Technology greater than the sum of its parts

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It is clear that improving glycaemic control reduces the risk of microvascular complications in type 1 diabetes (T1D) and, to a lesser extent, also reduces macrovascular risk (Diabetes Control and Complications Trial Research Group, 1993). The challenge for people with diabetes is to reduce their HbA_{1c} level without unacceptable disruption to normal life.

The most feared risk of tight glycaemic control in T1D is hypoglycaemia (Anderbro et al, 2010). Much progress has been made in recent years in reducing the risk of hypoglycaemia while maintaining tight glycaemic control. The use of continuous subcutaneous insulin infusion via an insulin pump would be considered by many to be the state-of-the-art regimen for the management of T1D, and there has been growing interest in combining an insulin sensor with an insulin pump to move towards a close-loop system or "artificial pancreas".

This important study (Bergenstal et al, 2010; summarised alongside) of just under 500 people with T1D from 30 centres in the USA and Canada provides the first substantive evidence that the closed-loop approach to treatment may be beneficial. Children and adults who were unable to achieve target glycaemic control were randomised to either multiple daily insulin injections (a continuation of their usual therapy) or sensor-augmented insulin pump therapy. Results were analysed at 1 year.

The main finding was that the combined sensor and pump produced a significant reduction in HbA_{1c} levels compared with multiple daily injections (7.5 vs 8.1% [58 vs 65 mmol/mol]; $P<0.001$). This reduction in HbA_{1c} using the combination of technologies was greater than would be expected from studies of sensors or pumps alone. Not surprisingly, Bergenstal et al reported that the greatest benefit was seen in those participants who wore the sensor most.

For the person with T1D, the price to be paid for use of these technologies – in addition to wearing a pump – is the regular replacement of the sensor electrode.

From a health economics perspective this technology is expensive. Huang and colleagues (2010; summarised below) highlight the considerable uncertainty around the cost-effectiveness of glucose sensor technology. The health economics arguments for the technology are mainly based on the potential reduction in microvascular complications. If the reduction in rates of hypoglycaemia are included, the case is strengthened, yet people who had experienced severe hypoglycaemia were excluded from Huang et al's study. This is understandable when their primary outcome was change in HbA_{1c}, but is disappointing as this group are one of the most likely to benefit from use of the technology.

Anderbro T, Amsberg S, Adamson U et al (2010) Fear of hypoglycaemia in adults with type 1 diabetes. *Diabet Med* **27**: 1151–8

Diabetes Control and Complications Trial Research Group (1993) The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* **329**: 977–86

DIABETES CARE

CGM: A cost-effective diabetes technology

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓

1 Although continuous glucose monitoring (CGM) enables people with T1D to achieve better glycaemic control, its cost-effectiveness is uncertain.

2 A societal cost-effectiveness analysis was performed on a study population from the Juvenile Diabetes Research Foundation CGM trials.

3 Direct costs (e.g. CGM technology and training) and indirect costs (e.g. time spent on diabetes care) and quality-of-life (QoL) effects were calculated for the 6-month period.

4 Analyses revealed improved QoL and glycaemic control, and indicated that CGM is a cost-effective technology.

Huang ES, O'Grady M, Basu A et al (2010) The cost-effectiveness of continuous glucose monitoring in type 1 diabetes. *Diabetes Care* **33**: 1269–74

NEW ENGLAND JOURNAL OF MEDICINE

Sensor-augmented pump therapy gives better HbA_{1c} results

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

1 Sensor-augmented pump therapy, where an insulin pump is combined with continuous glucose monitoring, aims to improve glycaemic control without increasing the risk of hypoglycaemia by providing a "closed-loop" system.

2 The authors sought to determine whether people with T1D and poor glycaemic control using conventional, multiple daily insulin injections and blood-glucose testing could achieve better results using sensor-augmented pump therapy.

3 Participants comprised 485 people with T1D (329 adults; 156 children) who were randomised to either sensor-augmented pump therapy or to their usual regimen of multiple daily insulin injections and followed-up for 1 year.

4 At baseline, mean HbA_{1c} level was 8.3% (67 mmol/mol) for both groups; at 1 year, the mean HbA_{1c} level was 7.5% (58 mmol/mol) for people in the sensor-augmented pump therapy group, compared with 8.1% (65 mmol/mol) for those in the multiple injection group ($P<0.001$).

5 More people reached the HbA_{1c} target of <7% (<53 mmol/mol) in the sensor-augmented pump therapy group, with no difference in the number of hypoglycaemic events between the groups.

6 The authors concluded that sensor-augmented pump therapy resulted in significantly better glycaemic control in both adults and children with T1D.

