

## Technology

### CSII confers a greater reduction in severe hypoglycaemia than MDI



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Despite increasing evidence for the benefits of delivering insulin by continuous subcutaneous insulin infusion (CSII) over multiple daily injections (MDI), there has still been some scepticism about the magnitude of this benefit, and whether it applies to long-acting insulin analogue-based MDI to the same extent as isophane insulin-based or insulin lente-based MDI therapy.

The original NICE guidance on CSII therapy from 2003 reflected a conservative interpretation of the potential benefits of CSII based on meta-analyses of randomised controlled trials, most of which predated 1990. To address this lingering scepticism, Pickup and Sutton have performed a meta-analysis (summarised alongside) of randomised controlled trials, and before-and-after studies – that is, studies comparing outcomes of MDI therapy before CSII initiation with those after CSII initiation. The studies chosen for the meta-analysis have been published since 1996, and so reflect modern pump technology; four of the studies used insulin glargine as the long-acting component of MDI therapy.

There are two important conclusions from the meta-analysis. Firstly, HbA<sub>1c</sub> levels and rates of severe hypoglycaemia were significantly reduced when using CSII compared with MDI, and the

higher the rate of severe hypoglycaemia or HbA<sub>1c</sub>, the greater the benefit from CSII. There is a good linear correlation between baseline rates of severe hypoglycaemia and HbA<sub>1c</sub> and the reduction achieved; so, for example, at a baseline HbA<sub>1c</sub> of 9%, an absolute reduction of around 1% would be expected. Secondly, while the relatively few studies using glargine-based MDI resulted in large confidence intervals, there was still a significant HbA<sub>1c</sub> reduction with CSII compared with MDI in these studies, which is of the same magnitude as that achieved with CSII in the isophane insulin-based or insulin lente-based studies.

Thus, CSII appears equally superior to all MDI-based regimens, and a person with higher HbA<sub>1c</sub> levels should not be denied CSII on the assumption that his or her poor control is indicative of problems complying with the insulin regimen, rather than a failure of MDI-based therapy for that individual. It is the information from this meta-analysis that was crucial to the NICE review of pump therapy (NICE, 2008), and, in particular, the recommendation that CSII be considered for adults and adolescents with an HbA<sub>1c</sub> > 8.5% despite optimised MDI, in addition to the existing indication for those suffering from disabling hypoglycaemia. Implementation of this evidence-based recommendation should extend pump usage from around 2% to around 20% of adults and adolescents with type 1 diabetes.

NICE (2008) *Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (review of technology appraisal guidance 57)*. NICE, London

### DIABETIC MEDICINE

### Greater reduction in severe hypoglycaemia with CSII than MDI

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

1 Continuous subcutaneous insulin infusion (CSII) and multiple daily insulin injections (MDI) are treatment methods for intensifying insulin therapy in people with type 1 diabetes.

However, the comparative efficacy of CSII and MDI had remained an area of controversy.

2 This authors of this paper performed a literature review of the Medline and Embase databases to find randomised controlled trials or before-and-after studies comparing CSII and MDI, published between 1996 and 2006.

3 Sixty-one studies were identified in the search, with 21 matching the inclusion criteria and giving 22 data sets, due to one study reporting results in two groups of people.

4 Severe hypoglycaemia in individuals using MDI was found to be associated with duration of diabetes, and was more frequent than in the CSII group.

5 HbA<sub>1c</sub> levels were higher in those on MDI therapy than in those using CSII ( $P=0.042$ ). In those individuals who switched from MDI to CSII due to poor glycaemic control, the reductions in HbA<sub>1c</sub> were the greatest.

6 Compared with MDI, severe hypoglycaemia was reduced with CSII, especially in those individuals with higher initial severe hypoglycaemia rates whilst being treated with MDI ( $P<0.001$ ).

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. *Diabetic Medicine* 25: 765–74

### HORMONE AND METABOLIC RESEARCH

### Continuous glucose monitoring useful in people with cystic fibrosis

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

1 This study aimed to investigate glucose tolerance in individuals with cystic fibrosis, and to ascertain the efficacy of continuous subcutaneous

glucose monitoring in these individuals.

2 Glucose tolerance was determined using an oral glucose tolerance test, and glucose levels were analysed using continuous subcutaneous glucose monitoring for 3 days.

3 Peak glucose levels >200 mg/dL (11.1mmol/L) were observed in 36% of individuals with apparently normal glucose tolerance; thus, continuous subcutaneous glucose monitoring might be a useful tool for the early detection of hyperglycaemia.

Moreau F, Weiller MA, Rosner V et al (2008) Continuous glucose monitoring in cystic fibrosis patients according to the glucose tolerance. *Hormone and Metabolic Research* 40: 502–6

## DIABETES &amp; METABOLISM

## Poor glycaemic control despite frequent SMBG

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

**1** This study included people with type 1 diabetes ( $n=235$ ), type 2 diabetes receiving insulin treatment ( $n=635$ ), and type 2 diabetes receiving oral antihyperglycaemic agents ( $n=2689$ ) recruited from a French national database.

**2** All participants completed a questionnaire, and data relating to self-monitoring of blood glucose (SMBG) were analysed in order to ascertain the factors affecting SMBG testing in this patient population.

**3** Frequency of self-monitoring was higher in individuals with type 1

diabetes: 58% of them performed SMBG the recommended three times per day, particularly females and those who had increased awareness of the meaning of HbA<sub>1c</sub>.

**4** In people with type 2 diabetes treated with insulin, SMBG was performed the recommended two times per day by 74% of them, particularly those with a history of at least one severe hypoglycaemic episode, and those with increased awareness of the meaning of HbA<sub>1c</sub>.

**5** Although almost all individuals receiving insulin performed SMBG, it had no correlation with their glycaemic control, which remained poor. Despite a lack of formal recommendations, nearly one-third of people with type 2 diabetes receiving oral antihyperglycaemic treatment also performed SMBG.

Lecomte P, Romon I, Fosse S et al (2008) Self-monitoring of blood glucose in people with type 1 and type 2 diabetes living in France: the Entred study 2001. *Diabetes & Metabolism* **34**: 219–26

## CLINICAL ENDOCRINOLOGY

## Continuous glucose monitoring is useful for insulinoma management

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

**1** This study investigated the benefits of continuous glucose monitoring in the management of individuals with insulinoma.

**2** Three individuals with suspected insulinoma were included in this study; following biochemical confirmation of the condition, participants were evaluated for hypoglycaemia awareness.

**3** At the beginning of the study, all participants demonstrated

hypoglycaemia unawareness; continuous glucose monitoring was implemented upon diagnosis, and demonstrated that both moderate and severe hypoglycaemia were experienced for a proportion of the time (6.1%, 21.9% and 71%, and 1.4%, 11.4% and 48.1% for patients 1, 2 and 3, respectively).

**4** Continuous glucose monitoring showed a reduction in hypoglycaemia after therapy with diazoxide and octreotide, and cure of insulinoma was also confirmed by continuous glucose monitoring.

**5** The authors conclude that continuous glucose monitoring is a useful tool not only for detecting hypoglycaemia and hypoglycaemia unawareness, but also for monitoring patients' response to therapy and confirming cure after treatment.

Munir A, Choudhary P, Harrison B et al (2008) Continuous glucose monitoring in patients with insulinoma. *Clinical Endocrinology* **68**: 912–8