Well-Being and Symptoms in Relation to Insulin Therapy in Type 2 Diabetes

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OBJECTIVE — To determine the influence of insulin therapy on physical symptoms, emotional and general well-being, and treatment satisfaction in patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS — A descriptive prospective 2-year cohort study was performed. The study population consisted of 272 eligible NIDDM patients of Dutch origin ≥40 years of age who had a known diabetes duration ≥3 months and who were treated with diet and/or oral hypoglycemic agents. Dependent variables in the logistic regression analysis were scores on the Type 2 Diabetes Symptom Checklist, the Profile of Mood States, and questions regarding general well-being and treatment satisfaction. Potential determinants under study were age, sex, known diabetes duration, insulin dose, duration of insulin therapy, comorbidity, baseline and change in metabolic parameters and cardiovascular risk factors.

RESULTS — A baseline and 2-year questionnaire were available for 157 patients (58%). During follow-up, 39 of them (24.8%) were treated with insulin. Initiation of insulin therapy was significantly associated with improved glycemic control (mean HbA_{1c} 8.2 ± 1.4 [SD] to 7.4 ± 0.9%, $P = 0.001$) and weight gain (BMI 27.1 ± 3.9 to 28.6 ± 4.3 kg/m², $P = 0.000$). Of all symptom and well-being scores, only feelings of emotional fatigue worsened significantly, although modestly (0.4–1.7 on a scale of 0.0–10.0, $P = 0.02$). Although diabetes management with insulin was experienced as more demanding ($P = 0.04$), treatment satisfaction scores were not adversely influenced (2.5–1.9, $P = 0.39$). High insulin doses were significantly and independently associated with high symptom scores (total score, hypoglycemic score) and with low mood (displeasure score, anger, tension, emotional fatigue) and perceived state of health.

CONCLUSIONS — Initiation of insulin therapy in type 2 diabetes improves glycemic control effectively, has little influence on physical and psychological well-being dimensions, and does not affect treatment satisfaction.

There is growing evidence that optimization of glycemic control may reduce the incidence of retinopathy, nephropathy, and neuropathy to the same extent in type 1 and type 2 diabetes (1–5). Some reports even suggest a reduction in macrovascular complications with lowering of glycemic level in type 2 diabetes (1,6–9). To achieve and maintain good glycemic control, ~5–10% of the type 2 diabetic patients should be transferred to insulin therapy each year (10–13). In symptomatic, poorly regulated patients, despite oral hypoglycemic agents, treatment with insulin is generally accepted. In patients with less pronounced hyperglycemic complaints, however, the step towards insulin therapy is often delayed. Anxiety about reducing actual quality of life by initiation of insulin injection therapy may partly explain this reluctant attitude of physicians. Apparently, the increased risk of chronic complications in the future is considered less important. An often unwittingly negative attitude of health care providers toward insulin may be an important source of worsening patients' well-being (14).

On the other hand, anecdotal case reports share the experience of many diabetologists that insulin therapy may result in marked improvement in well-being (15–17). This may be true not only for patients complaining of the classic hyperglycemic triad (thirst, polyuria, and weight loss), but also for those who experience only vague symptoms, such as itch, fatigue, drowsiness, or feelings of depression, which are often not ascribed to hyperglycemia. Improved glycemic control itself may positively influence well-being by minimizing symptoms associated with hyperglycemia (18). Diabetes education, accompanied by empathy of educators and the experience that insulin therapy is easier than expected, can increase well-being as well (19–21).

In a structured care setting, we expected a significant glycemic improvement due to initiation of insulin therapy without major adverse effects on subjective well-being. The objective of this study was to determine prospectively (2 years) the influence of insulin therapy on different dimensions of quality of life in type 2 diabetic patients with moderate to poor glycemic control. These dimensions included physical symptoms, mood states, general well-being, and treatment satisfaction.

RESEARCH DESIGN AND METHODS

Study population

Since 1992, 445 NIDDM patients ≥40 years of age in 22 general practices have been followed for 2 years in a regional shared-care diabetes project in Amsterdam (22). Reasons for nonparticipation and dropout were described elsewhere (22). Excluded from well-being analysis were patients with newly diagnosed NIDDM ($n = 94$) or with a non-Dutch origin ($n = 91$), since questionnaires were not validated for them, and patients treated with insulin at baseline ($n = 12$). Of the eligible 272 known NIDDM patients of Dutch origin, self-report questionnaires were available for 237 (87%) at baseline, 184 (68%) after 1 year, and 168 (62%) after 2 years of follow-up. Of the 157 patients

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Abbreviations: DSC-type 2, Type 2 Diabetes Symptom Checklist; GP, general practitioner; OR, odds ratio; POMS, Profile of Mood States.

