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Quality of life and treatment satisfaction in adults with Type 1 diabetes: a comparison between continuous subcutaneous insulin infusion and multiple daily injections

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Abstract

Aims The aim of this case–control study was to compare quality of life (QoL) and treatment satisfaction in adults with Type 1 diabetes (T1DM) treated with either continuous subcutaneous insulin infusion (CSII) or multiple daily injections (MDI).

Methods Consecutive patients aged between 18 and 55 years, and attending diabetes clinics for a routine visit, completed the Diabetes-Specific Quality-of-Life Scale (DSQOLS), the Diabetes Treatment Satisfaction Questionnaire (DTSQ) and the SF-36 Health Survey (SF-36). Case (CSII) and control subjects (MDI) were recruited in a 1 : 2 ratio.

Results Overall, 1341 individuals were enrolled by 62 diabetes clinics; 481 were cases and 860 control subjects. Cases had a longer diabetes duration and were more likely to have eye and renal complications. Age, school education, occupation and HbA_{1c} were similar. Of control subjects, 90% followed glargine-based MDI regimens and 10% used NPH-based MDI regimens. On multivariate analysis, after adjusting for socioeconomic and clinical characteristics, scores in the following areas of the DSQOLS were higher in cases than control subjects: diet restrictions ($\beta = 5.96$; $P < 0.0001$), daily hassles ($\beta = 3.57$; $P = 0.01$) and fears about hypoglycaemia ($\beta = 3.88$; $P = 0.006$). Treatment with CSII was also associated with a markedly higher DTSQ score ($\beta = 4.13$; $P < 0.0001$) compared with MDI. Results were similar when CSII was compared separately with glargine- or NPH-based MDI regimens.

Conclusions This large, non-randomized, case–control study suggests quality of life gains deriving from greater lifestyle flexibility, less fear of hypoglycaemia, and higher treatment satisfaction, when CSII is compared with either glargine-based or NPH-based MDI regimens.

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Keywords continuous subcutaneous insulin infusion, multiple daily injections, quality of life, questionnaires, Type 1 diabetes

Abbreviations CI, confidence interval; CSII, continuous subcutaneous insulin injection; DSQOLS, Diabetes-Specific Quality-of-Life Scale; DTSQ, Diabetes Treatment Satisfaction Questionnaire; MDI, multiple daily injections; OR, odds ratio; QoL, quality of life; SF-36, SF-36 Health Survey; T1DM, Type 1 diabetes

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Introduction

Since the report of the Diabetes Control and Complications Trial, healthcare providers have been working with their Type 1 patients to optimize glycaemic control either through multiple daily injection (MDI) or continuous subcutaneous insulin infusion (CSII) therapy. The results of this study also renewed interest in the role of CSII therapy in improving glycaemic outcomes, because it offers a more physiological method of insulin administration.

Trials comparing CSII with MDI in adults with Type 1 diabetes (T1DM) have focused mainly on easily measurable outcomes such as glycated haemoglobin, showing that CSII results in a modest but worthwhile improvement in glycaemic control [1]. Nevertheless, the relative benefits of CSII and MDI in terms of flexibility of lifestyle and quality of life (QoL) have rarely been investigated, and some of the implications for patients such as the psychological impact of wearing a device for 24 h every day have not been quantified. The latter could represent an obstacle, particularly in women, because of alteration in body image. Furthermore, poorer health-related QoL in women has been widely described [2–5], but it is not known whether CSII exerts a different effect on QoL in women as opposed to men. Overall, studies examining the impact of CSII on QoL in T1DM have been conflicting, making a judgment about the QoL benefits of insulin pump use difficult [6]. Furthermore, QoL has been investigated within randomized trials or cohort studies including small numbers of patients, usually treated with CSII for the first time [7–11]. Some of these studies do suggest that CSII treatment is associated with less severe hypoglycaemia, better QoL, increased coping ability and greater freedom. A recent randomized trial comparing CSII with NPH-based MDI in 272 T1DM patients has confirmed that CSII therapy was associated with a marked reduction in hypoglycaemic events and better QoL [12]. Nevertheless, no data are currently available comparing CSII with long-acting insulin analogue-based MDI regimens (insulin glargine and detemir), which have widely replaced NPH-based MDI in clinical practice, mainly on the grounds of the documented reduction in the risk of hypoglycaemia [13,14].

The aim of this large case–control study was to assess QoL and patient satisfaction in a large cohort of adults with T1DM treated with either CSII or MDI (glargine-based or NPH-based), under routine clinical conditions.

