Efficacy of an Education Program for People With Diabetes and Insulin Pump Treatment (INPUT): Results From a Randomized Controlled Trial

Dominic Ehrmann,[1,2] Bernhard Kulzer,[1,2,3] Melanie Schipfer,[1] Bernhard Lippmann-Grob,[3] Thomas Haak,[3] and Norbert Hermanns[1,2,3]

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OBJECTIVE

Continuous subcutaneous insulin infusion (CSII) is the most advanced form of insulin delivery, but it requires structured education to provide users with the necessary knowledge/skills and to support their motivation. Currently, no structured education program designed to provide this training has been evaluated. We developed a CSII-specific, structured education program (Insulin Pump Treatment [INPUT]) and evaluated its impact on glycemic control, behavior, and psychosocial status.

RESEARCH DESIGN AND METHODS

This was a multicenter, randomized, parallel trial with a 6-month follow-up. Eligible participants (age 16–75 years) currently were treated with insulin pump therapy. Participants were randomly assigned (1:1) to the INPUT program or to usual care using a computer-generated algorithm, with study center as the stratification factor. The primary outcome was HbA_{1c} change from baseline to 6 months. Secondary outcomes were incidence of severe hypoglycemia and changes in behavioral and psychosocial measures.

RESULTS

Between 1 April 2016 and 26 April 2016, 268 people with diabetes and a mean duration of CSII therapy of 9.5 years were randomly assigned to the INPUT group (n = 135) or control group (n = 133). At 6 months, HbA_{1c} improved in the INPUT group (8.33 ± 0.8 vs. 8.04 ± 0.9; $P < 0.0001$) but not in the control group (8.33 ± 1.0 vs. 8.27 ± 1.0; $P = 0.11$). The between-group difference in HbA_{1c} reduction was significant, favoring INPUT (−0.28% vs. −0.06%, Δ −0.22%, 95% CI −0.38 to −0.06; $P = 0.0029$). The incidence rate ratio of severe hypoglycemia was 3.55 times higher for participants in the control group than for those in the INPUT group (95% CI 1.50–8.43; $P = 0.0041$).

CONCLUSIONS

The INPUT education program led to a significant improvement in glycemic control and incidence of severe hypoglycemia in insulin pump users.

[1]Research Institute Diabetes Academy Mergentheim, Bad Mergentheim, Germany
[2]Department of Clinical Psychology and Psychotherapy, University of Bamberg, Bamberg, Germany
[3]Diabetes Clinic Mergentheim, Bad Mergentheim, Germany

Corresponding author: Norbert Hermanns, hermanns@fidam.de.

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The introduction of continuous subcutaneous insulin infusion (CSII) therapy in the late 1970s paved a new road for the treatment of insulin-dependent diabetes (1). With CSII therapy, it was possible to mimic normal physiologic insulin secretion more closely through continuous infusion of rapid-acting insulin over 24 h a day (basal rate) and manually administered boluses for prandial control at mealtimes without additional insulin injections. Over the years, several advances have been introduced (e.g., temporary basal rates, bolus delivery options, automated bolus calculators) that allow users to individualize their therapy to optimize glycemic control (2). Importantly, CSII is a cornerstone of future improvements in diabetes therapy and developments toward closed-loop systems (3).

With these advanced features, the use of CSII offers significant advantages over traditional therapy with multiple daily injections (MDIs) of insulin in terms of treatment flexibility and avoidance of injections. However, given the higher costs associated with CSII therapy, the magnitude of its effects, despite being clinically relevant, could be higher but are only moderate. Meta-analyses have demonstrated significant reductions in HbA_{1c} levels (-0.3%) with CSII therapy compared with MDIs of insulin (4,5). The beneficial effects of CSII therapy on hypoglycemia are inconclusive (5,6).

A possible reason for the underwhelming efficacy of CSII therapy may be that users do not fully use the features offered by their pump because a more frequent use of pump features was found to be associated with better glycemic control (7–9). In a clinical survey conducted in 40 specialized diabetes practices that assessed the usage of pump features in >1,000 people with diabetes, 25% of CSII users did not use temporary basal rates and ~75% did not have multiple basal profiles (10). Furthermore, various bolus options for better postprandial control (e.g., dual wave, square wave) were used by 49% of respondents, and bolus calculators were used by 67%. Lack of education and diminished motivation may be the reasons why pump users do not effectively use these technological features (7).

However, psychological barriers also must be considered. In particular, aspects of adherence and empowerment need to be addressed when treating diabetes with an insulin pump (11) because the high behavioral demand of CSII therapy, the need for more consistent engagement (12,13), burnout (14), depression (15), and perceived impairment of body image (16) have an impact on adherence to and outcomes of CSII therapy. In addition, people with diabetes can have many misconceptions about the capabilities of CSII therapy. These misconceptions can be accompanied by unrealistic expectations (17) and lead to negative emotional reactions to CSII therapy (e.g., feeling burdened, vulnerable, stigmatized) (18). In sum, CSII therapy can be considered the most demanding insulin regimen (11,19).