(58%) for whom a baseline and 2-year questionnaire were evaluable, insulin therapy was initiated in 39 subjects (25%).

Study protocol

At entry and at least at 3-month intervals, glycemic control of participating patients was determined. At the annual review of complications and cardiovascular risk factors, a set of questionnaires was administered to assess well-being. Within 2 weeks, general practitioners (GPs) received the results (except answers to questionnaires), accompanied by protocollized therapy advice, which they discussed with their patients. If necessary, diabetes education concerning nutrition or self-monitoring of blood glucose and insulin injection technique was provided by a dietitian or diabetes educator, respectively. Patients were told that insulin therapy might be required because of gradual worsening of β-cell function and not because of poor lifestyle habits.

If HbA_{1c} target values (i.e., HbA_{1c} of 7.0%, reference 4.3–6.1%) were not met in patients treated with maximal doses of oral hypoglycemic agents (i.e., 15 mg glyburide and 1,700 mg of metformin) even after application of self-monitoring of blood glucose, intermediate-acting NPH insulin at bedtime was added to sulfonylurea therapy. If unsuccessful, this was followed by NPH insulin twice daily without oral agents. The next step was the combination of short-acting and NPH insulin with two or more injections a day (22).

Outcome measures

Quality of life has physical (complaints), emotional (mood), cognitive (e.g., satisfaction), and social aspects. Because we expected changes in diabetes-specific complaints (by reduction of HbA_{1c}) and mood (17), two feasible questionnaires concerning these aspects were applied that had been shown to be sensitive to change. The Type 2 Diabetes Symptom Checklist (DSC-type 2) was used to assess frequency and perceived burden of diabetes-related symptoms (23). The DSC-type 2 is a self-report questionnaire that consists of 34 items covering 6 dimensions: hyperglycemic, hypoglycemic, neuropathic (subdivided into pain symptoms and sensory symptoms), psychological (subdivided into fatigue and cognitive distress), cardiovascular, and ophthalmological. Each item is scored on a frequency scale and, if a symptom is present, also on a discomfort scale. Multiplication of each frequency by its corresponding discomfort score yields weighted scores for each item. From these, a weighted score for each subdimension can be calculated. The DSC-type 2 explicitly refers to the month preceding the visit. For a total symptom score, all subscale scores are summed.

The Dutch shortened Profile of Mood States (POMS) was used to measure current emotional well-being (24,25). The POMS (32 items) consists of four negative dimensions (depression, anger, fatigue, and tension) and one positive dimension (vigor), explicitly referring to "the past few days, including today" (21). Subscale scores and an aggregate mood score can be calculated. Following Van der Does et al. (18), a displeasure score was derived as the sum of the depression, anger, and tension dimension scores, forming a more pure measure of mood state less influenced by physical fatigue. All subscores on the DSC-type 2 and POMS were transformed to a 0–10 scale, in which the lower score indicated a higher level of well-being.

Both the DSC-type 2 and the POMS have proven to be responsive to clinically relevant changes in type 2 diabetic patients Cross-sectionally, low HbA_{1c} was significantly correlated with a positive mood, as well as with low diabetes-related symptom scores (18,23).

Eight questions were used to assess general (cognitive) well-being. Referring to the previous 3 months, subjects were asked to score their perceived health ("How would you describe your current state of health?") and to give overall evaluations of their quality of life ("How did you feel, all things considered?"; "How satisfied were you, all things considered with your life?") and perceived burden of treatment ("Do you experience the treatment of your diabetes as demanding?"). To score the satisfaction with medical care, four statements were applied; the aggregate forms the treatment satisfaction score. Answers were given on 1–5 Likert scales; a lower score again indicated a higher level of well-being and satisfaction.

Potential determinants

HbA_{1c} was determined by ion-exchange high-performance liquid chromatography, using a Modular Diabetes Monitor System (reference value 4.3–6.1%; Bio-Rad, Veenendaal, The Netherlands). BMI was calculated as weight (kilograms) divided by height (meters) squared. Systolic and diastolic blood pressure were measured in sitting position with a digital blood pressure monitor (Omron Hem-405, Tokyo). Fasting total cholesterol, HDL cholesterol, and triglycerides were measured by enzymatic techniques (Boehringer Mannheim, Mannheim, Germany).