Research design and methods

Study design and population

This case–control study was carried out between January and December 2006. Consecutive patients with T1DM, aged between 18 and 55 years and attending diabetes clinics for a routine visit, were enrolled as cases if they had been on treatment with CSII for ≥ 6 months, irrespective of the type of insulin infusion pump used. Patients were enrolled as control subjects if they had never been treated with CSII and had been receiving at least four insulin injections per day for ≥ 6 months. Each centre was asked to recruit 10 case and 10 control subjects. Since it is possible that in those clinics frequently using CSII, patients offered this treatment could differ systematically from those treated with MDI, an additional control group was identified, following the same eligibility criteria, in centres without experience in the use of insulin pumps.

Patients were not included in the study if they were pregnant or had psychiatric problems limiting their ability to complete the questionnaires.

All patients gave written informed consent. The local research ethics committee at each institution approved the study protocol.

Measurements

All data concerning demographics and specific diabetes history were collected by participating physicians on *ad hoc* forms. Because normal ranges for HbA_{1c} varied in the different centres, the percentage change with respect to the upper normal value (actual value/upper normal limit) was estimated and multiplied by 6.0. This allowed us to normalize HbA_{1c} values with respect to a value of 6.0% [15].

Eye complications were defined as the presence of any grade of diabetic retinopathy or maculopathy on dilated eye examination, or cataract. Renal complications included micro- or macroalbuminuria, elevated serum creatinine levels (> 132 μmol/l) and dialysis/transplantation. Diabetic neuropathy was defined as the presence of symptomatic somatic or autonomic neuropathy. Cardiovascular complications included coronary heart disease, myocardial infarction, stroke, and revascularization procedures. Peripheral vascular complications were defined as the presence of intermittent claudication, ulcers, gangrene, and non-traumatic amputations.

At study entry, all patients completed a questionnaire including the Diabetes Specific Quality of Life Scale (DSQOLS), the Diabetes Treatment Satisfaction Questionnaire (DTSQ) and the SF-36 Health Survey (SF-36). The questionnaire was anonymous, and its link with the information collected by participating physicians was ensured by a numerical code.

Diabetes Specific Quality of Life Scale

The DSQOLS was designed to assess specifically the four main components of QoL (i.e. physical, emotional, and social burdens along with daily functioning) in patients with T1DM [16]. After its initial release, the questionnaire was revised to include a new set of questions investigating fears about hypoglycaemia. Furthermore, three additional items in the 'diet restrictions' scale, two additional items in the 'daily hassles' scale and one item in the 'physical complaints' scale were also added [17]. The scale comprises 57 items covering six areas: social relations (11 items), leisure time flexibility (six items), physical complaints (nine items), worries about future (five items), diet restrictions (nine items), daily hassles (six items) and fears about hypoglycaemia (11 items). Answers are given on a six-point Likert scale, and the scores range between 0 and 100, with higher

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scores indicating better QoL or higher satisfaction. The translation and cultural adaptation of the Italian version of the instrument were performed using standard forward/backward techniques to ensure conceptual equivalence [18]. The psychometric validation of the Italian version of the instrument was performed specifically for this study. All of the subscales of the DSQOLS showed excellent psychometric properties. In particular, for all of the subscales, Cronbach's coefficient largely exceeded the minimum accepted value of 0.70 (social relations 0.90, leisure time flexibility 0.88, physical complaints 0.86, worries about future 0.83, diet restrictions 0.87, daily hassles 0.82, fear about hypoglycaemia 0.92). Likewise, item–scale correlation was extremely satisfactory ($r \geq 0.40$) for all but one item of the physical complaints subscale ($r = 0.36$).

Diabetes Treatment Satisfaction Questionnaire

The DTSQ has been specifically designed to measure satisfaction with diabetes treatment regimens [19]. The instrument was originally developed to detect changes in satisfaction related to changes in treatment modalities, but it is also appropriate for comparing levels of satisfaction in subjects using different treatment regimens. It is composed of eight items, six of which are summed in a single score ranging from 0 (very dissatisfied) to 36 (very satisfied). The remaining two items are treated individually and explore the perceived frequency of hyperglycaemic and hypoglycaemic episodes, with higher scores indicating a higher frequency. The Italian version of the instrument has been previously translated and validated [20].

SF-36 Health Survey

The SF-36 is the most widely used generic health status measure [21]. It includes eight health concepts: physical functioning, role limitations due to physical problems, bodily pain, general health perception, energy/vitality, social functioning, role limitations due to emotional problems, and mental health. For each dimension item scores are coded, summed and transformed on to a scale from 0 (worst possible health state) to 100 (best possible health state). The SF-36 has been used in large population studies and in many different clinical conditions, showing excellent psychometric properties [22]. It has been translated and validated in several languages, including Italian [23].