Structured diabetes education has been recognized as an integral component of diabetes therapy for decades and has been integrated into many guidelines for the treatment of diabetes (20,21). Although structured diabetes education programs have been evaluated successfully, especially in type 1 diabetes, general education on intensified insulin therapy (e.g., basal-bolus therapy, carbohydrate counting, insulin-to-carbohydrate ratio) has not been shown to be equally beneficial for people with diabetes using CSII compared with MDI (22). CSII-specific education programs that facilitate the effective use of insulin pumps and address the psychosocial barriers of CSII use are needed. This need was highlighted by the National Institute for Health and Care Excellence (20) and the American Diabetes Association (23), calling for structured education for CSII users.

Although almost all studies on the effectiveness of CSII therapy used some sort of instruction (6), these trainings did not resemble a structured education program. Consequently, existing CSII education has varied across different practices. Thus, a standardized, structured education program specifically developed for CSII users that provides the skills and knowledge required for effective use of insulin pump features and addresses psychological barriers could augment the beneficial effects of CSII therapy and standardize CSII education.

We developed a CSII-specific structured education and treatment program (Insulin Pump Therapy [INPUT]) that is based on a self-management approach that incorporates clinical, technological, and psychosocial components. To assess the efficacy of this program, we conducted a randomized controlled trial of current CSII users to evaluate whether participation in this education program is more effective at lowering HbA_{1c} than usual care.

RESEARCH DESIGN AND METHODS

Study Design

This investigator-initiated study was designed as an open-label, parallel, randomized controlled trial with a 6-month follow-up. It was conducted in an outpatient setting of 26 CSII-specialized secondary care practices (study centers) throughout Germany. Ethics approval was obtained from the ethics committee of the German Psychological Association (NH 012016; Berlin, Germany).

Participants

Only people with diabetes currently treated with CSII therapy were eligible for the study. If CSII therapy was only recently (<6 months) initiated, the principal investigator of a study center had to confirm that those participants received a device-specific introduction on using their specific pump model before participation. Additional inclusion criteria were age 16–75 years; prior participation in a structured diabetes education program on intensive insulin therapy (to guarantee that all participants had the proper knowledge and basic skills to treat their diabetes with insulin); screening HbA_{1c} 7.5–13% (58–119 mmol/mol); ability to understand, speak, and write the German language; and informed consent (if necessary, informed consent of parents). Exclusion criteria were diabetes duration <1 year, severe organic disease preventing regular participation in the education courses, pregnancy, severe cognitive impairment, current treatment of a psychiatric disorder, or renal disease requiring dialysis.

Eligible people with diabetes and CSII therapy were recruited at each study center. Before inclusion, participants were fully informed both orally and in writing about the study and gave written informed consent. Participants received no monetary compensation for participation in this study.

Randomization and Masking

Participants were randomly assigned to one of two groups: *1*) participation in the INPUT treatment and education program or *2*) waiting list control group with treatment as usual. Thus, both groups used CSII therapy but differed only in whether they participated in the INPUT program.

Randomization was performed centrally at the study coordinating center, whose staff were not involved with recruitment or treatment of study participants. A computer-generated algorithm (SYSTAT 12.0; Systat Software, Chicago, IL), with study center as stratification factor and a 1:1 allocation, was used. After a study center recruited 6–16 participants and completed the baseline assessment for all recruited participants, the center contacted the study coordinating center, and block randomization was performed, with the block size depending on the participant pool for each study center (n = 6–16). Because of the nature of the intervention, blinding of participants as well as the diabetes educators who provided the intervention was not possible.

Procedure

The INPUT program is a structured education program that consists of 12 sessions, with each lasting 90 min. INPUT is conducted as a group program (three to eight participants per group) The specific content of INPUT is provided in Supplementary Table 1. INPUT is based on the self-management/empowerment approach and focuses on empowering participants to use their insulin pump effectively in daily life. Participants were educated about basal rates and their adaptation as well as about the effective use of temporary basal rates, programming different basal profiles, and adjusting prandial insulin administration with various bolus options. Training in recognizing problematic patterns in their glucose values and strategies to fix these were covered extensively throughout the course. Participants also were trained in how to use their insulin pump to avoid acute complications, such as hypoglycemia and diabetic ketoacidosis. Another key topic of INPUT is the psychosocial impact of CSII therapy. Throughout the course, emotional and motivational obstacles as well as negative attitudes toward diabetes and CSII therapy were addressed (e.g., barriers to CSII therapy, being dependent on a technical device, concerns about pump failures, positive error management). A key element of INPUT is individual goal setting. Participants discussed the individual goals they wanted to achieve within the course, reflected on the status of their goal attainment, and assessed their handling of barriers. Between sessions, participants were instructed to complete various materials (e.g., worksheets for individual goal setting and attainment, exercises about carbohydrate counting, glucose logs). Family members, partners, or friends were invited to attend the 10th lesson, during which social support issues were addressed.

INPUT was conducted by a single certified diabetes educator in person on the premises of each study center. These diabetes educators were trained for 12 h to ensure a standardized conduct of INPUT. This prestudy training was conducted by a diabetologist and psychologists who addressed the medical and psychological components of INPUT. In addition, diabetes educators received a written curriculum. Before the study start, each study center received an initiation visit. Major changes of CSII therapy were supervised by the diabetologist.

The study consisted of two decisive measurement points spanning three study phases. First, 2 weeks before the start of the intervention phase, baseline assessments were conducted. At baseline, participants completed several questionnaires, and blood samples for HbA_{1c} analysis were collected and sent to a central laboratory. Second, participants randomly assigned to the INPUT group received the biweekly intervention, whereas control group participants continued with CSII therapy without additional education. Third, 6 months after the end of the intervention, follow-up measurements were taken, assessing the same variables as the baseline measurements.

