# A Randomized Trial of Continuous Subcutaneous Insulin Infusion and Intensive Injection Therapy in Type 1 Diabetes for Patients With Long-Standing Poor Glycemic Control

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**OBJECTIVE** — To assess in a randomized crossover trial the efficacy of continuous subcutaneous insulin infusion in improving glycemic control and health-related quality of life in type 1 diabetic patients with long-standing poor glycemic control.

**RESEARCH DESIGN AND METHODS** — A total of 79 patients in 11 Dutch centers were randomized to 16 weeks of continuous subcutaneous insulin infusion followed by 16 weeks intensive injection therapy or the reverse order. Glycemic control was assessed by $HbA_{1c}$, self-reported hypoglycemic events, and blood glucose memory meter read outs. Changes in quality of life were assessed by self-report questionnaires administered at baseline and 16 weeks.

**RESULTS** — As the drop-out rate after crossover was high (17 of 79 patients [22%]), we analyzed the trial as a parallel clinical trial, using data of the first half of the crossover phase only. At 16 weeks, mean $HbA_{1c}$ was 0.84% (95% CI −1.31 to −0.36) lower in the continuous subcutaneous insulin infusion group compared with the insulin injection group ($P = 0.002$). Stability of blood glucose self-measurement values, expressed as SD of the nine-point blood glucose profiles, improved in the insulin pump group by 29.3 ± 41.1 vs. 8.2 ± 36.5% in the injection group ($P = 0.039$). The number of mild hypoglycemic episodes per patient-week was 0.99 (95% CI 0.11–1.87) higher in the insulin pump group ($P = 0.028$). Weight gain was similar in both groups. Scores on the Short-Form 36-Item subscales 'general health' and 'mental health' improved in the continuous subcutaneous insulin infusion group, compared with stable values in the injection group ($P = 0.048$ and 0.050, respectively).

**CONCLUSIONS** — Continuous subcutaneous insulin infusion improves glycemic control and some aspects of health-related quality of life in patients with a history of long-term poor glycemic control.

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**Abbreviations:** DCCT, Diabetes Control and Complications Trial; SF-36, 36-Item Short-Form Survey; SMBG, self-monitoring of blood glucose.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

**See accompanying editorial on p. 2100.**

Rapid-acting insulin analogs have been shown to result in moderately lower $HbA_{1c}$ values as compared with unmodified human insulin, both when used as mealtime insulin in multiple injection therapy (1–7) and as insulin for continuous subcutaneous insulin infusion (8–11). With the use of rapid-acting insulin analogs, two relatively small trials thus far have compared continuous subcutaneous insulin infusion and multiple injection therapy. The first, a crossover study in 40 patients found a 0.35% lower $HbA_{1c}$ with insulin pump treatment as compared with injection therapy (12). However, patients had been on insulin pump therapy using unmodified human insulin for a mean of 5.5 years before entering the trial, limiting the external validity of this study. The second, a parallel clinical trial, found no difference in $HbA_{1c}$, with a follow-up of 9 months (13). Thus, the evidence supporting the widespread and rapidly increasing use of continuous subcutaneous insulin infusion by an estimated 200,000 type 1 diabetic patients (14) seems relatively scarce.

The aim of our study was to compare efficacy in improving glycemic control and quality of life of continuous subcutaneous insulin infusion and intensive injection therapy in patients with long-standing poor glycemic control. The reason for selecting poorly regulated patients, who have often been excluded from participation in clinical trials, is that they are the most obvious candidates for treatment intensification. Moreover, the relationship between $HbA_{1c}$ and the development of long-term diabetic complications, as shown in the Diabetes Control and Complications Trial (DCCT), is steeper where $HbA_{1c}$ is higher (15). Thus, a lowering in $HbA_{1c}$ results in a greater absolute benefit in terms of prevention of long-term diabetic complications when baseline $HbA_{1c}$ is high. Poor glycemic

control is a prevalent problem in type 1 diabetes; ~30% of the well-motivated DCCT cohort had an average $HbA_{1c}$ >8.5% in the 4-year follow-up period following the DCCT (16).