Study hypotheses

Based on the scant data available, we hypothesized that CSII could have a positive impact primarily on those aspects more closely related to diabetes treatment: lifestyle flexibility and burden perception. Given the conflicting results regarding the impact of CSII on treatment satisfaction and broader aspects of QoL, we did not formulate any specific *a priori* hypothesis, and simply performed exploratory analyses.

Sample size estimation

Sample size was chosen to detect with a statistical power of 85% an excess risk of 50% [odds ratio (OR) 1.5] for MDI patients compared with CSII patients to have a QoL score within the lower quartile of the distribution of that score in the entire study population (with $\alpha = 0.05$). Assuming a case–control rate of 1 : 2, 473 case and 946 control subjects were needed. The actual number of control subjects recruited (860) only slightly decreased the study power from 85% to 82% [24]. The same sample size allowed us to detect with > 85% statistical power a small effect size of 0.20, when mean scores were compared between case and control subjects [25].

Statistical analysis

Data are summarized as mean ± SD for continuous variables and percentages for categorical variables. Patient characteristics according to study group were compared using χ^2 statistics for categorical variables and Mann–Whitney *U*-test or unpaired *t*-test for continuous variables. QoL scores, adjusted for age, gender and diabetes duration, were compared using an ANCOVA model.

To control simultaneously for the possible confounding effect of the different variables investigated, multiple logistic regression and multiple linear regression with stepwise variable selection were also used. In logistic regression analyses, QoL and satisfaction scores were dichotomized (lower quartile of the distribution vs. other quartiles). The results are expressed in terms of ORs with their 95% confidence intervals (CIs). An OR > 1 indicates a greater risk for patients treated with MDI to have a score in the lowest quartile compared with patients on CSII. Since the dichotomization of the dependent variables could lead to a loss of information, multiple regression was also performed, using each score as a continuous dependent variable. Results are expressed as β parameters with their associated *P*-values. In all the multivariate analyses the following covariates were tested: age, gender, school education, marital status, occupation, body mass index, diabetes duration, HbA_{1c}, number of diabetes complications, insulin regimen (CSII vs. MDI), ability to perform carbohydrate counting, and ability to self-manage insulin doses.

All the analyses were performed using SAS Statistical Package Version 9.1 (SAS Inc., Cary, NC, USA) [26].

Results

Overall, 62 diabetes clinics enrolled 1341 patients, of whom 481 used CSII and 860 used MDI. Of the latter, 648 were recruited by the same centres which also enrolled CSII patients ($N = 50$), whereas 212 were identified in those centres ($N = 12$) without any experience in insulin pump infusion therapy.

The mean duration of CSII therapy was < 1 year in 16% of the patients, 1–3 years in 52.8% and > 3 years in 31.2% of the patients. Of control subjects, 773 (90%) took glargine-based MDI regimens and 87 (10%) NPH-based MDI regimens. Median duration of glargine therapy was 24.6 months (interquartile range 13.1–32.6).

Patients' characteristics are reported in Table 1. Cases differed from control subjects in several sociodemographic and clinical characteristics. In particular, the proportion of women and married individuals was higher in patients treated

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Table 1 Patients' characteristics

	CSII ($N = 481$)	MDI ($N = 860$)	P*
Gender			< 0.0001
Male	206 (42.8)	467 (54.3)	
Female	275 (57.2)	393 (45.7)	
Age (years)	35.1 ± 10.9	34.9 ± 12.4	0.4
School education (years)			0.07
≤ 5	6 (1.3)	22 (2.6)	
6–8	113 (23.5)	231 (26.7)	
9–13	263 (54.7)	470 (54.4)	
> 13	99 (20.6)	141 (16.3)	
Occupation			0.5
Employed	320 (69.4)	598 (69.7)	
Retired	19 (4.1)	46 (5.4)	
Unemployed/student	122 (26.5)	214 (24.9)	
Marital status			0.0002
Single	202 (42.0)	460 (53.2)	
Married	259 (54.0)	364 (42.1)	
Divorced/widowed	20 (4.2)	40 (4.6)	
Body mass index (kg/m^2)	24.4 ± 3.5	24.1 ± 5.3	0.031
Diabetes duration (years)	18.4 ± 10.2	14.9 ± 9.8	< 0.0001
HbA_{1c} (%)	7.6 ± 1.3	7.7 ± 1.3	0.35
Eye complications	153 (31.9)	188 (21.8)	< 0.0001
Renal complications	54 (11.3)	52 (6.0)	0.0007
Cardiovascular complications	16 (3.3)	29 (3.4)	0.9
Peripheral vascular complications	13 (2.7)	13 (1.5)	0.12
Neuropathy	60 (12.5)	73 (8.5)	0.02
Carbohydrate counting	268 (56.3)	344 (40.3)	< 0.0001
Self-management of insulin doses	387 (80.5)	571 (66.5)	< 0.0001