Outcomes

The primary outcome was the change in HbA_{1c} from baseline to the 6-month follow-up. HbA_{1c} was measured in a central laboratory using high-performance liquid chromatography (Automated Glycohemoglobin Analyzer HLC-723G11; Tosoh) (normal range 21–43 mmol/mol [4.1–6.1%]). Laboratory personnel were blinded to the randomized treatment allocation of the study participants.

As a secondary outcome, the incidence of severe hypoglycemic events (requiring third-party assistance or medical intervention [injection of glucagon or glucose or associated with hospitalization]) during the 6-month study period were assessed and verified by interview and documented in severe adverse event forms. The following secondary outcomes were assessed at baseline and the 6-month follow-up to analyze change:

- Diabetes distress was evaluated with the Problem Areas in Diabetes Scale, which assesses psychosocial adaptation to the burden of living with and treating diabetes (Cronbach α [CR-α] = 0.95) (24).
- Depressive symptoms were assessed with the German version of the Center for Epidemiologic Studies Depression Scale (CR-α = 0.89) (25).
- Health-related quality of life was assessed by the EuroQol EQ-5D (test-retest reliability = 0.60) (26).
- Diabetes self-management was assessed with the Diabetes Self-Management Questionnaire, a self-reported measure of participants' level of self-management (CR-α = 0.84) (27).
- Treatment satisfaction with the current treatment was assessed with a 10-item questionnaire (CR-α = 0.79) (28).
- Hypoglycemia awareness was assessed with the German version of a hypoglycemia awareness questionnaire (29), which indicates the severity of hypoglycemia unawareness (CR-α = 0.69).
- Diabetes empowerment was assessed by the German short version of the Diabetes Empowerment Scale, a measure of diabetes-related psychosocial self-efficacy (CR-α = 0.89) (30).
- Attitudes toward insulin pump therapy were assessed through a new German language questionnaire (CR-α = 0.74) consisting of six subscales measuring perceived benefits (achieving better glycemic control, gaining more flexibility), perceived barriers (impaired body image, technological dependence), and ease of use (importance of functionality, importance of design) (31).
- Use of insulin pump features (temporary basal rates, basal rate profiles, bolus options, bolus calculator, analysis software, pairing with continuous glucose monitoring [CGM]) was assessed through self-report.

Key demographics (age, sex, education, BMI) as well as medical information (diabetes type, diabetes duration, duration of CSII therapy, late complications [retinopathy, nephropathy, neuropathy, diabetic foot syndrome, coronary heart disease]) were retrieved from patient files and documented through a case report form completed by study personnel.

Statistical Analysis

On the basis of the assumption of an expected HbA_{1c} difference between the two groups of 0.3% and an SD of 0.8% for each group (effect size = 0.375), power analysis revealed that 228 participants per group were needed to achieve a power of $1 - \beta = 0.80$ with a two-sided α-error of 0.05. Assuming a nonevaluable rate of 15% (e.g., not suitable for per-protocol analysis), a total of 268 participants was needed. Primary and secondary outcomes were analyzed with ranks using van der Waerden scores (i.e., area transformation) because of skewed distribution. ANCOVAs with treatment group as the between factor and baseline values as covariates were conducted for primary and secondary outcomes. The α-level was set to 0.05. The per-protocol sample included participants with complete data for the primary outcome and without major protocol violations (attendance at >50% of INPUT sessions). For the primary outcome, intention-to-treat analysis was performed, including all participants who completed baseline measurement. Missing values were replaced with baseline values. The difference in incidence of severe hypoglycemia was analyzed through zero-inflated Poisson regression analysis to account for overdispersion of zeros. Exploratory secondary analyses were conducted to identify baseline factors as possible moderators of change in HbA_{1c}. Separate linear regression analyses were performed for each baseline factor, with HbA_{1c} at follow-up as the dependent variable controlling for baseline HbA_{1c}. The main effect of the moderator variable and group as well as the interaction term between group and moderator variables were included to test for moderation. The following moderator variables were tested: age, sex, baseline HbA_{1c}, use of CGM technology, duration of CSII therapy, age of onset of CSII therapy, previous diabetes education (number, years since last course, regimen at last course), diabetes distress, depressive symptoms, empowerment, treatment satisfaction, recruited pool size, and study center. In addition, secondary tests of possible mediators were performed using linear