In patients treated with insulin, hypoglycemic events were recorded at each visit or telephone call. They were asked to verify perceived hypoglycemia by self-monitoring of blood glucose. A hypoglycemia grade 3 was defined as a hypoglycemic event that required oral carbohydrates given with the help of others. A hypoglycemic coma was scored as a hypoglycemia grade 4. At entry, patients were asked to score (yes/no) a comorbidity questionnaire with six items (arthralgia, low back pain, headache/migraine, abdominal pain, severe lung disease, and malignancy). Not only changes, but also baseline values, were considered as potential determinants of well-being parameters.

Statistical analysis

Baseline clinical characteristics in patients who did or did not complete the baseline and final questionnaire were compared with χ^2, unpaired t, or Mann-Whitney U tests when appropriate. To compare baseline with final results, paired t (fasting blood glucose, HbA_{1c}, BMI) or Wilcoxon's tests (questionnaires) were applied. Spearman's rank correlation coefficients were calculated to detect any univariate relationship between the changes in outcome measures during 2 years of follow-up and all potential determinants in patients treated with insulin. Changes in outcome measures were dichotomized at their median value and analyzed as dependent variables by means of logistic regression analysis. Multivariate stepwise logistic regression analysis of potential determinants, corrected for age and sex, was performed. If more than one (nearly) significant ($P < 0.15$) relationship was detected, these variables were entered in the model to detect any independent association of potential determinants and change in outcome measures. The role of a determinant in determining subdimensions of quality of life was expressed as the odds ratio (OR). The OR per unit difference, adjusted for all other determinants, is expressed by calculating the antilog of the regression coefficient b of a determinant (e^b).

RESULTS — Comparison of patients who did complete baseline and final questionnaires (n = 157 [57.7%]) with those who did not (n = 115) revealed some dif-

Table 1—*Baseline characteristics of study population*

Final therapy	Transferred to insulin	Remaining on diet/tablets
n (% of total)	39 (24.8)	118 (75.2)
Women	26 (66.7)	74 (62.7)
Age (years)	66.5 ± 9.8	66.8 ± 10.0
Diabetes duration (years)	7.3 ± 5.0	5.3 ± 4.9*
Diabetes therapy†		
Nutritional advice	1 (2.6)	50 (42.4)
Sulfonylurea and/or metformin	38 (97.4)	68 (57.6)
HbA_{1c} (%)	8.2 ± 1.4	6.6 ± 1.3†
BMI (kg/m^2)	27.1 ± 3.9	27.8 ± 4.0
Systolic blood pressure (mmHg)	150.2 ± 18.3	147.8 ± 18.7
Diastolic blood pressure (mmHg)	87.3 ± 12.6	86.2 ± 10.2
Total cholesterol	6.1 ± 1.1	6.3 ± 1.3
HDL cholesterol	1.2 ± 0.3	1.2 ± 0.3
Triglycerides	2.1 ± 1.2	1.9 ± 1.1
Comorbidity	0.5 ± 0.7	0.9 ± 1.1*

Data are *n* (%) or means ± SD. *$P < 0.05$; †$P < 0.001$.

ferences. The first group was younger (66.7 ± 9.9 vs. 69.5 ± 12.5 years; $P = 0.045$) and leaner (BMI 27.7 ± 4.0 vs. 29.0 ± 4.9 kg/m^2; $P = 0.022$) and had a slightly lower baseline HbA_{1c} (7.0 ± 1.5 vs. 7.6 ± 1.5%, $P = 0.000$) and final HbA_{1c} (6.8 ± 1.0 vs. 7.2 ± 1.3%; $P = 0.004$). The groups were similar in terms of sex, diabetes duration, and change in HbA_{1c} or BMI. Available questionnaires revealed no differences in baseline emotional or general well-being or in treatment satisfaction. Patients for whom follow-up questionnaires were not available reported more complaints (median DSC-type 2 score [$n = 76$] 1.4 vs. 0.9; $P = 0.01$).

Insulin therapy was initiated in 30 of the 157 patients (19.1%) the 1st year and in 9 patients (5.7%) the 2nd year. After 2 years of follow-up, 21 of the 39 patients (53.8%) were treated with sulfonylurea at meals and NPH insulin (mean dose 22.4 ± 14.9 U [range 6–54]) at bedtime, while 18 applied 2 injections a day (mean dose 58.3 ± 23.8 U [28–104]) without oral agents. Mean duration of insulin therapy during follow-up was 14.7 ± 7.1 months.