*χ^2 statistics for categorical variables and Mann–Whitney U-test or unpaired t-test for continuous variables. n (%) or mean ± SD.

with CSII. The percentage of individuals with higher levels of school education was not significantly different in cases from control subjects. Cases also had longer diabetes duration and were more likely to have microvascular complications. Furthermore, CSII patients were more likely to self-manage insulin doses and use carbohydrate counting. Overall, similar differences were present when comparing cases with each of the two control groups separately (data not shown). Mean age and HbA_{1c} were similar in case and control subjects.

All patients completed the QoL questionnaires. Raw, unadjusted QoL and satisfaction mean scores, and age, gender, and diabetes duration-adjusted scores are reported in Table 2. Scores were similar in control patients enrolled in centres using CSII and those not using this regimen, apart from the DTSQ score (25.9 ± 0.23 vs. 27.0 ± 0.4, $P = 0.02$) and the Bodily pain dimension of the SF-36 (81.8 ± 0.9 vs. 85.8 ± 1.6, $P = 0.03$). Both differences, although statistically significant, were associated with a very small effect size (< 0.20), suggesting that such differences were not clinically relevant. Therefore, all the analyses are based on the comparison between cases and the combined control group.

DSQOLS

Crude DSQOLS scores were significantly higher in CSII patients than in control subjects for 'diet restrictions', whereas MDI patients had significantly higher scores than CSII patients for 'leisure time flexibility' and 'physical complaints' dimensions (Table 2). When mean DSQOLS scores were adjusted for age, gender and diabetes duration, patients treated with CSII had a significantly higher score than those treated with MDI for the dimension 'diet restriction', whereas there were no major differences for the other subscales (Table 2). On multivariate regression analysis, after also adjusting for socioeconomic and clinical characteristics, cases had significantly higher scores than control subjects in the following areas of the DSQOLS: diet restrictions ($\beta = 5.96$; $P < 0.0001$), daily hassles ($\beta = 3.57$; $P = 0.01$) and fears about hypoglycaemia ($\beta = 3.88$; $P = 0.006$). Logistic regression analysis further confirmed that, compared with cases, control subjects had a 70% higher likelihood of having a score in the lower quartile for the 'diet restrictions' and 'fear of hypoglycaemia' DSQOLS scores (OR 1.7; 95% CI 1.3, 2.0 for both scores).

Women had lower scores than men for all the domains investigated, but the patterns of association with insulin delivery modalities were the same in both genders (data not shown).

Since 90% of the patients in the control group were treated with glargine-based MDI regimens, the overall results can be interpreted as a comparison between CSII and glargine-based MDI. As an additional analysis, we determined whether QoL and satisfaction scores differed when comparing cases separately with patients treated with glargine-based MDI regimens or NPH-based MDI regimens. For the comparison between CSII and glargine-based MDI, results were similar to the overall results. For the comparison of DSQOLS scores between CSII and NPH-based MDI, they were of the same magnitude as in the whole control group; however, they did not reach statistical significance, due to the very small number of patients treated with NPH-MDI (data not shown).

DTSQ

Mean crude and adjusted DTSQ scores were significantly higher in CSII than MDI patients, and were associated with a lower perceived frequency of hyperglycaemic episodes (Table 2). Multivariate regression analysis confirmed that treatment with CSII was associated with a markedly higher DTSQ score ($\beta = 4.13$; $P < 0.0001$) compared with MDI. These findings are further reinforced by the results of the logistic regression, showing that control subjects, compared with cases, had a more than threefold risk of having a DTSQ score in the lowest quartile (OR 3.3; 95% CI 2.5, 5.0).

Age, gender and diabetes duration-adjusted DTSQ scores were significantly higher with CSII than either glargine- or NPH-based MDI regimens (30.2 ± 0.3, 26.2 ± 0.2 and 25.8 ± 0.6, $P < 0.0001$ for CSII, glargine-based MDI and NPH-based MDI, respectively).