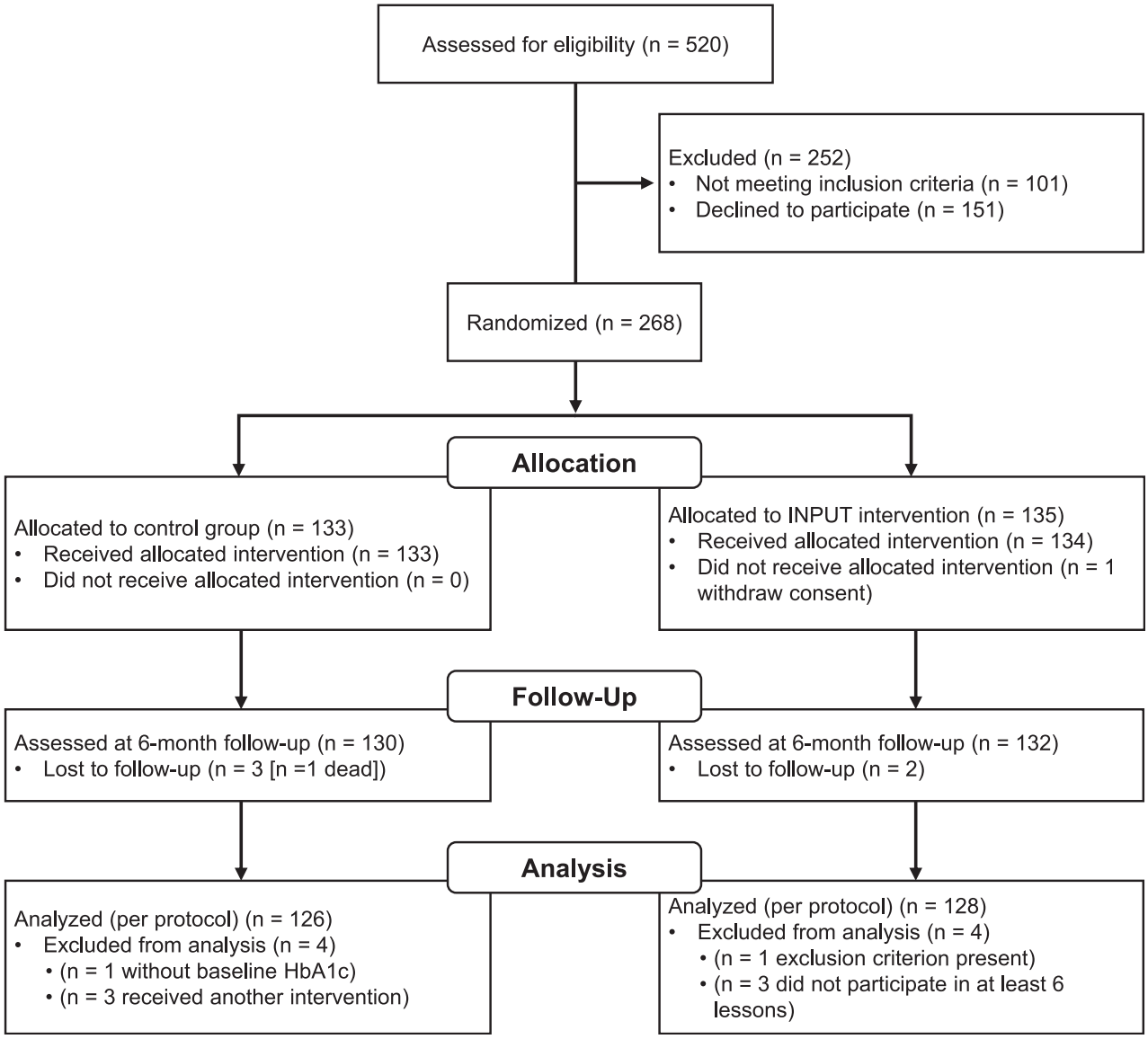

Figure 1—Trial profile.

regression analyses and the Sobel *z* statistic for mediation. SPSS version 24.0 software was used for all statistical analyses except the zero-inflated Poisson regression for which the statistical package R 3.4.3 was used.

RESULTS

Recruitment and Baseline Data

Participants were recruited between 1 April 2016 and 26 April 2016. Follow-up measurements were completed in February 2017. Each study center contributed one patient pool (median pool size 9, interquartile range [IQR] 7–12). As planned, 268 participants were randomly assigned to either the INPUT intervention or the control group, and data from a total of 254 participants were analyzed for the per-protocol population (Fig. 1). As seen in Table 1, only one participant with type 2 diabetes and CSII therapy was recruited. Participants were performing CSII therapy for almost one-half of the time since their diabetes diagnosis, and the majority initiated CSII therapy at an adult age. However, CSII duration showed a wide range, with most participants performing CSII therapy for <8 years; however, as shown in Table 1, participants performing CSII therapy for <1 year also were included. Table 1 also shows that 21–30% received their last structured education on intensive insulin therapy while performing MDI therapy and thus, never received structured education while