## RESEARCH DESIGN AND METHODS

### Study design

Originally, this trial was designed as a double 16-week multicenter open-label crossover study and was conducted in 11 centers in the Netherlands. The trial was monitored and carried out according to International Conference on Harmonisation/Good Clinical Practice guidelines (17). The crossover phase reported in this article was preceded by a 14-week qualification phase that will be reported in more detail separately. The main reason for including a qualification phase in the trial was to exclude patients not able to comply with the demands of a good clinical practice trial, especially in terms of a minimum frequency of self-monitoring of blood glucose (SMBG), and to study the phenomenon of a 'study effect'. The qualification phase comprised a short re-education and intensification of the frequency of outpatient clinic visits. At week 2, a 30-min re-education session was scheduled with the diabetes nurse specialist. This session included checking for possible deficits in the following self-care areas: insulin injection technique; SMBG; self-regulation of insulin dose in anticipation of physical activity and meals, and in case of holidays and illness; actions to be taken in case of hypo- or hyperglycemia storage of insulin and self-monitoring strips; the advice to keep bedtime insulin dosage constant, solely to be adjusted on consistent out-of-range glucose values at awakening; and finally, the advice to take additional carbohydrate in case of a glucose value <8 mmol/l at bedtime. There were five outpatient clinic visits in the 14-week qualification phase. A minimum frequency of SMBG of two per day was mandatory in this phase. A minimum of 70% of these measurements had to be made to qualify for randomization. Following the qualification phase and crossover part, the study was concluded with a 24-week follow-up phase, consisting of three bimonthly routine visits to the outpatient department.

### Participants

Participants were recruited from the outpatient clinic population from the participating centers. In these centers, routine care for type 1 diabetic patients comprises approximately four outpatient contacts per year with a physician and on-demand consultation with a diabetes specialist nurse and/or dietitian. A medical psychologist can be consulted in many centers. All these consultations, as well as the use of insulin, insulin delivery devices (including insulin pens and pumps), and materials for SMBG are fully reimbursed in the Netherlands. Inclusion criteria were type 1 diabetes (defined as diabetes diagnosed at or before age 30 years with a C-peptide level ≤0.20 nmol/l at a concomitant glucose level ≥7.0 mmol/l, or diagnosed at or before age 40 with a C-peptide level ≤0.05 nmol/l at a concomitant glucose level ≥7.0 mmol/l), age between 18 and 70 years, persistent poor control while on three or more insulin injections a day (defined as a mean of all $HbA_{1c}$ values measured ≥8.5% in the last 6 months before the trial). Exclusion criteria were severe active retinopathy (requiring laser therapy), impaired hepatic function (alkaline phosphatase or alanine aminotransferase at least two times the upper limit of normal), nephropathy (defined as a serum creatinine >150 μmol/l), insulin resistance (defined as the use of >1.5 units insulin/kg body wt), substance abuse, cardiac disease (decompensated heart failure NYHA III and IV, unstable angina pectoris, or a myocardial infarction within the last 12 months), uncontrolled hypertension (blood pressure ≥180/110 mmHg), insulin allergy, and past or current psychiatric treatment for schizophrenia, organic mental disorder, or bipolar disorder. Women were excluded if they were (or intending to become) pregnant or breastfeeding. Diabetic complications were classified as follows: presence or absence of retinopathy following fundoscopy by an ophtalmologist, polyneuropathy (defined by abnormal vibration sense at the metatarsal joint of a large toe), and nephropathy (microalbuminuria, i.e., urinary albumin 30–300 mg/24 h, or proteinuria, i.e., urinary albumin >300 mg/24 h). The protocol was approved by the respective institutional ethics committees before patients gave written informed consent.

### Randomization

Subjects were randomized with scratch labels to insulin pump treatment followed by injection treatment, or the reverse order. The randomization list was generated by computer. Permuted blocks of six were used for each center. The numbered scratch labels were sequentially assigned to patients by the coordinating center after the glycemic inclusion criterion for the crossover phase, an $HbA_{1c}$ ≥7.5% at the end of the qualification phase, had been fulfilled. The trial was necessarily unblinded.