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Table 2 Crude mean scores (± SD) and age, gender and diabetes duration adjusted mean scores (± SE) in case and control subjects

	Crude scores			Age, gender, and diabetes duration adjusted scores		
Quality of life dimensions	CSII	MDI	*P**	CSII	MDI	*P***
DSQOLS						
Social relations	78.2 ± 19.5	79.7 ± 19.0	0.11	78.4 ± 0.90	79.6 ± 0.66	0.30
Leisure time flexibility	74.4 ± 24.0	77.1 ± 22.7	0.05	74.6 ± 1.07	77.1 ± 0.79	0.07
Physical complaints	70.1 ± 19.9	72.3 ± 19.8	0.028	70.5 ± 0.92	72.1 ± 0.67	0.17
Worries about future	45.5 ± 25.1	46.2 ± 24.3	0.66	46.2 ± 1.15	45.8 ± 0.84	0.79
Diet restrictions	65.9 ± 21.7	60.4 ± 23.0	< 0.0001	65.5 ± 1.05	60.8 ± 0.77	0.0003
Daily hassles	67.6 ± 23.1	65.6 ± 22.7	0.06	67.6 ± 1.08	65.7 ± 0.79	0.16
Fears about hypoglycaemia	65.9 ± 23.0	63.9 ± 24.4	0.25	66.3 ± 1.10	63.9 ± 0.81	0.08
DTSQ						
DTSQ	30.1 ± 5.1	26.2 ± 6.1	< 0.0001	30.2 ± 0.27	26.2 ± 0.2	< 0.0001
Perceived hyperglycaemia	3.2 ± 1.4	3.4 ± 1.5	< 0.0001	3.2 ± 0.07	3.4 ± 0.05	0.004
Perceived hypoglycaemia	2.5 ± 1.4	2.6 ± 1.5	0.42	2.5 ± 0.07	2.6 ± 0.05	0.14
SF-36						
Physical functioning	91.0 ± 14.8	92.1 ± 14.0	0.017	90.9 ± 0.66	92.2 ± 0.49	0.13
Role physical	77.3 ± 32.9	81.3 ± 30.4	0.038	78.1 ± 1.46	81.0 ± 1.08	0.12
Bodily pain	80.6 ± 24.6	83.5 ± 22.6	0.04	81.8 ± 1.07	82.8 ± 0.78	0.44
General health perception	57.0 ± 21.9	59.5 ± 21.2	0.06	57.8 ± 0.97	59.0 ± 0.72	0.33
Role emotional	74.4 ± 36.6	78.3 ± 33.9	0.066	75.2 ± 1.65	78.0 ± 1.21	0.18
Energy-vitality	60.7 ± 19.4	64.3 ± 18.6	0.0006	61.3 ± 0.87	63.8 ± 0.64	0.019
Mental health	66.9 ± 19.4	69.4 ± 18.6	0.019	67.4 ± 0.88	69.0 ± 0.64	0.16
Social functioning	74.4 ± 24.7	77.9 ± 22.1	0.03	75.2 ± 1.09	77.5 ± 0.79	0.09

*Mann–Whitney *U*-test; **ANCOVA test.

SF-36

Mean SF-36 scores were higher in MDI than in CSII patients; nevertheless, when the scores were adjusted for age, gender and diabetes duration, they did not significantly differ between cases and control subjects, with the single exception of a higher energy/vitality score for patients in the control group (Table 2). After adjusting for additional potential confounders, no differences were detected for SF-36 subscales, either in multiple or logistic regression analyses. Similarly, no difference emerged when SF-36 scores in CSII patients were compared separately with patients treated with either glargine or NPH.

Discussion

To our knowledge, this is the largest study assessing QoL and treatment satisfaction in adults with T1DM treated with either CSII or MDI. It is also the first study comparing CSII with glargine-based MDI regimens. The involvement of large numbers of patients enrolled in over 60 centres throughout Italy allowed us to obtain a realistic picture of the impact of insulin treatment on subjective outcomes, outside the context, often artificial, of small randomized trials.

Both generic and disease-specific instruments were used to ascertain whether CSII could have an impact on broader aspects of health-related QoL, such as those investigated with the SF-36, or rather a more specific effect on those dimensions more likely to be affected by diabetes treatment. In fact, whereas SF-36 measures overall physical functioning and psychological well-being, the DSQOLS has a specific focus on the impact of diabetes and its treatment on lifestyle flexibility, the perception of burdens and restrictions, and the fears/worries related to complications. Further to its impact on QoL, we wanted also to determine whether the two modalities of insulin delivery had a different effect on treatment satisfaction. The latter is generally considered as a separate dimension, since higher treatment satisfaction does not necessarily translate into improved health-related QoL perception.