Table 1—Baseline characteristics of the intention-to-treat population

	INPUT group (*n* = 135)	Control group (*n* = 133)	*P* value
Age (years)	42.8 (14.2)	44.3 (14.3)	0.383
Median (IQR)	45.0 (29.5–53.0)	45.0 (34.0–55.0)	0.477
Sex			0.01
Male	44 (33)	64 (48)	
Female	91 (67)	69 (52)	
Education (years)	11.3 (2.2)	11.5 (2.3)	0.534
BMI (kg/m^2)	28.2 (5.7)	27.9 (5.5)	0.633
Diabetes type			1.000
Type 1	134 (99.3)	133 (100)	
Type 2	1 (0.7)	0 (0)	
Duration of diabetes (years)	22.6 (12.4)	23.2 (12.7)	0.717
Median (IQR)	21.0 (12.5–32.8)	21.0 (13.0–30.1)	0.688
Screening HbA_{1c}			0.604
mmol/mol	68.2 (8.7)	68.8 (10.0)	
%	8.4 (0.8)	8.4 (0.9)	
HbA_{1c} (central laboratory)			0.808
mmol/mol	67.2 (9.1)	67.5 (10.3)	
%	8.3 (0.8)	8.3 (0.9)	
Self-monitored blood glucose measurements (mean number per day)	5.4 (1.8)	5.2 (1.9)	0.424
Structured diabetes education			
Number of courses	4.6 (3.6)	4.3 (3.2)	0.468
Time since last education (years)	4.7 (4.2)	4.2 (3.6)	0.252
Duration of CSII therapy (years)	10.1 (8.0)	8.9 (6.8)	0.184
Median (IQR)	7.8 (4.0–14.3)	7.3 (3.6–13.5)	0.328
Participants on CSII therapy			
<1 year	6 (4.4)	8 (6.0)	
<5 years	39 (28.8)	48 (36.1)	
<10 years	86 (63.6)	83 (62.4)	
≥10 years	49 (36.3)	50 (37.6)	
Age of onset of CSII therapy (years)	32.6 (13.7)	35.3 (14.8)	0.120
Median (IQR)	31.8 (23.2–41.1)	34.5 (23.2–46.9)	0.144
Participants on CSII therapy			
<12 years	8 (5.9)	3 (2.3)	
<18 years	20 (14.8)	19 (14.4)	
≥18 years	115 (85.2)	114 (85.6)	
Therapy regimen at last education			0.081
CSII therapy	94 (69.6)	105 (78.9)	
MDI therapy	41 (30.4)	28 (21.1)	
Late complications			
Participants with at least one	63 (46.7)	54 (40.6)	0.317
Number of complications	0.8 (1.1)	0.8 (1.1)	0.981
Severe hypoglycemia (third-party assistance + medical intervention)			
Total number of events (rate per patient-year)	27 (0.40)	27 (0.41)	0.993
Number of affected participants (%)	13 (9.6)	15 (11.3)	0.644

Data are mean (SD) or *n* (%) unless otherwise indicated. Late complications (from medical records): retinopathy, nephropathy, neuropathy, coronary heart disease, diabetic foot syndrome.

on CSII therapy (not accounting for the nonstructured technical instruction about pump use).

Primary Outcome

HbA_{1c} improved in the INPUT group (−0.28% [−3.1 mmol/mol]; $P < 0.0001$) but did not change in the control group (−0.06% [−0.7 mmol/mol]; $P = 0.11$). The between-group difference of this change in HbA_{1c} was highly significant in favor of INPUT (−0.22% [95% CI −0.38 to −0.06%]; $P = 0.0029$) (Table 2). These results were corroborated by analyzing the intention-to-treat population (−0.21% [95% CI −0.36 to −0.06%]; $P = 0.0061$). Improvement of HbA_{1c} in the INPUT group was present along the whole HbA_{1c} range because the distribution of follow-up HbA_{1c} values can be clearly distinguished from the distribution of baseline HbA_{1c} values (Fig. 2). In contrast, the distribution of HbA_{1c} values for the control group showed a great overlap of baseline and follow-up, indicating that HbA_{1c} remained constant. Additional sensitivity analysis revealed that participants in the INPUT group had a twofold higher chance of achieving optimal glycemic control at the 6-month follow-up (HbA_{1c} <7.5% [58 mmol/mol]) compared with the control group (odds ratio 1.98 [95% CI 1.04–3.78]; $P = 0.0372$).

Secondary Outcomes

In the 6 months after the end of the intervention, a total of 55 events of severe hypoglycemia requiring third-party assistance or medical intervention were reported (11 events in the INPUT group and 44 events in the control group [0.17 vs. 0.70 events per patient-year]) (Table 3). The results of the zero-inflated Poisson regression analyses showed that the incidence rate ratio (IRR) of severe hypoglycemia was 3.55 times higher for participants in the control group than for those in the INPUT group (95% CI 1.50–8.43; $P = 0.0041$). Events of severe hypoglycemia requiring third-party assistance but without medical assistance for recovery were less frequent in the INPUT group than in the control group (11 vs. 35 events, incidence rate 0.17 vs. 0.56 events per patient-year). The IRR for such an event was 4.26 times higher for participants in the control group than in the INPUT group (95% CI 1.77–10.23; $P = 0.0012$). Nine of the 55 episodes of severe hypoglycemia required medical assistance for recovery; all 9 events took