In Table 1, baseline characteristics are shown separately for those who were, and those who were not transferred to insulin. Changes in well-being parameters between these groups were not compared statistically, since baseline HbA_{1c}, which determined the transfer to insulin, differed by definition (8.2 ± 1.4 vs. 6.6 ± 1.3%, $P <$ 0.001).

Tables 2 and 3 present the distribution of glycemic control, mood, general well-being, and treatment satisfaction at baseline and after 1 and 2 years of follow-up. In insulin-treated patients, HbA_{1c} was lowered effectively, and this was associated with moderate weight gain of 4.2 ± 3.7 kg. The low median and 75th percentile values of the outcome measures indicate that the distribution of the scores is highly skewed toward a high quality of life. After initiation of insulin therapy, patients tended to have a modest increase in hypoglycemic complaints and neuropathic pain. The DSC-type 2 subdimension "physical fatigue," consisting of items "overall feeling of fatigue," "fatigue in the morning when getting up," and "increased fatigue in the course of the day," showed no change. The scores of the POMS subdimension "emotional fatigue," which included such elements as "tired out," "dead beat," "fagged out," "burned out," and "exhausted," increased significantly, and the dimension "anger" showed a trend. As expected, insulin therapy enhanced the experienced burden of treatment. However, overall measures of complaints, mood, general well-being, and treatment satisfaction did not change significantly.

Potential determinants of measures of well-being were studied by means of rank correlation and logistic regression analysis. In univariate logistic regression analysis, a rise in BMI (per kilogram per square meter), adjusted for age and sex, was significantly correlated with an increase in DSC-type 2 sum score (OR 0.52; CI 0.28–0.96) and POMS dimension "fatigue" (OR 0.53; CI 0.29–0.99). A rise in insulin dose (per international unit) showed a significant correlation with an increase in DSC-type 2 sum score (OR 0.96; CI 0.92–0.99) and "hypoglycemic" dimension (OR 0.95; CI 0.92–0.99); in POMS dimensions "anger" (OR 0.96; CI 0.93–0.99), "fatigue" (OR 0.96; CI 0.93–0.99), "displeasure" (OR 0.97; CI 0.94–1.00), and POMS sum score (OR 0.97; CI 0.95–1.00); and in perceived health status (OR 0.93; CI 0.88–0.95). In multivariate forward and backward stepwise logistic regression analysis, including insulin dose and change in BMI and adjusted for age and sex, insulin dose only was independently related to outcome measures, as mentioned above, while the beta of the change in BMI was not statistically significant in the models (Table 4). Other potential determinants, such as age, sex, comorbidity, hypoglycemia, baseline and change in HbA_{1c}, metabolic parameters, and cardiovascular risk factors, were not related to any of the outcome measures. Only two patients experienced a severe hypoglycemia (4.4/100 insulin-treated patient-years).

The 118 patients treated with diet and/or oral hypoglycemic agents did not show any change in glycemic control or BMI or in any of the quality-of-life parameters. They tended to experience diabetes treatment as less demanding (median 2 to 1, $P = 0.06$).

CONCLUSIONS — To improve quality of life in the short and long term (in the latter by preventing complications), insulin therapy is generally accepted in symptomatic type 2 diabetic patients failing to respond adequately to oral hypoglycemic agents. In relatively asymptomatic patients, the step toward insulin therapy is more controversial because it is uncertain whether the long-term gain in quality of life will outweigh the anticipated loss of well-being associated with the burden of injecting insulin and the risk of hypoglycemia. This study shows that in relatively asymptomatic type 2 diabetic patients with moderate to poor glycemic control in general practice, initiation of insulin results in effective reduction of HbA_{1c} without major adverse influence on the short- to intermediate-term (mean duration of insulin therapy 1.2 years) quality of life. Because patients were relatively asymptomatic, with low baseline scores on symptom and well-being items, an improvement in quality of life during follow-up was not to be