Our study shows that, despite having more severe disease (higher prevalence of complications, longer diabetes duration), patients treated with CSII have HbA_{1c} levels almost identical to those of individuals treated with MDI, without any negative impact on QoL. On the contrary, CSII patients showed a lower perception of diabetes-specific burdens and restrictions. These findings are in line with those of a previous randomized trial comparing CSII vs. NPH-based MDI, showing that patients treated with CSII feel less limited in the aspects related to diet and everyday activities [12]. Diabetes and its treatment negatively affect QoL, particularly in terms of diet restrictions imposed by traditional treatment regimens [27]. Therefore, effective treatment strategies must enable patients to achieve good glycaemic control and, at the same time, they should interfere as little as possible with an independent and flexible lifestyle. The ability to increase flexibility in moment-to-moment

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living is the reason most frequently cited by individuals who have chosen CSII [1]. It allows the patient to modify insulin availability hour by hour, making possible the performance of activities that would otherwise be risky: missing or delaying meals, sleeping late on weekends, or engaging in vigorous exercise.

In our study, the use of CSII was also associated with a markedly higher treatment satisfaction score in comparison with individuals treated with either glargine-based MDI or NPH-based MDI regimens. Previous small studies utilizing the DTSQ have failed to show differences in treatment satisfaction between CSII- and MDI-treated patients [9,28]. In studies assessing treatment satisfaction with different instruments, mixed results have been obtained. In particular, CSII has been associated with higher satisfaction in one study [12], whereas no major differences were documented in another study [8]. None of these studies compared CSII vs. glargine-based MDI.

Another important observation derived from our study is that patients treated with CSII have less fear of hypoglycaemia, in line with a previous study showing that the switch from NPH-based MDI to CSII was associated with a decrease in the incidence of hypoglycaemic episodes and a parallel decrease in the fear of hypoglycaemia [10]. What our study adds is that CSII patients have less fear of hypoglycaemia not only in comparison with NPH-MDI patients, but also with respect to patients treated with glargine-based MDI, despite the documented lower risk of hypoglycaemia with glargine compared with NPH [13,14]. Hypoglycaemia is undoubtedly a serious concern for diabetic patients, and fear of hypoglycaemia can negatively affect the acceptance of insulin therapy and the ability to lower HbA_{1c} levels effectively through intensive treatment [29]. The increased confidence in CSII therapy can in turn further improve treatment satisfaction.

We were unable to show any major difference between CSII and MDI patients for the broader aspects of health-related QoL investigated by the SF-36 health survey. In a randomized trial involving 79 patients, the initiation of CSII was associated with an improvement in the mental health and general health dimensions of the SF-36 in comparison with MDI patients [9]. In another trial involving 272 patients randomized to CSII- or NPH-based MDI, no differences in perception of physical health, but a significant improvement in perception of mental health with CSII were documented using the SF-12 questionnaire [12]. It should be stressed that, contrary to randomized trials, in our study the baseline characteristics of CSII and MDI patients were different, with the former having a longer duration of diabetes and higher prevalence of complications. It is also worth noting that the proportion of women was significantly higher in insulin pump users than in MDI-treated individuals, thus suggesting that CSII is preferentially chosen by, or offered to, female patients, who generally tend to report poorer health-related QoL than men.

For all these reasons, one would expect poorer health-related QoL in CSII patients, as the comparison of raw scores seems to suggest. Nevertheless, when gender and diabetes duration were taken into account, the differences became non-significant; such a lack of significant differences in SF-36 scores between CSII and MDI patients would suggest a positive effect of CSII, although this remains to be proven in additional studies.

As a final consideration, it has been argued that some patients could be physically and emotionally uncomfortable with wearing an external device, which is dependent on mechanical functioning and more obviously advertises a patient's diabetes to the outside world than does injection therapy. In our study we were unable to detect any psychological harm associated with CSII therapy, either in the whole cohort, or when the analyses were performed separately on males and females (data not shown). The high proportion of women among CSII users seems also to suggest that women do not perceive the pump as cosmetically unacceptable. This is probably a consequence of the technical features of new pumps, which are small and lightweight compared with the early ones. The newer pumps are also more reliable, and may have alarms for empty cartridges, low batteries, occlusion of tubing and faulty electronics, giving rise to less fear of undetected malfunction, which was a problem with some of the older pumps [1]. Overall, the lack of significant differences in favour of MDI, despite the very large number of patients enrolled, excludes any detrimental effect of CSII on QoL.