Table 2—Changes in primary and secondary outcomes from baseline to follow-up

	Per-protocol population ($N = 254$)							
	INPUT ($n = 128$)			Control group ($n = 126$)				
	Baseline	Follow-up	Follow-up to baseline change (95% CI)	Baseline	Follow-up	Follow-up to baseline change (95% CI)	Adjusted between-group difference (95% CI)	*P* value*
Primary outcome: change in HbA_{1c}								
HbA_{1c} (mmol/mol)	67.5 (9.3)	64.4 (10.4)	−3.1 (−4.4 to −1.8)	67.6 (10.5)	66.9 (11.0)	−0.7 (−1.9 to 0.6)	−2.4 (−4.2 to −0.6)	0.0029
HbA_{1c} (%)	8.33 (0.8)	8.04 (0.9)	−0.28 (−0.40 to −0.17)	8.33 (1.0)	8.27 (1.0)	−0.06 (−0.18 to 0.05)	−0.22 (−0.38 to −0.06)	0.0029
Secondary outcomes								
Patient reported								
Diabetes distress (range 0–100)#	28.32 (16.26)	23.03 (15.98)	−5.29 (−7.51 to −3.06)	27.46 (16.25)	27.97 (18.33)	0.51 (−1.62 to 2.65)	−5.60 (−8.53 to −2.67)	0.0003
Depressive symptoms (range 0–60)#	15.87 (9.21)	14.41 (9.39)	−1.46 (−2.73 to −0.18)	13.42 (8.28)	14.05 (9.26)	0.63 (−0.64 to 1.91)	−1.31 (−2.21 to −0.41)	0.0478
Health-related quality of life (range −1 to 1)+	0.90 (0.14)	0.92 (0.12)	0.02 (−0.001 to 0.04)	0.90 (0.12)	0.90 (0.12)	0.00 (−0.01 to 0.02)	0.02 (−0.01 to 0.04)	0.2107
Diabetes self-management (range 0–10)+	6.65 (1.14)	7.11 (1.06)	0.46 (0.29–0.62)	6.60 (1.38)	6.61 (1.44)	0.01 (−0.15 to 0.17)	0.46 (0.25–0.68)	0.0002
Treatment satisfaction (range 10–60)#	28.54 (6.95)	26.00 (6.53)	−2.54 (−3.61 to −1.46)	28.80 (6.93)	29.75 (7.03)	0.95 (−0.28 to 2.18)	−3.61 (−5.02 to −2.19)	<0.0001
Hypoglycemia awareness (range 0–7)#	0.94 (1.38)	0.87 (1.38)	−0.06 (−0.31 to 0.18)	1.14 (1.48)	1.20 (1.60)	0.06 (−0.19 to 0.30)	−0.21 (−0.51 to 0.10)	0.1852
Diabetes empowerment (range 0–33)+	25.15 (4.80)	26.76 (4.44)	1.61 (0.80–2.42)	24.63 (5.21)	25.02 (5.33)	0.40 (−0.36 to 1.15)	1.43 (0.45–2.41)	0.0048
Attitudes toward CSII therapy (mean item scores; range 0–4)								
Flexibility+	3.27 (0.56)	3.40 (0.55)	0.13 (0.03–0.23)	3.34 (0.49)	3.33 (0.52)	−0.01 (−0.09 to 0.08)	0.10 (−0.02 to 0.21)	0.0799
Glycemic control+	3.05 (0.62)	3.22 (0.58)	0.17 (0.08–0.26)	3.03 (0.53)	3.02 (0.59)	−0.01 (−0.10 to 0.09)	0.18 (0.07–0.30)	0.0024
Impaired body image#	0.86 (0.72)	0.83 (0.71)	−0.03 (−0.12 to 0.07)	0.77 (0.59)	0.78 (0.59)	0.01 (−0.10 to 0.11)	−0.00 (−0.13 to 0.12)	0.9890
Technological dependence#	1.24 (0.73)	1.15 (0.77)	−0.09 (−0.20 to 0.03)	1.13 (0.70)	1.19 (0.75)	0.06 (−0.05 to 0.17)	−0.11 (−0.26 to 0.03)	0.1317
Functionality+	3.00 (0.76)	3.16 (0.67)	0.16 (0.05–0.28)	3.08 (0.72)	3.05 (0.66)	−0.03 (−0.12 to 0.06)	0.16 (0.03–0.29)	0.0085
Importance of design#	2.69 (0.76)	2.63 (0.84)	−0.05 (−0.17 to 0.07)	2.56 (0.78)	2.60 (0.75)	0.04 (−0.07 to 0.15)	−0.05 (−0.20 to 0.10)	0.6048

Data are mean (SD) unless otherwise indicated. *P values for between-group differences using transformed van der Waerden scores. #Negative values of change mean improvement. +Positive values of change mean improvement.

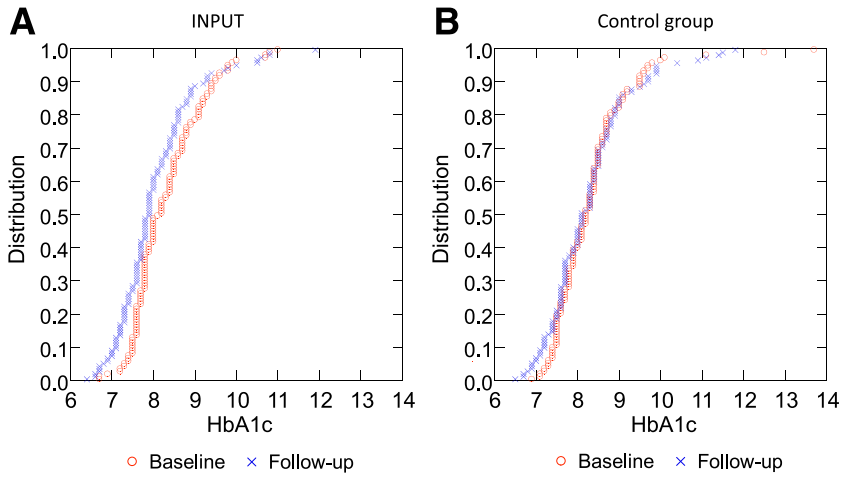

Figure 2—Distribution of HbA_{1c} values at baseline and at follow-up. *A*: INPUT group. *B*: Control group.

place in the control group (incidence rates 0.00 vs. 0.14 events per patient-year). The proportion of participants who were affected by severe hypoglycemia requiring medical intervention was significantly lower in the INPUT group (0.0% vs. 4.8%; $P = 0.0144$). The beneficial effects on HbA_{1c} and severe hypoglycemia were achieved even though basal insulin doses remained unchanged (Supplementary Table 2).

