Technology

Long-term efficacy of insulin pump therapy

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There is surprisingly little data on the long-term efficacy of insulin pump therapy. Maintenance of improved glycaemic control after transferring from multiple daily injections to continuous subcutaneous insulin infusion (CSII) is crucial to any cost-effectiveness analysis of CSII.

The NICE appraisal of CSII (TA151) concluded that cost-effectiveness of CSII could be expected when initiated for high HbA_{1c} when the pre-CSII HbA_{1c} was ≥69 mmol/mol (8.5%) and, therefore, the likely reduction would be ≥10 mmol/mol (0.9%) (NICE, 2008). The evidence base for this came from a meta-analysis of six randomised controlled trials and 20 before/after cohort studies (Pickup et al, 2008). The mean duration of CSII in these studies ranged from 6–48 months, but only four studies went beyond 24 months. Therefore, there is concern that the cost-effectiveness of CSII may be overstated if HbA_{1c} reduction is not maintained long term. The studies from Orr et al and Nixon et al (both summarised alongside) provide some welcome insight into how effective HbA_{1c} control can be maintained in the long term with CSII.

Orr et al report on a large cohort of 200 adults with type 1 diabetes who had a mean duration of pump therapy of 6.1 years from Kingston, Ontario, Canada. Mean HbA_{1c} decreased from 72 mmol/mol (8.7%) to a nadir of 58 mmol/mol (7.5%) at 6 months. Thereafter the reduction in HbA_{1c} was not as great, but mean HbA_{1c} remained lower than at initiation, ranging from 62–66 mmol/mol (7.8–8.2%).

Thirty-nine people had a duration of CSII usage greater than 10 years. This group showed a similar pattern of HbA_{1c} reduction, but past the 10-year mark the mean HbA_{1c} was 64 mmol/mol (8.0%), having been 74 mmol/mol (8.9%) at initiation. Thus for this cohort, CSII remained cost-effective in regards to the NICE appraisal at over 10 years.

Whilst this study found, as others have previously, that the greater the starting HbA_{1c} the bigger the reduction in HbA_{1c} on CSII, those starting CSII with an HbA_{1c} >86 mmol/mol (10.0%) rarely reached target HbA_{1c}. However, in contrast to the other participants of the study, this group with the particularly high HbA_{1c} on starting CSII, showed a continued reduction in HbA_{1c} over time, with a mean HbA_{1c} of 64 mmol/mol (8.0%) at 8–10 years.

The study also considered what factors influenced the ability to achieve the target HbA_{1c} of ≤53 mmol/mol (7.0%) in the cohort as a whole. In addition to a high HbA_{1c} at initiation, mental illness, smoking and missed appointments were associated with a failure to achieve target HbA_{1c}.

In a second study, Nixon et al report on a smaller cohort of 35 adults with type 1 diabetes from Guy's Hospital, London. The participants all had an HbA_{1c} of ≥64 mmol/mol (8.0%) at CSII initiation and a duration of pump usage of at least 5 years. HbA_{1c} declined from a mean of 78 mmol/mol (9.3%) at initiation to a nadir of 61 mmol/mol (7.7%), and then worsened to 65 mmol/mol (8.1%) at 5 years. The authors were able to identify three cohort groups in terms of HbA_{1c} response – 31% of participants had a sustained reduction in HbA_{1c}, maintained <64 mmol/mol (8.0%) throughout; 57% had an initial reduction in HbA_{1c} at 2 years then a deterioration at 5 years, although HbA_{1c} remained significantly lower than at CSII initiation (69 vs 78 mmol/mol [8.5 vs 9.3%], respectively); and 12% showed no significant improvement in HbA_{1c}. There were no obvious associations to explain the failure to improve HbA_{1c} in the third group, although non-responders did have a higher BMI.

Encouragingly, both studies would appear to confirm that for the vast majority of users, CSII reduces HbA_{1c} over the long term and that the mean sustained reduction in HbA_{1c} at least meets NICE criteria for cost-effectiveness. There is probably a small percentage of individuals who will not achieve any significant reduction in HbA_{1c} and as Nixon et al observe, what we now require is the identification of the factors that prevent improvement in HbA_{1c}, and whether these are modifiable or not. In this way, CSII can be targeted to those who will benefit, and appropriate measures can be put in place to support pump users to recover optimised control should HbA_{1c} start to rise. ■

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Diabetes Technol Ther

Long-term CSII efficacy: HbA_{1c} and associated predictors

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 The long-term efficacy of continuous subcutaneous insulin infusion (CSII) was investigated. HbA_{1c} was used as a measure of glycaemic control and demographic factors potentially associated with glycaemic control were investigated as predictors of pump efficacy.

2 In total, 200 people with T1D were involved in this retrospective observational study of real-world clinical data in Ontario, Canada. Said data were collected 3 months prior to pump initiation and up to 15 years after.

3 The cohort's mean age and duration of T1D at initiation were 35.4 years and 22.4 years, respectively, and there were 23 individuals who were under the age of 18 years at initiation.

4 Mean HbA_{1c} at initiation was 72 mmol/mol (8.7%) and decreased to a nadir of 58 mmol/mol (7.5%) 6 months' post-initiation (standard deviation=1.0; $P<0.001$). HbA_{1c} slowly increased after this time, but remained lower than pre-CSII HbA_{1c} ($P<0.001$).

5 Most of the improvement in HbA_{1c} occurred in the first 6 months after initiation, regardless of pre-CSII HbA_{1c} levels. The authors suspect that the initial drop in HbA_{1c} was related to higher adherence towards the recommended pump practices at initiation, which then decreased over time.