### Interventions

Subjects were seen at 2, 4, 8, 12, and 16 weeks after randomization. All patients used a Glucotouch or One Touch Profile memory glucose meter (Lifescan, Milpitas, CA). All patients were advised to note at least two blood glucose self-measurements per day in a diary and a seven-point profile (preprandial, 90 min postprandial, and before bedtime) once every week for the first 4 weeks and once every other week thereafter. The last profile before each visit was extended to a nine-point profile with a measurement 5 h after going to bed and before breakfast the next day. Dosage adjustment recommendations were derived from an algorithm based on these nine-point home blood glucose profiles in the treatment period. The algorithm advised to adjust preceding insulin doses when glucose measurements were outside the targeted 5.0- to 7.0-mmol/l range preprandially and the 5.0- to 9.0-mmol/l range postprandially. At bedtime, a 7.0- to 10.0-mmol/l range was advised.

In those randomized to injection therapy, 80% of the previously given premeal human insulin dose was given as insulin aspart (NovoRapid; Novo Nordisk AS, Bagsvaerd, Denmark) before meals, and subjects were advised to add the prandial dose decrement to their nighttime NPH insulin dose (Insulatard; Novo Nordisk AS), leaving the total daily insulin dose unchanged. When the interval between two daytime injections was >5 h, additional NPH doses were added in this group: 40% of the previously given premeal human insulin dose was given as NPH insulin and 60% was given as insulin aspart for each interval exceeding 5 h (18). Insulin aspart was adjusted on the postprandial measurements, and NPH was adjusted on the preprandial measure-

ments. The recommended injection site for mealtime insulin, using the NovoPen 3, was the abdomen; for NPH insulin it was the thigh.

In those randomized to continuous subcutaneous insulin infusion, protocoled education was given on pump usage. This did not include carbohydrate counting. The wearable Disetronic H-TRONplus insulin pump was used, with insulin aspart as pump insulin (19). The starting dose was 90% of the previously used total insulin dose per day or 80% when hypoglycemia was a problem to the patient. It was advised to start with one basal rate, or two at the most—the nighttime rate then being 0.2 units/h lower than the daytime rate. Initially, 50% of the total daily dose was given as basal insulin, the rest equally divided, before each meal. In the continuous subcutaneous insulin infusion group, mealtime bolus insulin aspart was adjusted according to the postprandial measurements and the basal rate was adjusted according to the preprandial measurements, targeting for the same glucose levels as in the injection therapy group.

### Objectives

The primary objective was to compare the efficacy in improving glycemic control of continuous subcutaneous insulin infusion and insulin injection therapy in diabetic patients in persistent poor control. The secondary objective was to investigate possible different effects of these modes of treatment on health-related quality of life.

### Outcome measures

The primary outcome measure was change in $HbA_{1c}$ in both randomization groups from baseline to 12 and 16 weeks (the mean of these two values was taken). Blood was sampled for $HbA_{1c}$ at these three time points. Secondary outcome measures were number of hypoglycemias, means of blood glucose values at the nine points in the blood glucose profiles, SD of all measurements in these profiles, and changes in dimensions of the quality-of-life measures. $HbA_{1c}$ values were assessed using an ion-exchange high-performance liquid chromatography (Mono S; Amersham Pharmacia Biotech, Uppsala, Sweden; reference value 4.3–6.1%). Mild hypoglycemia was defined as a value ≤3.9 mmol/l at SMBG in the last 3 weeks of the study confirmed in the meter read outs. Severe hypoglycemia was defined by requirement of third-party help.

Self-report questionnaires were introduced to the patient by a diabetes nurse specialist and filled out by the patient during the baseline visit and at 16 weeks after starting the assigned mode of therapy. The Medical Outcome Study 36-Item Short-Form Survey (SF-36) is a validated generic 36-item instrument that measures health-related quality of life (20). Using simple questions that the individuals score, it gives reproducible measures of health concepts for a large number of illnesses. It measures eight health concepts: physical functioning, physical role functioning, social functioning, bodily pain, mental health, emotional role functioning, vitality, and general health perceptions. According to the instruction manual, scores on all domains were standardized from 1 to 100, the latter representing optimal health.