Finally, some of the potential limitations of our study need to be discussed. First, this was not a randomized trial, and patients who were offered and accepted CSII therapy could differ systematically from those treated with MDI. To overcome this problem, we included a separate control group identified in centres without any experience in insulin pump therapy. Nevertheless, we did not document any major difference in QoL and treatment satisfaction when comparing control patients sampled in centres using or not using CSII. This allowed us to combine the two control groups. Furthermore, results were confirmed after adjusting the analysis for a large array of possible confounders.

Second, QoL and treatment satisfaction in CSII patients in our study reflect those of individuals who have accepted this treatment and coped with it. We cannot exclude that the psychological impact of wearing the pump could be particularly negative if the treatment was offered to individuals who do not meet the desired requirements [30]. Overall, we believe that the study results closely reflect the impact of different insulin treatment modalities in routine clinical practice conditions.

In conclusion, our study has confirmed the findings of previous small studies suggesting CSII is not associated with deterioration in QoL. On the contrary, it is associated in both genders with a lower perceived burden of disease and higher treatment satisfaction compared with NPH-based MDI. In addition, this is the first large study suggesting QoL gains deriving from greater lifestyle flexibility, less fear of hypoglycaemia, and higher treatment satisfaction, when CSII is compared with glargine-based MDI regimens. These findings are useful when weighing the benefits of different insulin therapy modalities against costs.

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Competing interests

A.N. in the last 12 months has received fees for speaking from Sanofi Aventis and LifeScan Italia and a fee for organizing education from Novo Nordisk; he has also received funds for research from LifeScan Scotland Ltd. E.B. and P.P. are employees of Fondazione Medtronic Italia, Sesto San Giovanni (MI), Italy.

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References

1 Colquitt JL, Green C, Sidhu MK, Hartwell D, Waugh N. Clinical and cost-effectiveness of continuous subcutaneous insulin infusion for diabetes. *Health Technol Assess* 2004; **8**: 1–171.
2 Centers for Disease Control and Prevention (CDC). Self-rated fair or poor health among adults with diabetes—United States, 1996–2005. *MMWR Morb Mortal Wkly Rep* 2006; **55**: 1224–1227.
3 Huang GH, Palta M, Allen C, LeCaire T, D'Alessio D; Wisconsin Diabetes Registry. Self-rated health among young people with Type 1 diabetes in relation to risk factors in a longitudinal study. *Am J Epidemiol* 2004; **159**: 364–372.
4 Koopmanschap M; CODE-2 Advisory Board. Coping with Type II diabetes: the patient's perspective. *Diabetologia*. 2002; **45**: S18–S22.
5 Glasgow RE, Ruggiero L, Eakin EG, Dryfoos J, Chobanian L. Quality of life and associated characteristics in a large national sample of adults with diabetes. *Diabetes Care* 1997; **20**: 562–567.
6 Barnard KD, Lloyd CE, Skinner TC. Systematic literature review: quality of life associated with insulin pump use in Type1 diabetes. *Diabet Med* 2007; **24**: 607–617.
7 Boland EA, Grey M, Oesterle A, Fredrickson L, Tamborlane WV. Continuous subcutaneous insulin infusion. A new way to lower risk of severe hypoglycemia, improve metabolic control, and enhance coping in adolescents with Type 1 diabetes. *Diabetes Care* 1999; **22**: 1779–1784.
8 Tsui E, Barnie A, Ross S, Parkes R, Zinman B. Intensive insulin therapy with insulin lispro: a randomized trial of continuous subcutaneous insulin infusion versus multiple daily insulin injection. *Diabetes Care* 2001; **24**: 1722–1727.
9 DeVries JH, Snoek FJ, Kostense PJ, Masurel N, Heine RJ. Dutch Insulin Pump Study Group: A randomized trial of continuous subcutaneous insulin infusion and intensive injection therapy in Type 1 diabetes for patients with long-standing poor glycemic control. *Diabetes Care* 2002; **25**: 2074–2080.
10 Linkeschova R, Raoul M, Bott U, Berger M, Spraul M. Less severe hypoglycaemia, better metabolic control, and improved quality of life in Type 1 diabetes mellitus with continuous subcutaneous insulin infusion (CSII) therapy; an observational study of 100 consecutive patients followed for a mean of 2 years. *Diabet Med* 2002; **19**: 746–751.