Assessment of the secondary outcomes showed that the INPUT group experienced a significantly greater reduction of diabetes distress (Δ −5.60 [95% CI −8.53 to −2.67]; $P = 0.0003$) and depressive symptoms (Δ −1.31 [95% CI −2.21 to −0.41]; $P = 0.0478$) than the control group (Table 2). Compared with the control group, the INPUT group also showed a greater improvement in diabetes self-management (Δ 0.46 [95% CI 0.25–0.68]; $P = 0.0002$) and satisfaction with CSII therapy (Δ −3.61 [95% CI −5.02 to −2.19]; $P < 0.0001$). After participation in the INPUT program, participants showed a larger improvement in diabetes-specific empowerment compared with the control group (Δ 1.43 [95% CI 0.45–2.41]; $P = 0.0048$). With regard to attitudes toward CSII therapy, participants in the INPUT group also indicated that they perceived more benefits of CSII (higher flexibility and better glycemic control) and rated the functionality of their pump as more important than participants in the control group. There were no differences between the groups in health-related quality of life and hypoglycemia awareness.

There were also behavioral changes in the usage of pump features (Table 4). Participants in the INPUT group self-reported more use of temporary basal rates and bolus options than participants in the control group.

Secondary Analyses

Only the interaction between the INPUT group and age of onset of CSII therapy and recruited pool size had a significant impact on the primary outcome (Supplementary Table 3), indicating a moderating effect of those factors on change in HbA_{1c}. An older age at onset of CSII therapy in the INPUT group was associated with lower HbA_{1c} values at follow-up. A larger group size in the INPUT group was associated with lower HbA_{1c} values at follow-up, hence greater improvement in HbA_{1c}.

Mediator analyses revealed that INPUT had an indirect effect on the improvement of HbA_{1c} through increased diabetes self-management and the new use of CGM technologies (Supplementary Table 4). However, INPUT had an independent effect on HbA_{1c} reduction, even after controlling for these mediators.

Intervention Implementation

Attendance rates were high, with a mean number of INPUT sessions attended of 10.9 ± 1.7 (median 11 sessions, IQR 10.25–12 sessions). After the last education session, participants in the INPUT group were asked about the conduct of the program. These fidelity measures indicated that key elements of the INPUT intervention were implemented according to the curriculum, with an implementation rate of 72.0–90.4% (Supplementary Table 5). In addition, the INPUT curriculum contained the testing of basic therapy parameters (e.g., basal rate). At the end of the intervention phase and even during the 6 months after, significantly more INPUT participants completed these tests compared with the control group (Supplementary Table 5), indicating the successful implementation of the intervention.

Safety Information

Over the total study duration (time since baseline, including the intervention phase

Table 3—Rate of severe hypoglycemia in the 6 months after the intervention

Severe hypoglycemic event	INPUT (n = 128)	Control group (n = 126)	IRR (95% CI)	P value
All events: third-party assistance + medical intervention				
Number of events (rate per patient-year)	11 (0.17)	44 (0.70)	3.55 (1.50–8.43)	0.0041*
Number of affected participants (%)	6 (4.7)	9 (7.1)		0.44+
Third-party assistance without medical intervention				
Number of events (rate per patient-year)	11 (0.17)	35 (0.56)	4.26 (1.77–10.23)	0.0012*
Number of affected participants (%)	6 (4.7)	6 (4.8)		1.00+
Only medical intervention				
Number of events (rate per patient-year)	0 (0.0)	9 (0.14)	12.548#	0.0004#
Number of affected participants (%)	0 (0.0)	6 (4.8)		0.0144+

*Zero-inflated Poisson regression for IRR. +Fisher exact test for comparison of the difference in affected participants. #Likelihood ratio χ^2 derived from omnibus test (IRR not applicable because of zero events in the INPUT group).

Table 4—Self-reported behavioral changes in using pump features

	Per-protocol population (*N* = 254)				
	INPUT (*n* = 128)		Control group (*n* = 126)		
Use of	Baseline	Follow-up	Baseline	Follow-up	*P* value*
Temporary basal rates	1.00 (0.00–3.00)	2.00 (1.00–3.00)	1.00 (0.00–3.00)	1.00 (0.00–3.00)	0.0139
Different basal rate profiles	0.00 (0.00–1.00)	0.00 (0.00–1.00)	0.00 (0.00–1.00)	0.00 (0.00–0.00)	0.090
Bolus options	2.00 (0.00–3.00)	2.00 (1.00–4.00)	1.00 (0.00–3.00)	1.00 (0.00–3.00)	0.0095
Bolus calculator	4.00 (0.00–4.00)	4.00 (2.25–4.00)	4.00 (1.00–4.00)	4.00 (1.00–4.00)	0.475
Analysis software	0.00 (0.00–1.00)	0.00 (0.00–1.00)	0.00 (0.00–1.00)	0.00 (0.00–1.00)	0.081
Pairing with CGM	0.00 (0.00–0.00)	0.00 (0.00–0.50)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.478

Data are median (IQR). 0 = not at all; 1 = one to three times a month; 2 = at least once a week; 3 = several times a week; 4 = daily. **P* values for between-group differences of change (Kruskal-Wallis test).

until the 6-month follow-up), a total of 19 serious adverse events of severe hypoglycemia requiring medical intervention were reported (3 in the INPUT group, 16 in the control group). One participant in the waiting control group died shortly before the 6-month follow-up as a result of a myocardial infarction.