To assess treatment satisfaction, we used the validated Diabetes Treatment Satisfaction Questionnaire. It comprises six items, on which subjects rate their satisfaction concerning different aspects of treatment (21). Items are summated to a sumscore, while two additional items, one on hypoglycemia and one on hyperglycemia are handled separately.

### Sample size

At the design phase, we anticipated the possibility that we would have to analyze the trial as a parallel randomized clinical trial, because of the demanding character of the study protocol and an expected high drop-out rate. Forty-eight patients were calculated to be required for each arm to have an 80% chance of detecting (at the two-sided 5% level) a 0.75% difference in $HbA_{1c}$, with an assumed SD of 1.3%. Following abstract presentation of the crossover trial mentioned in the introduction, in which no drop out at the moment of crossover was seen, we assumed we would be able to analyze our trial as a crossover trial and stopped inclusion after having 79 patients randomized (12).

### Statistical analysis

All analyses were prespecified in a statistical analysis plan. We analyzed the differences in change between groups from baseline to 16 weeks in biomedical variables with the independent samples *t* test and in quality-of-life levels with the Mann-Whitney *U* test, reporting exact *P* values. Missing baseline values were carried forward from earlier measurements during the qualification phase, if possible. Missing values at 16 weeks of treatment were carried forward from 12-week measurements, if available, for the SD of nine-point blood glucose profiles, body weight, and insulin use. For the comparison of stability of glycemic control, the SD of the nine-point blood glucose profiles was taken as an individual end point. A minimum of four measurements made was required to produce such an end point. Changes in SDs in the nine-point blood glucose profiles in the two groups from baseline to 16 weeks were compared. The number of missing values at 16 weeks was as follows: $HbA_{1c}$ end point: 0; SD of nine-point blood glucose profiles: 3; hypoglycemia: 8; body weight: 1; insulin use: 1; SF-36 general health: 4; SF-36 mental health: 5; and treatment satisfaction: 4. Data are presented as means ± SD with 95% CIs or median (25th, 75th percentile). Analyses were performed using SPSS 9.0. (22). No interim analysis was performed.

## RESULTS

### Patient flow, changes during the qualification phase, and baseline characteristics at randomization

A trial schedule is given in Fig. 1. Data on the number of patients approached were available from 4 of the 11 centers only. A total of 150 subjects were asked to participate in these four centers; 47 were enrolled.

In total, 89 patients entered the qualification phase. During the qualification phase, mean $HbA_{1c}$ decreased from 10.02 ± 1.5 to 9.34 ± 1.4%, $P < 0.001$, at 10 weeks and remained stable at 9.25 ± 1.3% at 14 weeks ($P < 0.001$ compared with baseline, $P = 0.29$ compared with 10 weeks). Insulin dosage remained unchanged at 0.9 ± 0.26 units · 24 $h^{-1}$ · kg body $wt^{-1}$ at baseline vs. 0.9 ± 0.34 units · 24 $h^{-1}$ · kg body $wt^{-1}$ at 14 weeks ($P = 0.23$). Frequency of SMBG increased from 5.0 measurements per week (25% 2.0, 75% 15.5) to 18.0 (14.7, 22.7; $P = <0.001$). Eight patients dropped out and two were excluded from randomization, because $HbA_{1c}$ had come down to below the predefined limit of 7.5% ($n = 1$) or because frequency of SMBG was judged to be too low ($n = 1$) (23).