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11 Bruttomesso D, Pianta A, Crazzolara D, Scaldaferri E, Lora L, Guarneri G *et al*. Continuous subcutaneous insulin infusion (CSII) in the Veneto region: efficacy, acceptability and quality of life. *Diabet Med* 2002; **19**: 628–634.
12 Hoogma RP, Hammond PJ, Gomis R, Kerr D, Bruttomesso D, Bouter KP *et al*. Comparison of the effects of continuous subcutaneous insulin infusion (CSII) and NPH-based multiple daily insulin injections (MDI) on glycaemic control and quality of life: results of the 5-nations trial. *Diabet Med* 2005; **23**: 141–147.
13 McKeage K, Goa KL. Insulin glargine: a review of its therapeutic use as a long-acting agent for the management of Type 1 and 2 diabetes mellitus. *Drugs* 2001; **61**: 1599–1624.
14 Rosenstock J, Dailey G, Massi-Benedetti M, Fritsche A, Lin Z, Salzman A. Reduced hypoglycemia risk with insulin glargine: a meta-analysis comparing insulin glargine with human NPH insulin in Type 2 diabetes. *Diabetes Care* 2005; **28**: 950–955.
15 Franciosi M, Pellegrini F, De Berardis G, Belfiglio M, Cavaliere D, Di Nardo B *et al*. The impact of blood glucose self-monitoring on metabolic control and quality of life in Type 2 diabetic patients: an urgent need for better educational strategies. *Diabetes Care* 2001; **24**: 1870–1877.
16 Bott U, Muhlhauser I, Overmann H, Berger M. Validation of a diabetes-specific quality-of-life scale for patients with Type 1 diabetes. *Diabetes Care* 1998; **21**:757–769.
17 Bott U, Ebrahim S. Further development of a quality-of-life measure for IDDM patients. *Diabetologia* 1998; **41**: A74 (Abstract).
18 Ware JE Jr, Gandeck BL, Keller SD, the IQOLA Project Group. Evaluating instruments used cross-nationally: methods from the IQOLA Project. in quality of life and pharmacoecoeconomics. In: Spilker B, ed. *Clinical Trials*, 2nd edn. Philadelphia: Lippincott-Raven Publishers, 1996: 681–692.
19 Bradley C. Diabetes Treatment Satisfaction Questionnaire (DTSQ). In: Bradley C, ed. *Handbook of Psychology and Diabetes*. Chur, Switzerland: Harwood Academic Publishers, 1994: 111–132.
20 Nicolucci A, Giorgino R, Cucinotta D, Zoppini G, Muggeo M, Squatrito S *et al*. Validation of the Italian version of the WHO-Well-Being Questionnaire (WHO-WBQ) and the WHO-Diabetes Treatment Satisfaction Questionnaire (WHO-DTSQ). *Diabetes Nutr Metab* 2004; **17**: 235–243.
21 Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; **30**: 473–483.
22 McHorney CA, Ware JE Jr, Lu JF, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. *Med Care* 1994; **32**: 40–66.
23 Apolone G, Mosconi P. The Italian SF-36 Health Survey: translation, validation and norming. *J Clin Epidemiol* 1998; **51**: 1025–1036.
24 Dupont WD, Plummer WD Jr. Power and sample size calculations. A review and computer program. *Control Clin Trials* 1990; **11**: 116–128.
25 Chassany O, Sagnier P, Marquis P, Fullerton S, Aaronson N, for the European Regulatory Issues on Quality of Life Assessment Group. Patient-reported outcomes: the example of health-related quality of life—a European guidance document for the improved integration of health-related quality of life assessment in the drug regulatory process. *Drug Inf J* 2002; **36**: 209–238.
26 *SAS® Language*, Version 9.1. Cary: SAS Institute Inc., 2002–2003.
27 Bradley C, Speight J. Patient perceptions of diabetes and diabetes therapy: assessing quality of life. *Diabetes Metab Res Rev* 2002; **18** (Suppl 3): S64–S69.
28 Hoogma RP, Spijker AJ, van Doorn-Scheele M, van Doorn TT, Michels RP, van Doorn RG *et al*. Quality of life and metabolic control in patients with diabetes mellitus Type 1 treated by continuous subcutaneous insulin infusion or multiple daily insulin injections. *Neth J Med* 2004; **62**: 383–387.
29 Davis RE, Morrissey M, Peters JR, Wittrup-Jensen K, Kennedy-Martin T, Currie CJ. Impact of hypoglycaemia on quality of life and productivity in Type 1 and Type 2 diabetes. *Curr Med Res Opin* 2005; **21**: 1477–1483.
30 Pickup J, Keen H. Continuous subcutaneous insulin infusion at 25 years: evidence base for the expanding use of insulin pump therapy in Type 1 diabetes. *Diabetes Care* 2002; **25**: 593–598.

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