Table 2—*Glycemic control, complaints, and mood during 2 years of follow-up*

	Follow-up							
	Transferred to insulin (years)				Remaining on diet or tablets (years)			
	0	1	2	*P**	0	1	2	*P**
n	39	35	39		118	92	118	
Glycemic control								
Fasting blood glucose (mmol/l)	10.3 ± 2.3	8.2 ± 3.3	7.0 ± 2.1	0.000	7.8 ± 1.6	7.9 ± 2.0	8.2 ± 2.2	0.08
HbA_{1c} (%)	8.2 ± 1.4	7.7 ± 1.1	7.4 ± 0.9	0.001	6.6 ± 1.3	6.4 ± 0.9	6.6 ± 1.0	0.85
BMI (kg/m^2)	27.1 ± 3.9	28.0 ± 4.4	28.6 ± 4.3	0.000	27.8 ± 4.0	27.7 ± 4.0	27.7 ± 4.1	0.46
Complaints (DSC-type 2)								
Hyperglycemic	0.8 (3.8)	0.8 (2.9)	1.5 (2.9)	0.70	0.8 (2.5)	0.6 (1.7)	0.6 (2.1)	0.43
Hypoglycemic	0.0 (1.4)	0.0 (0.6)	0.3 (1.7)	0.06	0.0 (1.1)	0.0 (1.1)	0.0 (1.1)	0.96
Neuropathic pain	0.0 (2.1)	0.4 (2.5)	0.4 (3.1)	0.11	0.4 (1.7)	0.0 (0.8)	0.0 (1.1)	0.27
Sensory neuropathic	0.3 (1.5)	0.3 (1.5)	0.6 (2.0)	0.32	0.0 (1.1)	0.3 (1.0)	0.3 (1.4)	0.38
Fatigue	1.3 (4.0)	0.8 (3.1)	1.3 (4.0)	0.77	1.3 (3.8)	0.8 (3.3)	0.9 (3.1)	0.21
Cognitive distress	0.4 (2.1)	0.4 (1.3)	0.4 (2.2)	0.93	0.4 (1.7)	0.4 (2.1)	0.4 (1.7)	0.51
Cardiovascular	0.4 (1.3)	0.0 (1.7)	0.4 (1.3)	0.71	0.4 (1.3)	0.2 (1.3)	0.4 (1.7)	0.92
Ophthalmological	0.3 (1.0)	0.3 (1.3)	0.3 (2.0)	0.19	0.0 (0.8)	0.0 (0.7)	0.0 (1.0)	0.86
Total: DSC-type 2 score	0.8 (2.2)	0.7 (2.1)	1.3 (2.3)	0.16	0.9 (1.8)	0.7 (1.5)	0.7 (1.7)	0.36
Mood (POMS)								
Depression	0.0 (0.7)	0.3 (0.9)	0.0 (1.1)	0.41	0.3 (1.6)	0.5 (2.0)	0.6 (1.9)	0.39
Anger	0.4 (1.4)	0.4 (1.4)	0.5 (2.1)	0.12	1.1 (2.5)	0.9 (2.5)	0.7 (2.1)	0.62
Tension	0.8 (2.5)	0.8 (2.9)	1.3 (2.8)	0.37	1.7 (4.2)	2.1 (3.8)	1.7 (3.3)	0.40
Total: displeasure	0.5 (1.5)	0.8 (1.4)	0.7 (2.1)	0.46	1.2 (2.3)	1.2 (2.6)	1.0 (2.5)	0.96
Fatigue	0.4 (2.2)	0.8 (2.5)	1.7 (2.5)	0.02	1.3 (3.6)	1.3 (2.9)	0.8 (3.3)	0.56
Vigor	5.0 (6.6)	5.3 (7.1)	5.0 (7.3)	0.40	5.0 (7.0)	5.5 (7.0)	5.0 (6.5)	0.06
Total: POMS score	1.5 (2.4)	1.6 (2.5)	1.5 (2.9)	0.56	1.8 (3.1)	1.8 (2.9)	1.6 (3.0)	0.94

Data are means ± SD or medians (75th percentiles). Scales of outcome measures are 0.0 (best) to 10.0 (worst well-being). *Paired *t* or Wilcoxon's tests were applied to compare baseline and final values.

expected. The 157 of 272 eligible patients (58%) who returned baseline and 2-year questionnaire were younger, leaner, and better controlled and reported fewer complaints at baseline than the nonresponse group. It is questionable whether this has biased the results significantly because changes in HbA_{1c}, BMI, baseline well-being, and treatment satisfaction did not differ between responders and nonresponders. Our findings are in agreement with a recently reported randomized controlled