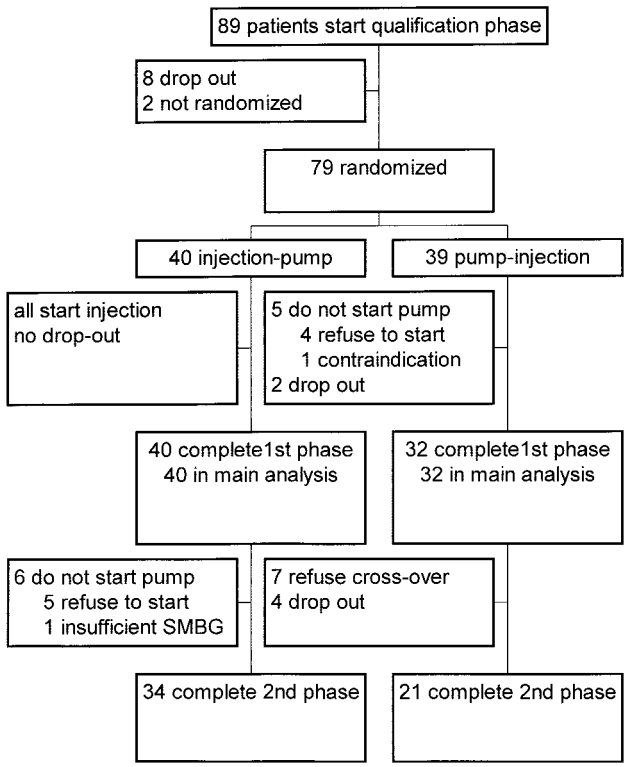


**Figure 1**—*Trial profile.*

Patients were randomized between 1 December 1999 and 23 November 2000. The two treatment groups were comparable with respect to demographic variables, disease characteristics, and quality-of-life variables measured at baseline (Table 1). One patient required extensive laser therapy following randomization and therefore could not start pump therapy. Reasons for dropout in the first half of the crossover phase were a serious adverse event (femur fracture, $n = 1$) and no show at follow-up visits ($n = 1$); in the second half, reasons included an adverse event (fluid retention on insulin aspart, $n = 1$), no show at follow-up visits ($n = 1$), and an increase in hypoglycemia rate upon resuming injection therapy ($n = 1$).

Because of the high drop-out rate after crossover, we analyzed the trial as a parallel clinical trial, using the data of the first half of the crossover phase only. In total, after randomization or crossover, nine patients (11.4%) refused to start insulin pump treatment.

Of the 55 patients having concluded the trial, 54 entered and completed the follow-up period. In the insulin injection group, the insulin algorithm resulted in the use of two NPH insulin injections per day in 25 patients (62.5%) and one NPH insulin injection in the remaining 15 patients (37.5%).

### Biomedical outcome measures

Change in $HbA_{1c}$ in the insulin pump group was significantly greater than in the insulin injection group: $-0.91 \pm 1.28$ vs. $-0.07 \pm 0.70\%$, $P = 0.002$, difference 0.84% (95% CI $-1.31$ to $-0.36$). The mean glucose value in the 24-h glucose profiles was lower, though not significantly, in the insulin pump group at seven of the nine time points (Fig. 2). The SD of glucose values measured in the nine-point blood glucose profiles, reflecting glycemic variability, declined more in the insulin pump group than in the injection group: $-1.35 \pm 1.88$ in the insulin pump group versus $-0.40 \pm 1.77$ in the injection group, $P = 0.039$, mean difference $-0.95$ (95% CI $-1.83$ to $-0.05$). Mild hypoglycemic episodes increased in the insulin pump group as compared with the injection group: $0.98 \pm 2.02$ vs. $-0.02 \pm 1.18$ episodes per patient week, $P = 0.028$, difference 0.99 (95% CI 0.11–1.87) episodes per patient week. The number of patients suffering severe hypoglycemic episodes was similar in either group: three in the insulin pump group and six in the injection group ($P = 0.48$). Over the whole study period, one episode of ketoacidosis in both the insulin pump and the injection group occurred. Change in weight was similar in both groups:

