DIABETES

Closed-loop insulin delivery helps meet glycaemic targets

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

1 Closed-loop insulin delivery, assessed over approximately 30 hours, was compared with a 3-day assessment of open-loop control.

2 The closed-loop delivery was based on subcutaneous glucose sensing and subcutaneous insulin delivery calculated using a model of β-cell multiphasic insulin response to glucose.

3 Data were collected from ten volunteers with type 1 diabetes (two men and eight women) with a mean age of 43.4 ± 11.4 years and a duration of diabetes of 18.2 ± 13.5 years.

4 Fasting plasma glucose was reduced from 160 ± 66 mg/dl at the start of close-loop delivery (07:00) to 71 ± 19 mg/dl (preprandial) by 13:00.

5 The next morning, fasting glucose for closed-loop delivery was similar to the target of 120 mg/dl (124 ± 25 mg/dl; $P > 0.05$).

6 Open- and closed-loop mean glucose levels were 133 ± 63 and 133 ± 52 mg/dl, respectively ($P > 0.65$).

7 Under closed-loop insulin, glucose was in the range 70–180 mg/dl 75% of the time, compared with 63% of the time for open-loop delivery.

8 The two treatments had a similar incidence of hypoglycaemia, which was never categorised as severe.

9 The authors conclude that automated external closed-loop insulin delivery can effectively manage glucose levels.

Steil GM, Rebrin K, Darwin C et al (2007) Feasibility of automating insulin delivery for the treatment of type 1 diabetes. *Diabetes* **55**: 3344–50

Bright future for closed-loop therapy?

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Clearly, the goal of diabetes care is to prevent or cure the condition. There has been understandable excitement in recent years about islet cell transplantation and where that may lead in the next few years. In the meantime, the aim of insulin therapy is to produce normal glucose control with no risk of hypoglycaemia.

However good our insulin regimens are, they are clearly a long way from reproducing normality. Insulin pumps are better but are only as good as the input information. Continuous glucose-sensing devices give us a great deal more information about what is happening to glucose control within the body. The next obvious move is to try and combine the devices and close the loop. There are three key components to any closed-loop delivery system. First, there needs to be a monitoring device that measures ambient glucose at appropriate intervals. This information then needs to be processed to determine when and how much, if any, insulin needs to be administered. The third part is the insulin pump that is instructed to administer the insulin. Key features of the system would be safety (avoidance of over- or underdosing with insulin), durability (the system needs to perform for indefinite periods) and reliability (the sensing device needs to continue to function efficiently for weeks or even months).

There is debate about whether the best device would be external or internal, intravascular, intraperitoneal or subcutaneous. The problem so far has been to develop an algorithm that converts an interstitial fluid glucose value into an order to deliver insulin. Owing to the lag between sensing glucose and the action of administered insulin, the device needs to use glucose values to predict what is going to happen in the next few minutes. As we all know, predicting the future even in the short term is not easy.

The paper summarised to the left does not fulfil all these essential criteria but does represent a proof of principle. It is possible, at least for a few days, to automate the process of insulin adjustment. The results are not astounding but are a significant step along the path.

It is easy to imagine that in 15 years time we will have an implantable system that removes the need for daily management of blood glucose. The question is, will other advances have removed the need for this technology?

DIABETES, OBESITY AND METABOLISM

Metformin improves insulin sensitivity and glycaemic control in type 1

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

1 The effect of adjuvant metformin on control of type 1 diabetes and quality of life was investigated in this 3-month, open-labelled pilot study.

2 Sixteen individuals aged 18–40 years were enrolled and were administered 500–850 mg metformin twice daily.

3 Insulin sensitivity increased from $0.86 \pm 0.33 \times 10^{-4}$ to $1.17 \pm 0.48 \times 10^{-4}$ μU/ml/min ($P = 0.043$), resulting in reduced insulin requirement and mean daily blood glucose levels. Quality of life also improved significantly ($P < 0.002$) and BMI decreased over a 2-year period (0.05 ± 0.05 kg/m^2; $P = 0.042$).

4 HbA_{1c} levels and body composition were not affected; however, a retrospective review of 30 individuals with type 1 diabetes receiving metformin for at least 4 months demonstrated a significant initial HbA_{1c} reduction ($P = 0.01$) that diminished with prolonged treatment.

