the resources available and partly because of an assumption that people with poorly controlled Type 1 diabetes might have been reluctant to invest five full days in diabetes management training.

The authors’ hypothesis is that those who have long-standing poor control can be difficult to motivate to invest time in their diabetes management, and this was supported by frequent cancellation and postponement of appointments by StenoABC participants, which led to extended follow-up for some. However, it was encouraging to see how those with long duration of Type 1 diabetes were still willing to change their approach, by taking on advanced carbohydrate counting with, or without, ABC.

Strengths of this study include robust design and relatively large number of participants. Lack of blinding is, of course, a limitation, but was inevitable because of the nature of the study.

In conclusion, based on the present and previous studies, adults with Type 1 diabetes should be offered training in advanced carbohydrate counting and automated bolus calculator use. The benefits are both statistically significant and clinically relevant, while costs and the risk of side effects are low.