**Table 1**—*Clinical characteristics of the randomization groups*

| | Insulin pump group | Insulin injection group |
|---|---|---|
| Characteristic | | |
| n | 39 | 40 |
| Males | 21 (54) | 21 (53) |
| Age (years) | 36.2 ± 10.3 | 37.3 ± 10.6 |
| Diabetes duration (years) | 17.6 ± 9.8 | 18.0 ± 9.4 |
| Smoking | 18 (46.2) | 26 (65.0) |
| Weight (kg) | 77.3 ± 13.6 | 79.8 ± 13.5 |
| Retinopathy | 19 (48.7) | 17 (42.5) |
| Nephropathy | | |
| Microalbuminuria | 11 (28.2) | 8 (20.0) |
| Proteinuria | 4 (10.2) | 4 (10.0) |
| Neuropathy | 4 (10.2) | 6 (15.0) |
| $HbA_{1c}$ (%) | 9.27 ± 1.4 | 9.25 ± 1.4 |
| Mild hypoglycemic episodes (*n*/patient-week) | 2.13 ± 2.05 | 1.97 ± 1.53 |
| Insulin use (units · $kg^{-1}$ · $24\ h^{-1}$) | 0.90 ± 0.28 | 0.88 ± 0.39 |
| SD glucose self measurement | 4.57 ± 1.66 | 4.85 ± 1.70 |
| SF-36 general health | 61.4 ± 20.5 | 59.8 ± 37.0 |
| SF-36 mental health | 80.0 (64.5, 84.0) | 78.0 (63.0, 92.0) |
| DTSQ | 28.8 ± 3.9 | 27.4 ± 4.9 |

Data are *n* (%), means ± SD, or median (25th, 75th percentiles). DTSQ, Diabetes Treatment Satisfaction Questionnaire.

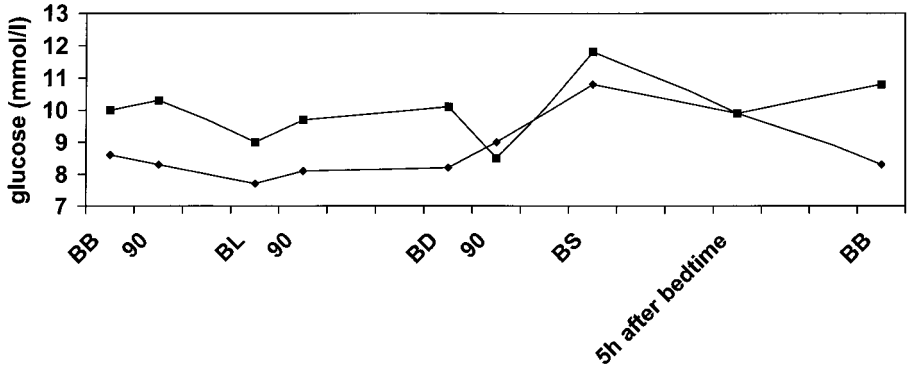


**Figure 2**—*Glucose profiles, a time series of averaged values, at 16 weeks in the insulin pump group (◆) and the injection group (■). BB, before breakfast; 90, 90 min postprandial; BL, before lunch; BD, before dinner; BS, before sleeping.*

0.60 ± 2.94 vs. 0.88 ± 2.74 kg, $P$ = 0.68, difference −0.28 (95% CI −1.63 to 1.07). Insulin requirements decreased in the insulin pump group and remained stable in the injection group: −15.8 ± 15.06 vs. 2.9 ± 17.01 units/day, $P < 0.001$, difference −18.76 units/day (95% CI −26.45 to −11.07).

Of the 54 patients who entered the follow-up phase of the trial, 44 (81%) chose continuous subcutaneous insulin infusion as their mode of treatment. No substantial differences in baseline variables were noted between these 54 patients and the 79 patients randomized. $HbA_{1c}$ at the end of the 24-week follow-up phase was similar to that at the end of 16 weeks of continuous subcutaneous insulin infusion in the first half of the crossover phase in these 44 patients: 8.46 vs. 8.21%.

### Health-related quality of life

The scores on the general health and mental health subscales of the SF-36 improved more in the insulin pump treatment group, as compared with the injection therapy group: +5.9 versus −1.2 ($P$ = 0.048) and +5.2 vs. −0.6 ($P$ = 0.050), respectively.

### Treatment satisfaction

Change in overall treatment satisfaction as assessed using the Diabetes Treatment Satisfaction Questionnaire was not different between groups: +1.3 in the insulin pump treatment group versus +0.2 in the injection therapy group ($P$ = 0.199).