5 Adjuvant metformin therefore improves insulin sensitivity, glycaemic control and quality of life in overweight adults with type 1 diabetes.

Moon RJ, Bascombe LA, Holt RI (2007) The addition of metformin in type 1 diabetes improves insulin sensitivity, diabetic control, body composition and patient well-being. *Diabetes, Obesity and Metabolism* **9**: 143–5

"The sensor-augmented pump improved glycaemic control in the short term for young people with type 1 diabetes."

"Optimal HbA_{1c} before stopping any contraception should therefore be used as the gold standard definition of pre-pregnancy care in women with diabetes."

DIABETES

Intensive glycaemic treatment effect on coronary artery calcification

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

1 Coronary artery calcification (CAC), a measure of atherosclerosis, was assessed in the Epidemiology of Diabetes Interventions and Complications (EDIC) study – a follow up of the Diabetes Control and Complications Trial (DCCT) type 1 diabetes cohort.

2 Computed tomography was used to measure CAC in 1205 people involved in the EDIC study 7–9 years after the DCCT ended.

3 CAC measurements of >0 Agatston units were prevalent in 31% of participants, while only 8.5% presented with CAC >200 Agatston units.

4 In the primary retinopathy prevention cohort, intensive glycaemic treatment was associated with significantly lower geometric mean CAC scores and a lower prevalence of CAC above 0 Agatston units than conventional treatment. These differences were not observed in the secondary intervention cohort.

5 In the combined cohort, there was a lower incidence of CAC of above 200 Agatston units.

6 CAC was also significantly associated with a large waist-to-hip ratio, smoking, hypertension, hypercholesterolaemia and mean HbA_{1c} levels.

7 During the DCCT if an individual had received prior intensive treatment for diabetes they had a lower risk of atherosclerosis largely owing to reduced HbA_{1c}.

Cleary PA, Orchard TJ, Genuth S et al (2007) The effect of intensive glycemic treatment on coronary artery calcification in type 1 diabetic participants of the Diabetes Control and Complications Trial/ Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study. *Diabetes* **55**: 3556–65

BJOG

Pre-pregnancy care reduces risk of adverse outcomes

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

1 Women with pre-gestational type 1 diabetes (n=423; mean age: 28.3 years; SD: 5.5 years) were examined to test the effect of planning and care on adverse outcomes, including early pregnancy loss, major congenital anomaly and perinatal death.

2 Data were collected on care parameters such as whether or not the pregnancy was planned, if rubella antibody status was recorded, if there was pre-pregnancy counselling, if folic acid was taken pre-conception and whether or not an optimal HbA_{1c} level of <7% had been achieved before contraception was discontinued.

3 Miscarriage occurred in 54 (12.8%) women, ectopic pregnancy in two and molar pregnancy in one. Abortion was induced in seven (1.7%) pregnancies owing to a fetal anomaly and a further 12 babies (3.3% of live births) had a major congenital anomaly.

4 The lowest rate of complications was associated with prior optimal HbA_{1c} levels (OR: 0.2; 95% CI: 0.06–0.67), which led to a five-times smaller odds ratio of adverse outcomes.

5 Optimal HbA_{1c} before stopping any contraception should therefore be used as the gold standard definition of pre-pregnancy care in women with diabetes.

Pearson DW, Kernaghan D, Lee R et al (2007) The relationship between pre-pregnancy care and early pregnancy loss, major congenital anomaly or perinatal death in type I diabetes mellitus. *BJOG* **14**: 104–7

JOURNAL OF PEDIATRICS

Sensor-augmented pump improves short-term glycaemic control

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

1 Sensor-augmented pumps combine real-time continuous glucose monitoring and an insulin pump.

2 An HbA_{1c} of less than 8% is only achieved in 30% of children with type 1 diabetes.

3 This study aimed to assess if glycaemic control is improved in young people with type 1 diabetes using a sensor-augmented pump.

4 The participants (n=10; mean age: 14.1±2.6 years; diabetes duration: 9.1±3.3 years) used an insulin pump for at least a year and their HbA_{1c} was measured during research visits at weekly intervals for a month.

5 The mean HbA_{1c} decreased from 8.1±0.9% at baseline to 7.8±0.9% at study end.

6 Following seven subcutaneous glucose measurements, the mean glucose value decreased from 167±19 mg/dl at test points 1 and 2 to 155±22 mg/dl for tests 6 and 7.