Bergenstal RM, Tamborlane WV, Ahmann A et al (2010) Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes. *N Engl J Med* **363**: 311–20

"The closed-loop system delivering insulin plus high-gain glucagon significantly reduced the frequency of hypoglycaemic episodes as well as the need for carbohydrate treatment."

DIABETOLOGIA

Onset of T1D in young adulthood affects long-term earnings

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 There is little in the literature on the effect of developing T1D in young adulthood.

2 As this is a time when choices in education are made, followed by establishment in the workplace, the onset of a chronic disease such as T1D may affect earnings.

3 The authors aimed to determine whether the onset of T1D in young adulthood would affect adults' annual income.

4 Data before and after the onset of T1D were obtained from the Econ-Diabetes Incidence Study in Sweden database, which contains socioeconomic data for young adults who developed diabetes between 1983 and 2005, and controls.

5 This study examined data from 3650 people born between 1949 and 1970 who developed T1D between 15 and 34 years of age and data from 14 629 controls. Education and progression of annual earnings were compared, before and after the onset of diabetes, with those of the controls.

6 There were no significant differences in earnings between the before-onset and control groups.

7 The onset of diabetes was associated with progressively lower earnings each year compared with the controls. Ten years after the onset of diabetes people earned 4% less; 20 years after, they earned 10% less.

8 It was concluded that the onset of T1D in young adulthood has a long-term, detrimental effect on earnings.

Steen Carlsson K, Landin-Olsson M, Nyström L et al (2010) Long-term detrimental consequences of the onset of type 1 diabetes on annual earnings – evidence from annual registry data in 1990–2005. *Diabetologia* **53**: 1084–92

DIABETES CARE

GADAs and IA-2As predict progression to T1D

Readability	✓✓✓
Applicability to practice	✓
WOW! factor	✓✓

1 The presence of GAD antibodies (GADAs) and islet antigen-2 antibodies (IA-2As) combined can be used to predict the development of T1D in first-degree relatives of people with T1D.

2 This study sought to determine whether the presence of GADAs and IA-2As combined predicted the development of T1D over 27 years in a general population.

3 A population-based sample of 3475 Finnish people (aged 3–18 years) were screened for GADAs and IA-2As in 1980; 2375 were resampled in 1986. Participants were observed until the end of 2007 for the development of T1D.

4 Initial GADAs and IA-2As identified 61% of people who developed T1D over the next 27 years.

5 Screening for GADAs and IA-2As is, it was concluded, a useful T1D predictor.

Knip M, Korhonen S, Kulmala P et al (2010) Prediction of type 1 diabetes in the general population. *Diabetes Care* **33**: 1206–12

DIABETES CARE

Strong link between high HbA_{1c} and both CVD and CHD risk

Readability	✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 The authors sought to determine the relationship between HbA_{1c} and coronary heart disease (CHD), stroke and cardiovascular disease (CVD).

2 This observational study comprised 7454 people (aged 20–65 years) with T1D (1–35 years' duration).

3 Participants were followed-up for 5 years; endpoints were fatal/non-fatal CHD, fatal/non-fatal stroke, fatal/non-fatal CVD and total mortality.

4 In total, 4186 participants had a baseline HbA_{1c} level of 5.0–7.9% (31–63 mmol/mol) and 3268 were within 8.0–11.9% (64–107 mmol/mol).

5 Each percentage-point increase in baseline HbA_{1c} or updated mean HbA_{1c} was associated with risk increases of 31–34% for fatal/non-fatal CHD and 26–32% for fatal/non-fatal CVD.

6 Higher HbA_{1c} was found to progressively increase the risk of CHD and CVD.

Eeg-Olofsson K, Cederholm J, Nilsson PM et al (2010) Glycaemic control and cardiovascular disease in 7454 patients with type 1 diabetes. *Diabetes Care* **33**: 640–6

DIABETES CARE

Closed-loop delivery with high-gain glucagon reduces hypoglycaemia

Readability	✓✓✓
Applicability to practice	✓
WOW! factor	✓✓

1 Despite advances in insulin delivery and blood glucose monitoring, hypoglycaemia remains a common complication of T1D therapy.

2 A novel, automated, sensor-controlled, closed-loop insulin delivery system, that included an amperometric glucose sensor that controls insulin delivery as well as administering glucagon to prevent hypoglycaemia was developed.

3 Thirteen adults with T1D participated in one closed-loop study with insulin plus placebo and in one study with insulin plus glucagon; seven received high-gain glucagon and six received low-gain glucagon.

4 The closed-loop system delivering insulin plus high-gain glucagon significantly reduced the frequency of hypoglycaemic episodes as well as the need for carbohydrate treatment.

Castle JR, Engle JM, Youssef JE et al (2010) Novel use of glucagon in a closed-loop system for prevention of hypoglycaemia in type 1 diabetes. *Diabetes Care* **33**: 1282–7