Table 3—*General well-being and treatment satisfaction during 2 years of follow-up*

	Follow-up							
	Transferred to insulin (years)				Remaining on diet or tablets (years)			
	0	1	2	*P**	0	1	2	*P**
n	39	35	39		118	92	118	
General well-being (based on past 3 months)								
How did you feel?	2 (3)	2 (3)	3 (3)	0.19	2 (3)	2 (3)	2 (3)	0.18
How satisfied are you with your life?	2 (2)	2 (2)	2 (3)	0.56	2 (3)	2 (3)	2 (3)	0.53
How do you judge your health?	2 (3)	2 (3)	2 (3)	0.56	2 (3)	2 (3)	2 (3)	0.83
How demanding do you experience your treatment of NIDDM?	2 (3)	3 (3)	3 (4)	0.04	2 (2)	2 (2)	1 (2)	0.06
Treatment satisfaction								
I am very satisfied with my current medical care.	1 (1)	1 (1)	1 (1)	0.94	1 (1)	1 (1)	1 (1)	0.91
Some aspects of my current medical care can be improved.	1 (4)	3 (4)	1 (4)	0.48	3 (4)	3 (4)	2 (4)	0.02
Sum: satisfaction score†	2.5 (4.1)	2.5 (4.2)	1.9 (4.4)	0.39	3.1 (5.0)	3.7 (5.0)	2.5 (5.0)	0.33

Data are medians (75th percentiles). Likert scale of outcome measures is 1 (very much or totally agree) to 5 (not at all or totally disagree). *Wilcoxon's test was applied to compare baseline and final values. Scale 0.0 (very satisfied) to 10.0 (very dissatisfied).

Table 4—*Multiple logistic regression analyses of the relationship between final insulin dose and change in outcome measures, adjusted for age and sex*

	Final insulin dose (U)
Complaints (DSC-type 2)	
Hypoglycemic	0.95 (0.92–0.99)
DSC-type 2 score	0.96 (0.92–0.99)
Mood (POMS)	
Anger	0.96 (0.93–0.99)
Displeasure	0.97 (0.94–1.00)
Fatigue	0.96 (0.93–0.99)
POMS score	0.97 (0.95–1.00)
General well-being	
Health status	0.93 (0.88–0.95)*

Data are OR (95% CI). An OR <1.00 means a worsening in quality-of-life dimension per unit increase in insulin dose. *In this model, age (years) was also independently related to health status: 0.81 (0.69–0.95). Other potential determinants not independently related to any of the outcome measures were omitted.

trial (26). More studies support the statement that insulin therapy is well accepted, even in the elderly (27,28).

Although the detected change in complaints and well-being items was very modest, the independent association with insulin dose applied is remarkable (Table 4). Several plausible hypotheses may explain this finding at least partly. First, we and others have found that an increasing insulin dose is associated with a rise in body weight, and this may worry patients (29,30). Second, a high insulin dose may cause (asymptomatic) hypoglycemia, which gives rise to feelings of anger, displeasure, and fatigue (31). Third, high insulin doses may worry patients (and doctors), which in turn may lead to the perception that their diabetes has become more severe (14,32). One may not use this association as an argument against high-dose insulin therapy in these patients, although it may be a(nother) reason to apply a therapy regimen that is effective at the lowest insulin dose and causes the lowest weight gain and risk of hypoglycemia (20). We could not reveal a significant relationship between the incidence and/or severity of hypoglycemia and worsening of well-being, probably due to the low incidence of severe hypoglycemia (two events; 4.4/100 insulin-treated patient-years). This low incidence rate of severe hypoglycemia has been reported earlier in insulin-treated patients with type 2 diabetes (13,33). In contrast to our previous findings in non–insulin-treated patients, no association between HbA_{1c} and quality of life improvement was found, probably because of the experienced burden of daily injections and occurrence of (asymptomatic) hypoglycemia (18). These adverse experiences may have reduced the expected gain in well-being. Our study did not reveal any association between insulin dose and worsening of neuropathic symptoms, as suggested by others (34).

In agreement with our hypothesis, initiation of insulin effectively lowers HbA_{1c} and did not affect to an important degree the well-being or satisfaction of patients in our study group. Only a modest weight gain and a minor increase in emotional fatigue and burden of treatment was observed. Therefore, this study supports the advice of Taylor (35), which states: "Insulin treatment should be started before rather than after a year or two of hyperglycemic malaise," provided structured care is available (35).

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