7 Nine children experienced mild hypoglycaemia but the mean number of 5-minute events decreased during sensor-augmented pump use.

8 The most common treatment change was increasing one or more basal rates on the pump (42%). Others included decreasing basal rates (15%), increasing insulin-to-carbohydrate dose (30%), increasing the amount of insulin given in the correction algorithm (9%) and changing exercise regimens (4%).

9 The sensor-augmented pump improved glycaemic control in the short term for young people with type 1 diabetes. Hypo- and hyperglycaemic episodes were also reduced in frequency.

Halvorson M, Carpenter S, Kaiserman K, Kaufman FR (2007) A pilot trial in pediatrics with the sensor-augmented pump: combining real-time continuous glucose monitoring with the insulin pump. Journal of Pediatrics **150**: 103–5

Type 1 diabetes

DIABETES CARE

Continuous glucose monitoring improves glycaemic control

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

1 A new, continuous glucose monitoring device, Guardian RT, allows users to set alarms for hyper- and hypoglycaemic events.

2 A 3-month randomised trial assessed 156 people with type 1 diabetes (81 young people aged 8–18.9 years and 81 adults aged 19–59.5) and an HbA_{1c} level above or equal to 8.1%.

3 The three treatment groups were: continuation of conventional self monitoring; Guardian RT continuously; Guardian RT biweekly for 3-day periods.

4 Baseline HbA_{1c} levels were 9.5 ± 1.1, 9.6 ± 1.2 and 9.7 ± 1.3% in the continuous Guardian RT, biweekly Guardian RT and control groups, respectively.

5 Compared with controls, continuous glucose monitoring significantly reduced HbA_{1c} by 0.6 ± 0.8 versus 0.2 ± 0.8% ($P=0.008$) at 1 month, and 1.0 ± 1.1 versus 0.4 ± 1.0% ($P=0.003$) at 3 months. Noncontinuous Guardian RT levels were not significantly different from controls.

6 At 3 months, 50% of continuous glucose monitoring users had a reduction in HbA_{1c} of ≥1% and 26% had a reduction of ≥2%. Individuals on the new device also made insulin, dietary or lifestyle changes based on the information the monitor provided.

7 Continuous glucose monitoring therefore improves glycaemic control in individuals with poor self monitoring. Long-term efficacy and clinical feasibility should now be investigated.

Deiss D, Bolinder J, Riveline JP et al (2007) Improved glycemic control in poorly controlled patients with type 1 diabetes using real-time continuous glucose monitoring. *Diabetes Care* **29**: 2730–2

METABOLISM: CLINICAL AND EXPERIMENTAL

Rising incidence of diabetic ketoacidosis

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

1 The incidence of diabetic ketoacidosis (DKA) is increasing.

2 Since ethnic minorities are more prone to type 2 diabetes, this study investigated the characteristics of ethnic minority people prone to DKA over a 3-year period.

3 DKA was observed in 168 individuals, 97% of whom were Hispanic or African–American. Type 2 diabetes also presented in 32%.

4 New-onset diabetes was recorded in 25% of patients and was most common in type 2 diabetes ($P<0.0001$) and African–Americans ($P=0.008$). Type 2 diabetes was also more prevalent in African–Americans than type 1 diabetes ($P=0.04$)

5 Hispanic patients with type 1 diabetes were most likely to be re-admitted with DKA ($P=0.0001$).

6 Acidosis was more severe for type 1 diabetes than type 2, as demonstrated by significantly lower pH ($P=0.03$), lower bicarbonate ($P=0.02$) and a larger anion gap ($P=0.005$). The creatinine levels were also lower and associated with precipitating causes.

7 New-onset diabetes led to higher HbA_{1c} levels but this trend was similar in type 1 and 2 diabetes.

8 The only reported mortality was in 2% of the African–Americans with type 2 diabetes.

9 DKA is occurring more frequently in type 2 diabetes and new-onset type 2 diabetes accounts for approximately 60% of new cases of DKA. Therefore, primary prevention of diabetes is very important.

Nyenwe E, Loganathan R, Blum S et al (2007) Admissions for diabetic ketoacidosis in ethnic minority groups in a city hospital. *Metabolism: Clinical and Experimental* **56**: 172–8