**CONCLUSIONS** — In this trial in patients with type 1 diabetes with long-standing poor glycemic control, insulin pump treatment resulted in a greater reduction in $HbA_{1c}$ as compared with intensive insulin injection treatment (difference 0.84%). This can probably be explained by the superior basal insulin supplementation administered by continuous subcutaneous insulin infusion, resulting in a lower and more stable glucose profile. Improved stability was reflected in our study by a significantly lower SD in 24-h glucose profiles in the insulin pump group. In contrast, NPH insulin shows a more erratic absorption pattern, with a reported intraindividual variability of 25% (24). Previously, we have shown the superiority of continuous subcutaneous insulin infusion to injection therapy during the night in achieving a less variable fasting glycemia (25). Our trial confirms that continuous subcutaneous insulin infusion can effectively counteract the dawn phenomenon and the waning of NPH insulin in the second half of the night (26,27). Recently, long-acting insulin analogs have been developed as alternatives for NPH insulin. Further research comparing CSII using rapid-acting insulin analogs and injection therapy using rapid-acting analogs in combination with long-acting analogs seems warranted. However, it should be noted that so far, the use of long-acting analogs has not been shown to result in a lower $HbA_{1c}$ than the use of NPH insulin, despite a lower frequency of hypoglycemic events associated with it (1,28,29). The daytime profiles indicate that both regimens were equally effective in correcting postprandial excursions, also supporting the notion that CSII is superior in basal insulin supplementation.

One may argue that the advantage found in the insulin pump group may be partially due to the more extensive education given to this group. However, several controlled trials investigating the effect of education in type 1 diabetic patients failed to show improvement in glycemic control (30–32). Moreover, the general education given in the 14-week qualification phase resulted in a stable $HbA_{1c}$ before randomization, providing a real baseline $HbA_{1c}$ on which a proper comparison can be made of two different treatment modalities.

A major difference between our trial and former trials lies in the selection of patients with long-standing poor glycemic control. To our knowledge, this is the first trial investigating the efficacy of two treatment modes in this specific group of patients, who can be considered to represent the primary target population for either intensification of insulin injection therapy or for continuous subcutaneous insulin infusion (14). The improvement in $HbA_{1c}$ in this population in long-standing poor glycemic control can be expected to result in a larger benefit in terms of prevention of long-term diabetic complications than a similar improvement in a population with fairly good glycemic control (15).

Insulin pump therapy is not a panacea for all patients in poor glycemic control. Only those with a readiness to change can be expected to benefit. In our trial, a readiness to change was apparent from objectively performed SMBG at least twice a day during the 14 weeks preceding randomization and willingness to participate in a good clinical practice trial. Nine patients (11.4%) refused to start insulin pump therapy, while seven (8.9%) refused to restart injection therapy following the intended crossover, illustrating the importance of patient preference and motivation for a specific mode of therapy.

The observed improvement in $HbA_{1c}$ in the insulin pump group was accompanied by a small absolute increase in mild hypoglycemic episodes. This is in contrast with an earlier trial in well-controlled patients, in whom a 0.35% improvement in $HbA_{1c}$, a stabilization of glucose values, and an unchanged incidence of hypoglycemic episodes were seen (12). Possibly, the larger improvement in $HbA_{1c}$ in our population (0.84 vs. 0.35%) overrides the effect of stabiliza-

tion of glucose values on the frequency of hypoglycemic episodes.

The improvement in $HbA_{1c}$ in the insulin pump group was accompanied by a small weight gain only. This is probably attributable to the 23% reduction in insulin dose in this group.

Health-related quality of life improved with insulin pump therapy. To our knowledge, this trial is the first randomized trial to investigate this issue. The discomfort of always having to wear the pump and the increased rate of mild hypoglycemia apparently were counterbalanced by the achieved improvement in glycemic control in these patients with long-standing poor control. No difference in treatment satisfaction could be noted, perhaps due to lack of sensitivity of the scale used or to the ceiling effect, which is found to be associated with this questionnaire (33).

In conclusion, in patients with a history of long-term poor control, continuous subcutaneous insulin infusion improves glycemic control and some aspects of health-related quality of life. Therefore, we suggest that continuous subcutaneous insulin infusion should be considered in patients with long-standing poor glycemic control and readiness to change.

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## APPENDIX

### Members of the Dutch Insulin Pump Study Group

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