6 It is worth noting that continuous glucose monitoring was used by only 2% of the participating cohort during any portion of the follow-up.

7 Poor pre-pump HbA_{1c}, missed appointments, mental illness, and smoking were predictors for those who were less likely to achieve an HbA_{1c} target of ≤53 mmol/mol (7.0%) on CSII.

Orr CJ, Hopman W, Yen JL, Houlden R (2015) Long-term efficacy of insulin pump therapy on glycemic control in adults with type 1 diabetes mellitus. *Diabetes Technol Ther* **17**: 49–54

Diabetic Medicine

Patterns of HbA_{1c} change over 5 years post-pump initiation

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! Factor	✓✓✓✓

1 The UK-based authors investigated patterns of long-term HbA_{1c} change among people with T1D managed by continuous subcutaneous insulin infusion (CSII), who began pump therapy after having poorly controlled T1D while on multiple daily injections (MDIs) of insulin.

2 Thirty-five adults (28 women) who had elevated HbA_{1c} of ≥64 mmol/mol (8%) on MDIs when they were switched to CSII were studied. Computerised data records of at least 5 years were analysed.

3 The cohort could be split into three sub-groups based on differing patterns of 5-year HbA_{1c} change. Group A – those with improvements followed by a deterioration (57%); group B – those with improvements that were sustained (31%); and group C – those where HbA_{1c} did not change significantly from baseline (12%).

4 The baseline HbA_{1c} was similar between groups, but only group B maintained an HbA_{1c} <64 mmol/mol (8%) for the whole 5-year period.

5 There were no significant differences between groups A, B and C for age, proportion of men versus women, duration of diabetes or fear of hypoglycaemia score. The only significant difference was for BMI; BMI was higher in group C versus group A or group B (31.0±5.2 kg/m^2 vs 25.9±3.3 kg/m^2 vs 25.2±3.1 kg/m^2; P=0.02 for both).

6 The authors come to the conclusion that non-responders of CSII are likely to be overweight or obese.

Nixon R, Folwell R, Pickup JC (2014) Variations in the quality and sustainability of long-term glycaemic control with continuous subcutaneous insulin infusion. *Diabet Med* **31**: 1174–7

Ir J Med Sci

Pre-pregnancy care

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! Factor	✓✓✓

1 The efficacy of insulin pump therapy versus multiple daily injection (MDI) therapy was investigated for pre-pregnancy care (before conception) among women with T1D.

2 In a cohort of 464 women (40 treated with pump therapy) in Dublin, Republic of Ireland, a retrospective review took place to compare HbA_{1c} control and pregnancy outcomes.

3 In those who attended pre-pregnancy care, the pump group had lower HbA_{1c} levels than those using MDI at booking to antenatal services (P=0.03).

4 Gestational age at delivery and birth weight did not differ between groups, but higher Caesarean section rates were associated with pump use (P<0.001), duration of diabetes (P=0.002) and parity (P=0.006).

5 Pre-pregnancy care and pump usage can lower HbA_{1c} peri-conception.

Neff KJ, Forde R, Gavin C et al (2014) Pre-pregnancy care and pregnancy outcomes in type 1 diabetes mellitus: a comparison of continuous subcutaneous insulin infusion and multiple daily injection therapy. *Ir J Med Sci* **183**: 397–403

J Diabetes Sci Technol

Meal bolus insulin delivery with an AP system

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 Different meal-time bolus strategies were compared when using an artificial pancreas (AP) system.

2 In a trial of 53 people with T1D (age range 12–65 years), four settings were assessed: standard bolus delivered with the meal (n=51); standard bolus delivered 15 minutes prior to the meal (n=40); over-bolus of 30% delivered with the meal (n=40); and bolus purposely omitted (n=46).

3 Meal carbohydrate (CHO) intake was 1 g of CHO/kg of body weight up to a maximum of 100 g. For the fourth strategy, the maximum was 50 g.

4 The AP system handled the four bolus situations safely, but there were elevated post-prandial glucose levels in most people. This was most likely secondary to suboptimal performance of the algorithm.

Chase HP, Doyle FJ 3rd, Zisser H et al (2012) Multicenter closed-loop/hybrid meal bolus insulin delivery with type 1 diabetes. *J Diabetes Sci Technol* **16**: 623–32

J Diabetes Sci Technol

JewelPUMP™: Accuracy of insulin delivery

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 The JewelPUMP™ (JP) is a new patch pump based on a microelectromechanical system that operates without any insertion plunger.

2 The infusion accuracy of the JP was evaluated for the first time *in vitro* and *in vivo* in the current report.

3 Thirteen people with T1D used the JP while simultaneously using their own pump for 2 days.

4 The JP was filled with physiological serum and showed a reduced absolute median error rate in vitro over a 15-minute observation window compared to other pumps, but there was no difference over 24 hours.

5 The JP was also found to be easier to wear than conventional pumps.

Borot S, Franc S, Cristante J et al (2014) Accuracy of a new patch pump based on a microelectromechanical system (MEMS) compared to other commercially available insulin pumps: results of the first in vitro and in vivo studies. *J Diabetes Sci Technol* **8**: 1133–41

"The authors conclude that non-responders of continuous subcutaneous insulin infusion are likely to be overweight or obese."

Commentary references

NICE (2008) *Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus* (TA151). NICE, London. Available at https://www.nice.org.uk/guidance/ta151 (accessed 25.02.15)

Pickup JC, Sutton AJ (2008) Severe hypoglycaemia and glycaemic control in type 1 diabetes: meta-analysis of multiple daily insulin injections compared with continuous subcutaneous insulin infusion. *Diabet Med* **25**: 765–74