CONCLUSIONS

In this randomized controlled trial, participants in both study groups performed CSII therapy without achieving optimal glycemic control. The results demonstrate that the INPUT education program reduced HbA_{1c} to a greater extent than usual treatment. These effects were seen in participants with short-term as well as long-term duration of their CSII therapy. The magnitude of the HbA_{1c} improvement was comparable to the effects achieved by switching from MDI therapy to CSII therapy, as reported in meta-analyses (4,5). Therefore, the effect of INPUT on HbA_{1c} can be regarded as clinically meaningful.

Of note, lowering HbA_{1c} did not lead to worsening of hypoglycemia problems. In contrast, the incidence of severe hypoglycemia requiring third-party assistance could be reduced after participating in the INPUT program. Thus, glycemic control was substantially improved in INPUT participants not only by improving HbA_{1c} but also by reducing the risk for severe hypoglycemic episodes.

INPUT also led to self-reported behavioral changes toward a more frequent use of the technological features of the insulin pump. After participation in INPUT, participants indicated that they used temporary basal rates and bolus options more frequently.

In addition to improving clinical outcomes, INPUT effectively improved psychosocial outcomes. Major psychological burdens, such as diabetes distress and depressive symptoms, were reduced through participation in INPUT. The detrimental effects of diabetes distress and depression have been widely recognized (32–34). In addition, reducing diabetes distress has been reported to confer beneficial effects on the course of depression (35,36). Thus, by reducing diabetes distress and depressive symptoms, participation in the INPUT program may reduce the burden associated with having diabetes or its regimen, which might positively affect prognosis.

Of note, relevant baseline variables such as age and sex and baseline levels of patient-reported outcome measures did not moderate the effect of INPUT, indicating a stable effect of INPUT across various subgroups. The only two significant moderators were age of onset and recruited pool size, indicating that INPUT is most beneficial for patients with an older age at onset of CSII therapy and larger groups. Larger groups might have led to more observational learning and more discussion and motivation through enhanced social support. However, the size of the INPUT group was limited to three to eight participants according to the study protocol. Thus, inferences about group sizes with more than eight participants cannot be made. Furthermore, the mediator analyses suggest that INPUT reduced HbA_{1c} through increased diabetes self-management and increased use of CGM technologies. Although these mediating effects demonstrate an indirect effect of INPUT, there was still an independent effect of INPUT on HbA_{1c}.

This study was the first to our knowledge to demonstrate the efficacy of a structured diabetes education program specifically designed for CSII therapy. In the only other study with a structured CSII-specific education program, the Relative Effectiveness of Pumps Over MDI and Structured Education (REPOSE) study, the authors found no superior effect of CSII therapy in combination with CSII-specific education on glycemic control, hypoglycemia, or most psychosocial outcomes (37). However, some major differences exist between the REPOSE study and the current study. In the current study, all participants had received structured education on intensive insulin therapy before inclusion and were already performing CSII therapy, whereas in the REPOSE study, patients were switched to CSII therapy. Therefore, the effect of INPUT can be regarded as a specific education effect that is independent of switching to CSII therapy. Because CSII therapy costs notably more than MDI therapy, a relatively inexpensive intervention such as structured CSII-specific group education potentially could enhance the cost-effectiveness of this treatment approach.

The following limitations must be taken into account. First, the waiting control design cannot exclude an attention effect that should be considered. In addition, because the intervention was group education, enhanced peer support may have contributed to some of the effects. However, as the mediation analysis demonstrated, INPUT also had indirect effects on the primary outcome through specific behavioral changes. Thus, the attention and peer support effects cannot account fully for the findings. Second, incidence of severe hypoglycemia relied on self-report. Although study personnel validated the self-reports of severe hypoglycemic episodes, these episodes could not be validated by glycemic data. In addition, the effects on hypoglycemic episodes relied only on a small number of patients.

Similarly, use of pump features also relied on self-report. Third, almost all participants had type 1 diabetes. We decided to keep the only participant with type 2 diabetes in the analyses because this participant was recruited according to the study protocol, fulfilled all inclusion criteria, and completed the study in compliance with the study protocol. Although the majority of CSII users have type 1 diabetes, the number of people with type 2 diabetes on CSII therapy is growing. Hence, the generalizability of the study is limited. Fourth, diabetes education programs are complex interventions (38) and therefore, depend on factors such as experience of the diabetes educator and group composition. However, diabetes educators were trained for 12 h in the conduct of INPUT, received a written curriculum, and had an initiation visit shortly before the study start to ensure a standardized conduct. A strength of the study was that the intervention was delivered in a naturalistic setting of regular diabetes care, which also may have led to the extremely small dropout rate.

In summary, this randomized controlled trial demonstrated that addressing the human factor within CSII therapy through structured, CSII-specific education leads to improvements in medical, behavioral, and psychosocial outcomes. Improvement in glycemic control was comparable to the effect of CSII therapy itself and was accompanied by a reduction of severe hypoglycemia. Taken together, the INPUT program can be considered an effective intervention that addresses skills and knowledge as well as psychological barriers and has beneficial effects on multiple clinically relevant outcomes.

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